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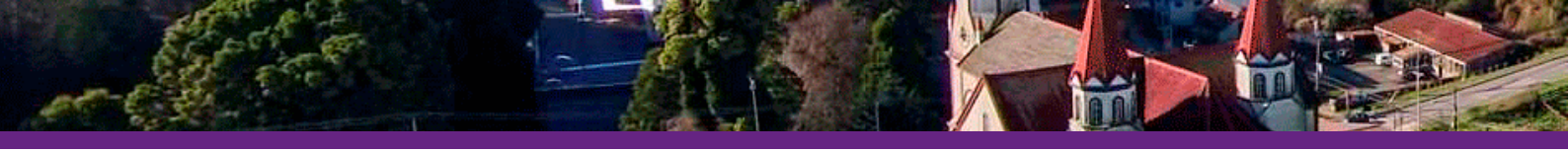

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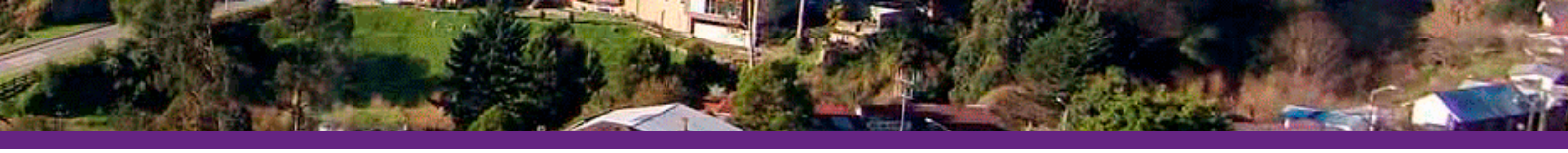

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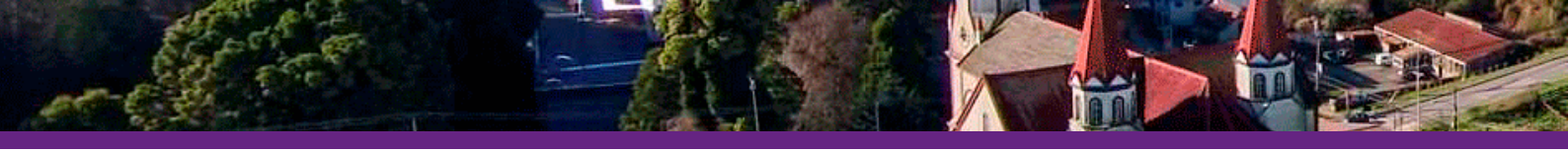

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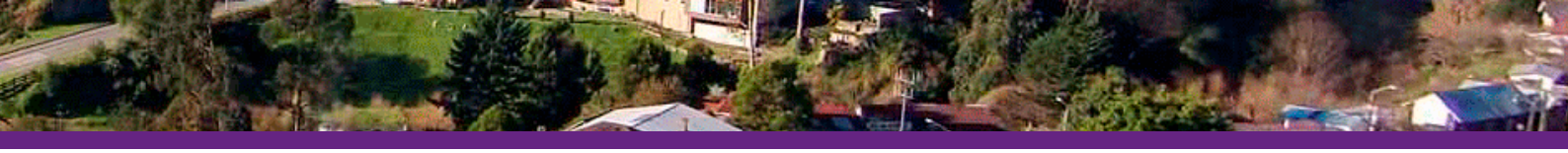


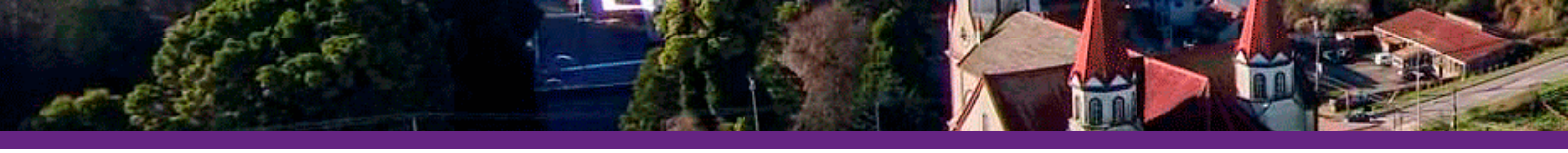
CONFERENCIA INAUGURAL

My Long Journey with Calcium, a Remarkable Universal Second Messenger

Hidalgo C [1] Department of Neurosciences, CEMC and Physiology and Biophysics Program, ICBM, Faculty of Medicine, Universidad de Chile

The pioneering studies of Sydney Ringer in 1882-83 showed that heart contraction requires Ca^{2+} ions. In the 1960's three independent German, Japanese and US teams showed that Ca^{2+} binding to troponin C allows actin-myosin interaction and muscle contraction, and described relaxation via Ca^{2+} uptake by the muscle SERCA pump. Many subsequent studies showed that Ca^{2+} is a highly versatile intracellular signal that operates over a wide temporal range to regulate many different cellular processes.

I first became acquainted with Ca^{2+} in the 1960's when I studied Ca^{2+} efflux from the squid giant axon under the guidance of Eduardo Rojas; we reported in 1968 that this high energy-demanding process requires mitochondrial function. My later work in Boston (1974-1983) showed that the physical state of the lipids surrounding the SERCA pump control its activity; this work provided key information on the mechanisms underlying active transport across biological membranes. On returning to Chile in 1983, I continued to work on Ca^{2+} signaling in striated muscle and in the 90's I began studying Ca^{2+} signaling in neuronal cells, studies which I continue up to now. We discovered and reported that cellular redox state controls calcium signals; this crosstalk is important for conditions entailing cellular oxidation, such as aging and neurodegenerative diseases. In parallel, I have been actively involved in promoting science and the participation of women in science in our country. I will present in my lecture a narrative account of my research, made possible by many collaborators, and my involvement in other activities.



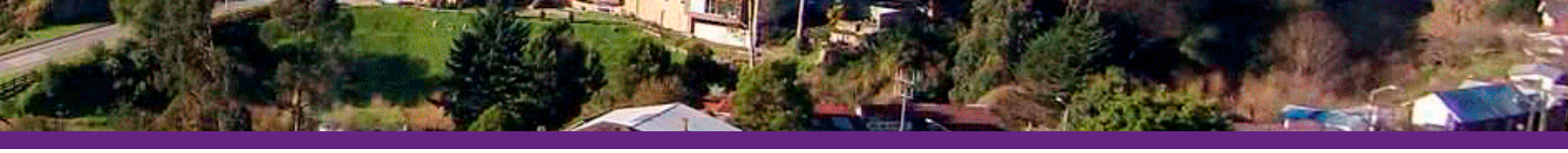
CONFERENCIA
DR. HERMAN NIEMEYER

Resurrección de proteínas ancestrales para el estudio de las trayectorias evolutivas de la adaptación de proteínas a ambientes extremos

Guixe Victoria [1]
(1) Laboratorio de Bioquimica y Biología Molecular, Departamento de Biología, Facultad de Ciencias, Universidad de Chile

Life inhabits all possible places on Earth. Archaea, the third domain of life, comprises organisms that are metabolically very diverse and able to thrive in both terrestrial and aquatic environments, with extreme conditions (extremophiles) of temperature, salinity, pressure, pH or a combination of them (polyextremophiles). A major question is how the proteins and enzymes of such organisms have evolved to cope with these extreme conditions. Then, we are interested in what are the structural and functional principles underlie the capacity for adaptation. By using ancestral enzyme reconstruction, we will address the structural and functional traits that allow protein adaptation through evolution in the ADP-dependent kinase family. Specifically, we will illustrate the functional and structural changes that enable these enzymes to be active and folded at high salt concentrations, at low temperatures, and how substrate specificity was achieved from bifunctional ancestors. We will show that cold- adaptation of catalysis relies on an increased structural flexibility due mainly to the absence of two ionic interactions which is an ancestral trait in the psychrophilic branch of this enzyme family. Also, we will illustrate that the halophilic character is an ancient trait in the evolution of the ADP-dependent kinase family and that these enzymes adapt to saline environments by a non-canonical strategy different from the one currently proposed. Finally, the study of ancestral enzymes of increasing historical age allows us to explore the mechanism underlying the change of protein function during natural evolution, illuminating the evolutionary basis for substrate recognition.

Fondecyt 1150460

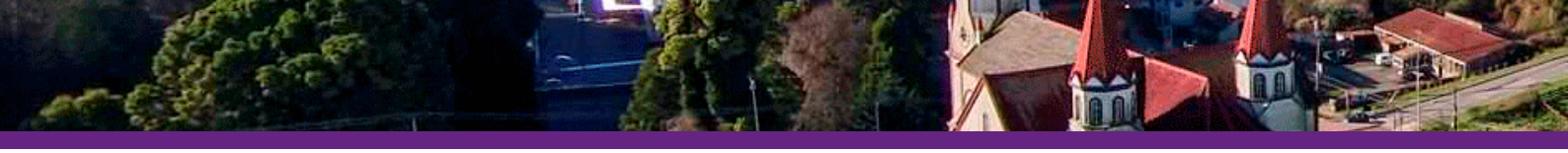


CONFERENCIA
DR. DANKO BRNCIC

Grapevine, a woody fruit crop scrutinized from the perspective of its genetic constitution

Hinrichsen Patricio [1] (1) Plant Genetics & Biotech, INIA, LA PLATINA Instituto de Investigaciones Agropecuarias, Centro de Investigación La Platina. Santa Rosa 11.610, Santiago, Chile. (+56-2) 25779110; (*) phinrichsen@inia.cl

Grapevine (*Vitis vinifera* L.) is one of the first domesticated plant species, originated from the Trans-Caucasus valleys surrounding the Black Sea to Central Europe. The species was brought into America by Spanish conquerors five centuries ago and become naturalized all along the continent in the Mediterranean areas, wonderfully adapted to this part of the New World. Chile has become a key player in the production of table grape (first world exporter) and wine (top five). During the last 25 years, I have been involved in the study of this marvelous fruit crop, being a close witness of the raise of the knowledge on this species, from the understanding of its genetic diversity and population structure, through the unveiling of the complexity and uniqueness of its genome organization, to the identification of markers, genes and genomic regions associated to quali- and quantitative traits of productive significance. In this opportunity, I will summarize the modest but significant contributions we have done regarding the characterization of the Criolla varieties diversity and the up-to-now challenging intra-cultivar variability, to the development of markers and identification of genes related to berry quality in table grapes, combining genomic and phenotypic characterizations.



CONFERENCIAS SOCIEDAD CHILENA DE EVOLUCIÓN

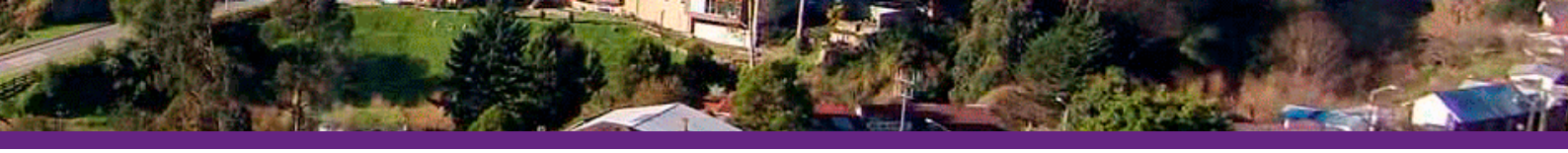
Premio a la Trayectoria en Biología Evolutiva 2018

Searching the chromosomal footprints in space and time. Studies examples .(Buscando las huellas cromosómicas en el espacio y el tiempo. Ejemplos de estudio)

Lamborot Madeleine [1]
(1) Ciencias Ecológicas, Ciencias, Universidad de Chile

Speciation or the formation of new species constitute an important wide topic of general interest, full of controversies, which necessarily must be study at different levels and from a multidisciplinary perspective involving evolutionary scientists. From the chromosomal point of view, it is accepted that numerous related organisms can differ in their chromosomalcharacteristics, sometimes in extreme degrees. Numerous models of chromosome speciation have been proposed, in which thechromosomal mutations could play an important role by reducingrecombination contributing to the reproductive isolation.

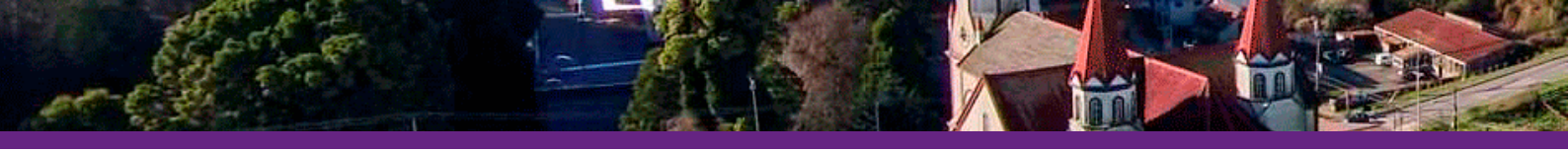
The somatic and meiotic chromosomes characterizationfocussed on big groups of organisms in Chile: Gryllidae andMogoplistidae; Iguanidae, mainly *Liolaemus*, helped to understand the great diversity and the possible causalrelationship between chromosomal changes and speciation. Two excellent species biological models to understand the meaning of the chromosome variation and the origin of the mutations: 1) The endemic *Liolaemus monticola* complex, with several chromosome races, hybrid zones,whose complexity increase South to North, it is spatially fragmented, as our geography, forming a metapopulation system. I illustrate how chromosome mutation originated in the germline must pass over the selective meiotic barriers conducive to viable gametes, thenby hybridization to be established as heterozygote, perpetuated as such, to disappear, or be fixed in homozygosis; then to expand in a demo and/or to colonize new environments, to replace or becomeextinct. 2) the complex *Liolaemus chiliensis,* with different ploidies(2n*;3n;2n/3n)*.With these species we can follow the parental, intermediated and thederived chromosome footprints in the space and the time.



Convergent evolution in cetacean inner ears.

Cooper N [1], Travis Park[1]
Department of Life Sciences (Vertebrates) Natural History Museum, London

Odontocetes (toothed whales) are the most successful marine mammal lineage. The catalyst for their evolutionary success is their ability to use echolocation - a form of biological sonar that allows them to sense their environment using high-frequency sound, which is produced in the forehead and detected by the cochlea. In recent years, several studies have identified different echolocation types, largely correlated with habitat, with an emerging consensus that the morphology of the cochlea is an excellent proxy to distinguish both of these in extant and extinct taxa. Given this strong influence on cochlear shape, we tested whether convergent evolution of the cochlea has occurred within Odontoceti. To do this we used SURFACE; a method that fits Ornstein-Uhlenbeck (OU) models with stepwise AIC (Akaike Information Criterion) to identify convergent regimes on a phylogeny. We fit SURFACE models to a phylogeny of odontocetes and identified three convergent regimes: True's and Cuvier's beaked whales; sperm whales and all other beaked whales; and kogiids and Dall's porpoise. We then used distance-based convergence metrics to test whether these convergences were statistically significant. We then discuss factors that may have driven these convergent shifts.



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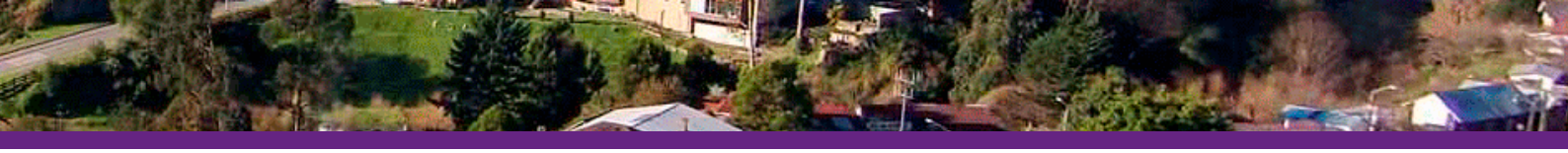
Epigenetic mechanisms in the process of speciation

Frias Daniel [1]
(1) Instituto de Entomología, Ciencias Básicas, Universidad Metropolitana de Ciencias de La Educación

There are described many concepts of species and modes of speciation. However with the advent of *Central Dogma of Molecular Biology* the principal mechanisms these process was reduced to the structural genes. Inside this framework, mutations was considered as the principal font of new genetic varaibilities that drive the speciation. However, with the advent of epigenetics we now know that there are also other complementary molecular mechanisms and evolutionary epigenetic forces that drive speciation and explain biodiversity in all domains of the tree of life. Here indicated and discuss the new epigeneic mechanisms that drive the origin of new species such as viruses, transposable genetic elements, DNA and histone methylations and ncRNAs. Now, we know that endogenous simbiont viruses they have a role in the origin of vivipary and also in the formation of placenta in mammals. Transposons explain some paramutations and also adaptatives phenotypic variations. NcRNAs have roles in numerous biological process such as splicing, RNA editing, epimutations, heterochromatinization, imprinting and development, processes that explain the phenotypic variation and adaptation. Some of these epigenetic tags that occurs during the ontogeny of a individuals, there are not erased and are inhredity transgenerationally to the next generations.Thus the individuals of a populations could change epigenetically without a mutations in its genome and emerge as a different species. The «paradox of C value» has demostrated that this hypothesis or, "epigenetic speciation", is factible.



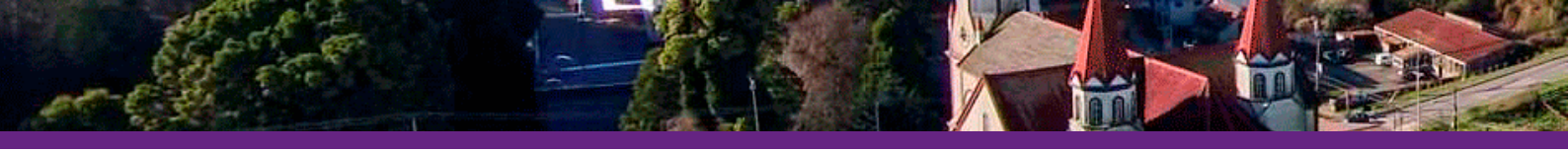
Cytogenetics: an announced death?".

Artoni R [1]
(1) Biología Estrutural, Moleular e Genética, Universidade Estadual de Ponta Grossa

Departamento de Biología Estrutural, Molecular e Genética, Programa de Pós-Graduação em Biología Evolutiva, Universidade Estadual de Ponta Grossa, Avenida Carlos Cavalcanti, 4748, 84030-900, Ponta Grossa, PR, Brasil. rfartoni@gmail.com

The study of chromosomes has fundamental importance in the interpretation of the genetic laws and demonstrate a level of variability still unknown by the researchers of the Natural Selection. Even at the beginning of the last century, curiosity exploded in the discovery of the karyotype of eukaryotes. Among the fish was no different, with the highlight that only after the advance of the "hypotonic shock" is that the resolution of chromosomes stimulate the investigation in fish. From the 70´s until today, we live an escalation of descriptions and seems to have no end, given the biological diversity of this group of vertebrates. However, fish are fascinating also in their chromosomes and present emblematic examples of the sex chromosomes, supernumerary and other numerical and structural changes at different levels. Population polymorphisms and interspecific variations only increase with the refinement of chromosomal banding techniques, and especially with the advent of localization of DNA sequences (gene and / or repetitive) by the fluorescence *in situ* hybridization. However, classical questions remain unanswered and modern literature no longer presents the same space for descriptive papers, even if they address an undisclosed diversity. In this scenario, we glimpse the survival of cytogenetic. Today we live in the OMICS era, analysis of megadata and the excitement by the use of techniques of high cost and great power of resolution. However, the answer to broad questions in biology goes through the study of chromosomes. Or do we have all the answers for cell differentiation, sex determination, epigenetic response to global climate change, viability of interspecific hybrids among many others?

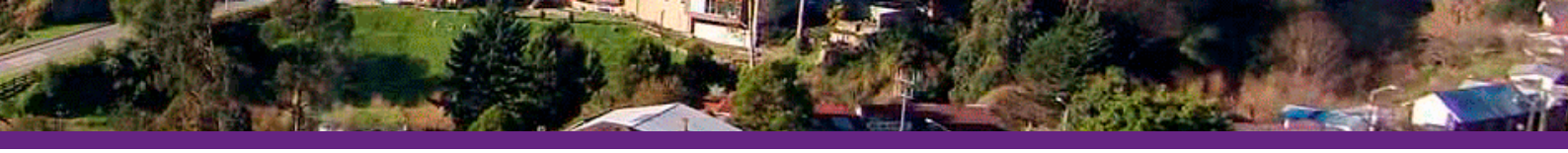
Financial support CNPq: research productivity grants (process nº 303376/2017)



Selective dinucleotide interactions and periodicities: a proof of dna polarity and double-strand conditions.

Valenzuela Carlos Alberto [1]
(1) Programa de Genética Humana, ICBM, Medicina, Universidad de Chile

The distribution of dinucleotides whose bases are separated by 0, 1, 2… K nucleotide sites showed a big distance to the random or neutral distribution, indicating a huge selective inter-nucleotide interaction. This interaction is present in prokaryotes and eukaryotes over 6,000 and 1,000,000 nucleotide sites of separation. The distance to the neutral distribution measured by a Chi-square value showed a periodicity with 3K periodicity. A 5'-3' dinucleotide in the index strand implies a parallel 3'-5' and an anti-parallel 5'-3' dinucleotide in the complementary strand. Within the index strand the selective condition of the parallel and anti-parallel dinucleotide was tested by assuming the relative selective distance to the index dinucleotide. The dinucleotides with equal parallel and anti-parallel were used to test the double strand selective value. High selective values of the double strand nature of DNA and its 5'-3' polarity were found. The antiparallel dinucleotide showed similar pattern of selection as the index dinucleotide, however, the parallel dinucleotides showed a great selective distance of to the index dinucleotide.

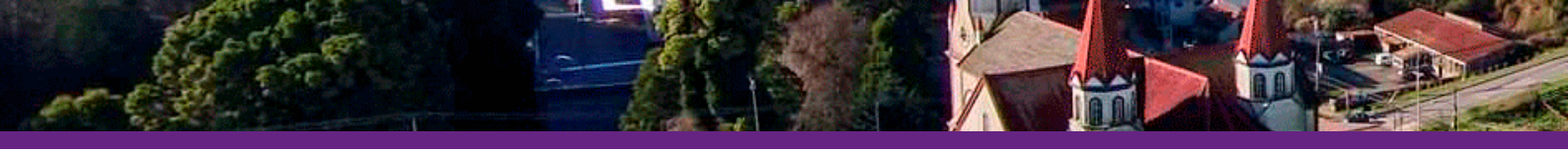


CONFERENCIAS SOCIEDAD CHILENA DE NEUROCIENCIA

CONFERENCIA Premio a la Trayectoria Sociedad Chilena de Neurociencia 2018
Dopamine and Neuropeptides

Katia Gysling
Department of Cell and Molecular Biology, Faculty of Biological Sciences, Pontificia Universidad Católica de Chile.

Neuropeptides were originally thought as modulators of neurotransmission. However, the evidence shows that they play a significant role as neurotransmitters. Furthermore, the evidence shows that there is a significant interaction between neuropeptides and classical neurotransmitters. A good example of this is the interaction of the dopamine (DA) system with several neuropeptide systems such as opioidergic, cholecystokininergic, orexinergic and corticotropin releasing factor (CRF) family allowing a fine tuning of the activity of dopaminergic neurons as well as other neurons such as glutamatergic inputs from the basolateral amygdala to prefrontal cortex. There have been significant challenges for the advance of knowledge of how neuropeptides function due to their nature. For instance, there are still few non-peptide agonists and antagonists for neuropeptide receptors. In addition, neuropeptides work at the nanomolar levels making very difficult their determination in specific brain regions. In last years, we have been studying the interaction between the DA and CRF system and its role in the interaction between stress and addiction. Available evidence showing key molecular events that could explain such interaction will be discussed.



Endogenously generated processes: A new paradigm in Systems Neuroscience

Maldonado Pedro E [1]
(1) Neurociencia, Medicina, Universidad de Chile

Most of our knowledge about neuronal mechanisms of perception comes from experiments where a stimulus is presented while the ensuing neuronal perturbation is analyzed. This scheme has brought us substantial knowledge about how the brain can respond to sudden changes in the environment. However, this experimental paradigm neglects a key fact about perception, which is that most of the time, the brain itself is the one that originates a sensory change by initiating motion of the sensory surfaces. In stark contrast to what happened during this passive processing, active sensing putatively enables the brain to processes sensory stimulus at times precisely locked to the self-action and thus engage modulatory mechanisms that exploit predictions about the nature and timing of the incoming stimuli. Here I will report studies in the visual cortex of human and other primates, that show that motor signals modulate neuronal activity in a timely precise manner which is consistent with closed-loop models of the sensory perception. This active sensing signal is an example of many other endogenously generated processes such as corollary discharge, active inference, and intrinsic ignition among others, which may trigger substantial changes in our models of the brain because of an increasing complexity of multiple types of perturbations to the different neuronal networks.

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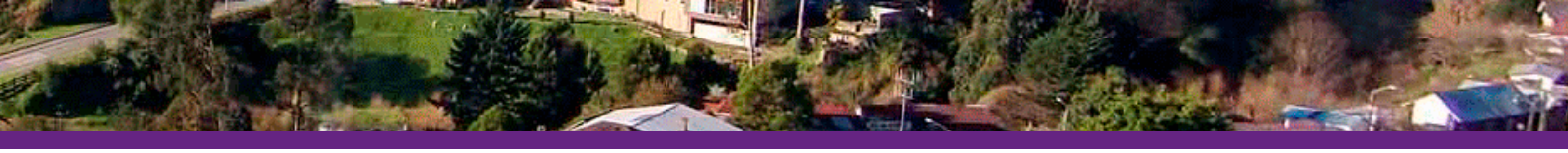
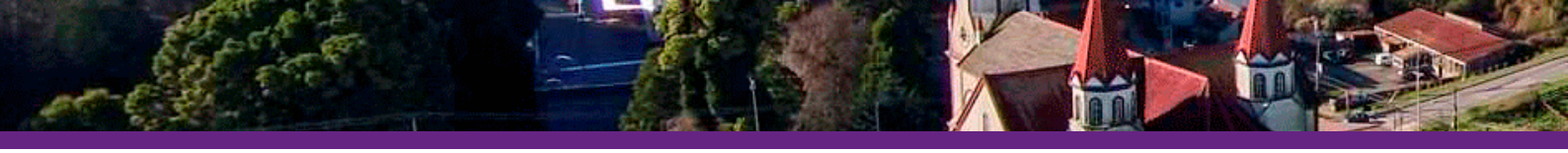


The ole of glutamate receptors in constructing cortical inhibitory circuits in health and disease

McBain Christopher James [1]
(1) Laboratory of Cellular and Synaptic Neurophisiology, NICHD, National Institutes of Health

Circuit computation requires precision in the timing, extent, and synchrony of principal cell firing that is largely enforced by parvalbumin-expressing, fast-spiking interneurons (PVFSIs). To reliably coordinate network activity, PVFSIs exhibit specialized synaptic and membrane properties that promote efficient afferent recruitment such as expression of high-conductance, rapidly gating, GluA4-containing AMPA receptors. We found that PVFSIs upregulate GluA4 during the second postnatal week coincident with increases in the AMPA clustering proteins NPTX2 and NPTXR. Moreover, Glu4A is dramatically reduced in NPTX2(-/-)/NPTXR(-/-) mice with consequent reductions in PVFSI AMPAR function. Early postnatal NPTX2(-/-)/NPTXR(-/-) mice exhibit delayed circuit maturation with prolonged critical period permissive for giant depolarizing potentials. Juvenile NPTX2(-/-)/NPTXR(-/-) mice display reduced feedforward inhibition yielding a circuit deficient in rhythmogenesis and prone to epileptiform discharges.

Memory loss in Alzheimer's disease (AD) is attributed to pervasive weakening and loss of synapses. In a mouse model of AD amyloidosis, *Nptx2-/-* results in reduced GluA4 expression, disrupted rhythmicity, and increased pyramidal neuron excitability. Postmortem human AD cortex shows profound reductions of NPTX2 and coordinate reductions of GluA4. NPTX2 in human CSF is reduced in subjects with AD and shows robust correlations with cognitive performance and hippocampal volume. These findings implicate failure of adaptive control of pyramidal neuron-PV circuits as a pathophysiological mechanism contributing to cognitive failure in AD. Our findings demonstrate an essential role for NPTXs in controlling network dynamics highlighting potential therapeutic targets for disorders with inhibition/excitation imbalances such as schizophrenia and AD.

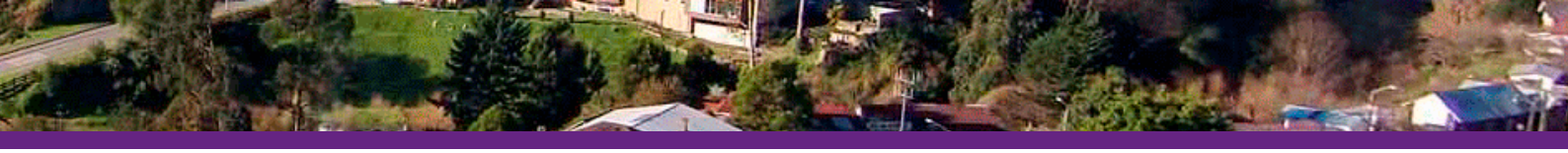


Human pain channelopathies

Bennett David [1](1) Nuffield Department of Clinical Neurosciences, Medical Science Division, University of Oxford

There has been significant progress over the last decade in understanding the molecular basis by which sensory neurons transduce and subsequently transmit noxious (ie. tissue damaging) stimuli giving rise to the sensation of pain. Over this same period we have recognized that mutations in such ion channels (many of which are selectively expressed in sensory neurons) can result in primary neuropathic pain disorders. An excellent example is the voltage gated ion channel Na_V 1.7 encoded by the gene SCN9a. Loss of function mutations in this ion channel result in congenital inability to experience pain and gain of function mutations can cause a number of distinct neuropathic pain disorders including erythromelalgia, paroxysmal extreme pain disorder and small fibre neuropathy. There is a correlation between the impact of mutations on the biophysical properties of the ion channel and the severity of the clinical phenotype. A further example is TRPA1 a mutation in which causes a familial episodic pain disorder characterized by proximal pain. The fact that mutations in such channels can cause monogenic pain disorders makes them attractive analgesic drug targets. Secondary neuropathic pain disorders such as traumatic neuropathy or painful diabetic neuropathy are also associated with altered expression of multiple ion channels which contribute to hyperexcitability. We are trying to improve the stratification of neuropathic pain patients by linking the clinical phenotype with genotype with the ultimate aim of optimizing analgesic drug selection on an individualized basis. As well as inherited channelopathies we are now recognizing nauto-immune channelopathies for instance mediated by antibodies to CASPR2. These provide novel therapeutic opportunities.

Fondecyt 1161019



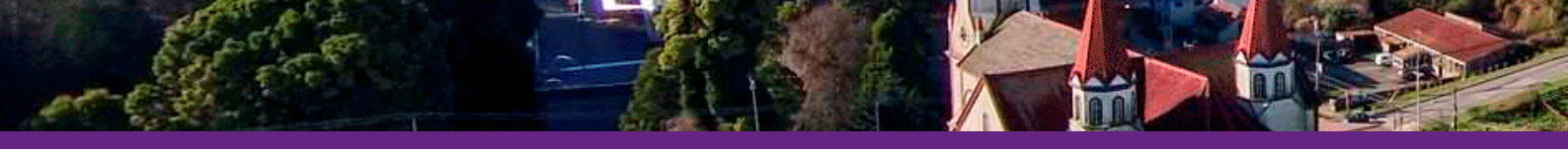
SIMPOSIOS
SOCIEDAD DE GENÉTICA DE CHILE

Genética y Genómica del Cáncer
Coordinadora: Katherine Marcelain

Mutaciones fundadoras en BRCA1 y BRCA2 en pacientes chilenas con cáncer de mama

Carvallo Pilar [1], Tapia Teresa[1], Alvarez Carolina[1](1) Biología Celular y Molecular, Ciencias Biologicas, Pontificia Universidad Católica de Chile

El cáncer de mama es la primera causa de muerte por cáncer en Chile, por lo cual se ha constituido como una de las prioridades en Salud Pública. La detección temprana de un tumor maligno es relevante para prevenir la metástasis y mejorar la calidad de vida de una paciente con cáncer de mama, por lo cual la detección de mutaciones de alto riesgo al cáncer de mama es de suma importancia en familiares sanos. Hace más de 20 años BRCA1 y BRCA2 fueron descritos como los dos genes cuyas mutaciones causan un alto riesgo a cáncer de mama y/u ovario, siendo hasta hoy los más relevantes en esta enfermedad. El análisis de BRCA1 y BRCA2 ha sido realizado en mujeres con cáncer de mama hereditario de diversas poblaciones del mundo, detectándose que entre el 10 y el 50% de ellas presentan una mutación. Nuestro grupo ha realizado la detección de mutaciones en BRCA1 y BRCA2 por los últimos 18 años en un total de 460 pacientes con cáncer de mama, tanto en casos hereditarios como en pacientes sin historia familiar. Hemos encontrado un total de 25 mutaciones en 76 pacientes índice, de las cuales 9 son recurrentes entre nuestras pacientes. La genotipificación de 11 marcadores STR en ambos genes revelaron un ancestro común para cada variante patogénica. Generamos un panel de 9 mutaciones fundadoras que dan cuenta del 78%de las pacientes portadoras de mutación, que es único en Latinoamérica, y uno de los pocos descritos en poblaciones del mundo.



Targeted sequencing of tumors reveals new therapeutic opportunities for gallbladder cancer patients

Marcelain Katherine [1], Toro Jessica[1], Diez Daniela[1], Alejandro Blanco[2], Oliveira Luciana[1], Villamán Camilo[1], Lorenzo-Bermejo Justo[3], Armisén Ricardo[1,2]
(1) Departamento de Oncología Básico-clínica, Facultad de Medicina, Universidad de Chile
(2) Centro de Excelencia en Medicina de Precisión (CEMP), Pfizer
(3) Institute of Medical Biometry and Informatics, University of Heidelberg

Chile has the highest incidence and mortality rates of Gallbladder Carcinoma in the word, being one of the leading causes of death by cancer in Chilean woman. Worldwide distribution of the disease is very distinctive, with a very low presence in developed countries. Thus, basic research and clinical trials seeking treatment opportunities are scarce, leaving this disease neglected. In the last few years, the introduction of next-generation sequencing technologies (NGS) to the clinical practice has allow the advancement in the identification of somatic mutations responsible for promoting or driving cancer progression and that have become the target for specific therapies in a broad number of cancers. This advancemente has also increase the knowledgment in gallbladder carcinoma, although at a very discrete level if compared with more prevalent cancers such as breast or lung adenocarcinoma. TP53 is the most frequently mutated gene (>50%), followed by CDKN2A, CDKN2B, ARID1A and SMAD4. Our results show that most mutations correspond to loss of function mutations (67% vs 33% gain of function). Importantly, among mutated genes, there are some that are targeted for therapies in other type of cancer. For instance, EGFR, ERBB2, KRAS, TSC1, BRCA1, ATM, PIK3CA. Thus, it is feasible to expect that these therapies would also be useful for gallbladder cancer patients. Moreover, some of these genes have also shown a synthetic lethal effect in other type of tumors, expanding the range of opportunities for treatment in these patients.

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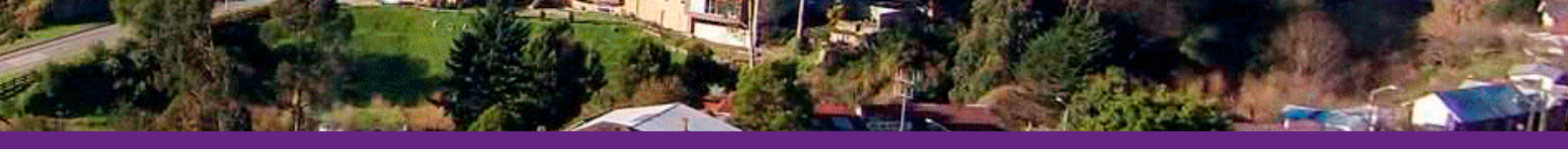

A comprehensive description of the molecular epidemiology of somatic mutations in actionable genes in Non-small cell lung cancer Chilean patients.

Armisen Ricardo [1]
(1) Pfizer Chile, Center of Excellence in Precision Medicine

Advances in precision medicine, which treats patients with therapies directed against the specific molecular alterations driving their cancers, have transformed oncology. This approach requires identification of the molecular alterations generating the cancer, the development of targeted therapies, and the validation of companion diagnostics assays to identify patient populations for clinical trials and eventual implementation. Thanks to global efforts, such as TCGA or ICGC, today it is possible to establish that a set oncogenic actionable driver mutations is found in about a 64% of lung adenocarcinomas patients.

The general aims of NIRVANA study (NCT03220230) are the validation of more sensitive and high-throughput technologies for the study of non-small cell lung cancer genomics alterations, and the generation of a comprehensive, high quality, clinical, pathological, and genomics data in Chile, Brazil and Peru. So far, mutation prevalence of 52 genes was analyzed in 1253 NSCLC tumor samples from the NIRVANA Chilean patients. After the variant calling and quality filtering process, potential somatic mutations were annotated to classify them as known or novel variants.

The prevalence of genomic alterations in the 52 genes is similar to previous studies. For example, ALK fusions were present in 3.83% of the tumors. Among the 973 DNA variants with a deleterious effect, 63% of them corresponded to novel variants that could be of clinical interest. Compared to the default variant calling process of known variants, this strategy increases by approximately 5-times the potential of finding new mutations for further analyses and new therapeutic opportunities.
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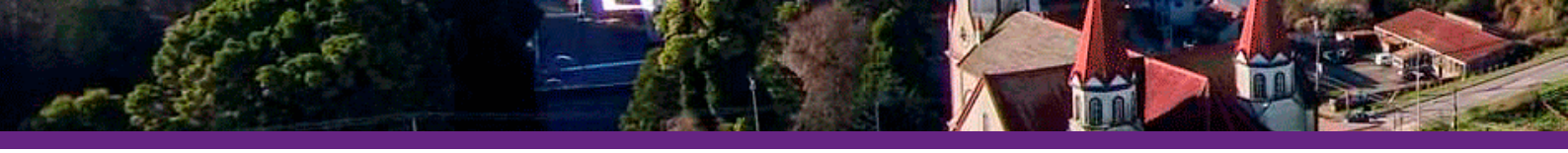

Exome-wide analysis of bi-allelic alterations identifies a Lynch phenotype in the Cancer Genome Atlas

Harismendy Olivier [2,1], Buckley Alexandra R.[4,3], Ideker Trey [2,5], Carter Hannah [2,5], Schork Nicholas J. [3]
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(2) Moores Cancer Center , University of California at San Diego (UCSD)
(3) Human Biology Program. , J. Craig Venter Institute
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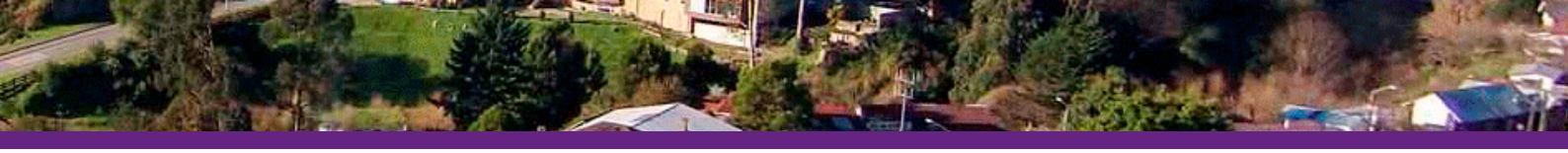
(5) Division of Medical Genetics, Department of Medicine., University of California at San Diego (UCSD)

Cancer susceptibility genes generally require the somatic alteration of the remaining allele to drive oncogenesis. Whether combined germline and somatic bi-allelic alterations are universally required for germline variation to influence tumor mutational profile is however unclear. Here we performed an exome-wide analysis of the frequency and functional effect of bi-allelic alterations in The Cancer Genome Atlas (TCGA). We integrated germline variant, somatic mutation, somatic methylation, and somatic copy number loss data from 7,790 individuals from TCGA to identify germline and somatic bi-allelic alterations in all coding genes. We used linear models to test for association between mono- and bi-allelic alterations and somatic microsatellite instability (MSI) and somatic mutational signatures. We discovered significant enrichment of bi-allelic alterations in mismatch repair genes, and identified 6 bi-allelic carriers with elevated microsatellite instability (MSI), consistent with Lynch syndrome. In contrast, we find little evidence of an effect of mono-allelic germline variation on MSI. Using MSI burden and bi-allelic alteration status, we reclassify two variants of unknown significance in *MSH6* as potentially pathogenic for Lynch syndrome. Extending our analysis of MSI to a set of 127 DNA damage repair genes, we identified a novel association between methylation of *SHPRH* and MSI burden. We find that bi-allelic alterations are infrequent in TCGA, but most frequently occur in *BRCA1/2* and MMR genes. Our results support the idea that bi-allelic alteration is required for germline variation to influence tumor mutational profile. Overall, we demonstrate that integrating germline, somatic, and epigenetic alterations provides new understanding of mutational profiles.



Construyendo una ruta hacia la investigación genómica colaborativa en Chile

Coordinador: Boris Rebolledo

Human population genomic studies: international and local initiatives on data sharing

Repetto Gabriela [1], De Ferrari Giancarlo[2], Lecaros Juan Alberto[3], Miquel Juan Francisco[4], Rebolledo Boris[1], Verdugo Ricardo[5,6]
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(4) Departamento de Gastroenterología, Facultad de Medicina, Pontificia Universidad Católica de Chile
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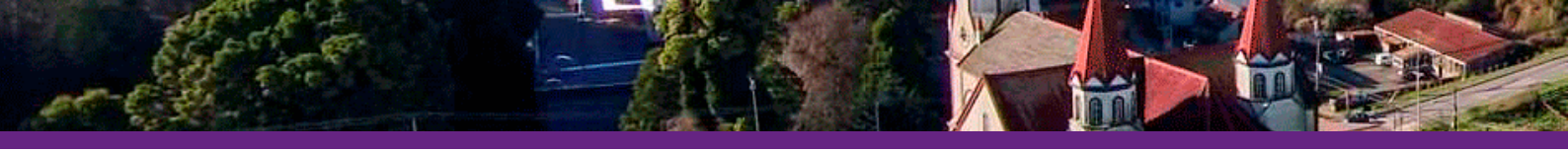
(6) Departamento de Oncología Básico-Clínico, Facultad de Medicina, Universidad de Chile

The generation of relevant benefits for population and individual health derived from the genomics revolution requires, among other needs, access to reference databases. For example, accurate clinical interpretation of whole-genome and whole-exome sequences requires comparison of the patient´s linked genomic and phenotypic data with variant reference data of both healthy and affected individuals. The robustness of such comparisons is made possible by sharing genomic and associated clinical data. The recognition of the need for data access has lead several countries, institutions and publishers to promote data sharing and access, with the purposes of allowing the maximum returns from the investment in research, reducing waste and promoting transparency. On the other hand, these same countries are enacting strict general data protection laws, making it difficult to share personal data across borders. This tension has led to the concept of safe and responsible data sharing, that aims at allowing society to benefit from research, while protecting the rights and privacy of participants. This presentation will describe international and local initiatives that promote responsible data sharing, such as the Global Alliance for Genomes and Health, METADAC, ClinVar, datoscientificos.cl, as well as the perspective of participants.

Fondecyt 1171014 (GR), 1180848 (GdF)



Chilean Human Genomic Data Sharing Initiative

Lecaros Juan Alberto [1], De Ferrari Giancarlo[2], Miquel Juan Francisco[3], Rebolledo Boris[4], Repetto Gabriela[4], Verdugo Ricardo[5,6]
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(2) Instituto de Ciencias Biomédicas, Medicina y Ciencias de la Vida, Medicina, Universidad Andrés Bello
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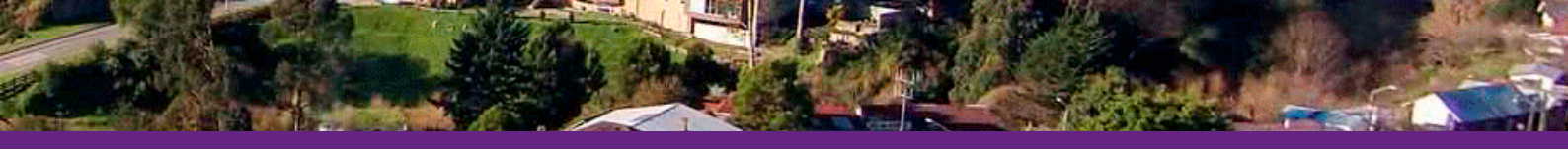
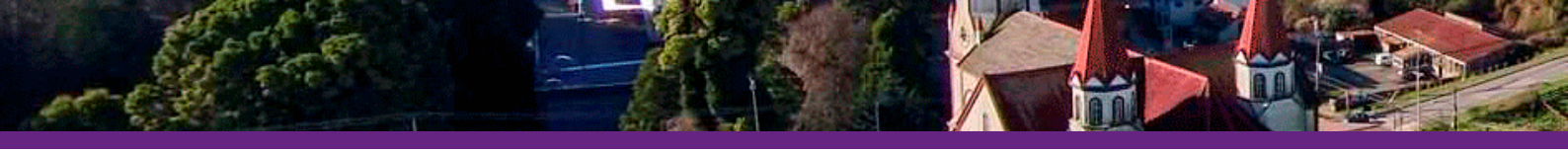
The sharing of genomic and health-related data is relevant in order to improve human well-being and health through scientific research.In order to develop a culture of responsible use of open access genomic data, it is necessary to have harmonized standards of quality, security, protection of privacy and confidentiality of data.The international research community has shown its concern in developing recommendations for responsible sharing of genomic data, highlighting the initiative of the Global Alliance for Genomics and Health (GA4GH) and the Human Variome Project (HVP). In this context, we present the Chilean Human Genomic Data Sharing Initiative, whose mission is to promote a culture of responsible sharing of human genomic data in Chilean researchers and research groups, following the recommendations of HVP and GA4GH. This local initiative, the second in LA, has a structure formed by three pillars (Genomic Data, Ethics and Regulatory Policies, Data Security), and an organization and governance directed by an executive committee and a steering committee, supported by an international advisory board.



The Personal Data Protection Bill draft, how will it impact on biomedical scientific research?

Leturia Francisco Javier [1]
(1) Miembro del Consejo para la Transparencia del Gobierno de Chile, Facultad de Derecho, Pontificia Universidad Católica de Chile

In times of increasing digitalization of society, our legislator, aware of the need to update our standards of protection and use of personal data, has begun the discussion of a bill that almost completely changes the current regulations (Law No. 19,628 on protection of privacy in 1999), which is clearly insufficient and obsolete in this new context. For this reason, this bill (Bulletin No. 11.144-07) seeks to modernize and make more flexible the normative and institutional framework for the treatment of personal data, in contexts of massive use of digital technologies and advances in genetic research, in order to allow a fair balance between the protection of privacy and access to information. Undoubtedly, one of the important challenges of this project is the regulation of the use of personal health data by information technologies (electronic clinical records, the provision of telemedicine services, the use of big data in health) and in research in precision medicine. This conference aims to analyze and discuss what should be the standard of protection that the new law should give to health data and how that new standard will impact on biomedical scientific research.



Gaps and challenges for sharing human genomic data in Chile

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(2) Proyecto ChileGenómico, Programa de Genética Humana, Facultad de Medicina, Universidad de Chile

There is general agreement about the pivotal role that genomic data will play in the medicine of the future. Precision medicine is already a reality in oncology and other areas such a pharmacogenomics are not far behind. The decreasing prices of sequencing technologies and the evolution of bioinformatic pipelines will make it feasible for any person to purchase his/her own whole-genome sequence, either for medical purposes or just for personal interest. Even some companies may offer that service for "free" in the future because of the value in the information that is collected. This will create tremendous opportunities for research, eliminating the need to spend big funding in large-scale genomics projects. However, the right conditions must be in place for people to safely share their sensitive genomic data to third-parties including legal protection, tools to encrypt and to safely share data, and even the right economic incentives for individuals who are the "owners" of the data. These aspects are far from resolved even in industrialized countries. In Chile, although a few research projects have generated significant amounts for genomic data, we have difficulties for sharing data, which are related to legislative and regulatory gaps, precarious infrastructure, funding shortage, lack of trained personnel in bioinformatics and IT security, and a general culture of mistrust. I will present future perspectives about genomics data sharing, current gaps and challenges to make it a reality in Chile, and my personal vision on how to overcome them.

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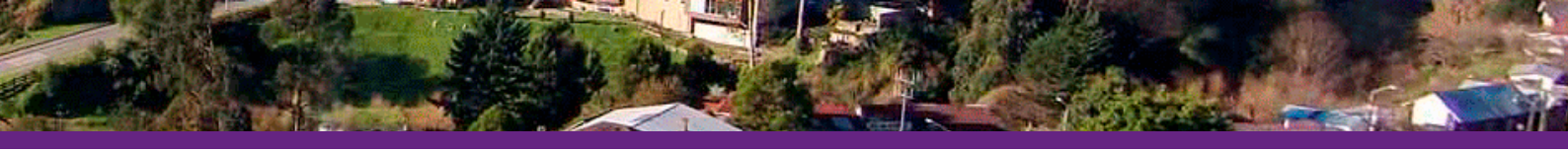


Parkinson Disease (PD):molecular insights, new mechanisms and innovative therapies

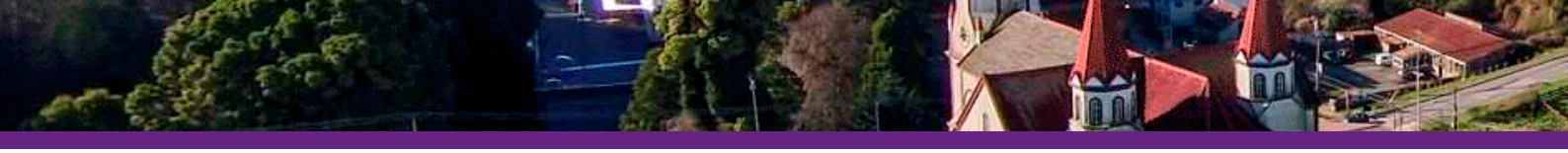
Coordinadora: Gabriela Repetto

Is Parkinson's disease a lysosomal disorder?

Klein Andrés D. [1]
(1) Centro de Genética y Genómica, Facultad de Medicina, Universidad del Desarrollo

Common forms of Parkinson´s disease (PD) have long been described as idiopathic, with no single penetrant genetic factor capable of influencing disease etiology. Recent genetic studies indicate a clear association of variants within several lysosomal genes as risk factors for idiopathic PD (iPD). The emergence of novel variants suggest that the etiology of idiopathic PD may be explained by the interaction of several partially penetrant mutations that, while seemingly complex, all appear to converge on cellular clearance pathways. These newly evolving data are consistent with mechanistic studies linking a-synuclein toxicity to lysosomal abnormalities, and indicate that iPD bears a striking resemblance to Mendelian lysosomal storage disorders (LSDs) at a genetic and biochemical level. Furthermore LSDs and PD are highly variable disorders, where patients can present a spectrum of symptoms. The genetic basis of such extraordinary phenotypic variability is largely unknown. The LSD-PD resemblance offers novel pathways to exploit for the development of disease-altering therapies for iPD that target specific components of the lysosomal system.

Funding: Pew Innovation Fund and Fondecyt 1180337 andresklein@udd.cl



22q11.2 deletion syndrome and Parkinson disease

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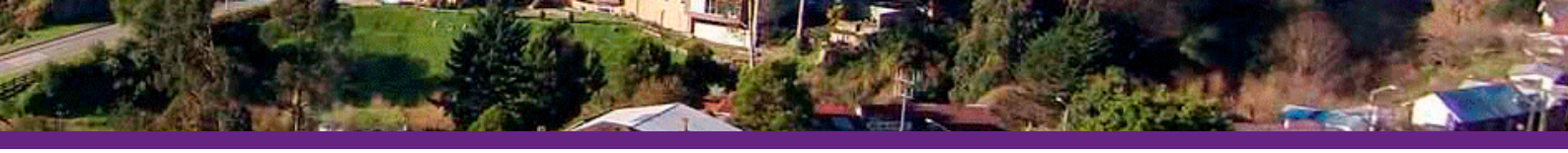
(2) ?s Heeren Loo Zorggroep, , Amersfoort, The Netherlands
(3) Department of Nuclear Medicine, Academic Medical Center, Amsterdam, the Netherlands

Background:
22q11.2 deletion syndrome (22q11.2DS) is the most common human microdeletion syndrome, affecting about 1 in 3000 live births. 22q11.2DS is associated with a 20 to 70-fold increased risk of Parkinson's disease (PD), especially with early-onset (<45 years), responsible for approximately 0.5% of early-onset PD.

Methods:
A review of the current knowledge on PD in 22q11.2DS.

Results:
Neuropathological and dopaminergic imaging findings, core motor symptoms of PD, and response to standard treatments appear similar in 22q11.2DS-associated PD in comparison to those seen in idiopathic PD. Less typical features include the average age of motor onset being earlier in 22q11.2DS (~40 years), the complex comorbidity, pre-existing psychiatric conditions, early dystonia and a history of seizures. In addition, medication-induced parkinsonism and undifferentiated parkinsonism appear to be also prevalent in 22q11.2DS.

Conclusion:
The author will discuss that further recognition of 22q11.2DS and study of 22q11.2DS-associated PD could provide insights into the mechanisms underlying PD in the general population, and that 22q11.2DS may serve as an identifiable PD model to study prodromal PD and disease-modifying treatments. Also, he will discuss possible pathophysiological mechanisms underlying 22q11.2DS-associated PD.



The journey of dopaminergic deficit to parkinson disease

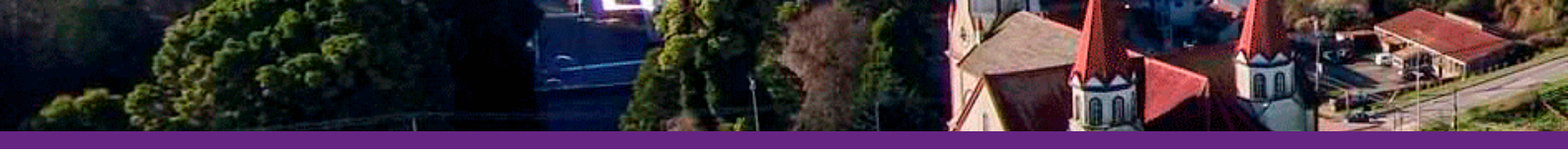
Juri Carlos [1]
(1) Neurología, Medicina, Pontificia Universidad Católica de Chile

Background:
The deficit of dopamine is the hallmark of Parkinson´s disease (PD). However, there is a long way from the beginning of the dopaminergic lost until the onset of the typical motor manifestations of PD. This prodromal phase of the disease is actually a source of tremendous interest.

Methods:
Review of the literature in the field of pre-motor or prodromal phases of PD.

Results:
The onset of Dopaminergic neuronal loss begins at least 7 to 10 years before the clinical manifestations of PD. During this period, numerous non motor symptoms as olfaction loss, constipation, affective and cognitive disturbances and REM sleep behavior disorders are apparent and prelude the debut of the classical clinical manifestations. The pathophysiological mechanisms involved in this process and the possible biomarkers for early detection will be discussed.

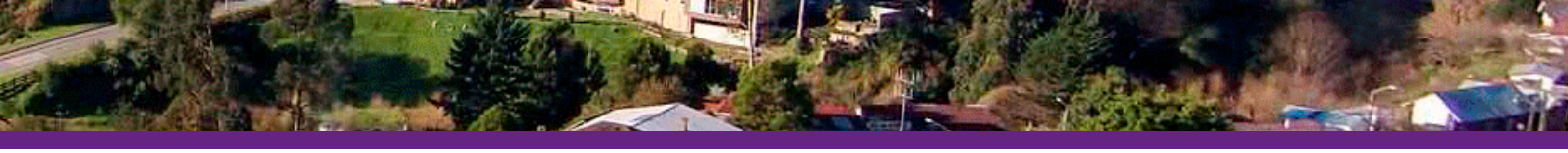
Conclusion:
The prodromal phase of PD is a new frontier for the understanding of the neurodegenerative disorders and opens a new window for possible neuroprotective strategies in PD.
CJ supported by FONDECYT 11130534.



Spinal cord stimulation for Parkinson´s disease: reaching the brain without touching it

Fuentes Romulo [1]
(1) Departamento de Neurociencias, Facultad de Medicina, Universidad de Chile

Since the discovery circa 1960 that dopaminergic deficit was a key player in Parkinson's disease motor impairment, pharmacological approaches compensating dopaminergic activity have been widely used for symptomatic treatment. On a different approach, the electrical stimulation of deep nuclei of the brain (Deep Brain Stimulation - DBS) has also proven effective in alleviating motor symptoms and has been used for several decades. Yet, this method requires the chronic implant of stimulation electrodes in the brain. DBS is believed to act by modulating the activity of the neuronal circuits involved in motor control, namely the cortico – basal ganglia – thalamic – cortical (CBTC) loop. But what if we could modulate the same circuit without implanting electrodes in the brain? Electrical stimulation of the somatotactile afferents of the spinal cord have overt effects on the CBTC circuit and have showed in animal models and patients it can improve parkinsonian motor symptoms.



SIMPOSIO
SOCIEDAD CHILENA DE EVOLUCIÓN

Integrando disciplinas para el estudio de las Zoonosis.

Coordinador: Ricardo Campos

Ecoepidemiology of a generalist microparasite: the case of *Leptospira* spp in Mediterranean Chile

Correa Juana Paola [1], García De Cortazar Rodrigo[1], Ramírez-Estrada Juan[2], Bacigalupo Antonella[3], Cattan Pedro E.[3], Botto-Mahan Carezza[3]
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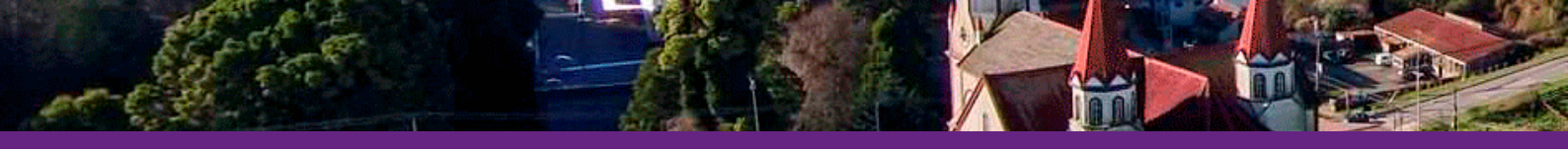
(2) Departamento de Ecología, Pontificia Universidad Católica de Chile
(3) Departamento de Ciencias Biológicas Animales, Facultad de Ciencias Veterinarias y Pecuarias, Universidad de Chile

Leptospira spp is a widely-distributed micro-parasite common in tropical areas, which causes disease in humans and other mammals. It has been suggested that the host community structure and some environmental characteristics could influence the persistence and abundance of these bacteria of complex transmission cycle. In Mediterranean Chile, even though the climate could restrict the environmental persistence of *Leptospira*, there are cases of disease. Previous studies in this area showed that rodent communities are more infected in agricultural sites than in wild ones, with the introduced *Rattus norvegicus* explaining the high infection levels in agroecosystems. In this study we examined the infection by *Leptospira* in rodents from agricultural sites of Mediterranean Chile in two seasons (summer and spring), evaluating whether there is an association between rodents diversity and infection in *Rattus* spp, as well as if there are infection-associated costs in *Rattus* spp, by using their space use and survival as proxys. It was detected spatio-temporal variability in infection levels between sites, with the highest overall infection in spring (Fisher-test, p=0.013). No association between infection and diversity (H') was detected, neither no effect of *Leptospira*-infection on mortality in *Rattus* spp. However, there was a marginally significant tendency in infected-*R. norvegicus* to use smaller areas than non-infected ones (Kruskal-Wallis test, P=0.0501); this species also showed high infection-level (31.9%). *Leptospira*-infection is widely distributed in rodents of Mediterranean Chile, being introduced rodents relevant for their high levels of infection. Temporal-trends in the infection levels should be examined with more detail in future studies.

FONDECYT Postdoctorado 3140543, FONDECYT 1170367 and 1140650. Acknowledgments: P. Arroyo, N. Lártiga, G. Rojo, N. Morales, C. Saez, E. Yefi, R. Salgado, Y. Cerda, F. Llanquín, and the land-owners that permit this study



Molecular epidemiology, challenges and transdisciplinary opportunities for collaborative research in "one health"

Verdugo Cristobal Cristian [1]
(1) Instituto de Medicina Preventiva Veterinaria, Ciencias Veterinarias, Universidad Austral de Chile

As in past centuries, the globalization of goods and services has not only meant economic growth, it has also been associated with a greater number of emerging and reemerging diseases. Through commercial routes, endemic infectious agents which were well adapted to specific geographical areas, have been exposed to new populations without immunological history, resulting in the emergence of important infectious outbreaks in humans and animals. In this line, it is estimated that about 75% of emerging infectious diseases are zoonotic. The growing possibility of the transmission of agents between different species has led to the need to address human and animal health as a whole, which has been embodied in the concept of "one health".

Technological advances in the field of molecular biology have allowed rapid and specific diagnostic of infectious agents. Additionally, advances in sequencing methods have enabled us to observe the population variability of different pathogens, going beyond the traditional absent/present scenario. However, the integration of those techniques to traditional methods of epidemiology has not been easy, where there is an important need to integrate disciplines such as population genetics and phylogeny into the epidemiology research.

Three diseases where the author has been involved (Rift Valley Fever in Kenya, Paratuberculosis in New Zealand, and Avian Influenza in Chile), will be presented as study cases, showing the application of molecular methods to epidemiological problems, their current limitations, as well as knowledge gaps for possible transdisciplinary collaborations.

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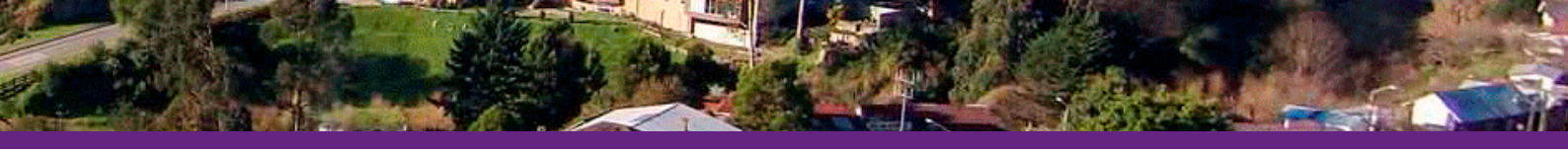

Understanding the *Trypanosoma cruzi* cycle in coastal islands of Chile. An integrative parasitological, ecological and evolutionary approach

Campos-Soto Ricardo [1], Díaz-Campusano Gabriel[1], Rives-Blanchard Ninette[2], Quiroga Nicol[3], Muñoz-San Martín Catalina[4], Torres-Pérez Fernando[1]
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Chagas disease is one of the main zoonoses mediated by vectors in America. The etiological agent is the protozoan *Trypanosoma cruzi*, transmitted mainly by hematophagous insects of the subfamily Triatominae. *T. cruzi* cycle alternates between triatomines and mammalian host species; birds and reptiles are refractory to infection. *Mepraia* genus are Triatomines endemic of Chile that play an important role in *T. cruzi* transmission in the wild cycle and are potential vectors for humans. In addition to the continental distribution, *Mepraia* populations have been reported inhabiting in islands of northern Chile, these insects feed mainly on seabirds and reptiles. In these islands infected *T. cruzi* insectshave been detected. If birds and reptiles are refractory to infection, what is the origin of the infected *T. cruzi* vectors in islands? Suggested hypotheses are: 1. The presence of *Mepraia* in insular areas are explained through passive dispersion by marine birds; 2. Infected *Mepraia* specimens are originated from ancestral habitats with a complete *T. cruzi* cycle that were separated by vicariance.

To clarify the insular *T. cruzi* cycle, infection rate of *Mepraia* and small mammals were studied in three islands. *Mepraia* mtDNA gene sequences were used to estimate divergence dates and migrations between insular and continental populations.

Results show a complete *T. cruzi* cycle with infected *Mepraia* and *Abrothrix* rodent. Divergence dates are congruent with sea level and tectonic changes that originate the islands during the Pleistocene. Divergence dates, shared haplotypes and migration suggest that the origin of island vectors can be explained by vicariance and dispersion.

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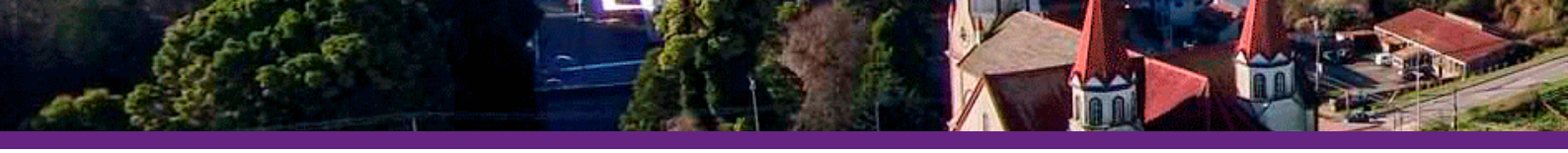

Hantavirus evolution and its host in Chile

Torres-Perez Fernando [1], Boric-Bargetto Dusan[1], Vial Cecilia[2], Palma R. Eduardo[3]
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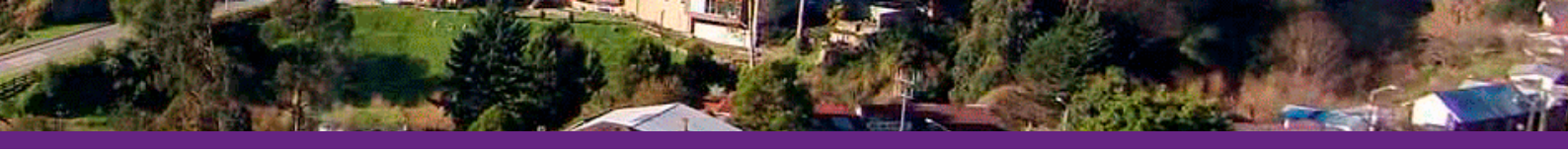
Emerging zoonotic diseases are a major concern among scientists studying infectious diseases at different scales, and may cause new or previously unrecognized diseases. In such emergencies, viruses represent an important group as human pathogens. For understanding the phenomenon of the emergence of a specific pathogen, it is essential to understand the epidemiology, ecology and evolutionary processes responsible for the appearance and spread of that pathogen.

Hantavirus cardiopulmonary syndrome (HCPS) is an emerging infectious disease that produces a variable number of human cases every year, with a case-fatality ratio between 30 and 50%. HCPS was first reported in Chile in 1995, and Andes Orthohantavirus (ANDV) is responsible for the more than 500 cases of HCPS reported in Chile. Serologically confirmed human hantavirus infections have occurred throughout a wide latitudinal distribution extending from the regions of Valparaíso (32° to 33°S) to Aysen (46°S) in southern Patagonia. This wide latitudinal range spans contrasting geographic features and landscapes ranging from a Mediterranean to deciduous Temperate Forests. Here we describe the phylogeographic structure of ANDV and its associated rodent host for understanding ANDV viral evolution integrated with spatio-temporal reconstruction of ANDV lineages. Results will help to identifying emerging patterns and gain new insights about the understanding of the ANDV disease dynamics.

Funding: CONICYT PIA-Anillo 1408, FONDECYT 1171280, 3180237, 1170761



SIMPOSIO SOCIEDAD CHILENA DE NEUROCIENCIA

Evolution and comparative biology of sensory systems and associated neural circuits

Coordinadores: Adrian Palacios-Nicolas Palanca

The evolution of amniote hearing organs

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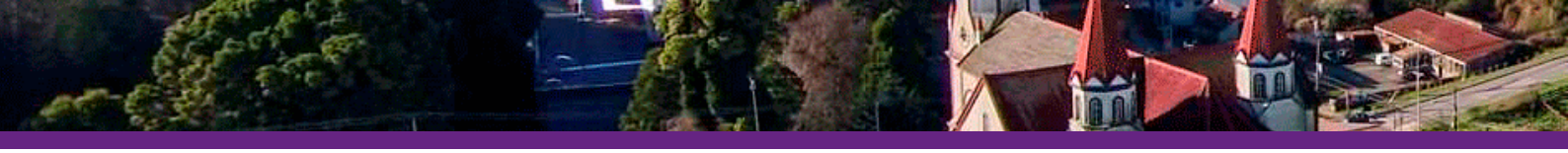
The major lineages of amniote vertebrates separated before significant formative evolution of the hearing organ began. Thus each lineage started with a small, simple sensory organ, likely consisting of a few hundred hair cells that responded to sound frequencies of up to about 1 kHz. Chelonians have retained this level of organization to date, whereas archosaurs, lepidosaurs and mammalian lineages evolved their ears along unique paths. Following the independent evolution of middle ears in the Triassic, most hearing organs expanded both in size and in frequency-response range, while specializing groups of hair cells in a lineage-specific but partly functionally parallel fashion. The resulting hearing organs differ hugely in size (~200-fold differences in length) and frequency-response range (max. 1 kHz to max ~200kHz, or about 4 to 9 octaves), but not greatly in sensitivity or frequency selectivity (with rare exceptions). Reversals have occurred, as, e.g., in the snakes, which reduced their middle ears and reverted to a chelonian-style auditory sensory epithelium. The independent evolution of middle and inner ears over more than 200 million years has resulted in an enormous variety of acoustic sensors whose specific morphological and functional patterns reveal specific adaptations to survival.



The avian auditory system, a view from comparative biology

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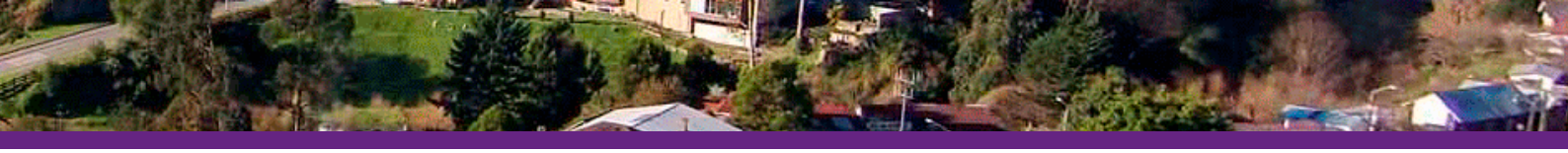
The auditory midbrain (inferior colliculus, IC) contains neurons that represent auditory space. The external nucleus of the barn owl's IC is the textbook example of a two-dimensional auditory space map, assembled by combining brainstem representations of the two binaural cues interaural time difference (ITD) and interaural level difference (ILD). However, the barn owl is unique in that its asymmetrically formed facial disk transforms ILD into a cue for sound source elevation. In contrast, for most animals, ITD and ILD are both cues for sound source azimuth. We recently showed, using headphone stimulation, that in the chicken IC, ITD selectivity was disproportionately more common among low-frequency units, while ILD-only selective units were predominantly tuned to high frequencies. This suggests that ITD and ILD cues provide complementary information for sound localization, according to the duplex theory, and very similar to mammals. However, the brainstem circuits that first represent ITD and ILD and convey these to the IC are fundamentally shared between owls and chickens, and different to mammals. This talk will summarize data across birds and mammals and emphasize the importance of being aware of the different physical cues available to different animals for inferring the evolution of auditory neural circuits and the selective pressures acting on them.



Adaptations of Cetacean Retinal Pigments to Aquatic Environments.

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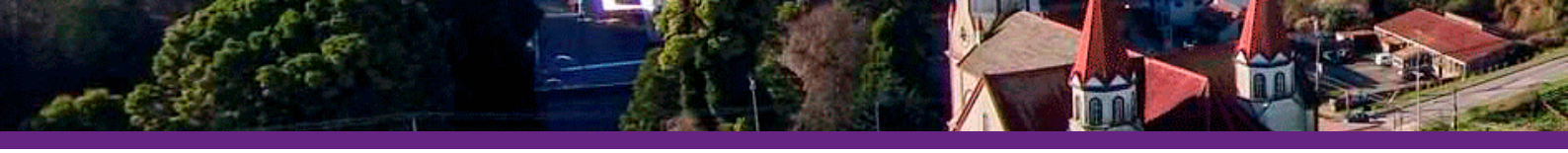
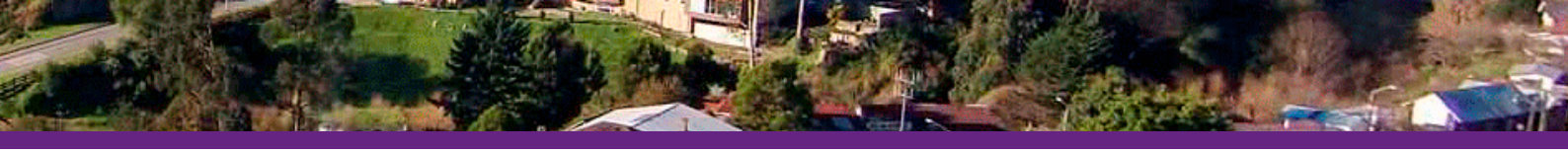
The underwater environment places unique constraints on the vision of cetaceans compared to their terrestrial mammalian counterparts. Water absorbs and filters light affecting both the intensity and spectral distribution of light available for vision. Therefore, the aquatic environment restricts the spectral distribution of photons and limits the distance at which objects may be observed. The cetacean eye possesses numerous anatomical, cellular and molecular adaptations to the underwater light environment that increase photon capture in a light-limited environment. These adaptations include a powerful spherical lens, a unique corneal design allowing for acute vision in both air and water, as well as a blue reflective optic tapetum. There are also molecular adaptations that influence the spectral sensitivity of both the rod and cone visual pigments. In addition, it appears that the melanopsins, the visual pigment expressed in a small subset of ganglion cells in mammalian retinae, from cetacean rod monochromats may possess a mechanism that inhibits relatively rapid deactivation of thelight-activated melanopsin. This mechanism would result in prolonged pupil constriction resulting in a very useful mechanism in the prevention of photobleaching of rod pigments under photopic conditions.



Processing of sound direction in Archosaurs, reptiles and turtles

Carr Catherine [1](1) Department of Biology, College of Computer, Mathematical and Natural Sciences, University of Maryland, College Park

Sound source segregation depends on mechanisms that enhance directionality, like detection of interaural time differences (ITD). Birds, crocodilians, turtles and lizards have brainstem circuits for detection of ITDs that appear homologous. In birds and crocodilians these circuits form maps of ITD composed of delay lines and coincidence detectors. Lizards, however, have coupled ears, and all lizard auditory nerve fibers have strongly directional responses, i.e. a peripheral specialization obviates the need for central computation of ITD. Current work suggests lizard brainstem auditory circuits may enhance the already strong lateralization by simple EI-type neural processing, but with no clear maps of auditory space. Thus the processing of sound direction in the bird, alligator and lizard CNS is different, but all three groups have mechanisms for enhancing sound source directionality and all have grossly similar neural circuits.



Dissecting ion channel gating

Coordinador: Alan Neely

Coupling between voltage sensor and permeation pathway in Hv1 proton channels

Gonzalez Carlos [1,2,3], Carmona Emerson[2], Neely Alan[2], Alvarez Osvaldo[5,4], Latorre Ramon[2]
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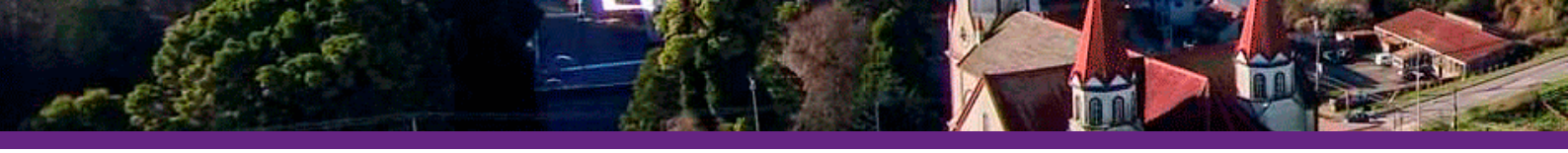
Hv1 is a voltage gated proton channel with an exquisite selectivity. The most accepted proton permeation mechanism for Hv1 consists of proton hopping along a stable water wire. To test the validity of such mechanism, we determined unitary conductance using fluctuation analysis of the wild type channel as well as in point mutations in the putative Hv1 channel pore region. Mutations of residues N264 and D222 affect unitary conductance and selectivity. Based on molecular dynamics and quantum dynamics simulations, we propose that a proton wire underlies the permeation mechanism in Hv1 channel, in which D222 and D160 are reversibly protonated in a process modulated by N264. Both D160 and D222, but not N264, are conserved in the non-conductive voltage-sensing domain of Ci-VSP. Notably, when the equivalent residue in Ci-VSP is replaced by an Asn (Ci-VSP R232N), Ci-VSP turned into a cationic channel with proton selectivity. To test the coupling wit voltage sensor, we have characterized the gating current elicited by the monomeric proton channel with the aim of understanding the voltage-dependent processes that control channel opening. We found that the voltage sensor displacements are more complex than previously thought and consist of numerous well-defined states. However, most of the charge is displaced in a single transition that probably leads to channel opening. Importantly, the fact that gating currents precede the development of proton currents is a direct demonstration that the charges contained in one voltage sensor undergo several conformational changes before proton channel opening.
Fondecyt#1180464 Millennium Initiative P029-022-F



Global fit and kinetic model as a tool to dissect allosteric regulation by auxiliar subunits

Neely Alan [1,2], Contreras Gustavo[2], Savalli Nicoletta[3], Olcese Riccardo[3], Gonzalez-Leon Carlos[1,4], Latorre Ramon[5], Castillo Karen[2]
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(5) Centro Interdiciplinario de Neurociencia

Members of the superfamily of voltage-gated channels are characterized by a tretrameric architecture of four voltage-sensing domain (VSD) surrounding a central pore. The dominant view emerging from studies on the prototypical *Shaker* potassium channel is that upon membrane depolarization, the charge-carrying forth membrane segment of each VSD moves upward and that this movement forces the gate regulating permeation of the central pore into the open state. This strict coupling preclude channel opening in the absence of VSD activation and predict that the probability of being open decreases logarithmically with voltage as it approaches zero with a slope proportional to the number of charges displaced during VSD activation (gating charges). This rule breaks down in other member of the family as Calcium-activated potassium channels (BK) and voltage-dependent calcium channels (CaV) where auxiliary subunits modulate the coupling between charge movement and pore opening. We will describe a global fit strategy combining gating currents, fluorescence signals and ionic currents to extract allosteric constant coupling VSD to the channel´s gate in the presence and absence of different auxiliary subunits. The main findings are that in CaV channel, VSD contribute negligibly to channel opening in the absence of α2δ subunit and in BK channels, we identified an additional step in the path to channel opening that become relevant only when the pore forming subunit of the channel co-exist with the different ß-subunits.

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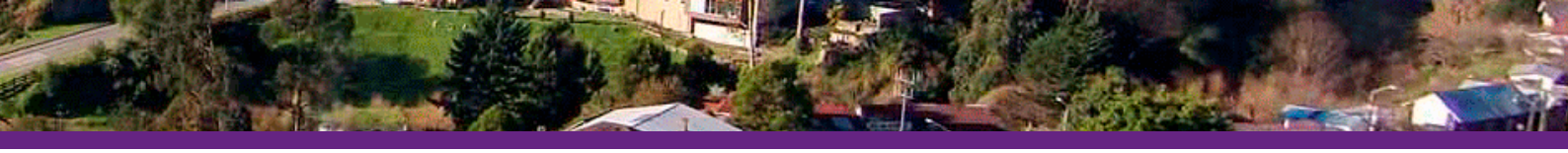

Disease causing mutation that alter hemichannel gating

Garcia Isaac [1,2]
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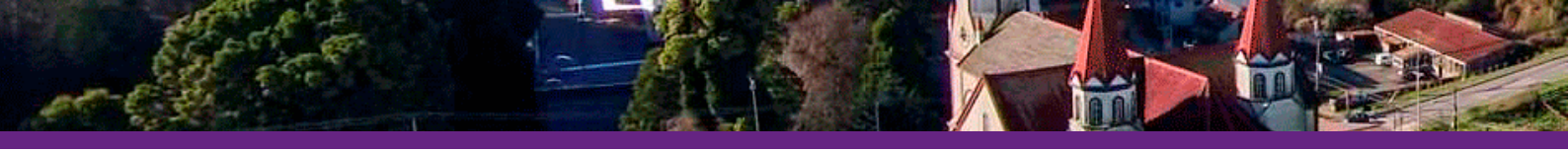
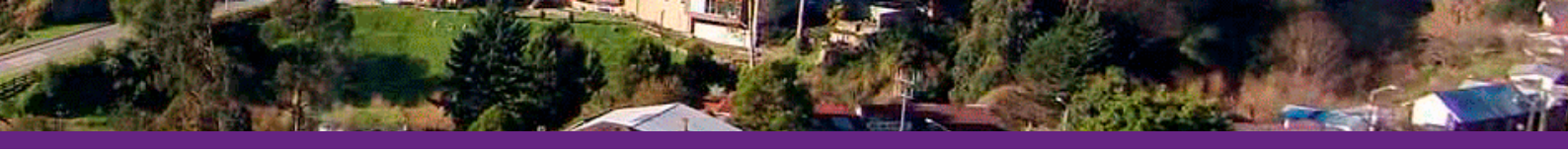
Mutations in connexin 26 (Cx26) hemichannels result in syndromic deafness that affects the cochlea and skin. These mutations lead to gain of function hemichannel phenotypes by unknown molecular mechanisms. We have investigated the biophysical properties of the syndromic mutant, Cx26G12R (G12R). We found that macroscopic hemichannel currents do not saturate upon depolarization and deactivation is faster during hyperpolarization, suggesting that these channels have impaired fast and slow gating. Single channel recordings show large increase in open probability, and transitions to the subconductance state are rare and short-lived, demonstrating an inoperative fast gating mechanism. Molecular dynamics simulations show that R12 favor a interaction R99 in the intracellular loop. Disruption of this interaction recovers the fast and slow voltage-dependent gating mechanisms. These results suggest that the mechanisms of fast and slow gating in connexin hemichannels are coupled and provide a molecular mechanism for the gain-of-function phenotype displayed by the syndromic G12R mutation.



Chemistry at the membrane: an unnatural approach in a natural setting

Sharona Gordon [1]
(1) Physiology & Biophysics, University of Washington

The study of ion channel and transporters is at a technological apex, with high-resolution structural studies using cryoEM joining better-established high-resolution functional studies with patch-clamp electrophysiology. Limitation of these approaches, however, have left a gap in our understanding of membrane protein dynamics, particularly outside the ion-conducting pore. Using amber codon suppression to introduce a fluorescent, noncanonical amino acid along with transition metal ion FRET, we have developed a system to measure short-distance rearrangements within a membrane protein in a native cellular environment.



Exploring key molecular determinants in cold sensing and neuropathic pain

Coordinadora: Margarita Calvo

Human pain channelopathies; Navs and beyond.

Bennett David [1]
(1) Nuffield Department of Clinical Neurosciences, Medical Science Division, University of Oxford

Peripheral neuropathic pain arises as a consequence of injury to sensory neurons; the development of ectopic activity in these neurons is thought to be critical for the induction and maintenance of such pain. Local anaesthetics and anti-epileptic drugs can suppress hyper-excitability however these drugs are complicated by unwanted effects on motor, CNS and cardiac function and alternative more selective treatments to suppress hyper-excitability are therefore required. I will discuss pharmacogenomics as an alternative strategy. We used a glutamate-gated chloride channel (GluCl) modified to be activated by low doses of Ivermectin (but not glutamate) and found that this was highly effective in silencing sensory neurons and reversing neuropathic pain related hypersensitivity. Activation of GluCl expressed in either rodent or human iPSC-derived sensory neurons *in vitro* potently inhibited their response to both electrical and algogenic stimuli. Silencing is achieved both at nerve terminals and the soma and is independent of membrane hyperpolarisation and instead likely mediated by lowering of the membrane resistance. Using intrathecal adeno-associated virus serotype-9 based delivery, GluCl was successfully targeted to mouse sensory neurons *in vivo*, resulting in high level and long lasting expression of GluCl selectively in sensory neurons. This enabled reproducible and reversible modulation of pain related hypersensitivity following nerve injury with no side effects observed. These findings demonstrate the importance of aberrant afferent input in the maintenance of neuropathic pain and the potential for targeted chemogenetic silencing as a new treatment modality in neuropathic pain.

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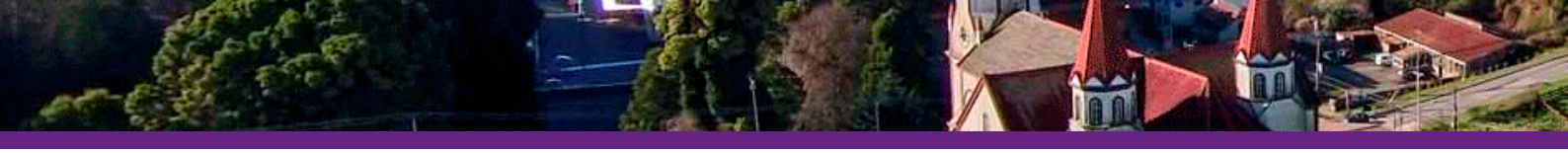
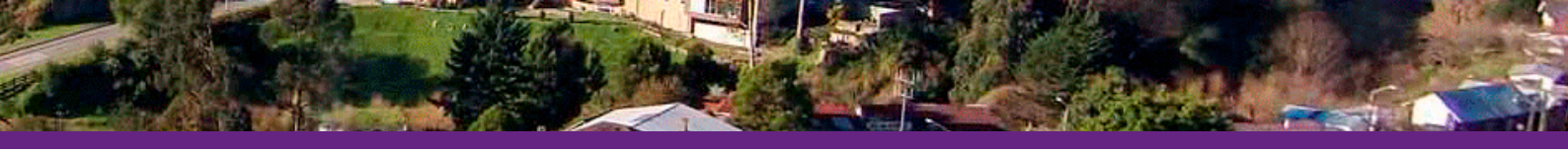


Evolution of the TRPM8 channel as a key cold transductor

Pertusa María [1], Rivera Bastián[1], González Alejandro[1], Ugarte Gonzalo[1], Madrid Rodolfo[1]
(1) Departamento de Biología, Facultad de Química y Biología, Universidad de Santiago de Chile

TRPM8, a calcium-permeable cation channel activated by cold, menthol and voltage, is the main molecular entity responsible for detection of cold temperatures in the somatosensory system. Several molecular determinants involved in TRPM8 responses to chemical agonists have been described; however, the residues or regions that mediate the activation by cold and voltage remain more elusive. In order to identify structural domains involved in TRPM8 sensitivity to temperature, we took advantage of the differences displayed by mouse (mTRPM8) and chicken (cTRPM8). While mTRPM8 displays larger responses to cold than cTRPM8, the avian ortholog shows a higher sensitivity to menthol compared to the mouse channel, in both HEK293 cells and primary somatosensory neurons. Using a combination of calcium imaging and patch clamping, and building multiple functional chimeras between these orthologs, we identified a region encompassing positions 526-556 in the N-terminus, whose replacement by the cTRPM8 homolog sequence potentiated its response to agonists. More importantly, we found that the characteristic cold response of these orthologs is due to non-conserved residues located within the pore loop, suggesting that TRPM8 has evolved by increasing the magnitude of its cold response through changes in this region. Our results reveal that these structural domains are critically involved in cold-sensitivity and functional modulation of TRPM8, and support the idea that the pore domain is a key molecular determinant in temperature responses of this thermo-TRP channel.



Role of the excitability brake potassium current I_{KD} in damage-triggered cold hypersensitivity

Madrid Rodolfo [1,3], González Alejandro[1], Ugarte Gonzalo[1], Restrepo Carlos[1], Herrera Gaspar[2], Piña Ricardo[1], Orio Patricio[2], Pertusa María[1,3]
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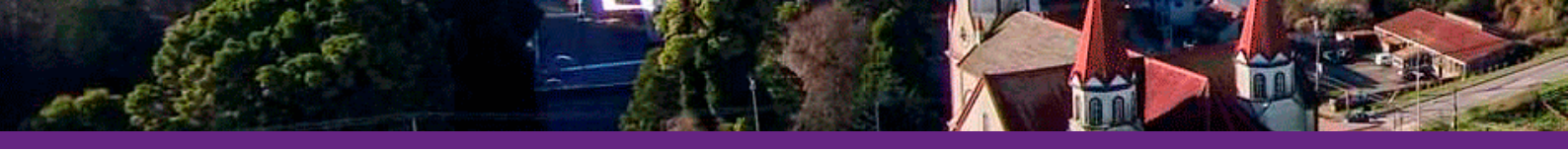
(2) CINV, Instituto de Neurociencia, Universidad de Valparaíso
(3) Millennium Nucleus of Ion Channels-Associated Diseases, (MiNICAD), Universidad de Santiago de Chile

Painful hypersensitivity to innocuous cold, or cold allodynia, is a common symptom of neuropathic and inflammatory pain following peripheral nerve injury. The mechanisms underlying this disabling sensory alteration are not entirely understood. In primary somatosensory neurons, cold-sensitivity under physiological conditions is mainly determined by a functional counterbalance between cold-activated TRPM8 channels and Shaker-like Kv1.1-1.2 channels underlying the excitability brake current I_{KD}. We have recently show that cold allodynia induced by chronic constriction injury (CCI) is related to an increase in the proportion of cold-sensitive neurons (CSNs) in dorsal root ganglia contributing to the sciatic nerve and a decrease in their cold temperature threshold. I_{KD} current density is reduced in high-threshold CSNs from CCI mice compared to sham animals, with no differences in cold-induced TRPM8-dependent current density. The electrophysiological properties and neurochemical profile of CSNs revealed an increase of nociceptive-like phenotype among neurons from CCI animals compared to sham mice. Thus, a reduction in I_{KD} current density shifts the thermal threshold of individual CSNs to higher temperatures and induces cold-sensitivity in former cold-insensitive neurons expressing low levels of TRPM8 current. Taken together, our results suggest that cold allodynia is due to a functional downregulation of I_{KD} in both high-threshold CSNs and in a subpopulation of polymodal nociceptors expressing TRPM8, providing a general molecular and neural mechanism for this sensory alteration.

FONDECYT 1161733 (RM, MP), 1130862 (PO), 11130144 (MP), DICYT 021843PP (MP, RM) and Millennium Nucleus of Ion Channels-Associated Diseases (MiNICAD) (RM, MP).



Kv1 channels behave as an intrinsic compensatory mechanism that reduces neuropathic pain

Gonzalez Luis Martin[1], Diaz Paula[1], Bennett David[2], **Calvo Margarita [1]**
(1) Fisiología, Ciencias Biológicas, Pontificia Universidad Católica de Chile
(2) Nuffield Department of Clinical Neurosciences, Oxford University

Neuropathic pain (NP) following peripheral nerve injury is associated with hyperexcitability in damaged myelinated sensory axons which begins to normalise over time. We investigated the composition and distribution of shaker type potassium channels (Kv1 channels) within the nodal complex of myelinated axons following injury. At the neuroma that forms after damage, expression of Kv1.1 and 1.2 (normally localised to the juxtaparanode) was markedly decreased. In contrast Kv1.4 and 1.6, which were hardly detectable in the naïve state, showed increased expression within juxtaparanodes and paranodes following injury, both in the rat and in humans. Within the dorsal root (a site remote from injury) we also noted a redistribution of Kv1 channels towards the paranode. Blockade of Kv1 channels with αDTX after injury reinstated hyperexcitability of A-fibre axons and enhanced mechanosensitivity. Changes in the molecular composition and distribution of axonal Kv1 channels, therefore represents a protective mechanism to suppress the hyperexcitability of myelinated sensory axons that follows nerve injury.

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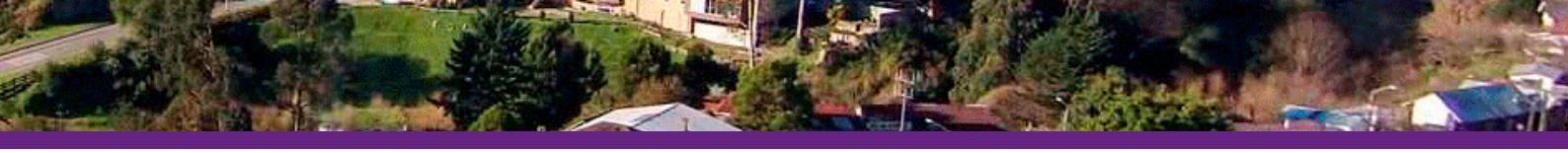

Recent progress on the mechanisms of neurological dysfunction in epilepsy

Coordinador: Juan Carlos Saez

Alvarez Alejandra [1], Vargas LM1[2], Chandia A1 A1[3], Lara M4 M4[4], Jimenez P1[5], Leal N1[6], Gutierrez D1[5], Carvajal F2[7], Zanlungo S3[8], Cerpa W2[9], Rojas P4,[10]
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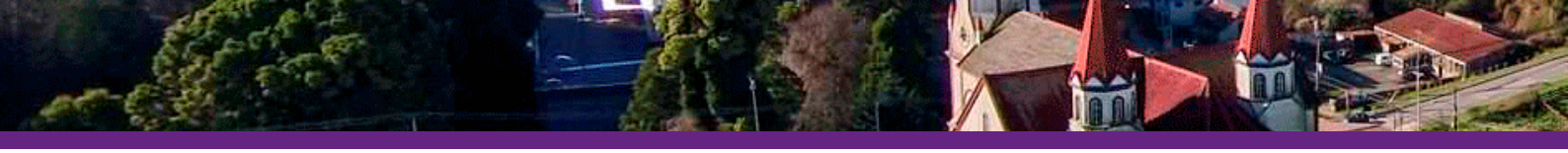
(10) 4Department of Biology , University of Santiago, Chile. [1]Cell Signaling Laboratory, Centro UC de Envejecimiento y Regeneración (CARE), [2]Pathology and Neuronal Function Laboratory, Department of Cellular and Molecular Biology, Biological Sciences Faculty and [3]Department of Gastroenterology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile.[4]Department of Biology University of Santiago, Chile.

Epilepsy is a highly prevalent neurological disorder characterized by epileptic seizures, which interrupt the normal functions of the brain. During temporal lobe epilepsy (TLE) it may be seen neuronal death in the hippocampus, gliosis, aberrant axonal growth and significant decrease in the density of dendritic spines. However the mechanisms that drive the chronic progression of TLE remains elusive. Previously, we have reported that c-Abl signaling pathway participates in the neuronal apoptosis and synaptotoxicity in Alzheimer disease. The c-Abl activation has been recently reported in patients with TLE.

Here we show that c-Abl is activated and mediates the neuronal death in excitotoxicity models in vitro. Moreover c-Abl in activated in TLE mice model and its inhibition using Imatinib or GNF-2 has a significant anticonvulsant effect in TLE mice model. Particularly, in TLE mice model the Y1472 GluN2B phosphorylation (phospho-NR2B) membrane levels are decreased, however when the mice were treated with Imatinib or GNF-2, phospho-NR2B membrane levels were recovered. Moreover, c-Abl-knockout mice induced to TLE model showed decreases in the loss of dendritic spine, apoptosis an important anticonvulsant effect, indicating an important role of c-Abl in the epilepsy damage. Our results reveal a critical regulatory mechanism of c-Abl kinase over the NR2B surface levels subunit, which is related to the prevention of the damage observed in epilepsy.

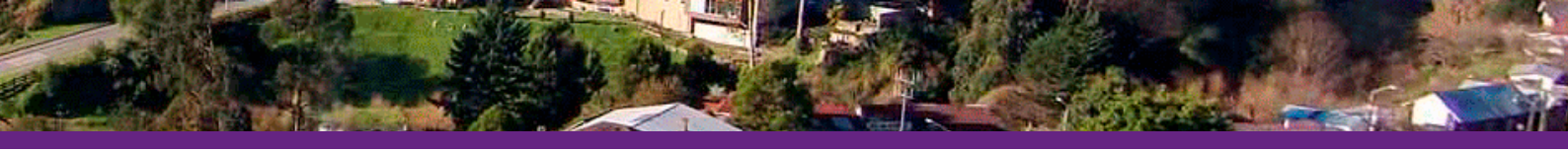
Acknowledgements: FONDECYT 1161065, CARE-Chile-UC AFB170005, FONDEF D10E1077.



Spatial pattern separation deficits in a pharmacological rodent model of temporal lobe epilepsy

Fuentealba, P.
Laboratory of Neural Circuits, Centro de Neurociencia UC, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile.

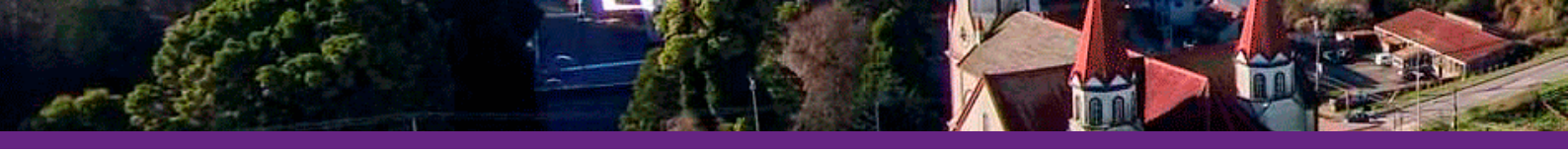
Temporal lobe epilepsy is a common form of focal epilepsy characterized by a latent period followed by the emergence of recurrent seizures. The mechanisms underlying epileptogenesis have been largely studied, and one of the most characterised pharmacological models is the local injection of kainate. One of the temporal areas most affected by epilepsy is the dentate gyrus, which is essential for the implementation of pattern separation, a cognitive function necessary for the formation of discernible memories. Pattern separation heavily relies on the integrity of neurogenesis. Thus, we anticipated that spatial pattern separation would be compromised in epilepsy. To test this, we used the pharmacological rodent model of kainite injections in the amygdala to generate generalized seizures. We found that injected animals performed poorly in behavioural tests involving pattern separation in a degree proportional to the magnitude of epileptiform activity observed in the hippocampus. Importantly, seizures did not take place during behavioural testing, so they did not exert a direct effect on animal behaviour. Instead, chronic damage produced to neurogenesis is more likely to explain our results. This is consistent with results showing that detrimental effects of epilepsy on dentate gyrus neurogenesis not mediated by direct action of electrographic seizures.



Targeting the piriform cortex as therapeutic treatment for epilepsy

Lau Geoffrey [1]
(1) Department of Biomedical Sciences, City University of Hong Kong

Epilepsy is a neurological disorder that affects the global population and is characterized by recurrent seizures. Temporal lobe epilepsy (TLE) is the most common type of seizure which neural activity can spread across to other brain regions. TLE is generally thought to involve structures in the limbic system such as hippocampus, amygdala and the piriform cortex. The anterior piriform cortex (APC) is the largest primary cortical area receiving direct input from the olfactory bulb and is critical for odor learning and recognition. The APC is epileptogenic due to its recurrent connections with the endopiriform nucleus, which has one of the lowest seizure thresholds in the brain. To investigate the role of APC in epileptogenesis, we manipulated neuronal activity in APC using viruses that express DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) via stereotaxic injection. We focused on manipulating excitatory and inhibitory balance in the APC by controlling the activity of parvalbumin (PV) interneurons via chemogenetic technology. Our preliminary results revealed that manipulation of activity in APC can be an effective method for treating epileptic seizures that are otherwise intractable.



Role of glial connexin- and pannexin- based channels in epilepsy

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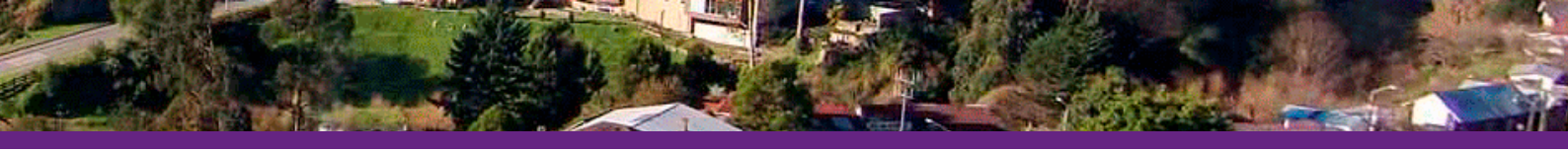
Epilepsy, the most common neurological disorder, is defined by the presence of spontaneous and recurrent seizures. The etiopathogenesis is diverse but a common factor appears to be the inflammatory processes. Notably, all current treatments for epilepsy are directed to molecular targets located in neurons but not in glial cells. The latter express pannexin channels and connexin hemichannels (Cx HCs). The putative role of pannexin1 channels has been documented by others. In this work, we propose the critical role of glial connexin hemichannels (Cx HCs) in controlling the increase in neuronal activity. To study this possibility, male adult mice were treated acutely or chronically with an epileptogenic agent; pentilentetrazol (PTZ), a GABAA receptor antagonist. Convulsions were evident after ~7 min of PTZ administration,followed by several hours of low motor activity and sporadic muscle spasms and ~70% survival. A potent and selective Cx HC blocker D4, identified by virtual screening using the NCI database was used to test our hypothesis. In mice pretreated with D4, the PTZ-induced epileptic seizures were avoided in most cases, when this was not the case, the frequency of seizures decreased and recovery was faster, behaving as control animals with 100% survival. Also, D4 completely inhibited the PTZ –induced glial HCs activity. These results strongly suggest glial Cx HCs as potential therapeutic targets for epileptic conditions that involve a neuroinflammatory process.

Acknowledgements: Fondo Nacional de Desarrollo Científico y Tecnológico (FONDECYT) grant No 1150291 (to JCS), and P09-022-F from Iniciativa Científica Milenio (ICM)-ECONOMIA, Chile (to JCS).



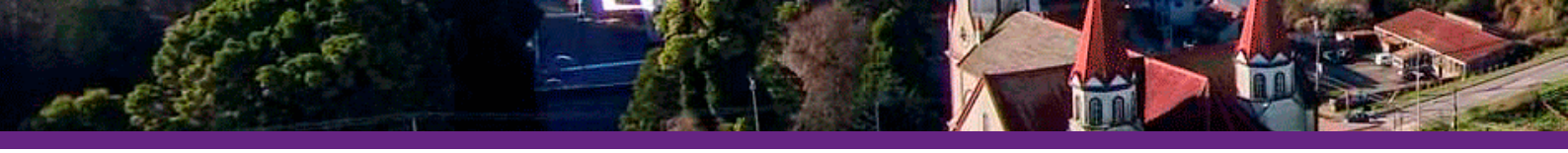
Glial cells in pathophysiology: from the central nervous system and beyond

Coordinadores: David Andrade – Fernando Ortiz

"Glial cells in pathophysiology: from the central nervous system and beyond"

Ortiz Fernando C [1]
(1) Mechanisms of Myelin Formation and Repair Lab, Instituto de Ciencias Biomedicas, Facultad de Ciencias de la Salud, Universidad Autónoma de Chile

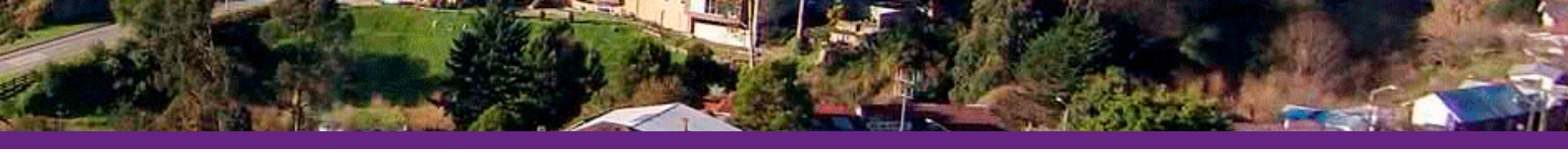
The relevance of glial cells in the induction, maintenance, and progression of disease conditions has received an increasing focused attention in the past few years. This symposium aims to discuss recent evidence on the contribution of glial cells to central nervous system pathophysiology as well as its underlying mechanisms. In particular, the discussion will be articulated around the role of astrocyte activity on epilepsy and glial cell contribution to oxygen sensing and cardiovascular diseases. Finally, a common cellular mechanism of glial pathogenesis will be discussed. The group of speakers is formed by two international leader scientists in the field of neuroscience along with two young Chilean researchers. We will cover basic and translational research allowing the audience for understanding cellular and molecular mechanisms behind both glial cell dysfunction and neuron-to-glial communication impairment. We expect that this symposium will allow delineating new pathways involved in altered glial cell function and neuron- to-glia interaction.



Astrocyte gliotransmission increases excitatory synaptic transmission in the epileptic hippocampus

Audinat Etienne [1]
(1) L´Université Paris Descartes

Epilepsy is characterized by unpredictable recurrent seizures resulting from abnormal neuronal excitability. Increasing evidence indicates that aberrant astrocyte signaling to neurons plays an important role in driving the network hyperexcitability, but the underlying mechanism that alters glial signaling in epilepsy remains unknown. Increase in glutamate release by astrocytes participates in the onset and progression of seizures. Epileptic seizures are also accompanied by increase of tumor necrosis factor alpha (TNFα), a cytokine involved in the regulation of astrocyte glutamate release. We have therefore tested whether TNFα controls abnormal astrocyte glutamate signaling in epilepsy. Combining Ca2+ imaging, optogenetics and electrophysiology, we report that TNFα triggers a Ca2+-dependent glutamate release from astrocytes that boosts excitatory synaptic activity in the hippocampus through a mechanism involving autocrine activation of P2Y1 receptors by astrocyte-derived ATP/ADP. In a mouse model of temporal lobe epilepsy such TNFα-driven astrocytic purinergic signaling is permanently active, promotes glial glutamate release and drives abnormal synaptic activity in the hippocampus. Blocking this pathway by inhibiting P2Y1 receptors restores normal excitatory synaptic activity in the inflamed hippocampus. Our findings indicate that targeting the coupling of TNFα with astrocyte purinergic signaling may be a therapeutic strategy for reducing glial glutamate release and normalizing synaptic activity in epilepsy.



Control of brainstem respiratory circuit activity by astrocytes

Gourine Alexander [1]
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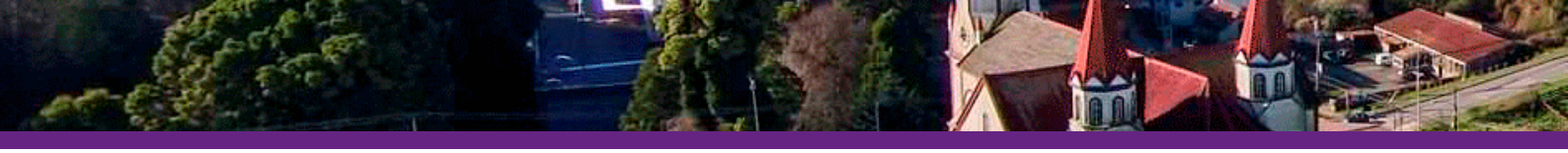
Astrocytes are implicated in modulation of neuronal excitability and synaptic function, but it remains unknown if these glial cells can directly control activities of motor circuits to influence complex behaviors in vivo. We focused on the vital respiratory rhythm-generating circuits of the preBötzinger complex (preBötC) and determined how compromised function of local astrocytes affects breathing in conscious experimental animals (rats). Our data indicate that astrocytes modulate the activity of CNS circuits generating the respiratory rhythm, critically contribute to adaptive respiratory responses in conditions of increased metabolic demand and determine the exercise capacity.



Hemichannels in neuron-glia crosstalk

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The brain performs exceptionally complex and dynamic tasks based on the coordinated interaction of neurons and astrocytes. The latter have emerged as crucial players in the regulation of synaptic transmission and neuronal function. Indeed, these cells express virtually all known types of neurotransmitter receptors, allowing them to detect neuronal activity and respond to it through the release of bioactive molecules known as "gliotransmitters". Several mechanisms of gliotransmitter release have been documented, and one of them involves the opening of two types of channels: hemichannels and panexons. These channels are composed of the oligomerization of six subunits of connexins or pannexins, respectively. In normal astrocytes, both hemichannels and panexons have a low activity but enough to ensure the release of relevant amounts of gliotransmitters to the extracellular medium, including ATP, glutamate, adenosine and glutathione. Here we show that two endogenous cannabinoids (CBs): methandamide and 2-arachidonylglycerol, as well as a synthetic CB: WIN, prevent the activation of astrocytes, as well such as the hemichannel-mediated release of gliotransmitters induced by the β-amyloid peptide. On the other hand, we also show several findings indicating that adolescent rats exposed to ethanol exhibit an increased opening of hemichannels and panexons in hippocampal astrocytes, as well as alterations in astroglial arborization and elevated levels of pro-inflammatory cytokines. The persistent opening of hemichannels and panexons could be detrimental to normal communication between glial cells and neurons. The specific inhibition of these channels could prevent astrocyte and neuronal dysfunction and the subsequent reduction in cell survival.

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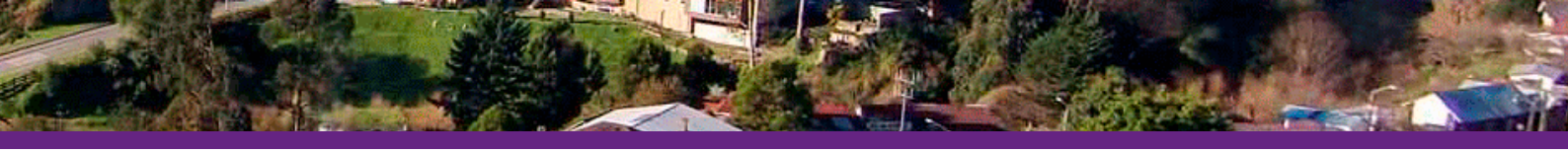

Glial cells in cardiovascular disease: a new player in pathophysiology?

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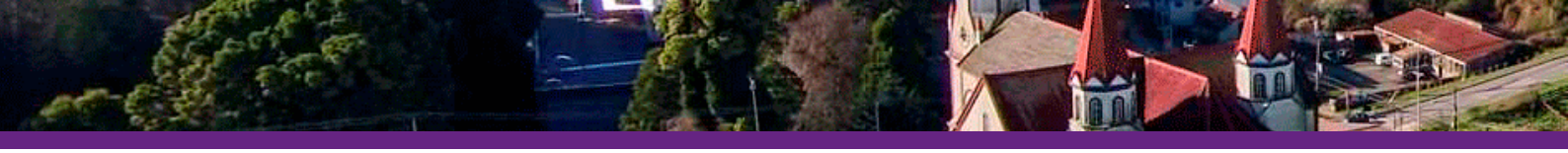
(1) Physiology, Pontificia Universidad Católica dStee Chile

Major hallmark in heart failure (HF) include breathing pattern irregularities. The precise mechanism underpinning oscillatory breathing patterns in HF are not known. Recent evidence suggests that astrocyte-dependent purinergic signaling within the RTN may contribute to regulate breathing. Therefore, we aimed to determine: i) if the RTN is responsible for triggering oscillatory breathing, ii) if purinergic signaling is altered in the RTN and, iii) if RTN astrocytes are involved in breathing alterations. Repetitive photoexcitation of pLenti-PRSX8-ChR2-YFP-expressing RTN neurons was performed to assess the contribution of RTN to resting breathing oscillations. RTN micropunches were obtained to determine P2X7R expression and ATP levels. P2X7R-/-mice were used to study breathing stability. In addition, AAV-GFAP-P2X7R-GFPwas stereotaxically injected in the RTN. Activation of ChR2-expressing RTN neurons leads to increases in breathing variability. HF rats displaydecreased ATP bioavailability and reduced P2X7Rexpression in the RTN. Interestingly, P2X7Rdeletion in mice recapitulates the altered breathing patterns observed in HF. Accordingly, P2X7R overexpression selectively targeted into astrocytes within the RTN in HF rats normalized breathing disorders and oscillations. In summary, our results show that repetitive RTN chemoreceptor neurons activation is capable of driving ventilatory disordersin normal rats. Also, our results show that P2X7R signaling is required for breathing regularity in healthy conditions and its lack may be related to decrease of astrocyte-mediated ATP signaling into RTN from HF rats.

Supported by FONDECYT 1180172.



Stress, Resillience and Neuropsychiatric Disorders

Coordinador: Alexies Dagnino

Novel insights into the circuitry and mechanisms associated to stress, anxiety and depression.

Stehberg Jimmy [1]
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We shall review new insights into the circuitry and mechanisms associated to stress, anxiety and depression. First, despite several studies in human imaging suggesting that the insula is involved in anxiety and its overactivation is a hallmark of anxiety-related disorders, no attempt has been made to date to elucidate the role of the insula in anxiety and unveil its position within the accepted brain circuitry subjacent to anxiety. Here we show in rodents using *in vivo* pharmacology that the insula is critical for anxiety, it is located downstream from the amygdala within the brain circuitry for anxiety and is pivotal in mediating the effects in anxiety of both main stress hormones, adrenaline and glucocorticoids. Secondly, although much is known about the effects of chronic stress in hippocampal neurons, few studies have reported on the role of astrocytes in chronic stress and depression. Here we show that chronic stress induces increased release of gliotransmitters from astrocytes in the ventral hippocampus, including glutamate, ATP and possibly D-serine. The pharmacological blockade of astroglial release of gliotransmitters via connexin 43 hemichannels in the hippocampus induces a decrease in NMDAR transmission and antidepressants effects, both of which can be prevented by addition of glutamate and D-serine, suggesting that enhanced astroglial release of gliotransmitters contributes to the pathophysiology of depression. Based on this novel mechanism, we have developed antidepressant drug candidates that target astroglial release of gliotransmitters glutamate and D-serine and can have fast NMDAR-dependent antidepressant effects when administered to rodents systemically.

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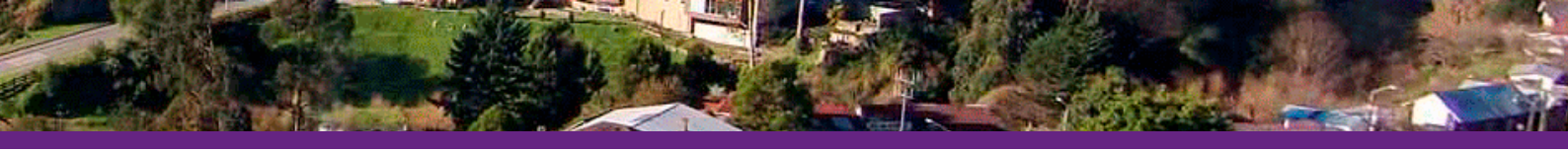
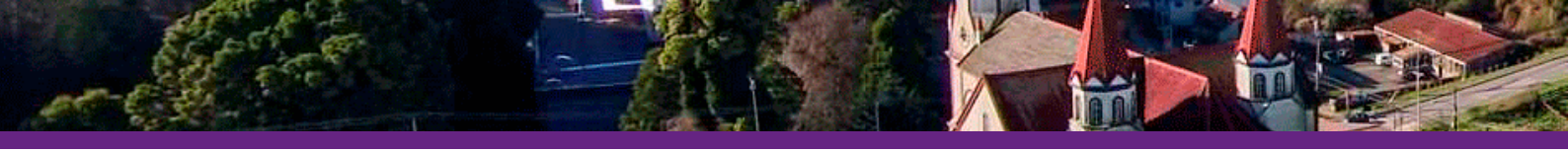


Brain oscillations in stress and resilience.

Dagnino Alexies [1]
(1) Laboratory of Stress Neurobiology, Faculty of Sciences, Universidad de Valparaíso

Deficit in social behavior and persistence of fear memory are common in several stress-related neuropsychiatric disorders. The nucleus accumbens (NAc) and basolateral amygdala (BLA) are brain areas involved in social behavior and fear memory, respectively. Speculation about a possible role of neural oscillations on susceptibility and resilience to stress has emerged. Male *Sprague-Dawley* rats were subjected to social defeat stress and then a microelectrode array was implanted in the NAc. LFP activity was acquired using a wireless recording system in two conditions; non-social (open field), and social—where the rats interacted freely and continuously with a conspecific in an ecological manner. We found that gamma-band power in the NAc was higher in those rats that were resilient to stress during social interaction. Surprisingly, gamma oscillations in those rats that were susceptible to stress did not vary between social and non-social conditions. These findings suggest that gamma oscillations in the NAc may play a key role in the susceptibility to stress. On the other hand, we evaluated whether chronic stress affects the neuronal activity in BLA during recall of fear memory. Rats were trained in a fear conditioning protocol and then were implanted in BLA. We found that power of 4-6 Hz oscillations from BLA was increased during recall of fear memory. Seven days after recall, 4-6 Hz oscillations decreased in control animals, while they remained enhanced in the stressed rats. These results suggest that enhancing of 4-6 Hz oscillations could be related to persistence of fear memory in stressed animals.

This work was funded by Anillo de Ciencia y Tecnología Grant Nº ACT1403 and FONDECYT Grant N° 1141276 to Alexies Dagnino-Subiabre. Labsite: www.stress.cl



Cannabinoids, stress and Antidepressant Drugs: Is there a Link?

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(1) Pharmacology, Ribeirão Preto Medical School, University of São Paulo

Although several studies and clinical reports have demonstrated the efficacy of antidepressants, such as escitalopram, their clinical application is often associated with delayed therapeutic response, important side effects and low rates of response due treatment-resistance. Similar to clinically used antidepressants, cannabinoids can also regulate anxiety and depressive symptoms. Although the mechanisms of these effects are not completely understood, recent evidence suggests that changes in endocannabinoid system could be involved in some actions of antidepressants. Chronic antidepressant treatment modifies the expression of CB1 receptors and endocannabinoid (EC) content in brain regions related to mood and anxiety control. Moreover, both antidepressant and cannabinoids activate mitogen-activated protein (MAP) kinase and phosphoinositide 3-kinase(PI3-K)/Akt or PKB signalling, intracellular pathways that regulate cell proliferation and neural cell survival. Facilitation of hippocampal neurogenesis is proposed as a common effect of chronic antidepressant treatment. Genetic or pharmacological manipulations of cannabinoid receptors (CB1 and CB2) or enzymes responsible for endocannabinoid-metabolism have also been shown to control proliferation and neurogenesis in the hippocampus. Preliminary results from our groups suggest that cannabinoids participate in the behavioral and neuroplastic events induced by chronic treatment with escitalopram. Moreover, the combination of sub-effective doses of antidepressant and cannabinoids reduces the latency for the behavioral effects produced by the former. We believe that considering the widespread brain distribution of the EC system, a better understanding of this possible interaction could contribute to the development of therapeutic alternatives to mood and anxiety disorders.

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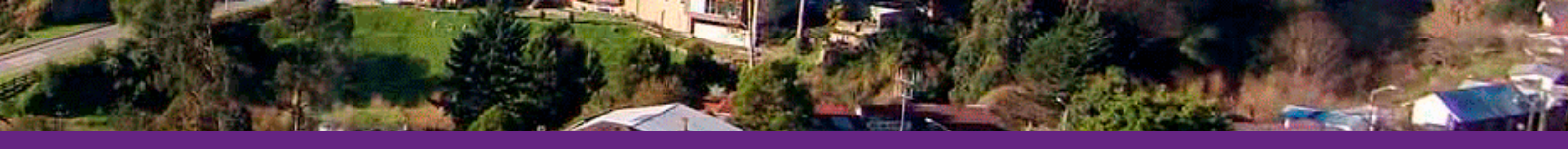

Human cortical responses to stress

El-Deredy Wael[1], Weinstein Alejandro[2], Gallagher David [2]
(1) Centro de Investigación y Desarrollo en Ingeniería en Salud, Engineering, Universidad de Valparaíso
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We propose a common framework for cognitive/mental stress (mental arithmetic, cognitive load, time pressure) and environmental stress (load noise, extreme heat/cold, geographical altitude), based on Hockey 1997 [and following on from Kahneman's effort theory, 1973] whereby increased physiological activity [e.g. cortisol or adrenaline], up to a point, correlates with maintenance of cognitive or motor performance under stress. In Kahneman´s (1973) model, regulation of goals and actions required the operation of a compensatory control mechanism, which allocates resources dynamically.

Such compensatory control mechanism is required not only for maintaining tasks under disturbance from stressors, but for preventing the loss of task goals under all circumstance, including increased processing demands. We review the relationship between the HPA axis and brain imagining studies, with a particular focus on cortical measurements using EEG and fNIRS. So far the most consistent marker for elevated cortisol is increased resting frontal EEG asymmetry in the alpha band, which in turn has been linked to a reduced approach motivation and emotional dysregulation. We argue that the challenge for research on the relationship between stress, HPA axis and Brain function is in identifying the determinants of optimal physiological responses that preserve performance under disturbance from stressors, and the point at which such responses become maladaptive.

References
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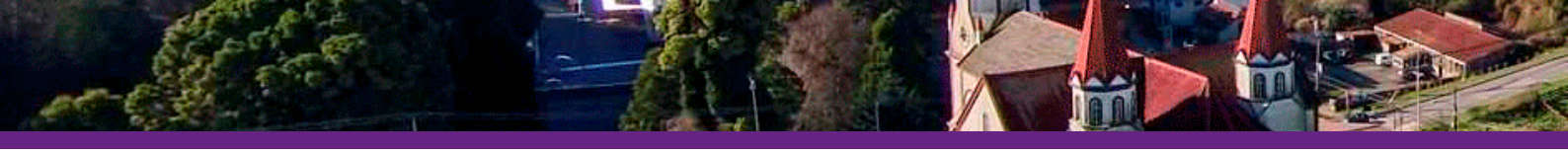

SIMPOSIO
JÓVENES NEUROCIENTÍFICOS

Coordinador: Oliver Schmachtenberg

Episodic stimulation of central chemoreceptors neurons elicits cardiorespiratory plasticity in heart failure: uncovering a new phenomenon in the progression of the disease

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Enhanced central chemoreflex gain is observed in models of heart failure (HF) and is closely associated with cardiorespiratory disorders. Ventilatory long-term facilitation (vLTF), a form of neuronal plasticity, may play a role in the induction of breathing disturbances in several pathological conditions; However, this neurophysiological mechanism has not been previously explored in HF. We hypothesized that episodic hypercanic stimulation (EHS) of chemoreceptor neurons from the retrotrapezoid nucleus (RTN), a major source of chemoreflex regulation in the brainstem, elicits vLTF and triggers cardiorespiratory disorders in HF rats. HF was induced by volume overload in male Sprague-Dawley rats. Whole body plethysmography was used to study breathing patterns. A brief EHS paradigm was used to elicit vLTF (10 cycles of FiCO27%, 5min). Cardiac autonomic function was assessed by heart rate variability analysis. RTN neurons were selectively ablated by stereotaxic injection of saporin toxin conjugated to substance P in the RTN (SSP-SAP 0.6 ng/30nL). 90 minutes post-EHS, ventilatory long-term depression was observed in control animals, which was not observed in HF animals (ΔVE -5.5±2.1 vs. 1.2±1.3 mL/min, respectively). Furthermore, EHS resulted in autonomic imbalance, cardiorespiratory coupling, and ventilatory disturbances in HF. The effects of EHS in HF were markedly attenuated by SSP-SAP treatment. Importantly, EHS-induced cardiorespiratory disturbances were related to the entrainment of the respiratory and sympathetic activity in HF animals (167.5 ± 30.5 vs. 85.4 ± 11.3% coherence, respectively). Our results show that in HF rats, EHS triggers vLTF and elicits long-term cardiorespiratory abnormalities, which are largely dependent on RTN chemoreceptor neurons.

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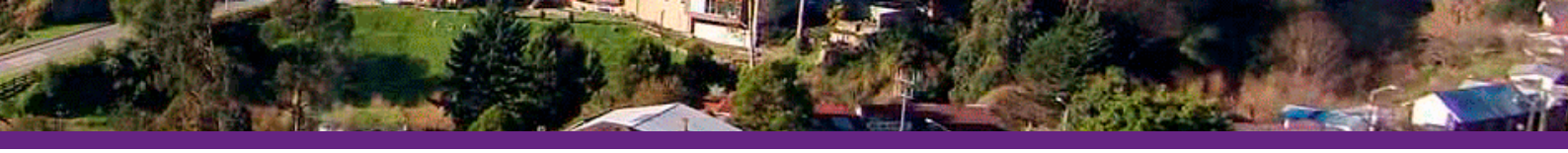

Epigenetic regulation of the RhoA pathway by the histone methyl-transferase G9a promotes neuronal development

Wilson Carlos [1], Giono Luciana[2], Rozés Victoria[1], Fiszbein Ana[2], Kornblihtt Alberto[2], Cáceres Alfredo[1]
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(2) Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE UBA -CONICET), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires

Neurons are polarized cells characterized by both the axonal and somato-dendritic compartments. Mechanisms controlling polarization have been studied, but its genetic regulation has remained largely unexplored. In this regard, epigenetics is the most global mechanism regulating gene expression, based on histone and DNA modifications that remodel chromatin conformation. In neurons, REST is an epigenetic factor capable of inhibiting gene expression by recruitment of several enzymes, including the histone methyl-transferase G9a. Sequentially, G9a methylates the Lys9 of histone 3, a code for gene repression. However, little is known about its contribution to neuronal development. Using primary cultured neurons and in utero-electroporated mouse brains, we now show that G9a suppression impairs neuronal polarization by halting axonal development, an event mediated by a microtubule stability-dependent mechanism. After bioinformatics and molecular biology approaches, we detected that REST/G9a targets the RhoA signaling pathway, which is critical for both microtubule dynamics and neuronal development. Axonal growth inhibition after G9a suppression was reversed by Y-27632 treatment, an inhibitor of the RhoA-effector ROCK. Moreover, the loss of function of G9a increased both RhoA activity and transcription of RhoA activators (GEFs), suggesting that REST/G9a targets this pathway during development. In summary, our data propose an epigenetic control of the RhoA pathway with direct effects on neuronal development. Further research will be required to describe the spatio-temporal regulation of this machinery and its impact on neuronal physiology in health and disease.

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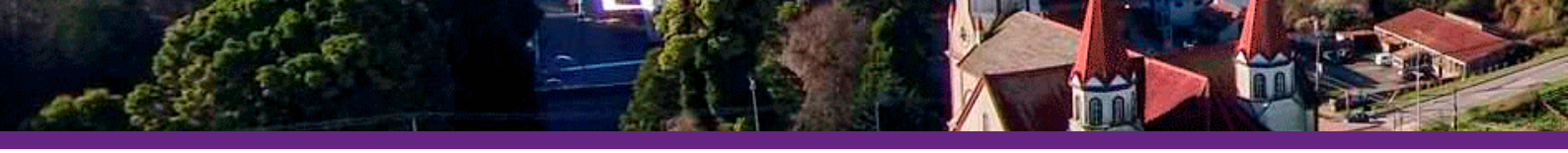

Decrease in central chemosensitivity after perinatal fluoxetine exposure is associated with changes in serotonin receptors contribution

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Breathing is a vital behavior, generated by the brainstem and modulated by several chemosensory nuclei. A main chemosensory nucleus, the raphe nucleus (RN), contains serotonergic neurons that project into the respiratory neural network. Besides, serotonin regulate the development of neural circuits. Selective serotonin reuptake inhibitors (SSRI), such as fluoxetine, are often used during pregnancy. However, the effects of chronic SSRIs exposure during perinatal stages on breathing and its modulation by central chemoreceptors in the offspring are unknown. Here, *we* report the first evidence that fluoxetine exposure during perinatal period decreases the central chemoreception in mice. Fluoxetine (7mg/kg/day s.c.) was administered to the dams from gestational day 5 to postnatal (P) day 12. We found perinatal exposure to fluoxetine reduced: the ventilatory responses to hypercapnia in offspring from P8 up to adulthood, number of c-Fos positive neurons in RN. As also, a reduction of the respiratory responses to hypercapnia recorded from brainstem slices (BS) at P8 - P20. By contrast, acute administration of fluoxetine (500 ng/mL) unmodified the respiratory responses to acidosis/alkalosis in BS suggesting a mechanisms different to direct activation of 5HT receptors. In fluoxetine-exposed mice, concentration-response curves on BS by local administration of the 5HT1A receptor agonist 8-OH-DPAT, reduced the maximal respiratory response and the 5HT2A/2C receptor agonists, DOI and NBOH-2C-CN, increased it. Our results reveal that fluoxetine chronic exposure decreased central chemoreception associated to changes in the serotonin receptors responsiveness. These results support the necessity to further investigate the potential risk/benefits of using SSRI during pregnancy.

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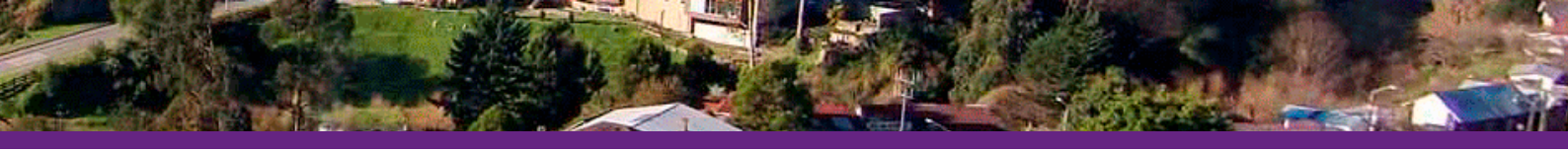

D-serine is a mediator in the central chemosensory control of breathing

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Central chemoreception is essential for adjusting breathing to physiological demands, and for maintaining CO2 and pH homeostasis. While CO2 induce the adaptive increases in breathing through the release of ATP from astrocytes on ventral surface of the medulla oblongata and the activation of chemoreceptor neurons in the retrotrapezoid nuclei, the astrocytes-ATP-mediate mechanism is not imitated in caudal chemosensitivity nucleus. How astrocyte also release D-serine, an agonist for the glycine-binding site of the NMDA receptor (NMDAR), and NMDAR antagonism reduces the CO2-induced hyperventilation by unknown mechanisms, we evaluate the role of D-serine as a mediator of central chemosensitivity. We show that astrocytes in the mouse caudal medullary brainstem can synthesize, store, and release D-serine in response to elevated CO2 levels. By other site, the application of D-serine to brainstem slices preparations (1-100 μM in bath) and the systemic (single intraperitoneal, 250 mg/kg) and raphe nucleus (stereotaxic injection, 30-300 μM) D-serine administration to unrestrained and awake mice increases the respiratory frequency. Interestingly, D-serine is mediating the central chemoreception since the inhibition of Dserine synthesis (with phenazine -ethosulphate or -methosulphate), or the enzymatic degradation of D-serine (with D-amino acid oxidase), or the sodium fluoroacetate-induced impairment of astrocyte functions decrease the basal respiratory frequency and the CO2induced respiratory response in vivo and in vitro. Our results confirm the existence of astrocytic release of D-serine induced by hypercapnia mediates the respiratory response in caudal medullary chemosensory nuclei, improving our knowledge about the glutamatergic contribution to central chemoreception.

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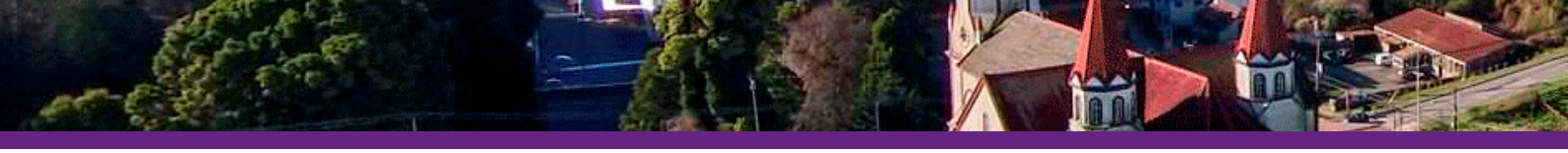

SIMPOSIOS
SOCIEDAD DE BIOLOGÍA DE CHILE

Molecular Biology of the Neuron. Local versus long-distance signaling

Coordinadora: Francisca Bronfman

The actin-binding protein drebrin controls resistance to oxidation stress in neurons

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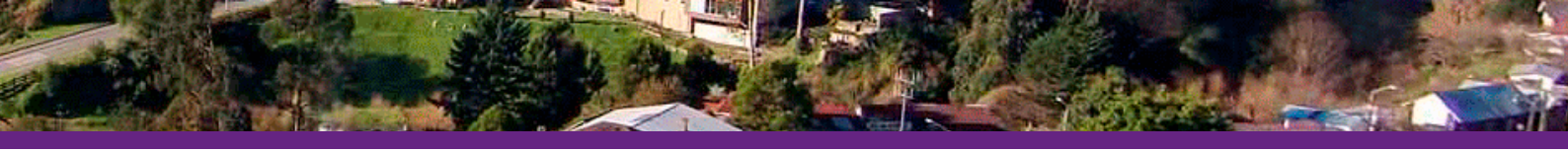
Drebrin (DBN) regulates cytoskeletal functions during neurite outgrowth, dendritic spine development and synapse transmission, and is thought to contribute to structural and functional synaptic changes occurring during aging and Alzheimer's disease. We have identified that DBN is able to coordinates stress signalling with cytoskeletal dynamics, via a mechanism that is dependent on the kinase ataxia-telangiectasia mutated (ATM). An excess of reactive oxygen species (ROS) stimulates ATM-dependent phosphorylation of DBN at serine-647, which enhances protein stability and accounts for improved stress resilience in dendritic spines. Our data point towards a master regulatory function of ATM-DBN in integrating cytosolic stress-induced signalling with the dynamics of actin remodelling to provide protection from ROS-triggered synapse dysfunction. We hypothesize that DBN protein abundance governs actin filament stability to contribute to the consequences of oxidative stress in physiological and pathological conditions.



Neuronal polarity: when cytoskeleton meets membrane dynamics

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(2) Geroscience Center for Brain Health and Metabolism (GERO), Santiago, Chile
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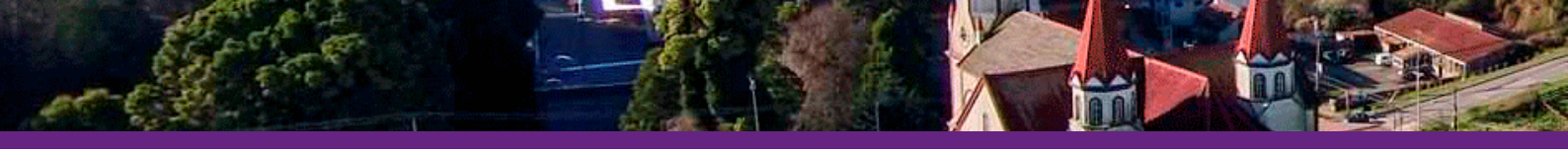
Neurons are highly polarised cells that contain two compartments that differ in their molecular composition and functions, the axon and dendrites. The acquisition of polarity in neurons is regulated by several cellular mechanisms that include membrane and cytoskeleton dynamics amongst others. Both microtubules and actin microfilaments are involved in the polarised distribution of organelles and membrane vesicles. Noteworthy, membrane derived components also can regulate locally the dynamics of cytoskeleton.
In this presentation we will present evidenced showing that different vesicles associated to small GTPases from the Rab family control axon and dendrite morphology. In addition we will discuss how subsets of these vesicles can locally regulate the activity of proteins that control actin dynamics. These results show that membrane and cytoskeleton dynamics are intertwined processes that need to be concertedly regulated to define neuronal shape.

Supported by FONDAP grant 15150012 and Fondecyt 1180419



Role of signaling endosomes and long-distance signaling in BDNF-mediated dendritic arborization

Moya-Alvarado Guillermo[1], Stuardo Nicolás[1], Gonzalez Andrés[1], Lezana Juan Pablo[1], **Bronfman Francisca C [1]**
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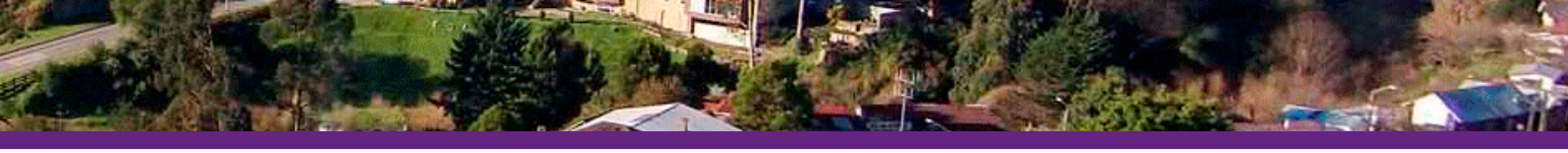
Neuronal morphology is regulated by several molecular and cellular processes including cytoskeletal rearrangement, membrane trafficking, signaling pathways and activation of specific transcription factors. How extracellular clues coordinated and integrate all these processes is not well understood. Brain Derived Neurotrophic Factor (BDNF) is broadly express in different circuits of the central nervous system (CNS) and binds its receptorTrkB triggering different signalling pathways including ERK1/2, PLC-gamma and PI3K-mTORtoinducedendritic growth. BDNF and its receptor TrkB are key regulators of neuronal morphology in central neurons acting locally or through long-distance signaling. Long-distance signaling is regulated by signalling endosomes, an endocytic organelle that transmit trophic signals from axons to cell bodies to regulate transcription using the microtubule-base motor dynein. We will discuss our resent results as how BDNF integrate different cellular processes to induce dendritic branching from the soma or axons, including the role of different signaling pathways, RabGTPases and transcription factors.

Basal CONICYT AFB 170005 (CARE UC) and Fondecyt 11201146



Take the long way home: axonal transport, organelle dynamics and neurodegenerative diseases

Gibbs KL[1], Rhymes ER[1], Fellows AD[1], Sleigh JN[1], Tosolini AP[1], **Schiavo Giampietro [1]**
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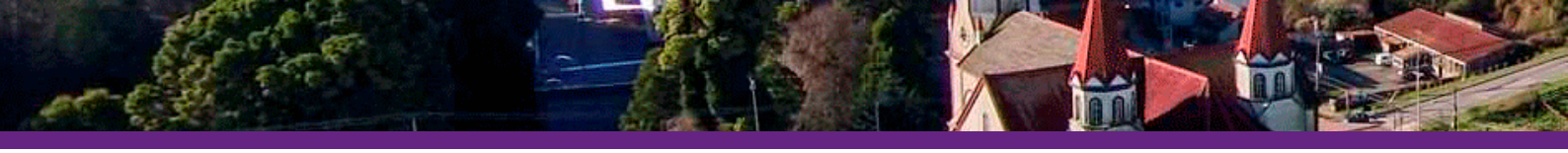
Axonal transport is essential for the maintenance of neuronal function, and deficits in this process contribute to neuronal degeneration. In particular, defects in axonal transport of mitochondria and axonal signalling endosomes have been observed in amyotrophic lateral sclerosis (ALS) models, such as SOD1(G93A) mice, already at the pre-symptomatic stage, suggesting that alterations in this pathway may have a causative role in motor neuron degeneration. However, conclusive proof of the key role of axonal transport defects in ALS pathogenesis is still lacking.

We set out to identify compounds able to specifically enhance axonal transport, thereby rescuing the deficits observed in SOD1(G93A) mice. Testing the effectiveness of these compounds in vivo would conclusively prove the role of axonal transport defects in ALS pathogenesis.

We have screened a small-molecule inhibitor library for pharmacological enhancers of axonal retrograde transport, which might be used to normalise the rate of this pathway in ALS neurons. Inhibitors of p38 MAPK were identified in this screen and were found to correct deficits in axonal retrograde transport of signalling endosomes in cultured SOD1(G93A) motor neurons and *in vivo*. Our findings demonstrate that the pathogenic effect of p38 MAPK on axonal retrograde transport is reversible and identify a potential therapeutic strategy for ALS.

Interestingly, we found that the rate of axonal transport of signalling endosomes varies in motor neurons innervating different types of muscles, and is differentially affected by ALS, suggesting a close interlink between axonal transport rate, muscle type, and motor neuron function and survival.



Simposio conjunto de la Sociedad de Biología de Chile y la Sociedad de Evolución de Chile

Ciencia, educación y comunicación: una mirada desde distintos actores.

Coordinadores: Pamela Morales y Marco A. Méndez

Broadcasting Evolution: Public communication of science from the beginning of our academic career

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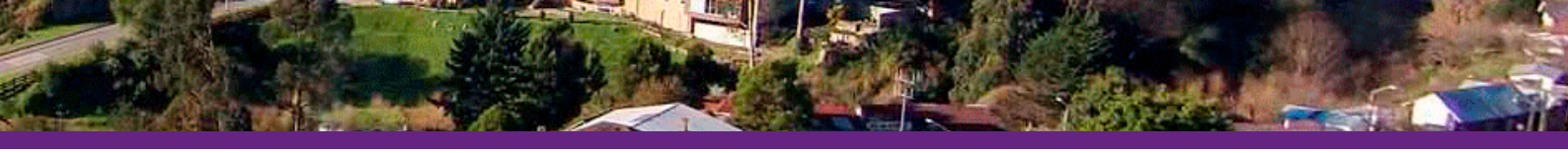
(2) Educación, Ciencias Sociales, Universidad De Chile

Scientific communication or Public communication of science is a labor that few scientist do or want to do, either because of scares resources, time or motivation. As a consequence, one of the main criticism to scientist is the distance they represent with the rest of the society. This reflects on the knowledge gap of our public when it comes to scientific topics and particularly the kind of research done in Chile. In this context, our team confronted this knowledge gap in evolutionary biology by contributing with educational material for students in secondary school, based on research topics of local scientists and on their educational curriculum according to MINEDUC. In this presentation, we will show the labor behind our work, from a perspective of a young researcher initiating its career in academy, with all the limitations and challenges, but overall the motivation and benefits that they imply. With this, we would like to open a discussion on, When, how and to whom do you communicate science to? And What is required to fulfill this labor? We would like to bring forward the importance that scientific communication has in the society and motived researcher to talk to the public about what they have learned, discovered or experience during their career. By communication science to secondary school students, we expect to increment the value the society has for science, and hopefully enhance the conditions of research in Chile.

Departamento de Postgrado y Postítulo, Vicerrectoría de Asuntos Académicos, Universidad de Chile.



De novo genome sequencing in the classroom offers unique opportunity for original research by secondary school students

Allende Miguel [1], Gaete Alexis[2], Urra Claudio[3], Díaz Lorena[1], Nardocci Gino[3], Maldonado Jonathan[2], Meneses Claudio[3], Hodar Christian[2], González Mauricio[2]
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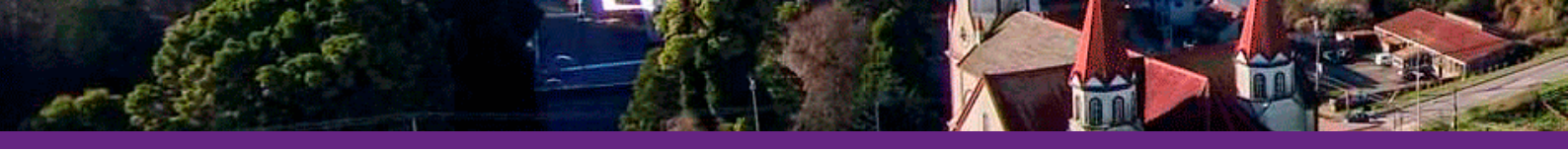
(3) Centro de Regulación del Genoma, Facultad de Ciencias Biológicas, Universidad Andrés Bello

New low-cost sequencing technologies hold the promise of widespread use of genomic analysis in almost any environment and, very likely, by the lay person. To pave the road to a full understanding of this cultural and technological change by the next generation of citizens, the Chilean 1000 Genomes Initiative has carried out a genome sequencing experiment in 10 Chilean schools distributed widely throughout the country. Schools were selected on the basis of an essay competition while striving for regional representation, gender balance and opportunities for underprivileged institutions. Scientists from the Centers of Excellence participating in the 1000 Genomes Initiative traveled to the schools and carried out the sequencing experiment simultaneously in all 10 schools. We selected the common pill bug (Armadillium sp.) to sequence; the arthropods were captured in the field by the students and DNA was extracted in a University lab to comply with restrictions on the use of animals in schools. Genomic DNA purification, library construction and loading of the samples on the sequencers (Oxford Nanopore Technologies MinIon sequencers) was done by the students. During the event, students also received basic bioinformatic training and carried out exercises aimed at learning molecular biology concepts. The results, which describe the genome sequence of the pill bug for the first time, will be published in a mainstream scientific journal with all participants as co-authors. We describe the educational opportunities and lessons learned from this unique experience.

FONDAP 15090007



The Diploma in Science Communication at the Faculty of Sciences – University of Chile

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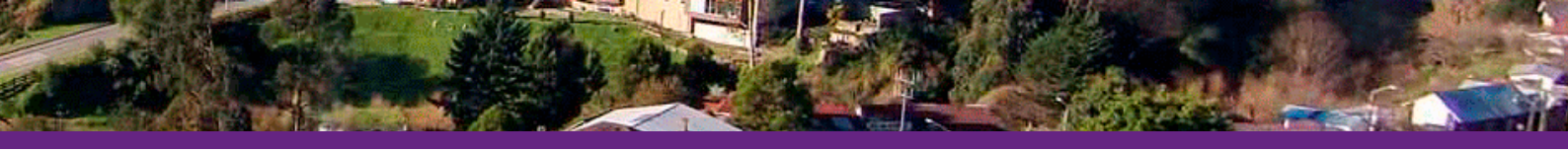
The Diploma in Science Communication, is the first science communication training program in Chile. The staff of professors includes scientists, journalists and a sociologist. The goal of the Diploma is to promote that graduates can design strategies, messages and products that serve as a bridge between the world of science and the non-scientific community. Specifically, it seeks to: examine the relationship between science and society, develop appropriate communication skills for the dissemination of science, understand the specific requirements of different audiences, generate scientific communication materials for different communication platforms, and explore the possibilities available for science communicators in Chile. The program takes 6 months and is divided into four modules that mix theory and practice. Briefly the following topics are examined: scientific communication, philosophy and sociology of science, written and oral communication tools, current societal controversies regarding science (climate change, GMOs, vaccines). We also teach basic project formulation skills, funding and evaluation strategies Finally, we explore hands on the basics of radio, digital and visual communication. Along the year, students learn to generate clear, attractive and concise messages, and to develop communicational projects with which they can access competitive funds. The program has 58 graduates, mostly scientists (biologists, physicists, chemists, geologists) and journalists (media, institutional and freelance), but has also attracted a diversity of professionals, among them school teachers, designers, audiovisual producers and publicists. Graduates successfully perform in the field of science communication, access jobs, have been accepted to graduate degrees in complementary areas, and develop new professional interactions. Diplomado en Comunicacion de la Ciencia, Universidad de Chile.



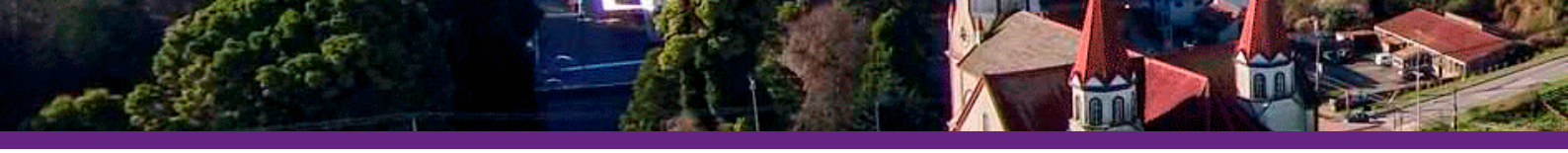
Science in the media: the necessary and strategic relationship between scientists and journalists

Espinoza Cristina [1]
(1) Área de Comunicaciones, Facultad de Ciencias Físicas y Matemáticas, Universidad de Chile

Spreading science beyond papers is nowadays another requirement to obtaining funding to do science. However, a large part of these results is still far from the general public. Most of Chileans believe that "scientists make little effort to inform the public about their work", and that makes they are not interested in increasing public investment in science (National Survey of Social Perception of Science and Technology in Chile, Explora-Conicyt, 2016). The media are a way to shorten the gap between scientists and society because it opens doors for more people to learn about and be interested in the research that is carried out in Chile. But publishing about science in the media is not easy for journalists or scientists, not only because there is little space, but because the lack of information and preparation persists among journalists, and lack of trust persists among scientists.

This presentation will provide information about what it means and what is behind writing about science for media -from a communication medium and from the communications area of the Faculty of Physical and Mathematical Sciences of the University of Chile-, when an investigation can be news and how to achieve it, the importance of promptly answering a request for an interview, among other reflections on how to make a fruitful scientists-journalists relationship. It is essential to understand the benefits for scientists of developing the ability of explaining their research in simple terms and the whole potential of communicate it in an interview.

Diplomado en Comunicacion de la Ciencia



Sociedad de Microbiología de Chile

Interacción patógeno hospedero

Coordinador: Fernando Valiente
Co-coordinador: Claudia Saavedra

Contribution of pathogenicity islands in *Shigella flexneri*

Toro Cecilia S. [1], Marcoleta Alicia[1], Henríquez Tania[1], Bravo Verónica[1], Díaz Patricia[1], García Camila[1], Salazar Juan Carlos[1], Hermosilla Germán[1], Ulloa María Teresa[1], Santiviago Carlos[2], Oñate Ángel[3], Marvasi Massimiliano[4], Shah Ajit[4]
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(3) Departamento de Microbiología, Facultad de Ciencias Biológicas, Universidad Austral de Chile
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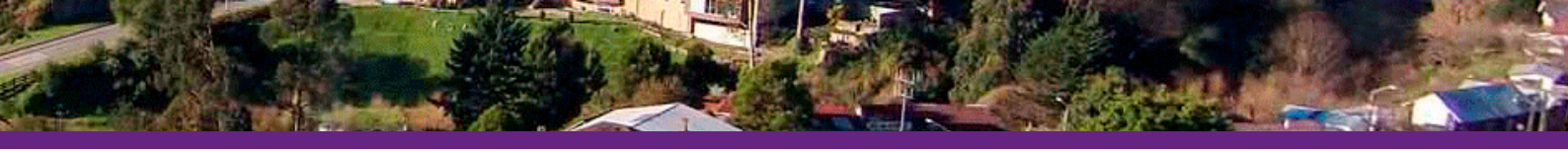
Shigellosis is a syndrome of acute diarrhea, which often progresses to dysenteric. The study of pathogenicity islands (PAI) in *Shigella* has made it possible to understand the mechanisms used by this facultative intracellular pathogen to produce disease exclusively in humans. In our laboratory we have studied the contribution of the *Shigella* pathogenicity islands SHI-1 and SRL.

The *she* PAI or SHI-1 in *S. flexneri* 2a encodes, among others, the SigA protein, which, according to its gene sequence, belongs to the family of SPATE (Serine protease autotransporters of Enterobacteriaceae). SigA produces cytopathic effect on HeLa cells, but not cytotoxic. Through dissemination assays in the TC7 cell line, it was determined that the mutant strain (ΔsigA) and the catalytic site mutant (Δ*sigA* / pGSigA-S260A) have reduced capacity to invade HeLa compared with the wild strain, without altering the ability of dissemination in vitro. On the other hand, a strain of *S. flexneri* lacking the gene transformed with *sigA* present a greater ability to invade epithelial cells, results that supporting SigA as a synergistic factor of virulence in the process of invasion of *Shigella* to the intestinal epithelium.

The SRL PAI of *S. flexneri* 2a YSH6000 encodes the locus SRL, which confers resistance to four antibiotics. However, there is no information whether it participates in other metabolic processes in addition to iron uptake by the *fec* operon. Therefore, the role of SRL in bacterial metabolism was evaluated by phenotypic microarrays, comparing wild strain YSH6000 and an spontaneous deleted-SRL mutant. The only difference was that the mutant lost the ability to metabolize in the presence of D-aspartic acid as the sole carbon source. Bioinformatic analysis of the SRL sequence revealed that the *orf8-orf9* genes belong to this island code for an aspartate racemase and a transporter, respectively. The findings obtained by HPLC-MS / MS corroborated the aspartate racemase activity in the reference strain and in the strains complemented with the region in question. The presence of racemases in enterobacteria and the participation of D-amino acids, not only forming structures but also as mediators of chemical signals, opens up interesting fields to explore.
Financiado por Anillo ADI- 08/2006, FONDECYT 1040539, 1130394.



Microbiota and immune response in aquaculture

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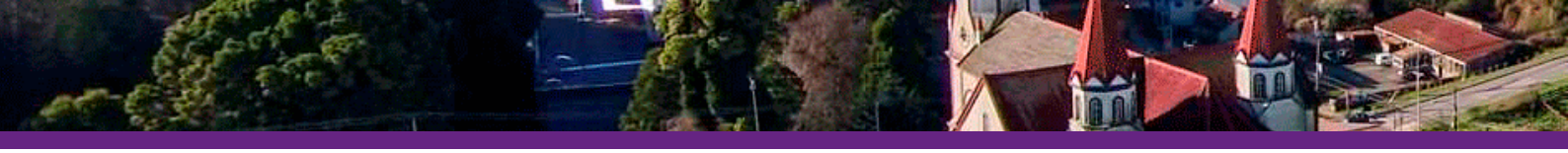
The microbiota is a complex community of microorganisms that is established on the mucous membranes and surfaces of multicellular organisms. This microorganisms plays an important role in assimilation of nutrients, behavior, protection against pathogens and in the adequate maturation of the immune system. Most of the knowledge about the role of the microbiota comes from studies in mammals and zebrafish as a model, however the biological role of the microbiota in species of aquaculture interest such as Atlantic salmon or Rainbow trout is unknown. Our laboratory is focused on understanding how the microbiota of these aquaculture species helps the adequate immunostimulation, in order to develop alternatives to the treatment of antibiotics to fight viral and bacterial diseases based on the stimulation of the immune system and the competition between microorganisms. Through the use of antibiotics we have observed that the reduction of the microbial load produces an increase in the inflammatory response and a reduction of leukocyte populations in the immune organs of the fish. These changes are not reversed even after 15 days post treatment with antibiotics which suggests that through the microbiota the antibiotics could have a prolonged effect on the immune status of the fish. We have also identified microorganisms of the microbiota with antagonistic activities against some fish pathogens and managed to use some microorganisms as immunostimulatory peptide release systems with successful results in the reduction of viral and bacterial load in challenge experiments. As a whole, our results suggest that the study of the microbiota may be a new target in aquaculture for the development of alternative treatments to the use of antibiotics and vaccines.

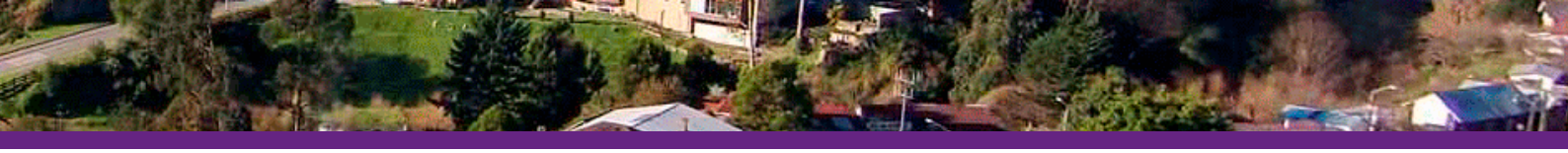


Role of the Transcription Factor ArcA on the genetic modulation of *Salmonella* Typhimurium during the infection of murine neutrophils

Saavedra Claudia [1]
(1) Facultad de Ciencias Biológicas, Universidad Andres Bello

During the infection cycle of pathogens, some cells from the host's immune system, such as neutrophils, use microbicide mechanisms to eliminate themincluding the highly toxic compounds known as Reactive Oxygen Species (ROS), specifically neutrophils use HOCl. Pathogens like *Salmonella* Typhimurium,however, have the ability to overcome these microbicides mainly due to its genetic modulation and consequently adapting efficiently to overcome toxic-related stress. Recently we have found that the Transcriptional Factor ArcA responds to changing oxygen levels and is activated in response to the conditions found inside neutrophils triggering the modulation of several key genes that allow the bacteria to survive. Here we showthat after the production of HOCl inside the phagocytic cell the presence of the *arcA* gene influences on the survival of *S.* Typhimurium and participates on the expression of genes associated with ROS resistance(*katE, msrA, ompD, ompW, cadB* and *sipC*). Additionally, we have found from *in vitro* studies that some routes are enriched in the presence of HOCl, such as Fatty Acid Degradation, Oxidative Phosphorylation and Lysine Degradation, consequently we carried out the validation of genes that codify for proteins that participate in these routes and found that ArcA has a role in the regulation of genes related to this functions inside neutrophils, postulating it as an important asset for the pathogen to achieve a successful infection aiding in the adaptation to adverse conditions found in the phagosome.

FONDECYT 1160315 Palabras clave: Salmonella Typhimurium, ArcAB, neutrophils.



Anti-carcinogenic drugs (ACDs) that promote the assembly of RNPs modulate HIV-1 gene expression

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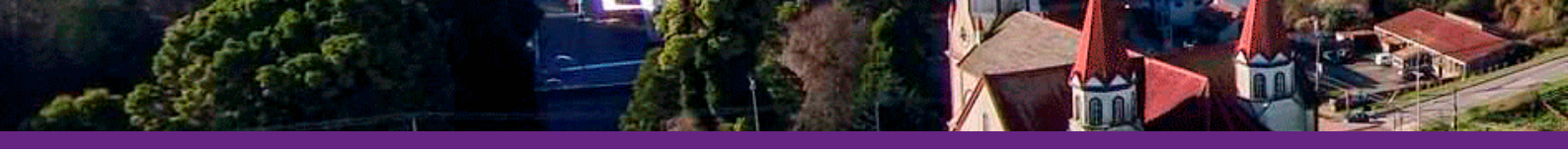
HIV-1 is member of the lentivirus subfamily of theRetroviridae and the etiologic agent of AIDS. Following viral infection, the host cell responds by mounting a robust anti-viral immune responseto create an inhospitable environment for viral replication, causing both the shut-off of protein synthesis and stress granules (SGs) assembly. Previously, we showed that HIV-1 Gag protein suppresses SG assembly, but when not possible, it not only lifts the SG blockade, but also results in impaired virus production and infectivity. Given that several reports have been shown that anti-carcinogenic drugs (ACDs) can induce the assembly of SGs, we tested several types of ACDs on HIV-1 expressing cells. Using quantitative cell analysis coupled with bioimaging methods, we found that Vinca alkaloids modulates HIV-1 replication on cells that have SGs assembly, which indicates a potential use of ACDs as complementary antiretroviral therapy (ART).

This work is supported by FONDECYT Nº11140502 and Nº 1180798.



INCORPORACIONES SOCIEDAD DE GENÉTICA CHILE

ADAR1 Transcriptome editing promotes breast cancer progression through the regulation of cell cycle and DNA damage response

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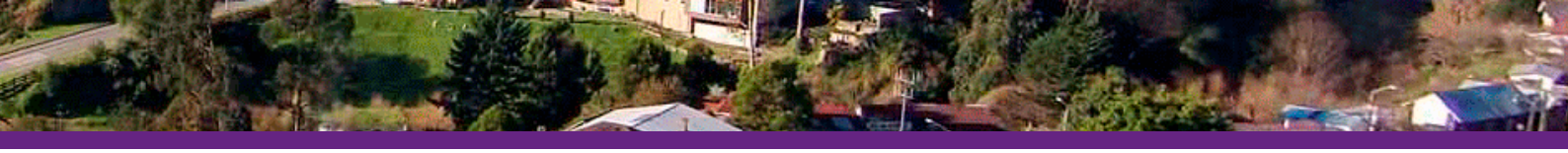
DNA and RNA editing are novel mechanisms involved in cancer progression. In recent years, genome-wide works have been shown that the double stranded RNA-specific adenosine deaminase (ADAR1) modify an important proportion of genes involved in cell cycle control, DNA damage response and transcriptional processing, suggesting an important role of ADAR1 in the regulation of those processes. While a limited number of edited sites occur on exonic regions, the mayor proportions of those edited sites are located on intronic or 3'UTR regions, where have been shown that ADAR1 activity is increased in transcripts associated to DNA damage response, cell cycle progression and apoptosis processes on those regulatory mRNA regions. Despite the phenotypic implicances of ADAR1 in different cancer models, it has not been fully addressed the ADAR1 role on DNA damage response and proliferation in breast cancer (BC). In this work, we shown that ADAR1 expression significantly correlates with proliferation related mRNAs, and previously reported ADAR1 target edited transcripts. Moreover, ADAR1 *knock down* produces significant changes in mRNA stability of edited transcripts involved in DNA damage response and DNA replication. In addition, MCF7 and ZR-75-1 ADAR1 knock down cells shown a decreased proliferation, viability and an increased apoptosis, compared to control cells, showing that *knock down* cells exhibit a significant decrease of their DNA damage response activation. Taken together, our results shows that ADAR1 plays an important role in BC progression through the regulation of mRNA stability and expression of those genes involved in proliferation and DNA damage response.

FONDECYT 1151446 (RA), FONDECYT 1151435 (KM), CONICYT Doctoral fellowship (EAS, AIS) and CORFO 13CEE2-21602 (RA).



INCORPORACIONES SOCIEDAD CHILENA DE EVOLUCIÓN

Demographic processes and genetic diversity: The case of *Bombus dahlbomii* and *Bombus terrestris* (Hymenoptera: Apidae) in Chile

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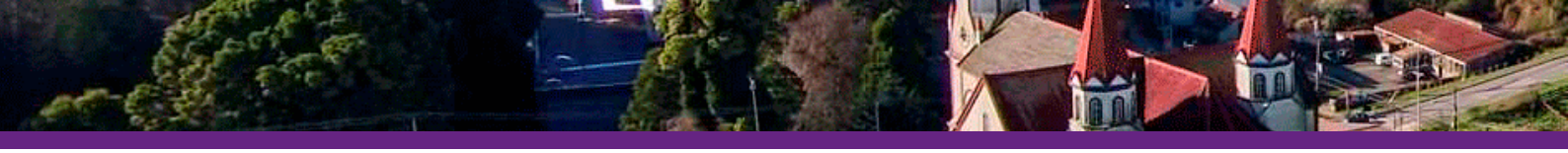
The invasive species are an important component of global change. The colonization, establishment and subsequent range expansion events have an effect in genetic diversity of invasive species. The impact of invasive species on native species has been widely recognized for decades. Native species could have their population size reduced (given interespecific competition, e.g. competition for floral resources and nest sites, and pathogen infections from invasive species) and subsequent loss of genetic diversity by genetic drift. *Bombus dahlbomii* is a native species from Chile and the southern-most bumblebee species worldwide. This species has had a drastic reduction of his population size in the last 20 years, coincident with the introduction of *Bombus terrestris* into Chile in 1996. *Bombus terrestris* was introduced to pollinate tomatoes in Quillota, and has had a quick demographic and geographic expansion to the south of Chile. These species are a good model to evaluate the effects of contrasting demographic processes (population size decrease in *B.dahlbomii* and demographic expansion in *B.terrestris*) in genetic diversity. We used 10 microsatellites and mitochondrial marker COI. Our results show a high genetic diversity in *B. dahlbomii* populations and the signs of bottleneck in the recent past in southern populations suggest a low effect of population decline in genetic diversity. In *B.terrestris,* analyses of genetic population structure suggest a high structure, especially in population from the north of the range distribution. This genetic structure is remarkable in invasive species, and could explain the colonize and adaptation potential in new environments of *B. terrestris.*

CONICYT 21140012



Pleistocene glaciations, paleolakes and orography: three important components of the genetic structure and historic demographic patterns of *orestia agassii* in the margin of the chilean altiplano

Cruz-Jofré Franco [1,2], Fabres Alejandra[1], Araya Carolina[3], Rojas Carla[1], Morales Pamela[1], Pastenes Luis[4], Vila Irma[1], Méndez Marco A.[1]
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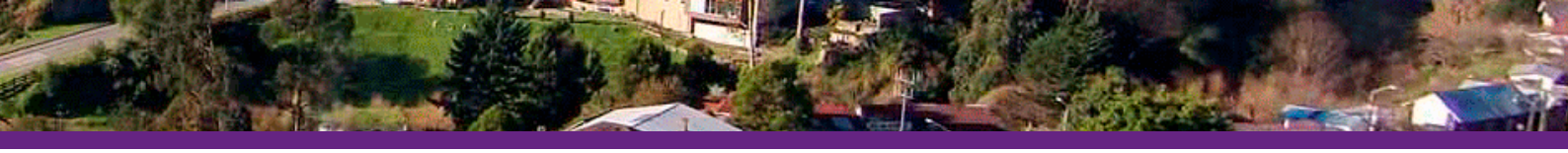
Orestia agassi is a species with a wide distributional range, which goes from the basin of the Urubamba River (Peru), Región de Tarapacá (Northern Chile), to the basin of Uyuni Saltpan (Bolivia). Geographic barriers and geological changes have been proposed as the mechanism that causes genetic differentiation in other species of the genus (i.e. *O. ascotanensis*). Here, we evaluated the effects that the geographical altitude and past climate change has on the genetic diversity and differentiation process between populations using two mitochondrial markers (Dloop and Cytb) and eight microsatellites. We sampled 15 localities in the basins of Isluga and Cariquima Rivers that have an altitudinal gradient that goes from the origin of both (4,200 m a.s.l) to the mouth of the river in the Coipasa Saltpan, Bolivia (3,700 m a.s.l.). We observed high genetic structure, with three well defined clusters. Two of these correspond to the localities at a higher latitude (>4,000m a.s.l), which present the least diversity and a clear genetic differentiation between each other, associated to its permanent isolation. The third genetic group, corresponds to the fish populations located at a lower altitude (near 3,700 m a.s.l), these present a higher genetic diversity and a recent gene flow. We discuss the effects of the paleolake Tauca (16-14 ka AP), and of the current variations of water level effected by the South American Summer Monsoon on the observed diversity and genetic structure
FONDECYT 1140543, 1140540, 3140483 CONICYT-PCHA/doctorado nacional/2012-21120972, CONICYT-PCHA/doctorado nacional/2015-21150821 y Vicerrectoría de Investigación y Postgrado, Universidad Santo Tomás.



Systematics and past biogeographical events: the case of *Heleobia* (Caenogastropoda: Truncatelloidea) from the Andean Altiplano

Valladares Moisés [1], Fabres Alejandra[1], Puillandre Nicolas[2], Prié Vincent[3], Barrera Soraya[4], Sarmiento Jaime[4], Collado Gonzalo[5], Méndez Marco[1]
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(3) Service Recherche et Développement, Biotope
(4) Colección Boliviana de Fauna (MNHN-IE), Campus Universitario UMSA, Museo Nacional de Historia Natural (Sección Peces)
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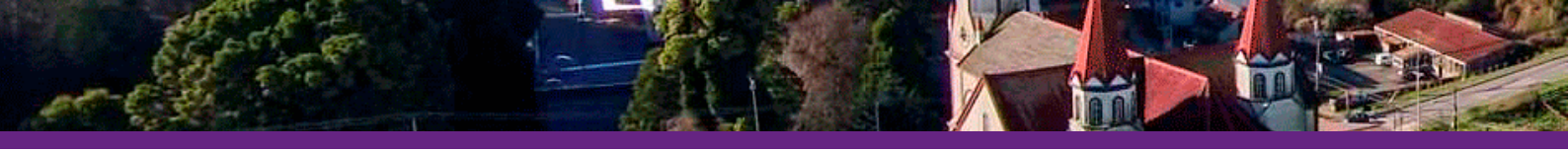
The genus of freshwater gastropods *Heleobia* Stimpson, 1865 comprises several species distributed in the southern cone of South America and presents numerous taxa that are endemic to the Andean Altiplano. Species delimitation in *Heleobia* is a difficult task because these snails are similar in shell morphology, hence in this group the taxonomy is uncertain, and many populations remain unknown. In the Altiplano, the distribution patterns of *Heleobia* and co-distributed taxa suggest that the scenario of evolutionary divergence and diversification processes may involve a mix of different speciation processes (in terms of vicariance, dispersal and founder events), mainly modulated by geological and environmental changes that continuously reshape the aquatic systems (Plio-pleistocenic events). In this study, we analysed mtDNA and nucDNA markers of the *Heleobia* species from the Altiplano of Bolivia, Chile and Perú under an integrative taxonomy framework. We compared primary species hypotheses (according to DNA sequences) with morphology and distribution, to delimit the *Heleobia* species in the Andean Altiplano and reconstruct their phylogenetic relationships. Besides, we focus on the implications of environmental and historical constraints and how local conditions relate to genetic divergence in *Heleobia*. Furthermore, we discuss the mechanisms and processes that have stimulated the divergence in the group and propose biogeographical scenarios that could explain the current distribution of the genus in a dynamic environment such as the South American Altiplano.

CONICYT-PCHA/Doctorado Nacional/2014-21140226; FONDECYT 1140540; FONDECYT 11130697; ECOS-CONICYT C15B02.



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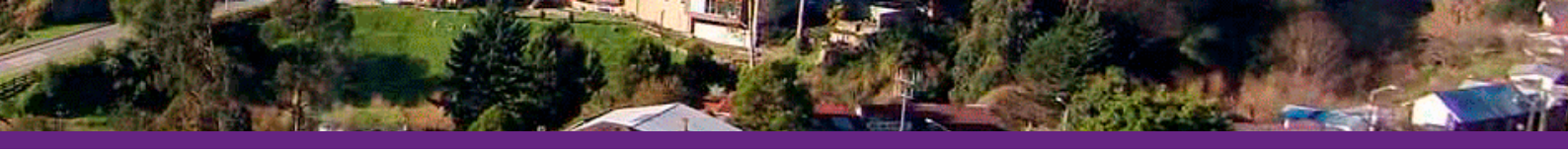
Sociedad de Genética de Chile

The landscape of non-coding RNAs in the archaeon Sulfolobus genus

Aliaga-Tobar Victor[1,2], Arias-Carrasco Raúl[1], Thuong Le[3], Verenja-Albers Sonja[3], Orell Alvaro[4], Maracaja-Coutinho Vinicius[1]. [1]Laboratory of Integrative Bioinformatics - LIB, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile. [2]Programa de Doctorado en Genómica Integrativa, Vicerrectoría de Investigación, Universidad Mayor. [3]Molecular Biology of Archaea, Institute of Biology II - Microbiology, University of Freiburg. [4]Terrestrial Microbiology, Max Planck Institute. (Sponsored by Vinicius Maracaja-Coutinho)

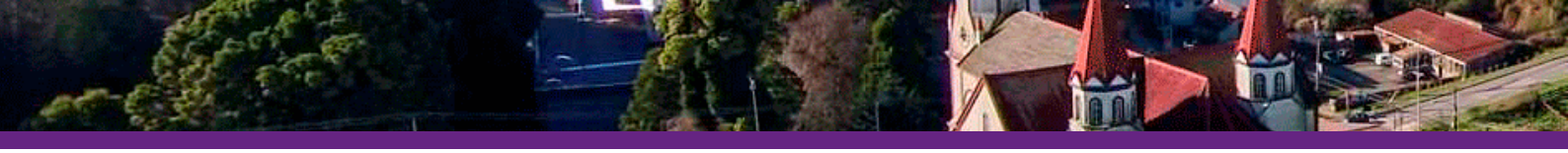
Non-coding RNAs (ncRNAs) are known to have key roles in gene regulation, nucleotides modification, transposable elements silencing and defense against foreign genetic material. In Archaea, ncRNAs are as abundant as in Bacteria. However, its identification has been confined to a few species and little efforts have been performed to extend the repertoire in non-models Archaea. In *Sulfolobus*, an archaeal genus that contain species widely used as models for the study of extreme-environment adaptation. Transcriptome sequencing has allowed the identification of ncRNAs in several species, mainlyt *S. solfataricus* and *S. acidocaldarius*. However, the number of complete available genomes for this genus cover more than 20 strains, and a limited number of computational methodologies have been applied to identified the real complete repertoire of ncRNAs in these microorganisms. In order to extend the ncRNA repertoire in the *Sulfolobus* genus, we performed an exhaustive identification using three complementary in-house developed approaches: sequence similarity, secondary structure inference and transcriptome data analyses. We identified a variation of 350-600 ncRNAs in each genome, including classes described for the first time in Archaea, totallying more than 1400 ncRNAs spreaded over 28 *Sulfolobus* species. Curiously, ~80% of predicted ncRNAs presented no annotations based on databases comparisons. Additional insights were obtained from transcriptome, sequence conservation and experimental analyses. It revealed the presence of validated promoter regions controlling their biogenesis, expressed ncRNAs under specific conditions and predominance of species specific-ncRNAs. Our findings suggests that the complexity of the non-coding transcriptome in Archaea is still an opened avenue for future research.
Fondecyt 11161020 and PAI-CONICYT PAI79170021



Integrated use of DNA Barcoding and cytogenetic analysis for species delimitations in Orestias genus of the Chilean Altiplano.

Araya-Jaime Cristian[1], **Lam Natalia [2]**, Iturra Patricia[3], Mendez Marco[4], Vila Irma[4]. [1]Laboratório de Biología e Genética de Peixes., IBB, Universdade Estadual Paulista, Botucatu-SP.. [2]Departamento de Producción Animal, Facultad de Ciencias Agronómicas, Universidad De Chile. [3]Programa de Genética Humana,ICBM., Facultad de Medicina, Universidad de Chile. [4]Departamento de Ciencias Ecológicas, Facultad de Ciencias, Universidad de Chile.

Orestias is one of freshwater fish genus with more species present in Chile. At present, eight species have been described which are distributed from the Lauca National Park, in Arica and Parinacota region, to the Salar de Ascotán in Antofagasta region. The species diversity has been explained by an allopatric speciation processes, as a consequence of their habitat fragmentation during the Pleistocene. Cytogenetic studies in *Orestias* have established that the diploid number of chromosomes varies from 48 to 55 chromosomes, being the 2n = 48 the karyotype the most frequent. It is remarkably, that each of the Chilean *Orestias* species possesses different cytogenetic attributes. Unfortunately, the cytogenetic characteristics lack taxonomic value. In this context, we analyzed partial sequences of the Cytochrome Oxidase I (COI) gene from *O. ascotanensis, O. gloriae, O. laucaensis* and populations from Isluga, Caquena, Paquisa and Huasco, in order to evaluate if the cytotypes recognized by cytogenetic analysis correspond to species recognizable by DNA Barcoding approach and molecular delimitation of species. The analysis of this set of sequences resulted in the recognition of each cytotype as an Operational Taxonomic Unit (UTO), with genetic divergence values (K2P) averaging 3%. In this way, we conclude that the integrated use of cytogenetic analysis and DNA Barcoding can improve the identification and delimitation of the Operational Taxonomic Units within *Orestias*, information that becomes relevant for taxonomic, phylogenetic and conservation studies.
Proyectos FONDECYT 1110243 y 1140543.



Detecting native ancestral components in human populations from Patagonia

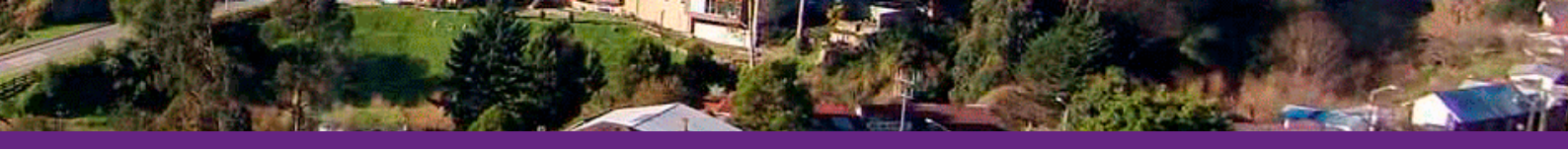
Pezo Patricio Alejandro[1], Moreno-Estrada Andrés[2], Verdugo Ricardo[1,3], Moraga Mauricio[1,4]. [1]Instituto de Ciencias Biomédicas, Facultad de Medicina, Universidad de Chile. [2]Laboratorio Nacional de Genómica y Biodiversidad (LANGEBIO), Irapuatp, México, CINVESTAV. [3]Departamento de Oncología Básico Clínica, Facultad de Medicina, Universidad de Chile. [4]Departamento de Antropología, Facultad de Ciencias Sociales, Universidad de Chile.

Introduction and Objectives:
Patagonia, located in the southern part of South America, is known to be one of the last places to be populated by modern humans 13,000 years ago. The first archeological sites show that the first settlers were terrestrial hunter-gatherers that occupied oriental Patagonia (Argentina). Based on genetic tools there are two non-excluding hypothesis of occupation, including an Andean route, and a Coastal Pacific route from occidental Patagonia (Chile) with a posterior trans-Andean corridor due of the ice sheets limits in Chilean Patagonia. The objective of this work is to elucidate the ancestral genetic components in currents populations from Patagonia.

Material and Methods:
A total of 152 individuals descendant from Patagonia populations were genotyped and then imputed for 2.176.679 SNPs.

Results and Conclusions:
We explore the genetic structure through ancestry component analysis using PCA, ADMIXTURE and TRACTs. The first principal component differentiates our samples between European and Native Ancestry. The global ancestry analysis (ADMIXTURE) reveals evidence of sub-structure within the Native American component splitting into one northern component (Andean), another from Central/South Chile (Pehuenche/Huilliche) and another from Austral Patagonia (Kaweskar and Yamana). In addition, these results shown a new component exclusive to Austral populations from Patagonia (Kaweskar and Yamana). According to TRACTs, we can describe also the presence of Andean component before the European arrival, being the highest component in Yamana (40%). The presence of these components might reflect a possible connection between the Andean highlands and the population of Patagonia trough an oriental route.

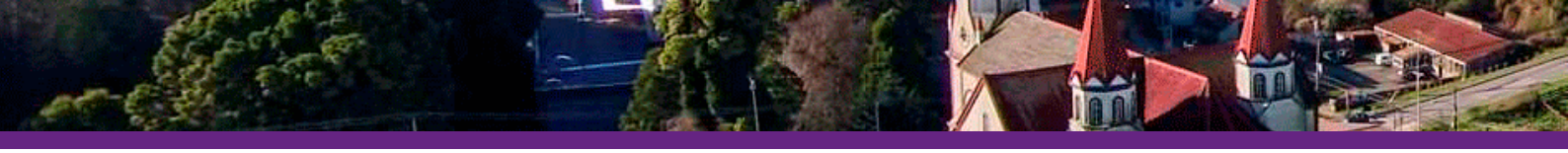
Funding: CONICYT USA2013-0015, FONDECYT 1140544 and 1181889, Beca Doctorado Nacional 2014 Nº 21141094



The role of the presence of congenners during the ontogeny on an adequate morphological, physiological and behavioral development in *drosophila melanogaster* larvae.

Del Pino Francisco Rodrigo[1], González F.[1], Zamora M.[1], Espinoza P.[1], Álvarez Eduardo[1], Godoy-Herrera Raúl[1]. [1]Programa de Genética Humana, Medicina, Universidad de Chile.

During development, the environment surrounding the organism significantly influences the expression of morphological, physiological and behavioral traits. Environmental signals that influence development can come from many sources in nature, of particular importance to many organisms are the sensory inputs emitted by congeneric organisms that are in the same space and time. In this study, we investigated the role played by the social interactions during larval development in *D. melanogaster* on the size, weight and behavior of preadults. For this, an isomaternal line of the Canton S strain of *D. melanogaster* was first constructed, which allowed us to experiment with a genétically homogeneous population of individuals. In a Petri dish 4 cm in diameter filled halfway with Burdick culture medium, larvae of the aforementioned isomaternal line were bred in two different ways; i) a single egg per capsule was deposited and ii) 30 eggs were deposited per capsule, when the larvae reached 96 hours of age, we proceeded to weigh them, measure them and record their locomotor activity. The isolated larvae exhibited a significantly lower weight and length than those reared in the group, in addition they showed a locomotor activity and a rotation rate lower than those that developed with congeners. Our results suggest that social isolation during larval development alters the weight, size and way of exploring the environment in pre-adults of *D. melanogaster*.

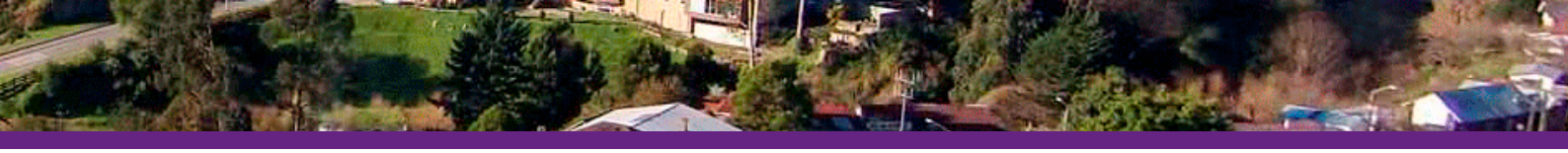


Genetic-by-early life-nutrition interactions in sleep behavior and brain morphology in drosophila

Olivares Gonzalo H.[1], Núñez Franco[1], Vega-Macaya Franco[1], Candia Noemi[1], Zúñiga Nolberto[1], Verdugo Ricardo A.[2], Olguín Patricio[1]. [1]Program of Human Genetics, Department of Neuroscience, Faculty of Medicine, Universidad de Chile. [2]Program of Human Genetics, Departamento de Oncología Básico-Clínico, Faculty of Medicine, Universidad de Chile. (Sponsored by Gonzalo Alberto Olivares Herane)

Sleep can be defined as a reversible state of inactivity, which is controlled by circadian and homeostatic factors, and which is conserved across most metazoans. In vertebrates and Drosophila, starvation leads to suppression of sleep, however, it has not been studied whether early-life nutrition during development affects sleep variation and to what extent it is influenced by the morphology variation of the brain structures controlling sleep, such as the mushroom bodies (MBs) in flies. To answer this question we characterize sleep traits and MBs morphology in a subgroup of flies of the Drosophila Genetic Reference Panel (DGRP) raised under prenatal nutritional restriction (NR). The DGRP is a collection of wild origin of 205 sequenced isogenic lines that represent the genetic variation of a natural population. Therefore, the genetic variation of DGRP can be associated with the variation of specific phenotypes using GWA studies. Using this panel, we determined that genetic-by-early-life-nutrition interaction contributes to variation of MBs morphology and sleep traits. By performing GWA analyses we identified single nucleotide polymorphisms (SNPs) associated with the sensitivity of MBs morphology and sleep traits to nutrition. Using this data we infer gene networks that underlie the differential response to NR in Drosophila sleep and MBs morphology. These results shed light on how prenatal NR results in adaptations of development, and how they contribute to shape brain function during adult life.

Acknowledgments: This work was supported by ANILLO ACT-1401 and BNI ICM P09015F

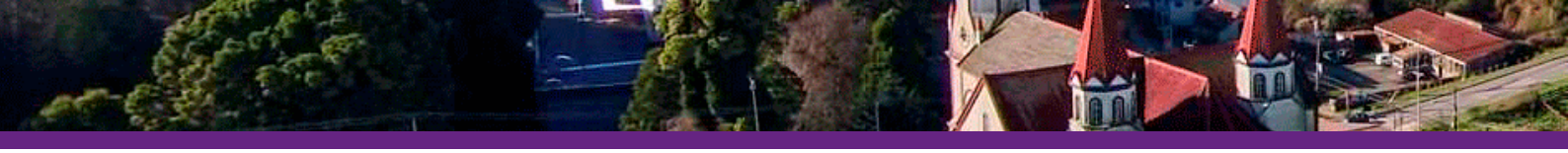


Search of genes involved in the differential activation of the TORC1 signaling pathway by glutamine in Saccharomyces cerevisiae

Kessi EI[1], Salinas F[3,2], Larrondo LF[4,3], Martínez C[2,1]. [1]Departamento de Ciencia y Tecnología de los Alimentos, Universidad de Santiago de Chile (USACH). [2]Centro de Estudio en Ciencia y Tecnología de los Alimentos (CECTA), Universidad de Santiago de Chile (USACH). [3]Millennium Institute for Integrative Systems and Synthetic Biology (MIISSB), Santiago, Chile. [4]Departamento de Genética Molecular y Microbiología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Casilla 114-D, Santiago, Chile. (Sponsored by Claudio Martínez)

Saccharomyces cerevisiae is the main species responsible for the alcoholic fermentation in the production wine, being one of the main problems the deficiency of nitrogen in the must, which can lead to stuck or sluggish fermentations. A major challenge is to identify the genetic basis underlying the phenotypic variability in nitrogen consumption and metabolism, with emphasis on the study of TORC1 signaling pathway, given its central role in responding to nitrogen availability and influencing growth and cell metabolism. However, the mechanism by which different nitrogen sources activates TORC1 is not completely understood, with the study of allelic diversity appearing as an alternative to identify genes involved in this process. Using a recently developed microculture method, which uses the luciferase gene as a reporter, representative strains of clean lineages described in *S. cerevisiae* (North American 'NA', Sake 'SA', West African 'WA' y Wine/European 'WE') were phenotyped. Among them, strains SA and WE showed the greatest phenotypic differences. Subsequently, a recombinant population composed of 96 segregants derived from these two strains was phenotyped. The phenotypic data obtained were used to carry out a linkage analysis, from which several candidate genes were obtained. Currently, these candidate genes are being validated by a reciprocal hemizygosity analysis, in order to corroborate that they are involved in the phenotype under study.

CONICYT/FONDECYT [grants 1150522 and 11170158], CONICYT/Beca Doctorado Nacional [grant 21150700] and MIISSB Iniciativa Científica Milenio-MINECON.

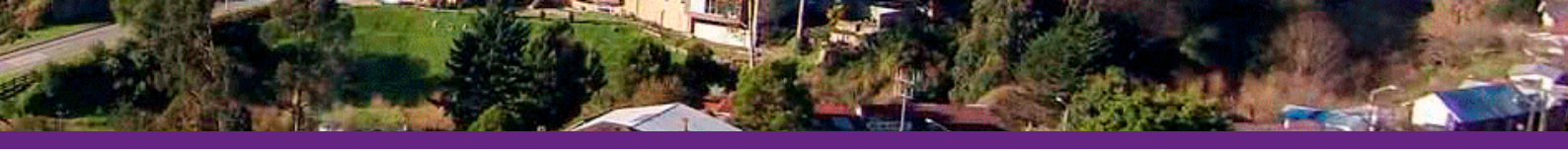


Experimental evolution of Saccharomyces eubayanus populations to improve fermentative capacities

Mardones Wladimir[1,2], Urbina Kamila[1,2], Nespolo Roberto[3,2], Cubillos Francisco A.[1,2]. [1]Departamento de Biología, Facultad de Química y Biología, Universidad de Santiago de Chile. [2]Millennium Institute for Integrative Biology (iBio), Santiago, Chile..[3] Institute of Environmental and Evolutionary Science, Universidad Austral de Chile, Valdivia, Chile. (Sponsored by Francisco A. Cubillos Riffo)

The Lager beer yeast *Saccharomyces pastorianus* is a natural hybrid between *Saccharomyces cerevisiae* and the cryotolerant yeast *S. eubayanus*. The latest was recently found in Patagonia, however only a handful of studies have evaluated its potential for beer production. In general, wild *S. eubayanus* strains have lower fermentative rates compared to commercial *S. pastorianus* genetic stocks, producing beer with lower ethanol concentrations. Recently, our group isolated hundreds of *S. eubayanus* strains from Central and South Chile. A phylogenetic analysis using *COX2* demonstrates an extensive genetic diversity between Chilean isolates, with 4 structured subpopulations and which are not necessarily distributed based on geographic distance. The above indicates a dynamic interaction of the populations probably due to the absence of natural barriers. To improve the fermentative capacities of these wild strains, we adopt an experimental evolution strategy. Ten genetically identical groups combining 30 different strains from three populations (Villarrica, Puyehue and Coyhaique) were incubated during approximately 200 generations in a restrictive ethanol containing media (9% v/v). The initial adaptation process to the restrictive media was moderate, but from the 50th generation an appreciable tolerance was detected. Additionally, was observed that the maxima growth rate was achieved after the 150 generations. Other traits, such as: flocculation or fermentation capacity were also evaluated. The evolved strains represent a novel platform to produce "wild beers" containing greater ethanol concentrations.

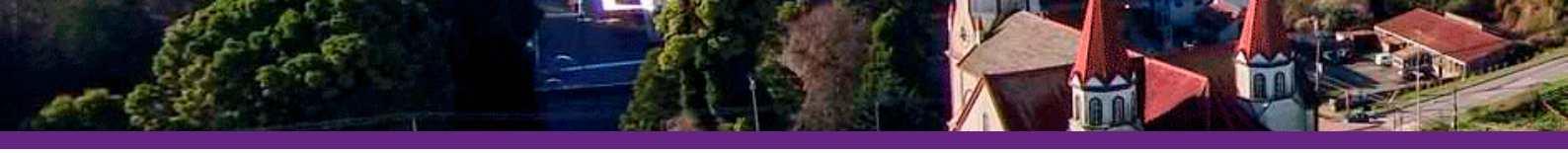
This research is funded by Instituto Milenio iBio – Iniciativa Científica Milenio MINECON



Extending the search for berry size selection markers in table grape (vitis vinifera l.): new ssrs derived from snp/indels and candidate genes

Burgos Matías[1], Jiménez Pablo[1], Bustos Sofía[1], Muñoz-Espinoza Claudia[1], **Hinrichsen Patricio[1]**. [1]Plant Genetics & Biotech, INIA, LA PLATINA. (Sponsored by FONDECYT 1171378)

In the framework of a table grape breeding program, we previously identified 38 polymorphisms of the SNP and InDel types with association to this largely quantitative trait. In this work, our aim was to identify SSR markers located in the vicinity of these SNPs/InDels, as well as SSRs close to seven genes, also associated to berry size. To approach this search, regions of 1 Mb from the *Vitis vinifera* reference genome (12X.2) surrounding the 44 markers and genes selected were analyzed using the SAMTOOLs and MISA softwares, considering a minimum of five repeats as threshold. A total of 29,173 SSRs were found, with an average density of 0.7 SSR per Kb. Mono-nucleotidic repeats (69.4%) were discarded, due to inherent difficulties in their experimental evaluation. The length of microsatellites varied from five to 55 repeats. From the preliminary screening of 17 regions distributed in 13 chromosomes, primers have been designed for 308 SSRs. A subset of 285 SSRs were evaluated using four table grape varieties with contrasting phenotypes for berry size as a first screening; 115 of them (40.4%) showed polymorphic patterns, while 18.9% were monomorphic and 40.7% did not amplify or were non-informative. Subsequently, the set of 115 polymorphic SSRs were analyzed in a group of 12 contrasting table grapes varieties and segregants; using this second screening, 18 SSRs with partial association to berry size were identified. These results will be discussed in the context of the potential use of these markers for table grape breeding.
Financed by FONDECYT 1171378 to PH.



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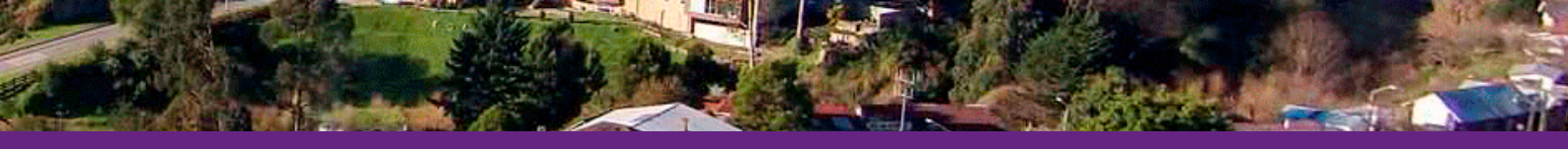
The effect of gut microbiota on the thermal physiology of Drosophila subobscura

Jaramillo Angélica[1], **Castañeda Luis[2]**. [1]Instituto de Ciencias Ambientales y Evolutivas, Facultad de Ciencias, Universidad Austral de Chile. [2]Programa de Genética Humana, Instituto de Ciencias Biomédicas, Facultad de Medicina, Universidad de Chile.

Higher and fluctuating environmental temperatures influence ectotherm physiology and biotic interactions such as host-microbiota interactions. Particularly, gut microbiota has an important role in host nutrition, which is related to many host physiological traits especially those energetically expensive such as thermal tolerance. The present work has two goals: (1) we compared the heat tolerance between axenic (germ-free flies) and conventional *Drosophila subobscura* flies, and (2) we characterized the gut microbiota before and after a heat shock using 16S rRNA metabarcoding. At 35ºC assays, we found that conventional flies exhibited higher thermal tolerance than axenic flies and that males showed higher thermal tolerance than females. However, no effects of gut microbiota or sex were found at higher assayed temperatures. On the other hand, we found a significant interaction between heat shock and sex on richness: female and male showed similar richness before the heat shock, and richness decreased after the shock but the decrease was stronger on males than females. Similar findings were found for Shannon and phylogenetic diversity. We also found significant effects of heat shock and sex on the gut microbiota community. Conclusions: (1) gut microbiota has a role on heat tolerance, suggesting an effect on fly nutrition that constrains heat tolerance only in chronic thermal stress; (2) heat shock changes the *Drosophila* gut microbiota, reducing its richness and diversity. We will continue exploring the role of gut microbiota on heat tolerance and to address what are the physiological mechanics allowing to increase the resistance to stress environmental challenges.

FONDECYT 1140066, ENLACE 09/18 UChile



Evolution of the brain size of mammals: A macroecological overview

Inostroza-Michael Oscar Esteban[1], Hernandez Cristian Esteban[1], Rodriguez-Serrano Enrique[2], Avaria-Llautureo Jorge[1], Rivadeneira Marcelo M[4,5,3]. [1]Laboratorio de Ecología Evolutiva y Filoinformática, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción. [2]Laboratorio de Matozoología, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción. [3]Departamento de Biología Marina, Facultad de Ciencias del Mar, Universidad Católica del Norte. [4]Laboratorio de Paleobiología, Centro de Estudios Avanzados en Zonas Aridas. [5]Departamento de Biología, Universidad de La Serena.

Multiple hypotheses have been developed to explain the evolution of large relative brain sizes (RBS) in mammals. However, all of these are idiosyncratic and/or clade-specific and are based on the costs or advantages associated with large RBSs. Given that both costs and benefits coexist in the species, it is necessary to adopt an approach that allows us to study the evolution of this trait in a broader sense. This can be accomplished by studying the frequency distribution of RBS, which shows an over-representation of species with RBS ~ 0; that is, relative brain sizes as expected for a species of given body size. This pattern suggests the existence of an optimal relative brain size (ORBS), where species with values close to ORBS would be mostly represented because there is a maximization between the costs and advantages associated with their brain size. To test this hypothesis, we constructed a brain-size database of 1564 mammal species. With this database together with the phylogeny of this clade, we studied the evolution of RBS, evaluating the existence of an ORBS by using models based on Ornstein-Uhlenbeck evolutionary process. Our results support the existence of multiple changes in the evolutionary regime of mammalian RBS, together with the existence of multiple ORBSs. The results show that the process of expanding the brain size of mammals is a highly complex process that does not correspond to be a universal one and which could be dominated by the presence of different ORBSs, modeled by different clado-dependent evolutionary histories

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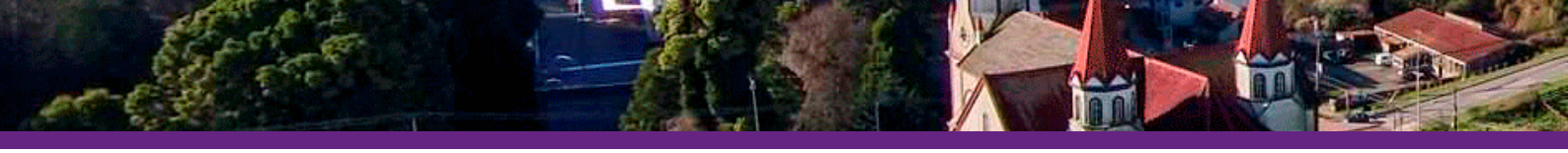

Population genetics of the trans Pacific haploid-diploid red alga (Gracilaria chilensis) and the effects of its cultivation in Chile

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Gracilaria chilensis is the only algae truly cultivated in Chile. Here, two kinds of populations coexist but differ in their habitat. Natural populations are usually sexual and fixed on rocky shores, while farms are asexual, free-floating or embedded in soft sandy substrate. We propose that cultivation may enhance changes in life history traits otherwise naturally linked to habitats characteristics and reproductive modes. Exploring two different types of molecular markers, SNP's (ddRAD) and microsatellites, we confirm high levels of clonality in most farms with widespread clones shared at a regional level. Furthermore, since hard and soft bottom habitats exhibit important differences in terms of turbidity, light intensity, desiccation, and level of burial/abrasion affecting the thalli, we hypothesized the presence of genetic differentiation to be associated with adaptive divergence between fixed and floating populations. 1206 variable SNPs, with 35 outlier loci, revealed that in Chile, regardless of the type of SNPs, genetic differentiation between locations was likely linked to habitat (estuaries vs rocky-platforms, with higher oceanic exposure) and the local history of the population (e.g., modified by earthquakes or human activities). Additionally, we investigated natural, free-floating populations, in New Zealand (NZ), where *G. chilensis* in not yet farmed/cultivated, to compare and explore whether the population structure in Chile is more likely linked to habitat/environmental conditions or cultivation/anthropogenic impact. In NZ, a system naturally lacking genetic and demographic signatures linked to cultivation practices, any discrepancy found between fixed vs. free-floating populations, would rather be linked to differences in habitat, further supporting our hypothesis.

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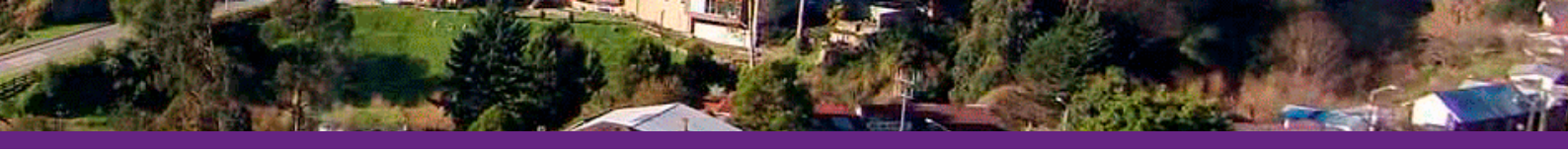

Testing the Island Rule in the sigmodontine rodent Abrothrix olivacea in Chilean Patagonia

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Islands represent natural scenarios to test evolutionary trends in the morphology of vertebrate taxa. For example, in mammals, a tendency to insular gigantism and dwarfism is predicted for small and big body size individuals inhabiting the mainland, respectively. This trend is named the "Island Rule" and could be explained in terms of the insular ecological release, immigration selection and resource limitation. The rodent *Abrothrix olivacea* is asmall sigmodontine mammal distributed from the south of Peru to the Chilean and Argentinian Patagonia. In the Patagonian range, this species is distributed along the mainland and nearby islands, setting a promissory scenario to test such evolutionary phenomenon. We hypothesize bigger body size of the insular individuals of *A. olivacea* in the Patagonian islands with respect to the mainland conspecifics. We measured standard body size and cranial traits with a digital caliper (± 0,02 mm precision) for a total of 75 individuals. Linear multivariate analyses were used to test our hypothesis (principal component analysis and discriminate analysis). In general, we did not observe significant differences between insular and mainland individuals. However, individuals from "Isla Wellington" resulted in significant bigger body sized in contrast to the mainland forms. Interestingly, individuals from such island have been recently considered a new subspecies of *A. olivacea (A. o. markhami).* **We discussed our results in terms of the historical migrations routes followed for this rodent** in the Patagonia. In order to corroborate our previous results, we are currently applying geometric morphometric tools on tree-dimensional cranial models.

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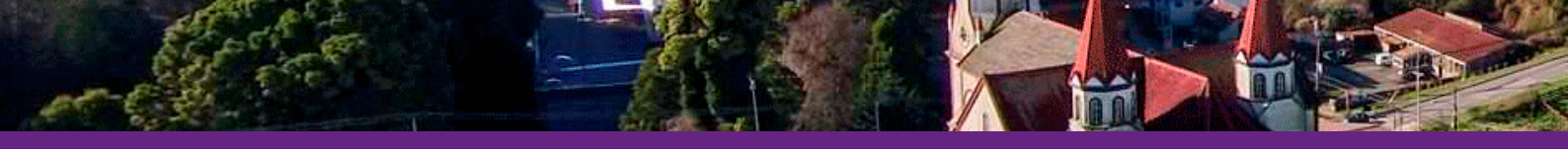

Evolutionary history of interdigital membrane and dynamics of the climate niche in the tropical salamander genus Bolitoglossa (Caudata: Plethodontidae)

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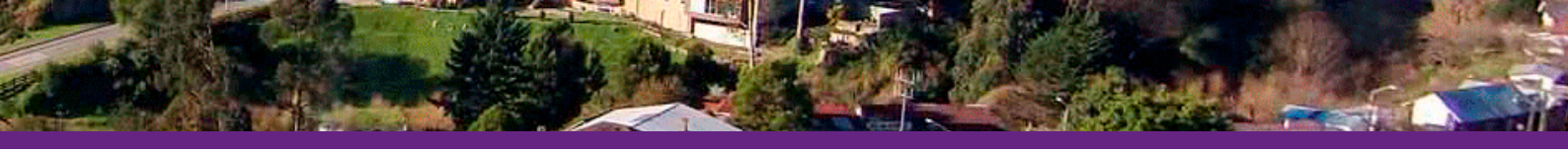
The tropical salamander of the genus *Bolitoglossa* is the most widely distributed within the family Plethodontidae, with 132 currently recognized species, whose distribution range from northeastern Mexico to Brazil; seven subgenera have been recognized and the monophyly of the genus is well supported by molecular data. However, studies to understand trait evolution and dynamics of the climate niche have not been evaluated. We carried out the divergence dating analyzes for 84 species of *Bolitoglossa* using mitochondrial DNA data (16S-CytB). For discrete traits we generated a matrix with characters related to the type of habitat use and foot traits. We fit a single-rate model and reconstruct ancestral states at internal nodes in the tree. We obtained the marginal ancestral states with an empirical Bayesian posterior probabilities. For evaluate the dynamics of the climate niche, we obtained 3440 occurrences for all species, then we extracted the values of climatic indexes. We perform a fast estimation of ML ancestral states and we estimated the variances and 95% confidence intervals for each node. Our results show that the free interdigital membrane represents the ancestral trait; moreover, there is a tendency to change from free to extensive membrane in arboreal habitats. With respect to the climate niche, there are two large groups with similar climatic ranges, the clades corresponding to the subgenus *Eladinae*, and basal clades of the *Bolitoglossa* phylogeny. However, it is necessary to evaluate in depth if climatic suitability can be a factor that has led to speciation within the genus.



Body size and phylogeny influence the geographical and bathymetric distribution of cephalopods

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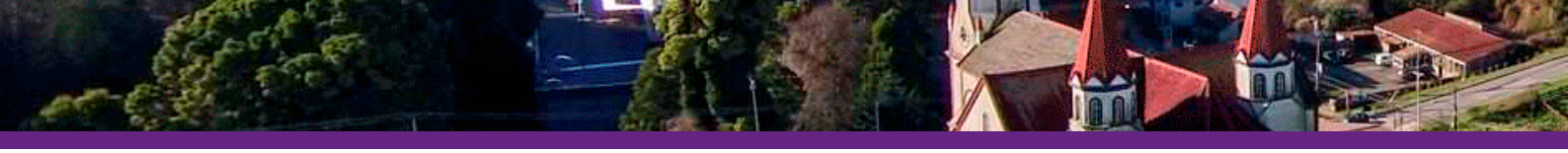
Macroecological studies have mainly focused on exploring the relationships between body size and geographical distribution at large scales, whether regional, continental or even global, with most of them being conducted on terrestrial species. Few studies have been carried out on aquatic species, and even less have considered the importance of phylogeny in the observed patterns. In this context, cephalopod mollusks possess large geographic and bathymetric ranges as well as a wide range of body sizes, which make them a very good study model to evaluate macroecological hypotheses. Here, we evaluated the potential relationships between body size (i.e. mantle length) with geographical (latitudinal range and area) and bathymetric (depth range) distribution of 43 species of cephalopods distributed worldwide. To test the macroecological hypothesis, we evaluated the phylogenetic signal and correlated evolution of previous traits (i.e. body size and distribution) to assess the role of ancestral-descendant relationships on the distribution of the cephalopods using a molecular phylogeny of the 43 species based on mitochondrial genomes. The analyses showed the existence of a relationship between body size and geographic and bathymetric distribution, where the area of distribution showed the best fit. In addition, significant differences were evidenced between benthic and pelagic species for both geographic and bathymetric distribution. Phylogenetic signals were high for all traits (body size and distribution). Geographic and bathymetric distribution of cephalopods evolved related to body size where larger cephalopods (e.g., jumbo squid, giant squid) have wide distributions and small size species (e.g., pygmy squid and octopus) have reduced distributions.



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Astrocytes from raphe obscurus nucleus contribute to the respiratory response to elevated CO2

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Homeostatic regulation of breathing is achieved through feedback information provided by peripheral and central respiratory chemoreceptors. Brainstem astrocytes are chemosensory interoceptors and they can release gliotransmitters in response to hypercapnia and acidosis. We addressed here whether astrocytes from the raphe obscurus (ROb) can modulate the respiratory response to hypercapnia *in vitro* and *in vivo*. In caudal brainstem slices obtained from neonatal CF1 mice, fictive respiration was recorded from the ventral respiratory column while were superfused with normocapnic (5% CO_2) or hypercapnic (10% CO_2) aCSF. Local acidification restricted to the ROb was performed by microinjection of aCSF-Pipes buffer (pH 6,5) during superfusion with either basal aCSF or aCSF containing fluoroacetate/glutamine (FA/Gln), a selective metabolic inhibitor of astrocytes, for 30 min. In conscious adult CF1 mice, injection of saline or FA/Gln was performed through a guide cannula, implanted 4 days before, into the ROb while ventilation was recorded by plethysmography during normocapnia or hypercapnia. Hypercapnia in slices increased the respiratory frequency (fR) in about 30% whereas local acidosis of the ROb with aCSF-Pipes increased this fR in about 21%. Application of FA/Gln reduced both the basal fR and the hypercapnia-induced increase in fR in about 20%. In conscious adult mice microinjections of FA/Gln, decreased the hypercapnia-induced ventilatory response in fR, tidal volume (V_T) and minute volume (V_E). These results are compatible with the notion that caudal medullary astrocytes from ROb are interoceptors mediating central chemoreception.

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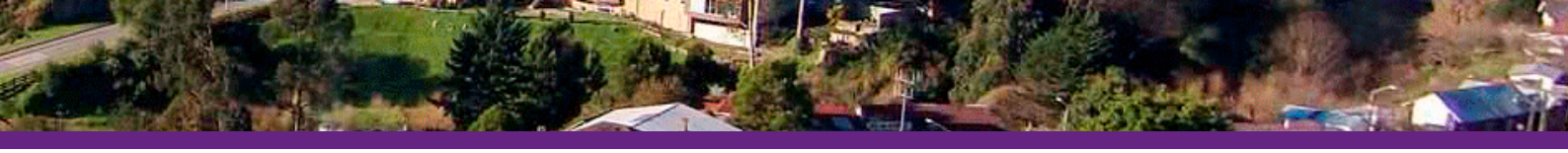

Avian thalamorecipient pallial cells indeed express a mammalian cortical phenotype

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Despite seemingly differences in cytoarchitecture and early gen patterning, avian and mammalian pallial territories exhibit structural similarities that point to share a common anatomical organization from early ancestry. The cell-type homology hypothesis, based on similarities in circuitry and neurochemistry, state that layer-specific cortical cell populations have specific equivalences with cell populations forming the nuclear masses of the avian pallial DVR. In the canonical neocortical circuit, layer 4 glutamatergic cells receive thalamic inputs and connect reciprocally, in a columnar fashion with cells in the upper layers 2 and 3. Similarly, in the avian DVR cells at the nucleus entopallium receive visually driven thalamic afferents and sustain columnar arranged reciprocal connections with cells in the intermediate nidopallium and ventral mesopallium. Interestingly, layer 4 specific molecular markers such as EAG2 (ether-a-go-go 2, a potassium channel gene) and RORβ (RAR-related orphan receptor beta, a transcription factor gene), as well as the vesicular glutamate transporter 2 (VGLUT2), are also expressed massively at the entopallium. At present, it is unknown whether the entopallial neurons expressing EAG2, RORβ and VGLUT2 are involved in the columnar projection circuit. We investigated such issue in chicks (*Gallus gallus*) by combining injections of a fluorescent retrograde neural tracer (CTB-AF555) into the entopallial targets, with fluorescent "*in situ*" hybridization. We found that most "column forming" entopallial cells were VGLUT2+ and also expressed EAG2 and RORβ. These results demonstrate that the avian forebrain contains cell types with connectional and molecular features of layer 4 cortical neurons, further supporting the cell-type homology hypothesis.

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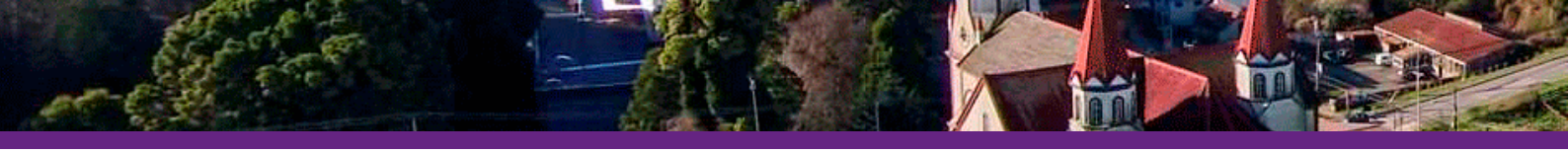

Envelope analysis as a tool for the identification of epileptic EEG patterns in rats

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Epilepsy has been mainly characterized by the occurrence of tonic-clonic seizures (TCS) but also by electroencephalographic (EEG) alterations, such as interictal activity during stages of sleep-wake cycle (SWC). There is little evidence available that has quantified the morphology and magnitude of these alterations. This research means to study the electroencephalographic abnormalities in an animal model of temporal lobe epilepsy induced by pilocarpine, using the Coefficient of Variation of the Envelope (CVE) of EEG, in order to characterize and quantify morfological alterations in SWC stages. Epilepsy was induced in 13 rats using a single dose of pilocarpine, while a second group of rats was used as control group. After being implanted for chronic polysomnography, all rats were recorded during two undisturbed days at least. A 4 hours sleep deprivation was performed on 6 epileptic subjects, in order to evaluate the time course of SWC alterations and its interaction with sleep homeostasis. Using envelope analysis, it is observed a global alteration of EEG morphology. Significative differences were found in delta and theta bands when epileptic and control groups were compared. Epileptic animals display almost complete abolition of sawtooth-shaped theta activity during REM sleep. In addition, a new pattern of synchronized slow waves (delta-s), that depart from the physiological delta of non-REM sleep, was found. At the same time, it is observed that delta-s describes the canonical homeostatic pattern of delta waves, suggesting that delta-s is part of non-REM sleep dynamics. This pattern of activity might be a new target to study epilepsy.

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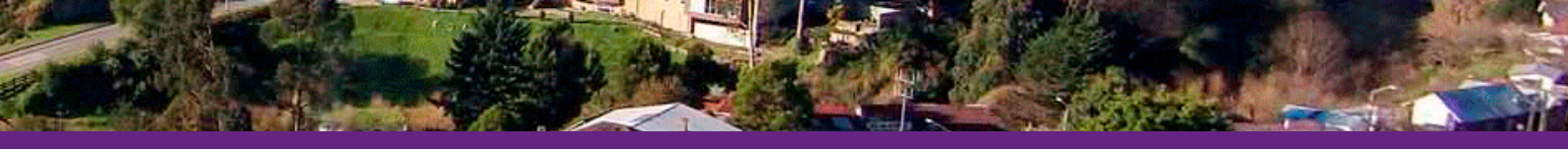

(NO SE PRESENTÓ)

Innocuous and noxious cold specificity emerge from the variability of slowly inactivating Shaker-like current density in a TRPM8-dependent model of peripheral receptor.

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In mammals, the cold-transducer channel TRPM8 is expressed in nociceptive and non-nociceptive peripheral axonal endings that differently encode innocuous and painful perceptions of cold, respectively. The cold detection threshold of these afferents is tuned by the expression of slowly inactivating voltage-gated K+ currents of Shaker-like channels (I_{KD}), and the deficient expression of these channels after nerve injury is linked to the development of axonal hyperexcitability and hyperalgesic states. It is unknown how I_{KD} affects the dynamics of the cold-evoked response and action potential firing of TRPM8-expressing peripheral axonal endings. Using a computational approach, we study this problem in a conductance-based model of TRPM8-dependent cold receptor containing I_{KD}, were the functional expression of this current is represented in the parameter controlling its maximal density. We have shown that reducing I_{KD} alone can shift the detection threshold of the response to cold stimuli, producing changes in cold sensitivity like those observed in rodent models of peripheral nerve injury. The analysis of the model revealed that, above a certain density range, I_{KD} affects the cold-evoked response through a change in the dynamics of action potential (AP) initiation. Bifurcation analysis shows that a large density of I_{KD} introduces a qualitative difference in the dynamics of the model, by changing a saddle-node bifurcation (Class I excitability) into a subcritical Hopf bifurcation (Class II). Our results establish a dynamical basis by which fast currents with no intrinsic temperature-dependency could participate in encoding cold stimuli as innocuous or noxious in TRPM8-expressing afferents.

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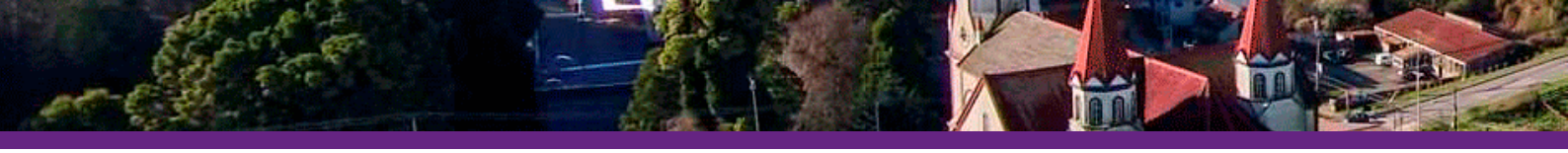

Connectivity structures shape bistable collective cortical dynamics on a large-scale model

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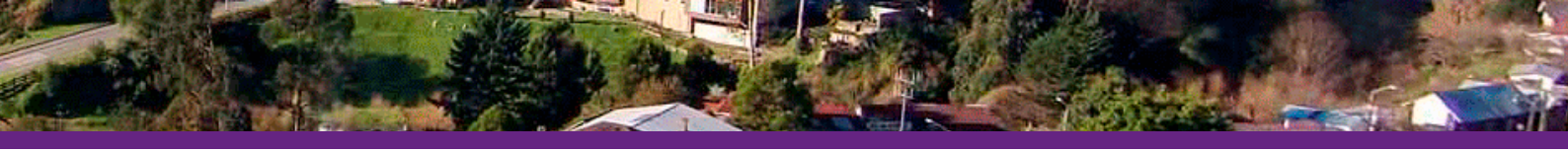
Large-scale brain models have been used to study cortical activity, in which the long-distance connections between areas are from diffusion imaging studies while local dynamics derive from mean-field model. The collective dynamics of the model show at least two cortical activity states within a window of coupling gain, G. The bistable dynamics arise between the bifurcations at the minimum (G_-) and maximum (G_+) values. However, which structures contribute to sustain and shape the collective cortical dynamics has not been elucidated yet. We studied the collective dynamics from three models based on known network properties: small-world network, degree-preserving network and a connectivity pattern version of Human network. To account for the local and global connectivity structures on the networks, we used the degree and k-core decomposition, respectively. We removed connections from either sparsely (low degree/ not belong to critical k-core) or highly (high degree/ belong to critical k-core) connected structures, and next, we compared their effect on the bifurcation G_- and G_+. We find that bistable dynamics in Human cortex depends partially on the specific weight of the connections. In structural models, the increase of node activity at the bifurcations correlates both with a high degree nodes and a critical k-core sub-network. The sustain of the two cortical states depends on subsets of highly connected nodes and sub-networks. Therefore, it is necessary to consider the network properties and their connectivity structures when investigating states in collective cortical dynamics.



Characterization of the voltage-gated proton channel currents on myeloid-derived suppressor cells

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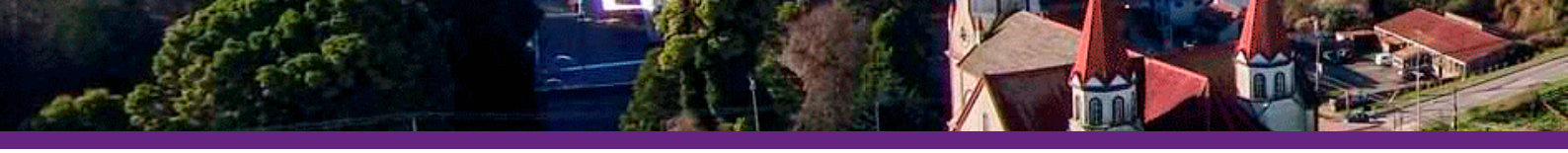
Myeloid-derived suppressor cells (MDSCs) are a cell population with a heterogeneous phenotype and high immunosuppressive activity. The presence of MDSCs on the tumor microenvironment promotes progression and metastasis of cancer by suppression of the immune response. One of the molecular mechanisms behind the suppressive activity of MDSCs involves the activity of NADPH oxidase, an enzyme whose function has been previously demonstrated requires the presence of voltage-gated proton channel (Hv1) in other cells of the immune system as macrophages, dendritic cells and granulocytes. Previous data obtained in our laboratory confirmed the presence of Hv1 on these cells by flow cytometry and immunofluorescence. In order to determine if Hv1 expressed in MDSCs is functional, we performed a biophysical characterization of their proton currents. MDSCs were obtained *in vitro* by culturing progenitor cells from the bone marrow of healthy C57BL/6 mice in media supplemented with granulocyte-macrophage colony-stimulating factor (GM-CSF) for four days. Proton currents were measured the fourth day of culture by the whole-cell patch-clamp technique. MDSCs currents were voltage- and pH-dependent with slow kinetics of activation. Our results suggest a high proton selectivity channel that additionally, is strongly inhibited by Zn+2 and 5-Cl-2-GBI. These results agree with the presence of a functional dimeric Hv1 in MDSCs, which we propose is intimately related to the immunosuppressive function of these cells. Acknowledgements: Fondecyt 1180464to C.G., 1150273 to R.L. and CINV as Millennium Institute supported by the Millennium Scientific Initiative.



Gating charge displacement in a monomeric voltage-gated proton (Hv1) channel

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Voltage-gated proton (H_v1) channel, a voltage sensor and a conductive pore contained in one structural module, plays important roles in many physiological processes. Voltage sensor movements can be directly detected by measuring gating currents, and a detailed characterization of Hv1 charge displacements during channel activation can help to understand the function of this channel. We succeeded in detecting gating currents in the monomeric form of *Ciona*-Hv1 channel. To decrease proton currents and better separate gating currents from ion currents, we used the low-conducting Hv1 mutant N264R. Isolated ON-gating currents decayed at increasing rates with membrane depolarization, and the amount of gating charges displaced saturates at high voltages, two hallmarks of currents arising from the movement of charged elements within the boundaries of the cell membrane. The kinetic analysis of gating currents revealed a complex time course of the ON-gating current characterized by two peaks and a marked Cole-Moore effect. Both features argue that the voltage sensor undergoes several voltage-dependent conformational changes during activation. However, most of the charge is displaced in a single central transition. Upon voltage sensor activation, the charge is trapped and only a fast component that carries a small percentage of the total charge is observed in the OFF. We hypothesize that trapping is due to the presence of the arginine side chain in position 264, which acts as a blocking ion. We conclude that the movement of the voltage sensor must proceed through at least five states to account for our experimental data satisfactorily.

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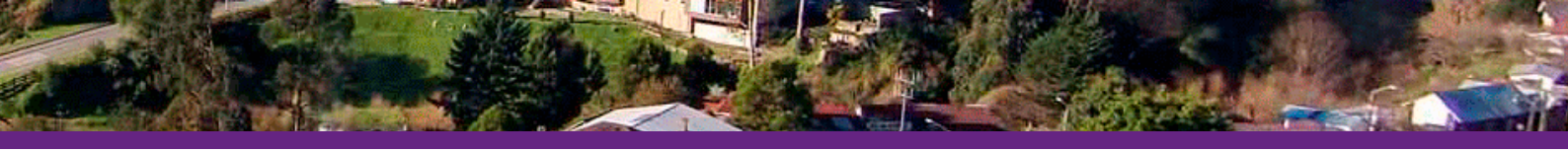

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Metabolic-modeling based on brain proteomics and transcriptomics of aged astrocytes allows characterizing mechanisms of aging

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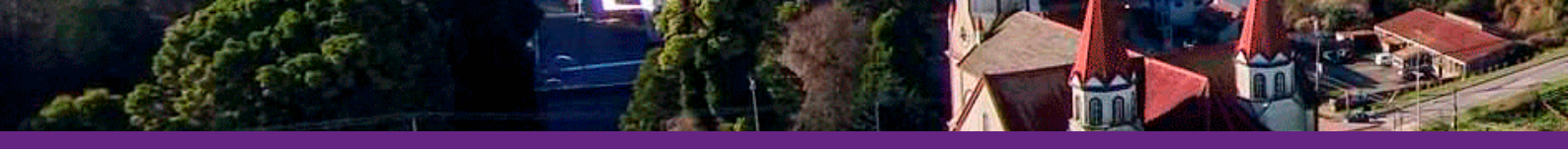
Introduction:
The neuron-astrocyte metabolic module is characterized by regulation of energy and glutamate metabolism in astrocytes during neuronal activity. Astrocytes exposed to activity-related potassium and glutamate rising induce glycolysis and suppress oxidative phosphorylation, while they uptake glutamate and convert it to glutamine to subsequently shuttle it back into neurons. These mechanisms allow augmenting oxygen availability for neurons and avoiding glutamate excitotoxicity. Recent transcriptomics studies on aging astrocytes have revealed lowered expression of respiratory chain components and glycolytic enzymes, while over-expressed glutamate dehydrogenase.

Objective:
This work aims at determine how those astrocytic age-related changes affect the neuron-astrocyte metabolic module from an *in-silico* modeling perspective. Methods: A flux model for the neuron-astrocyte module based on mouse brain-cell specific proteomics was build using linear optimization techniques. Aging-related changes from astrocyte transcriptomics were added to the model as perturbed weights in the objective function. Attainable metabolic phenotypes were calculated for a range of oxygen and glucose uptake rates.

Results:
Aging strongly impaired astrocytic ATP production both from glycolysis and oxidative phosphorylation. Remarkably, glutamate fate in astrocytes shifted from glutamine efflux to Krebs cycle, possible to compensate lowered ATP synthesis.

Conclusion:
Omics-based reconstruction of the neuron-astrocyte flux network allowed characterizing possible mechanisms of aging, particularly those related to impaired energy and disrupted glutamate/glutamine cycle.

This research was supported by grant 15150012 from FONDAP Program to CG-B. Also, the supercomputing infrastructure (Leftraru cluster) of the National Laboratory for High-Performance Computing (NLHPC; ECM-02) of the Center for Mathematical Modeling (CMM) at the University of Chile partially supported this research.

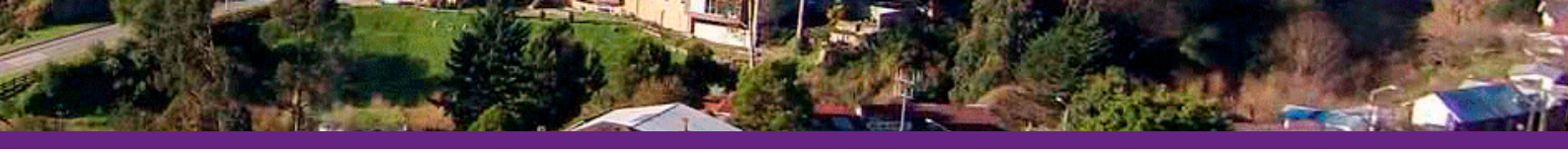


A computational study of the single nucleotide polymorphism of bdnf leading to the v66m mutant

Bernal Yanara A.[1], **Matute Ricardo A.**[1,2]. [1]Departamento de Ciencias Químicas y Biológicas, Universidad Bernardo O´Higgins. [2]CIBQA, Universidad Bernardo O`higgins. (Sponsored by Ricardo A. Matute Morales)

The precursor of BDNF (proBDNF) is synthesized and processed in the endoplasmic reticulum and Golgi, been enzymatically cleaved by intracellular (furin) or extracellular (metalloproteinase-2, -9, plasmin) proteases. A polymorphism of BDNF (V66M), located in the prodomain of BDNF, which interacts with the p75NTR, has been associated with cognitive disorders. The V66M affect the release of mBDNF, but effects on the processing are unclear. In this work, BDNF homology models were constructed, on which molecular dynamics (MD) of three replicates were performed for 50 ns. In order to assess critical interactions, computational calculations of quantum chemistry were performed, considering interactions with the sidechains of the surrounding residues in a radius of 10Å centered in the Valine/Methione mutation. Our calculations suggest that the interactions of electrostatic nature are critical for the functionality of the molecule. Docking and MD of the BDNF-MMP9, BDNF-Furin and proBDNF-p75NTR were performed to qualitatively compare and characterize the differences in the binding of the native and mutant protein. The mutant shows fluctuation patterns with fewer hydrogen bridges, and exist difference in the interaction of the mutant molecule with furin, MMP9, and p75NTR, when compared to the native structure. Overall, our studies in silico suggest that the mutated proBDNF can be involved in the activation of the p75NTR that induced LTD. In addition, with this computational analysis, it was possible to suggest structural and dynamic protein/protein and protein/receptor changes in the processing of the mutant BDNF, results allow to understand the effects of this mutation in memory and learning.

This work was funded by the FONDECYT Grant No. 1181260. We also acknowledge the National Laboratory of High Performance Computing NLHPC (ECM-02).

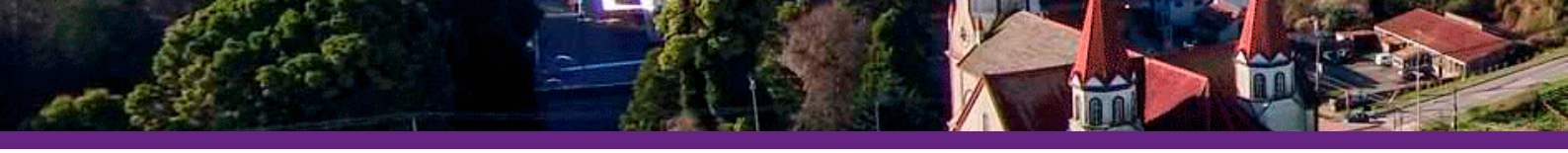


Marsupial in vivo assays illuminate the development and evolution of neocortical circuits

Suárez Rodrigo[1]. [1]Queensland Brain Institute, The University of Queensland. (Sponsored by Rodrigo Suárez)

The six-layered neocortex integrates sensory-motor functions, and mediates higher-order cognitive processes such as attention, learning and language. However, subtle defects in cortical circuit formation can lead to conditions such as autism, attention deficit disorders and schizophrenia. Most of our knowledge on healthy and pathological cortical development comes from studies in rodents and primates, as only mammals evolved a neocortex. However, important questions remain open due to the lack of experimental paradigms to study its early development, inside the uterus, *in vivo*. Here I will present a marsupial model of extra-uterine cortical development (inside the pouch), the Australian fat-tailed dunnart (*Sminthopsis crassicaudata*). Dunnarts breed very well in captivity and allow multiple events of cell-specific gene manipulation with unprecedented detail as compared to rodents, as their cortex develops mostly postnatally. Their cortical connectome shows conserved mammalian features, despite the absence of a corpus callosum, and the transcriptional control of neocortical development suggests a molecular logic that arose before the split of modern Therian lineages. Moreover, the skull of pouch-young dunnarts is highly translucent, hence very amenable for optical monitoring and control of neocortical neuron activity at stages equivalent to prenatal humans and rodents. In-pouch electroporation of GCaMP6s in cortical pyramidal neurons, followed by two-photon imaging *in vivo*, reveal patterns of calcium activity shared with rodents and humans. These features highlight the potential impact of laboratory marsupials to study the genetic and environmental influences on cortical development, while also providing important clues on the evolution of developmental systems in the brain.

Australian Research Council (Discovery Early Career Researcher Award, DE160101394; Discovery Project, DP160103958)



Prodromal sleep signs of Parkinson's Disease in 22q11 Microdeletion Syndrome patients: Envelope Analysis of Rapid Eye Movement (REM) sleep electromyogram

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The damage of neural mechanisms responsible of physiological muscle atonia that normally occur during REM sleep, provoke a pathological condition known as REM sleep behavior disorder (RBD), whose cardinal sign is REM sleep without atonia (RWA). RWA is a prodromal manifestation of Parkinson's Disease (PD) as largely anticipates other pathological motor signs. Evidences support that 22q11 microdeletion syndrome (22q11DS) patients present higher risk for early onset PD. The aim of present report is to compare sleep electromyogram (EMG) in 22MDS patients with healthy controls and patients diagnosed with RBD, by means of EMG envelope analysis. One full-night video-polysomnographic (v-PSG) record was successfully obtained in seven 22q11DS adult patients and eight healthy controls. Polysomnographic records of seven RBD patients were also analyzed. The envelope analysis of the EMG evaluate magnitude of muscle tonus and phasic activity by means of the envelope amplitude (EA) and coefficient of variation of the envelope (CVE) respectively. Whole night 30-second epochs of EMGs were projected in a CVE vs. EA phase portrait. The EMGs portraits were mapped to discriminate high-tone+phasic region respect to the atonia+non-phasic region. REM sleep epochs of healthy controls cluster in the atonia+non-phasic region, whereas that of RBD patients invade the high-tone+phasic region. Three of seven 22q11DS patients exhibit a RBD-like phase portrait for chin. Forearms of controls and 22q11DS present similar EMG portraits and differ from RBD patients. 22q11DS patients may have prodromal RBD manifestations according to chin EMG envelope parameters.

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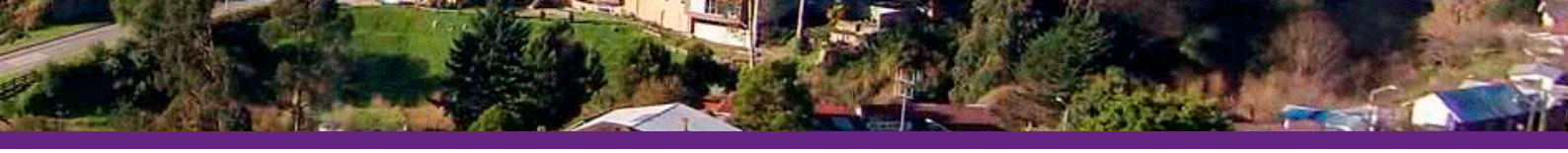

Polyunsaturated fatty acids increase the activity of pannexin 1 channel via free fatty acid receptors.

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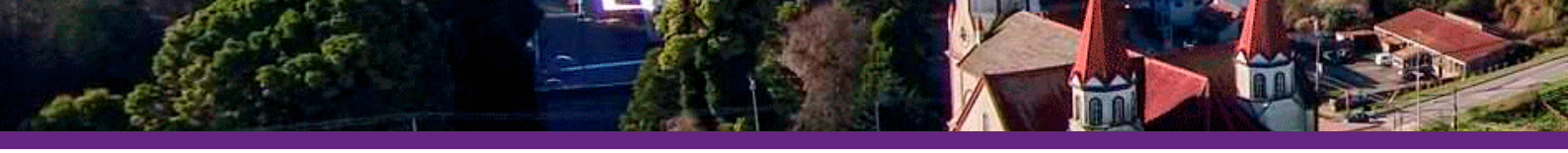
Background:
Free fatty acids (FFAs) regulate diverse cellular functions. Also, several free fatty acid receptors (FFARs) have been identified. In particular, FFAR1 and FFAR4 are activated by medium- and long-chain FFAs. Pannexin 1 (Panx1) is a glycoprotein expressed in diverse organs and tissues, such as adult skeletal muscle, and can formed channels (Panx1-Ch) permeable to ions and small signaling molecules. Panx1 channel is known to play critical roles in maintaining functional integrity of diverse tissues. Here, we evaluated the regulation of Panx1-Ch activity induced by FFAs via FFARs.

Methods:
Skeletal muscles obtained from wild type (WT) and KO-Panx1 (KO) mice were used. Also, HeLa-Panx1 cells were used. The expression of Panx1, FFAR1 and FFAR4 were evaluated by PCR. The activity of Panx1-Ch was estimated by evaluating the cellular uptake of ethidium (Etd). The polyunsaturated FFAs, linoleic acid (LA) and alpha-linolenic acid (ALA), were used. GW5908 and GW1100, agonist and antagonist of FFARs, respectively, were used.

Results:
Skeletal myofibers isolated from WT mice showed expression of Panx1, FFAR1 and FFAR4 mRNA. Also, myofibers isolated from WT mice showed increase of Etd uptake upon treatment with LA (100 μM) or ALA (100 μM). This response was not detected in myofibers isolated from KO-Panx1 mice. Moreover, HeLa-Panx1 cells showed increase of Etd uptake upon stimulation with LA, ALA or GW9508 (100 μM), which was blocked by GW1100 (20 μM).

Conclusion:
LA and ALA increase the activity of Panx1-Ch through a FFAR-dependent pathway.

Funded by FONDECYT: 11160536 (CP); 1150291 (JCS); ICM-Economía P09-022-F (JCS).



Mucins expression in Clara cells of distal airway associated to increase in expression of Notch1/Hes1 during primary infection by *Pneumocystis carinii*

Méndez Andrea [1], Rojas Diego Andrés[1], Ponce Carolina Angélica[1], Bustamante Rebeca[1], Vargas Sergio Luis[1] (1) Laboratorio de Infecciones Respiratorias, Programa de Microbiología y Micología, ICBM, Facultad de Medicina, Universidad de Chile

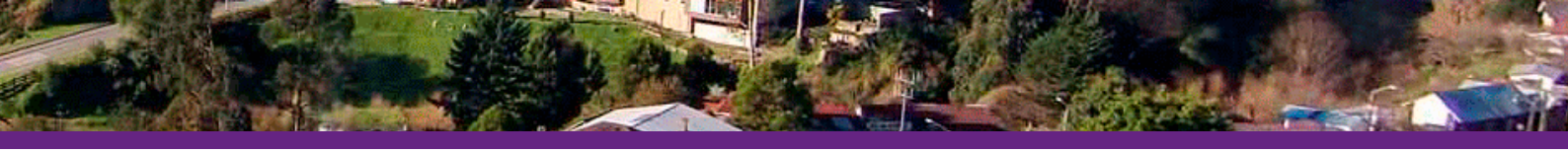
Introduction:
Clara cells can originate goblet cells by transdifferentiation, which is regulated by Notch. It has been demonstrated that this mechanism is associated to increase in goblet cells in modls of asthma, however this has not been studied in *Pneumocystis*infection. Due to distal airway is lacking of goblet cells, we aimed to determine coexpression of Clara and goblet cells markers in distal airway along with its association with changes in Notch signaling during primary infection by *Pneumocystis.*

Methods:
Frequency of Clara and goblet cells, colocalization of CC10 and MUC5B markers, from Clara and goblet cells, respectively, and mitosis by IIF and confocal microscope, along with levels and expression of CC10, MUC5B, Notch1 and Hes1 by western blot and qRT-PCR were measured in lungs of immunocompetent rats infected by *Pneumocystis.*

Results:
Frequency of goblet cells in distal airway was increased in infection (p=0.0036). These cells expressed MUC5B. mRNA levels of MUC5B showed a 2.7 fold increase (p=0.0275). No differences were observed in frequency of Clara cells, whereas mRNA levels of CC10 were increased (p=0.0006) and peptidic levels of CC10 were reduced (p=0.0118). Colocalization of CC10/MUC5B in epithelium of distal airway was observed in infection, with no evidence of mitosis. mRNA levels of Notch1 and Hes1 were increased in infection (p=0.0031 y p=0.0127).

Conclusion:
Primary infection by*Pneumocystis*was associated with increase in goblet cells, colocalization of CC10 with MUC5B in distal airway, and increase in expression of Notch1/Hes1, suggestive of cellular transdifferentiation.

FONDECYT Regular 1140412

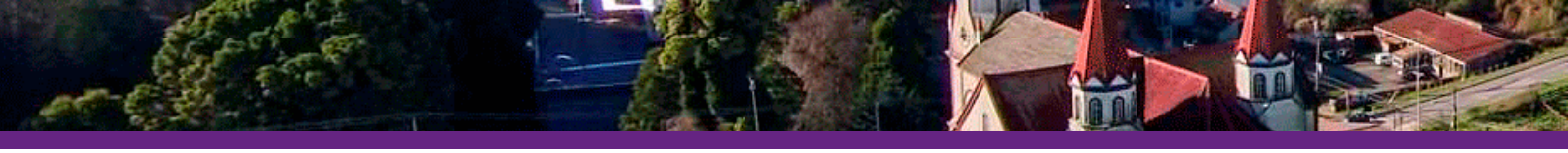


Pro-inflammatory cytokines are highly expressed in astrocytes located in the nucleus of the solitary tract of rats exposed to chronic intermittent hypoxia

Oyarce Maria Paz[1], Iturriaga Rodrigo [1](1) Laboratorio de Neurobiología, Ciencias Biologicas, Pontificia Universidad Católica de Chile

Chronic intermittent hypoxia (CIH) is the main risk factor for develop systemic hypertension in obstructive sleep apnea. We propose that CIH enhances the carotid body (CB) chemosensory drive to the brainstem and hypothalamic nuclei related to the cardiorespiratory control, such as the nucleus of the solitary tract (NTS), producing oxidative stress and inflammation. Thus, we studied if CIH increases IL-1β, IL-6 and TNF-α in the caudal portion of NTS, the primary site of CB inputs. Male Sprague-Dawley rats (250 g) were exposed to CIH (5% O2, 12 times/h, 8 h/day) for 7-28 days. Rats were euthanized, and brains were removed and processed to measure proinflammatory cytokines in the cNTS by immunofluorescence, and their co-localization with neurons (NeuN) or astrocytes (GFAP). Chronic activation of neurons in the cNTS was measured by FosB immunofluorescence. The immunofluorescence analysis showed a significant increase of IL-1β, IL-6 and TNF-α after 28 days of CIH in the cNTS compared to control rats. Co-localization studies showed that pro-inflammatory cytokines were highly expressed in astrocytes compared to neurons. In addition, we found a significant increase the number of FosB positive neurons in the cNTS of rats exposed during 28 days to CIH. Present results suggest that pro-inflammatory cytokines may be involved in the maintenance of hypertension in the cNTS of CIH-exposed animals.

FONDECYT 1150040



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Effect of cortisol on the immune activity of skeletal muscle cells of rainbow trout (Oncorhynchus mykiss) challenged in vitro with Piscericketia salmonis

Carrizo Victoria Belen[1], Valenzuela Cristián[1], Aros Camila[1,2], Altamirano Claudia[2], Valdés Juan Antonio[1], Molina Alfredo[1]. [1]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias de la Vida, Universidad Andrés Bello. [2]Laboratorio de Cultivos Celulares, Escuela de Ingeniería Bioquímica, Pontificia Universidad Católica de Valparaiso.

The rainbow trout is the second species with the highest commercial value after the Atlantic salmon in Chile. Skeletal muscle is the bigger tissue in fish and is the final product of the industry. This tissue can be affected by the stress generated during aquaculture activities, which could decrease the immune system, and generate an increase of the rates of infection due pathogens. Recently, our research group reported that skeletal muscle is able to respond against infections by pathogens and is an important focus of immune reactions in fish. Studies have shown the immunosuppressive effect of stress in lymphoid organs, however, there is few antecedents that relate skeletal muscle as an organ with immune activity and there is no data about the effect of the stress in this activity. In this context, the objective of this work was to determine the effect of cortisol over the innate immune activity of skeletal muscle cells of trout challenged with *Piscericketia salmonis*. Primary cultures of trout myoblasts were performed and treated with cortisol (100 ng / ml) for 1 hour. Later, the cells were challenged with *P. salmonis* for 4, 6 and 8 hours. The expression level of genes associated with the innate immune system and genes involved in the glucocorticoid pathway were evaluated by qPCR. An up-regulation of the molecules associated with stress and the cytokine suppressor molecules was observed, while the expression of the genes of the innate immune system corresponding to anti/proinflammatory cytokines were down-regulated

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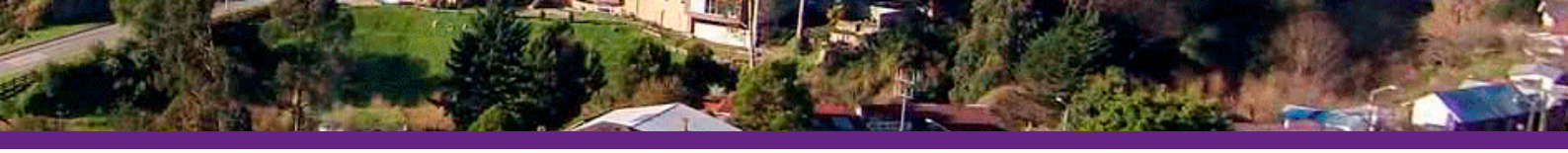
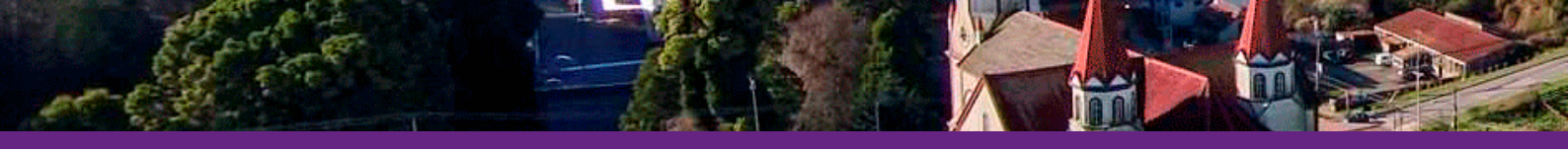


Evaluation of the non-genomic effects of cortisol on the activation of the PKA and PKC signaling pathways in rainbow trout myotubes (Oncorhynchus mykiss)

Figueroa Consuelo Pilar Verena[1], Aedo Jorge[1], Fuentes Marcia[1], Boltaña Sebastian[2], Molina Alfredo[1], Valdés Juan Antonio[1]. [1]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias de la Vida, Universidad Andrés Bello. [2]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción.

Glucocorticoids are critical regulators of cellular processes that allow vertebrates overcome to different stressors. In teleost, cortisol is the main circulating glucocorticoid and it is involved in the metabolic and physiological response to stress. Cortisol exerts its cellular effects through two distinct mechanisms: genomic and non-genomic signalling pathways. The genomic signalling has been extensively studied, whereas the non-genomic, on the other hand, is far from clear. Among the pathways that are potentially involved in this non-genomic signalling are PKA and PKC. However, the regulation of PKA and PKC signalling pathway owing this alternative action of cortisol in the skeletal muscle is unknown. Therefore, in this work we evaluated the impact of non-genomic cortisol action over PKA and PKC activation in rainbow trout myotubes. Rainbow trout myotubes were differentiated *in vitro* until day 12 and treated with physiological doses of cortisol or cortisol-BSA. Cortisol-BSA is a membrane impermeable analogous of cortisol, exclusive inductor of non-genomic action. Then, total proteins were extracted from myotubes and a Western blot was carried out against phosphorylated substrate of PKA and PKC. We found differences on the level of phosphorylation of PKA and PKC substrates in myotubes incubated 60 minutes with cortisol and cortisol-BSA comparing to vehicle. These results suggest that both PKA and PKC signalling pathways are modulated through the non-genomic cortisol action in fish myotube.

FONDAP 15110027, FONDECYT 1171307, and FONDECYT 1171318



Genomic scale identification of target genes of the transcription factor Mig1 in the context of glucose repression.

Valenzuela Luis Alfonso[1], Sepúlveda Dionisia [1,2], Baeza Marcelo[1,2], Alcaíno Jennifer [1,2], Cifuentes Victor[1,2]. [1]Departamento de Ciencias Ecologicas, Facultad de Ciencias, Universidad de Chile. [2]Centro de Biotecnología, Facultad de Ciencias, Universidad de Chile.

In yeast, the presence of glucose in the culture media inhibits the transcription of a set of genes, a mechanism known as catabolic repression, which is mediated by the transcription factor Mig1. In order to identify, on a genomic scale genes, that are regulated by Mig1, a chromatin immunoprecipitation assay followed by next-generation sequencing (ChIP-seq) was performed. For this, the two native *MIG1* alleles of a *X. dendrorhous* wildtype strain, were replaced by homologous versions fused to a sequence encoding for the FLAG3x epitope, which is recognized by a commercial anti-FLAG3x monoclonal antibody. After 36 hours of culture using glucose as the sole carbon source, the ChIP-seq assay was performed to identify the regions of the genome to which the transcription factor Mig1 binds *in vivo*. These regions were compared to the location of genes that showed differential expression by RNA-seq assays between the wildtype and the *mig1-* mutant strains of *X. dendrorhous* . The R/Bioconductor software was used to analyze the RNA-seq data and it was found that 365 genes presented a differential expression. On the other hand, using the MACS2 software and the ChIP-seq data, it was determined that Mig1 binds to 671 regions in the genome. When crossing both results, genes encoding proteins involved in several functions stand out; for example, the major facilitator superfamily (*mfs*), ABC transporters, urea transporters and gilcosyltransferases. These results allow us to determine which genes are directly regulated by Mig1 binding in order to infer gene regulatory networks as a next step.

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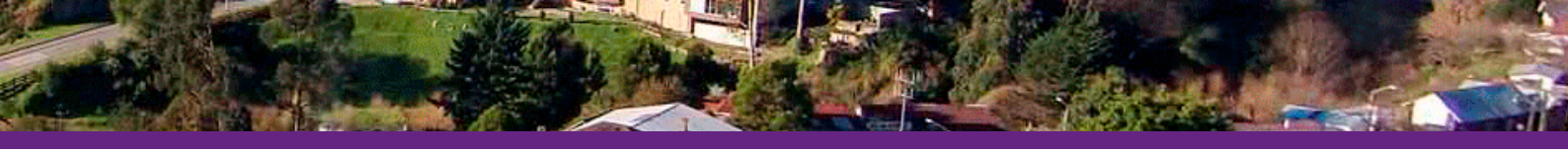

The pangenome of Leishmania spp: a comparative genomic study

Martinez J. Eduardo[1,2,3], Molina Cristian[2,4], Nourdin-Galindo Guillermo[2,5], M. Martin Alberto J.[3], Maracaja-Coutinho Vinicius[2]. [1]Programa de Doctorado en Genomica Integrativa, Vicerrectoria de Invesitigacion, Universidad Mayor. [2]Advanced Center for Chronic Diseases - ACCDiS, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile. [3]Network Biology Laboratory, Centro de Genomica y Bioinformatica, Ciencias, Universidad Mayor. [4]Lircaytech. [5]Instituto de Bioquímica y Microbiología, Facultad de Ciencias, Universidad Austral. (Sponsored by Vinicius Maracaja-Coutinho)

Leishmania comprises about 30 described species, of which around 20 are infective for humans. Reported annual infections vary from 0.7-1.3 million for cutaneous leishmaniasis and between 200,000-400,000 cases for visceral leishmaniasis. Focusing on the evaluation of structural and functional divergences within leishmania species, we performed a pangenomic analysis of 26 strains belonging to 16 species available at complete genome/chromosome level in TriTrypDB and NCBI, identifying metabolism signatures for different groups of *Leishmania* spp. We employed novel ORF predictions using three different algorithms, and carried out functional annotations with an in house pipeline against a myriad of public databases. Predictions were validated using RNAseq data. Finally, we implemented a pipeline based on presence-absence binary matrix which were used to define the pangenome of Leishmania genus. We found an open pangenome composed by 15,987 genes, with a core genome of 3,223 (20.2%) genes shared within all genus, and an auxiliary genome composed by 6,165. Using metabolic pathways enrichment, we found that most of the unique genes are mainly involved in cellular processes and mechanisms of response and adaptation to different environments, as well as, host specific virulence factors. Furthermore, we were able to identify different genes subsets shared and unique to species with distinct clinical manifestations and evolutionary history. This study could be useful for the future development of specific diagnosis tests, as well as for the identification of target genes for vaccines and therapeutics development.

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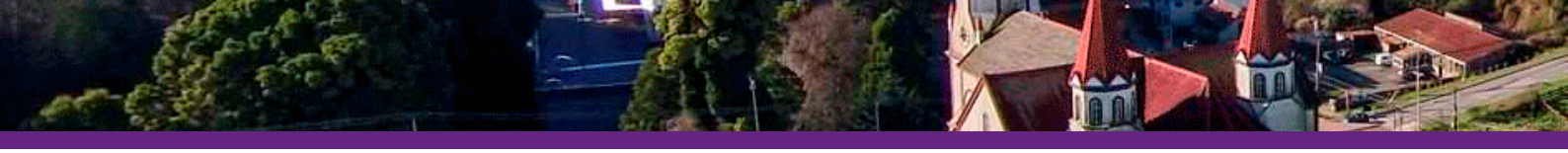
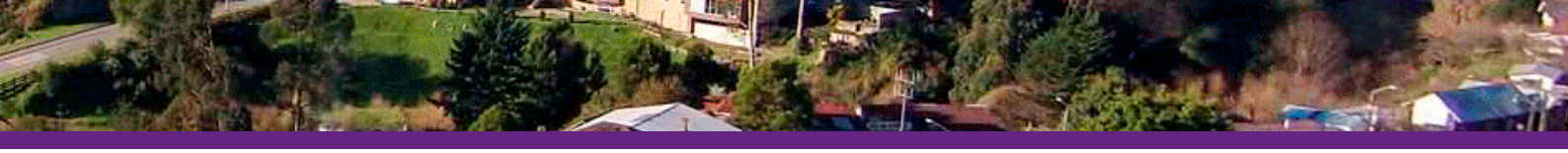


Origen independiente y retención diferencial de genes nodal y factores de diferenciacion del crecimiento en vertebrados

Opazo Juan C.[1], Zavala Kattina[1], Toloza Jessica[1]. [1]Instituto de Ciencias Ambientales y Evolutivas, Facultad de Ciencias, Universidad Austral de Chile. (Sponsored by Juan C. Opazo)

Los factores de diferenciación de crecimiento 1 (GDF1) y 3 (GDF3) así como los genes nodales son miembros de la superfamilia del factor de crecimiento transformante (TGF-β) que están involucrados en procesos fundamentales de desarrollo temprano que estan conservados en los vertebrados. La historia evolutiva de estos genes todavía está en debate debido a las definiciones ambiguas de las relaciones homólogas asi como el número de linajes de genes existentes. El objetivo de este estudio fue desentrañar la evolución de los genes GDF1, GDF3 y nodales de los vertebrados, haciendo hincapié en la comprensión de las relaciones de homología, número de linajes y su origen evolutivo. Nuestros resultados revelaron que los genes GDF1 y GDF3 encontrados en anuros y mamíferos son productos de eventos de duplicación independientes de un gen ancestral en el ancestro de cada uno de estos linajes. La principal implicación de este resultado es que los genes GDF1 y GDF3 de anuros y mamíferos no son ortólogos 1: 1. Por otra parte Nuestros resultados mostraron que existirían dos linajes de genes nodales los cuales habrían sido retenidos diferencialmente durante la historia evolutiva del grupo.

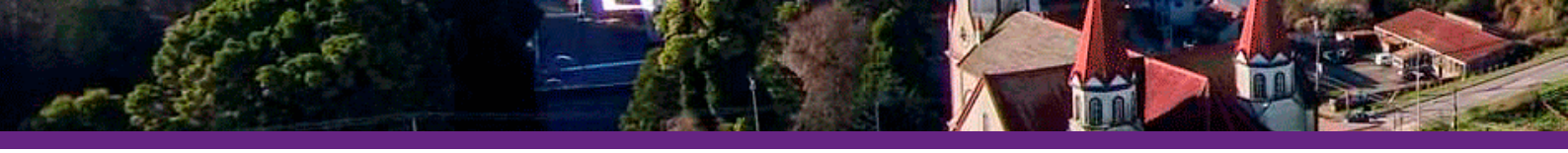
FONDECYT 1160627



Evolution of Average Shape, disparity and allometry in the ground beetle genus Ceroglossus

Benitez Hugo[1], Püschel Thomas[2]. [1]Departamento de Recursos Ambientales, Facultad de Ciencias Agronomicas, Universidad de Tarapacá. [2]School of Earth and Environmental Sciences, University of Manchester.

Ground beetles, are one of the largest groups in Coleoptera, containing more than 40.000 species described from around the world. Many of them are adapted to their terrestrial lifestyle and lose their ability to fly by decreased flight muscle power, jointed elytron, and devolution of wings.In the present research, a particular small group of ground beetles from Chile and Argentina belonging to the genus *Ceroglossus* (8 sp) (Coleoptera: Carabidae) were studied.The aim of this study is to address two questions regarding the evolution of body shape in a comparative context: 1) does the *Ceroglossus* body shape evolve across the genus? and 2) Is there any evolutionary influence of the allometry in the shape diversification of the genus*?* To study these morphological changes, geometric morphometrics as a tool for analyzing shape variation was used.Moreover, we also used comparative methods for mapping the shape data onto the phylogeny. The phylomorphospace shows minimun overlaps in the shape space with few possible homoplasy as the *Ceroglossus ochsenii* and *C. guerini*. It is noticeable that the level of the phylogenetic signal was lower than expected (p value: 0.052), nevertheless the reason of this could be related to the number of species of the genus related and the number of individual per species was lower in few groups. Future field work are needed for more concise conclusion. The methods applied in this study were useful for a first exploration of the pattern of shape evolution and allometry, as well as their evolutionary significance.



Evaluation of protein-protein interaction between the Dap1 and the cytochrome P450 enzyme Cyp61 in Xanthophyllomyces dendrorhous

González Ana María[1], Gómez Melissa[1], Barahona Salvador[1], Sepúlveda Dionisia[1], Baeza Marcelo[1], Cifuentes Víctor[1], Alcaíno Jennifer[1]. [1]Ciencias Ecológicas, Ciencias, Universidad de Chile.

Xantophyllomyces dendrorhous is a basidiomycete yeast of commercial interest as it produces the carotenoid astaxanthin. In this yeast, three cytochrome P450 enzymes have been characterized: Cyp51 and Cyp61, involved in ergosterol biosynthesis and CrtS, involved in astaxanthin biosynthesis. In organisms such as *S. pombe*, a positive regulator of P450s has been described, named as Dap1 (*Damage activated protein 1*), which is involved in the ergosterol synthesis. In *X. dendrorhous*, a homolog to Dap1 has been identified and characterized, where it has been observed that its mutation affects the synthesis of carotenoids and sterols. The aim of this work was to evaluate the interaction of the *X. dendrorhous* Dap1 protein with Cyp61 by co-immunoprecipitation (Co-iP). For this, a strain harboring the Dap1 protein fused to the FLAG epitope and the Cyp61 protein fused to the HA epitope was constructed through the *DNA assembler* technique and transformation. This strain was used to perform Co-iP assays of protein extracts using an anti-FLAG antibody and magnetic beads linked to protein A/G. After Co-iP, a protein band of approximately 63 KDa, which corresponds to the expected size of the Cyp61-3XHA protein, was observed by western-blot analysis using the anti-HA antibody. The presence of Dap1-FLAG was also confirmed by western-blot using the anti-FLAG antibody. These results indicate protein-protein interaction between the *X. dendrorhous* Dap1 and Cyp61 proteins.

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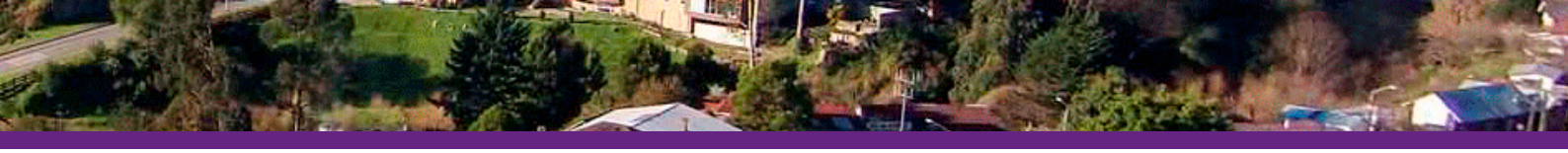

Genome sequence and RNA expression profiles of Orestias ascotanensis (Teleostei; Cyprinodontidae) reveal strategies for adaptation to extreme environmental conditions

Montecino Martín[1], Di Genova Alex[2], Nardocci Gino[1], Hodar Christian[3], Valdivieso Camilo[4], Morales Pamela[4], Gutiérrez Rodrigo[5], Orellana Ariel[6], Gonzalez Mauricio[3], Glavic Alvaro[4], Méndez Marco[4], Maass Alejandro[2], Allende Miguel[4]. [1]Instituto de Ciencias Biomédicas, Facultad de Medicina, Universidad Andrés Bello. [2]Centro de Modelamiento Matemático, Facultad de Ciencias Físicas y Matemáticas, Universidad de Chile. [3]Instituto de Nutrición y Tecnología en Alimentos, Universidad de Chile. [4]Departamento de Biología, Facultad de Ciencias, Universidad de Chile. [5]Departamento de Microbiología y Genética Molecular, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile. [6]Centro de Biotecnología Vegetal, Facultad de Ciencias de la Vida, Universidad Andrés Bello. (Sponsored by Martín Alejandro Montecino Leonard)

Orestias ascotanensis (Cyprinodontidae) is a teleost pupfish inhabiting springs of the *Ascotan* saltpan in the Chilean Altiplano (3,700 masl) and therefore exposed to extreme environmental conditions. This species is part of a tribe (Orestiini) inhabiting both freshwater and salt-lake environments distributed along the central Andes range which shows allopatric divergence in the southern Altiplano and sympatric distribution in Lake Titicaca. We have *de novo* sequenced the genome of *O. ascotanensis* at high coverage, representing the first sequenced teleost from a Puna desert environment. Comparative analysis of the *O. ascotanensis* genome sequence to those of other previously sequenced Teleosts, points to potential adaptive mechanisms in this species including paralog expansion in families of genes that have been associated with stress resistance to metal ions, salinity and DNA repair after UV exposure, a set that partially overlaps with genes that are currently under positive selection pressure. We also provide evidence supporting a role for miRNAs expressed in this species, as they are predicted to target mRNAs coding for proteins classified in these same categories. Together, our results shed light on the mechanisms operating during adaptive evolution of Andean fishes in response to environmental stress conditions. Furthermore, we propose that lakes and streams from the Puna represent new natural laboratories suitable for exploring the adaptive strategies developed by the inhabitant species.

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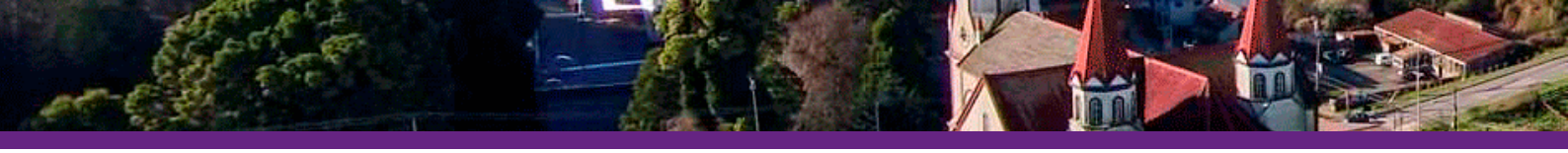

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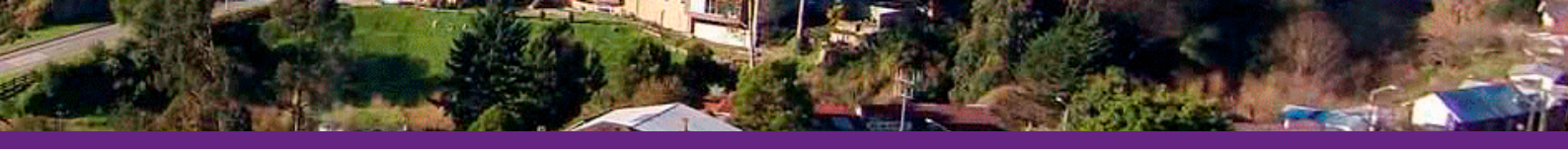
Phylogeny and historical biogeography of the genus Octopus in America

Pardo-Gandarillas María Cecilia[1], Cifuentes-Bustamante Alina[1]. [1]Departamento de Ciencias Ecológicas, Facultad de Ciencias, Universidad de Chile.

Benthic octopuses of the family Octopodidae comprises over 170 species inhabiting tropical and temperate ecosystems worldwide. Specifically, the Octopus genus comprises over 68 species, 30 of them inhabiting the Americas at both side (Atlantic and Pacific). Geomorphological events associated to the formation of the Isthmus of Panama trigged evolutionary processes such as dispersal and vicariance, which caused diversification of the Octopus genus in America. To test this hypothesis, three mitochondrial genes (COI, COIII and 16S) were sequenced in 33 specimens belonging to 14 species (Octopus, Robsonella, Enteroctopus, Muusoctopus) from North, Central and South America. Additionally, sequences from 83 species of the superfamily Octopodoidea were obtained from GenBank. The phylogenetic relationships, origin and divergence time as well as the ancestral distribution were estimated, including a total of 97 species. As in previous studies, phylogenetic results showed that the genus Octopus is polyphyletic; however, one of the Octopus clades corresponding only to the American species revealed to be monophyletic, contrasting with other Octopus species from different continents. Biogeographic, phylogenetic and divergence time evidenced a concordance with the geological time of the formation of the Isthmus of Panama, initiating this divergence during the Oligocene in the Caribbean Sea, which through dispersion and vicariance processes originated the current species that inhabit the Atlantic and Pacific coast of America.

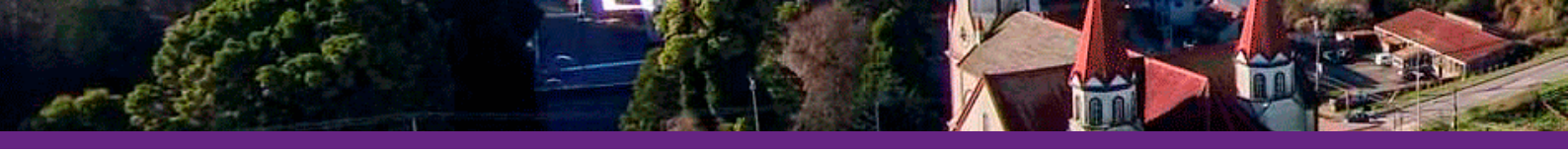


Genetic patterns of Ectinogonia pretiosa (Coleoptera, Buprestidae) in the Salar de Atacama: a complex history of joining and splitting of lineages in a changing oasis in time

Anguita-Salinas Simón[1,2], Zúñiga-Reinoso Álvaro[3], Poulin Elie[2,1]. [1]Departamento de Ecología, Facultad de Ciencias, Universidad de Chile. [2]Instituto de Ecología y Biodiversidad, Universidad de Chile. [3]Zoological Institute, Faculty of Mathematics and Natural Sciences, University of Cologne.

During the climatic oscillations of the Pleistocene, the Atacama Desert in northern Chile experienced repetitive processes of expansion and contraction. In this region the greatest richness of species for *Ectinogonia* genus is found. These buprestids are flying and plant-dependent beetles, they are endemic to the western slope of the Andes mountain range, where many of the species have restricted distribution. *Ectinogonia pretiosa* is one of them, distributed almost exclusively in Salar de Atacama (22°S-24°S). This species is associated to small patches of shrubland on alluvial plains. Considering the history of the environment and distribution of this species, this study aims to evaluate the effects of climatic cycles on the micro-evolutionary processes of *E. pretiosa*. For it, 40 specimens of *E. pretiosa* were sampled in San Pedro de Atacama (N=20) and in Socaire (N=20). Subsequently, fragments of the 16S and COI genes were amplified. An haplotype network was reconstructed to explore the distribution of genetic diversity among sampling sites. Additionally, a phylogeny of *Ectinogonia* genus was reconstructed, emphasizing the species from northern Chile. The haplotype network shows an extended topology with no sign of geographic structure, while the phylogeny shows two paraphyletic evolutionary units of *E. pretiosa*. The results suggest that *E. pretiosa* is composed of two independent lineages sharing a geographical area and host plant, originated by isolation-conexion during climatic oscillations, resulting in the current genetic pattern of the species.

Acknowledgments: This study was supported by CONICYT PIA AFB170008



Genomic variation in the chilean endemic crayfish parastacus PUGNAX, reveals high structure and cryptic diversity

Victoriano Pedro F.[1], **Muñoz-Escobar Christian[1]**, Vega-Drake Karina[1], Muñoz-Ramírez Carlos[2], D'Elía Guillermo[3]. [1]Departamento de Zoología, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción. [2]Centro de Investigación en Biodiversidad y Ambientes Sustentables (CIBAS), Facultad de Ciencias, Universidad Católica de La Santísima Concepción. [3]Instituto de Ciencias Ambientales y Evolutivas, Facultad de Ciencias, Universidad Austral de Chile. (Sponsored by Pedro Francisco Victoriano Sepúlveda)

For old and low vagility taxa, widely distributed in low connected scenarios, high structure and cryptic diversity are expected. In Chile, *Parastacus pugnax* also known as "camarón de vega", is part of a Gondwanan family and inhabits low connected environments. Given the large exploitation for human consumption and threat by land use change, knowledge of its levels of intraspecific diversity in the geographical context is crucial to conserve its real diversity. With the recent methods of Next-generation sequencing it is possible to have a large genomic coverage to answer such questions. We obtained, through the RADSeq method, genomic information of 95 individuals of *P. pugnax* from 42 localities throughout their distributional range. From 16,007 loci and Maximum Likelihood analysis (RAxML), the results suggest the existence of at least 4 lineages of deep divergence and distributed allopatrically. By using an analysis of genetic structure using fast-STRUCTURE, four clusters with high probability of individual assignment were detected, concordant with our tree clades. These results provide evidence of cryptic diversity beyond the previous hypothesized species of *Parastacus* and highlight the complexity of their evolutionary history.

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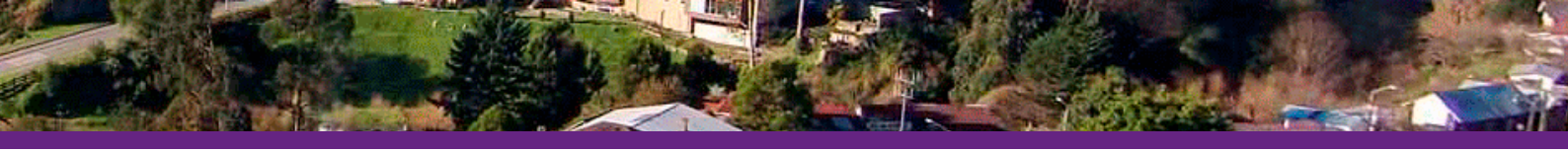
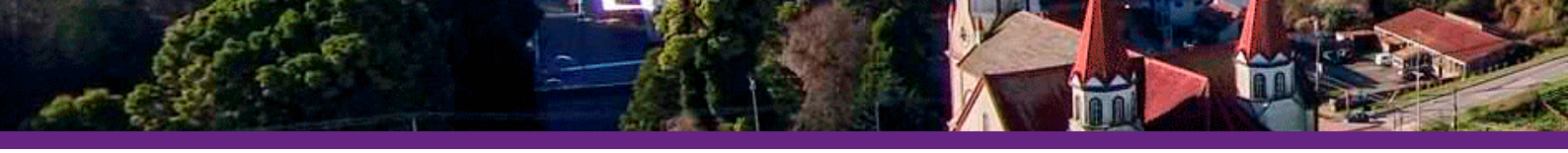


Phylogenetic and biogeographical patterns of southern hemisphere temperate forest's woody taxa

Tamburrino Ítalo Francisco[1], Jara-Arancio Paola[1], Arroyo Mary T. Kalin[2]. [1]Departamento de Ciencias Ecológicas, Facultad de Ciencias, Instituto de Ecología y Biodiversidad, Universidad de Chile. [2]Departamento de Ciencias Ecológicas, Facultad de Ciencias, Universidad de Chile. (Sponsored by Paola Jara-Arancio)

Southern hemisphere temperate forests concentrate the highest levels of tree diversity of some woody taxa and present distinctive features that differentiate them from their northern equivalents, that are often explained by their common Gondwanic origin, while the importance of biogeological events in the Cainozoic has been neglected in the study of the actual patterns of biodiversity. Reconstructing the phylogenetic relationships of the species ocurring within the area of interest is a crucial step in the integration of the evolutionary dimension in the understanding of community assembly and the patterns of species distribution, an important issue when defining conservation priority sites. The aim of this study is to propose a hypothesis for the phylogenetic relationships of the taxa present in the southern temperate forests, conformed by territories in New Zealand, southeast Australia and southwest South-America, at a genera level and identifying biogeographical patterns in the studied lineages. To do so, a list of tree species for the three territories was made from bibliography; georeferences and genetic sequences were downloaded from GBIF and Genebank respectively for all available taxa. Phylogenetic reconstructions using rbcL and matK plastid genes were made for selecting one representative specie from each genera, finally generating a 172 genera phylogenetic tree. The reconstruction shows coherence with APG IV classification system and a phylo-Sørensen index clustering analysis indicates significative lower dissimilarity between the Australasian forests respect the Southamerican territory. Thanks to Beca Magister Nacional 22170321, Fondecyt 1180454 and Instituto de Ecología y Biodiversidad Proyecto AFB170008.

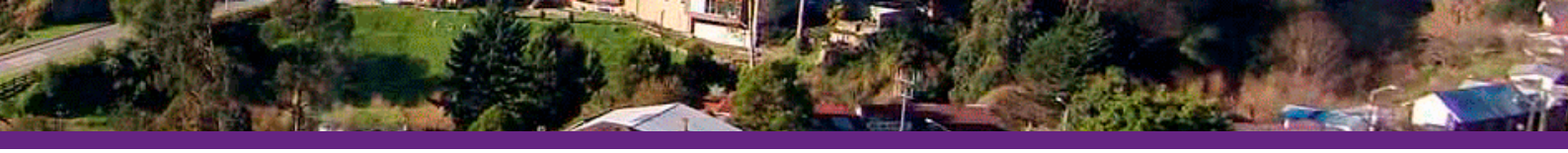
Beca Magister Nacional 22170321, Fondecyt 1180454 e Instituto de Ecología y Biodiversidad Proyecto AFB170008.



Exon Capture reveals co-occurrence without hybridization of ecologically similar species within an Adaptive Radiation of Hawaiian spiders

Cotoras Darko D.[2,1], Bi Ke[3,4], Brewer Michael S.[5], Lindberg David R.[2,6], Prost Stefan[2,7], Gillespie Rosemary G.[8]. [1]Entomology, California Academy of Sciences. [2]Integrative Biology, University of California, Berkeley. [3]Museum of Vertebrate Zoology, University of California, Berkeley. [4]Computational Genomics Resource Laboratory , University of California, Berkeley. [5]Department of Biology, East Carolina University. [6]Museum of Paleontology, University of California, Berkeley. [7]Department of Biology, Stanford University. [8]Environmental Science, University of California, Berkeley.

The early stages of adaptive radiation are key to understand the dynamics of rapid diversification events. The chrono-sequence of the Hawaiian Islands provides an ideal system to explore this fundamental process. Here, we focus on a radiation of long jawed spiders, genus *Tetragnatha*, to examine the genetic signatures of early events of speciation. Specifically, we investigated how ecologically similar species have differentiated genetically in the course of an adaptive radiation. Using a transcriptome-based Exon Capture approach, we examined relationships between populations of three closely related species (*T. brevignatha, T. waikamoi* and*T. macracantha*) from the youngest of islands of the Hawaiian chain, Lana'i, Maui and Big Island. The data shows that the originally described three species could be separated in at least five genetic clades. A key finding is that *T. waikamoi*, is widespread across East Maui, while the other species (juxtaposed with *T. waikamoi*) are localized and more closely related to populations on other volcanoes. Regardless the phylogenetic proximity there is no evidence of hybridization between these species. The fact thatmultiple genetic lineages exist on a single volcano on Maui suggests that there are no inherent dispersal barriers and the observed limited distribution of taxa might reflect some degree of competitive exclusion. Therefore, the ability of close relatives of the same ecomorph to interact, without admixture, may provide the conditions necessary for ecological divergence and independent evolution of ecomorphs associated with adaptive radiation.



Which are the main drivers of differences in phylogeographical patterns in Eudyptespenguin species?

Frugone María José[1,2,3], Noll Daly[1,2,3], Ramos Barbara[1], Lowther Andrew[4], Pistorius Pierre[5], Dantas Giselle[6], Petry Maria Virginia[7], Bonadonna Francesco[8], Steinfurth Antje[10,9], Polanowski Andrea[11], Raya Rey Andrea[12,13], Lois Nicolas[12,14], Pütz Klemens[15], Trathan Phill[16], Wienecke Barbara[11], Poulin Elie[2,3], Vianna Juliana[1]. [1]Departamento de Ecosistemas y Medio Ambiente, Pontificia Universidad Católica de Chile. [2]Laboratorio de Ecología Molecular, Departamento de Ciencias ecológicas II, Ciencias, Universidad de Chile. [3]Instituto de Ecología y Biodiversidad (IEB), - . [4]Fram Centre, Norwegian Polar Institute. [5]Department of Zoology, DST/NRF Centre of Excellence at the Percy FitzPatrick Institute for African Ornithology,Nelson Mandela University . [6]PPG in Vertebrate Zoology, Pontificia Universidade Católica de Minas Gerais . [7]Laboratório de Ornitologia e Animais Marinhos, Universidade do Vale do Rio dos Sinos . [8]CEFE UMR 5175, CNRS, Université de Montpellier. [9]RSPB Centre for Conservation Science, Royal Society for the Protection of Birds . [10]DST-NRF Centre of Excellence, Percy FitzPatrick Institute of African Ornithology, University of Cape Town. [11]Australian Antarctic Division, - . [12]Consejo Nacional de Investigaciones Científicas y Técnicas (CADIC-CONICET), Centro Austral de Investigaciones Científicas . [13]Instituto de Ciencias Polares, Ambiente y Recursos Naturales, Universidad Nacional de Tierra del Fuego. [14]Laboratorio de Ecología y Comportamiento Animal. Instituto de Ecologia, Genética y Evolución de Buenos Aires , Consejo Nacional de Investigaciones Científicas y Técnicas (IEGEBA-CONICET) . [15]Antarctic Research Trust, - . [16]British Antarctic Survey, - .

In the Southern Ocean Antarctic, sub Antarctic and subtropical waters are delimitated by oceanic fronts. Due to the drastic physicochemical changes, is suggested that they could impose a barrier to dispersal. Also, displacements of oceanic fronts associated to past climate changes would promote diversification of lineages throw long term reproductive isolation. Such hypothesis is proposed for *Eudyptes* penguins, particularly rockhopper penguins (*E. moseleyi*, *E. chrysocome*and *E. filholi*), nevertheless genetic structure or diversification processes associated to oceanic fronts haven't been tested in other *Eudyptes* penguins, like the wide-distributed Macaroni penguins (*E. chrysolophus*) and how interspecific differences would be reflected in genetic patterns of Eudyptes penguins. Our aim was to evaluate if oceanic fronts represent an equally efficient barrier to dispersal in rockhopper and macaroni penguins and asses their role in generating genetic structure and in diversification processes in these species, associated to past climate changes. To do so, we analyzed two mtDNA and two nuclear markers from 13 locations of macaroni and rockhoppers penguins. Population structure were observed for Rockhopper and Macaroni penguin associated to the PF. PF and STF act as barrier in these species, but their efficiency to limit genetic flow can vary between species and colonies. In Rockhopper penguins, geographic distance between colonies and dispersal capabilities seem to be relevant elements at explaining phylogeographical patterns. Finally, we didn't find lineage differentiation within macaroni penguins that could be related to past climate changes and oceanic fronts, as in the case of rockhopper penguins.

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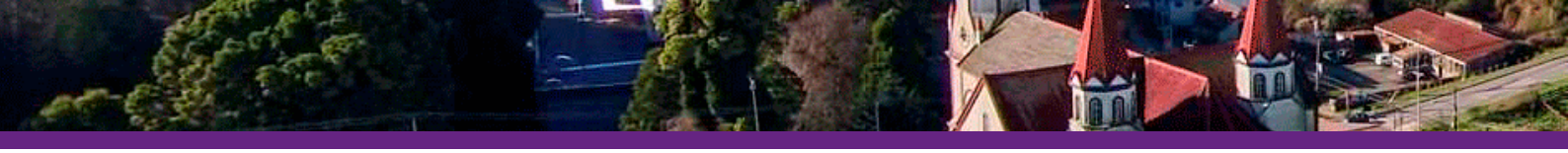

Population genomic shows low genetic differentiation and absence of local adaptation of adelie penguin along the Antarctic Peninsula and the Ross Sea

Noll Daly [1,3,2], Segovia Nicolás[3,4], Trathan Phill [5], Dantas Gisele PM[6], Gonzalez-Acuña Daniel[7], Massaro Melanie[8], Poulin Elie[3,2], Bowie Rauri[9], Bi Ke[9], Wang Cynthia[9], Vianna Juliana[1]. [1]Laboratorio de Biodiversidad Molecular, Departamento de Ecosistemas y Medio Ambiente, Agronomía e Ingeniería Forestal, Pontificia Universidad Catolica de CHile, [2] Laboratorio de Ecología Molecular, Departamento de Ciencias Ecológicas, Ciencias, Universidad de Chile, [3] Instituto de Ecología y Biodiversidad (IEB), Universidad de Chile, [4] Departamento de Biología Marina, Facultad de Ciencias del Mar, Universidad Católica del Norte, [5]High Cross, Madingley Road, Cambridge, UK CB3 0ET, British Antarctic Survey (6) PPG in Vertebrate Zoology, Pontificia Universidade Católica de Minas Gerais, [7]Departamento de Ciencias Pecuarias, Facultad de Ciencias Veterinarias, Universidad de Concepción, [8]School of Environmental Sciences and Institute for Land, Water and Society, Charles Sturt University, Australia, [9]Department of Integrative Biology, Museum of Vertebrate Zoology, University of California Berkeley

Adaptive polymorphisms of species between different regions of its distribution, allows to understand aspects related with the adaptive variation at molecular level and the possible role of the environment in the persistence of populations to climate change. Adelie penguin (Pygoscelis adelie), is distributed around Antarctica and previous studies using mtDNA have described two divergent lineages; one around Antarctic continent, and another in the Ross Sea. In this study, 53 individuals from colonies located in distant geographic regions such Scotia Arc, northern, central and southern Antarctic Peninsula and Ross Sea were sequenced using double-digest restriction site-associated DNA sequencing (ddRAD). A total of 45,211 SNPs distributed throughout the genome were obtained. Even if our results recovered the differentiation previously described between Ross Sea and maritime Antarctic, multivariate analyses showed subtle difference and Fst values were very low considering that both populations described as different evolutionary units. Likewise, little but significant genetic structure between northern and southern colonies of Antarctic Peninsula were detected. The coloies from Central and Southern area were the most differentiated, while the Northern and Scotia Arc colonies did not show differences. However, the ancestry admixture reveals a single ancestral population. We found high number of loci under neutrality (20,331) and balancing selection (24,879) models, but very few loci with evidence of positive selection were found. The strong signal of stabilizing selection suggest that adelie penguin is highly specialized to Antarctic climate, and that changes in the environment could disfavour the persistence of populations of this species.

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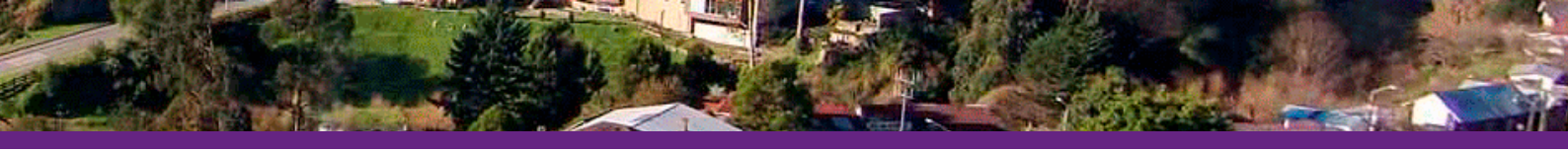

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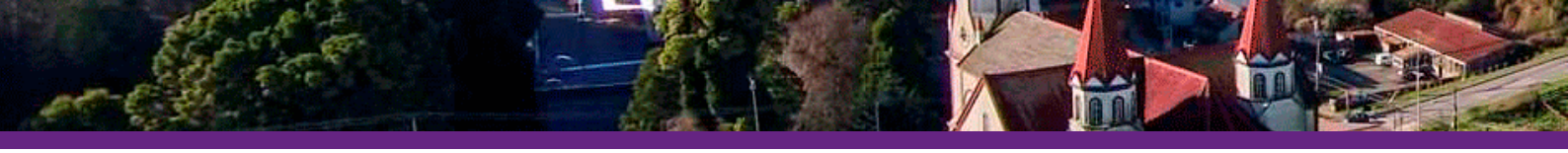
Epigenetic alterations in an ALS mouse model

Jury Nur [1,2], Abarzua Sebastian[1,2,3], Díaz Ivan[1,2], V. Guerra Miguel[1], Martinez Pablo[1,2], Varela-Nallar Lorena[1], Montecino Martín[1,3], Van Zundert Brigitte[1,2]. [1]Instituto de Ciencias Biomédicas (ICB), Facultad de Medicina y Facultad de Ciencias de la Vida, Universidad Andrés Bello, Chile. [2]Centro de Envejecimiento y Regeneración (CARE-UC), Pontificia Universidad Católica de Chile. [3]Center for Genome Regulation, FONDAP, Chile. (Sponsored by Brigitte Van Zundert)

Mutations in *SOD1* (mutSOD1) cause motoneuron pathology and death in amyotrophic lateral sclerosis (ALS). We determined whether the profiles of epigenetic modifications at nucleosomal histone proteins are altered in mutSOD1 transgenic mice. Primary astrocyte cultures and CNS tissue obtained from mutSOD1 mice were analyzed by immunostaining and western blot assays using antibodies that detect repressive (H3K9me2/me3, H3K27me2/me3) and active (H3K9Ac, H3K27Ac) histone epigenetic modifications as well as the DNA damage-associated histone mark gamma-H2A.X. Epigenetically dysregulated genome sequences in ALS astrocytes were detected by chromatin immunoprecipitation with antibodies against H3K9me3 followed by genome-wide sequencing (ChIP-seq). Immunostaining and western blot assays revealed that cultured mutSOD1astrocytes display a strong reduction in the number of nuclear H3K9me2/3 foci and at the overall level of nuclear H3K9me2/3 signal. Also, H3K9me2/3 loss was detected in ALS astrocytes and neurons in the spinal cord and motor cortex. ChIP-seq analyses revealed that global H3K9me3 enrichment at the transcription start sites is similar in mutSOD1 and control astrocytes. Interestingly, however, we identified particular gene sequences that exhibit changes in the H3K9me3 mark distribution. Our data indicate that a loss of epigenetic control can contribute to the pathogenesis and disease development in ALS.

Fondecyt 1181645 (BvZ), CARE-UC AFB 170005 (BvZ), Núcleo UNAB DI-4-17/N (BvZ, LVN), FONDECYT 1150933 (LVN), FONDAP 15090007 (MM), Conicyt 201161486 (NJ), Conicyt 21151265 (SA), Conicyt 21151563 (PM).

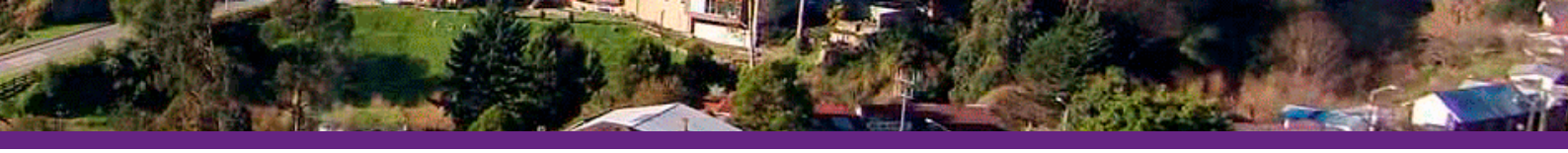


Lipophorin receptors participate in the development of Drosophila melanogaster mushroom body

Rojo Francisca[1], Marzolo María Paz[1], Campusano Jorge[1]. [1]Biología Celular y Molecular, Ciencias Biológicas, Pontificia Universidad Católica de Chile.

The very low density lipoprotein receptor (VLDR) and apolipoprotein E receptor 2 (ApoEr2) are two proteins that in addition to their involvement in lipid uptake, have been recognized as receptors for Reelin. This is an extracellular glycoprotein that is responsible for neuronal migration, cerebral cortex patterning and neural plasticity. The Reelin effect depends on its receptors VLDR and ApoEr2, and is mediated by Dab1. In *Drosophila melanogaster*, Lipophorin receptors (LpRs) mediate lipid uptake. Two LpRs have been described in *Drosophila*, LpR1 and LpR2, which are homologues of VLDR and ApoER2. Here we evaluated the role of LpRs in the development of *Drosophila* mushroom body (MB), a brain structure serving as the "fly hippocampus". We assessed whether mammalian Reelin (mReelin) affects the number and length of neurites in *Drosophila* MB neurons in culture prepared from wild-type flies and animals mutant for LpR1 and LpR2, and Dab, the fly homologue of vertebrate Dab1. Additionally, fly brain general anatomy was evaluated in these mutants. Our results support the idea that Lpr1 and LpR2 participate in MB development and that this effect is mediated by Dab.

Funded by Fondecyt 1141233 and Puente-PUC (JMC) and Fondecyt 1150444 (MPM). FR is supported by Conicyt Doctoral Fellowship.



c-Abl participates in the missorting of Tau and axon initial segment stability regulation

Cáceres Alvaro[1,2], Gutierrez Daniela[1,2], Leal Nancy[1,2], Álvarez Alejandra[1,2]. [1]Cellular & Molecular Biology, Biological Sciences, Pontificia Universidad Católica de Chile. [2]CAREChile-UC, Pontificia Universidad Católica de Chile.

Introduction:
The Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive synapse loss and neuronal death, leading to progressive cognitive decline and memory impairment. In the AD brain, the Tau protein associated to axonal microtubules, is hyper phosphorylated and present an abnormal localization in the somatodendritic compartment. The loss of the diffusion barrier on the axon initial segment (AIS) had been implicated in the missorting of Tau in AD. Our group has shown that the Aβ peptide induced c-Abl tyrosine kinase activation. Imatinib, a c-Abl specific inhibitor prevents tau hyperphosphorylation and apparently, its somatodendritic mislocalization. Therefore, we asked if c-Abl regulates the AIS stability contributing to Tau missorting.

Materials and methods:
We treated hippocampal culture neurons (13 DIV) with Aβ peptide at different time points and evaluated Tau phosphorylation and its distribution along the neuronal process. Additionally, we followed the AIS scaffold protein, AnkyrinG by immunofluorescence in Aβ treated neurons during c-Abl inhibition with Imatinib.

Results:
We found that c-Abl inhibition prevents the phosphorylation and missorting of Tau to the somatodendritic compartment induced by Aβ. Futhermore, we observed that the loss of AnkyrinG induced by Aβ was depend on c-Abl inhibition. Interestingly, c-Abl could be regulating the stability of the axon initial segment and contributing to the Tau pathology in AD.

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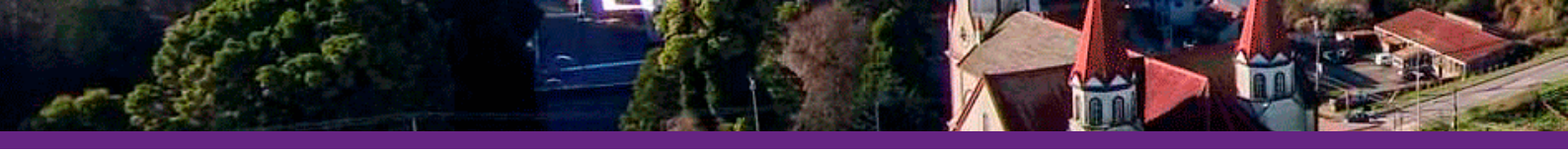


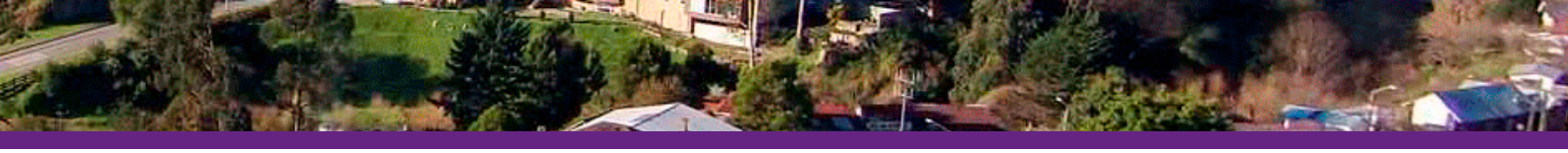
(NO SE PRESENTÓ)

Subthreshold Ca2+-dependent modulation of vesicle release dynamics and docking site occupancy at single central synapses

Blanchard Kris[1,2], Llano Isabel[2], Bacigalupo Juan[1], Marty Alain[2], Trigo Federico[2]. [1]Departamento de Biología, Facultad de Ciencias, Universidad de Chile. [2]UMR8118, Université Paris Descartes. (Sponsored by European Research Council (ERC) Grant To Alain Marty)

In several neurons of the CNS, subthreshold somatodendritic activity can spread passively into the axon and transiently enhance spontaneous and spike-evoked synaptic transmission in a Ca^{2+}-dependent and graded manner. Available evidence about the underlying mechanism of this type of synaptic plasticity, called "analog" or "analog to digital" facilitation (ADF), remains largely incomplete for the majority of central synapses, mainly due to the experimental inaccessibility to the small presynaptic boutons. Here we use both Ca^{2+} photolysis and imaging at individual presynaptic terminals of the rat cerebellar molecular layer interneurons (MLIs), combined with whole-cell paired recordings from synaptically connected MLIs, to report a novel subthreshold-Ca^{2+}-dependent mechanism for ADF whereby the fraction and the kinetics of the pool of vesicles available for immediate release, the Readily Releasable Pool (RRP), are modulated by changing the docking site occupancy probability in single synaptic contacts. Our results add a new dimension in the understanding of how subthreshold activity modulates information flow in neuronal circuits.

Beca doctorado nacional CONICYT

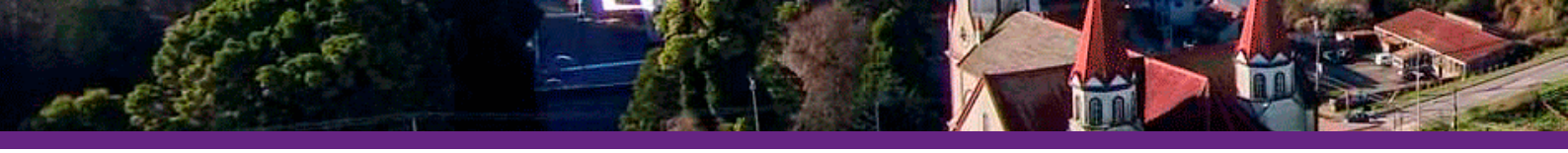


Chronic administration of ketamine during late adolescence reduces neurogenesis and alters the inhibitory synaptic transmission in the dorsal dentate gyrus during adulthood

Santander Odra [1], Pérez-Lizama Miguel[2], García Francisca[2], Guerra Miguel[3], Varela-Nallar Lorena[3], Chávez Andrés E.[4], Fuenzalida Marco[2]. [1]Programa de Doctorado en Ciencias mención Neurociencias, Facultad de Ciencias, Universidad de Valparaíso. [2]Instituto de Fisiología, Facultad de Ciencias, Universidad de Valparaíso. [3]Centro de Investigaciones Biomédicas (CIB), Facultad de Ciencias Biológicas y Facultad de Medicina, Universidad Andrés Bello. [4]Centro Interdisciplinario de Neurociencia de Valparaíso (CINV), Facultad de Ciencias, Universidad de Valparaíso.

Adult neurogenesis occurs through the proliferation of precursor cells, which migrate to specific regions and differentiate into neurons with characteristics indistinguishable from existing nature neurons. Alterations in the production of new neurons and GABAergic disruption have been linked to neurodevelopment disorders, such as Schizophrenia (SZ). Since neurodevelopment processes persist into adulthood, the question arises; does abnormal neurodevelopment in SZ extend into adulthood and affect neurogenesis? However, whether GABAergic disruptions are related to abnormal neurogenesis during adulthood remains unclear. Previously we observed that ket-treatment decrease the synaptic transmission in dorsal hippocampus (dHPC), whereas ventral hippocampus was not affected. Here, using immunofluorescence (IF) and electrophysiology techniques, we examined whether administration of an NMDAR antagonist (ketamine, ket) in rats during late adolescence impair neurogenesis and GABAergic transmission in the dorsal dentate gyrus. Ket treatment decreased both the expression of Ki67 and doublecortin in the subgranular zone, which were molecular markers for proliferation and differentiation, respectively. Interestingly, the IF and voltage clamp recording reveal that the ket administration reduced both the expression of parvalbumin (PV) and GABAergic synaptic efficacy in the granular dentate gyrus neuron. Also, we observed by current clamp recording that Ket administration did not affect passive or active membrane properties in mature granular neurons. Taken together, these results could be key to understand whether abnormal neurogenesis during adulthood as a crucial factor for the pathogenesis of the SZ.

FONDECYT 1171006 and Anillo ACT1414 (MFN); FONDECYT Postdoctorado 3160442 (MAP), Conicyt Fellowship 21181214 (OS) and Conicyt Fellowship 21181497 (MG); PMI UVA 1402 (FG); FONDECYT 1150933 (LVN); FONDECYT 1151091 and CINV P09-022-F

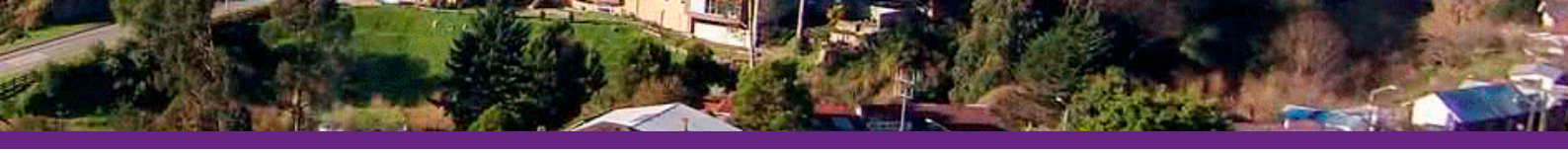


A novel role of TMBIM proteins in sculpting the Drosophila glutamatergic synapse

Delgado María Graciela [1], Lisbona Fernanda[2], Alvaro Glavic[2], **Delgado Ricardo [2]**. [1] Immunité et Cancer, Institut Curie, PSL Research University, INSERM U932. [2]Departamento de Biología, Facultad de Ciencias, Universidad de Chile.

Experience-dependent structural synapse modifications condition animal behavior. Morphogens (BMP/TGFb and Wnt) and neurotrophins (BDNF) have been shown to be key players sculpting synaptic structure. However, the molecular cell death mechanisms, fundamental in shaping the nervous system during early development, as well as autophagy, essential for degradation of missfolded proteins and turnover of cytoplasmic materials, have been poorly investigated regarding its contribution to synapse function. We aimed to investigate the role of putative *Drosophila* genes of Transmembrane BAX-inhibitor-1 Motif-containing (TMBIM): *Lifeguard (CG3814)* and *recS1 (*CG9722) in *Drosophila* neuromuscular junction (NMJ) synaptic. Both genes, which appear as a novel candidate to regulate cell death, could have a role in determine synaptic structure. To assess their role we use the binary UAS-Gal4 expression system to manipulate their expression in motorneurons of third instars larvae. Using immunofluorescence confocal microscopy to analyze the NMJ synapse structure, we have found that RNA-mediated silencing either *Lfg* or *Recs1*, led to a reduction in motorneuron synapse size; whereas, overexpression of either *Lfg* or *Recs1*, induced synapse enlargements and consequently an increase of the excitatory junction currents (EJCs). Furthermore, we have found that NMJ synaptic enlargement evoked by starvation in *wt* flies was abolished in*recS1* knock-out flies. Additionally, we found that *lfg* and *recs1* knock-out abolished the EJCs enlargement exhibited *dunce* mutant larvae (cAMP-phosphodiesterase mutant). Altogether, suggesting a role for TMBIM proteins in structural synaptic plasticity, involving the cAMP signaling.

Supported by PAIFAC to RD and Grant Conicyt PIA ACT1401 (AG)

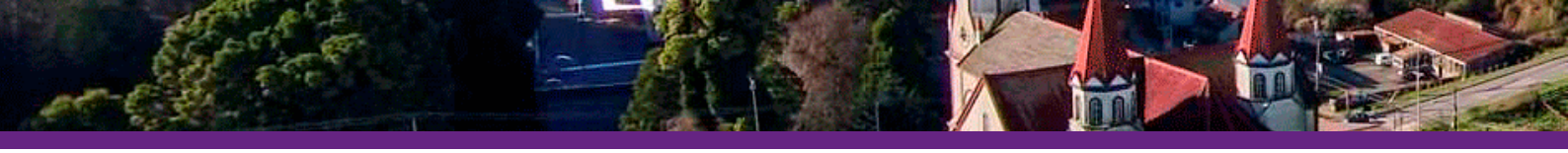


MPH recover impaired hippocampal plasticity in a mouse model of ADHD induced by prenatal nicotine exposure

Contreras Darwin[1], Piña Ricardo[1], Ugarte Gonzalo[1], Albornoz Michelle[1], Klagges Jorge[1], Morales Diego[1], Morales Bernardo[1], Rozas Carlos[1]. [1]Biología, Química y Biología, Universidad de Santiago de Chile.

Attention Deficit/Hyperactivity Disorder (ADHD) is a neuropsychiatric disorder characterized by hyperactivity/impulsivity and inattention. Methylphenidate (MPH) is the main medication used to treat ADHD. In this work we studied the effect of MPH on hippocampal synaptic plasticity in an animal model of ADHD generated by prenatal nicotine exposure (PNE). Using electrophysiological approaches and Western blot analysis we investigated TBS-dependent LTP in CA3-CA1 synapses of hippocampus and the insertion of AMPA receptors in the postsynaptic membrane. Our results show that PNE mice have a reduced LTP compared to controls (No PNE): from 152,9±0,68% n=10,12; to 127,0±0,81% n= n=10,15. This effect was reverted after oral administration of MPH 1mg/Kg: from 127,0±0,81% to 151,9±1,34; n=9,14. Consistent with these results, a significant decrease in phosphorylation ratio for GLUA1-Ser831 was found in PNE mice that showed reduced LTP versus controls mice (PNE: 0,67±0,05; No PNE: 0,93±0,01). Also, using voltage-controlled technique, we recorded the rectification index (RI) of the current mediated by AMPA receptors. Our results show that PNE animals present a rectification compared to controls: PNE (IR: 0,256±0,03, n=4,5), NoPNE (IR: 0,726±0,09, n=5,5) and that this effect was reverted after administration of MPH: from PNE (IR: 0,256±0,03, n=4,5) toPNEMPH (IR: 1,93±0,17, n=4,6). Taken together, these results suggest that oral administration of MPH reestablished the LTP observed in PNE mice, we hypothesized that this effect is possibly by insertion/mobilization of AMPA receptors in the CA3-CA1 synapses. This evidence shows the molecular mechanism by which MPH would be exerting its effect in the treatment of ADHD.

Support: FONDECYT 1161524 (BM); CONICYT FELLOWSHIP 21141188 (DC); FONDECYT 3170249 (RP).



COMUNICACIONES LIBRE ORAL VIII SOCIEDAD DE GENÉTICA DE CHILE

Differentiated genetic susceptibility for the development of depressive symptomatology in relation to early stress experiences

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Depression is a pathological alteration of mood. It is estimated that it will be the first cause of disability worldwide by the year 2030. Some genetic polymorphisms may modulate sensitivity to environmental factors such as early stress. These polymorphisms would be located in genes related to the functioning of neuroendocrine pathways that are altered in individuals with depression. The hypothesis of this work is "there is interaction between two polymorphisms located in the SLC6A4 gene, with early stress experiences in developing depressive symptomatology". 673 students from the Universities of Chile and La Frontera of Temuco, ages 18 to 25, were recruited. They were asked to answer online questionnaires about depressive symptomatology (BDI) and early stress experiences (CTQ). DNA samples, obtained from peripheral blood, were genotyped in house. Once the genetic data, the antecedents of early stress and the depressive symptomatology information were obtained, the statistical analysis was performed considering variable by variable, relations of pairs of variables and models of interaction between the three variables. 44.7% of the participants had antecedents of trauma, being the most frequent emotional abuse (27.8% of the cases). Emotional abuse experiences have a significant effect on the score obtained in the BDI. The 12R/10R genotype of the STin2 polymorphism showed a protective effect, particularly in men. These findings imply that knowing the background of emotional abuse and genotypes of the STin2 polymorphism of the SLC6A4 gene, would help to predict susceptibility for the development of depressive symptoms.

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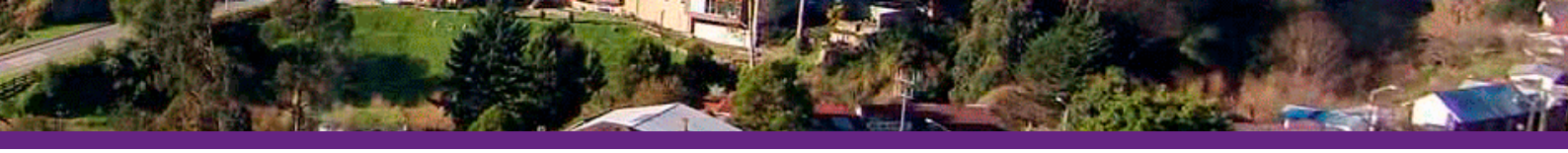


Prodromal manifestations of Parkinson disease in adults with 22q11.2 microdeletion syndrome

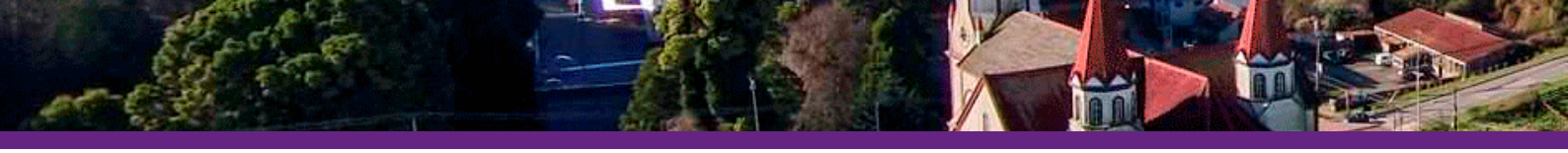
Repetto Gabriela[1], Cuiza Analía[1], Chaná Pedro[3,2], Villanueva Katiuska[4], Fritsch Rosemarie[5], Juri Carlos[6], Kramer Vasko[7], Ocampo Adrian, Ornstein Claudia, Cordova Teresa. [1]Centro de Genética y Genómica, Medicina, Universidad del Desarrollo. [2](CETRAM), Centro de Trastornos del Movimiento. [3]Neurología, Universidad de Santiago de Chile. [4]Instituto de Ciencias Biomédicas, Medicina, Universidad de Chile. [5]Psiquiatría, Medicina, Universidad de Chile. [6]Neurologia, Medicina, Pontificia Universidad Católica de Chile. [7]Medicina Nuclear, Positron Med.

Background:
Parkinson disease (PD) is the second most common neurodegenerative disorder. The classical motor symptoms are preceded by a decade by non-motor, prodromal manifestations: anosmia, autonomic dysfunction, REM-sleep behavior disorder (RBD), and loss of basal ganglia dopaminergic neurons. Chromosome 22q11.2 microdeletion syndrome (22q11DS) was recently recognized as a cause of PD. Aim: to assess the presence of prodromal PD in adults with 22q11DS.

Methods:
Instruments according to the International Parkinson and Movement Disorder (MDS) research criteria for prodromal PD; clinical, cognitive and molecular characterization of 22q11DS. Results: We report the results on the first 20 participants: 9 males and 11 females, median age 28 years. Fifteen had the common 3Mb deletion, and 3 had the nested 1.5Mb deletion. Full-scale IQ median was 73 (range 52-96). Four patients had psychosis and were receiving antipsychotic medication. UPDRS motor score average was 9.3 (range 1-16, normal 0); four patients had olfactory scores in the anosmia range. Home polysomnograms in 9 participants showed no signs of RBD. PET-CT showed increased, symmetric 18F-PR04-MZ pre-synaptic dopamine (DAT) signaling compared to age and gender-matched controls (130% of controls in the caudate nucleus, 115% in putamen).

Discussion:
These initial results suggest the presence of prodromal findings. The observed increase in dopamine signaling on PET-CT may be related to haploinsufficiency of COMT, located within the deletion region and involved in dopamine metabolism. Caution should be taken when interpreting these results, due to the limited sample size and the lack of validated screening tools for patients with cognitive deficits.

Funded by Fondecyt-Chile #1171014 and Fundacion Puelma

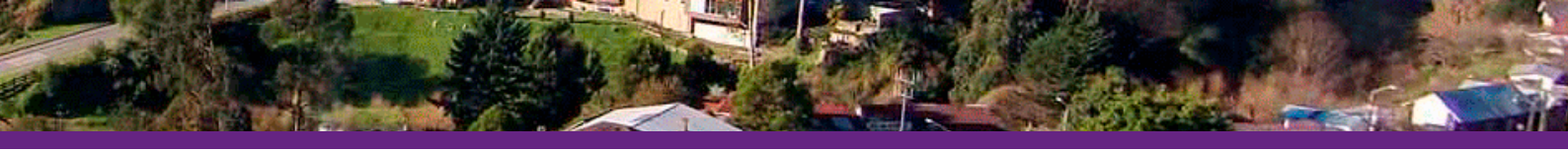


Genetic Variants in pre-miR-182 and TNRC9 are associated with breast cancer susceptibility in Chilean population

Morales Sebastián Felipe[1], De Mayo Tomas [2], Jara Lilian[3]. [1]Genética Humana , Medicina , Universidad De Chile. [2]Genética y Genomica , Facultad de Medicina , Universidad del Desarrollo. [3]Programa de Genética Humana, Facultad de Medicina, Universidad de Chile.

Breast cancer (BC) is one of the most frequent tumors affecting women worldwide. Single-nucleotide polymorphisms (SNPs) in microRNAs (miRNAs) likely contribute to BC susceptibility. Using Sanger sequencing, we detected rs4541843:C>T (pre-miR-182 boundaries) in 99 *BRCA1/2*-negative BC patients from high-risk families. While mir-182 is known to be involved in breast carcinogenesis, there are no association studies in the literature regarding the contribution of rs4541843 to BC susceptibility. Therefore, we evaluated the association of the SNP rs4541843:C>T with BC risk in non-carriers of *BRCA1/2* mutations from a South American population. The SNP was genotyped in 440 *BRCA1/2*-negative Chilean BC cases and 1048 controls. The frequency of rs4541843-T was higher in cases than controls (0.46 vs. 0.31, p=0.01). Furthermore, homozygous T/T- and T-allele carriers (C/T + T/T) had a significantly increased BC risk (OR=1.5 [95% CI 1.0-2.2] p=0.03 and OR=1.2 [95% CI 1.0-1-5] p=0.01, respectively), indicating that the T allele is positively associated with BC susceptibility. This is the first association study on rs454183 and BC risk. In our previous work, we showed that TNRC9-rs3803662:C>T was significantly associated with familial BC risk. Given that TNRC9is a target of miR-182, and that both the TNRC9 rs3803662-T and pri-miR-182 rs454183-T alleles are associated with elevated BC risk, we evaluated their combined effect. Risk of familial BC increased in a dose-dependent manner with the number of risk alleles (p-trend=0.0005), indicating an additive effect.

Grant Sponsor: Fondo Nacional de Desarrollo Científico y Tecnológico (FONDECYT). Grant Number: 1150117



Patients' PBMCs transcriptional response to Andes hantavirus infection: longitudinal analysis

Ribeiro Grazielle[8], Vial Pablo[8], Cuiza Analia[8], Ferres Marcela[1], Calvo Mario[2], Perez Jose Luis[3], Ferreira Leonila[4], Rioseco Maria Luisa[5], Graf Jerónimo[6], Leon Luis[7], **Vial Cecilia[8]**. [1]Departamento de Enfermedades Infecciosas e Imunología Pediatrica, Medicina, Pontificia Universidad Católica de Chile. [2]Hospital Base de Valdivia, Facultad de Medicina, Universidad Austral de Chile. [3]Hospital Base San Jose de Osorno, Facultad de Medicina, Universidad Austral de Chile. [4]Unidad de Cuidados Intensivos, Hospital Clinico Regional Guillermo Grant Benavente. [5]Departamento de Infectologia, Hospital de Puerto Montt Dr. Eduardo Schütz Schroeder. [6]Unidad de Cuidados Intensivos, Facultad de Medicina, Clinica Alemana. [7]Instituto de Ciencias Biomedicas, Ciencias de la Salud, Universidad Autónoma de Chile. [8]Instituto de Ciencias e Innovación en Medicina, Programa Hantavirus, Medicina, Universidad Del Desarrollo.

Andes hantavirus (ANDV) is endemic to Chile and Argentina, causing hantavirus cardiopulmonary syndrome (HCPS). It affects young, previously healthy people with a case fatality rate of 30%. Host-related immune mechanisms rather than direct viral cytopathology are postulated to be responsible for the principal manifestations of the disease, along with infection of endothelium which can disrupt tight junctions among them causing leakage. Cells of the immune system, including follicular dendritic cells, macrophages, and lymphocytes are also infected. Our goal is to better understand the role of the hosts immune responses in the progression towards HCPS, by longitudinally characterize the transcriptional profile of the peripheral blood mononucleated cells (PBMCs) isolated from ANDV infected patients, and healthy subjects as controls. Total RNA was extracted from PBMCs isolated from peripheral blood of healthy controls and patients infected with ANDV on days 1, 3, 5 and 60 post hospitalization. Isolated RNA was sequencedat the Broad Institute (Illuminas HiSeq, 50M reads paired-end). We analyzed 10 ANDV patients and four healthy controls. We found that during the acute phase, mainly in day 1, there was an enrichment of GO processes related to cell metabolism, humoral immune response and inflammatory response. On day 60 genes in these GO processes have levels similar to healthy controls, suggesting the full recovery of these patients. Future directions of this study include the analysis of differential expression by gene, to help us understand the mechanisms involved in the pathogenesis of HCPS. Transcriptome analyzes were performed with STAR, Deseq2 and GOseq. Fondecyt1161447.

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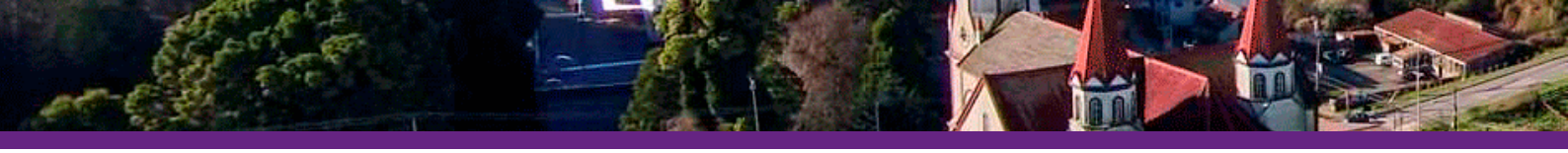
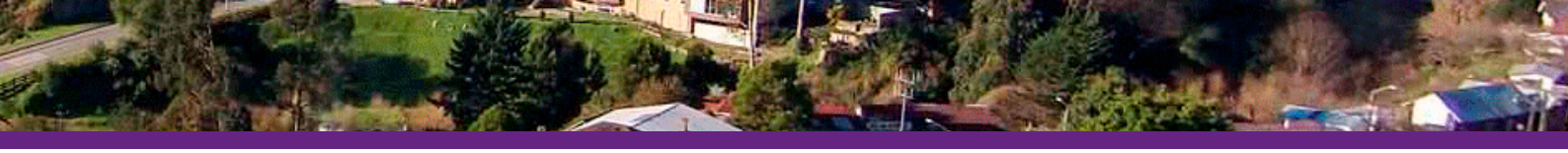


Variants in tcf7l2 and eca confer genetic risk to the development of diabetes mellitus type-2 and diabetic nephropathy

Krall Paola[1], Peralta Natalia[1], Nualart Daniela[1], Lavoz Carolina[1], Elgueta Osvaldo[2], Ardiles Leopoldo[1], Flores Claudio[1], Mezzano Sergio[1]. [1]Instituto de Medicina, Facultad de Medicina, Universidad Austral de Chile. [2]Programa Salud Cardiovascular, Centro de Salud Familiar Externo de Valdivia.

Diabetes mellitus type-2 (DMT2) is a chronic disease that is the leading cause of end-stage renal disease due to diabetic nephropathy (DN). A role in DN has been described for Gremlin (GREM1) and for an indel (I/D) in the Angiotensin-Converting-Enzyme (*ACE*) gene. Chile has the highest prevalence of DMT2 in Latin America, but the genetic susceptibility to develop DMT2 or DN remains unknown. Our aim was to explore the association of polymorphisms in genes related to *GREM1* and *ACE* with DMT2-DN. Methods: A retrospective case-control study was performed in the XIV Region that considered control subjects (n=140) and DMT2 patients without DN (n=80) or with DN (n=101). The following polymorphisms were studied: rs1129456(*GREM1*), rs7903146(*TCF7L2*), rs34231037(*VEGFR2*), rs4819554(*IL-17RA*), indel-18 pb(*VEGF)* and the indel~300pb (*ACE)*. Allelic and genotypic frequencies were analyzed to determine Odds ratio (OR). Results: The T allele (*TCF7L2)* was associated to DMT2 (OR=1.53, 95%IC=1.08-2.18, p=0.009). Additionally, the D allele (*ACE)* was associated to DN (OR=1.62, 95%IC=1.06-2.47, p=0.01), as well as to early DN development (OR=2.22, 95%IC= 1.10-4.46, p=0.01). Conclusions: Particular variants in *TCF7L2* (T allele) and *ACE* (D allele) are highly prevalent in the study cohort (30-50%) and present a potential clinical value as risk alleles in DMT2 and DN of early development. Further studies are required to determine if the TCF7L2 genotype modulates the GREM1 expression in the DMT2-DN kidney. A second cohort is required to validate *TCF7L2* and *ACE* as susceptibility genetic markers in the Chilean population, in order to consider them to design preventive strategies in DMT2-DN.

FONDECYT Regular 116-0465, FONDECYT de Iniciación 111-40242

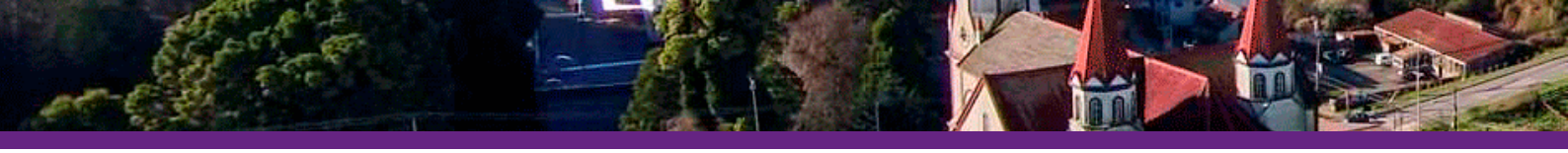


Alteration of pericentromeric heterochromatin leads to defective centromere formation, chromosomal segregation errors and aneuploidy

Pola Víctor [1], Sagredo Eduardo A[2], Cappelli Claudio[1], Inostroza Víctor[1], Armisén Ricardo[1,2], Marcelain Katherine[1]. [1]Oncología Básico-Clínica, Medicina, Universidad de Chile. [2]Centro de Excelencia en Medicina de Precisión, Pfizer.

Chromosome segregation defects leads to aneuploidy and chromosome instability, a hallmark of advances cancers. Pericentromeric heterochromatin (surrounding the centromere) provides a structural scaffold for centromere formation, being essential for safeguarding of chromosome stability. Previous data from our group show that the Ski protein (a transcriptional co-repressor) is localized on pericentromeric chromatin of some mitotic chromosomes, occupying Beta Satellite (BSR) and Human Satellite II (HSATII). Moreover, we found the presence of this protein modulates H3K9 acetylation/trimethylation (H3K9ac/me3) pattern on repetitive regions, critical modifications for pericentromeric heterochromatin formation. In this work we aimed to evaluate whether a defective pericentromeric heterochromatin lead to defects on centromere formation and subsequent chromosomal segregation errors. To address this, we decreased levels of Ski using a specific shRNA in a non-transformed breast epithelial cell line (MCF10A) and performed several technics such as chromatin immunoprecipitation (ChIP), Western Blot, indirect immunofluorescence and qRT-PCR assays. Our results show that Ski knockdown in MCF10A cells, resulted in altered levels of epigenetic marks associated to heterochromatin and to an aberrant localization of HP1 alpha in asynchronic as well as mitotic cells. Moreover, we found that these alterations spread to the centromere, evidenced by a significant decrease of CENP-A incorporation on Alpha Satellite DNA and decreased alpha-satellite transcripts expression. Finally, the analysis of MCF10A shSki revealed that these cells exhibit significant chromosomal segregation defects, micronuclei formation and aneuploidy. This findings indicate that Ski is necessary to centromere formation, which impacts on the faithful chromosome segregation and genome stability.

Supported By FONDECYT 1151435



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Fine sensorimotor coupling modulates working memory

Loyola Rocio[1,2,3], Rodrigo Vergara-Ortúzar [1,2], Crstóbal Moenne-Loccoz [1,2], Pedro Maldonado-Arbogast [1,2], [1]Departamento de Neurociencias, Facultad de Medicina, Universidad de Chile, [2]Biomedical Neuroscience Institute, BNI, [3]Departamento de Educación Diferencial, Facultad de Filosofía y Educación, UMCE.

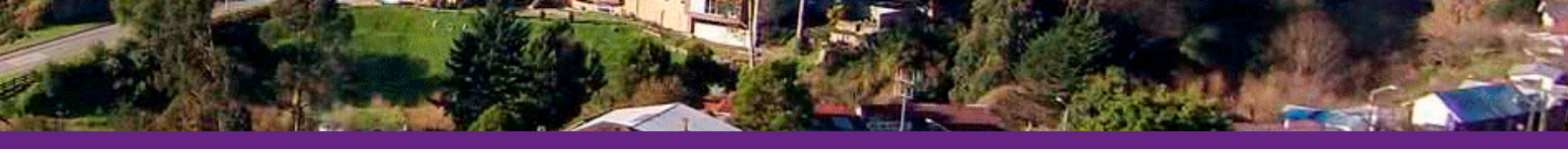
Classic studies of working memory (WM) required passively waiting for the appearance of a stimulus, while during natural behavior, sensory activation is typically the consequence of self-initiated movements. We conjecture that this sensorimotor coupling would modulate WM processes. 26 subjects were studied in a WM test in three conditions: coupled, were participants pressed a button for the stimuli, decoupled where was a delay between the presentation of the stimuli and the pressure of the button and passive in which the stimuli appear automatically.

Behavioural results shows a statistically significant improvement of performance in the coupled condition versus the other two conditions, and a significantly worse performance of the passive condition with respect to the other two. No effect in response times were found.

Preliminary results in Event Related Potentials show that P100, N100 and P300 decreased their latency in coupled condition compared with the other two conditions.

These results suggest that fine sensorimotor coupling contributes to the mechanisms of the working memory. Our results confirm that fine temporal coupling is a critical feature of the sensorimotor modulations, as it has been previously shown in active sensing. The fact that this same effects are seen on several cognitive processes as perception, attention and now working memory, suggests that sensorimotor coupling could be a global mechanism of precise temporal modulation.

Funded by CONICYT-PFCHA 21150153 and ICM P09-015-F



Frontomedial negativity discriminates outcomes and intentions in trust-repayment behavior

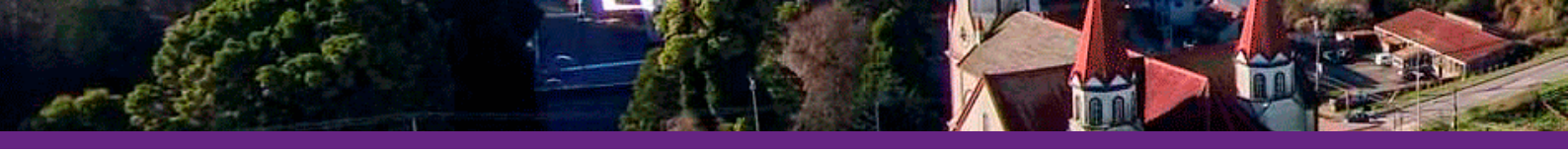
Aspé-Sánchez Mauricio[1], Mengotti Paola[2], Rumiati Raffaella[2], Rodríguez-Sickert Carlos [3], Guzmán Ricardo[3], Ewer John[4], Billeke Pablo[1]. [1]División de Neurociencias (neuroCICS), Centro de Investigación en Complejidad Social, Universidad del Desarrollo. [2]Cognitive Neuroscience Department, Scuola Internazionale Superiore di Studi Avanzati, Trieste. [3]Centro de Investigación en Complejidad Social (CICS), Universidad del Desarrollo. [4]Centro de Neurociencias de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso.
Altruism (an outcome-based behavior) and reciprocity (an intentions-based behavior) are crucial for the maintenance of cooperative interactions. However, their neurophysiological bases and specific contributions to the repayment of trust remain unclear.

Here, using a mixed version of the Dictator (DG) and the Investment game (IG), together with electroencephalography, we uncover *(i)* the interplay between altruism and reciprocity, and *(ii)* the neurophysiological activity underlying the integration of outcomes and intentions concerns in trust-repayment behavior.

We found that altruism is a basal component in the repayment of trust, and that reciprocity depends on a critical amount of perceived trust. Thus, assessing for altruism unmask, from trust-repayment behavior (clasically considered to be only positive reciprocity), three components: altruism, and positive and negative reciprocity.

In addition, event-related potentials (ERPs) analysis shows that subjects' feedback-related frontomedial negativities (FMN) differ between outcome *versus* intentions-based conditions, being more prominent in the outcome-based trials, but predicting subjects responses to trust in the intentions-based trials. Furthermore, source analysis suggests that brain structures, including dorsomedial prefrontal cortex (DMPFC), temporoparietal junction (TPJ), and dorsolateral prefrontal cortex (DLPFC), are responsible for this neurophysiological activity.

In summary, our work shows that trust-repayment behavior is composed of altruism, positive reciprocity, and negative reciprocity, and that outcomes and intentions are codified differently by FMN, being TPJ, DMPFC and DLPFC the brain structures that seems to be responsible of this neural activity.



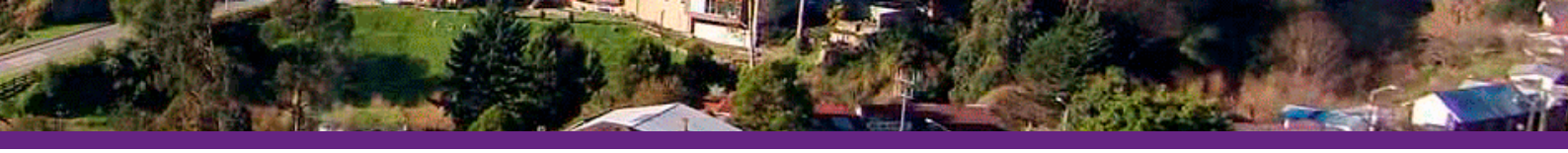
Finger temperature: A novel psychophysiological assessment of attention

Ávalos-Latín Camila[1], Vergara Rodrigo[1], Moënne-Loccoz Cristóbal[1], Egaña José[1], Maldonado Pedro[1]. [1]Neurociencias, Medicina, Instituto de Neurociencia Biomédica, Universidad de Chile. (Sponsored by Biomedical Neuroscience Institute, Universidad de Chile. FONDECYT Postdoctorado 3160403.)

Attention is targeted by a wide range of disciplines, for instance, to avoiding driving and industrial accidents, to understand and treat attentional deficit and hyperactivity disorder (ADHD), or to understand it as a cognitive phenomenon. Attention is usually assessed physiologically using EEG; however, little is known if we can improve the prediction of attentional performance including psychophysiological responses triggered by attentional demands. In this work, we aim to explore whether peripheral temperature, measured through finger skin temperature, can improve the prediction of attentional performance when compared with EEG spectral activity. We recruited 34 participants of ages ranging from 19 to 36 years old, from the Facultad de Medicina, Universidad de Chile. They went through four tasks: Baseline, Continuous Performance Task (CPT), the Flanker task (FT), and a Counting task (CT), 10 minutes each. These tasks were performed to measured baseline variation of body temperatures during a resting state (Baseline), sustain attention (CPT), resilience to distractors (FT), and attentional resources (CT). To predict attentional performance, we used multiple linear regressions, using an index of change in finger temperature, and EEG spectral bands Alpha, Theta, and Beta. Spectral activity presented an inverse association with Finger Temperature for all attentional tasks, while for the Baseline presented a positive slope. Finger temperature was able to estimate attentional performance and improving the predictions made using EEG spectral measurements alone. We conclude that our results address possible applications of finger temperature for attention research as well as in accident prevention, workload, and fatigue prediction.

Biomedical Neuroscience Institute, Universidad de Chile.

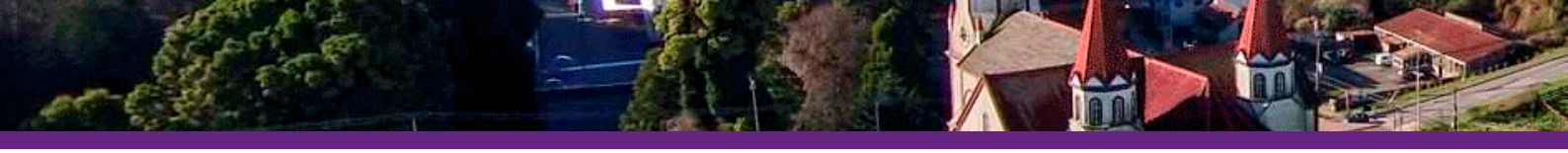
FONDECYT postdoctorado 3160403.



Impact of musical training on the fronto-parietal control network in selective and divided attention

Kausel Leonie[1,2], Zamorano Francisco[3,4], Billeke Pablo[3], Larrain-Valenzuela Josefina[3], Sutherland Mary-Elizabeth[3], Stecher Ximena[5], Schlaug Gottfried[6,7], Aboitiz Francisco[2]. [1]Psiquiatría, Medicina, Pontificia Universidad Católica de Chile. [2]Centro Interdisciplinario de Neurociencias, Pontificia Universidad Catolica de Chile. [3]CICS, Gobierno, Universidad del Desarrollo. [4]Radiología, Clínica Alemana de Santiago. [5]Neurología, Clínica Alemana de Santiago. [6]Neurology, Beth Israel Deaconess Medical Center. [7]Neurology, Harvard Medical School. (Sponsored by Francisco Aboitiz)

The ability to focus on one (selective attention-SA) or more stimuli at the same time (divided attention-DA) is a crucial capacity that allows us to cope successfully with our daily life. Since playing a musical instrument demands to pay attention to lots of simultaneous multimodal events, we hypothesized that the neural networks underlying these attention skills could be boosted in children who regularly learn and play a musical instrument. This study aimed to reveal the neural correlates of bimodal (auditory and visual) SA and DA for children (12.20.8 years) with (n=18) and without (n=17) musical training as measured by functional magnetic resonance imaging (fMRI, 3T Siemens Skyra). In the scanner, children solved a task that presented simultaneous visual (figures) and auditory (melodies) stimuli. They were asked to attend to the visual (visual SA), the auditory (auditory SA) or to both (DA) stimuli at the same time. To evaluate attention, they answered an auditory and visual memory task. Behavioral results showed that musically trained children compared to controls had more correct responses on both memory tasks in all attention conditions. fMRI results showed that musically trained children had significantly higher activation of fronto-parietal brain areas such as dlPFC and left medial superior parietal area in all attention conditions. Results support the hypothesis that musical training in childhood enhances the activation of the fronto-parietal network that underlies effective attentional control in these children. Results also suggest that musical training could be used as an intervention strategy for children with attentional problems.CONICYT Doctorate Scholarship 21140209 to LK.

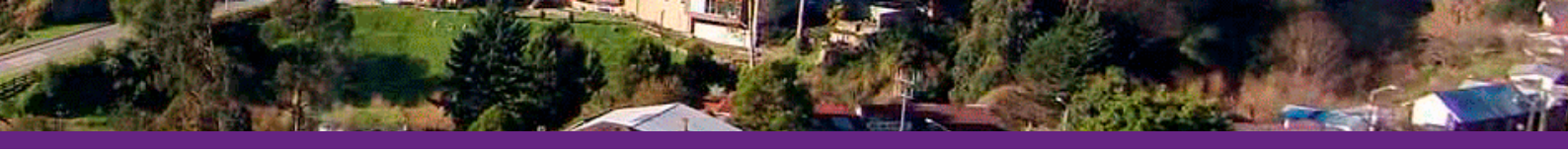


Does theta activity priming in lateral prefrontal cortex increase proactive cognitive control?

Martínez-Molina María Paz [1], Valdebenito-Oyarzo Gabriela [1], Larraín-Valenzuela Josefina[1], Stecher Ximena[2], Salinas Cesar[2], Zamorano Francisco[1], Billeke Pablo [1]. [1]División de Neurociencia (neuroCICS), Centro de Investigación en Complejidad Social, Facultad de Gobierno, Universidad del Desarrollo. [2]Departamento de Imágenes, Clínica Alemana de Santiago.

In conflictive situations, subjects have the ability to coordinate their thoughts and actions according to their objectives, but they are also able to integrate previously occurring events to anticipate control requirements, known as proactive cognitive control. Electroencephalography (EEG) studies have described that theta band activity over medial prefrontal cortex is associated with cognitive control, mainly with reactive cognitive control. Furthermore, using functional Magnetic Resonance Imaging (fMRI), proactive cognitive control has been associated to activity in dorsolateral prefrontal cortex (dlPFC). However, it is not clear if proactive cognitive control involves theta activity in these lateral prefrontal areas. We hypothesized that theta oscillatory activity in dorsolateral prefrontal cortex has a causal role in proactive cognitive control. In order to test this hypothesis, seventeen healthy subjects participated in two experimental sessions. First, subjects solved the multi-source interference task during an fMRI scan, and second, theta activity was induced in dlPFC with an fMRI guided Transcranial Magnetic Stimulation (TMS)-EEG experiment while subjects performed a go no-no task. Our initial results show a causal role for theta oscillatory activity of lateral prefrontal cortex in proactive cognitive control. As subjects anticipate the likelihood of requiring control, more lateral prefrontal activity occurred, specifically in superior frontal sulcus. In addition, non-invasive brain stimulation at theta frequency seemed to enhance this cognitive control. This TMS intervention could be used as a therapeutic target in pathologies associated with cognitive control difficulties such as Attention Deficit Hyperactivity Disorder.

FONDECYT 1181295



Posterior Parietal Cortex Encodes Value And Prediction Error During Decision-making Under Ambiguity

Valdebenito-Oyarzo Gabriela [1], Martinez-Molina María Paz[1], Larraín-Valenzuela Josefina[1], Stecher Ximena[1], Salinas Cesar[1], Zamorano Francisco[1], Billeke Pablo[1]. [1]División de Neurociencias (NeuroCICS) Centro de Investigación en Complejidad Social, Facultad de Gobierno, Universidad del Desarrollo.

The scientific evidence that unravels the neurobiological activity that codifies the value focuses mainly on the prefrontal cortex and the parietal cortex, however, the role of the Parietal Cortex is not yet clear. We hypothesize that the posterior parietal cortex encodes value and prediction error during decision-making under ambiguity. In our study, 39 healthy subjects participated in the first stage and we studied probabilistc task using fMRI. In second stage (13 healthy subjects) we study which the activity of predictior error during feedback in ambiguity conditions using TMS-EEG. The participants solved a probabilistic task that had two conditions: Ambiguity and non-ambiguity. Behavioral results: The results shows that the participants considerer the visible probability and outcomes in conditions of non-ambiguity, in conditions of ambiguity the subjetc considerer less the visible probability. Neurobiological results: We study which is the value activity that modulated the ambiguity condition and the activity of predictior error during feedback in ambiguity conditions, the results show neurobiological activity of PPC and IPS. The psicophysiological interaccion between coincidence áreas of value and prediction error of one ROI selected of PPC and the results shows interaction with Cingulate Anterior during decision-making under ambiguity. The Stimulacion using TMS-EEG in PPC and IPS show that the PPC and IPS encodes value and uPE under ambiguity.The stimulation with TMS in IPS show that PFC encodes *prefentially*PE in non-ambiguity and the stimulation with TMS in PPC show that PFC encodes *preferentially*PE in ambiguity.

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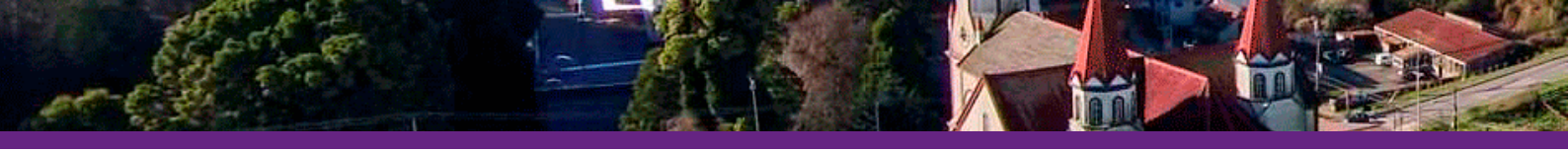

Prefrontal cortex theta frequency source activity during a novel planning task

Domic-Siede Marcos[1,2], Follet Brice[1], Valdés Joaquín[1], Santander Daniela[1], Perrone-Bertolotti Marcela[2], Ossandón Tomás[1]. [1]Departamento de Psiquiatría, Facultad de Medicina, Pontificia Universidad Católica de Chile. [2]Laboratoire de Psychologie et NeuroCognition, UMR (5105) CNRS (INSB), Université Grenoble Alpes. (Sponsored by Becas de Doctorado Nacional, Año 2015 Of CONICYT Scholarship: 21150295 And FONDECYT Regular: 1140996.)

Cognitive planning consists on a sequenced development of a plan to achieve a specific goal and is related with cognitive control function. Behavioral paradigms of planning are a current challenge in cognitive neuroscience and specifically when neural correlates would be assessed. Literature suggested that cognitive control tasks, in general, involve midline frontal activity on theta band. Nevertheless, there are not specific results for planning in terms of oscillatory activity and its sources origin. We designed a planning task adapted from the Porteus and Zoo Map Task. Twenty-seven healthy adults performed this planning task coupled to EEG recording. Participants were instructed to solve 36 mazes (which represents a zoo map) planning a path to visit animals following a set of rules (planning condition). We focus on theta frequency band to evaluate brain regions implication in planning processing. We performed brain source reconstruction using sLORETA. We showed an increase in bilateral local theta frequency sources activity in the prefrontal cortex during planning condition. Source reconstruction suggested that these bilateral theta activity increase was related with: fronto-polar cortices (Wilcoxon, left (L): z = 71, p=0.0036**; right (R): z = 92, p=0.0187*), Anterior Cingulate Cortices (Wilcoxon, L: z = 57, p=0.0009***; R: z = 67, p=0.0025**), Superior Frontal Gyri (Wilcoxon, L: z = 56, p=0.0008***; R: z = 58, p=0.0010**). Thus, our results present for the first time in the cognitive control literature brain correlates of the planning process and suggested a more prefrontal cortex demands as other literature results related to cognitive control.

Research supported by Becas de Doctorado Nacional, año 2015 of CONICYT scholarship: 21150295 and FONDECYT regular: 1140996.

Motor adaptation- an error based learning process, involves contributions from multiple cortical and subcortical regions of the human brain organized in widespread networks, in which the cerebellum seems to play a fundamental role. Large-scale synchronization of oscillatory activity could be an effective strategy to integrate the cerebellar function with the rest of the system, however there is no direct evidence of this proposal. To investigate the impact of cerebellar stimulation on motor adaptation and brain connectivity, we conducted a study where 18 healthy participants carried out a visuo-motor adaptation task in parallel to receive a protocol of cerebellar transcranial alternating stimulation (tACS), a form of electrical stimulation that could entrain the nervous system in a frequency-specific oscillatory activity. Applying tACS in different days, we yielded evidence that tACS at 50Hz, but not at 20Hz or sham, accelerated the rate of adaptation in parallel to enhance the event-related power modulation and phase-synchronization. This effect was evident for the comparison between tACS-50Hz and sham in a range of alpha and beta band (8-30 Hz). Notably, active tACS conditions (50Hz and 20Hz) imposed a particular modulation of neural activity that prevent a direct comparison between them in the 13-30Hz range. No changes in visuomotor coordination were detected. Our results support the notion that purkinje cell-deep nucleus, a key network for motor error processing, could be the target of tACS. Overall, tACS demonstrated the potential to entrain the nervous system in a function-related oscillatory activity, which bring the opportunity to modulate cognitive functions.
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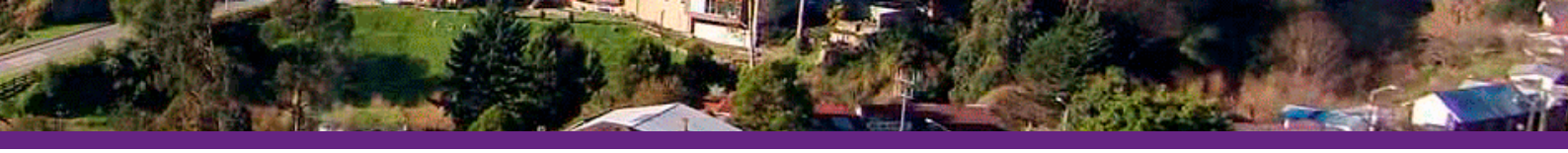


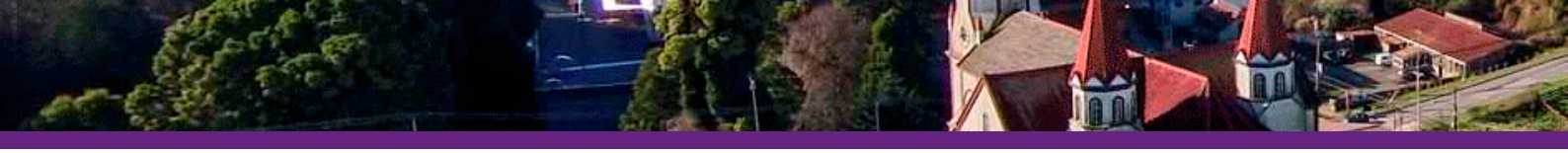
SESIÓN DE PANELES I

1)Theory of single-molecule biophysics on F1-ATPase

Matute Ricardo Andrés[1]. [1]Centro Integrativo de Biología y Química Aplicada (CIBQA), Campus Rondizzoni, Universidad Bernardo O`higgins.

Description of a theoretical and computational study of kinetic processes in F1-ATPase systems probed by single-molecule imaging experiments which provide information that is not available from ensemble experiments. Single-molecule experiments such as imaging and rotor manipulation have revealed that the rate constants of enzymatic steps, e.g., ATP binding, ATP hydrolysis, or phosphate release, show an exponential dependence on the stalled rotor angle. Hence, understanding the dynamical interplay of reactions and mechanical rotation in the protein is crucial to elucidate the biological function in the F1-ATPase enzyme. Taking into consideration the ideas underlying the theories of electron and group transfer reactions, I will describe a structure-based analytic model in order to treat the dynamical behavior observed in single-molecule experiments for F1-ATPase.

Dr. Matute acknowledges the FONDECYT Grant No. 1181260 and the NSF/XSEDE Allocation Grant MCB170140 (USA). The author also acknowledges the National Laboratory of High Performance Computing NLHPC (ECM-02).

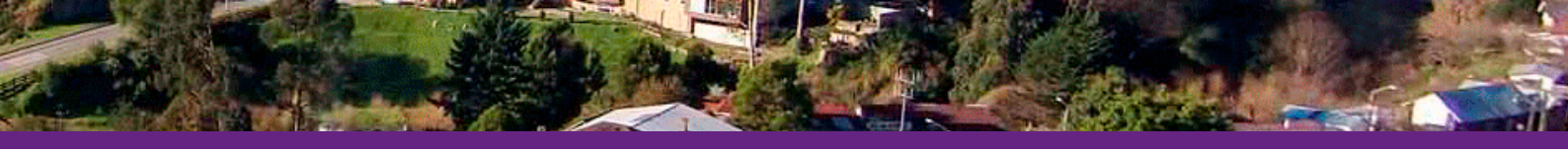


2) Effect of crowding stress over the proteolytic mechanisms in the skeletal muscle of rainbow trout (Oncorhynchus mykiss)

Ponce Claudia Andrea[1], Valenzuela Cristián[1], Avendaño-Herrera Rubén[1], Valdés Juan Antonio[1], Molina Alfredo[1]. [1]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias de la Vida, Universidad Andrés Bello.

Chile is the main producer of rainbow trout in the world. The constant need to increase production has led to the use of inappropriate practices such as high densities of culture. This generates an increase on stress in the individuals, which impact negatively different biological process in the organism. The skeletal muscle is one of the most affected tissues by the stress conditions. The protein degradation in this tissue is vital for the supply of energy and this catabolic process is mediated by different proteolytic pathways such as ubiquitin-proteasome, autophagy and calpain system. Nevertheless, the regulation of these proteolytic axis under stress conditions are not yet completely clear. In this context, we evaluated the stress effect "*in vivo*" generated by high stocking density in juvenile rainbow trout. First, the fish were keep in high cultivation densities (30Kg/m3) during 15, 45 and 60 days, using as control group fish on 10kg/m3. Skeletal muscle was sampled at each experimental point and RNA was extracted. Transcript levels of key genes related to proteolytic mechanisms in skeletal muscle were evaluated using RT-qPCR. It was observed an increase in the cortisol levels and an increase in the relative expression of genes like *calpain 1*, *calpain 2* and *calpastatin* associates to calpain complex. The autophagy associated gene *bnip3* was up-regulated. In the case of ubiquitin-proteosome system, just *Atrogin-1* was up-regulated. All these data suggest that stress conditions like crowding, promotes the muscle degradation through the up-regulation of the 3 principal proteolytic mechanisms described before.

FONDAP 15110027, FONDECYT 1171307, and FONDECYT 1171318

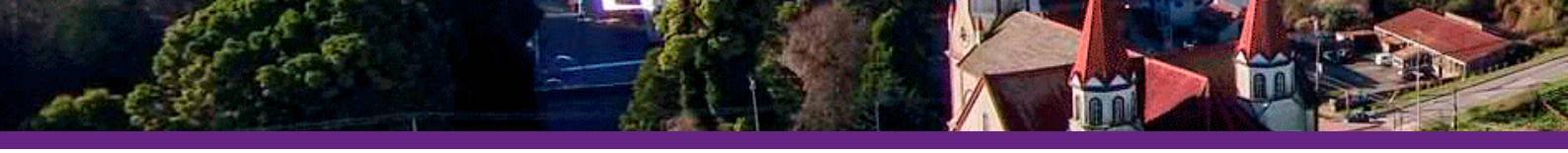


3) Calcium signals mediated by the inositol 1,4,5-trisphosphate receptor (IP3R) mediate the Ferroptotic cell death induced by acute inhibition of Glutathione Peroxidase 4

Campos Muñoz Joaquín[1], Aguirre Pabla[1], Hidalgo Cecilia[2], Nuñez Marco Tulio[1]. [1]Biology, Sciences, Universidad de Chile. [2]Biomedical Neuroscience Institute (BNI), Department of Neurosciences, CEMC and ICBM, Medicine, Universidad de Chile. (Sponsored by Marco Tulio Nuñez Gonzalez)

Ferroptosis is an iron-dependent cell death pathway that involves depletion of intracellular glutathione (GSH) levels and iron-mediated lipid peroxidation. In neurons, ferroptosis is similar but not the same as Oxytosis. Ferroptosis is experimentally caused by inhibition of the cysteine/glutamate antiporter xc−, which depletes cell of GSH, or by inhibition of GPx4, the only know enzyme that catalyzes the detoxification of lipid peroxides. In Ferroptosis, the events that occur between GPx4 inhibition and the execution of cell death are unknown. Here we show that in SH-SY5Y neuroblastoma cells, inhibition of GPx4 by RAS Selective Lethal Compound 3 (RSL-3) generated calcium signals, detected by FURA-2 and Fluo-3, coupled to increased oxidative damage, evidenced by Bodipy C11 oxidation and the formation of protein/4-HNE adducts. RSL-3-induced calcium signals and cell death were inhibited by xestospongin C, an inhibitor of IP3R calcium channels, by calcium chelation with BAPTA-AM, or by IP3R down-regulation by carbachol. We propose that acute inhibition of Gpx4 in SH-SY5Y cells induces IP3R-mediated calcium signals that promote Ferroptosis, acting before or in parallel to lipid peroxidation and cell death. Putative effectors of this pathway are discussed.

Supported by FONDECYT 1170053 and BNI P09-015-F grants to CH, and by PAIFAC Faculty of Science, VID U-Ayuda and FONDEF 17I10095 grants to MTN.

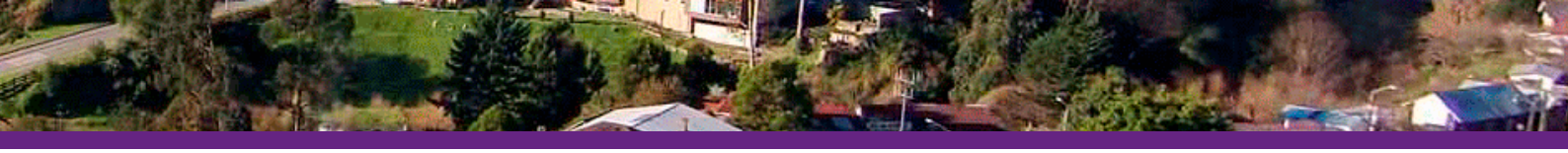


4) Periodic stimulation of RVLM-C1 neurons triggers long-term ventilatory disorders and sympathoexcitation

Andrade David Cristobal[1,2], Toledo Camilo[1,3], Arce-Alvarez Alexis[1], Hugo Diaz[1], Lucero Claudia[1], Rodriguez-Fernandez Maria[4], Del Rio Rodrigo[1,3,5]. [1]Lab. of Cradiorespiratory Control, Ciencias Biológicas, Pontificia Universidad Católica De Chile. [2]Centro de Investigación en Fisiología del Ejercicio, Facultad de Ciencias, Universidad Mayor. [3]Centro de Envejecimiento y Regeneración (CARE), Pontificia Universidad Católica de Chile. [4]Instituto de Ingeniería Biológica y Médica, Pontificia Universidad Católica de Chile. [5]Centro de Excelencia en Biomedicina de Magallanes (CEBIMA), Universidad de Magallanes.

Sympathoexcitation is dependent of catecholaminergic neurons from the rostral ventrolateral medulla (RVLM-C1). It has been proposed that RVLM-C1 neurons can modulate breathing. However, the relative contribution of RVLM-C1 neurons to the long-term breathing disorders and sympathoexcitation has not been determined. Therefore, we propose to determine if the activation of RVLM-C1 neurons in-vivo induces long-term ventilatory disorders and sympathoexcitation in rats. Sprague-Dawley rats (n=6;250±20g) were used. A lenti-viral-vector carrying the light-sensitive cation channel channelrhodopsin 2 (LVV-PRSX8-ChR2-YFP) was stereotaxically injected unilaterally into the RVLM to activate C1 neurons. In the contralateral side, LVV-PRSX8-ChR2-YFP was co-injected with an immuno-toxin recognizing dopamine-**β**-hydroxylase conjugated with saporin (D**β**H-SAP, 7.5 ng/150nl) to eliminate C1 neurons. Fibers optics were bilaterally implanted into the RVLM for photostimulation (10ms/20Hz/30s) in freely moving rats. Episodic stimulation of C1 neurons in vivo triggers a long-term ventilatory instability characterized by an increase of coefficient of variation of tidal volume (Post-stimulation vs. Pre-stimulation, $p<0.05$) (170.8±15.1 vs. 100.0±4.2%) and short-term breath to breath interval variability (169.7±12.9 vs. 100.0±5.6%) and sympathoexcitation (549.1±101.1 vs. 158.7±23.9%). In addition, we found that RVLM-C1 stimulation induces respiratory-sympathetic coupling (coherence between ventilation-sympathoexcitation) (194.6±22.9 vs. 100.0±17.69%) and active expiration (0.64±0.08 vs. 0.47±0.01 late/early expiratory phase). We found that ventilatory rhythm gets out of phase with heart rhythm after C1 activation (-0.40±0.10 vs. -0.18±0.02 1/Hz, $p=0.07$, LVVPRSX8-ChR2-YFP vs. D**β**H-SAP+LVVPRSX8-ChR2-YFP). These effects were not observed in the RVLM region treated with D**β**H-SAP toxin. Our results described a novel role of RVLM-C1 neurons into long-term modulation of breathing regularity and cardiac autonomic function in rats.

Supported by Fondecyt 1180172.

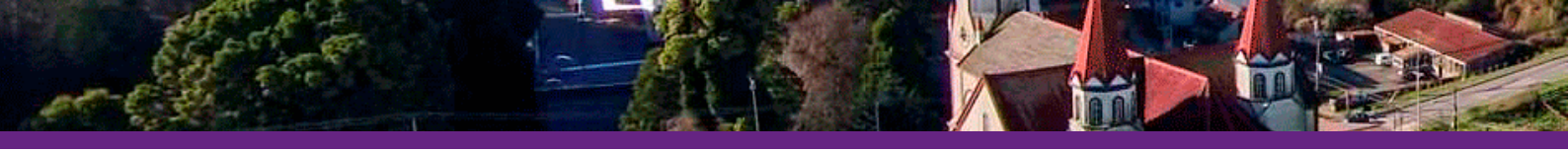


5) Frequency of apolipoprotein e (apoe) ε2, ε3 and ε4 genetic variant in healthy individuals of the Region of Antofagasta.

Urzua Ximena[1], **Placencia Pablo[1]**, Galvez Anita[1], Escobar Jorge[1]. [1]Laboratorio de Genética, Dpto. Biomédico, Ciencias de la Salud, Universidad de Antofagasta.

Genetic marker studies are relevant to evaluate the association among the existence of allelic variant and susceptibility to develop non-contagious diseases. Identification of certain allelic variants, such as the different isoforms of the of Apolipoprotein E (ApoE) gene, located in exon 4 of chromosome 19, may allow for early prevention of the development of several cardiovascular pathologies. The E3/4 variant has been related to higher risk of cardiovascular disease and increased levels of low-density lipoprotein cholesterol (LDL-C). Thus, the main goal of the present study was to evaluate genotypic distribution and allelic frequency of the isoforms **ε**2, **ε**3 and **ε**4 of ApoE gene and their effects on plasma lipid levels in a cohort of population in the city of Antofagasta. This study evaluated 127 healthy adult individuals of both gGender. Genomic DNA was extracted from peripheral blood leukocytes through the saline precipitation method. Genetic variants were determined by real-time PCR using TaqMan probes. Plasma was processed to quantitate total cholesterol, triglycerides, HDL and LDL. Lipid profiles were determined by colorimetric enzyme tests.

Anthropometric and clinical characteristics such as BMI and blood pressure were all among normal parameters. Genotypic distribution was E2/2=0.8%, E2/3=3.9%, E3/3=84%, E2/4=0.8%, E3/4=10.2% and E4/4=0%. Allelic frequencies were **ε**2=0.03, **ε**3=0.9 and **ε**4=0.06. Results showed that genetic variant did not change lipid profiles in all studied subjects. It is required to increase the sample size and conduct a case-control study to determine the potential impact of this genetic variant on our population. Programa Semillero de Investigacion. Vicerrectoria de Investigacion, Innovacion y Postgrado, Universidad de Antofagasta



6) Identification and transcriptomic profiling of the CAZyome of Xanthophyllomyces dendrorhous

Campusano Sebastián Leimir[1], Sepúlveda Dionisia[2,1], Baeza Marcelo[2,1], Alcaino Jennifer[2,1], Cifuentes Víctor[2,1]. [1]Departamento de Ciencias Ecológicas, Facultad de Ciencias, Universidad de Chile. [2]Centro de Biotecnología, Facultad de Ciencias, Universidad de Chile.

Xanthophyllomyces dendrorhous is a basidiomycetous yeast which is recognized for its ability to produce secondary metabolites of commercial interest such as carotenoids and mycosporines. This yeast can grow under various carbon sources, and the yield of products formation may be affected by glucose-mediated catabolite repression through protein Mig1 and the Cyp8-Tup1 complex. In this context, carbohydrate-active enzymes (CAZymes) play a key role since they are involved in diverse biological processes such as metabolism, protein modifications and secondary metabolites production. In this work, we aimed to identify and characterize the CAZyome of *X. dendrorhous*. Through Homology-to-peptide pattern analysis of predicted proteins, we identified 174 CAZymes (70 Glycosyl Transferases, 74 Glycoside Hydrolases, 2 Polysaccharide Lyases, 10 Carbohydrate Esterases, 11 Auxiliary Activities and 10 Carbohydrate-binding Modules), which forms the CAZyome of *X. dendrorhous*. 108 enzymes were functionally annotated and metabolic pathways were analyzed through Kyoto Encyclopedia of Genes and Genomes (KEGG) mapping. 65 CAZymes would be involved in glycan biosynthesis and carbon metabolism, 13 in genetic information processing, and 30 were annotated in diverse pathways such signaling and amino acid metabolism. By comparing the RNA-seq profiles of wild-type and mutant strains *mig1-*, *cyc8-* and *tup1-* cultured with glucose as the sole carbon source, we found 25 CAZymes differentially expressed (p-value >0.05) at least in one mutant strain. Our results suggest that there are some CAZyome members which may be affected by glucose-mediated catabolite repression in *X. dendrorhous* through the Cyc8-Tup1 complex and transcription factor Mig1.

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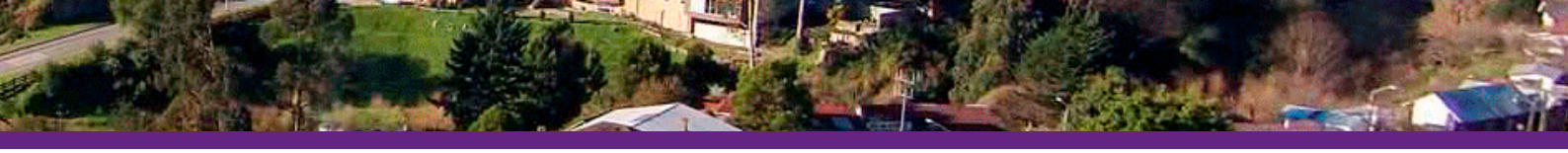
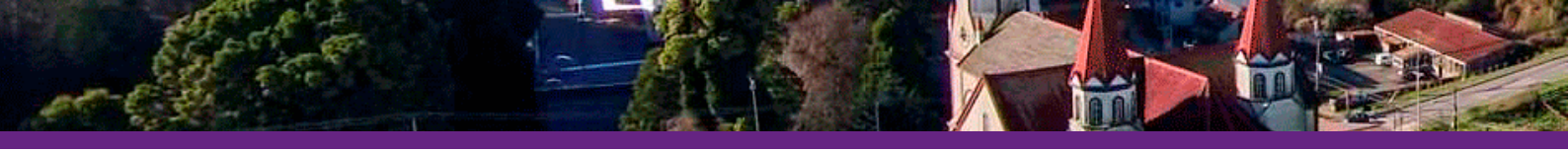


7) Effect of temperature on the activity and unfolding of an amylase secreted by the cold-adapted fungi Tetracladium sp

Peragallo Vicente Andrés[1], Rubio Constanza[1], Barahona Salvador[1], Cifuentes Victor[1], Alcaíno Jennifer [1], Baeza Marcelo[1]. [1]Ciencias Ecológicas, Ciencias, Universidad de Chile.

Tetracladium sp. is a fungi isolated from Antarctica, and secrete several enzymes of industrial/ biotechnological interest such as amylase. This enzyme hydrolyze **α**-glucosidic bonds and might hold interesting features as it is adapted to cold weather. It is assumed that enzymes from cold environments are more flexible, especially in their active sites, than mesophilic counterparts. The objective of this study was to determine the activity and unfolding of the amylase from *Tetracladium sp.* in a wide range of temperatures. The activity was measured using the dinitrosalicylic acid (DNS) method and the protein unfolding by the binding of the fluorescent dye SYPRO Orange (which binds to hydrophobic protein segments) using a qPCR thermal cycler. The enzyme activity begins to decrease from 40ºC, and it is completely lost at 55 ºC. An increment in the fluorescence of protein sample was observed in the same range of temperature. These results indicate that the loss of amylase activity due to temperature depends of the loss of global enzyme structure. Contrary, in other enzymes active at low temperatures the activity is lost at lower temperatures than the global protein structure. Our results strongly suggest, that the active site of amylase from *Tetracladium sp.* is not the more termolabile region of the enzyme, as occur in other cold-active enzymes.

Financiamiento: Proyecto Fondecyt 1180233

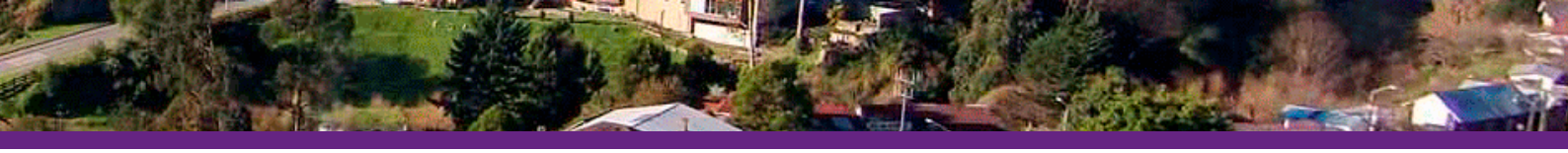


8) Effect of low temperature in growth of Antarctic yeasts

Zúñiga Sergio [1], Barahona Salvador[1], Alcaíno Jennifer[1], Cifuentes Victor[1], Baeza Marcelo[1]. [1]Ciencias Ecológicas, Ciencias, Universidad de Chile. (Sponsored by Marcelo Enrique Baeza Cancino)

The effect of low temperature on organisms has been studied extensively since it has structural and functional consequences in several cellular components. There is an increasing interest in the adaptation mechanisms developed by microorganisms to live at low temperatures, in the case of psychrophilic yeasts, due to their ecological importance and biotechnological/industrial applications. Most studies about cold response have been performed in mesophilic yeasts submitted to cold-stress. Our objective is to study the response of eight Antarctic yeast species (optimum growth temperatures between 10 and 30 ºC) to low temperatures, thus, first it is necessary to determine the stress conditions by low temperature for each one. The yeasts were grown in liquid medium at their respective optimum temperature to reach mid-log phase and then cultures were divided. One half was cultivated at the same temperature and the other at 4ºC, and the growth was monitored at 600 nm. The yeast *Wickerhamomyces anomalus* showed significant decrease in growth by incubation at 4ºC, while *Candida sake* was not affected. *Cryptococcus victoriae* displayed differences when exposed to 4ºC for 5 hours, later reactivating its growth. As can be seen, the response to cold-stress was variable among the yeast species tested, an aspect necessary to consider when designing experiments to study the global gene expression changes induced by cold-stress in these yeasts.

Proyecto Fondecyt 1180233

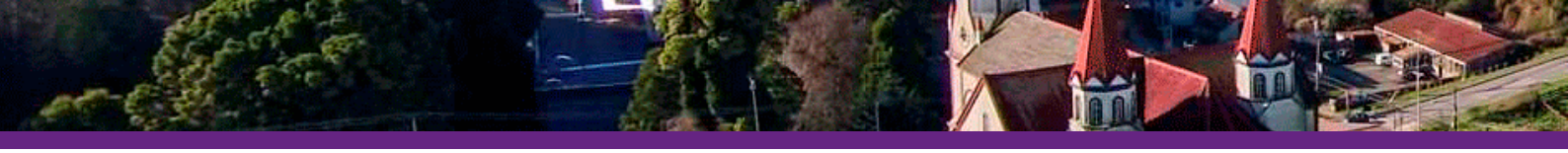


9) REM sleep in the dark: is there a closed loop control system? Experiments with photic masking

Ocampo-Garcés Adrián Pedro[1], Barrera Norma[1], Bassi Alejandro[1], Estrada Jorge[1], Diaz Javier[1]. [1]Laboratorio de Sueño y Cronobiología, Fisiología y Biofísica, Instituto de Ciencias Biomédicas, de Medicina, Universidad de Chile.

Eutherian mammals present (age-specific) stable quotas of Rapid Eye Movement (REM) sleep. If the stability of the REM sleep quota is determined by a closed loop control system (REM sleep homeostat) as has been proposed by "homeostatic models" of REM sleep, the temporal profile of REM sleep should behave as a hourglass process that keeps track of the insensitive to the activation of REM-on neurons targeted by photic masking.cumulated REM sleep time, so that REM sleep is promoted in response to REM sleep deficits and postponed when challenged by REM sleep excesses. Current models are mostly based on sleep deprivation experiments, including selective REM sleep deprivation (RD) in humans and rodent models. In the albino rat, short dark pulses (DP) transiently increase REM sleep amount by shortening the latency of NREM to REM sleep transitions, phenomenon known as photic masking. Photic masking provide a useful strategy to explore the REM sleep hourglass process in response to REM sleep excess. Male Sprague-Dawley albino rats were polysomnographically recorded and subjected to 4 hours of RD during the rest phase (zeitgeber time, ZT, 4-7; light:dark cycle= 12:12). REM sleep rebound magnitude was highly affected by DP: in the two hours after RD alone REM sleep amounted 10.9 minutes and when occurring in the presence of DP was 22.2 minutes. Instead of returning to baseline values, REM sleep after DP sustainedly exceeded predicted quota suggesting that REM sleep control system is defective in detecting REM sleep overshoots

Supported by Guillermo Puelma Foundation.



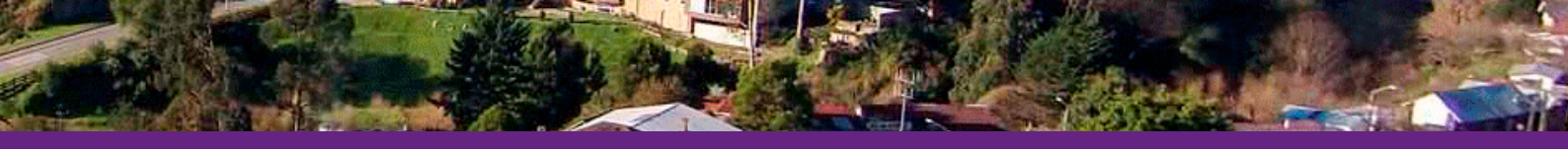
(NO SE PRESENTÓ)

10) Impact of membrane-initiated cortisol action in the early transcriptional response of rainbow trout (Oncorhynchus mykiss) skeletal muscle

Aedo Jorge [1], Antiqueo Paulette[1], Boltaña Sebastián[2], Bastías Macarena[3], Meneses Claudio[3], Molina Alfredo[1], Valdés Juan Antonio[1]. [1]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias de la Vida, Universidad Andrés Bello. [2]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción. [3]Centro de Biotecnología Vegetal, Facultad de Ciencias de la Vida, Universidad Andrés Bello.

Cortisol is the main hormone involved in the regulation of metabolic adjudgments during stress. Cortisol action is attributed to its interaction with intracellular glucocorticoid receptors and the modulation of targets genes (genomic action). However, cortisol also can interact with membrane components activating rapid signaling pathways with unknow contribution during the stress response. Therefore, in the present work we sought to identify potentially genes and biological process modulated through membrane-initiated cortisol action in fish skeletal muscle. Rainbow trout were pre-treated with metyrapone to inhibit endogenous cortisol synthesis and then intraperitoneally administrated with vehicle, cortisol and cortisol-BSA (membrane impermeable analogous of cortisol). After one, three and nine hours, plasma and skeletal muscle were collected. RNA from skeletal muscle of experimental and vehicle groups were sequenced using Illumina 2500 technology. RNA-seq analysis were performed using CLC genomic workbench software and functional annotation were performed using DAVID GO and KEGG tools. Plasma cortisol levels increased in both cortisol and cortisol-BSA groups respect to vehicle. 433 of 618 million high-quality reads from each condition were mapped onto reference genome rainbow trout. RNA-seq analysis shows 4153, 1391 and 1428 differential expressed genes between cortisol-BSA and vehicle group at one, three and nine hours, respectively. Functional annotation reveals that focal adhesion is the mainly process up-regulated at one and three hours under cortisol-BSA treatment, whereas growth-signaling pathways such: PPAR and FOXO signaling are modulated at 9 hours. Our results suggest that membrane-initiated cortisol action contributes in the regulation of the physiological response to stress in fish.

FONDAP 15110027, FONDECYT 1171307, and FONDECYT 1171318

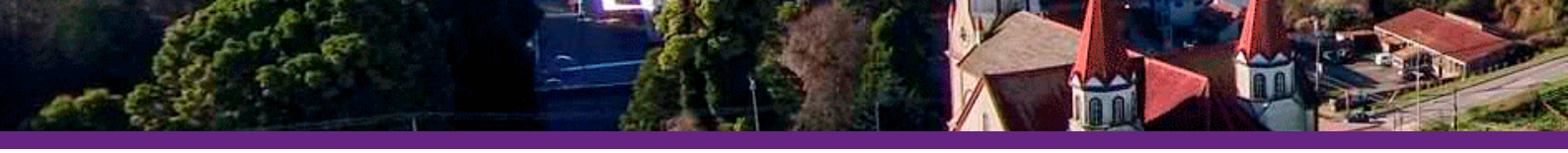


11) Impact of membrane-inititated cortisol action over the expression of corticosteroid receptors in rainbow trout liver (Oncorhynchus mykiss)

Ramírez Carolina Isabel[1], Aedo Jorge[1], Olivares German[2], Molina Alfredo[1], Valdés Juan Antonio[1]. [1]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias de la Vida, Universidad Andrés Bello. [2]Piscicultura de Rio Blanco, Escuela de Ciencias del Mar, Pontificia Universidad Católica de Valparaíso.

Stress is a condition in which the internal balance of the animal or homeostasis is disturbed by biotic or abiotic stimuli denominated stressors. The physiological response to stress is attributed mainly to the role of glucocorticoid hormones, with cortisol being the main glucocorticoid secreted in fish. The mechanism of action of cortisol is attributed to its interaction with glucocorticoid (GR) and mineralocorticoid (MR) receptor, and the subsequent modulation of target genes by hormone-receptor complex. Nevertheless, cortisol also signaling trough cell surface components in a poorly understood mechanism known as membrane initiated- or non-canonical cortisol action. Until now, the impact of non-canonical cortisol action over the regulation of the corticosteroid receptors has not been determined. Therefore, in this work we evaluate the levels of transcripts of *gr1, gr2* and *mr* in the liver of rainbow trout administrated during 1, 3 and 9 hours with cortisol and cortisol-BSA. The latter corresponds to a membrane-impermeable cortisol analogous and exclusive inductor of non-canonical effects. As a control group we include fish administrated with vehicle and only BSA. Our results reveal that cortisol and cortisol-BSA modulates *gr1*, *gr2* and *mr* gene expression in the liver of rainbow trout in a time-dependent way. It was observed that at 1 hour post-treatment with cortisol there is an increase in the transcript levels of gr1 and there is also an increase at 9 hours in fish administered with cortisol-BSA. This work suggest that membrane initiated-cortisol action contributes to modulates corticosteroid receptor in the liver of fish.

FONDAP 15110027, FONDECYT 1171307, and FONDECYT 1171318

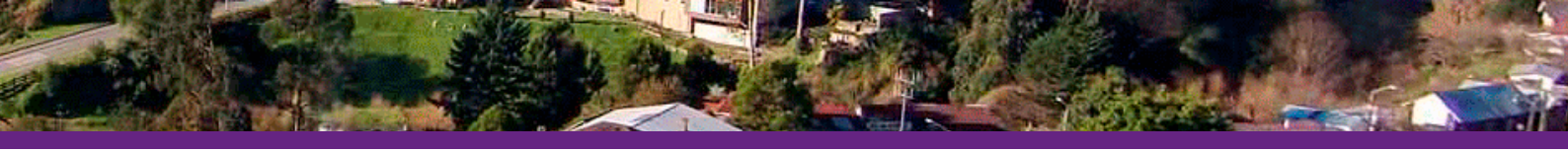


12) Effect of Wi-fi radiofrequencies on the production of secondary metabolites in vitro culture of the fungus Serpula himantioides

Oyarce Gabriela Antonieta[1], Torres Solange[1], Triviño Sergio[1], Ñanco Flavio[1], Bravo Arrepol Gastón[1], Hasbún Rodrigo[2], Becerra José [1]. [1]Laboratorio de Química y Productos Naturales, Ciencias Naturales y Oceanográficas, Universidad de Concepción. [2]Laboratorio de Epigenética Vegetal, Facultad de Ciencias Forestales, Universidad de Concepción. (Sponsored by Carlos Marcelo Baeza Perry)

Wi-fi is a technology of short-range wireless broadband that transmits at a frequency of 2,5 GHz, in the microwave-radiofrequency spectrum, and it has been positioned as one of the most used technological advances in the last years. It has been reported that direct exposition to radiofrequencies can induce physiological changes in different animals and plants species, which constitutes a source of stress. One of the degenerative effects Wi-fi can cause is the overproduction of reactive oxygen species, which can induce tissue damage and DNA alterations. As for fungi, while the effect of exposure to electromagnetic radiation in the UV spectrum has been extensively studied, the physiological effect that exposure to radiofrequencies such as Wi-fi might have is unknown. In that sense, the aim of this study was to evaluate changes in metabolism of the fungus *Serpula himantioides*, using gas chromatography - mass spectrometry (GC–MS), and measure the antioxidant activity of metabolites obtained from *in vitro* cultures of *S. himantioides* exposed to Wi-fi at 2,5 GHz. Our results show an increment in the fatty acids content, and an increased concentration of ergosterol, in total extracts from the fungus mycelium; and also an antioxidant activity increment of total extracts of *S. himantioides* culture medium, associated with an increment in the content of phenolic compounds. Taken together, our results suggest that direct exposition to Wi-fi radiation produces oxidative stress in the fungus *S. himantioides*.

To INNOVA BIOBIO 16CTEBI 2016- 67480 and FONDECYT 1151028 projects for granting the necessary resources to carry out this investigation.



13) Changes in potassium channel composition in myelinated sensory axons following injury

Diaz Paula[1], Calvo Margarita[1], Bronfman Francisca[1]. [1]Departamento de Fisiología, Ciencias Biológicas, Pontificia Universidad Católica de Chile.

Myelinated fibres have a special molecular organization of channel domains within the axon, which allows them to have saltatory conduction of the action potential. Voltage-gated sodium channels (Nav) are clustered at the nodes of Ranvier. Nodes are flanked by the paranode. Axoglial junction of the paranode is the juxtaparanode, a domain enriched in voltage-gated K+ channels Kv1.1 and 1.2. Kv1 have a general presynaptic function in suppressing terminal hyperexcitability. Sensory neurons in the peripheral nervous system have been shown to express Kv1 predominantly in the soma and juxtaparanodes of myelinated DRG neuron and an injury following axotomy result a decreased in Kv1.2 expression and a marked increase expression of Kv1.6. Rat DRG myelinated co-cultures were exposed to ascorbic acid to generate myelinating for 21DIV. Cultures with myelinated axons were subject to axonal transection to produce an injury by axotomy and KV1.2 and 1.6 expression in myelinating (MBP positive) axons at day 3-7 after transection analyzed by immunostaining. Sensory neurons in the peripheral nervous system have been shown to express Kv1 predominantly in the soma and juxtaparanodes of myelinated DRG neuron and axons following axotomy show a marked decrease in Kv1.2 expression. At later stages Kv1.2 are almost absent, but there is increased expression of Kv1.6. Our data shows that voltage-gated potassium channels composition in myelinated sensory axons change after injury. We are investigating how this alteration in the molecular composition represents a protective mechanism to suppress the hyperexcitability.

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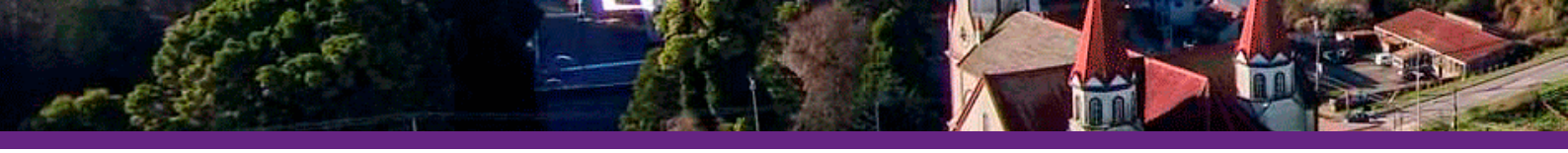
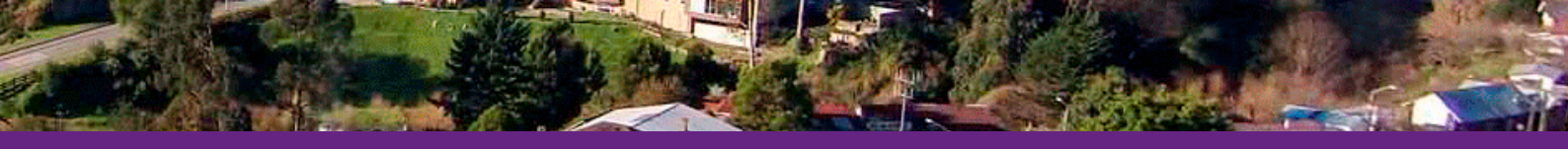


14) Novel Hv1 channel isoform isolated from bone-marrow derived cells of mouse

Peña Antonio[1], Alvear Juan[1], Villar Javiera[1], Carmona Emerson[1], Fernández Miguel[1], Picuntureo Matías[1], Navarro Nieves[1], Neely Alan[1], González Carlos[1]. [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso.

Myeloid-derived suppressor cells (MDSC) plays a key role in several physiological and physiopathological processes, among them cancer, showing immunosuppressive activity through inhibition of T lymphocytes by reactive oxygen species (ROS). ROS production is catalyzed by the enzyme NADPH oxidase (NOX). The activity of NOX induces a decreasing in the intracellular pH and an electrogenic imbalance, depolarizing the plasmatic membrane. These events regulate negatively the NOX activity, but positively the proton channel Hv1, accelerating its kinetics and opening probability, disipating the fall in the intracellular pH by extruding H+ outside the cell. Hv1 is a voltage-dependent channel selective for protons, expressed in many cells of the immune system, including bone-marrow derived cells (BMDC), which can be differentiated into MDSC, but it have not been reported isoforms of the channel in mouse. Three transcript variants of the Hvcn1 gene have been predicted *in silico*, two of them codificating for isoforms for the Hv1 protein. We hypothezise that all variants, including predicted are present in both MDSC and BMDC from mouse. To contrast the hypothesis we explored the transcript variants by RT-PCR. We identified three reported Hv1 transcripts and no predicted transcripts in MDSC and two of the three transcripts predicted in BMDC, one of them being predicted to codificate one of the two isoforms of the Hv1. We cloned this transcript by insertion into plasmid, transformation in bacteria and selection of positive clones for growth and plasmid DNA extraction. We made digestion and PCR controls to finally sequence the transcript isolated.

Proyecto FONDECYT Regular 2018 Nº 1180464,
FIB-UV Scholarship,
Millennium Science Initiative (CINV).



15) Attentional top-down and bottom-up pupil response attentional top-down and bottom-up pupil responseX

Brice Follet[1], Lachaux JP[2], Ossandon T[1]. [1]psiquiatria, Medicina, Pontificia Universidad Católica de Chile. [2]Neurosciencias, CRNL.

Many studies have shown that top-down attentional interest of the stimuli yields the pupil to dilate (Rieger and Savin-Williams 2012; Libby et al. 1973). However, in the same way, feature-based bottom-up saliency enhances a pupil response of dilation (Wang et al. 2014). From this perspective, a recent study has observed that pupil presents a greater dilation for attended areas of natural scenes when salience is lower (Mathôt et al. 2015). Authors interpret this phenomenom as a top-down effect because a lower saliency would require more cognitive resources. In order to distinguish top-down and bottom-up factors in the pupilar dilation marker and to attempt this hypothesis, we use a simple paradigm of rapid target letter detection while manipulating the saliency of the stimuli changing its color. This task requires high attentional maintaining and thus is considered difficult by its duration. Because theories of Locus Coeruleus activity (Aston-Jones and Cohen 2005, Bouret and Sara 2005) consider the phasic activity as a trial task-engaged behaviour contrary to the tonic mode reflecting a task disengagement, we compare the phasic and tonic effect of pupil dilation across 3 conditions: salient target, no-salient target, resting condition where subject looks the screen in listening music by headphones.

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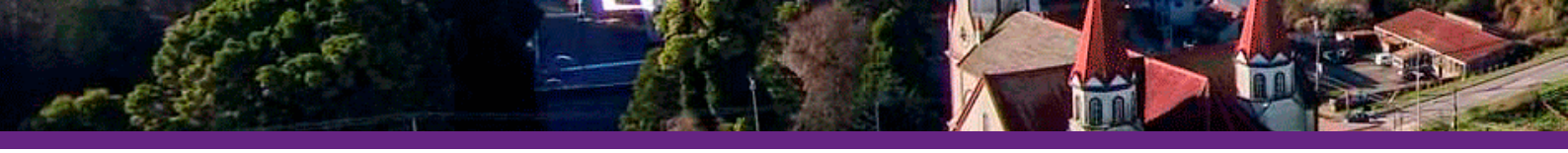
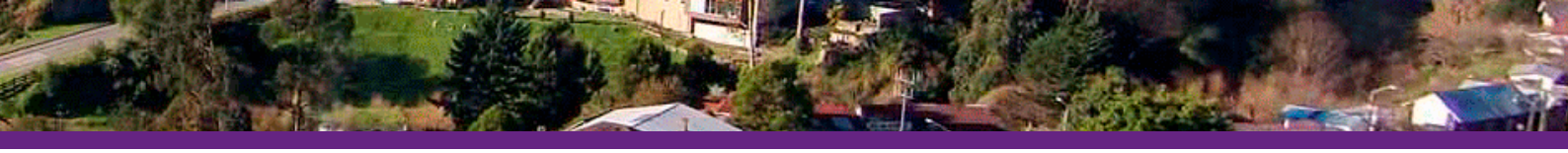


16) Impaired spatial pattern separation in a pharmacological model of temporal lobe epilepsy

Fuentes Constanza[1], Espinosa Nelson[1], Fuentealba Pablo[1]. [1]Circuitos Neuronales, Medicina, Pontificia Universidad Católica de Chile.

Temporal lobe epilepsy is a common form of focal epilepsy characterized by a latent period followed by the appearance of recurrent seizures. Patients with this type of epilepsy have reported difficulty distinguishing between past events, and the mechanism underlying epileptogenesis has been extensively studied with the kainic acid (KA)-injection model on mice. In this model, the epileptiform activity begins at the injection site, and spreads to the hippocampus. Thus, we proposed assessing the performance of this model, which could help us to discover a palliative treatment for this symptom on epileptic patients. A group of mice was unilaterally injected with KA in the amygdala (KA group), whereas another group was injected with saline solution (control group). Thereafter, performance was assessed for both groups in two behavioural tests: Novel Test (NT) and Spatial Pattern Separation (SPS). Behavioral performance was impaired in both tests for epileptic mice when compared to control mice. Indeed, in NT and SPS the control group spent more time exploring the new position, in comparison to the KA group. This suggests that KA-injected mice could not discriminate between a familiar and novel position of the objects tested[PF1] [CF2] . Furthermore, electrophysiological recordings confirmed epileptiform activity, ipsilaterally, and sometimes bilaterally in KA-injected mice. In conclusion, our results show that spatial pattern separation and others episodic memories is affected in epilepsy, likely by damage produced to the hippocampus, suggesting that the treatment should be focused to the dentate gyrus, the hippocampus area which is responsible of this type of memory function.

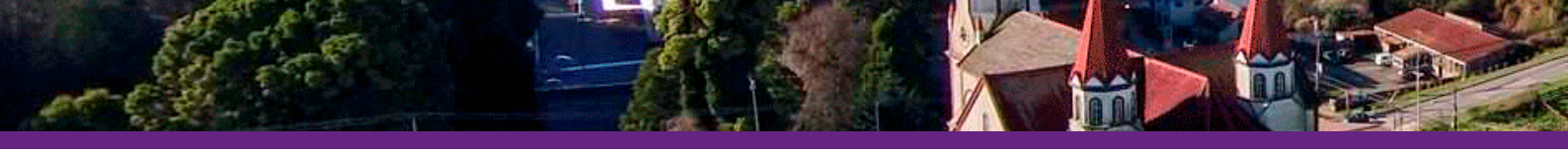


17) Ocular Movements facilitate the perceptual switch in Bistable Perception

Lorca Enrique[1], Zenteno Daniel[1], Madariaga Samuel[1], Concha Miguel[1], Devia Christ[1], Maldonado Pedro[1].
[1]Laboratorio de Neurosistemas, Departamento de Neurociencia, Facultad de Medicina, Universidad de Chile.

The possibility to alternate between two competing visual interpretation of an invariant physical stimulus is related to bistable perception. The neural mechanisms linked to the act of transiting between two perceptual states are still unknown. In the present study, we evaluate the role of ocular movements when a visual perceptual switch is reported. We recorded perceptual switch reports and ocular behavior from 25 subjects who had to observe 3 bistable stimuli, with 3 different sizes, in 2 conditions: free exploration and restriction of eye movement. We found that regardless the size of the stimulus during free viewing the ocular behavior is similar in every stimulus type. Moreover, the subjects report significant more perceptual changes when the instruction is free exploration compared with restriction of eye movement in two bistable stimuli. These results suggest that free ocular movements facilitate the perceptual switch in visual bistable stimulus modulating the switch in the perception in an invariant visual stimulus.

Funded by ICM P09 015 F



18) Neural and cognitive predictors of interoceptive behaviour

Morales Juan Pablo[1]. [1]Pontificia Universidad Católica de Chile.

Interoception is the ability to sense and perceive consciously internal states of the body. Three mains interoceptive indices have been reported, these are Interoceptive accuracy, Interoceptive learning and Interoceptive awareness. These behavioural indices present high variability in the population. However, the factors that explain the interoceptive behaviour in its different index have not been studied in an integrative statistical model. This project aims to build a statistical model to determine the factors that explain the interoceptive behaviour in its three main indices. Given the literature, two factors emerge as possible interoceptive predictors. These are, a) Neurophysiological factors: Functional connectivity in fMRI, heart evoked potential (HEP) and alpha band, b) Cognitive factors: attention, executive function and fluid intelligence. Our preliminary results show a strong correlation between some cognitive and neurodynamic variables with interoceptive performance, being both, the cognitive and neurophysiological activity necessary to explain the interoceptive behaviour. The relevance of this study lies in the growing interest to link interoception and its neural correlate with clinical disorders that present socio-cognitive functions altered, for example, anxiety, panic disorder and mood disorders. Finally, research with methodological nature like this plays a crucial role in orienting future investigations and generating new questions.

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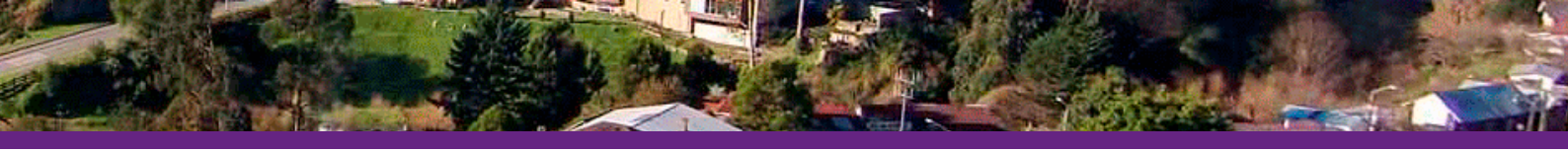
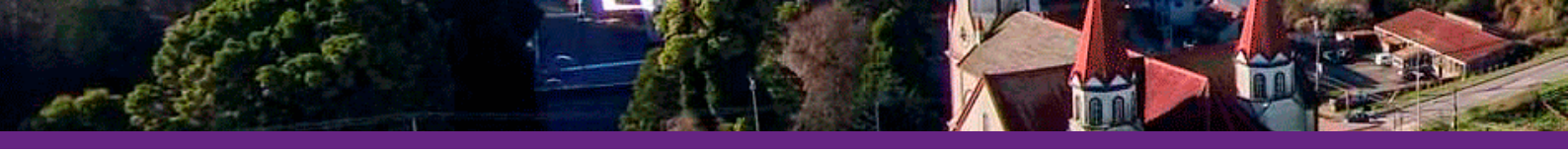


19) Effect of working memory training on attentional networks in pre-school children with symptoms of attentional deficit and hyperactivity disorder.

Oyarzún Felipe[1], Aboitiz Francisco [1], Cristian Rojas-Barahona[2]. [1]Psiquiatría , Medicina, Pontificia Universidad Católica de Chile. [2]Aprendizaje y Desarrollo , Educación, Pontificia Universidad Católica de Chile.

Attentional deficit and hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by problems in the control of attention. Working memory training has been shown to improve the control of attention in children diagnosed with ADHD. However, it is unknown what is the effect of the training on attention in children who are in an early stage of the development of this condition. Tywenty nine children with ADHD symptoms were recruited (mean age 65.6 ± 1.96 month) comparable in IQ, sex, age and SES. Fifteen children were part of the intervention group (they participated in a computer-based working memory training program for 12 sessions of 30 minutes each, three times a week) and 14 children in control group (they carried out during the same period activities that do not train working memory). In both groups the attentional network task was evaluated during an electroencephalographic record one month before and one month after the intervention. After training only the intervention group presented an increase in the modulation of the orienting network (greater amplitude of the P1 component; t-test $p<0,05$) and the executive network (greater amplitude of the early frontal P3 component; t-test $p<0,05$), but not in the alerting network (no differences in amplitude of the frontal CNV; t-test $p>0,05$). The control group did not present improvements in the modulation of the attentional networks after the intervention. The results suggest that working memory training may improve, one month later, the modulation of orienting and executive attentional networks in preschool children with ADHD symptoms.

Beca Doctorado Nacional, CONICYT Fondecyt regular 1151262

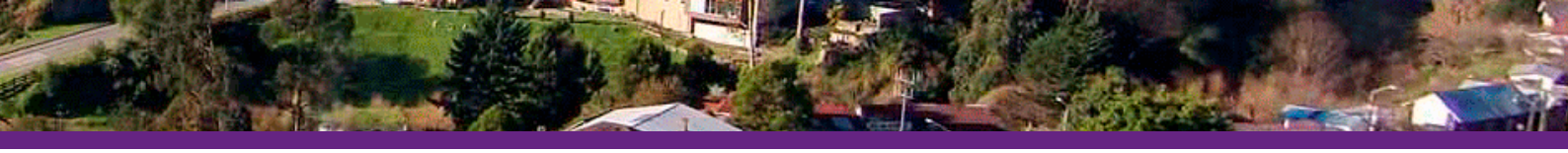


20) Correlational study between creativity and cognitive reserve in chilean population over 50 years

Riquelme-Herrera Camila [1,2], Rojas-Mancilla Edgardo[2]. [1]Escuela de Tecnología Médica, Facultad de Salud, Universidad Bernardo O`Higgins. [2]Departamento de Ciencias Químicas y Biológicas, Facultad de Salud, Universidad Bernardo O`Higgins. (Sponsored by Patricio Rojas Montecinos)

The cognitive reserve is the ability to optimize cognitive performance through the recruitment of different brain connections, which delays the onset of symptoms associated to age-related brain deterioration, including Alzheimer´s disease. On the other hand, the development of creativity has been associated with a reduction in the risk of cognitive deterioration, giving the opportunity to design and test neuroprotective strategies. In this study, the relationship between cognitive reserve and creativity in the Chilean population, over 50 years old, was evaluated. To address this issue, 75 Chilean adults between 50 and 90 years of age, apparently healthy, living in Santiago and regions, were evaluated. A sociodemographic survey, a cognitive reserve scale and a test of figurative creativity were applied. A medium correlation was found between the level of cognitive reserve and figurative creativity. In addition, a medium inverse correlation was observed between age and level of creativity and a medium correlation between the number of years of study and the level of figurative creativity. The multiple regression model showed that the main variables associated with greater creativity in the elderly are the years of education, age, bilingualism, social activity and variety of hobbies. These results suggest that fostering creativity among adults and older adults could raise their level of cognitive reserve and may reduce or delay the onset of Alzheimer´s symptoms.

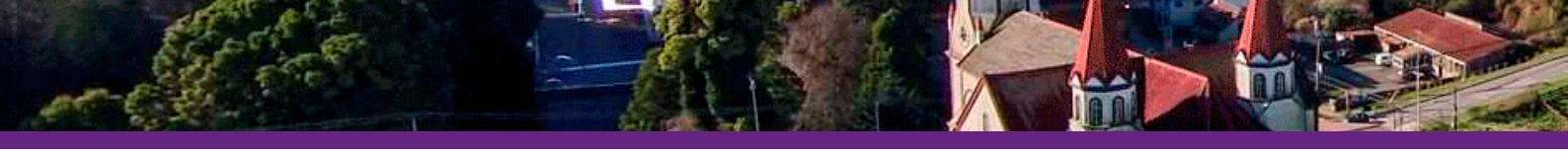
This work was supported by Dirección de Investigación, Universidad Bernardo O´Higgins.



21) Characterizing the developing of the Learning process in children with catecholaminergic imbalance: electrophysiological correlates of the emergence of a Learning Trial during a visuospatial working memory task

Santander Daniela[1], García Roberto[1], Domic Marcos[1], Arias Carolina[2], Ossandón Tomás[1]. [1]Psiquiatría, Medicina, Pontificia Universidad Catolica de Chile. [2]Genética y Enfermedades Metabólicas, Instituto de Nutrición y Tecnología de Alimentos, Universidad de Chile.

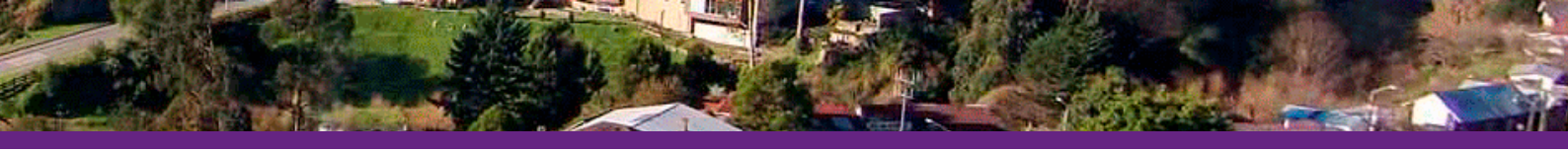
We have studied attentional dynamic in populations with different kinds of catecholaminergic imbalance: phenylketonuria (PKU), a metabolic-genetic disorder and Attention-Deficit-Hyperactivity-Disorder. We seek differences in working memory-performance and learning process. For this purpose, we studied 3 cohorts: PKU, ADHD, Controls Children (20 subjects each), who developed a visuospatial Working-Memory-task concurrently with Electroencephalographic recording. We used the Expectation-Maximization Algorithm (EM) to establish a Learning-Process obtaining the statistical definition of Learning-Trial (LT), i.e., the specific trial during the subject develops an inherent LP and is sustained throughout the task. The most of the subjects had LT during the first or second-third of the task, then we compared the spectral activity prior and posterior to the LT established for each subject, throughout a Cluster-based-permutation-test. We found differences in ADHD group in comparison to PKU group, during the average throughout all the trials Previous and Posterior to an LT, particularly in central electrodes. In the case of Control Group, we could see differences in Pre and Post trials also, principally concerning ADHD group, in Frontal Electrodes. The EM algorithm, allow us to identify with statistic certainty the subjects which develop learning during the execution of the task, altogether establishing a point of interest in wish we can focus our analysis, looking for Electrophysiological correlates of the memory. This same procedure could be used for comparing populations with different neural features, such as differences in catecholaminergic and attentional neurodynamics (ADHD) and in the patients with metabolical catecholaminergic imbalance, as in the case of the Phenylketonuric subjects..



22) Behavioral flexibility in dominant mice, an interplay between physiology and social behavior

Lara-Vasquez Ariel[1], Morán Constanza[1], Morales Cristian[1], Fuentealba Pablo[1]. [1]Centro Interdisciplinario de Neurocienica, Departamento de Psiquistria, Medicina, Pontificia Universidad Católica de Chile, Centro Interdisciplinario de Neurociencia . (Sponsored by PROYECTO ANILLO ACT. 1414 / PUC)

Behavioral flexibility refers to the adaptive changes in the behavior of an animal, in response to changes in the internal or external environment like social context. Prefrontal cortex (PFC) and hippocampus are two regions of the brain of mammals that comprise multiple circuits that mediate functions related to behavioral flexibility and dominance hierarchy related behaviors. Here we report ,in different litters mice group, the social behaviour in modified T-maze task and correlate its performance with the basal functional connectivity between PFC and hippocampus in the anesthetized mice. In behavioral experiments we found that dominant mice were the only social group that present an increase in their latencies in the collective T-maze task. In physiological experiments we found that the firing rate of PFC neurons discharged at high levels and have more activity during post hippocampal ripple (a characteristic oscillation of Hippocampus) compared with other subordinate mice. Thus, these results suggest that the cognitive processes in dominant mice present differences in behavior in a T-maze task and basal physiology. In addition, the higher activity in PFC could be related with more connectivity in this areas for process information about the behavior of others to detect, remember, and process information about social stimuli in the T-maze task. Current understanding of the neural mechanisms associated with behaviour flexibility and social hierarchy as well as related behavioural in a social context is limited. These data show new evidence about behaviour and cerebral circuits in relation to behavioural flexibility and social rank.

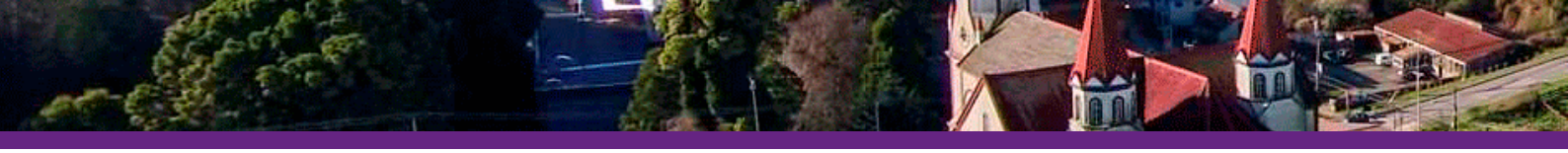


23)Resting-state brain switching dynamics in Parkinson's Disease

Astudillo Aland[1], Orio Patricio [2], Kotz Sonja[3], Trujillo-Barreto Nelson [4], El-Deredy Wael[1]. [1]Centro de Investigación y Desarrollo en Ingeniería en Salud, Universidad De Valparaíso. [2]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso. [3]Faculty of Psychology and Neuroscience, Maastricht University. [4]Division of Neuroscience and Experimental Psychology, The University of Manchester. (Sponsored by Wael El-Deredy)

Altered cognition in Parkinson's disease (PD), precede motor dysfunction. PD is associated with brain activity in cortical and subcortical regions, related to cognitive control, memory, attention and executive function. Thus, it is important to identify a causal link between brain activity and those cognitive alterations. EEG displays a repertoire of quasi-stationary spatiotemporal patterns that could be related to cognitive functions. Hidden Markov Model (HMM) have been successfully applied to characterize the underlying dynamical process of brain state switching behavior capturing spatiotemporal dynamics. Here, we use HMM to analyze brain states dynamics in EEG data at rest. We recorded 8min resting-state EEG (64 channels @500Hz) from healthy adults (N=17) and Parkinson's Disease (PD) adults (N=17). We computed power spectrum density (PSD) for each group. We used HMM to infer state parameters and state time courses. We computed topographical maps, fractional occupancies and other statistical measures from state dynamics. PSD is lower the PD group. State time courses differ between groups, showing different state participation in PD group. PD group shows less HMM-state changes than the control group. Specific patterns of EEG frequency and state dynamics distinguish between PD patients and healthy controls. Future work should relate such patterns to cognitive function, both to serve as markers of disease and disease progression, and as a framework for understanding the relationship between brain activation and cognition.

CONICYT-PFCHA/Doctorado Nacional/2017- 21172028; Fondecyt 1181076 (PO); and FONDECYT 1161378 (WeD) The Centro Interdisciplinario de Neurociencia de Valparaíso (CINV) is supported by the Ministerio de Economía (Proyecto P09-022-F, ICM-MINECON, Chile).



24) Abstract Aperiodic power spectra analysis in neuromodulatory disorder

Medel Vicente[1], Valdés Joaquín[1], Ossandón Tomás[1]. [1]Psiquiatría, Medicina, Pontificia Universidad Católica de Chile.

The internal dynamics and responsiveness to external stimuli fluctuates rapidly in the awake brain (Harris & Thiele, 2011). This rapid arousal variations in awake brain states has been indexed by characteristic evoked and spontaneous "noise" activity in cortical neurons (McGinley et al., 2015), which reveal that arousal is related to an asynchronous state (Renart et al., 2010). A possible gain control of this dynamic system could be neuromodulation. It has been shown that cortical computation under neuromodulatory control affects spontaneous cortical noise (Lee & Dan, 2012).

In the EEG power spectra, the temporal fluctuations have a characteristic "scale-free" behavior where power scales as a function of frequency according to a power law, $P(f) \propto f\beta$, which resembles long range autocorrelation (Linkenkaer-Hansen et al., 2001).This aperiodic components have been suggested to reflect population spiking activity (Manning et al., 2009), background cortical noise (Voytek & Knight, 2015), balance between excitation and inhibition (Gao et al., 2017), and behavioral changes (Podvalny et al., 2015). In this line, we hypothesize that neuromodulatory impairment disorders -such as ADHD- would have a specific biomarker in the aperiodic EEG power spectra, possibly reflecting background noise. We show a preliminary study comparing EEG power spectral slope between three different groups: a control group and ADHD with and without methylphenidate -a catecholaminergic reuptake inhibitor-.

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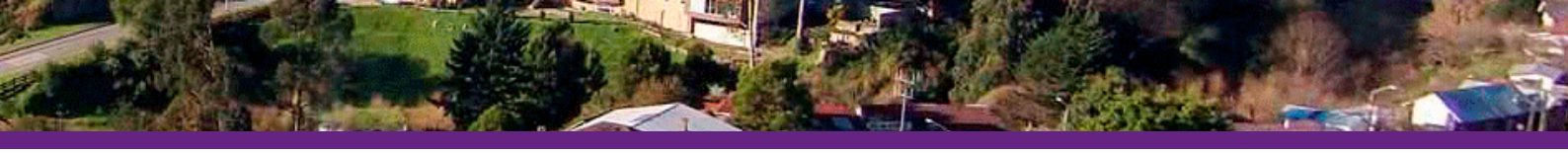
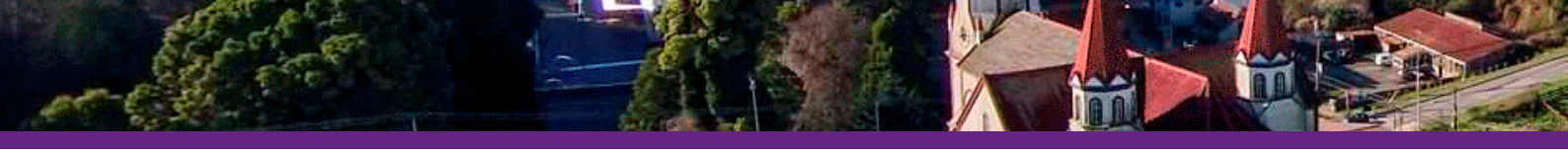


25) Multi stable dynamics in a brain inspired network model of Wilson Cowan oscillators depends on structural, connectivity and noise properties

Palma-Espinosa Javier[1], Coronel Carlos[1], Gatica-Briceño Marilyn[1], Castro Samy[1], Orio Patricio[2,1]. [1]Laboratorio de Neurociencia Computacional, Facultad de Ciencias, Universidad de Valparaíso. [2] Centro Interdisciplinario de Neurociencias de Valparaíso, CINV.

The brain allows organisms to respond to ever-changing external and internal stimuli with appropiate behaviours. In order to respond to this variable stimuli, the system must explore a large number of state configuration, which allows it to deal with sensory novelty and to learn from it. However, little is know about the origin of this dynamical diversity. One theory proposes that the multistability of the node, i.e., the stable points that each node´s dynamic has, may account for this repertory of state configurations. Additionally, interconnection among those nodes drives the dynamics of the neural network by imposing oscilatory regimes related to the coupling strenght between the nodes. In the first case, there is growing evidence that the noise is the mechanism that moves the system from one stable point to another one. In the second case, the interconnection of the nodes may lead to chaotic behaviour and thus, moving the oscilatory regime. In order to test how the network coupling (G) and the network structure modifies its dynamical diversity, we developed a neural network simulation by using a well known oscilatory model. Our results shows that network´s multistability is highly dependent to the node´s coupling strength, G. Also, the structure of the network modifies the multistability. Further analysis on the relationship between G and network structure needs to be adresses as this interaction may account for a more realistic process and the imbalance in dynamical diversity within the brain.

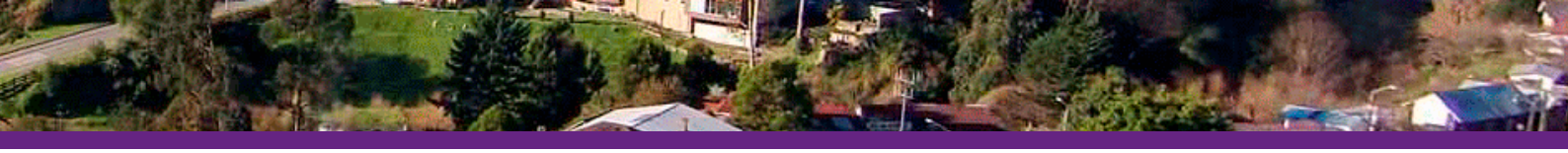


26) Dysregulation on glutamatergic system in cortical and limbic brain areas in an animal model of depression

Ardiles Nicolás[1,2], Chávez Andrés E.[2], Moya Pablo R.[1,2]. [1]Laboratorio de Neurogenética, Instituto de Fisiología, Facultad de Ciencias, Universidad de Valparaíso. [2]Centro Interdisciplinario de Neurociencia de Valparaíso (CINV), Facultad de Ciencias, Universidad de Valparaíso.

Major depressive disorder affects around 10% of the world´s population. Studies have shown alterations on glutamatergic system in brain regions that regulate mood and cognition. However, the mechanisms underlying the abnormal glutamatergic transmission in depression remain controversial. We hypothesized that chronic stress decreases expression levels of EAAT3 -a neuronal glutamate transporter- and induces changes in the expression and function of glutamate receptors. To test this hypothesis, mice were challenged to unpredictable chronic mild stress (UCMS) -a well validated model of stress-induced depression- and expression levels of EAAT3, NMDA receptors (NMDARs) and AMPA receptors (AMPARs) subunits in limbic and cortical regions were evaluated. In UCMS-mice a downregulation of EAAT3 in nucleus accumbens were observed with no changing in hippocampus and medial prefrontal cortex. Moreover, we found that NR2A- and NR2B-containing NMDARs as well as GluR1- and GluR2-containing AMPARs increased significantly in the hippocampus. NR2B and GluR1 also increased their levels in dorsal striatum, but NR2A decreased in medial prefrontal cortex. Further, we evaluated the impact of EAAT3 conditional overexpression (cOE) in pyramidal neurons in mice at the behavioral level. Compared to littermates, EAAT3 cOE mice were found to have increased anxiety-like behavior and showed a lower despair behavior, but no change in anhedonia in depressive-like behaviors. Altogether, these results indicate that dysregulation of glutamatergic components in the limbic-cortical areas is related to depressive-like behaviors. We suggest that stress-induced upregulation of AMPARs and NMDARs in the hippocampus could be related to maladaptive processes in memory and learning in depression.

Supported by Nucleo Milenio NuMIND (NC130011) and Millennium Institute CINV (P09- 022F).



27) Morphological and immunohistochemical characterization of retinal explants under different culture glucose levels

Cadiz Barbara[1], Pires Ronakarina[1], Vielma Alex[1], Calbiague Victor[1], Schmachtenberg Oliver[1]. [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Ciencias, Universidad de Valparaíso.

Diabetic retinopathy (DR) is one of the leading causes of decreased vision and blindness worldwide. It is due to an increase in glucose levels, which produce oxidative stress and neuronal damage. Retinal explants have been fundamental in the study of the physiopathology of the retina. The advantages of this models that it maintains the circuitry of the retina intact, and allows to perform pharmacological studies in conditions in which the vascular component is absent. The aim of this study was to determine whether different glucose conditions induce direct neuronal changes in the markers of oxidative stress and inflammation. For this, retinal organotypic cultures from postnatal day 14 C57BL/6 mice were maintained for up to 2 weeks in low (10.5 mM) and high (30 mM) glucose, fixed with 4% PFA, cryosectioned and mounted on microscope slides coated with polylysine. Immunohistochemistry for neuronal, glial (GFAP, TUBB3, NF, S100, nNOS), vascular (CD31), immune and oxidative stress markers (iNOS, N-Tyr) was performed. In 30 mM conditions an altered iNOS, N-Tyr, GFAP and TUBβ3 expression was observed, while the other markers did not show significant changes.These results indicate that retinal explants may be useful for the investigation ofglucose toxicity and experimental neurodegenerative diseases like diabetic retinopathy.

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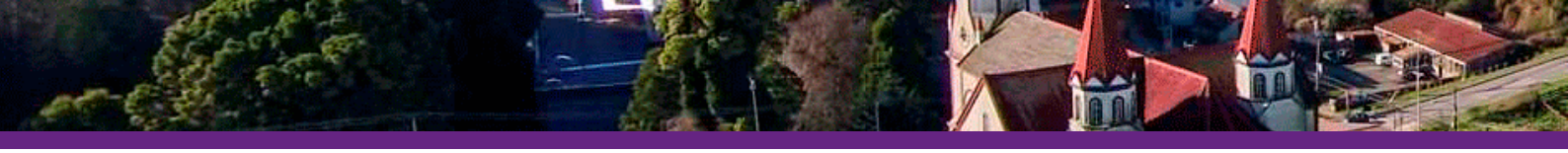

28) Exploring the potential of the pupillary light reflex as an early diagnostic tool for age-related neurodegeneration in Octodon degus

Ibaceta Cristobal[1], Palanca-Castan, Nicolas[1], Muñoz Vanessa[1], Neira David[1], Araya Joquin[1], Harcha Paloma[1], Palacios Adrian[1]. [1]CINV, Universidad de Valparaíso.

This work explores retina functionality as a target for early diagnosis of neurodegenerative diseases. To test this hypothesis, we used Octodon degus, a long-lived rodent that naturally develops age-related CNS changes. We evaluated pupillary light reflex (PLR) by measuring the contraction of the pupil in response to light stimuli and sorted them by normal (PLR+) or deteriorated (PLR-). Animals considered PLR- had a normalized horizontal contraction that was at least 10% lower than PLR+ animals in response to stimuli in optimal sensitivity range (470-500 nm). Since the PLR is driven by retinal ganglion cells (RCG), the retinas of these animals were recorded with a multielectrode array to evaluate their response to light. PLR- animals had signs of retinal deterioration, showing increased RGCs response in both firing rate (PLR- 1.32 + 0.07 Hz; PLR+ 0.85 + 0.07 Hz) and burst activity (PLR-: 0.060 + 0.008 Hz; PLR+: 0.041 + 0.006 Hz) when compared to PLR+ animals as well as a lower number of recovered receptive fields (PLR-: 3.2% vs PLR+: 14.5%). Neuronal death markers were present in the retina of PLR- animals and absent in PLR+ animals, indicating deterioration. Neuronal death markers were absent in the hippocampus of both PLR+ and PLR- animals. Further work will address whether the presence of neurodegeneration in the retina but not in the hippocampus of PLR- is a sign of isolated retinal neurodegeneration or if it predates CNS deterioration. In the latter case, PLR tests could be used to detect neurodegeneration in a non-invasive way.

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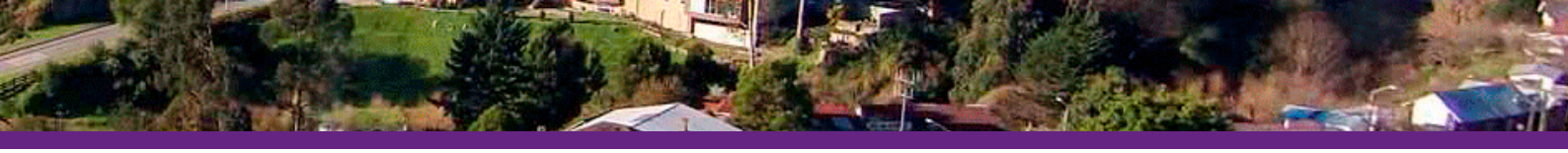
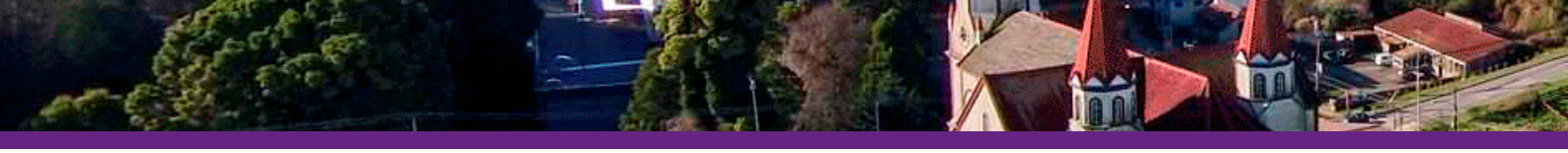


29) The lack of c-Abl improve behavioral performance in an animal model of Alzheimer´s disease

León Rilda[1,2], Morales Cristian[2], De La Fuente Catalina[1], Espinosa Nelson[2], Tiznado Vicente[2], Morán Constanza[2], Fuentealba Pablo #[2], Álvarez Alejandra #[1]. [1]Laboratorio de Señalización Celular, Facultad de Biología, Pontificia Universidad Católica de Chile. [2]Laboratorio de Circuitos Neuronales, Facultad de Medicina, Pontificia Universidad Católica de Chile.

c-Abl is a non-receptor tyrosine kinase that plays a role in neuronal development, neurogenesis and synaptic plasticity. Increasing evidence suggests that c-Abl play a role in the pathogenesis of Alzheimer's disease (AD). Our laboratory has shown that c-Abl is activated in both *in vitro* and *in vivo* AD models, and its activation is involved in synaptic loss and long-term potentiation inhibition induced by Aβ oligomers. Also, treatment with Imatinib, a c-Abl inhibitor, reduces neuronal loss, Aβ deposition and cognitive impairments in a transgenic AD mouse models. However, one of the limitations of those studies is the use of inhibitors since they lack the capability to cross the blood-brain-barrier and also can target other kinases. In the present study we assess the effect of the genetic ablation of c-Abl in APP/PSEN1 mice on behavioral performance and functional connectivity. We use a new transgenic strain of AD that has a brain-specific genetic deletion of c-Abl (APP/PSEN1/Abl-KO). We evaluated the cognitive performance through two different behavioral tests: Novel Object Recognition (NOR, hippocampus-non-dependent memory) and Object Location Memory (OLM, hippocampus-dependent memory). Also, we evaluated the functional connectivity in the hippocampal-prefrontal cortex axis, in order to establish a relationship between behavior and neuronal activity. We found that APP/PSEN1/Abl-KO mice recovered the ability to discriminate in OLM test. However, NOR test didnt show differences between groups. In addition, our data suggest that functional connectivity might be recovered in APP/PSEN1/Abl-KO mice. The present study contributes to the understanding of how c-Abl is involved in pathogenesis of AD.

Beca Doctorado Nacional 2016-21160057, FONDECYT 1161065 to AA, CARE-Chile-UC AFB170005, FONDEF D10E1077 # *Contributed equally*



30) Perceptual stability and discrimination of olfactory representations in a mouse model of FXS

Fuenzalida Rocío[1,2], Diego Becerra[2], Núñez Valentina[2], **Nuñez-Parra Alexia [2]**. [1]Magíster en Neurorehabilitación, Universidad Andrés Bello. [2]Laboratorio de Neurofisiología, Facultad de Ciencias, Universidad de Chile.

Fragile X syndrome (FXS) is the first monogenetic cause of autism and it is produced by the mutation of the *FMR1* gene encoding for the FMRP protein. One of the most prevalent symptoms in FXS are abnormal social behavior and an extreme sensitivity to daily life stimuli. Yet, compared to cognitive and social functioning, how sensory information is processed in FXS has been largely understudied. The olfactory system is one of the most conserved senses used primarily by rodents to survive and reproduce, which in addition to their stereotyped olfactory-mediated make it a highly attractive system to study the neurophysiological aspects of sensory perception in FXS. Olfactory information is integrated and ultimately decoded by a unique ensemble of pyramidal neurons (Pyr) in the olfactory cortex (OC). The OC is an autoassociative neuronal network, capable of storing and recalling odor-objects. Interestingly, the OC identifies an odor mixture as one odor-object without recognizing the different odorants that build them as independent units, even though the Pyr activation pattern will partially overlap to the ones of the single odorants. Therefore, the brain has to exhibit the ability to decorrelate partially overlapping patterns of Pyr activation and treat them as different, a process called pattern separation. We found that Fmr1-KO animals in a go-no go task can indeed learn to discriminate between a rewarded and a not rewarded odorant, but cannot morphed the stimuli mixtures to promote pattern separation. Our data suggests that inappropriate olfactory representations could in part rely on dysfunctional cortical processing.

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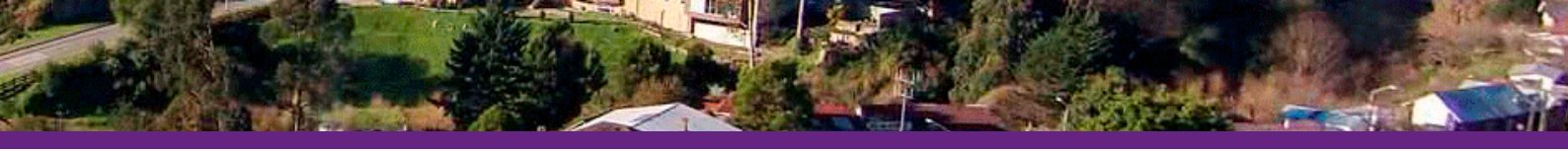
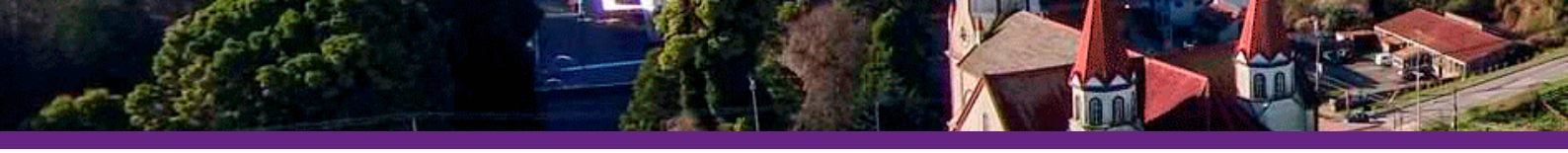


31) Effect of β-amyloid and neuroinflammation on Neurocan in an Alzheimer´s disease mouse model

Triviño JJ[1], Von Bernhardi R[1]. [1]Laboratorio de Neurociencia - CIM UC, Facultad de Medicina, Pontificia Universidad Católica de Chile.

Neuroinflammation takes part in various neurodegenerative diseases. In the case of **Alzheimers disease (AD),** neuritic (Aβ) plaque formation, neurodegeneration, and inflammatory activation of glia are consequences of microglia dysregulation, depending at least in part in age-related changes. The **Chondroitin Sulfate Proteoglycans (CSPGs)** have inhibitory functions over inflammatory pathways, and **Glycosaminoglycans (GAGs)** have importance in the formation of the Aβ plaque. **Neurocan** is a lectican CSPG component of the **extracellular matrix (ECM)** of the central nervous system (CNS), overexpressed during modeling and remodeling processes of the CNS. Neurocan has multiple functions, it can bind to various components of the ECM, and interacts with cell surface molecules. We postulate that Neurocan increases in response to neuroinflammation, and in the presence of Aβ plaques in AD models and promotes neuronal dysfunction. Young (6 m) and middle aged (12 m) adult C57BL/6 mice, wild type (WT), SRA KO (potentiation of inflammatory process) and APP/PS1 (which accumulate Aβ), were exposed to an inflammatory protocol (LPS intraperitoneal injection). TGFβ-1 and activation markers (TAU, HSP70, S100B) were evaluated by ELISA, and showed increased levels in response to inflammation and Aβ. Analysis of Neurocan by immunoblotting techniques (dot blot and western blot) indicated the presence and increased level of Neurocan in aged animals exposed to LPS. Histochemical studies of Hippocampus and Cortex in aged APP/PS1 animals showed a robust Neurocan labeling in association with Aβ, as opposed to WT mice that only showed a fine punctuated staining. Our results suggest that Neurocan could play a role in AD.

Support Grant FONDECYT 1171645 (RvB). The research is part of the Biochemistry research seminar, course BIO296F, by JJ Triviño.



32) RU-486 administration and gestational stress decreases maternal behavior and generate depressive-like behaviors in rats

Arriagada-Solimano Marcia[1], Iturra-Mena Ann[1], Dagnino-Subiabre Alexies[1]. [1]Laboratory of Stress Neurobiology, Institute of Physiology, Facultad de Ciencias, Universidad de Valparaíso.

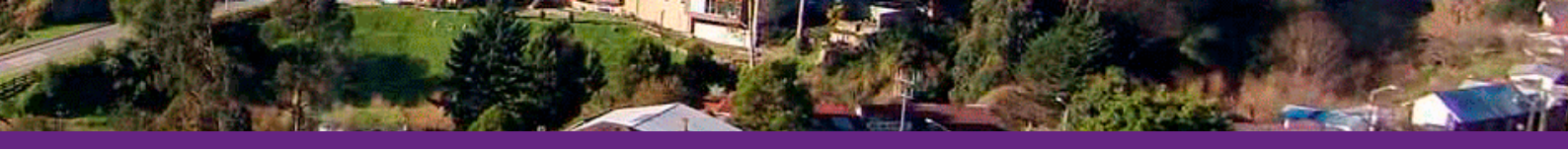
Introduction:
The maternal behavior during lactation in rats is vital for offspring development. Stress is an environmental factor that affects maternal behavior. In this regard, RU-486 is a glucocorticoid receptor antagonist.

Methods:
Sprague-Dawley rats were pregnant and then four experimental groups were formed: Vehicle, RU-486, Vehicle gestational stress (daily restraint stress 45 minutes/ 3 times per day) and RU-486 gestational stress. RU-486 was administered at gestation days 15, 18 and 21. Maternal behavior was evaluated using the Pup Retrieval Test at postnatal day 3, also was evaluated during day and night passive and active maternal behaviors. After weaning, depressive-like behaviors were evaluated by forced swimming. Additionally, anxiety-like behaviors and locomotor activity were analyzed by an open field and elevated plus maze tests, respectively.

Results:
Animals from RU-486 group spend more time to retrieve pups back to the nest, even dams can´t retrieve the entire nest in the Pup retrieval test. In addition, gestational stress and RU-486 administration decrease active and passive maternal behavior during the day. Also, dams with RU-486 administration spend more time floating during forced swimming test other groups.

Discussion:
Glucocorticoid's peak before partum is very important to oxytocin secretion, this hormone enables the maternal behavior. Both, RU-486 and gestational stress, could impair the oxytocin release.

Research support FONDECYT, Grant/Award number: 1141276, Anillo de Ciencia y Tecnología programa PIA of CONICYT grant number: ACT1403 and Master of Neurosciences University of Valparaiso.

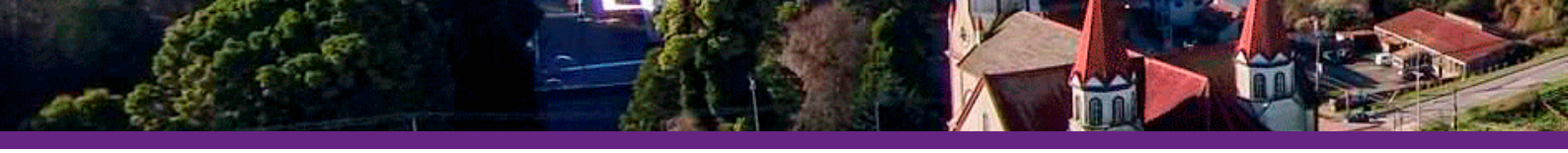


33)Hypercapnia-induced brainstem microglial cell activation in adult mice

Irribarra Estefanía[1], Cáceres-Vergara Daniela[1], Béltran-Castillo Sebastián[1], Von Bernhardi Rommy[2], Eugenín Jaime[1]. [1]Biología, Química y Biología, Universidad de Santiago de Chile. [2]Neurobiología, Medicina, Pontificia Universidad Católica de Chile.

Breathing is essential for life. It is generated by the respiratory pattern generator (RPG), neural network, distributed along the ventral (VRC) and dorsal (DRC) respiratory columns. The RPG is modulated by cells capable of sensing changes of CO2 and H+, located within the RPG or in nuclei projecting into the RPG. It has been found that neurons and astrocytes are chemosensitive. Given that microglia are cells functionally related with neurons and astrocytes, for instance through the release of gliotransmitters, our aim was to study whether brainstem microglia are sensitive to hypercapnic acidosis acquiring an activated phenotype in response to exposure to high concentrations of CO2. Adult CF1 mouse brains were fixed and processed to perform an immunohistochemistry against Iba-1, a microglia marker, after 90 min of breathing air (controls) or air enriched with 10% CO2 for 30 min. We found that hypercapnia induced increased cell body size and a reduction in the number of branches in microglial cells of brainstem chemosensitive nuclei such as NTS, raphe, and VRC. By contrast, microglia in hippocampus and cortex were unmodified by hypercapnia. Our results indicate that microglia can sense hypercapnia and be transformed into an activated phenotype in chemosensitive respiratory nuclei in the brainstem, suggesting their possible role mediating the ventilatory response to hypercapnia.

Supported by: Fondecyt 1171434 (JE), 1171645 (RvB), Postdoctoral Grant CONICYT 3180553(SBC)

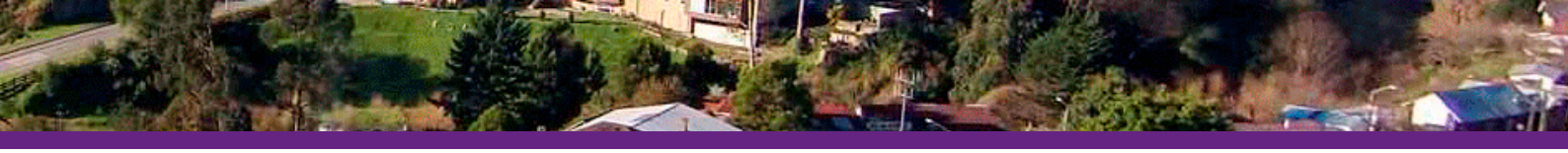


34) Alcohol exposure activates astroglial hemichannels and pannexons in the hippocampus of adolescent rats: effects on neuroinflammation and astrocyte arborization

Oyarzún Juan Esteban [2], Gómez Gonzalo[2], Rojas Consuelo[2,5], Falcón Romina[2], Maturana Carola[2], Labra Valeria[2], Salgado Nicole[2], Cortez Cristián[6], Cerpa Waldo[1,4], Quintanilla Rodrigo[3,4], Orellana Juan Andrés[2,4]. [1]Departamento de Biología Celular y Molecular, Facultad de Biología, Pontificia Universidad Católica de Chile, [2]Departamento de Neurología , Facultad de Medicina, Pontificia Universidad Católica de Chile, [3]Ciencias de la Salud, Facultad de Ciencias de la Salud, Universidad Autónoma de Chile, [4]Centro de Investigación y Estudio del Consumo de Alcohol en Adolescentes, P. Universidad Católica de Chile, U. Autónoma, U. Metropolitana de Ciencias de la Educación, [5]Departamento de Gastroenterología, Facultad de Medicina, Pontificia Universidad Católica de Chile, [6]Facultad de Ciencias, Universidad Mayor

Alcohol abuse increases burden disease and produces serious societal and economic consequences. Moreover, adolescents have a greater susceptibility to the influence of alcohol than adults, but the mechanisms of this phenomenon remain poorly understood. Astrocyte-mediated gliotransmission is crucial for hippocampal plasticity, where the opening of hemichannels and pannexons seems critical for this process. Here, we evaluated whether *in vivo*ethanol exposure affects the activity of these channels in hippocampal astrocytes, as well as neuroinflammation and astrocyte arborization. Adolescent rats were exposed to ethanol (3.0 g/kg) for two consecutive days at 48-h intervals over 14 days. Then, the opening of hemichannels and pannexons was examined in hippocampal slices by ethidium uptake. Furthermore, hippocampal cytokine levels and astroglial arborization were determined by ELISA or Sholl analysis, respectively. We found that adolescent ethanol exposure increased the opening of connexin 43 (Cx43) hemichannels and pannexin-1 (Panx1) in astrocytes. Blockade of p38MAP kinase, iNOS and COXs, as well as chelation of intracellular Ca^{2+}, drastically reduced the ethanol-induced channel opening in astrocytes. Importantly, ethanol-induced hemichannel/pannexon activity was correlated with increased levels of IL-1β, TNF-α, IL-6 in the hippocampus, as well as with profound alterations in astrocyte arbor complexity. Thus, we propose that uncontrolled opening of astrocyte hemichannels and pannexons may contribute not only to the glial dysfunction and neurotoxicity caused by adolescent alcohol consumption, but also to the pathogenesis of alcohol use disorders in the adulthood.

FONDECYT 1160710 and Anillo ACT1411

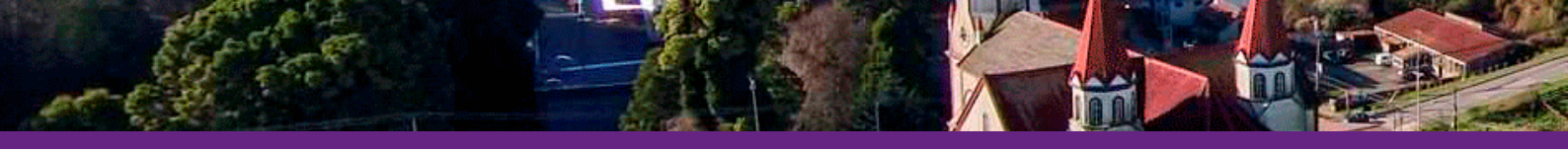


35) Intranasal Cotinine Plus Krill Oil Facilitates Fear Extinction, Decreases Depressive-Like Behavior, and Increases Hippocampal Calcineurin A expression in Mice.

Oliveros-Matus Patricia[1], Alvarez-Ricartes Nathalie[3], Mendoza Cristhian[2], Perez-Urrutia Nelson[2], Echeverria Florencia[1], Hernandez John[3], Susperreguy Francisco[3], Iarkov Alexandre[3], **Echeverria Valentina[3]**. [1]Neurociencias, Ciencias de la Salud, Universidad San Sebastian. [2]Departamento de Kinesiología, Ciencias de la Salud, Universidad San Sebastian. [3]Tecnología Medica, Ciencias de la Salud, Universidad San Sebastian.

In the post-traumatic stress disorder (PTSD), the failure to extinguish traumatic memories is one of the most complex and painful symptoms. The acquisition and extinction of fear memory involve several brain regions such as the hippocampus, the prefrontal cortex, and the amygdala. PTSD is treated with selective serotonin-reuptake inhibitors and psychotherapy, however, less than 60% of patients respond to treatments, and 70% suffer reinstatement of fear after extinction. Rodents have proven to be useful to investigate the effectiveness and molecular mechanisms of action of drugs for PTSD. Cotinine a tobacco-derived alkaloid facilitates fear extinction (FE), decreased depressive and anxiety behaviors, and improved working memory in mice subjected to fear conditioning (FC). In here, we investigated the effect of intranasal (IN) cotinine plus Krill oil (KO) in FE. Mice C57BL/6 were divided into five groups: 1. Control + vehicle; 2. FC + vehicle; 3. FC + IN Cotinine; 4. FC + IN Cotinine + KO; 5. FC + oral Sertraline. After FC mice were subjected to daily extinction trials for five days and then tested for depressive-like behavior and working memory. Cotinine and Cotinine + KO enhanced FE more effectively than sertraline alone. Unexpectedly, KO increased the consolidation of fear memory and inhibited FE. Cotinine like other antidepressants increased hippocampal calcineurin A expression.

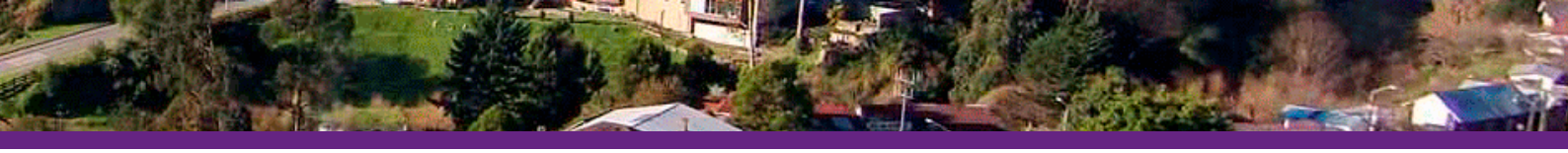
Fondecyt 1150194



36) Electrophysiological study of cognitive function through working memory in patients with multiple sclerosis

Figueroa Alejandra [1], Billeke Pablo[1], Zamorano Francisco[1], Cárcamo Claudia[2], Ciampi Ethel[2], Vásquez Macarena[2], Aboitiz Francisco[3]. [1]División de Neurociencia del Centro de Investigación en Complejidad Social, Gobierno, Universidad del Desarrollo. [2]Departamento de Neurología, Medicina, Pontificia Universidad Católica de Chile. [3]Laboratorio de Neurociencias Cognitivas, Psiquiatría, Pontificia Universidad Católica de Chile.

Multiple Sclerosis (MS) is a demyelinating disease of the Central Nervous System, provoking motor, cognitive and neurosychiatric symptoms. Memory impairment is one of the most commoncognitive deficits in MS. While working memory (WM) plays a crucial role in multiple cognitive functions, evidence in MS is scarce and contradictory regarding the nature of its cognitive impairment and its evolution. We studied the WM using the modified Sternberg Paradigm and electrophysiological recording. We researched a group of RRMS patients (relapsing-remitting multiple sclerosis) without cognitive alteration and a control group of healthy people. Participants watched arrays of 2, 4 or 6 consonants that had to be memorized. Then a black screen was shown and finally a target stimulus was displayed (consonant). The subjects had to respond whether the target stimulus was present on the array initially shown.We found significant differences in the reaction timing and correct responses in relation to the load of WM for both groups, whithout no significant differences between both groups. Regarding to Event-Related Potentials (ERPs), in both groups, we found a memory load modulation in amplitude of a late potential, which was higher in the control group. In time-frequency analyses, we found a difference between groups for memory load 6. Patients demonstrated a greater theta activity over left central a parietal electrodes. Hence, both electrophysiological features could reflect a sub-clinical alteration. Thus, differences in both late potentials and cortical oscillations would be useful for the early detecting and the following of the WM alterations in MS.



37) Serotonin modulates excitatory and inhibitory synaptic transmission in the inner retina

Di Berardino Claudia[1], Alcaíno Alejandro A.[1], Quiroz Camila A.[1], Estay Sebastián F.[1], Chávez Andrés E.[1]. [1]Centro Interdisciplinario de Neurociencia, Laboratorio de Neuromodulación y Fisiología Sináptica, Facultad de Ciencia, Universidad de Valparaíso.

Serotonin (5-HT) by modulating synaptic function and neuronal excitability regulates both cognitive and sensory functions. While numerous evidences indicate that the serotoninergic system is expressed in the vertebrate retina, little is known about the cellular and molecular mechanisms by which 5-HT can modulate synaptic transmission onto retinal ganglion cells (RGCs) and how a perturbation of the 5-HT system could affect visual functions. Here, using whole-cell voltage-clamp recordings in mouse acute retinal slices, we investigated how 5-HT regulates visual processing in the inner retina by assessing its effect on excitatory (EPSCs) and inhibitory (IPSCs) synaptic transmission onto RGCs. Bath application of fenfluramine, an agent that stimulates the release of 5-HT from vesicular storage, reduces the frequency but not the amplitude of spontaneous EPSCs (sEPSCs). Fenfluramine also reduce the frequency but not the amplitude of spontaneous IPSCs. Interestingly, a similar reduction in the frequency of sEPSCs and sIPSCs was observed in RGCs from SERT-/- mice compared to wild-type littermates, strongly suggesting that increased levels of 5-HT in the inner retina reduce both excitatory and inhibitory transmitter release in a presynaptic manner. We are currently investigating the identity of the specific 5-HT receptors underlying these observations.

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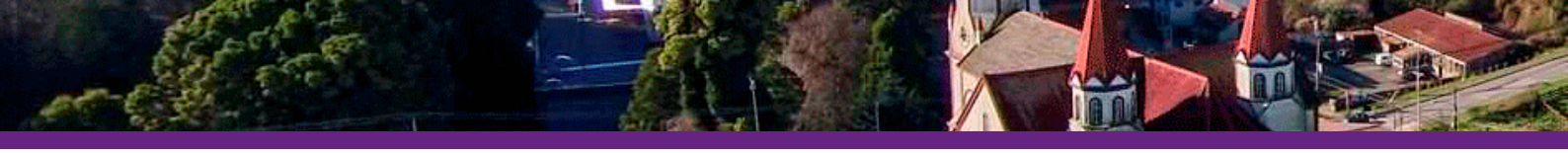
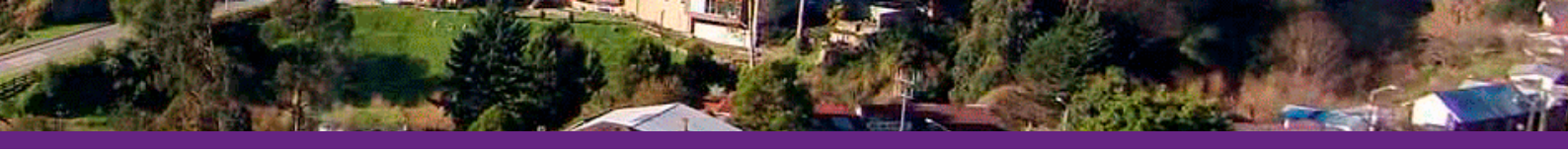


38) Astrogliar network disruption in Octodon degus during natural ageing

Harcha Paloma A[1], Neira David[1], Maripillán Jaime[1], Palanca-Castrán Nicolás[1], Martínez Agustín D[1], Palacios Adrián G[1]. [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Ciencias , Universidad de Valparaíso.

Neurodegenerative conditions associated with ageing have become one of the most dreaded diseases of older people. During normal ageing, there is a progressive decline of learning and memory functions, synaptic plasticity and adult neurogenesis. Under these conditions, a mild chronic inflammatory state mediated by the activation of glial cells increases neuronal death susceptibility. So far, increased astrogliar hemichannel (HCs) activity disrupting central nervous system (CNS) homeostasis and neuronal function, has been implicated in a series of neurodegenerative conditions that share molecular hallmarks related to natural age-related neuroinflammation. Nevertheless, the short-lived mice models commonly used in previous studies fail to represent entirely age-related diseases. Therefore, we evaluated the participation of astrocytes HCs in the ageing process of *Octodon degus,* a long-lived rodent that naturally develops CNS age-related changes, including synaptic dysfunction, amyloid plaques and neurofibrillary tangles, and consequently age-related changes. For this purpose, animals were sorted after pupillary light reflex response (PLR) in 3 study groups: young PLR+, old PLR+ and old PLR-. Thereafter, confocal immunofluorescence microscopy along with dye uptake assays in the presence of HCs-building proteins inhibitors were used in *ex vivo* coronal brain slices. We detected atrophy in astrocyte processes in both older groups, suggesting that syncytia disruption is a natural process. Nevertheless, only in the PLR- group, astrocytes present an increase of dye uptake mainly dependent of Cx43 HCs, implicating that glial homeostasis disruption is correlated with neurodeterioration of CNS. Therefore, we propose HCs as a new potential molecular target to reduce age-related neurodegenerative diseases.

CM P029-022-F, FONDECYT-1171240.

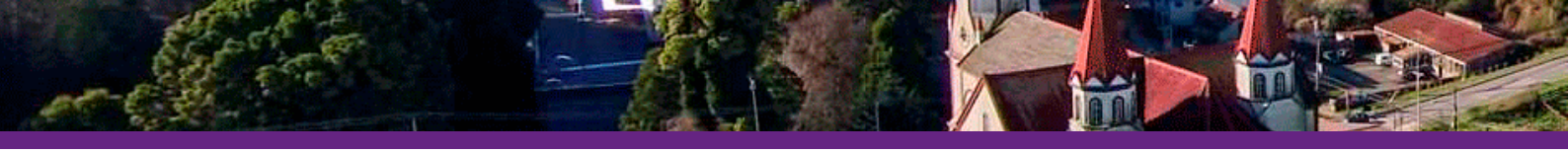


39) Activation of brainstem microglia by gliotransmitters

Marca Silvia Raquel[1], Irribarra Estefania[1], Cáceres-Vergara Daniela[1], Olivares María José[1], Von Bernhardi Rommy[2], Eugenín Jaime[1]. [1]Química, Biología y Química, Universidad de Santiago de Chile. [2]Centro de Investigación Médica, Medicina, Pontificia Universidad Católica de Chile.

The neural network responsible for generating the respiratory rhythm, the Respiratory Pattern Generator is located at the brainstem. Glia-neuron interactions are dynamic and glial cells can release gliotransmitters that affect neurons and other glial cells. ATP and D-serine released by brainstem astrocytes can affect the respiratory neural network. However, there is little evidence that both gliotransmitters could affect microglia which in turn could affect astrocytes or the neural network. In this work, brainstem microglia pure cultures will be exposed to different concentrations of ATP and D-serine, and their activation and phenotypic differentiation will be evaluated by changes in cellular morphology at 3 and 6h of exposure. Our results show that after 3h of incubation, 50% of microglia incubated with 100μM ATP and 60% with 1mM ATP were activated as evidenced by activated-like morphological changes. After 6h of ATP exposure, intermediate microglial morphology predominates. By contrast, after 3h of exposure to 10μM D-serine, activation was not observed; And only 10% of cells showed activated-like morphology when exposed to 100μM D-serine. After 6h of 10μM or 100μM D-serine exposure, 20% of microglia showed activation, being predominant the intermediate morphology at 3 and 6h of exposure. These results indicate that microglia can be activated by gliotransmitters potentially released by the astrocytes. Whether, activated microglia may contribute to the respiratory response induced by the activation of astrocytes or neurons is an open question.

With the support of Fondecyt 1171434 (JE) and 1171645 (RvB).

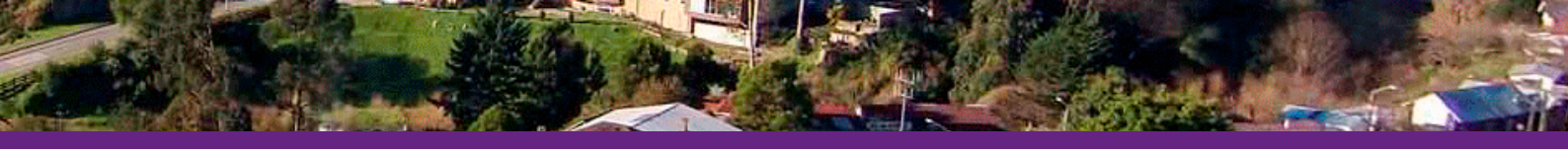


40)The TRP and TRPL light-dependent channels of Drosophila photoreceptors activated by mechanical stimulation in submicroscopic inside-out patches excised from the light-sensitive membrane

Delgado Ricardo [1], Christian Wilson[2], Bacigalupo Juan[1]. [1]Departamento de Biología , Facultad de Ciencias, Universidad de Chile. [2]Laboratorio de Bioquímica, Facultad de Ciencias Qumicas y Farmacéuticas, Universidad de Chile.

Drosophila phototransduction occurs in ~40,000 tightly packed highly specialized microvilli of photoreceptor cells. Light activates rhodopsin,thatcouples to G-proteinactivating phospholipase-C (PLC), whichcleaves phosphatidylinositol 4,5-bisphosphate into 1,4,5-inositol trisphosphate, diacylglycerol (DAG) and H+.Strong evidence supportsthat DAG mediates the opening of the light-dependent channels TRP and TRPL (Delgado and Bacigalupo, 2009, Delgado et al, 2014), the only channels in the microvilli. TRP and PLC are bound to scaffold protein INAD, but not TRPL. The mechanism linking the lipid to channel gating remains elusive. Recent whole-cell recording studies combining light and mechanical stimulation suggested that these channels are mechanosensitive (Hardie and Frenze, 2012). We addressed this question by recording TRP and TRPL single channel currents directly in sub-microscopic (~400 nm) inside-out patches excised from the photosensitive microvilli, under mechanical stimulation. We puffedonto these patches magnetic microspheres (~50 nm) coated with α-rhodopsin antibody to attach them to the membrane, and approached the patch pipette with a magnet to ~1 mm. The mechanical force (~0.1pN) instantlyand steadily opened the channels, which closed abruptly upon retractingthe magnet back (N = 9). This could be repeated multiple times in every patch.Patches containing TRP, TRPL or both channels were responsive, whilethe double mutant lacking both channels (*trp;trpl*) were not. As TRPL is not bound to the complex, our results strongly support thatlight inducesphysical changes on the photosensitive membranedirectly opening the channels.

Supported by Facultad de Ciencias, University of Chile (RD) and FONDECYT 1181361 (CW)

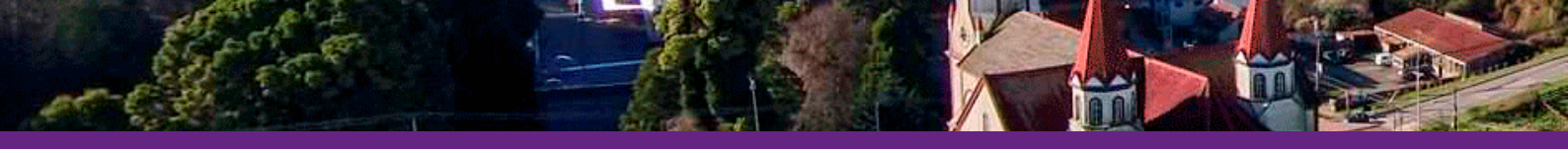


41)Changes on synaptic efficacy in CA1 region of dorsal hippocampus in Ket-treated rats.

García Francisca [1], Santander Odra[2], Pérez-Lizama Miguel[2], Bonansco Christian[2], Fuenzalida Marco[2]. [1]Programa de Doctorado en Ciencias Mención Neurociencias, Facultad de Ciencias, Universidad de Valparaíso. [2]Instituto de Fisiología, Facultad de Ciencias, Universidad de Valparaíso.

Ketamine (Ket), an NMDA-receptor antagonist, has been widely used as an animal model of schizophrenia (SZ), due its ability to induce molecular, synaptic plasticity and behavioral impairment. Previously we have shown that Ket-treated rats had a reduction in the mPFC GABAergic synaptic efficacy and an impaired mPFC-dependent cognitive function. Although clinical and animal research shown that hippocampus is involved in the pathophysiology of schizophrenia our previous results indicate that in our model the ventral hippocampus remains unchanged. However, in recent years it has become apparent that the contribution of the hippocampus to behavioral and cognitive tasks varies along its septal-temporal axis, due to they differ in their anatomical connections, gene expression and glutamate receptor subunit expression. Considering the structural and functional differences along septal-temporal axis, using electrophysiological approach we study whether Ket-treatment affect the excitatory/inhibitory synaptic efficacy and plasticity in the CA1 region of dorsal hippocampus in adult rats. The PPR analysis revealed that the Ket-treatment increases the pulse-paired ratio (PPR), as well as a reduction in the frequency of spontaneous EPSC and IPSC, suggesting changes in the presynaptic excitability and a reduction in the probability of glutamate and GABA release, which could be underlying the cognitive alterations caused by Ket. These results suggest a possible role of dorsal hippocampus in the impaired synaptic plasticity and cognitive symptoms occurring in schizophrenia.

FONDECYT 1171006, Anillo ACT1414, NU-MIND 130011 (MFN); FONDECYT Postdoctorado 3160442 (MAP); PMI UVA 1402 (FG).

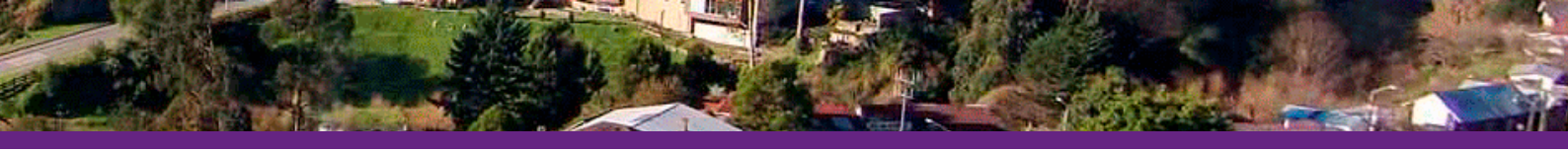


42)Change in Drosophila melanogaster social space over aging

Molina Daniela[1], Zárate Rafaella[1], Hidalgo Sergio[1], Valderrama Benjamín[1], Campusano Jorge[1]. [1]Biología Celular y Molecular, Ciencias Biológicas, Pontificia Universidad Católica de Chile.

Social interaction is one of the fundamental aspects of animal behavior and crucial to guarantee the survival of species. It is observed in a wide range of animals from simpler organisms such as bacteria to humans. A consequence of social interaction is social space, a concept that reflects the distance of an animal respect to its closest neighbor. Here we decided to investigate how the social space changes with aging in different genders, and whether this change depends on aminergic systems. For doing this, we worked with *Drosophila melanogaster*. About 40 flies were placed in a triangular vertical arena for 30 min. Afterwards we measured the social space index (SSI), a parameter that reflects how far away is a fly respect to its closest neighbor. We also measured serotonin and dopamine levels in fly brain by HPLC, at the ages at which the social experiment was carried out (3, 10 and 17 day old flies). Additionally, we measured the Preference Index (PI) a parameter that reflects the performance of the olfactory system in flies. Results show a reduction in SSI over aging, suggesting that older flies prefer to maintain a bigger distance between them. No change in whole brain dopamine or serotonin levels seems to explain these results. Interestingly, PI is decreased as flies age. Our results suggest that the increase in social space in older flies would be explained by impairments in the olfactory system in *Drosophila*. Future experiments will use genetic and pharmacological tools to corroborate these ideas.

FONDECYT 1141233. CONICYT 21170543



43) Cannabinoids decrease the frequency of the respiratory rhythm in mouse brainstem slices

Ochoa Sarmiento Martin[1], Cáceres Vergara Daniela[1], Eugenin Jaime[1]. [1]Laboratorio Sistemas Neurales, Química y Biología, Universidad de Santiago de Chile.

Justification:
The main psychoactive ingredient of the cannabis plant is the delta nine tetrahydrocannabinol (Δ-9 THC). This compound activates the CB1 receptor in the brain. Its synthetic analogue WIN 55.212-2 has 21 times more affinity for the CB1 receptor than THC. Both substances have the potential to permeate the blood-brain barrier and alter the functioning of the central respiratory network. However, the effect of cannabinoids on the respiratory rhythm is still under study and its mechanism of action is not completely understood.

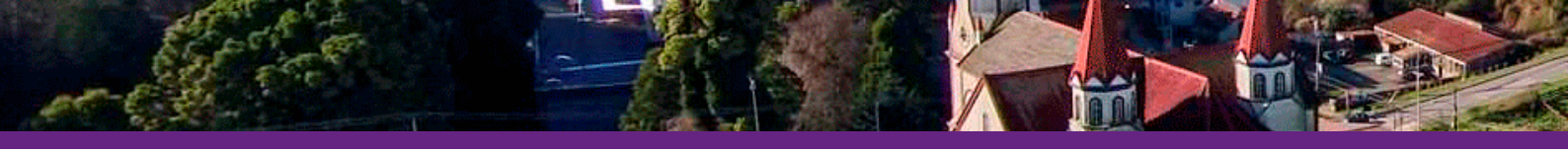
Objective:
To evaluate the effect of the topical application of the cannabinoid agonist WIN 55.212-2 on the fictive respiratory rhythm obtained in brainstem slices.

Methods:
The respiratory rhythm was recorded from the ventral respiratory column in medullary slices from P3 to P6 CF1 mice superfused with artificial cerebrospinal fluid (aCSF) equilibrated with O_2-CO_2 at 95 and 5% respectively in the absence and in the presence of 1uM and 5uM of WIN 55,212-2.

Main Results:
Superfusion of slices with 1uM and 5uM WIN 55-212 reduced the frequency of the fictive respiration

Conclusions:
Superfusion of cannabinoids of medullary brainstem slices significantly reduced the frequency of the respiratory rhythm. These results are relevant for understanding the modulation of the respiratory network during early postnatal life. Key words: Cannabinoids, respiratory rhythm, pre-Bötzinger

Suported by Fondecyt 1171434

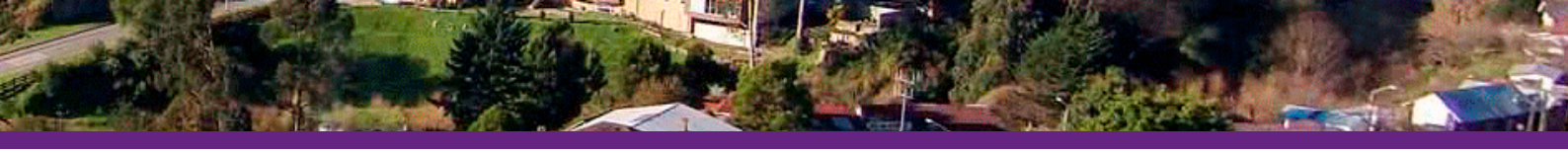


44) Spectral sensitivity of the eyes of Loxosceles laeta

Tapia Felipe[1], Olivares Jesus[1], Vielma Alex[1], Palacios Adrian[1], Schmachtenberg Oliver[1]. [1]Neurociencia, Ciencias, Universidad de Valparaíso.

Loxosceles laeta is a spider species native to South America, usually found in domestic habitats (synanthropic). The envenomation by this species, known as loxoscelism, is an important public health concern in many South American countries, especially in Chile. Despite its epidemiological importance, the biology of this species is poorly understood. Specifically, regarding the vision of this species there is no data available, and since spider eyes are far from being simple or having uniform characteristics among different families or genera, it is impossible to generalize results from other species. In the present study we were able to design an effective protocol to obtain electroretinographic recordings from *L. laeta* individuals and use them to produce spectral sensitivity curves for all three pairs of eyes. Our data shows the presence of three main sensitivity peaks, in the UV (382nm), blue (476nm) and green (532nm) ranges, pointing to the existence of three possible light sensitive pigments. Furthermore, we could not find differences between male and female individuals. It is also of note that we were not able to isolate the sensitivty curves of the putative visual pigments using selective adaptation because of the presence of an unidentified compensatory mechanism, which requires further study. This is the first study to date to analyze the visual capacities of this spider, and could help us understand its ecology and develop new control measures.

Beca CONICYT Doctorado Nacional. Millennium Institute CINV.

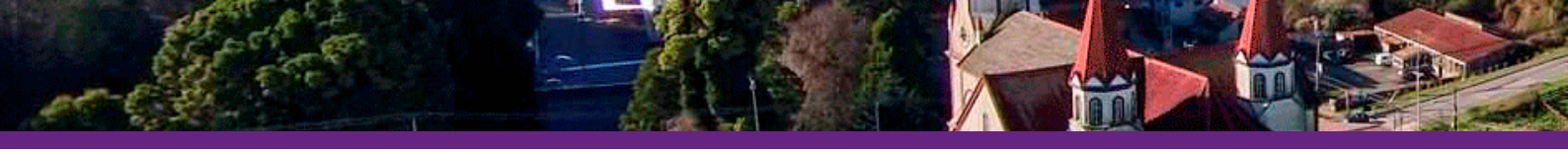


45) The role of sleep in the organization of spatial representations during memory formation

Valdivia Gonzalo[1], García Perez Alexandra[1], Tiznado Vicente[1], Espinoza Nelson[1], Fuentealba Pablo[1]. [1]Psiquiatría, Medicina, Pontificia Universidad Católica de Chile.

The development in the study of place cells discovered by O'Keefe (1971) has put the focus on the study of spatial representation of the environment in the processes and functions lead by the hippocampus. Among these functions, the hippocampus plays a preponderant role in the establishment of spatial memory, in which sleep is fundamental, suggesting a possible relationship between sleep and the establishment of spatial representations by place cells. In this line, there is a query if sleep participates in the consolidation and configuration of spatial representations. One possibility is that sleep affect the configuration of place fields in a post-sleep exploration when place cells are reactivated during slow wave oscillations in a post-learning sleep. In this study we will evaluate the influence of sleep on the variations in the configuration of a spatial map given by place cells during the spatial memory task Object in place recognition (OPR); and the reactivation and temporal coupling of place cell activity with the slow wave oscillations during the post-learning sleep phase. Here we will present our preliminary results showing that post-learning sleep enhances performance in the OPR task We expect to findand that the coupling of place cells activity with hippocampal oscillatory activity during sleep helps to establish specific spatial representations that allow to improve the performance of spatial memory. The study of sleep`s influence on spatial representations given by place cells in the hippocampus will allow us to understand the importance of this process in the performance of a cognitive function such as memory.

PIA Anillo ACT 1414

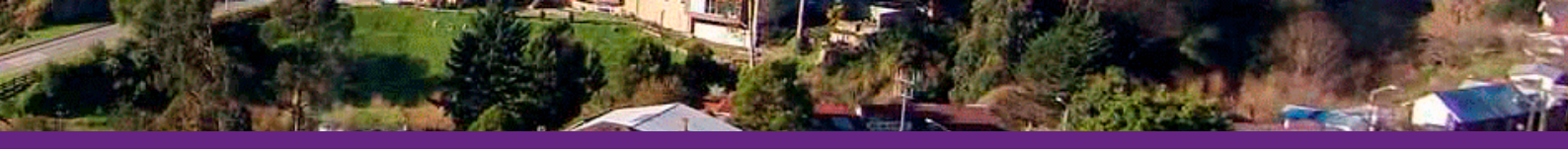


46) Comparative study of habenular network in actinopoterigeans: An inmunohistichemical and histological analysis

Weiss Camila[1,2], Ahumada-Galleguillos Patricio[1,2], Concha Miguel[1,2,3]. [1]Institute of Biomedical Sciences., Facultad de Medicina, Universidad de Chile. [2]Biomedical Neuroscience Institute, Universidad de Chile. [3]Center for Geroscience, Brain Health and Metabolism, Universidad de Chile. (Sponsored by Miguel Concha Nordeman)

In the vertebrate brain, the habenula (Hb) is part of an extended network interconnectingforebrain, midbrain and hindbrain. Remarkably, the efferent projections from Hb to the midbrain located interpeduncular nucleus (IPN) have been described in all species, from lampreys to mammals and teleostei. In turn, the IPN is a component of a local network involved in motor control and neuromodulation. In spite of its highly conserved character, few comparative studies have addressed the evolutionary history of this neural pathway. To do this, we have combined the description of expression patterns of immunohistochemical markers (ChAT, SP, TH and 5-HT) with classical histology (nissl stain) to have a comparative view of Hb-IPN system across different order of teleostei (Cipriniformes, Characifomes and Silurifomes) which are represented by *Danio rerio* (zebrafish), *Paracheirodon innesi* (neon tetra) and *Corydoras paleatus*, respectively. As an out group, we performed the same analysis in the Hb-IPN system of Polypterus senegalus (Polypteriformes), a non-teleost actinopterigean. Results will be discuss in relation to the Hb-IPN system organization into actinopterigeans, but considering the more general context of vertebrates.

ICM P09-015-F, Conicyt PIA ACT1402, Fondap 15150012, Fondecyt Postdoctoral 3160486



47) Olfactory coding of pattern separation in awake mice

Becerra Diego[1], Avello Felipe[1], Nuñez-Parra Alexia[1]. [1]Laboratorio de Neurofisiología, Ciencias, Universidad de Chile.

Being able to discriminate between chemically similar compounds is crucial to fruitfully engage with the dynamic environmental demands. The olfactory cortex (OC) exhibits unique neuronal activation patterns promoting the identification of an odor mixture as one odor-object without recognizing the different molecules composing it, even though the neuronal activation pattern will partially overlap to the ones of their single molecules forming the mixture. Therefore, OC relies on neuronal plasticity and modulation to achieve a balance between perceptual stability and perceptual discrimination (pattern separation). A process that is experience-dependent. Here, we used a Go/No-go task to study how cortical representations changes to promote pattern separation. Mice were trained in a 10 molecules absence-of-one-recognition-test, and 2 molecules mixture/components-separation-test. The former demands them to discriminate between two complex odorant mixtures differing only in one molecule (10o vs 10-1o). In the latter, the mice need to learn to discriminate between two reinforced molecules and its mixture (A or B vs AB). We found that regardless of concentration and number of components, the animals took longer to master mixture/components-separation-test. We hypothesize that pattern decorrelation is achieved in the first experiment by neuronal activation suppression, rendering the neuronal ensemble being recruited with 10o and 10-1o less similar with both higher concentration and time. On the other hand, discrimination between A, B, and AB, in addition to activity-mediated suppression must recruit new units that respond to the mixture but not to the components alone in order to achieve pattern separation.

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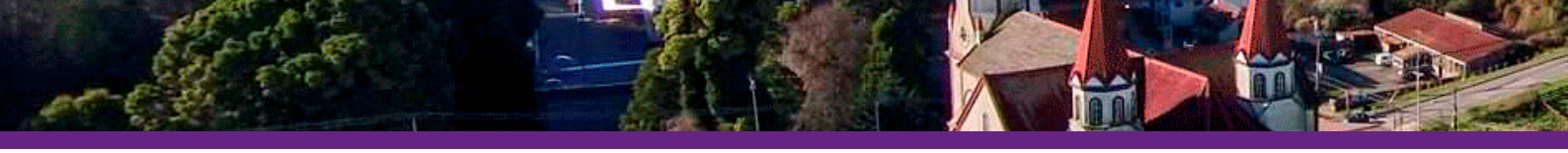
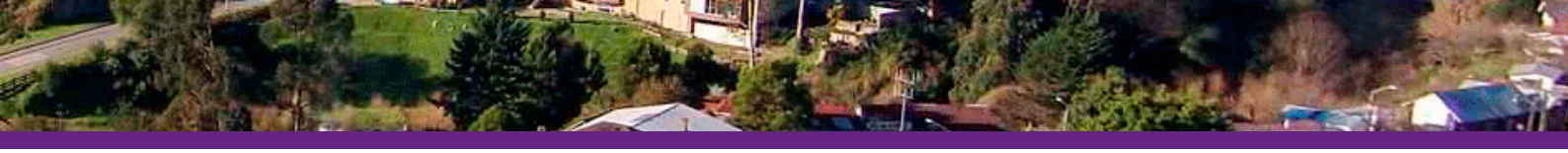


48) Deciding when to perceive: improvement of perception during active behavior

Concha-Miranda Miguel[1,2], Ríos Javier[3,2], Bou Joaquín[2], Maldonado Pedro[2]. [1]Biomedical and Neuroscience Institute, BNI. [2]Neurociencias, Facultad de Medicina, Universidad de Chile. [3]Neurosciencias, Facultad de Medicina, Universidad de Chile.

If stimuli presentation is evoked by a motor act, sensory discrimination and timing accuracy improves. We studied this phenomenon when rats had to locate the position of a brief light stimulus, either when the stimulus was elicited by a warning light (passive condition) or when it was generated by a lever press (active condition). We found that during the passive condition, rats had 66% of correct responses, vs a 77% of correct responses on active condition, which was significantly higher (t-test, p=0.006). Also, reaction times during passive condition was reduced from 1181 ms to 816 ms on the active condition (t-test, p=0.006). On the latter condition, the probability of detecting the side of the light stimulus was negatively correlated with the time lag between the motor act and the evoked light (r=-0.55, p=0.01) and with a 20% reduction on performance per 100 ms (P=0.018). This experiment shows that the mechanism that underlies sensory improvement during active behaviors have a constrained time dynamic, where the peak of performances occurs during the motor act, decreasing proportionally to the lag between the motor act and the stimulus presentation. This result is consistent with the evidence already found in humans of a precise time dynamic of the improvement of sensory acuity after a motor act and reveals an equivalent process in rodents. Our results support the idea that perception and action are precisely coordinated in the brain.

ICM P09-015-F



49) Activation of the phototransduction current in the rhabdomeric photoreceptors of the scallop Argopecten purpuratus

Díaz-Valdivia Alejandra[1], Vielma Alex[1], Schmachtenberg Oliver[1]. [1]Laboratorio de Fisiología Sensorial, Facultad de Ciencias, Universidad de Valparaíso.

Scallops have a large number of pallial eyes distributed in the middle mantle fold. Each eye includes a cornea, a biconvex lens, a concave mirror and two retinas. These organisms have unusual double retinas with two types of photoreceptors with particular properties. The ciliated photoreceptors display a hyperpolarizing response to light, and the rhabdomeric photoreceptors a depolarizing. In these invertebrates, the light sensitive channels TRP and TRPL are found in the microvilli of the rhabdomers. Certain components such as diacylglycerol (DAG), polyunsaturated fatty acids (PUFAs) and phosphatidylinositol biphosphate (PIP2) can open these channels, however, the evidence supporting a direct activation remains controversial. Furthermore, enzymes that degrade these compounds have a potential participation in the activation of TRP or TRPL channels. The objective of this study is to evaluate the activation of the phototransduction cascade in the rhabdomeric photoreceptors of *Argopecten purpuratus*. These experiments may finally solve the old mystery of the last step of invertebrate phototransduction.

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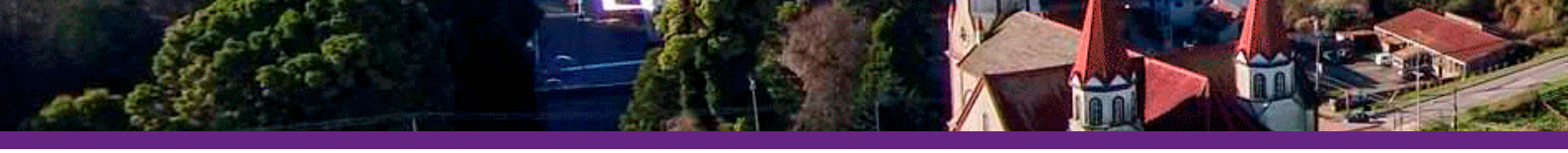
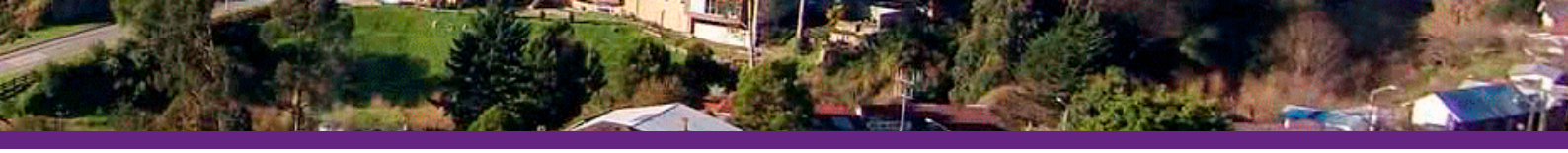


50) Modulation of TRPM8 function by basal phosphorylation

Moreno Claudio Ignacio[1], Rivera Bastián[1], Lavanderos Boris[1], Madrid Rodolfo[1], Pertusa María[1]. [1]Departamento de Biología, Facultad de Química y Biología, Universidad de Santiago de Chile.

TRPM8 is the main molecular entity responsible for detection of cold temperatures in the somatosensory system. This calcium-permeable cation channel is activated by cold, cooling compounds such as menthol, and voltage. It has been suggested that TRPM8 function could be regulated by several kinases that phosphorylate the channel in basal conditions, in both recombinant systems and cold thermoreceptor neurons. In order to explore the mechanism underlying this regulation, we evaluated the contribution of this posttranslational modification in TRPM8 function. To this aim, we have assessed the phosphorylation state of immunoprecipitated TRPM8 channels in basal conditions, identified the residues where this modification takes place, and evaluated channel function using calcium imaging in both HEK293 and F11 cells. We found that TRPM8 is phosphorylated in several residues within the N-terminal domain. The inhibition of the basal kinase activity using staurosporine enhances TRPM8 responses to cold and menthol, and causes a shift of 2ºC in its temperature threshold to warmer temperatures in both cell lines. Altogether, these results indicate that basal kinase activity acts as a negative modulator of TRPM8 function, and suggest that constitutive phosphorylated residues in TRPM8 channels tune their responses to cold and menthol.



51) Protein kinase c negatively modulates trpm8 channel activity

Rivera Bastián[1], Campos Matías[1], Lavanderos Boris[1], Madrid Rodolfo[1], Pertusa María[1]. [1]Departamento de Biología, Facultad de Química y Biología, Universidad de Santiago de Chile.

Transient receptor potential melastatin 8 (TRPM8) channel is expressed in primary somatosensory neurons and is activated by cold, cooling compound such as menthol, and by voltage. Several studies showed that protein kinases participate in the modulation of TRPM8 activity in both cold thermoreceptors and recombinant systems. In inflammatory conditions, the release of bradykinin activates Gq-coupled receptors and PKC, suggesting that this kinase could play a role in the modulation of TRPM8 in inflammation. To further explore the effect of PKC activation on TRPM8 function, we used either phorbol esters (PMA) and the proinflammatory mediator bradykinin, in combination with calcium imaging in native, recombinant systems and extracellular recordings in corneal free nerve endings of cold thermoreceptors. Our results show that the activation of PKC reduces the maximal response of TRPM8 to cold and menthol in both HEK293 cells and trigeminal neurons, causing a shift of 2°C in the temperature threshold of activation to lower temperatures, where the mechanism involve in this effect is product of the reduction in the amount of channels present in the plasma membrane. In corneal cold thermoreceptors, PMA reduces both the ongoing activity and the maximal response to cold. Altogether, these results suggest that PKC acts as a negative modulator of TRPM8 channels, suggesting a relevant role of this kinase in cold sensing in inflammatory conditions.

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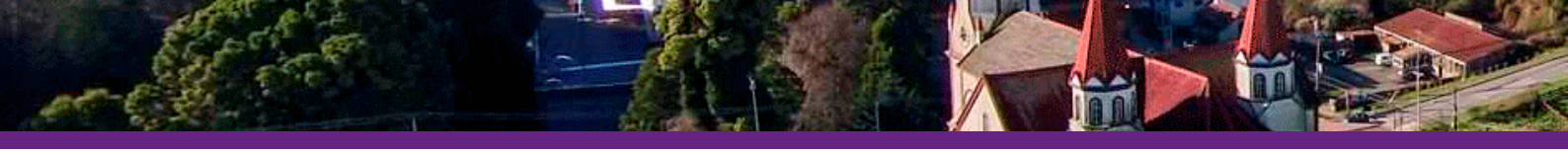

SESIÓN PANELES II

52) Parasite-mediated behavioral alteration in the home-range of the native rodent Phyllotis darwini

García De Cortazar Rodrigo[1], **Correa Juana Paola[1]**, Bacigalupo Antonella[2], Yañez-Meza Andrea[1], San Juan Esteban[1], Sandoval-Rodríguez Alejandra[1], Quiroga Nicol[1], Araya Raul[1], Botto-Mahan Carezza[1]. [1]Departamento de Ciencias Ecológicas, Facultad de Ciencias, Universidad de Chile. [2]Departamento de Ciencias Biológicas Animales, Facultad de Ciencias Veterinarias y Pecuarias, Universidad de Chile.

Parasites can generate physiological, morphological and behavioral modifications in their hosts. Some behavioral alterations are side-effects of parasitic infection, but others can be considered parasite adaptations that increase the probability of transmission. The protozoan ***Trypanosoma cruzi***, the causative agent of Chagas disease in humans, can be transmitted by triatomine insects (Hemiptera) to a wide variety of mammals. Previous studies have detected that small mammals acting as ***T. cruzi*** hosts, modify their use of space depending on the infection status and the presence of environmental stressful conditions. In this study, we evaluated the association between ***T. cruzi***-infection/burden and the home-range of ***P. darwini*** inhabiting a protected area. To this end, we constructed ***spider web*** like trapping grids to estimate the home-range of ***P. darwini*** by means of capture-mark-recapture procedure. We assessed the ***T. cruzi***-infection status and parasitic burden of ***P. darwini*** by qPCR. The home-range was used as response variable to fit a Generalized Linear Model including infection status (infected or not infected) and sex (male or female). Results indicate that the home-range of ***P. darwini*** ranged from 77 to 11536 m^2 and the parasitic load varied between 0.017 and 1103 par-eq/ml; but no association was detected between parasitic burden and home range ($p=0.67$). We detected a significant interaction between status and sex ($P<0.001$), where infected females exhibited a smaller home-range than those non-infected. We suggest that infected females might be using smaller areas due to the energetic cost associated to parasite resistance and reproduction.

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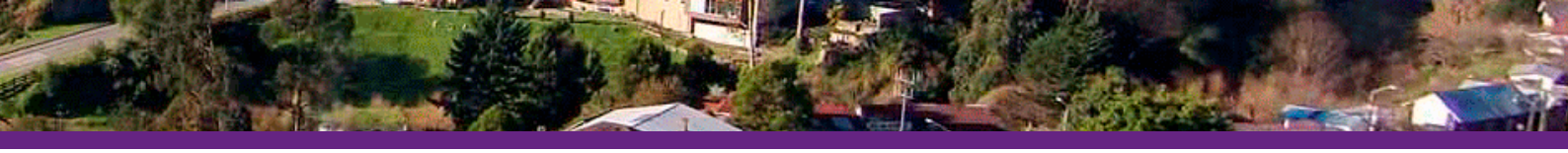
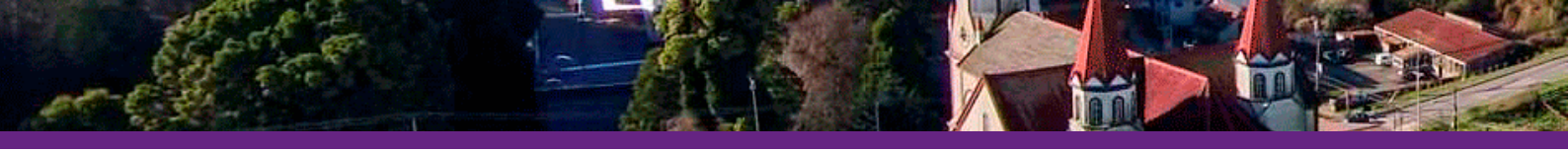


53) Abundance and seropositivity of andes orthohantavirus in oligoryzomys longicaudatus and abrothrix hirta [rodentia: sigmodontinae] in snaspe protected areas

Astudillo Roxana Loreto[1], Boric-Bargetto Dusan [2], Palma R. Eduardo [3], Torres-Pérez Fernando [2]. [1]Laboratorio de Zoología, Epidemiología y Evolución., Facultad de Ciencias, Pontificia Universidad Católica de Valparaíso. [2]Laboratorio Zoología, Epidemiologia y Evolución, Instituto de Biología, Facultad de Ciencias, Pontificia Universidad Católica de Valparaíso. [3]Departamento de Ecología, Facultad de Ciencias, Pontificia Universidad Católica de Chile.

There is only one strain and etiologic hantavirus agent in Chile, ***Andes Orthohantavirus*** (ANDV). ***Oligoryzomys longicaudatus*** is the primary reservoir of this strain, while new research shows that ***Abrothrix hirta*** is the second species with the highest seroprevalence. The Chilean government is responsible for protecting and regulating the territory natural wealth and biodiversity (e.g. through SNAPSE which covers around 19.2% of the national territory). SNASPE are intended to be areas less intervened compared to those un protected areas due to anthropogenic intervention, where fragmentation and habitat loss has been observed. Comparing these two typed of areas, it is expected that in SNASPE there is a greater abundance of ***O. longicaudatus*** and ***A. hirta***, and eventually higher prevalence of seropositive rodents to ANDV. A comparison of abundance and relative seropositivity was performed using ***O. longicaudatus*** and ***A. hirta*** in SNASPE and adjacent areas (not SNASPE). We sampled, 20 localities, 10 from SNASPE and 10 from unprotected areas. Results showed no significant differences in the total abundance and relative seropositivity between both areas. Among ecoregions,significant differences were obtained for ***O. longicaudatus*** in abundance for the Valdivian Forests. No significant differences were observed for the relative seropositivity in ecoregions for both rodents. The results suggest that both SNASPE and adjacent areas not SNASPE are important in determining the epidemiological potential for hantavirus, that should result in extensive information campaigns for population.

CONICYT PIA-ANILLO 1408, FONDECYT 1171280, 3180237, 1170761.

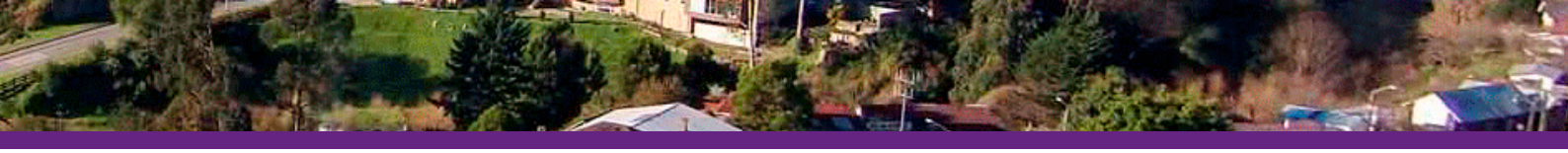


54) Relative Abundance and Seroprevalence to Andes Orthohantaviruses of Oligoryzomys longicaudatus [Rodentia: Sigmodontinae] in four Ecoregions of Chile

Cruz-Ormeño Javier[1], Stevenson Robert[1], R. Eduardo Palma[2], Boric-Bargetto Dusan[1], Torres-Pérez Fernando[1]. [1]Facultad de Ciencias, Instituto de Biología, Pontificia Universidad Católica de Valparaíso. [2]Departamento de Ecología, Pontificia Universidad Católica de Chile. (Sponsored by Fernando León Torres Pérez)

Oligoryzomys longicaudatus has a high epidemiological importance because it is the main reservoir of ***Andes Orthohantavirus*** (ANDV; ***Hantaviridae***), which produces the Hantavirus Cardiopulmonary Syndrome (HCPS). This species is endemic from Chile and Argentina, inhabiting the latter country from the Atacama Desert to Tierra del Fuego (27 ° S to 55 ° S). It is distributed in the ecoregions Mediterranean, Temperate Rainforests, Patagonian Rainforests and Magellanic Rainforests. Due to the different climatic and vegetation characteristics of each ecoregion it is possible to infer that there are differences in abundance and seroprevalence to ANDV in ***O. longicaudatus***. More than 900 specimens of ***O. longicaudatus*** were captured in the four aforementioned ecoregions between the years 2000-2009 and the presence of anti-ANDV antibodies was determined by SIA (Strip Immunoblot Assay). Relative abundance and seroprevalence were calculated in the four ecoregions. The results showed that the relative abundance is higher in the ecoregions of the Temperate Rainforests and Magellanic Rainforests, while relative seroprevalence is higher in the Mediterranean ecoregion. It is noteworthy that the seroprevalence of the Mediterranean ecoregion is more than twice that those from the remaining ecoregions. We discuss the impact of this results in terms of epidemiological measures of monitoring and prevention of the disease.

Funding: CONICYT PIA-Anillo 1408, FONDECYT 1171280, 3180237, 1170761

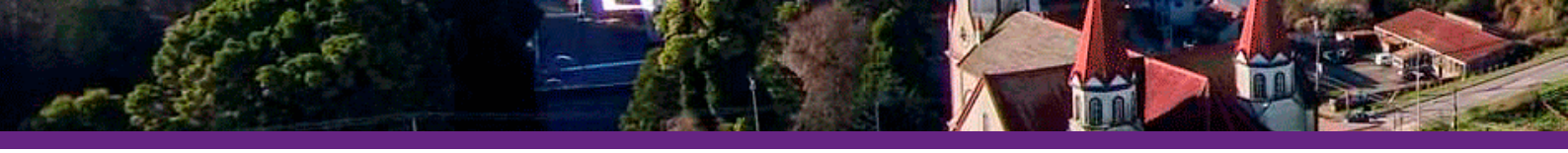


55) Infected rodent from the island reveal a complete Trypanosoma cruzi cycle in an insular zone of Chile

Diaz Campusano Gabriel[1], Campos-Soto Ricardo[1], Rives Ninette[2], Quiroga Nicol[3], Muñoz-San Martín Catalina[4], Torres-Pérez Fernando[1]. [1]Instituto de Biología , Facultad de Ciencias, Pontificia Universidad Católica de Valparaíso. [2]Pregrado, Facultad de Ciencias Veterinarias y Pecuarias, Universidad de Chile. [3]Departamento de Ciencias Ecológicas, Facultad Ciencias, Universidad de Chile. [4] Departamento de Ciencias Biológicas Animales, Facultad de Ciencias, Universidad de Chile.

Chagas disease is one of the main zoonoses mediated by vectors in America. The etiological agent is the protozoan ***Trypanosoma cruzi***, transmitted mainly by hematophagous insects of the subfamily Triatominae. ***T. cruzi*** alternates between triatomines and mammalian host species; meantime birds and reptiles are refractory to infection. Triatomines of the ***Mepraia*** genus are endemic of Chile, playing a role in the wild cycle of transmission of ***T. cruzi*** and are potential vectors for humans. In addition to the continental distribution, populations of ***Mepraia*** have been reported inhabiting in islands of northern Chile infected with ***T. cruzi***. Although it has been suggested that the insular insects feed mainly on seabirds and reptiles, the presence of small mammals cannot be ruled out. If birds and reptiles are refractory to infection, how were these vectors infected? One of the hypotheses is that the infected ***Mepraia*** specimens are originated from ancestral habitats with a complete ***T. cruzi*** cycle that were separated by vicariance. To clarify this question, small mammals and vectors were captured in three islands. DNA was extracted from blood of small mammals and from the gut in the insects. ***T. cruzi*** was detected by amplification of kDNA segment through PCR and qPCR. Results show infected ***Mepraia*** and ***Abrothrix*** specimens in Pan de Azucar Island. This results shows for the first time a complete ***T. cruzi*** cycle in an island, congruent with the vicariance hypothesis. Future phylogeographic analyses must be integrated to determine how long this cycle have been maintained in insular areas.

FODECYT N° 11170643 and 1171280



56) Intra-organismal genetic heterogeneity in modular macroalgae

Santelices Bernabé[1], Gallegos Cristobal[1], **Gonzalez Alejandra[2]**. [1]Ecologia, Ciencias Biológicas, Pontificia Universidad Católica de Chile. [2]Departamento Ciencias Ecologicas, Facultad de Ciencias, Universidad de Chile.

Genetic diversity is considered a key factor of population survival and evolution, especially in changing environments. Genetic diversity arises from mutations in the DNA sequence of cell lines and from there it reaches the level of organisms, populations, and regions. However, many previous studies have not considered the organism architecture or pattern of thallus construction, ignoring the potential genetic complexities that intra-organismal genetic heterogeneity could generate in modular organisms. In seaweeds, modularity and clonality exist in many species among the three major macroalgal divisions: Chlorophyta, Rhodophyta, and Phaeophyceae. Modular organization has been related to advantages in terms of rapid construction and recovery after the loss of individual modules, which have their own demographic properties as they are generated, mature, senesce and die. We made a mini-review melding concepts from terrestrial plant, invertebrate, and macroalgal fields. Then, we made links between growth pattern and genetic variation. Based on recent evidence from the literature, we suggest that modules also have their own genetic properties. Specifically, modular seaweeds have two possible sources of genetic diversity at the individual level: the heterozygosity of the genotypes composing the genet, and genetic heterogeneity among the modules within a genet (i.e., intraclonal genetic variability). Both sources of genetic diversity can have ecological and evolutionary consequences, and most of them must be considered in research on modular seaweeds. Linking intra-organismal genetic diversity, with clonal architecture and propagation styles may help us to understand important ecological and evolutionary processes, such as speciation modes, invasive capacities or farming potential.

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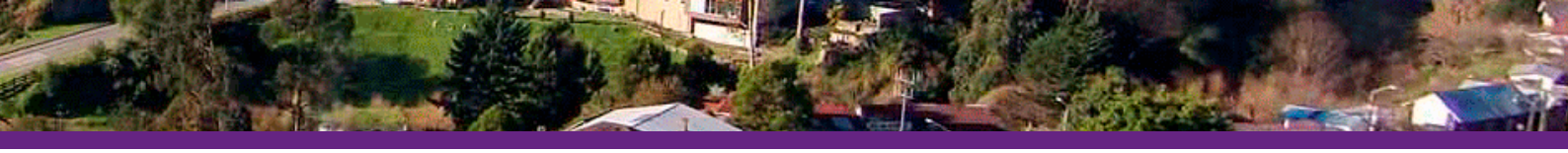
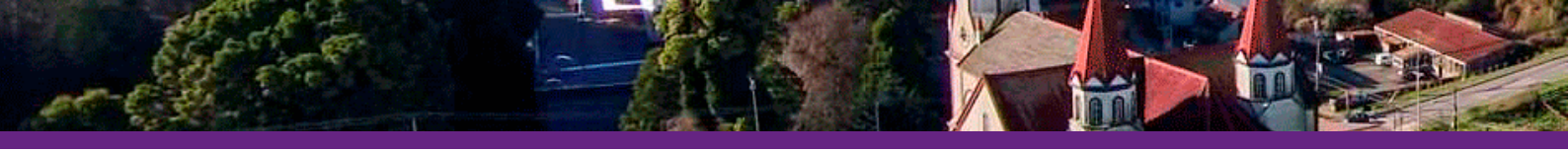


57) Intraorganismal genetic heterogeneity against climate change: the thermal stress tolerance in the brown macroalgae lessonia spicata

Hernández Juan[1], Beltrán Jessica[2], Santelices Bernabe[2], González Alejandra[1]. [1] Laboratorio Fitoecoevo. Departamento de Ciencias Ecológicas, Fac. de Ciencias., Universidad de Chile. [2]Departamento Ecología Departamento de Ecología, Facultad de Ciencias Biológicas., Pontificia Universidad Católica de Chile.

The intraorganismal genetic heterogeneity (IGH) involves the existence of different genomes in a single entity genetically heterogeneous. From an evolutionary and ecology perspective, therefore, IGH implies a higher tolerance to environmental changes compared to genetically homogeneous organism. Recently, a high frequency of IGH has been reported in natural ***Lessonia spicata*** populations, a brown macroalgae specie under intense harvesting pressure and with enormous ecological and socioeconomic importance. In order to test whether IGH confers higher thermal stress tolerance to this specie, we built plants genetically homogeneous (control) and with IGH by coalescence of sporophytes at different density and strain relatedness (half-sibs vs unrelated strains). All treatments were incubated for 30 days at 12°C (normal) and 18°C (stress). The thermal tolerance was evaluated in terms of specific growth rate of IGH organism vs genetic homogeneous. Our results indicate that IGH organisms showed higher growth rate at 12ºC and 18ºC compared to controls. However, under thermal stress (18°C) density and strain relatedness that conform the organism made the differences among the treatments. In conclusion, we suggest that organism of ***L. spicata*** with IGH have advantages compared to genetically homogenous. In addition, specific combination of density and strain relatedness of the fused sporophytes increase resilience capacity in terms of growth under thermal stress condition. In the light of these, IGH can be explain the persistence of natural populations of ***Lessonia*** under continuous ENSO events, and probably confer higher resilience under climate change.

PAIFAC-2015-2017, ENL020/16, FONDEF ID17I10080

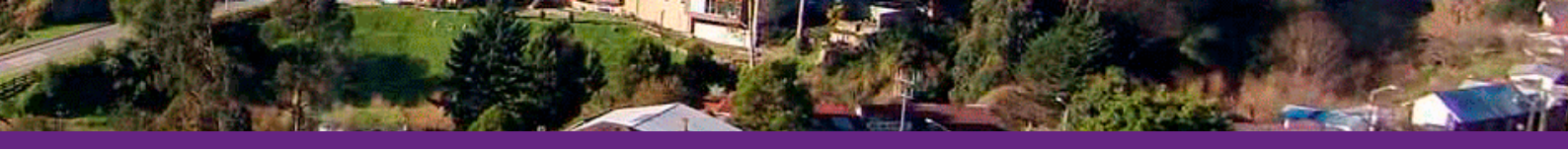


58) Evolutionary responses to selection on heat tolerance in Drosophila subobscuradepend on intensity of thermal selection

Mesas Andrés[1], Jaramillo Angélica[1], Castañeda Luis E.[1,2]. [1]Ecología y Evolución, Facultad de Ciencias, Universidad Austral de Chile. [2]Instituto de Ciencias Biomédicas, Facultad de Medicina, Universidad de Chile.

Heat tolerance represents the thermal limit at which ectotherms can perform. Then, the evolutionary potential of this trait has been deeply explored, but the heat intensity employed during experimental assays strongly influence the heat tolerance estimates: the lower the heat intensity, the lower the heat tolerance. This phenomenon has been explained because in chronic assays, individuals that use efficiently their energy resources can tolerance long thermal assay, which results in higher heat tolerance. In the present work, we explored the effect of heat intensity on the evolutionary response of heat tolerance and metabolic traits (i.e. metabolic rate, Glucose-6-Phosphate enzymes) in *Drosophila subobscura*. To accomplish this goal, we performed acute and chronic thermal selection on heat tolerance and we tested the correlated response of metabolic traits in both selected population. We hypothesized that chronic selected populations should exhibit a lower evolutionary response of heat tolerance than acute selected populations and that metabolic traits should exhibit correlated responses only in chronic selected populations. At the same time, modifications on metabolic machinery in chronic heat selection should affect fecundity and egg viability. We found that heat tolerance evolves after artificial selection but its evolutionary rate does not differ between both thermal selection. Metabolic rate did not exhibit a correlated response. Interestingly, enzymatic activity related to glucose and reproduction decrease/ increase in chronic selected populations, while a reduction of enzymatic activity related to lipids was found in acute selected individuals. Concluding that heat intensity had a profound effect on correlated traits to heat tolerance.

FONDECYT 1140066, Beca Doctoral CONICYT



59) Evolutionary divergence in the acoustic communication system of Chilean anuran: Evoked vocal and neural responses

Velásquez Nelson Andrés[1], López Carlos[1], Rojas Valentina[1], Moreno-Gómez Felipe[2]. [1]Laboratorio de Comunicación Animal, Ciencias Básicas, Universidad Católica del Maule. [2]Laboratorio de Bioacústica y Ecología del Comportamiento Animal, Ciencias Básicas, Universidad Católica del Maule.

The producing and receiver structures of acoustic signals and environment where these signals are propagated may present significant geographic variations. However, the proximate mechanisms involved in the establishment of these geographic variations have received little attention. Previous studies on ***Pleurodema thaul***have demonstrated a notable geographic variation at the morphological and behavioral level along with their distribution in Chile. To study as the learning for acoustic signals participate in the generation of geographic differences of advertisement calls in this species, we carried out playback experiments in two Chilean populations of ***P. thaul***(north: Totoral and south: Osorno). Additionally, electrophysiological recordings were carried out to characterize their neural responses in front of repetitive stimulations with acoustic signals similar to north and south populations. In both studied populations, males showed decreasing vocal responses during stimulation. Neural responses were consistent with vocal responses. Variation in both evoked vocal and neural responses of males of ***P. thaul***from both studied populations constitutes a support to a participation of learning for acoustic signals as an explicative mechanism of evolutionary divergence of the acoustic communication system in this species.

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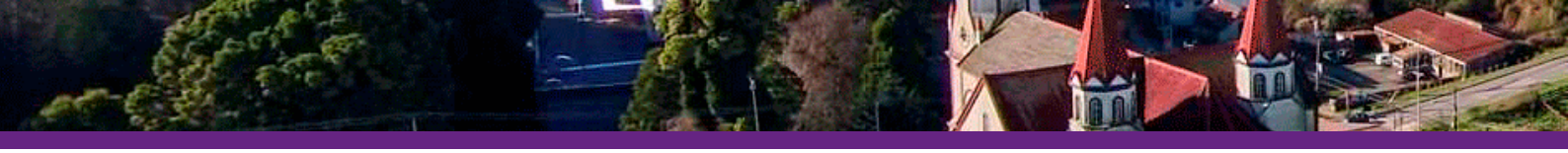
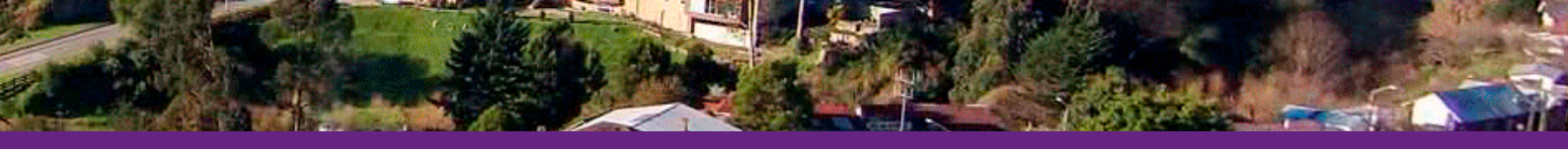


60) Current status of Abrothrix as a natural reservoir of Andes Orthohantavirus in Chile

Arriagada Honores Marisol [1], Boric Bargetto Dusan[1], Torres-Pérez Fernando[1]. [1]Instituto de Biología, Facultad de Ciencias, Pontificia Universidad Católica de Valparaíso.

Hantavirus is an RNA virus of the family Hantaviridae that causes the Hantavirus Cardiopulmonary Syndrome (HCPS). In Chile, the main reservoir of the Andes strain (ANDV) is ***Oligoryzomys longicaudatus***. Other seropositive rodents to ANDV have been described, such as ***Phyllotis darwini, Loxodontomys micropus***, ***Abrothrix olivacea, A. longipilis, and A. sanborni.*** These and other species are sympatric with ***O. longicaudatus***. Given the new taxonomic changes in the genus ***Abrothrix***, it is fundamental to determine which species are reservoirs of ANDV. ***Abrothrix*** individuals from the south of Chile were captured and the presence of ANDV in tissue samples was determined by serology and PCR. Mitochondrial DNA (cytochrome b) was extracted to infer the specific status of rodent species carrying ANDV. The results show ANDV can be found in ***Abrothrix hirta*** and ***Abrothrix manni***, which is relevant in the monitoring and prevention campaigns of HCPS in Chile.

CONICYT PIA-Anillo 1408, FONDECYT 1171280, 3180237, 1170761.



61) Morphological divergence in the genus orestias, ecological, sympatric and allopatric effects

Cruz-Jofré Franco[1,2], Maldonado Mabel[3], Vila Irma[4], Sarmiento Jaime[5], Barrera Soraya[5], Méndez Marco A.[1]. [1]Laboratorio de Genética y Evolución, Ciencias Ecológicas, Ciencias, Universidad de Chile. [2]Escuela de Medicina Veterinaria, Recursos Naturales y Medicina Veterinaria, Universidad Santo Tomás. [3]Centro de Limnología y Recursos acuáticos, Universidad Mayor San Simón. [4]Laboratorio de Limnología, Ciencias Ecológicas, Ciencias, Universidad de Chile. [5]Sección de Ictiología, Zoología, Museo Nacional de Historia Natural, La Paz, Bolivia.. (Sponsored by Marco Antonio Méndez Torres)

The genus ***Orestias*** is composed of 44 species distributed along the Altiplano of South America. Five complexes of species have been described: O. cuvieri, O. gilsoni, O. mulleri, O. lutea, recognized as an intra-lacustrine radiation, and O. agassii. The last complex show the widest distribution along the Central Andes, inhabits in many water systems (lakes, rivers, wetlands and springs). This scenario represents an opportunity to evaluate different degree of morphological divergence in two contrasting systems: allopatric and sympatric distribution. To evaluate the effect of environments and phylogeny on diversity of body shape, we performed a geometric morphometric analysis (44 species; 694 individual; 60 localities). We inferred a molecular phylogeny using two mitochondrial markers (Cyt_b; control region). We not found a relationship between Morphological and Genetic traits. In the morphometric analysis of Agassi complex, individuals from spring environment were greatly differentiated from those from rivers, lakes and wetlands. The comparison of groups with allopatric and sympatric distribution shows low level of differences, however in sympatric conditions fish show a widest forms and a largest centroid size. In the Titicaca Lake we found big-headed (robust fishes) and fishes with small heads and elongated bodies. In allopatric system the environment may the best explanation to body shape, robust and big head fishes were found in the spring environment. Instead, in river systems the hydrodynamic body is the rule. Fishes from wetlands show a high variability morphology and low correct classification, this last environment it is highly variable.

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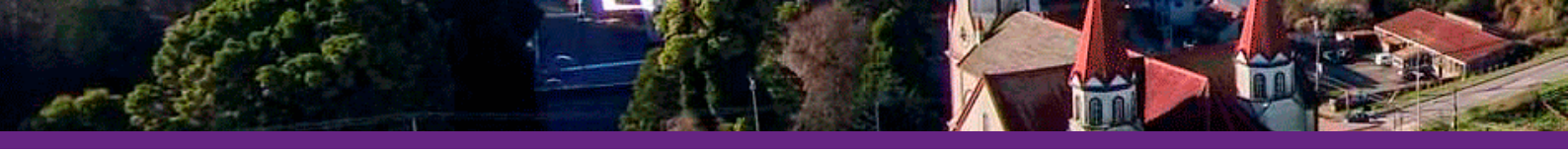
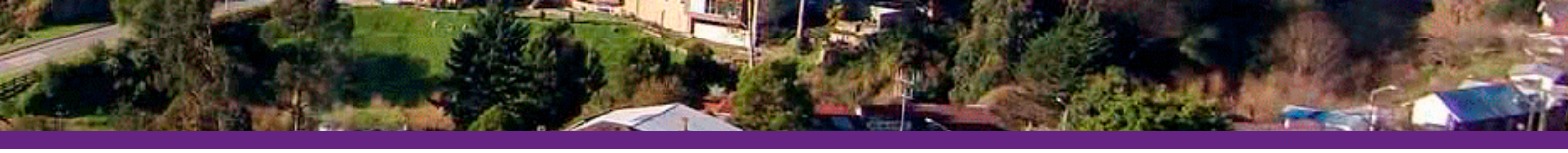


62) The role of rivers in the primary and/or secondary divergence of Thylamys elegans (Didelphimorphia: Didelphidae)

Boric-Bargetto Dusan Vladimir[1], Zúñiga-Reinoso Álvaro[2], Torres-Pérez Fernando[1], Rodríguez-Serrano Enrique[3], Hernández Cristián E[3], Palma Vásquez R Eduardo[4]. [1]Instituto de Biología, Facultad de Ciencias, Pontificia Universidad Católica de Valparaíso. [2]Institute of Zoology, University of Cologne. [3]Departamento de Zoología, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción. [4]Departamento de Ecología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile.

Three hypotheses have been formulated for the divergence of populations associated with rivers: 1) primary differentiation, with a river as a vicariant barrier, generating reciprocal monophyly of sister clades from opposite banks; 2) secondary differentiation, with a river as a barrier to the dispersion of previously differentiated populations, with lineages of opposite banks without sister clades and each lineage more related to the populations from where they dispersed than from the opposite bank; 3) dispersion of a population established on one bank towards the opposite bank, producing paraphyletic relationship and the river being a permeable barrier to gene flow. Furthermore, demographic predictions have been proposed for the riverine barrier hypothesis: Populations of opposite banks that diverged with a river as a vicariant barrier will not show signs of demographic expansion; while the populations of opposite banks that diverged previously in each bank and later they did not make secondary contact by a river as a barrier, will present a signal of demographic expansion. In this study, a phylogeographic approach was used to evaluate whether rivers have caused primary and/or secondary divergence in ***T. elegans*** lineages, analyzing the phylogeographic topology and demographic parameters of populations of each riverbank. Furthermore, an interpolate genetic landscape shape analysis shows a north-south gradient of the genetic distance, in agree with the highest phylogeographic structure found in the center and south of chile (32-35,5ºS).

Funding: FONDECYT 3180237, 1170761, 1170815, 1170486

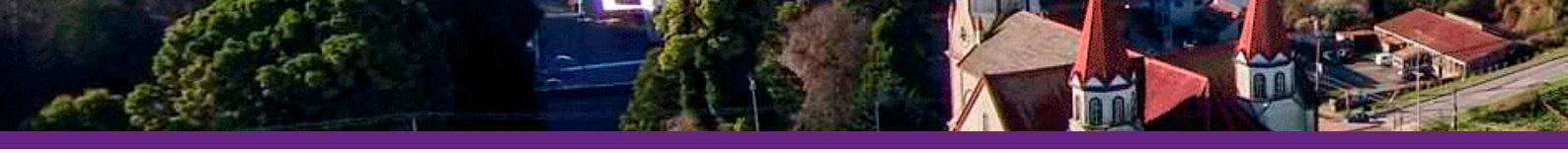


63) Between basin genetic divergence along the southwestern Andean margin: the case of Telmatobius water frogs (Anura:Telmatobiidae)

Fibla Pablo[1], Otalora Katherin[1], Méndez Marco[1]. [1]Departamento de Ciencias Ecológicas, Ciencias, Universidad De Chile. (Sponsored by Marco Antonio Méndez Torres)

The Andean margin in northern Chile is divided into a series of watersheds that are delimited by irregular reliefs, mountain ranges and volcanoes. These boundaries between basins would play a fundamental role in determining the phylogeographic patterns of the native aquatic fauna from this region, since they would function as barriers that restrict the genetic flow between populations in a predominantly desert area. We evaluated the levels of genetic differentiation between populations and the existence of phylogeographic structure in three allopatric species of aquatic toads of the genus ***Telmatobius***, distributed in different basins present in the western Andean margin in northern Chile: ***Telmatobius pefauri***, ***T. chusmisensis*** and ***T philippii***. A fragment of the mitochondrial control region and seven microsatellite markers were used in the analyses. It was possible to detect relatively high levels of genetic differentiation between populations that inhabit separate watersheds in the three studied species, with private haplotypes prevailing in each basin and shared haplotypes at low proportion. The microsatellite markers also evidenced this pattern and revealed low levels of recent genetic flow between adjacent basins, suggesting phylogeographic structure in at least two of the three studied species. Due to the fact that there are currently no current connections between the different basins analyzed, it is suggested that the phylogeographic pattern found here could be the effect of past hydrological connections. The results are discussed based on climatic events that could favor connections between basins during the past.

CONICYT PCHA/Doctorado Nacional/2014-21140355; FONDECYT 1140540.



64) Philogeography of a species with low vagility and low habitat connectivity: the history of the sweet crayfish parastacus pugnax (poeppig 1835) in coastal and andean basins

Rivera Lorena [1], Muñoz Carla[1], Muñoz-Escobar Christian [1], Vega-Drake Karina[1], D`Elía Guillermo[2], Victoriano Pedro F.[1]. [1]Departamento de Zoología, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción. [2]Instituto de Ciencias Ambientales y Evolutivas, Facultad de Ciencias, Universidad Austral de Chile. (Sponsored by Pedro Francisco Victoriano Sepúlveda)

The phylogeography of a species is shaped by biológical attributes of the taxon, geography and paleoclimatic dynamics. For old and low vagility taxa, a marked structure and high genetic-beta diversity is expected, especially in scenarios with complex paleoclimatic history. Parasticoidea crayfishes have an origin associated with the break of Gondwana. In Chile, the named "camarón de vega" ***Parastacus pugnax*** inhabits highly disaggregated environments and it is exploited as a food resource. The knowledge of this species mainly covers biological and ecological aspects, but its evolutionary diversity and the processes which generated it is unknown, which is a fundamental aspects for its conservation. Its range of distribution includes areas of contrasting geographic and historical attributes, such as Andean and coastal basins. We analyzed phylogeographically this species, using mtCOI sequences of 385 individuals from its central-southern range, contrasting both types of basins. The results show high structure and contrasting intra-basin demographic diversity-stability levels, which seems not to be associated with the Andean-coastal condition. The high number of lineages suggests numerous conservation units associated with complex environmental histories.

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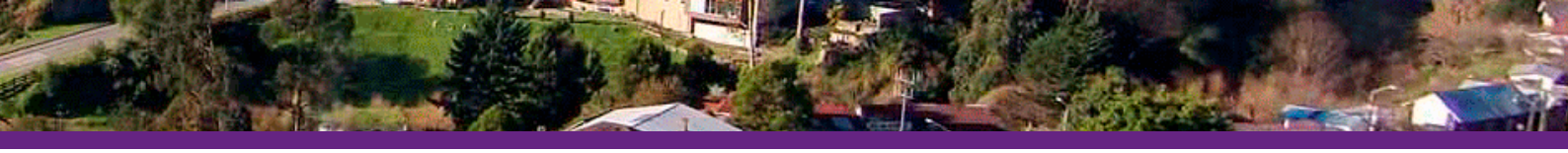
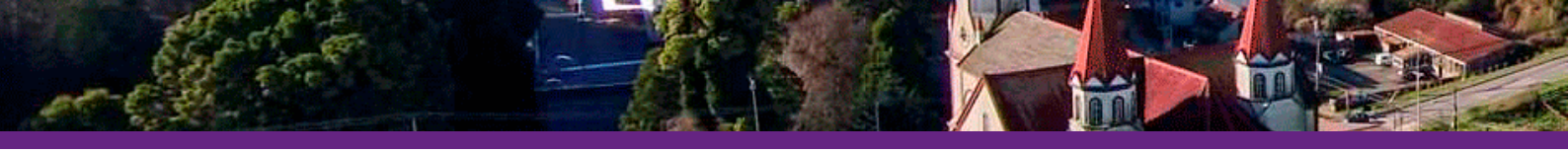


65) Integrative study of genetic and demographic data to improve the management units delimitation of Lessonia spicata, a brown macroalgae of economic importance

Morales Pamela[1], Salas Paulina[1], Santelices Bernabé[2], González Alejandra[1]. [1]Ciencias Ecologias, Ciencias, Universidad de Chile. [2]Departamento de Ecología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile.

Management units delimitation is a fundamental task for conservation of species of economic importance. The genus ***Lessonia*** is one of the commercially exploited brown macroalgae that have also an important ecological role as primary producers and bioengineer organisms. However, the increased demand has caused overexploitation affecting their natural populations and fisheries. As consequence, the culture and repopulation have been promoted, but without knowledge of the population genetic structure. The objective of this study is to combine demographic information and genetic analyses of the species ***L. spicata.*** Using six microsatellites markers, we observed that each population conform a differentiated genetic group and that there is absence of gene flow, implying low or none migration. Additionally, and specifically for the population of Pichicuy that have harvesting information since 2003, population viability analyses showed different scenarios of population persistence. However, it should still be considered as a management unit by itself given their disconnection with any other population. In a conservation biology context, these tools help the management units delimitation to protect exclusive genes and maximize the genetic diversity allowing the persistence of exploited species.

PAIFAC-2015-2017, ENL020/16, FONDEF ID17I10080



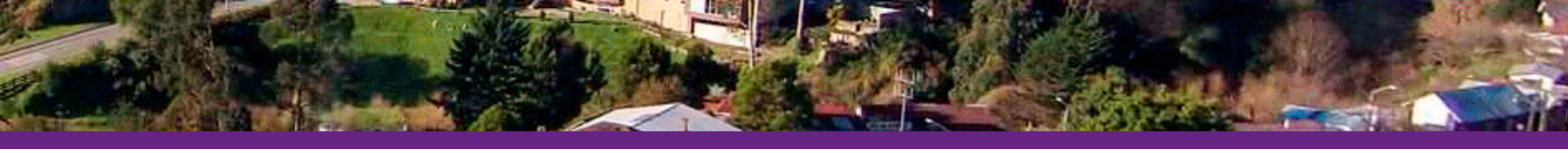
66) Development and characterization of microsatellite molecular markers for the eye mask frog Batrachyla taeniata (Girard, 1855)

Cisternas-Medina Ingrid[1], Ortiz Juan Carlos[1], Ferrada Sandra[2]. [1]Zoología, Ciencias Naturales y Oceanográficas, Universidad de Concepción. [2]Oceanografía, Ciencias Naturales y Oceanográficas, Universidad de Concepción.

Batrachyla taeniata (Anura: Batrachylidae) is a small frog species endemic to the temperate forests of ***Nothofagus*** that has a wide distribution in Chile and marginally in Argentina. In Chile, it extends from the Aconcagua province in the Valparaíso region to the Capitán Prat province in the Aysén region. In addition, it presents island distributions in at least three islands near the continent, Quiriquina, Mocha and Chiloé. This species cover approximately more than 1,500 km from north to south. However, their populations are threatened due to the change in land use, deforestation, and human settlements. Through massive sequencing runs in ION Torrent PGM, was built DNA fragment library, from which we finally isolated and characterized 25 microsatellite loci from 40 individuals. The number of alleles per locus ranged from 2 to 23, allele sizes varied between 110 and 268 bp, observed heterozygosity ranged from 0.205 to 1.000 and the expected heterozygosity between 0.21 and 0.93. We found evidence of deviations of HWE for 10 microsatellite loci, linked to high inbreeding coefficients, indicating a loss of heterozygosity in those particular loci. There was no linkage disequilibrium found within the microsatellite loci tested through the sequential Bonferroni correction. Results are also presented on the genetic variation and structure between some populations of ***B. taeniata*** with the 10 most polymorphic microsatellite loci. These microsatellite markers can be used to evaluate population problems such as low diversity and high genetic structure, with the purpose of optimize future conservation strategies for the populations of this species.

CONICYT Doctoral Scholarship 2012 and the National Doctorate Scholarship for operational expenses 21120202

The Agricultural and Livestock Service for the exempt resolution nº:6494/2006, 1470/2009, 3350/2015 Universidad de Concepción, Diuc Semilla Patagonia 205.113.066-1 and CA-099.09

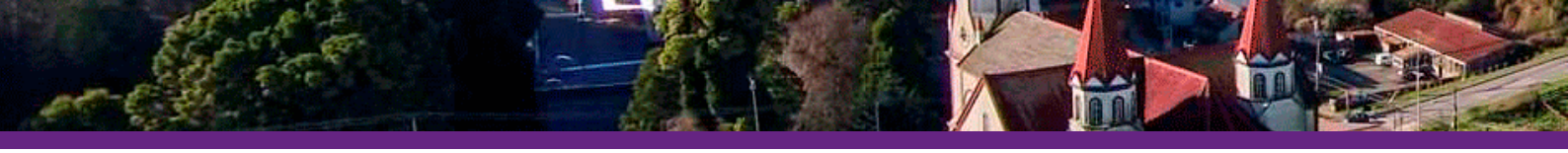


67) Monitoreo Genético de la Rata Negra (Rattus rattus) introducida en Chile

González Francisco[1], Jaksic Fabián M.[2,1], Suárez Catalina[1], Lobos Gabriel[3], Palma R. Eduardo[1]. [1]Departamento de Ecología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile. [2]Center of Applied Ecology & Sustainability, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile. [3]Centro de Gestión Ambiental y Biodiversidad, Facultad de Ciencias Veterinarias y Pecuarias, Universidad de Chile.

La rata negra (***Rattus rattus***) es una especie invasora que ha contribuido directamente a la extinción de varias especies nativas de animales y plantas, siendo además un reservorio de numerosas enfermedades zoonóticas. Estudios genéticos y taxonómicos en su rango nativo identificaron 6 linajes mitocondriales intraespecíficos, con características ecológicas y zoonóticas diferenciadas, sugiriendo planes de erradicación más focalizados. Este trabajo se enfoca en describir los posibles linajes mitocondriales de ***R. rattus*** en Chile, identificar su procedencia, y caracterizar su estructura genética poblacional. Desde muestras colectadas entre las regiones de Coquimbo y Aysén, obtuvimos secuencias parciales de ***Citocromo b*** y ***Región Control***, las que se analizaron mediante métodos filogenéticos y filogeográficos tradicionales. Nuestros resultados revelaron sólo presencia de linaje I de ***R. rattus***, distribuido en 8 haplotipos mitocondriales: un grupo dominante entre Coquimbo y Los Lagos; 4 haplotipos derivados del principal entre BíoBío y Aysén; y 3 haplotipos exclusivos de Coquimbo, Santiago y Los Ríos. El linaje I fue distribuido globalmente desde Europa durante la Era de la Conquista, por lo que ***R. rattus*** probablemente comenzó su invasión en Chile con la llegada de los primeros colonizadores en el siglo XVI. La alta diversidad de haplotipos, y una extensa historia portuaria, sugiere que esta invasión habría sido a través de la XIV región. Aunque la intensa actividad portuaria actual habría facilitado nuevas reintroducciones. El monitoreo genético de especies invasoras entrega una perspectiva histórica sobre su dinámica invasiva, identificando áreas prioritarias de muestreo y conservación, y zonas de alto riesgo de nuevas introducciones.

Proyecto FB-0002-2014 y Proyecto FONDECYT 1170761

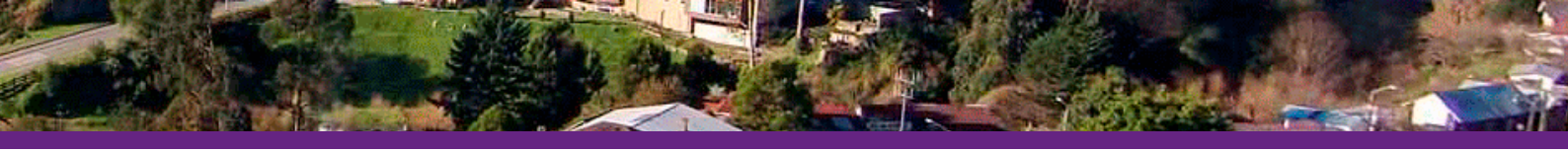


68) Consequences of the Andean Uplift on the historical biogeography of Abrotrichini (Rodentia, Sigmodontinae)

Toledo Macarena Ivette[2], Hernández Cristian E.[2], Palma R. Eduardo[1], Rodriguez-Serrano Enrique[2]. [1]Departamento de Ecología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile. [2]Departamento de Zoología, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción.

Among the high species richness of Neotropical rodents, Abrotrichini is the natural group, above genera level, which the distribution of its species is strongly related to the Andean domain. In this work, we evaluate the consequences of the Andean Uplift on the historical biogeography of this tribe. Then, we also evaluate the consequences of this major geological process on the diversification and morphological disparification of the group. Aiming to these objectives, we construct the most complete database for Abrotrichini including molecular, ecomorphological and distributional data. Our results show that earlier diversification and morphological differentiation events are related to the last pulse of Andean Uplift. Subsequent vicariance and dispersal events explain how the landscape change, owing to the Andean uplift, interacts with the geographic distribution of species richness of the tribe.

Financiamiento: Proyectos Fondecyt 1170486; 1170815; 1170761

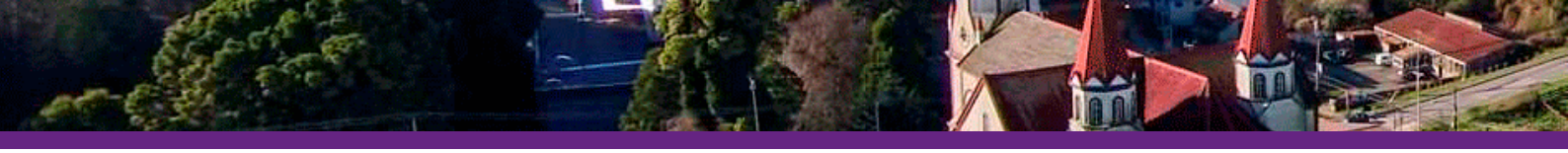


69) Comparing the influence of Andean orogenesis on the diversification patterns of the most diverse Sigmodontinae tribes (Rodentia, Cricetidae).

Vallejos Paulo[1], Castillo-Ravanal Boris[1], Inostroza-Michael Oscar[1], Pino Kateryn[1], Hernández Cristian E.[1], Palma R. Eduardo[2], Rodriguez-Serrano Enrique[1]. [1]Departamento de Zoología, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción. [2]Departamento de Ecología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile.

Considering the great diversity of sigmodontine rodents inhabiting the Neotropics, and their contrasting, and in some cases exclusive, pattern of species richness, this group stands as a relevant ground for testing general hypothesis related to the origin and diversification of Neotropical biota. Specifically, we evaluated several aspects of the influence of Andean orogenesis on the diversification patterns of the three most diverse and geographically contrasting tribes of Sigmodontinae: Oryzomyini with high species richness on the northern and central Andes, the western Amazonia, Guyanas and Cerrado; Akodontini with high species richness on central Andes and Atlantic Forest and; Phyllotini with species richness on central Andes and the Southern Cone. For the analysis we used state depended speciation models and event based biogeographical analysis on a calibrated phylogenetic tree for each tribe - model. Our results show that aspect related to the Andean uplift, and the consequences of this process on the environmental differentiation during the Plio-Pleistocene transition, are key to explain common and idiosyncratic responses of these tribes regarding their fast and geographically defined species accumulation.

Financiamiento: Proyectos Fondecyt 1170486; 1170815; 1170761

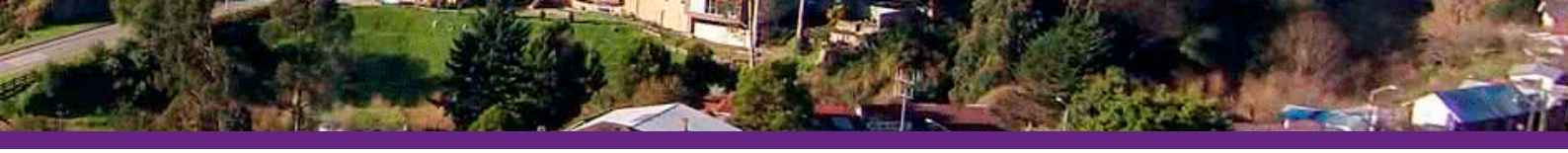


70) Tadpole or froglet? The evolution of development mode in egg-breeding frogs (hemiphractidae)

Armesto Luis Orlando[1], Palma Eduardo[1]. [1]Ecología, Pontificia Universidad Católica de Chile.

Egg-breeding frogs belong to the family Hemiphractidae and they are known to carry eggs on their backs, of which they may hatch in free-living aquatic larvae or froglets (direct development). This family is endemic to the Neotropics, inhabiting forests, Páramo and Puna environments. Although factors driving changes from a basic life cycle to direct development have been investigated, the results have not been clear. Thus, we aim to analyze the evolution of development mode and whether this trait evolved associated with habitat. We used the mitochondrial 16S y ND1 genes to estimate the phylogeny using parsimony and maximum likelihood (ML). We implemented the Pagel´s correlation analysis for detecting correlated evolution between developmental mode and habitat. Parsimony and ML reconstructions suggest that the most recent common ancestor of developmental mode and habitat was a direct-developer and forest, respectively. Free-living aquatic tadpoles evolved from direct-developing ancestors seven times, while clades living in forest colonized páramo habitats evolved five times. An asymmetric model was selected for both traits, showing that reproductive mode is an irreversible trait, while habitat is not. The Pagel´s correlation indicates that development mode and habitat evolved independently of each other. Pond-breeding and direct development species inhabit forest and páramo but they are not sympatric; probably the presence of species with free-living tadpole in a habitat may be explained by the absence of competence. Unlike previous works, we implemented methods and analyzes to evaluate reversibility and coevolution of traits, which allowed us to obtain results and conclusions better supported.

Comisión Nacional de Investigación Científica y Tecnológica (CONICYT)



71) The development of binocular specializations parallels the maturation of visually triggered aversive responses in the Octodon degus

Deichler Alfonso [1], Lopéz-Jury Lucy [1], Dover Rodrigo [2], Mpodozis Jorge[2], Marín Gonzalo[2]. [1]Departamento de Biología, Facultad de Ciencias, Universidad de Chile. [2]Biología, Ciencias, Universidad de Chile.

Eye orientation is a character tightly bounded to the visual ecology in vertebrates. High degrees of frontal binocularity has been widely linked to nocturnality and active visual behaviors such as hunting and eye-hand coordination. However, prey mammalian species, such as rodents, feature a dorsal band of binocular superposition functionally associated to reactive visual responses such as freeze and escape. Previous studies in our lab have demonstrated that this aerial binocular field is conserved among rodents with independence of their visual habits (diurnal, nocturnal or subterranean). Behavioral studies in mice show that escape behavior can be triggered by an overhead looming stimulus that mimics an approaching predator. These responses are classically described as innate behaviors. However the precise course of development of the escape responses in rodents has not been described so far. In ***Octodon degus*** pups (5 to 15 postnatal days) we found that the presentation of an overhead looming stimulus between P-5 and P-9 only triggers freezing, a response that switch toward escape at around P15. We also noted that at early ontogenetic stages the binocular field has not reached the expansion observed in adult degus, indicating that the transformation of aversive responses from freezing to escape run in parallel with the maturation of binocular specializations. Our results reinforce the link between the aerial binocular portions of the visual field and reactive responses triggered by visual stimulation, revealing the strong dependence that exist between the maturation of morphological characters of the visual system and the behavior it orchestrates.

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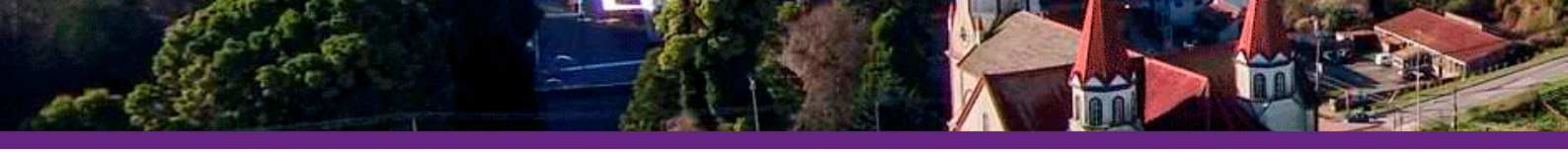

72) RNAmining: a deep learning stand-alone and web server tool for sequences coding prediction and RNA functional assignation

Ramos Thaís[2,1], Silva Cecília[3], Do Rêgo Thaís[3], Maracaja-Coutinho Vinicius[1]. [1]Advanced Center for Chronic Diseases - ACCDiS, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile. [2]Núcleo Multidisciplinar de Bioinformática, Universidade Federal do Rio Grande do Norte. [3]Departamento de Informática, Centro de Informática, Universidade Federal da Paraíba. (Sponsored by Vinicius Maracaja-Coutinho)

Non-coding RNAs (ncRNAs) are important players in the cellular regulation of organisms from different kingdom. Its investigation is routine in every transcriptome/genome project. Two key steps in ncRNAs research are the ability to distinguish coding/non-coding sequences, followed by their functional assignation. Here, we applied 5 machine learning algorithms (Naive Bayes, SMO, IBK, Random Forest and Deep Learning (DL)) in order to select the one (DL) with best performance to be used in a stand-alone tool and web-server for RNA coding potential prediction and functional assignation (RNAmining). Firstly, we evaluated it using randomly selected ncRNA sequences from Rfam and coding genes from RefSeq/NCBI. Then, we used coding/non-coding sequences from four organisms downloaded from Ensembl, and compared them with literature. All ncRNAs were filtered using a maximum-similarity cutoff of 80% (Levenshtein distance); and the coding/non-coding sequences had their tri-nucleotides counts analysed. The DL architecture used for each database was selected based on the Grid-search method, which scan the data to configure optimal parameters for a given model that minimize the validation error function. Tests were performed using Dense, LSTM and Convolutional Neural Network. The bests results were obtained with two convolutional followed by two fully connected layers. All tests were performed using 10-folds cross-validation. Analyses using Rfam database reached 99.3% of accuracy. The bests accuracies for each organism were: 97.82% (A. lyrata); 97.76% (D. melanogaster); 96.3% (E. coli); 94.33% (S. cerevisiae). We are currently integrating functional assignation analyses to RNAmining.

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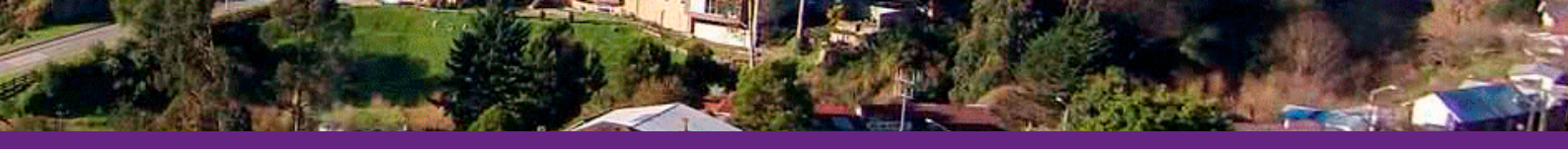

73) LABioinfo.org: an integrated web portal for user-friendly bioinformatics tools and genomic information on organisms of interest in Latin America

Correia Bruno[2,1,3], Ramos Thaís[4,3], Tobar Victor[3], Carrasco Raúl[3], Martínez Jesús[3], Maracaja Vinícius[1,5,3], Initiative LABioinfo[6]. [1]Research Unit, Beagle Bioinformatics. [2]Centro de Informática, Universidade Federal da Paraíba. [3]Advanced Center for Chronic Diseases - ACCDiS, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile. [4]Núcleo Multidisciplinar de Bioinformática, Universidade Federal do Rio Grande do Norte. [5]Research Unit, Instituto Vandique. [6]LABioinfo, Latin America Bioinformatics Initiative. (Sponsored by Vinicius Maracaja-Coutinho)

Latin America (LatAm) harbour over 30% of the world's biodiversity, is a major producer/exporter of important global commodities (e.g. salmon, sugarcane, mining) and is affected by important neglected diseases (e.g. leishmaniasis, malaria, dengue). To date, dozens of important organisms in LatAm has been sequenced and deposited in public databases. However, they are not made available with updated gene predictions/annotations in an integrated repository, as those available for USA (e.g. UCSC Genome Browser) or Europe (e.g. Ensembl). Particularly worrisome is the fact that most of the original publications of these genomes doesn't have authors from the region. This might be result of the absence of an initiative supporting bioinformatics and computational biology in a collaborative effort. Aiming to power-up the local data-driven biology ecosystem, we describe here a web-portal (LABioinfo.org) that integrates different computational solutions developed by LatAm groups; and an integrated database containing genomic information for +70 eukaryotic organisms of importance for local human health, economy and biodiversity protection. For that, we firstly integrated 13 softwares and databases developed by local teams, initially part of our initiative, in an user-friendly environment. These tools democratize transcriptomics, systems biology and non-coding RNAs analyses. Additionally, we implemented a Genome Browser containing gene predictions and functional annotations from +70 organisms of interest for the region. Our perspectives are to integrate more locally-developed tools, standardized coding/non-coding gene predictions for integrated genomes and novel organisms. We also hope to invite novel collaborators to be part of this initiative.

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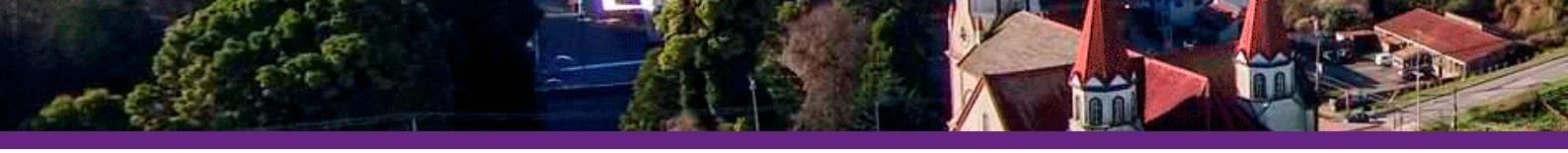

74) Tumor Mutation Burden and its important role in overall survival in LUAD

Oróstica Karen[1], Olivera-Nappa Alvaro[2]. [1] Departamento de Ingeniería Química y Biotecnología, Facultad de Ciencias Físicas y Matemáticas, Universidad de Chile. [2]Departamento de Ingeniería Química y Biotecnología, Facultad de Ciencias Físicas y Matemáticas, Universidad de Chile.

With the arrival of Next Generation Sequencing (NGS) new therapeutic strategies in cancer have been developed, based on the study of the genomic alterations present in tumour cells, which could have an important predictive value of the clinical response. Recently it has been proposed that the number of somatic mutations also known as Mutation Burden Tumor (TMB) reflects the problems of DNA repair and it could be associated with the response to treatments in different cancers. We reviewed data on 230 patients with LUAD and we calculated a TMB for a list of 52 actionable genes in cancer and genes that are mutated in at least 20% of patients. Then we analyzed the TMB for overall survival for both gene list using the Kaplan Meier method. We applied bi-clustering with heatmap function to all patient with the TMB for each gene list and then we compared the results. The males and patients over 60 years obtained a significant difference in survival with a P value of 0.034 and 0.02 respectively. The clustering obtained shows the interesting divide, an important cluster of patients has an only one mutated gene, Kras. Thus, our findings support to the idea of the important role of TMB in overall survival in LUAD but are necessary more research to continue to study the relationships between TMB and survival in LUAD and others cancers.

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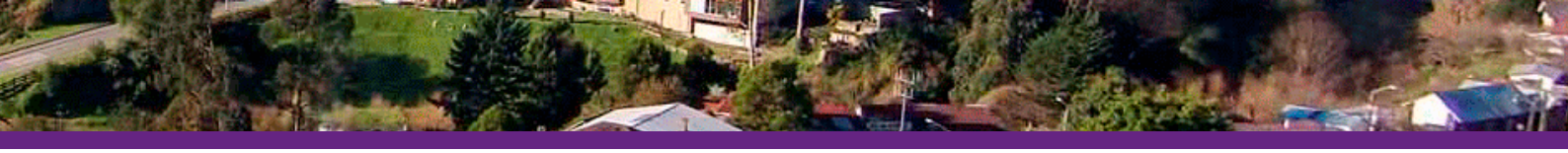
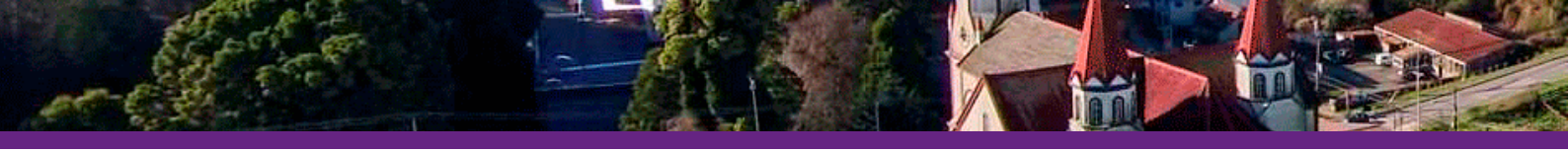


75) Use of a plasma focus device to induce DNA damage and cell death in a colorectal cancer cell line

Andaur Rodrigo [1], Jain Jalaj[2], Moreno José[2], Soto Leopoldo[2], Armisen Ricardo[3], Marcelain Katherine[4]. [1]Oncología básico-clínica, Facultad de Medicina, Universidad de Chile. [2]Center for Research and Applications in Plasma Physics and Pulsed Power, Comisión Chilena de Energía Nuclear, Santiago, Chile. [3]Departamento de Oncología Básico-clínica. Centro de Investigación y Tratamiento del Cáncer, Facultad de Medicina, Universidad de Chile, Centro de Investigación y Tratamiento del Cáncer. [4]Departamento de Oncología Básico-Clínica. Centro de Investigación y Tratamiento del Cáncer,, Facultad de Medicina, Universidad de Chile.

DNA double strand breaks (DSBs) are the most lethal form of ionizing radiations (IR) -induced DNA damage. In this sense, the effects of high doses of IR (> 1 Gy) are well known. However, although low doses of IR (0.2 to 0.6 Gy), can also induce DSB and cell death, the underlying mechanism of damage is not well understood. In this work, we aimed to study DNA damage and cell death using a plasma focus (PF) device, which delivers low doses of high energy pulsed X-rays and neutrons. Human colorectal cancer cells (DLD-1) were exposed to pulsed X-rays or neutrons from a PF device and to a continuous source of Xrays (0.6 – 12Gy), as controls. After irradiation, DNA damage and cell death were evaluated. We found that pulsed Xrays (0.12 Gy) induced a significant increase in DNA damage (~5 DSB/nuclei) and cell death (~10 %). Importantly, these results were similar to those induced using doses 5-fold higher of continuous Xrays (0.6 Gy). On the other hand, preliminary results indicate that exposure of DLD-1 cells to very low doses of neutrons (3.5 µGy) induced cell death, although DNA damage did not seems to be induced. These results suggest that the effect of IR on DNA damage is depending on the source of radiation and that pulsed x-rays and neutrons from a PF device are more effective on inducing cell death than continuous x-rays.

This work was supported by grant Anillo ACT172101 PIA Program, CONICYT and Fondecyt grant 1151435.



76) Partial trisomy 5 arisen from two small supernumerary marker chromosomes

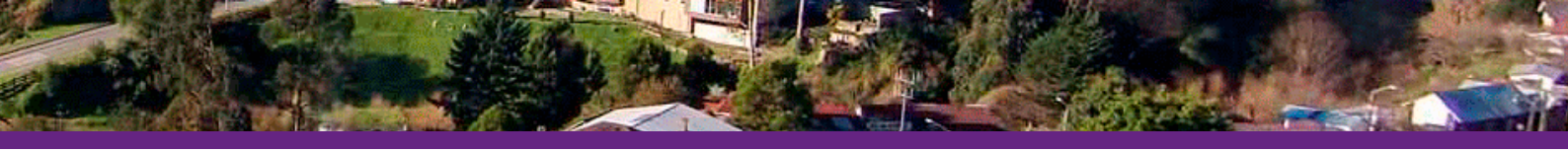
Curotto Bianca[1], Santa María Lorena [2], Martin Luz María[2], Faúndes Víctor[2], Morales Paulina[2], Peña Angela[2]. [1]Laboratorio Citogenética Molecular, INTA, INTA U. de Chile. [2]Laboratorio de Citogenética - Molecular, INTA, Universidad de Chile.

Introduction:
The phenotypes associated with an small supernumerary marker chromosome (sSMC) are highly variable, and depend on the chromosome, involved region and the percentage of mosaicism, if present. sSMC of almost all chromosomes have been described, including chromosome 5. However, we present the first case with two sSMCs derived from this chromosome.

Patient and Method:
A 2-years-and-4-months-old boy with dysmorphic features and moderate developmental delay was studied by conventional karyotyping and chromosomal microarray (CMA, 60K ISCA platform, Agilent). Results: G- and NOR-banding revealed mosaicism for 2 different sSMCs: one ring-shaped (mar1) and another analphoid without satellites (mar2). The CMA detected a pericentromeric chromosome 5p12q11.2 duplication, and an interstitial chromosome 5q13.2q14.1 duplication.

Discussion:
Although further structural characterisation is needed, mar1 may correspond to the pericentromeric chromosome 5 duplication and mar2 may correspond to the interstitial chromosome 5q duplication. The classical and molecular cytogenetic techniques allowed identifying the chromosomal origin in this patient and correlating his clinical features with these findings.

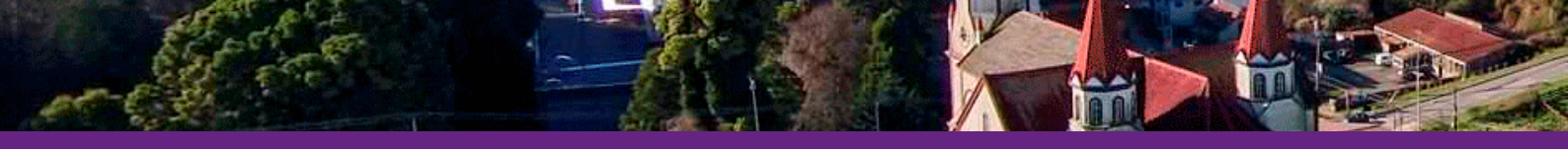
Propios del laboratorio de Citogenética- molecular. Instituto de Nutrición y de los alimentos. INTA Universidad de Chile.



77) Effect of social isolation during the development on the viability of *drosophila melanogaster*

Arriagada Jairo[1], Álvarez Eduardo[1], **Del Pino Francisco Rodrigo[1]**, Godoy-Herrera Raúl[1]. [1]Programa de Genética Humana, Medicina, Universidad de Chile.

In this research, we seek to know the effect of social isolation during development on the viability of ***D. melanogaster***. To this end, an isomaternal line of the Canton - S strain was constructed, making brother - sister crossing for 6 generations in order to have genetically homogeneous individuals. Thus, we can attribute to social relationships the differences in viability observed in socially isolated individuals with respect to individuals raised in the company of others. In acrylic capsules of 4 cm in diameter filled half with Burdick medium, a single egg was deposited from the indicated isomaternal line, in other similar capsules 30 eggs of the same indicated line were deposited, both types of capsules were left at 24 degrees Celsius. When following the larval development of individuals reared alone and accompanied, it was observed that only 27% of the isolated larvae managed to reach the state of pupa due to the contamination of fungi in the breeding site, instead 60% of the larvae reared in groups they reached pupation, not observing the presence of fungal contamination in these breeding media. Our results show that a social aspect such as the aggregation of larvae in ***D. melanogaster*** is very important to control fungal contamination of the breeding environment, critically affecting the survival of individuals in their vital environments. Finally, we want to emphasize that the social interactions during the development of ***D. melanogaster*** increases the ability to survive in the breeding sites.



78) Identification of genes that mediate the effects of genetic by early-life nutritional interaction on negative geotaxis behavior of *Drosophila melanogaster*

Candia Noemi [1], Nuñez Franco[1], Olivares Gonzalo[1], Verdugo Ricardo[2], Vega Franco[1], Olguin Patricio[1]. [1]Programa de Genética Humana, ICBM, Biomedical Neuroscience Institute (BNI), Departamento de Neurociencia, Medicina, Universidad de Chile. [2]Programa de Genética Humana, ICBM, Departamento de Oncología Básico-Clínico, Medicina, Universidad de Chile. (Sponsored by Patricio Olguin Aguilera)

Complex behaviors of animals are highly sensitive to environmental conditions. Nutritional restriction during development produces defects in the growth of the organism and behavioral alterations such as negative geotaxis. However, how prenatal nutritional restriction alters the behavior variation of the adult organism is unknown. To answer this question we used: i) a subset of isogenic lines from the ***Drosophila*** Genetic Reference Panel (DGRP), which captures the genetic variation of a natural population; and ii) an outbreed advanced intercross population (AIP) which was generated by round robin cross design of 40 DGRP lines. Larvae were raised under prenatal restriction and then their locomotor activity was evaluated by means of a negative geotaxis or climbing assay. Our results indicate that genetic by early life nutrition interaction contributes significantly to the phenotypic variance of this trait. In addition, they show that the effects of interaction are dependent on sex. Through genome-wide association studies (GWAS) and extreme quantitative trait loci (xQTL) analysis, we identified candidate genes associated with the sensitivity of negative geotaxis to early life nutrition. This work hopes to contribute to the understanding of the cellular and molecular mechanisms that mediate prenatal genetic-nutritional interaction in adult behavior.

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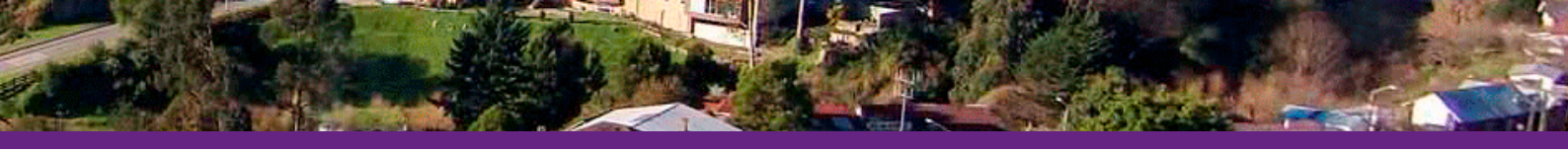

79) Identifying genetic networks influenced by nutritional conditions during early – life and their impact on sleep architecture of Drosophila melanogaster.

Núñez Franco[1], Olivares Gonzalo[1], Vega-Macaya Franco[1], Candia Noemi[1], Zuñiga Nolberto[1], Verdugo Ricardo[2], Olguín Patricio[1]. [1]Programa de Genética Humana, ICBM,Biomedical Neuroscience Institute(BNI), Departamento de Neurociencia., Medicina, Universidad de Chile. [2]Programa de Genética Humana, Departamento de Oncología Básico-Clínico., Medicina, Universidad de Chile. (Sponsored by Patricio Olguín)

Sleep is a behavioral state widely conserved throughout the animal kingdom, which is characterized by inactivity and highly variable patterns inter- and intra-species. These patterns vary in multiple characteristics including total sleep time, latency, sleep quality and daytime drowsiness, among others. In humans, it is known that high variability of these characteristics in an individual are hallmarks of sleep disorders and mental illness. The association between nutrition and its influence on sleep has been investigated in both vertebrates and invertebrates. Studies in ***Drosophila*** have shown that starvation leads to a suppression of sleep, however, the relationship between early-life nutrition and sleep traits variation has not been studied. To address this, we used the ***Drosophila*** Genetic Reference Panel (DGRP), a collection of 205 sequenced isogenic lines that represent the genetic variation of a natural population, allowing the association between genetic variants and sleep traits using genome-wide association studies (GWAS). Larvae of 40 different lines were grown on normal and nutritional restriction (NR) and sleep-related traits were characterized. We identified genes that are associated with the sensitivity of sleep traits to early-life nutrition by performing GWAS. Then we infer gene networks underlying genetic by early-life nutrition interaction on sleep patterns. Finally, we validated the contribution of these genes on sleep traits by using RNAi knockdown and/or P-element hypomorphic mutants. Our work shed light on the mechanisms that underlie genetic-by-early life nutrition interactions on sleep traits.

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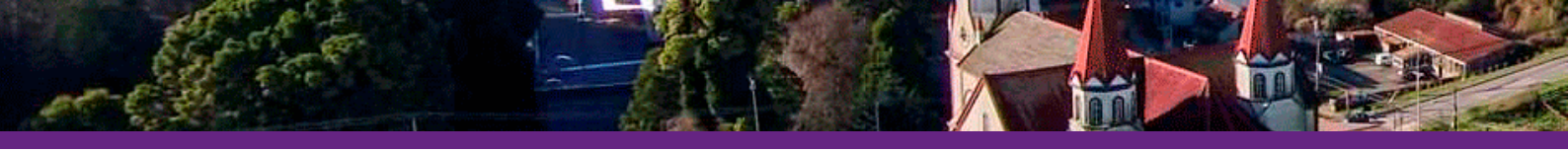

80) Uncovering the genetic basis of phenotypic heterogeneity in Parkinson's disease

Escobedo Tamara Patricia[1], Olivares Gonzalo H. [2], Candia Noemi[2], Núñez Franco[2], Olguín Patricio[2], Klein Andrés D.[1]. [1]Centro de Genética y Genómica, Facultad de Medicina, Universidad del Desarrollo. [2]Programa de Genética Humana, ICBM, BNI, Department of Neuroscience, Facultad de Medicina, Universidad de Chile.

Parkinson's disease (PD) is a progressive neurodegenerative disorder with a heterogeneous genetic etiology and a worldwide incidence of 8 to 18 patients/100,000 inhabitants. About 90% of cases are idiopathic, presumably due to genetic-by-environmental interaction (***GxE***). Accordingly, PD patients show a wide range of symptoms that vary in their penetrance and expressivity, these include motor and sleep defects, and reduced life expectancy. However, there are no studies with the aim of discovering the genetic basis of this variation. Here we use the natural genetic variation of the ***Drosophila*** genetic reference panel (DGRP), and a validated model of idiopathic PD in flies to uncover the gene networks underlying phenotypic heterogeneity in PD. The DGRP is a collection of 205 sequenced isogenic lines representing the genetic variation of a natural population. Thus, SNPs and variants found in the DGRP can be associated with the phenotypic variation using GWA studies. Idiopathic PD was induced by feeding adult male flies with 250 µM of Rotenone for 7 days. Our findings show that DGRP lines present variation in locomotor behavior and life expectancy in response to Rotenone. Broad-sense heritability (***H2***) and ***GxE*** interaction coefficient (***i2***), indicate a significant contribution of genetic and ***GxE*** in phenotypic variation. Finally, GWAS revealed new candidate genes underlying phenotypic variation of PD-like symptoms in flies. Validation of candidate genes and comparative analyzes using human genomic data will lead us to the discovery of personalized therapies to treat idiopathic PD

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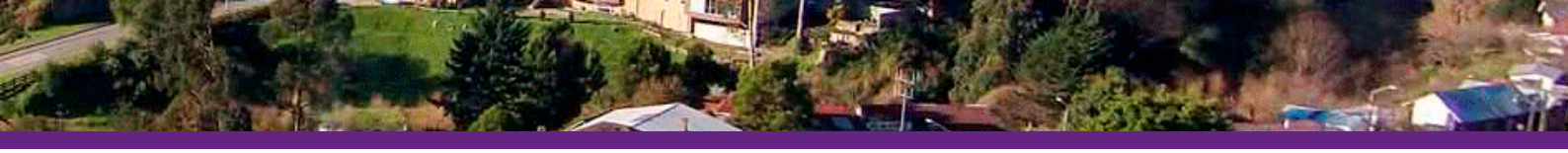
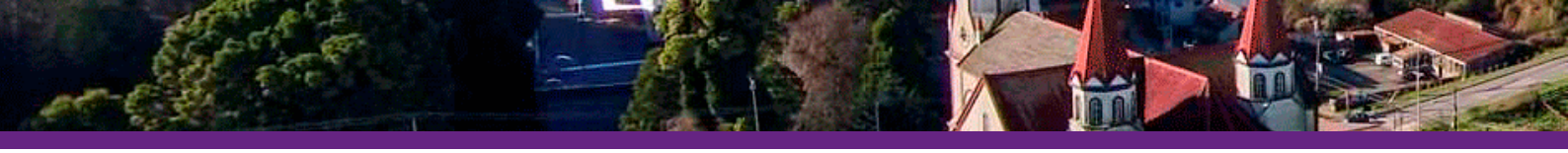
*Corresponding authors: **patricioolguin@med.uchile.cl**, **andresklein@udd.cl**



81) Optimization of a panel of microsatellite markers for maqui (Aristotelia chilensis (Mol.) Stuntz) genotypes traceability

Cona Matías[2], Castro María Herminia[2], Correa Francisco[1], Bastías Adriana[1], Sagredo Boris[1], Hinrichsen Patricio [2], [1]Biotecnología y Genética, INIA Rayentué, [2]Plant Genetics & Biotech, INIA, LA PLATINA

Aristotelia chilensis [Molina] Stuntz, better known as maqui, is a dioecius tree native to Chile and South of Argentina. These little blackberry-like fruits have been historically used as a source of food, dye and medicine. In last years, many studies have reported its high content in antioxidants, including anthocyanins and other polyphenols, even higher than other highly consumed berries such as blueberry (*Vaccinium sp*.). Currently, little is known about maqui genetics although there is some information describing genetic diversity of the species based on AFLP and microsatellite (SSR) markers, these later recently described. Based on these markers, the species appears as not having well defined populations. To asses an effective genetic differentiation protocol for maqui genotypes, we developed a new set of SSR markers. Firstly, primers were obtained by High-throughput sequencing (HTS) of genomic DNA. Secondly, we filtered through 28,575 SSRs of di, tri, tetra, penta, hepta and octanucleotide by amplicon size range of 130-280 bp; we also selected the largest motif repetitions. Thirdly, a total of 69 SSRs were obtained and subjected to screening for good amplification. We achieved a set of 13 SSRs giving highly polymorphic profiles in 60 individuals belonging to three populations from different geographical regions in Chile. Our results suggest that it is possible to efficiently differentiate between many genotypes of maqui. As an example of the usefulness of these markers, we were able to determine the fingerprinting for a set of lines of productive interest.

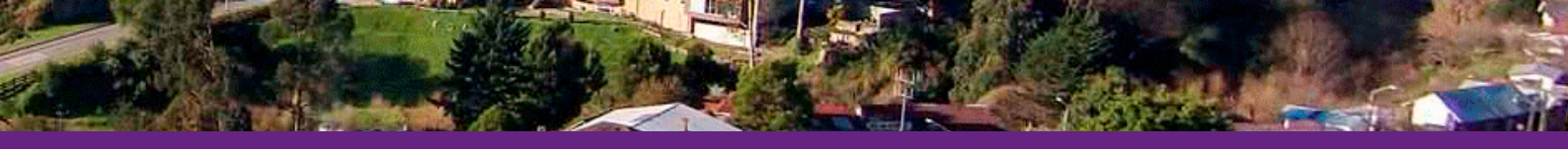


82) Gastric Cancer's Polygenic Risk Score calculated with genetics variants described in other populations is not related with Mapuche Ancestry in the Chilean population

Retamales Rocío Mariana[1], Tobar Calfucoy Eduardo[1], Yáñez Lara Cristian[1], Gonzalez Hormazábal Patricio[1], Verdugo Ricardo A.[1,2]. [1]Programa de Genética Humana, Facultad de Medicina, Universidad de Chile. [2]Departamento de Oncología Básico-Clínico, Facultad de Medicina, Universidad de Chile.

Introduction: Chile has a high Gastric Cancer's (GC) mortality rate (MR) compared to other Latin American countries and the rest of the world. Within Chile, MR is highest in the south, suggesting a relation with Mapuche ancestry. However, association between risk's alleles frequency for loci associated with GC and Mapuche ancestry hasn't been tested. In addition, non-genetic factors may give rise to similar geographic patterns of MR. Here, we used research resources generated by the ChileGenomico Project to formally test association between genetic risk for GC and Amerindian ancestry in the Chilean population. Methods: DNA samples from 2068 participants of ChileGenomico were selected to represent 30 communes of Chile. The ChileGenomico panel of Ancestry Informative Makers (AIMs) was complemented with SNPs reported to be associated with GC in the literature. Risk SNPs were selected by p value < 3E8 and Odd Ratio > 1.2. Genotyping of 150 Ancestry Informative Makers and 18 GC's SNPs was performed by the GT-seq protocol. A polygenic risk score for GC per individual was calculated by adding the published OR for each allele of the individual in log-scale. Association was assessed by linear regressions between global Amerindian and Mapuche ancestry and the polygenic risk score per individual. Results: 20 SNPs were selected, but only 18 assays passed quality control after sequencing. There wasn't significant association between Amerindian or Mapuche Ancestry and the polygenic risk score. **Conclusion:** Published SNPs associated with risk of GC do not account for population-level associations between Mapuche ancestry and GC mortality.

FONDEF grants D10I1007 and D10E1007, Conicyt scholarship 21160297.



83) Genetic Structure of the Rural Populations of the Upper Course of the Aconcagua River through Ancestry Informative SNPs

Orellana Michael[1], Moreno Andrés[2], Verdugo Ricardo[3], Véliz David[4], Moraga Mauricio[1,5]. [1]Laboratorio de Genética de Poblaciones y Evolución Humana, ICBM, Facultad de Medicina, Universidad de Chile. [2]Laboratorio Nacional de Genómica para la Biodiversidad, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional. [3]Laboratorio de Genética de Sistemas y Genómica Biomédica, ICBM, Facultad de Medicina, Universidad de Chile. [4]Departamento de Ciencias Ecológicas, Facultad de Ciencias, Universidad de Chile. [5]Departamento de Antropología, Facultad de Ciencias Sociales, Universidad de Chile.

Recent archaeological surveys in the Upper Course of the Aconcagua River suggest that since the Early Potter Period there are two culturally differentiated areas: the Putaendo valley and the Los Andes valley. Along with this, the geographical characteristics of the Aconcagua Valley, specifically the Aconcagua River, is presented as a possible geographic barrier that would influence the flow of people. In this study, the existence of genetic differences between the Upper Course populations of the Aconcagua river was evaluated given the cultural differences and the presence of the river as an important geographic barrier. 40 individuals from the Putaendo Valley, 28 individuals from the Santa María Valley and 45 individuals from the Los Andes Valley were genotyped for 148 ancestry informative SNPs. The ancestry results show that the three populations present on average proportions of the European (~ 54%), African (~ 6%), northern (~ 13%) and southern indigenous (~ 27%) ancestral components very similar. PCA shows that the valleys form a single cluster. The DA-1 of the DAPC shows a subtle difference between the valley of Putaendo and the rest of the valleys. The values of Fst between the populations are very low, although it shows concordance with the DAPC. The results suggest a low signal of genetic differentiation among the populations studied, although this may have been influenced by the process of miscegenation during European colonization or the number of markers and/or the potency of these to distinguish said differentiation.

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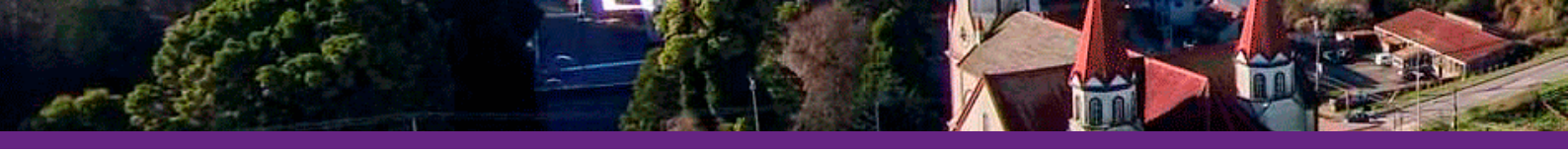
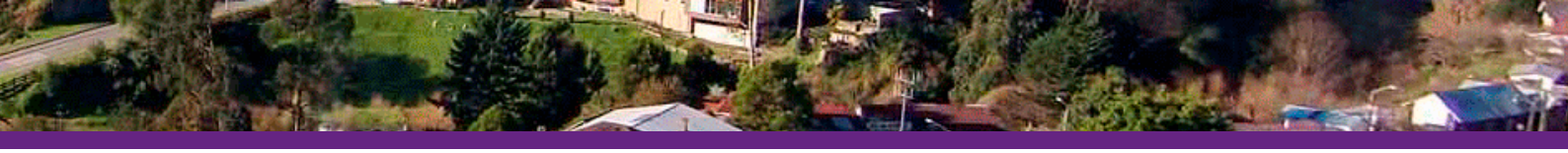


84) Genetic linkage and association analysis to identify genetic risk markers of gallstone disease and gallbladder cancer in Chile

Báez Benavides Pablo [1,2], Boekstegers Felix[3], Barahona Ponce Carol[3], Fischer Christine[4], Lorenzo Bermejo Justo[3], Marcelain Katherine[1]. [1]Department of Basic and Clinical Oncology, Medical Faculty, University of Chile. [2]Center for Medical Informatics and Telemedicine, Biomedical Neuroscience Institute, University of Chile. [3]Institute of Medical Biometry and Informatics, Statistical Genetics Group, University of Heidelberg. [4]Institute of Human Genetics, University of Heidelberg.

The role of a genetic risk factor for gallbladder cancer (GBC) and gallstone disease (GSD) (the main GBC risk factor) is supported on the association between ancestry and GSD/GBC prevalence, and the familial clustering observed in both diseases. Nevertheless, current knowledge about the genetic triggers of these pathologies is sparse. Our main goal was to identify genetic variants associated with GSD and GBC with familial clustering, and with the risk of sporadic GBC, through a three-step analysis: (1) genetic linkage analysis in families with GBC clustering; (2) search for candidate genes through an integrative functional annotation analysis; and (3) fine-mapping by genetic association based on cases and population controls. A total of 2,193 individuals were analyzed: 48 individuals (six GBC cases, 15 cholecystectomized, 27 unaffected) belonging to 7 families, 183 sporadic GBC patients and 1,962 controls. Two candidate linkage regions were identified: Chr9: 105016960-115983216 and Chr16: 105444-5995388, which harbored 128 coding genes: 95 on chromosome 9 and 33 on chromosome 16. By functional annotation, the list was reduced to 30 genes potentially relevant for the disease etiopathogenesis. Candidate gene association analysis revealed two variants associated with sporadic GBC risk: ***ABCA1*** rs363717 (OR = 1.84 95% CI 1.26-2.66) and ***SEC14L5*** rs1558562 (OR = 2.02 95% CI 1.4-2.95). These results suggest that both GBC and GSD with familial clustering, as well as sporadic GBC susceptibility in Chile, are associated at least in part with ***ABCA1*** and ***SEC14L5*** genetic variants.

FONDEF IT16I10051 (KM), FONDECYT 1151435 (KM), BMBF 01DN15021 (JLB) and BNI-ICM P09-015-F.

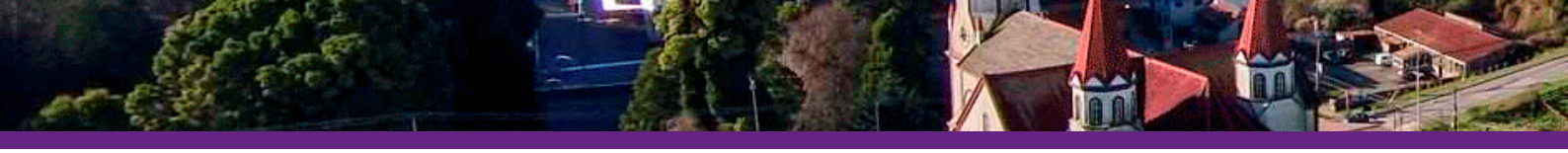


85) Identification of a miR-1245a-rs60611793 and its relation with early-diagnosis and high-gradebreast cancer susceptibility

Jara Lilian Elena[1], De Mayo Tomas[2], Morales Sebastian[3]. [1]Instituto de Ciencias Biomédicas, Medicina, Universidad De Chile. [2]Genética y Genomica, Facultad de Medicina, Universidad del Desarrollo. [3]Programa de Genética Humana, Facultad de Medicina, Universidad de Chile.

Breast cancer (BC) is one of the most frequent cancers affecting women worldwide. In Chile, BC has the highest mortality rate among cancers (15.69/100,000 women). Recent evidence supports a role for microRNAs (miRNAs) in BC development and progression. Single-nucleotide polymorphisms (SNPs) are the most common type of variation in the human genome. SNPs in miRNA genes can alter expression, maturation, or target binding affinity, thus contributing to the development of cancer. Studies have documented that SNPs in miRNA(s) targeting ***BRCA1/2*** genes alter ***BRCA*** gene expression levels. miR-1245a targets the ***BRCA2*** gene. Sequencing pre-miR-1245a in 107 ***BRCA1/2***-negative BC probands from high-risk families resulted in the identification of rs60611793, which corresponds to a 1-bp deletion. This variant was detected in an early-onset (diagnosis at 30 years of age), triple-negative (TN) BC case without a family history of BC. Given the clinicopathological features of the patient carrying the deletion, we used Sanger sequencing to screen for rs60611793 in another 181 early-onset and TN BC cases and 192 healthy individuals. The deletion was detected in another four BC cases and 3 of 192 controls. The five cases with the deletion had early-onset BC. However, there was no correlation between rs60611793 and histological BC type. Two of the five cases were poorly-differentiated ductal carcinomas, one was a medullar carcinoma, one was an ***in-situ*** carcinoma, and the histopathological report for the fifth case was unavailable. Therefore, this deletion could be related to the development of early-onset BC and high-grade malignant neoplasms, with no predominant ER/PR/Her2/Neu status.

Grant Sponsor: Fondo Nacional de Desarrollo Científico y Tecnológico (FONDECYT). Grant Number: 1150117

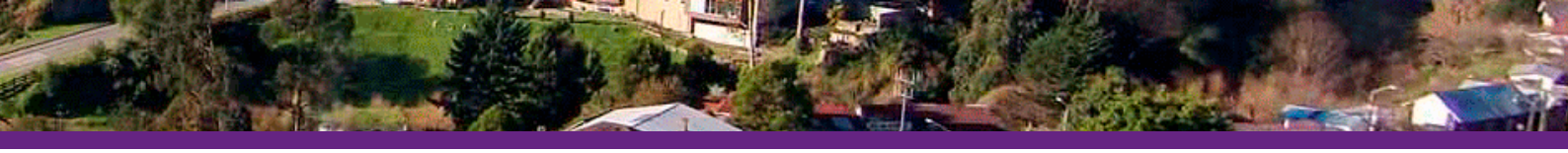


86) A National Registry of Patients with Inheritable Connective Tissue Disorders to identify genetic modifiers of clinical severity through Whole Exome Sequencing

Jimenez Yanireth[1], Cruz-Fernandes Leonor[1], Lay-Son Guillermo[1], Repetto Gabriela[1], **Calderon Juan Francisco[1]**. [1]Centro de Genética y Genómica, Medicina, Universidad del Dessarrollo.

Inheritable Connective Tissue Disorders (ICTDs) are those caused by mutations in genes that encode for proteins of the Extracellular Matrix (ECM). ICTDs affect patients since birth and their symptoms are present in the musculoskeletal system, skin, eye and respiratory system. The most life-threatening feature of these diseases is the enlargement and rupture of big vessels, most prominently, the aorta. These diseases include Marfan Syndrome, Loeys-Dietz Syndrome, Ehlers-Danlos Syndrome type IV, among others. They are all caused by mutations in genes that code for different effectors of the Transforming Growth Factor beta (TGFβ) signaling pathway, including ECM components that play active roles in the regulation of this pathway. Hypothesis: The wide range of phenotypic severity in ICTDs patients is likely caused by unknown genetic variants that modify the ECM-TGFβ signaling equilibrium beyond the effect of the pathogenic mutation. We aimed to collect a number of Chilean patients with ICTDs (n=200) in a database that encompasses every relevant clinical aspect in order to identify these genetic modifiers of clinical severity. Results: We have created a Chilean Registry of ICTDs as a platform for understanding the effect of genetic modifiers in the clinical course of ICTDs. This online database thoroughly integrates clinical information in a patient-centered structure, but also holds Whole Exome Sequencing (WES) data. This will enable us to generate relevant genotype-phenotype correlations for the diseases studied and will allow us to interrogate molecular mechanisms behind this variation through in vitro techniques and translate these findings into improved treatment of patients.

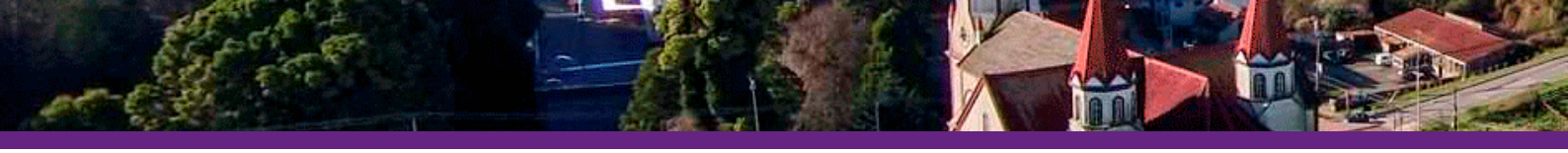
This project is funded by Fondecyt Initation Grant N°11170353



87) Glut-1 Deficiency Syndrome: A Case Report

Castillo Valentina Andrea[1], Zavala Maria Jesus[1], Castillo Silvia[1]. [1]Genética, Medicina, Universidad de Chile.

The glucose transporter type 1 deficiency syndrome (GLUT-1 SD) is a rare metabolic disorder, approximately 500 cases have been reported worldwide since the disorder was first identified in 1991. It is caused by mutations in the SLC2A1 gene that encodes for glucose transporter protein type 1 (GLUT1). The GLUT1 protein is embedded in the outer cell membrane, where it transports glucose into cells. This syndrome is classically characterized by drug resistant seizures, global developmental delay, encephalopathy, ataxia, hypotonia, microcephaly and hypoglycorrhachia. We present the case of a ten year old boy who was diagnosed with Epilepsy, Global developmetal delay and Ataxic Syndrome. The electroencephalogram showed epileptiform activity and the Magnetic Nuclear Resonance, metabolic study and laboratory profile were all normal. He received treatment with Benzodiacepines with mild response. Due to the severe clinical presentation molecular study was requested and a pathogenic variant in SLC2A1 gene was found (c.177del p.(Thr60Argfs*18)). The gold standard treatment for this syndrome is cetogenic diet which is highly effective, achieving an adequate control of Epilepsy in 80% of the patients.



88) Familial Mediterranean fever: A diagnosis to keep in mind

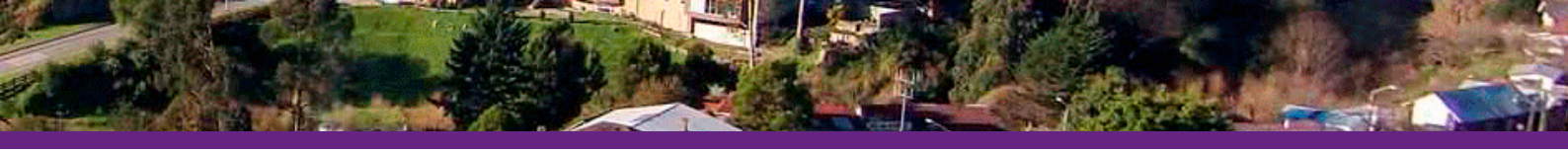
González María Isabel[1], Castillo Taucher Silvia[1]. [1]Genética , Medicina, Universidad de Chile.

Familial Mediterranean Fever is a chronic inflammatory disease of predominantly autosomal recessive inheritance, produced by mutations in the MEFV gene that is found on the short arm of chromosome 16, characterized by recurrent episodes of fever accompanied by peritonitis, pleuritis, arthritis or erysipelas-like erythema. An episode lasts on average 3 days, and its frequency is very variable.This disease is more frequent among Mediterranean populations (Jews from North Africa (non Ashkenazi), Armenians, Turks and Arabs). However, in recent years more cases have been reported in countries not related to this area.

There are no formal studies of epidemiology in Chile.

We present the case of 1 patient of Egyptian / Jewish ancestry, and the case of a family of German ancestry, all Chileans with semiology and characteristic evolution of familial Mediterranean fever and heterozygous positive molecular study.

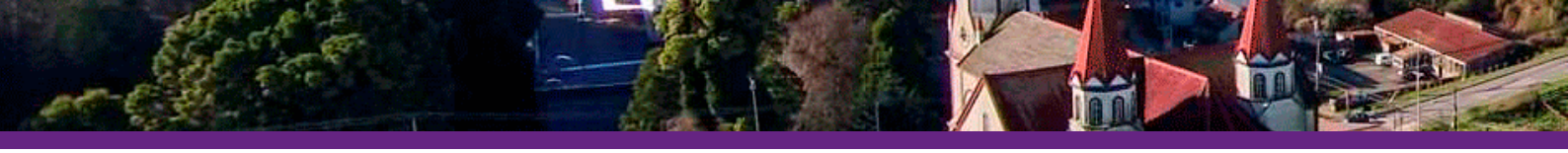
The lack of diagnosis in non-Mediterranean countries may be due to the lack of awareness of this disease. In Chile there are more cases given by migrations and their offspring, so it is very important to have it as a probable diagnosis in case of pain and fever of unknown origin.On the other hand, the familial Mediterranean fever is mainly of autosomal recessive inheritance, but dominant variants have been described. Both cases described in this work present the variant in which the disease manifests itself in its heterozygous form, generating an autosomal dominant inheritance, which would increase the number of affected individuals in the population.



89) A new case of Knobloch Syndrome in Chile

Huserman Jonathan[1], Nakousi Nicole[1], Castillo Silvia[1]. [1]Genética , Medicina, Universidad de Chile.

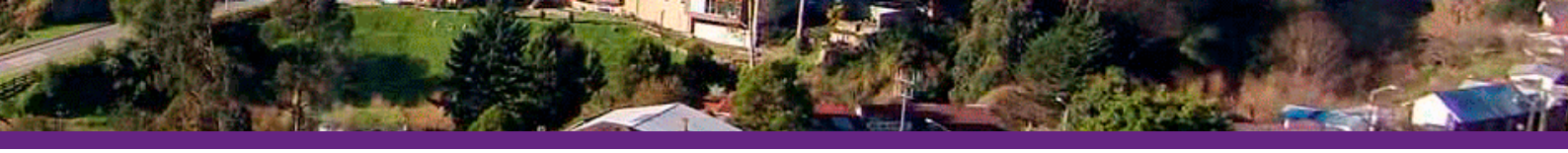
Knobloch Syndrome is a rare autosomal recessive hereditary disease. It is characterized by vitreoretinal degeneration, high myopia, retinal detachment, and encephalocele in variable degree associated with occipital skull abnormalities. Eye abnormalities can lead to unilateral or bilateral blindness at young age. The phenotype is highly variable, and can include neural, lymphatic or renal system affectation. Clinical case reports present mutations in the collagen XVIII-coding gene ***COL1A2***, mapped in chromosome 21q22.3. The protein product has three isoforms that are part of the basal membrane, and help to regulate proliferation and apoptosis, vital processes for structural maintenance of multiple tissues. 106 cases and 21 different mutations have been described since the first case report in 1972. Our patient is a new case of Knobloch Syndrome; the second daughter of a young, healthy consanguineous couple who was diagnosed with Stickler syndrome at 2 months old due to high myopia and facial dysmorphism. During follow-up, a round flat occipital depressible lesion was detected, and studied with imaging. Whole exome sequencing detects a probably pathogenic variant in homocygosis in the ***COL18A1*** gene. We present the first case report of Knobloch syndrome in Chile, together with a review of previous cases found in the literature.



90) Mutations in PPA2 gene as a cause of Sudden Unexpected Cardiac Arrest in a Chilean family

Nakousi Nicole[1], Castillo Silvia[3,2]. [1]Genética, Postgrado, Universidad de Chile. [2]Genética Clínica, Hospital Clínico Universidad de Chile. [3]Genética Clínica, Clínica Alemana.

Sudden unexpected death in infancy (SUDI) is one of the most important causes of post-neonatal deaths in the developed world. One in five cases carries potentially damaging mutations in genes associated with cardiomyopathy, or coding for ion channels. While mitochondrial fatty acid oxidation disorders may also present as SUDI, monogenic causes are rare. One of these involves the nucleus-contained PPA2 gene, where loss of function mutations in both alleles causes deficiency of the mitochondrial inorganic pyrophosphatase PPA2, leading to mitochondrial dysfunction and sudden cardiac arrest. We report the case of a family with two victims of SUDI. The parents, both healthy and non-related, have a healthy daughter from their first pregnancy. Their two following children, both males, died from cardiac arrest following an episode of vomit at ages 2 and 1 year, respectively. The oldest son presented myocarditis, left ventricular hypertrophy and inflammatory infiltrate in the anatomopathological study. The youngest boy and his parents were studied with whole exome and mitochondrial genome sequencing, which detected two heterozygous variants in gene PPA2. The presence of the c.894C>A p.(Ser298Arg) variant from the mother –of unknown significance- and the pathogenic c.514G>A p.(Glu172Lys) variant from the father behaved as compound heterozygous mutation in their son. This is the first case of a family with SUDI caused by PPA2 mutations reported in a Chilean family, and the first description of the variant p.(Ser298Arg) as a potentially damaging variant in the literature



91) Array Comparative Genomic Hybridisation (aCGH) study in 420 Chilean patients with neurodevelopmental disorders or congenital anomalies.

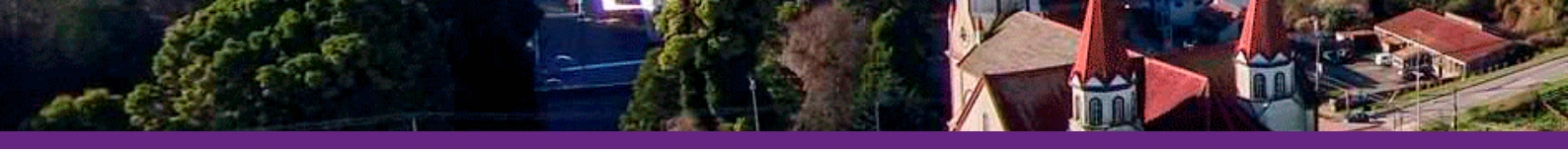
Santa María Lorena[1], Faundes Víctor[1], Morales Paulina[1], Curotto Bianca[1], Vilches Matías[1], Alliende María Angélica[1]. [1]Laboratorio de Citogenetica Molecular, INTA-Universidad de Chile.

Background:
Neurodevelopmental disorders (NDD) and congenital anomalies (CA) are conditions that begin and manifest since the infancy, that include psychomotor developmental delay, intellectual disability, autism spectrum disorder and dysmorphias in some cases. Up to 20% of NDD/CA are caused by genomic imbalance detectable only by aCGH.

Aim:
To analyse the results detected by aCGH in Chilean population with NDD/CA.

Methods:
Retrospective study that considered features such as sex, age, clinical diagnosis and molecular findings from all of the aCGH reports and in some cases parent studies, performed at INTA laboratory of Molecular Cytogenetics from 2013 to 2018.

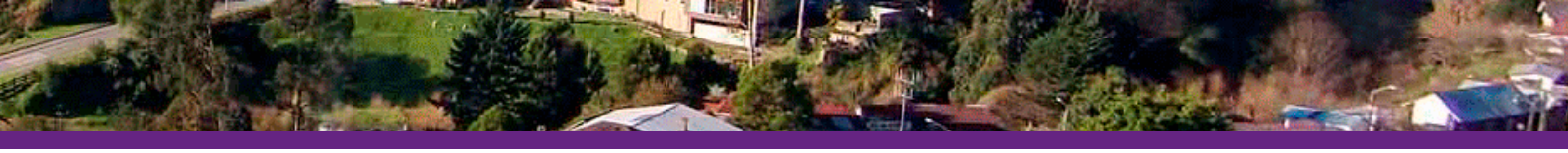
Results:
A total of 420 report were analysed. The median age studied was 5,4 years (range 2-9 y.o.) and 240 (57%) of them were masculine sex. Pathogenic (PV) or probably pathogenic variants (VLP) were found in 80 (19%) of cases, mainly deletions; of them 74 (92%) corresponded to interstitials microdeletions/ microduplications in different chromosomes and 6 (8%) involved sub-telomeric regions. **Conclusions:** The diagnostic yield and findings of aCGH in Chilean population are similar to those reported in international studies. Therefore, aCGH is a valid diagnostic tool in the Chilean population that allow an opportune therapeutic intervention, give prognostics and determine recurrence risk to affected family.



92) Polymorphic variant of the β2-adrenoreceptor gene (ADRB2) related to hypertension in Valdivia

Toloza-Villalobos Jessica [1], Caro Nataly[2], Gutiérrez María Luisa[2]. [1]Instituto de Ciencias Ambientales y Evolutivas, Facultad de Ciencias, Universidad Austral de Chile. [2]Técnología Médica, Facultad de Salud, Universidad Santo Tomás.

In this study we have investigate the distribution of frecuencies of ADRB2 allelic variants (Arg16Gly, Gln27Glu, Thr164Ile) in Valdivian population as well as the influence of SNPs as a risk factor for hypertension developmen. The study included 100 volunteers who were measured blood pressure and blood biochemistry (cholesterol, triglycerides, glycemia). The genetic analysis included a study of informative SNPs for our population, haplotype diversity, allelic and genotypic frequencies. The blood biochemistry analyzes were carried out in an ERBA equipment of the Santo Tomás University and the sequencing was carried out by the Macrogen. The analysis of the allelic sequences was carried out using the Geneious program and statistical analysis with the STATISTICA program. Our results show a relationship between the variables studied and essential hypertension. ANOVA test showed a significant effect of triglycerides on systolic pressure, which is explained by a predominance of volunteers with hypothyroidism and/or insulin resistance pathologies. The genetic analysis for ADRB2 showed allelic diversity with 16 haplotypes and only one informative SNPs for hypertension, which corresponds to the substitution of Arginine by Glycine in codon 16, which burned the vasodilatory effects of the adrenoreceptor-β2. The allelic frequencies for this codon were Guanine 0.478 and Arginine 0.521 what resembles frequencies in Latin American populations, but differs from those described in Asian or European studies.



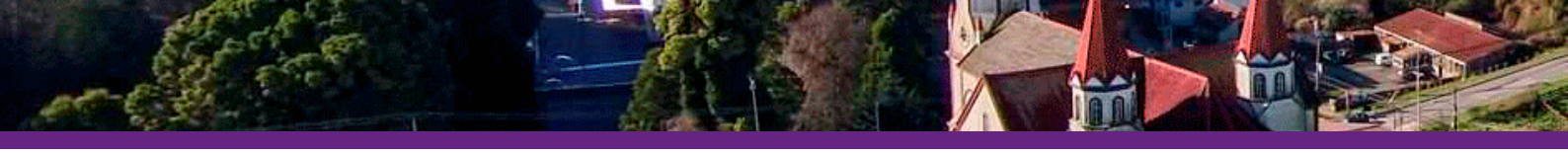
93) 3D meiotic cell division: an learning experience with augmented reality

Palma-Rojas Claudio Hernán[1], López- Cortés Francisco[1], Ibacache Camilo[1]. [1]Biología, Ciencias, Universidad de La Serena.

The aim of this work is to diversify the available resources, both for education and learning purposes of the meiotic cell division, which is a central content for genetics and cell biology courses.
Traditionally, to teach this process two-dimensional representations are in use (2D) that, in its own nature, have some explanatory limitations especially about the spatial disposition of the chromosomes.
For this reason, we developed an application with augmented reality of this process, since this technology offers an enriched environment of visualization that, in combination with other resources (texts, photographies, animations and videos) will allow the students in agreement to their interests and learning times , to raise and to answer their questions referred to the meiotic process, favoring the autonomous learning.

This application was designed for smartphones and tablets with the Android software for being this most used. In parallel with the previous thing, the targets were designed to make the visualization possible of the application and a work guide which includes a brief description of the stages of this process, including a questionnaire of auto evaluation.

Laboratorio de investigación e Innovación Tecnológica para la Educación en Ciencias (LIITEC-ULS) "MINEDUC-ULS 1795" y Departamento de Biología y Facultad de Ciencias, Universidad de La Serena



94) 3'UTR regulatory variants could contribute to the phenotypic variability of Niemann-Pick type C disease

Martínez Jose Rodrigo Waldemar[1], Klein Andrés[1], Rebolledo Boris[1]. [1]Centro de Genética y Genómica, Facultad de Medicina, Clínica Alemana, Universidad del Desarrollo. (Sponsored by Boris Rebolledo Jaramillo)

Niemann-Pick type C (NPC) is a rare and progressive disease characterized by premature death, disabling neurological manifestations and overall highly heterogeneous presentation, which makes it prone to underdiagnosis. A clinical report of monozygotic twins with NPC and extensive phenotypic heterogeneity was presented recently, and it suggested that the phenotypic variability could be explained by post-zygotic genetic variation. We are interested in the genetic determinants of NPC clinical variability. So, the aim of our study was to identify genetic variants that could contribute to the phenotypic heterogeneity observed in the twins. We analyzed the twin's whole exome sequencing data with a naïve approach first: variants were called with the GATK, FreeBayes, and Samtools pipelines, and considered as true those variants called by at least two pipelines. Then, we used VariantMetaCaller, a tool that uses Support Vector Machines to combine information provided by each pipeline to estimate a variant probability. Six variants, located at ZNF717 (Chr 3:75781272; C>A), ATG3 (Chr 3:112253058; C>CA), LOC101927157 (Chr 4:47916346; C>G) and in the 3'UTR of UGT2B15 (Chr 4:69512595; C>A), KIF13B (Chr 8:28927901; A>T) and SLC7A6 (Chr 16:68335537; T>C) were identified. miRNAs binding site disruption by 3'UTR variants was confirmed by TargetScan (**http://www.targetscan.org/vert_72/**), suggesting that gene expression regulation could be affected by these variants In conclusion, we identified six variants that could explain the phenotypic heterogeneity in NPC. Next steps include Sanger sequencing validation of the variants, and functional analyses to determine the contribution of the variants to the phenotype of NPC.

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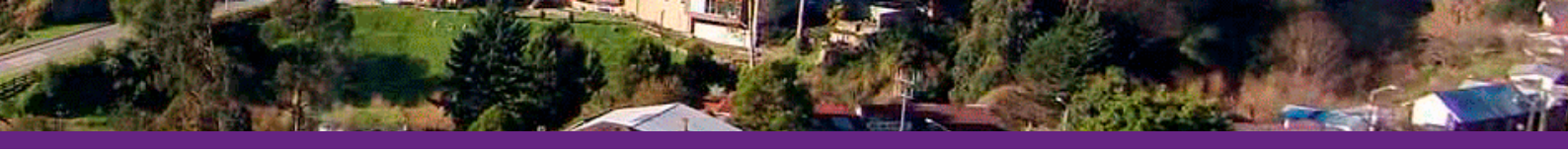

95) TumorSec: Design and optimization of a targeted-gene sequencing assay to improve the accuracy of oncological therapies.

Maureira Ignacio Andrés[1], Toro Jessica[1], Villaman Camilo[1,2], Salvo Mauricio[3,4], Verdugo Ricardo[5,1], Barajas Olga[1], Ahumada Mónica[1], Marcelain Katherine[1]. [1]Departamento de Oncología Básico clínico, Facultad de Medicina, Universidad de Chile. [2]Laboratorio ChileGenómico, Programa de Genética Humana, ICBM, Facultad de Medicina, Universidad de Chile. [3]Madison, Wisconsin, Roche Madison. [4]Roche Madison, Madison, Wisconsin, USA. [5]Laboratorio ChileGenómico, Programa de Genética Humana, Facultad de Medicina, Universidad de Chile.

Cancer represents the second cause of death in our country. In the recent years, the massification of next-generation sequencing technologies (NGS) has allow the advancement in the identification of somatic mutations responsible for promoting or driving cancer progression. These alterations have become the target for specific therapies. In this study, we designed a custom panel for targeted-gene sequencing by NGS. This panel (called TumorSec), allows the identification of mutations in 25 genes, which are predictors of response to specific therapies in solid tumors. Once the target regions were identified, an ***in silico*** analysis was done to compare three comercial alternatives for library preparation, two of them amplicon-based (Ampliseq Thermo and Ampliseq Illumina) and one capture hybridization system ("SeqCap EZ Custom target", Roche). ***In silico*** results show that coverage of the SeqCapEZ system was higher (99.77%) than the one for the Ampliseq platforms (89.3% and 80.7%, for Thermo and Illumina, respectively). Thus, SeqCapEZ system was chosen to perform a piloy study. Libraries were prepared using 6 samples of DNA extracted from frozen or formalin-fixed tumors. Technical replicates were included. Libraries were run in an Illumina MiSeq sequencer. Our preliminary data shows a 100% of coverage of the targeted regions, with >99% of reads with 100X deep. Even regions uncovered in the design, were patially covered in the assay. This data indicates that the SeqCapEZ system is appropriate to design and perform our custom-designed panel for identification of mutations that are predictive of the response to targeted-therapies in solid tumors.

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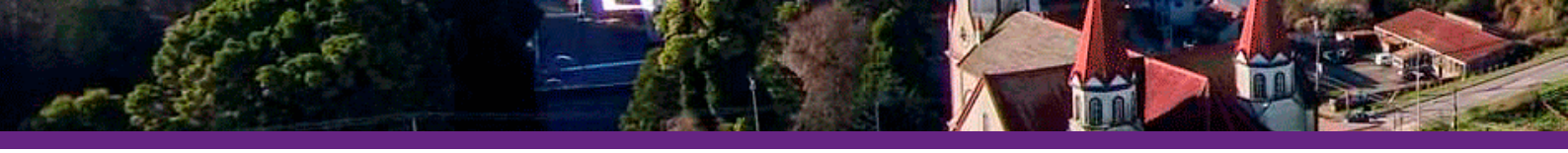


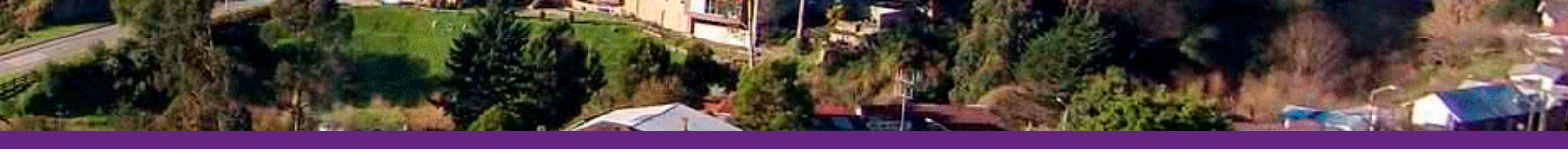
96) Mitochondrial genome contribution to the 22Q deletion syndrome variability

Rebolledo-Jaramillo Boris[1], Repetto Gabriela[1]. [1]Centro de Genética y Genómica, Facultad de Medicina Clínica Alemana, Universidad del Desarrollo.

Chr22q11.2 deletion syndrome (22q11DS) is one of the most frequent pathogenic rearrangements in humans (1 in 4000), and it accounts for ~2% of cases of congenital heart disease (CHD). The syndrome shows marked variable expressivity not associated with deletion size or parental origin, suggesting the presence of modifiers elsewhere in the genome.

We are interested in the genetic determinants of the presence/absence of CHD. There are six nuclear-encoded mitochondrial genes within the deletion region. Proper mitochondrial function is required for the morphogenesis of several structures including the heart, however, no study has evaluated the contribution of the mitochondrial genome variability to the 22qdel syndrome.
Using bioinformatics, we analyzed whole exome sequencing data from 54 patients with the deletion: 21 cases of CHD and 33 controls. We compared predicted deleterious single-nucleotide variants (rdSNVs), defined as missense variants where at least two of six predictors: SIFT, PolyPhen-2, MutationTaster, MutationAsessor, FATHMM and CADD, predicted damaging impact, but found no differences among cases and controls in terms of the mutational load. However, compared to randomly selected genes, nuclear-encoded mitochondrial genes had fewer rdSNVs (observed 8 SNV per individual, expected 22, p-value = 0.001), pointing to functional constraints of the mitochondrial network in 22qdel patients overall.
We also conducted a weighted combination of burden and SKAT test genome-wide and found 58 genes with p-value<0.05. Among those, two genes corresponded to nuclear encoded mitochondrial genes: COQ7 and NSUN4, but their role in CHD has yet to be elucidated.

Funding: FONDECYT 1130392, 1171014 and 3170280. Acknowledgments: FONDEQUIP EQM150093.

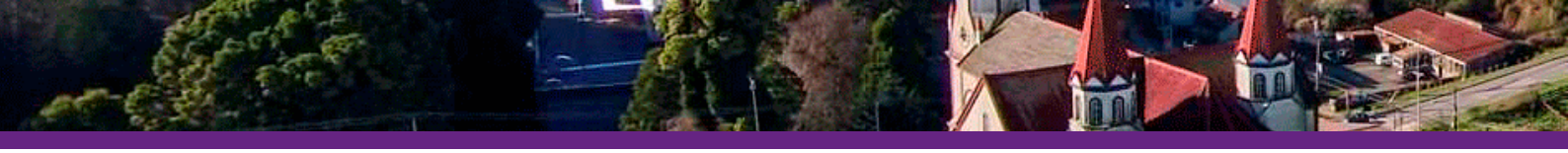


97) Primate genome analysis reveals two possible independent origins for trichromatic color vision in catarrhines

Toloza-Villalobos Jessica [1], Opazo Juan C.[1]. [1]Instituto de Ciencias Ambientales y Evolutivas, Facultad de Ciencias, Universidad Austral de Chile.

Primates are unique among mammals in having a substantial diversity in the type of vision they possess. Catarrhine primates, the group that includes apes and Old World monkeys, are characterized by possessing routine trichromacy, as they have the short, medium and long wavelength sensitive opsin genes. It has been proposed that routine trichromacy was originated by a single gene duplication event in the last common ancestor of the group. An alternative hypothesis postulates that routine trichromacy originated in the common ancestor of anthropoid primates; however, in New World monkeys the medium wavelength sensitive opsin gene would have been removed from their genome. The aim of this study is to unravel the history of duplication of the X-linked opsin genes, in order to understand the origin of routine trichromacy in catarrhine primates. Our results do not match with any of the proposed hypotheses, and show that routine trichromacy in apes and Old World monkeys originated independently in the last common ancestors of each group, and not in the last common ancestor of catarrhines or anthropoid primates as previously thought. Our data provide evidence that in both groups, descendent copies of the same ancestral gene may have been independently neofunctionalized to originate the same phenotype in both lineages.

Funding Fondecyt 3180679

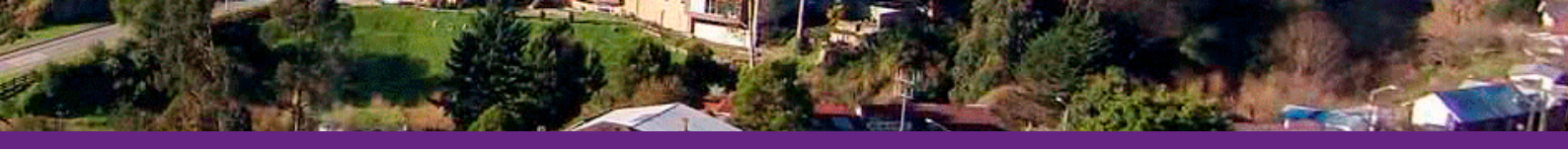


98) A mouse genetics strategy for identifying new therapeutic targets for lysosomal storage diseases

Durán Anyelo Alberto[1], Yáñez María José [2], Escobedo Tamara[3], Zanlungo Silvana [2], Klein Andrés D.[3]. [1]Doctorado en Ciencias e Innovación en Medicina, Universidad del Desarrollo. [2]Departamento de Gastroenterología, Pontificia Universidad Católica de Chile. [3]Centro de Genética y Genómica, Universidad del Desarrollo.

Lysosomal storage disorders (LSDs) include ~70 disorders due to deficiency of lysosomal proteins. Although there are treatments available for some LSDs, they have limited clinical benefits.. Therefore, innovative strategies for increasing enzyme activities are required.. Inbred mouse strains are great mapping tools; their genomes and transcriptomes are available. Our long-term goal is to identify putative modifier genes using the activity of lysosomal enzymes as a trait for genome-wide association studies (GWAS). We will determine the activity of several enzymes, including glucocerebrosidase (GBA; the enzyme mutated in Gaucher disease), hexosaminidase A/B (Tay-Sachs/Sandhoff disease) and a-galactosidase (a-gal; Fabry disease), in a collection of mouse tissues. Since the transcriptomes of inbred strains are known, we will check for potential correlations between the enzymatic activities and the mRNA levels of the recently identified genes. The best modifier candidates will be tested in patient-derived fibroblasts with missense mutations. As a proof of principle, in this research we performed a GWAS using the hepatic a-gal activities of 22 strains, which were published in Cell 1975;6(3):371-8, leading to the identification of a collection of putative modifier genes. Among them are ***Pde3b*** (p=3.9E-6) and ***Purg*** (p=3.9E-6). The correlations between the mRNA levels of these genes and a-gal activity are p=0.05 and p=0.03 respectively. Currently we are setting the conditions to determine the activity of GBA in mouse livers.. We expect that this strategy will allow us to identify modifier genes of several lysosomal enzymes which may help us to design novel strategies for diseases with lysosomal dysfunction.

This work is funded by Fondecyt grant N 1180337.

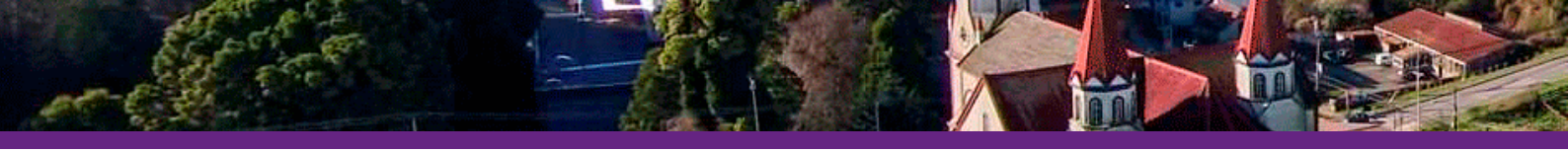


99) Productive response in adult zebrafish families to the inclusion of soybean meal in the diet and its effect on the intestine.

Leal Ricardo[1], Muñoz Sebastián [2], Lam Natalia[3], Feijoo Carmen Gloria[4], Araneda Cristian [5], Hernandez Adrián[6], Dantagnan Patricio[6], Ulloa Pilar [8,7]. [1]Agronomía, Medicina Veterinaria y Agronomía, Universidad de Las Américas . [2]Biotecnología, Facultad de Ciencias, Universidad Mayor. [3]Producción Animal, Facultad de Agronomía, Universidad de Chile. [4]Biología, Facultad de Ciencias Biológicas, Universidad Andrés Bello. [5]Producción Animal, Agronomía, Universidad de Chile. [6]Acuicultura, Escuela de acuicultura, Universidad Católica de Temuco. [7]Produccion Animal , Facultad de Agronomia, Universidad de Chile. [8]Escuela de Agronomía, Medicina Veterinaria y Agronomía, Universidad de Las Américas.

The intestinal inflammation is a multifactorial condition triggered by different insults, such allergens/ irritants present in the diet. In the case of cultured fish, and also in zebrafishsoybean meal (SBM) induces intestinal inflammation affecting both, fish health and growth. Promisingly, have been reported contrasting impacts on growth (negative vs. unaltered effect) in the same fish species, even when exposed to the same SBM% in feed. This suggests that there is a genetic variability underling the more tolerant fish to SBM diet, favoring growth. With the selection of SBM-tolerant fish could identify the genes and corresponding SNPs that confer intestinal tolerance to a SBM diet through RNA-seq. Initial analyse was performed in zebrafish. Two set population with the same genetic background and from 21 families were generated. One set of families was fed with a control diet (100FM) and the other set of family was fed with soybean meal diet (50SBM). Productive parameters of zebrafish fed with 100FM diet showed higher values than fish fed with 50SBM (weight gain, SGR). Individuals from the 5 % in both tails of the normal distribution from a population fed 50SBM were selected (50 mg vs 180mg). The degree of intestinal inflammation in selected fish was measured by qPCR through key marker genes (i.e. il-17a/ f1, il17a/f3, il-10, il-22) which allow establishing relationships between the degree of inflammation and growth phenotype. Individuals with different inflammatory conditions will be selected for future RNA-seq analysis to determinate the genetic variability.

Fondecyt de iniciacion 11170847

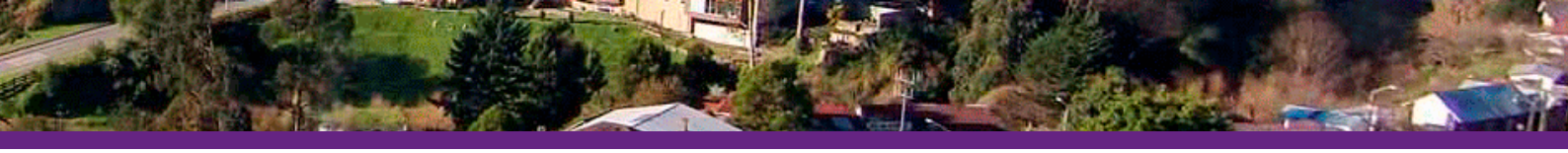


100) Characterization of the role of atlastin and its genetic modifiers in the neuromuscular junction and motor axons of adults Drosophila melanogaster

Ibacache Andres Patricio[1]. [1]Neurociencias - Genética Humana, Medicina, Universidad de Chile.

The hereditary spastic paraplegias (HSPs) correspond to a group of neurodegenerative disorders that generate weakness and spasticity of the lower limbs, as a result of degeneration of corticospinal motor neurons. Mutations in ***atlastin-1*** give rise to 10% of cases of early onset of this disease. How altered function of ***atlastin (atl)*** in neurons results in these defects has not been elucidated. In ***Drosophila*** knockdown of ***atl*** in larval motor neurons causes motor defects, however, an adult model allowing the study of degenerative processes associated to ***atl*** has not been developed. We have characterized the effects associated to ***atl*** knockdown in adult motorneurons and identified genomic regions that modify dominantly this phenotype. We hypothesize that locomotor defect is caused by neural and muscular degeneration, which are modified by ***atl*** genetic interactors. Here, we studied the degenerative process by analyzing the morphology of motor axons, neuromuscular junction (NMJ) and muscles of adult fly limbs with reduced expression of ***atl*** in motorneurons. Our results indicate that ***atl*** knockdown results in progressive defects of motor axons, NMJ and leg muscles. These phenotypes are modified dominantly by the genomic deficiencies, which enhance or revert the locomotor defects. Finally, we identified the ***homologous to sly-1 (slh)*** as a potential genetic modifier of ***atlastin***, whose decreased expression resulted in neuronal morphological defects. The identification of new genetic modifiers of ***atl*** in motorneurons will allow the design of new therapeutic strategies to treat the degenerative process associated to HSP.

This work was supported by ICM P09015F



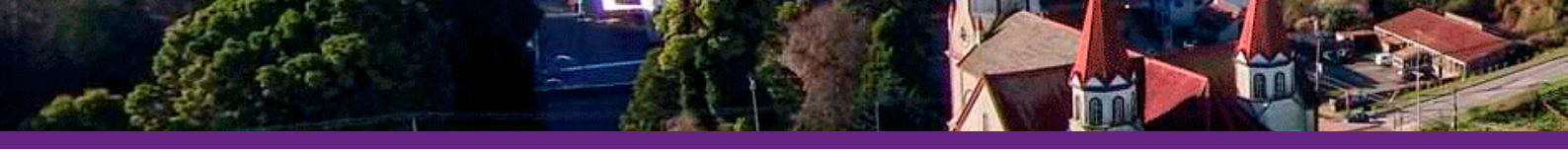
SESIÓN PANELES III

1)Expression of Irisin in rainbow trout (Oncorhynchus mykiss)

Espinoza Carlos Agustin[1], Aedo Jorge[1], Fuentes Marcia[1], Olivares German[2], Molina Alfredo[1], Valdés Juan Antonio[1]. [1]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias de la Vida, Universidad Andrés Bello. [2]Piscicultura de Rio Blanco, Escuela de Ciencias del Mar, Pontificia Universidad Católica de Valparaíso.

Irisin is a novel protein that in mammals has been widely studied, because of its potential use as a treatment for obesity and diabetes mellitus. However, the studies on teleost are limited. Irisin is the key mediator of the browning of white adipose tissue and that in teleost may be playing other roles as a regulator of different biological processes like muscular atrophy and cardiac physiology. With these reports, it might be possible that irisin is having more functions on other organs but they have not been studied. The localization of irisin and its expression profile is the first step to start to elucidate on wich organs and tissues could be having a function. In this work, we determined the profile expression of irisin through the evaluation of *fndc5*, and its localization on distincts organs and tissues in rainbow trout. Kidney, head kidney, liver, brain, gill, heart, intestine, spleen and skeletal muscle from juvenile rainbow trouts were sampled. RNA and proteins were extracted; RT-qPCR analysis was performed to evaluate transcript levels of *fndc5*, and Western Blot was carried to determine irisin location. Our results show that Irisin protein is present in spleen, intestine, heart, head kidney and skeletal muscle. Complementary, *fndc5* expression, preliminary results suggest that it is being expressed in brain, intestine, liver, spleen, gill, heart and skeletal muscle. This results may be indicating that irisin in rainbow trout could be contributing to different biological processes.

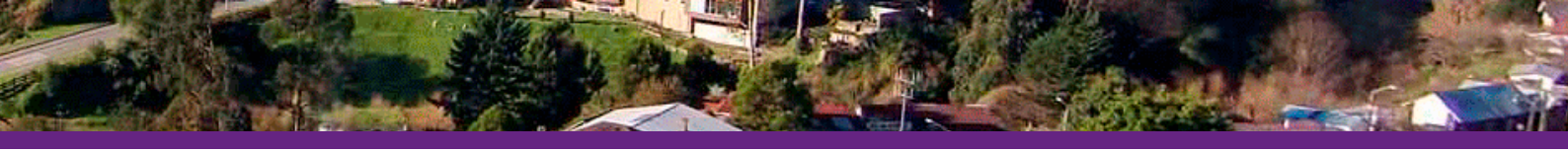
FONDAP 15110027, FONDECYT 1171307, and FONDECYT 1171318



2) Where does the initiation of the second wave of hematopoiesis take place in the human embryo?

Pereda Jaime Sixto[1], Valencia Bárbara[1]. [1]Escuela de Medicina, Ciencias Médicas, Universidad de Santiago de Chile.

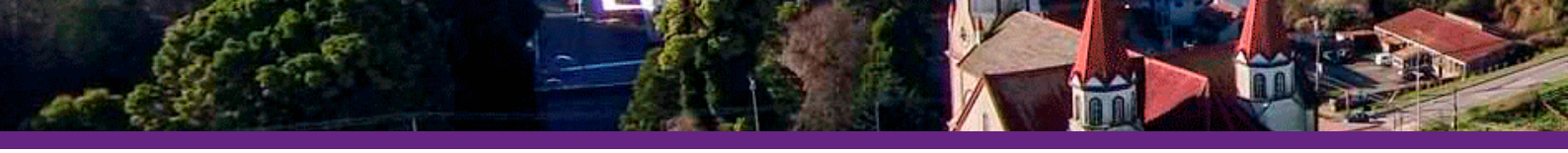
Embryonic hematopoiesis occurs in two generational waves. During the first wave primitive erythroblasts (PEs) and macrophages are generated. In the second wave mature definitive erythrocytes are produced. In the mouse, these two waves are initiated in the yolk sac (YS). In humans, the origin of the second wave remains unknown. In our work we give morphological evidence showing that the second wave occurs within the embryo. Six normal human embryos including their YS were study (aged 4, 5, and 6-week post fertilization [pf]), by light and scanning electron microscopy. The specimens were selected from the Embryo-fetal collection of the Universidad de Santiago, Chile. PEs were the only blood cells present at week 4 pf in embryo circulation. At the end of week 5 pf, a considerably increase in the number of PEs was seen in the embryo's circulation and in the liver. At the end of week 6, pf changes in the liver's structural organization were seen, indicating the beginning of hepatic hematopoiesis. Our results show that the second hematopoietic wave is produced not in the YS but within the embryo's body, because the vitelline stalk, the only link between the YS and the embryo, degenerates, preventing the transfer of blood cells toward the embryo at the end of week 5 pf. The second wave coincides with the generation of non-nucleated erythrocytes in the YS and their phagocytosis by the epithelial cells of the stomach. Iron generated in this degradative process may trigger the beginning of the second hematopoietic wave.



3) Brain size macroecological patterns of Marsupials

Espinoza Nicolas Andres[1], Rivera Reinaldo[1], Inostroza-Michael Oscar[1], Palma Eduardo[2], Rodriguez-Serrano Enrique [1], Hernández Cristián E.[1]. [1]Departamento de Zoología, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción. [2]Departamento de Ecología, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile.

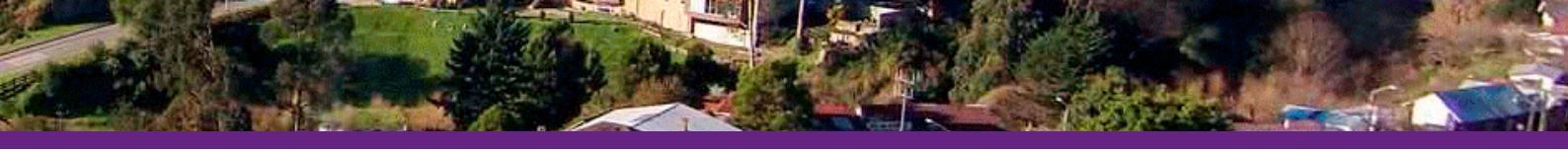
The brain is a metabolically expensive organ, consuming a disproportionately large amount of energy. Actually, the large amount of energy necessary for the development of big brains-assigned indirectly cost (Expensive-Tissue Hypothesis) or by increasing energy intake directly (Expensive Brain Hypothesis)- is also accompanied by higher parental investment for their development (Developmental Cost Hypothesis). These phenomena, result in significant costs for large-brained species, suggests a differential cost-benefit effect of brain sizes that could determine its current geographical distribution. Consequently, the environmental productivity will be the main driver of the current brain size distribution. To evaluate this hypothesis, based on the geographic distributions of marsupials and its brain sizes, we use spatial regression approaches (i.e. GAM + RAC) and AIC procedure to compare the effect of environmental variables over encephalization index (EQ) using three models: 1.- All environmental variables, including not energetic ones; 2.- Only significant variables (reduced model); and 3.- Only productivity variables (i.e energy model). The greater EQ values were observed in the American continent and not in the Asia-Oceania area, a pattern opposite to the richness distribution. The reduced model was selected, which include only environmental variables associated with water and energy and explain the 75% of the EQ spatial variability. These results sustain that the EQ spatial distribution of Marsupials is explained by the Energy-Water hypothesis, suggesting that the brain size is highly depending on water availability, and that only the energy availability is not enough to maintain the brainy marsupials.
FONDECYT 1170815, 1170486, 117076. R. Rivera were supported by a CONICYT Doctoral Fellowship (21160866) and Doctoral Fellowship from the Dirección de Postgrado of the Universidad de Concepción.



4) Alpha–LINOLENIC ACID DECREASES THE MYOGENIC DIFFERENTIATION OF C2C12 CELLS.

Gómez Gonzalo Ignacio[1], Avendaño Beatriz[1], Ortiz Fernando[1], Puebla Carlos[1]. [1]Instituto de Ciencias Biomédicas, Facultad de Ciencias de la Salud, Universidad Autónoma de Chile. (Sponsored by Fernando Ortiz)

Skeletal muscle is the largest organ in the human body. It has been reported that proinflammatory cytokines can inhibit myogenic differentiation. Inflammation is a complex process in which it has recently been related to disorders in intercellular communication through the pannexins channels (Panx-Chs). Linoleic acid (**Ω**-6, LA) and alfa-linolenic acid (**Ω**-3, ALA) are two types of polyunsaturated fatty acids (PUFAs). Recent studies have found association between PUFAs and inflammation. It is reported that PUFA **Ω**-6 and **Ω**-3 induce a less muscle development, and increase muscle extensor strength. Although there are antecedents in skeletal muscle that link Panx-Chs and free fatty acids as signaling molecules, the relationship of PUFA **Ω**-6 and **Ω**-3 in Panx-Chs has not yet been studied and how they influence myogenic differentiation. Here, we evaluated if "PUFAs affects the myoblast differentiation, changing the permeability of the cell membrane". C2C12 cells were stimulated with PUFA **Ω**-6 or **Ω**-3during their differentiation. The differentiated C2C12 cells to myotubes, compared to undifferentiated cells, have an increase in the activity of the non-selective channels in the cell membrane. The presence of ALA, but not LA, decreases the myogenic differentiation of C2C12 cells. Furthermore, in presence of ALA the levels of proinflammatory markers, as IL-1**β**, TNF-**α**, and production of nitric oxide was decreased. This effect was not observed in the presence of LA. Our data suggest that the differentiation of myoblast is reduced in presence of PUFA **Ω**-3 by changing proinflammatory markers.
Funded by FONDECYT Nº11160536 (CP)

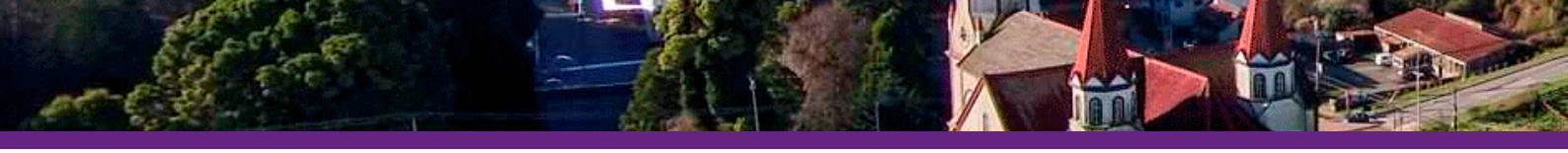


5) Obtaining genomic resources from RNA-seq in Red cusk-eel: SNPs, lncRNA and reference genes identification

Dettleff Phillip [1,2], Hormazabal Elizabeth[1,2], Meneses Claudio[3,4], Molina Alfredo[1,2,5], Valdés Juan Antonio[5,1,2]. [1]Laboratorio de Biotecnología Molecular, Universidad Andrés Bello. [2]INCAR, Centro Interdisciplinario para la Investigación Acuícola. [3]Centro de Biotecnología de Plantas, Universidad Andrés Bello. [4]FONDAP Centro de Regulación del Genoma, Universidad Andrés Bello. [5]CIMARQ, Universidad Andrés Bello. (Sponsored by Juan Antonio Valdes)

The red cusk-eel (*Genypterus chilensis*) is a native species with high potential to Chilean aquaculture diversification. However, exist few genomics resources for this species. Our objectives were: (i) Identify SNPs marker across the transcriptome of *G.chilensis;* (ii) identify long non-coding RNA (lncRNA);(ii) identify suitable reference genes from RNA-seq data to use in relative gene expression evaluation. We use a previously published reference transcriptome in our group to mapping RNA-seq libraries of muscle, liver and head kidney of *G.chilensis.* We identify SNPs marker using the Quality-based variant detection module (CLC Genomic Workbench), identifying more than 18,000 SNPs marker. For lncRNA identification, we use a series of successive filters based in several databases annotation to discard coding sequences. We identify a total of 14737 putative lncRNA in the transcriptome of *G.chilensis*. The expression of these lncRNAs among tissues showed 1910 lncRNA expressed simultaneously in all tissues, with 891, 1126 and 2017 lncRNA expressed exclusively in muscle, liver and head kidney, respectively. Finally, using the expression data of RNA-seq, we evaluated the expression stability using the RPKM normalized values of expression to calculate the coefficients of variation and the maximum fold change, ranking the genes according to expression stability, identifying several candidates with stable expression, posteriorly evaluated by qPCR, join to lncRNA and mRNA immune-related transcripts in response to stress. This work provides useful information for the future development of this aquaculture industry and to increase the biological knowledge of this species.

CONICYT FONDECYT Postdoctorado 3180283, CONICYT FONDAP 15110027.

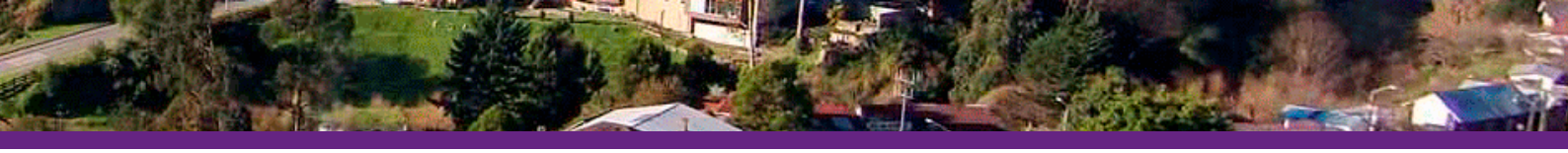


6) The transcription factor Sre1 of the SREBP pathway would be involved in the transcriptional regulation of genes from other biosynthetic pathways in the carotenogenic yeast Xanthophyllomyces dendrorhous

Gómez Melissa [1], González Ana M[1], Gutiérrez María S[1], Sepúlveda Dionisia[1], Barahona Salvador[1], Baeza Marcelo[1], Cifuentes Víctor[1], Alcaíno Jennifer[1]. [1]Departamento de Ciencias Ecológicas, Facultad de Ciencias, Universidad de Chile. (Sponsored by Jennifer Alcaíno Gorman)

In *Xanthophyllomyces dendrorhous*, sterols levels are probably regulated through the SREBP (Sterol Regulatory Element Binding Protein) pathway, because possible genes that would encode proteins of this pathway have been identified, being these called *SRE1* **and** *STP1*. *SRE1* **would encode the transcription factor Sre1 and** *STP1* **the protease Stp1 that generates the soluble form of Sre1 (Sre1N), which activates the expression of target genes through the recognition of the** Sterol Response Elements (SREs) present in the promoter region. Among the targets are found genes of the ergosterol pathway, the main sterol in fungi. Interestingly, the sterol levels would be involved in the regulation of the mevalonate and carotenoids pathways of *X. dendrorhous*. For example, it has been shown that in mutants that do not produce ergosterol increase the levels of various transcripts of these pathways and the total production of carotenoids increase, which return to a wildtype level when *SRE1* **and** *STP1* **are mutated. To confirm the regulation by Sre1 of some of these possible target genes, a ChIP protocol was optimized and applied in mutant strains of** *X. dendrorhous* **that express the 3xFLAG epitope fused to Sre1 by its N-terminus. To evaluate the functionality of the assay, primers that flank possible SREs in the promoter regions of some candidates genes were designed with the aim of obtaining the expected amplification using the immunoprecipitated DNA. These results allow to corroborate that the yeast effectively would has a functional SREBP pathway that is active in mutants that do not produce ergosterol.**

Funding from FONDECYT 1160202, and CONICYT Doctorado Nacional 21170613 fellowship.

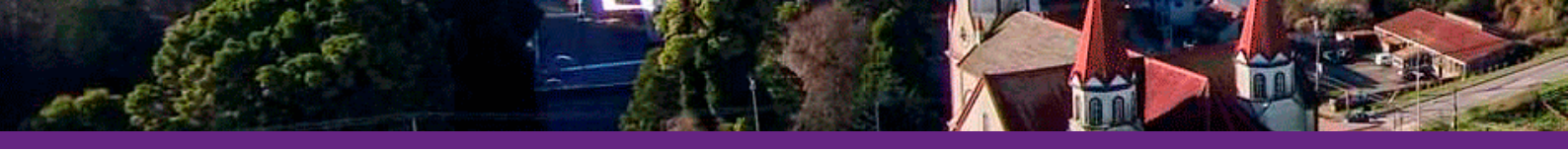


7) Identification and characterization of the ERG3 gene, involved in the biosynthesis of ergosterol in Xanthophyllomyces dendrorhous.

Venegas Maximiliano [1], Barahona Salvador[1], Dionisia Sepúlveda[1], Baeza Marcelo[1], Cifuentes Victor[1], Alcaíno Jennifer[1]. [1]Ecología, Ciencias, Universidad de Chile. (Sponsored by Jennifer Alcaíno Gorman)

Xanthophyllomyces dendrorhous is a basidiomycete yeast that produces carotenoids, mainly astaxanthin. Isopentyl pyrophosphate (IPP) is a precursor of astaxanthin and of ergosterol synthesis, which are the end products of the carotenoid and sterol pathways, respectively, in *X. dendrorhous*. Previous works suggest that both pathways would be regulated by the SREBP (*Sterol Regulatory Element Binding Protein*) pathway. The *X. dendrorhous* mutant *cyp61-*, does not produce ergosterol and overproduces carotenoids, suggesting that the absence of ergosterol is responsible for carotenoids overproduction. The goal of this work was to identify the *ERG3* gene,which encodes C-5 sterol reductase that catalyzes the conversion of episterol to 5,7,24 (28) ergostatrienol in the ergosterol biosynthesis, to obtain another ergosterol biosynthesis mutant and evaluate if this mutation generates the same carotenoids overproducing phenotype as in mutant *cyp61-*. The *ERG3* gene mutant (CBS-6938**Δ***erg3*) was obtained by gene replacement by homologous recombination. By RP-HPLC analysis of sterols and carotenoids, it was observed that this mutant does not produce ergosterol and it accumulates a sterol that is different from the ones accumulated in mutant *cyp61-*, and no carotenoid overproduction was observed in mutant **Δ***erg3*. In addition, the *HMGS* transcript level (gene controlling the synthesis of IPP) was evaluated by RT-qPCR and no significant differences in relation to the parental strain was observed, as it was observed in mutant *cyp61-*. In conclusion, the absence of ergosterol is not responsible for carotenoid overproduction in mutant *cyp61-*, but rather it is the change in sterol composition.

FONDECYT 1160202

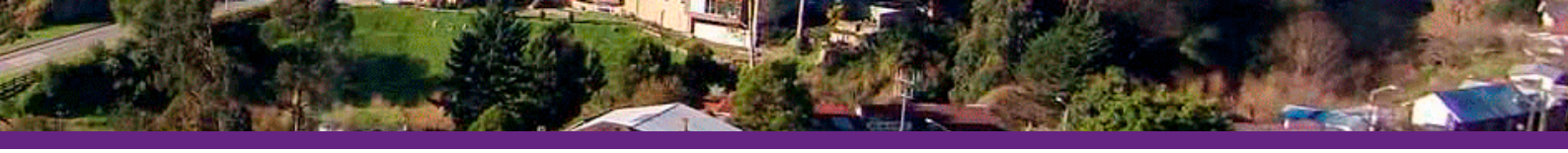


8) Developmental electrophysiological characterization of the consolidation of long-term memories after the early exposure to the task of OPR in sleep condition

García María Alexandra[1], Valdivia Gonzalo[1], Espinoza Nelson[1], Tiznado Vicente[1], Fuentealba Pablo[1]. [1]Psiquiatría, Medicina, Pontificia Universidad Católica de Chile. (Sponsored by Pontificia Universidad Católica de Chile)

Sleep following encoding favors the formation of episodic long-term memory (Rasch and Born,2013). Slow wave sleep (SWS) appears to support hippocampus-dependent spatial memory consolidation such as object in place recognition (OPR) (Inostroza and Born, 2013). It has been proposed that this process is supported by the phase-locking of three cortical rhythms along hippocampal replay: neocortical slow oscillations, thalamic spindles, and hippocampal sharp wave-ripples allowing hippocampal-neocortical long-term storage (Sirota et al., 2003; Mölle and Born, 2010; Latchoumane, et al. 2017; Staresina et al.,2015). During the first three postnatal week development detectable oscillations related to cognitive functions and synaptic plasticity appear (sharp waves, theta, gamma and ripples) possibly reflecting cortical maturational processes (Olini and Huber, 2014). Moreover, these immature networks are modified in experience-dependent manner (Martens et al, 2015). Allocentric spatial abilities emergence at an early stage, along with rat's sensorimotor repertoire (Altman J, et al., 1975; Tan H. 2017). Object recognition defined only by distal cues appears at P17-P31 (Ramsaran, Westbrook, & Stanton, 2016). We are particularly interested in study the oscillation phase-locking in sleep coupled with allocentric spatial emergence during development. To address this, Long Evans rats performed a OPR task during several postnatal days to evaluate discrimination. Our data suggest that there is a tendency to discriminate the object displace at P32 that is absent in the previous postnatal days. According to this, we aim to implant a multi tetrode drive in posterior parietal cortex, somatosensory thalamus, and dorsal hippocampus (CA1) for LFP and single units recording during sleep.

Proyecto Anillo **ACT1414**



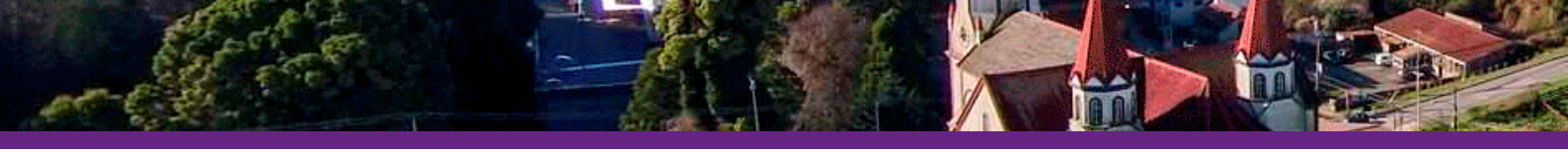
(NO SE PRESENTÓ)

9) Rapid Eye Movement (REM) sleep in humans: fast rebound after short-term sleep deprivation

Espinoza Danay[1], Córdova Teresa[1], Bassi Alejandro[1], Vivaldi Ennio[1], **Ocampo-Garcés Adrián Pedro[1]**. [1]Laboratorio de Sueño y Cronobiología, Fisiología y Biofísica, Instituto de Ciencias Biomédicas, de Medicina, Universidad de Chile.

REM sleep exhibit a stable quota that occupies one fifth of nocturnal sleep among adult humans. In contrast to most animal models that efficiently compensate REM sleep losses provoked by sleep deprivation, several reports document minimal REM sleep recovery (state rebound) after long-term total or selective REM sleep deprivation (RD) in humans. It could be argued that REM sleep rebound after long term deprivation may be interfered among others, by complex NREM-REM sleep interactions according to a zero-sum rule. Here, we explore REM sleep rebound after a short-term (5-hours) selective RD in healthy adults. Two full-night video-polysomnographic (v-PSG) record were successfully obtained in eight volunteers: first night was an undisturbed sleep night (BL condition), the second night started with 5 hours of selective REM sleep deprivation followed by four hours of recovery (5RD condition). REM sleep losses amounted on average 33.8 minutes during 5-hour deprivation period that corresponded to 75.4% of BL quota (paired t-test $p<0.001$). REM sleep attempts increased monotonically during deprivation procedure (repeated ANOVA $p<0.001$, with post-hoc multiple comparisons). REM sleep rebound amounted 30.9 minutes accounting for 91.5% of cumulated REM sleep debt (paired t-test $p<0.001$). 5-hours of selective RD provoked the canonical homeostatic REM sleep response, with increased propensity during deprivation followed by REM sleep rebound. REM/TST ratio was not affected by 5RD procedure suggesting that part of observed REM sleep excess occurs by an unspecific sleep increment. Short term deprivation procedures may help to evidence human REM sleep homeostasis refined from confounding factors.

Supported by Puelma Foundation; D.E. was awarded by CONICYT PhD Fellowship.



10) Expression profiles of genes and long non-coding RNA associated to ubiquitin proteasome pathway in coelomocytes, gonad and gut of red sea urchin (Loxechinus albus)

Gonzalez Joaquín Ignacio[1], Antiqueo Paulette[1], Estrada Juan Manuel[2], Molina Alfredo[1], Valdés Juan Antonio[1]. [1]Interdiciplinary Center for Aquaculture Research (INCAR), Facultad de Ciencias de la Vida, Universidad Andrés Bello. [2]Centro de Investigación Marina Quintay (CIMARQ), Facultad de Ciencias de la Vida, Universidad Andrés Bello.

The red sea urchin, *Loxechinus albus* is an economically important equinoderm distributed along the Chilean coast. This organism has a high market demand, which has led to overexploitation. The current high throughput sequencing techniques allows the construction of transcriptomes of non-model species like *Loxechinus albus*. The information from transcriptomes facilitates the work on cellular and molecular pathways that might be regulating gene expression, like long non-coding RNA. Among cellular pathways, the ubiquitin proteasome signaling is an excellent candidate to study due to the importance in different regulatory process like immune response, protein transport, DNA repair and protein degradation. In this work, genes associated with ubiquitin proteasome pathway where selected by functional annotation. The long non-coding RNA were obtained from *Loxechinus albus* transcriptome and selected through correlation analysis against candidate genes. Total RNA extraction and cDNA synthesis were performed from juvenile red sea urchin. RT-qPCR technique was used for measuring the expression of the genes previously chosen. Different expression profiles among tissues were obtained, which allowed us to determinate the overrepresentation of the pathway in coelomocytes of red sea urchin. This confirms this pathway's role in the immune system of this species of sea urchin.

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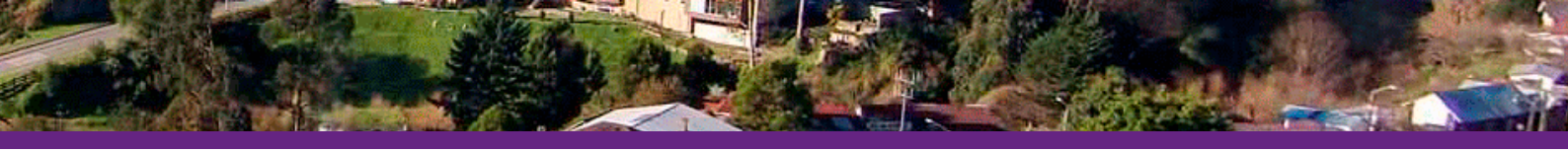


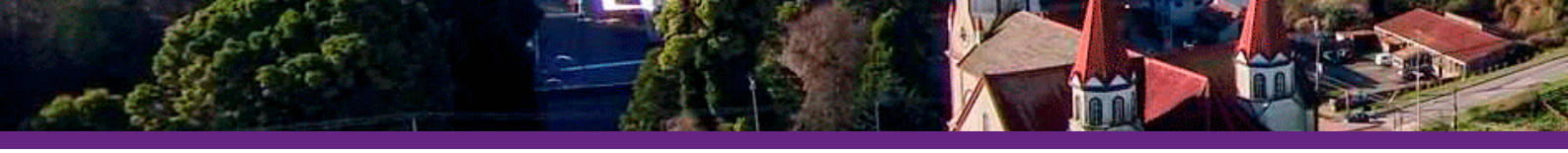
11) Role of the metabolites from the seaweed Chondracanthus chamissoi (C. Agardh) Kützing, 1843 in the process of inducing the primary settlement of mussel larvae of commercially important in Chile

Pinilla Macarena Fernanda [1], Tarifeño Eduardo[2], Llanos Alejandra[3], Hernández Víctor[1], Becerra José[1]. [1]Laboratorio de Química de Productos Naturales , Ciencias Naturales y Oceanográficas , Universidad de Concepción. [2]Departamento de Zoología, Facultad de Ciencias Naturales y Oceanográficas , Universidad de Concepción. [3]Departamento de Oceanografía , Facultad de Ciencias Naturales y Oceanográficas , Universidad de Concepción. (Sponsored by Carlos Marcelo Baeza Perry)

The national mussel farmer is the second aquaculture activity in the country and currently depends almost entirely on the seeds captured in natural banks. It is estimated that about 1 ton of seed is needed to produce 5.56 tons of mussels, but in recent years it has been difficult to maintain this volume of production due to the shortage of seeds of these organisms, which has affected production commercial of these species. The use of compounds with inducing action of primary settlement of mussel larvae to improve the uptake of seeds is currently being investigated. The presence of some of the compounds that are currently being tested in the settlement process of these and other marine invertebrates has been described in macroalgae. The ecological relationship that exists in Chilean coasts between algae of the Rhodophyta Division and Chilean Mytilidae, together with some field observations, suggests that there would be a chemical interaction between these organisms. This study proposes that metabolites of *Chondracanthus chamissoi* (Rhodophyta) possess the capacity to attract premetamorphic mytilids larvae and enhance their primary settlement process. The aim of this investigation is to determine the inductive effect of primary settlement of the larvae of mytilids of the crude extracts of *C. chamissoi.* To this end, the extraction of metabolites of the algae under study was carried out and the effectiveness in the induction of the settlement of larvae of mytilids was evaluated experimentally. In addition, the chemical and biological characterization of the extracts in study was carried out.

Acknowledgment

The financing granted by the FONDEF IDEA ID16I10154 Project and the CONICYT National Magister 2018 is appreciated.



12) Direct reprogramming of fibroblasts into chemically induced neurons following a small-molecule based protocol

Bodaleo Felipe Jose[1,2], Gudenschwager Camila[1,2], Lee-Liu Dasfne[1,2], Delgado Ricardo[2], González-Billault Christian[1,2,3]. [1](GERO), Geroscience Center for Brain Health and Metabolism . [2]Departamento de Biología, Facultad de Ciencias, Universidad de Chile. [3]., The Buck Institute for Research on Aging. (Sponsored by Christian Enrique González Billault)

The study of human central nervous is limited because of the scarcity of neurons available for direct analyses, and the use of murine neuronal models are mainly restricted to embryonic stages. In this scenario, the reprogramming of somatic non-neuronal cells into functional neurons is considered as a valid experimental approach. We implemented a cell-reprogramming methodology based in a pharmacological treatment, as described in Li et al., 2015. We have reprogrammed both mouse embryonic fibroblasts (MEF) and adult mouse dermal fibroblasts into chemically induced neurons (cIN). After the pharmacological treatment cells exhibit dramatic morphological changes, acquiring neuron-like morphology. After 7 days post-induction (dpi) cells start expressing the canonical neuronal marker bIII-tubulin as detected by immunocytochemistry (ICC) and real-time quantitative PCR (qPCR). As induction progress cells increase the levels of bIII-tubulin reaching its maximum of expression at 21 dpi, a time point in which MEF were slightly more susceptible to the reprogramming protocol than adult dermal fibroblasts. Classical neuronal cytoskeletal elements such as the dendritic microtubule-associated protein 2 (MAP2), the axonal protein tau and poly-glutamylated tubulin are also detected in cINs. Glutamatergic synaptic proteins such as synaptophysin-I and Homer 1 are also expressed at 21 dpi cIN. Finally, single-cell electrophysiological recordings show that the cIN present outward potassium currents elicited by different voltage pulses. In conclusion, the cINs exhibit neuron-like morphology, express neuronal proteins and respond to electrical stimuli. Further efforts will be focus on reaching maturation stages where cIN show different cell features of mature neurons.

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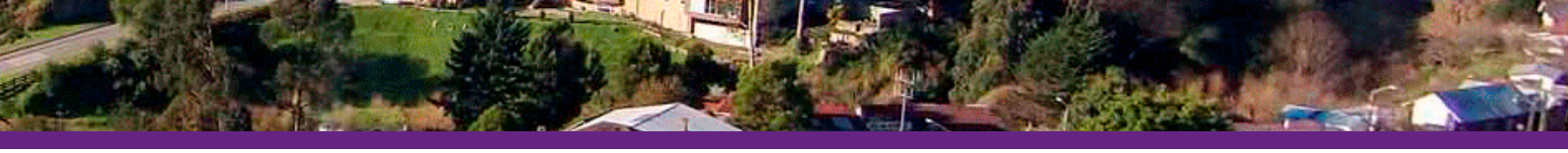

13) Temperature-dependence of activation parameters in a potassium channel from an antarctic limpet

Ferrada Juan[1], Barria Joel[1], Ugarte Gonzalo[1], Madrid Rodolfo[1], Pertusa Maria[1], **Rojas Patricio[1]**. [1]Departamento de Biología, Facultad de Quimica y Biología, Universidad de Santiago de Chile.

Voltage dependent potassium channels (Kv) are involved in repolarization of the of action potential. These channels present a steep dependance of temperature in vertebrates where the descent in temperature favors the closed state of the channel. On the other hand several Kv channesl from invertebrates show an opposite displacement in V0.5. In order To study the effect of the temperature on the gating properties of potassium channels of cold water invertebrates that live in the harsh conditions of the antarctic peninsula where the water temperatures can reach 0°C during the winter. we cloned the Kv1 channel from the antarctic limpet *Nacella concinna*(NCKv) and compared it to it´s ortholog from *Mus musculus* (mKv1.1). Whole-cell patch clamp recordings were performed in the transfected HEK293 cells at temperatures of 10°, 15°, 25° and 30 °C. When temperature is decreased, mKv1.1 undergo a right shift in V0.5, favoring the closed state of the channel, in contrast NCKv1 channels present a left-shift of V0.5, favoring the open state of the channel at lower temperatures in the same fashion as other cold water invertebrates. Besides the V05 from NCKv is right-shifted compared to mKv1.1, when both channels are compared to their physiological temperatures, their V0.5 are similar.

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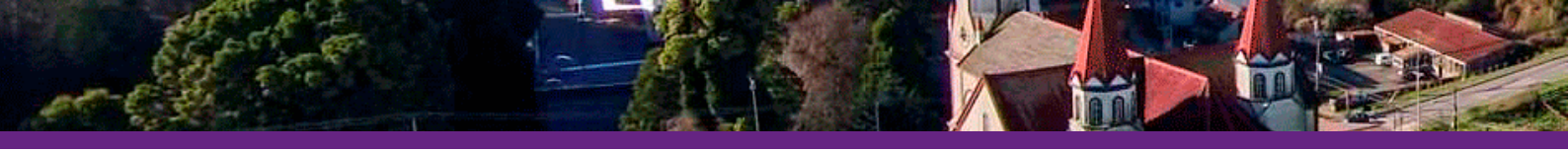
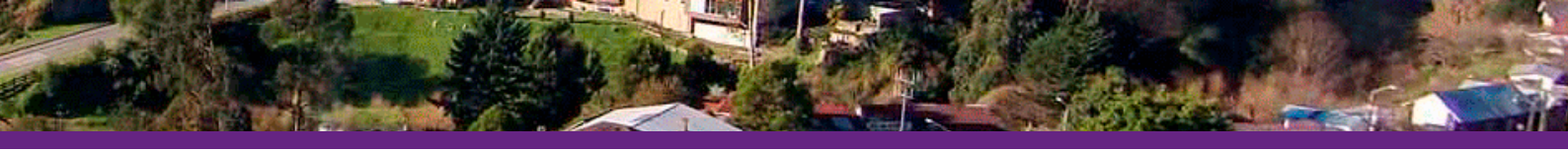


14) Multisensory integration in different states of consciousness

Artigas Claudio[1], Ivan Rubio[1], Rodriguez Eugenio[1]. [1]Psicología, Ciencias Sociales, Pontificia Universidad Católica de Chile.

The ability to integrate inputs from different senses in a single percept that cannot be easily decompose in their components is called multisensory integration. Basically, this is a process that need sharing of information from different areas separates from each other. This aspect can be achieved when the subject is awake, because long distance communication is lost when the subject is under anaesthesia or fall sleep. Nevertheless, several investigations have found that multisensory integration could happen when the stimulus are heavily masked (subliminal) or the subject is sleep. To tackle this question, we a visual stimulus and an auditory stimulus and show it to the subject with their eyes close. The presentation could be coordinate (both stimulus at 700 ms or 1000 ms) or discoordinate (One at 700 ms and the other at 1000ms) for 5 seconds. The subjects must respond as quickly as possible if the visual stimulus has a sound, or if the audio and visual stimulus were independent. We analyse the neural synchrony when the subjects are awake and when the subjects are in a state of drowsiness (transition to sleep). We saw that when the subjects are awake, they have a long-scale synchrony between occipital-centro parietal in the coordinate condition that it is absent when the subjets are in drowsiness. This support the model that MSI needs the activity of different areas, involving association areas and sensory cortices and that this dissapear when the state of the brain cannot sustain this activity.

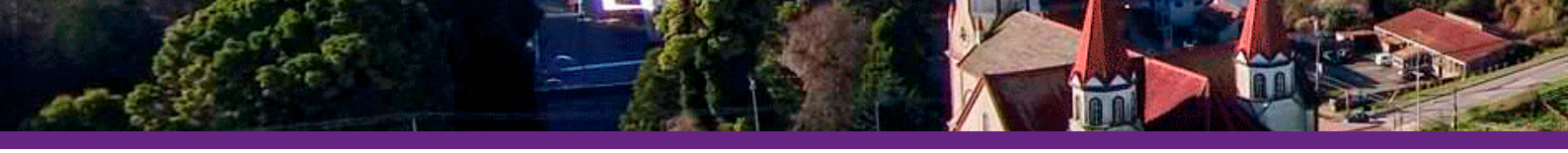


15) Neural dynamics of creative drawing

Cordero Evelyn[1], Barraza Paulo[2], Ivan Rubio[1], Aland Astudillo[3], Eugenio Rodríguez[1]. [1]Neurociencias, Psicología, Pontificia Universidad Católica De Chile. [2]CIAE (Centro de Investigación Avanzada en Educación), Universidad de Chile. [3]Centro de Investigación y Desarrollo en Ingeniería en Salud, Medicina, Universidad de Valparaíso.

Creativity in humans is a complex cognitive behavior commonly defined as the ability to generate responses that are novel, useful and relevant. In electrophysiological studies, a frequent finding is that creative ideation is associated with an increase in alpha potency, in relation to a baseline at rest, in frontal and bilateral posterior cortical sites. These findings suggest a close relationship between the increase in alpha power and inhibitory, descending control, which has been implicated in many different demands related to creativity, especially with tasks of verbal creative ideation. We wanted to study the neuronal dynamics underlying the process of creating a drawing. To do this, we have devised a paradigm where participants perform two drawing tasks associated with a concept. One task consists in drawing the symbol associated with the concept and the other in creating a new representation of the concept. In both cases, we analyze the ideation window of the drawing with respect to a baseline. Our preliminary results suggest that creative ideation in the figurative domain differs from the brain activation patterns observed during creative ideation in the verbal domain. We found a significant attenuation of occipital alpha during the creation task with respect to the task of symbolization and a significant increase of frontal and right parietal beta, possibly associated with a greater motor recruitment in creative tasks. The electrophysiological activation patterns found are coherent with processes of downward control and with internal attention, thus describing mental processes relevant to creative ideation.

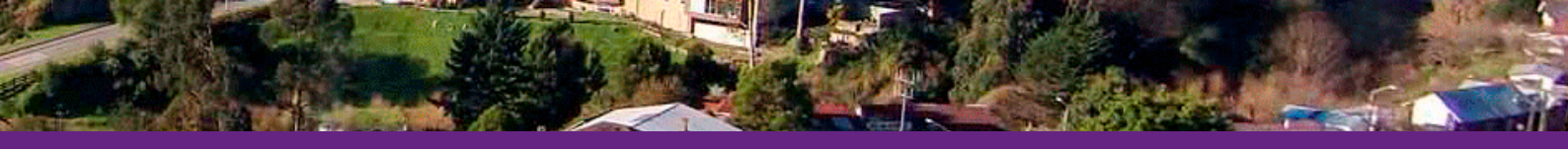
CONICYT Doctorado nacional



16) Influence of semantic consistency and perceptual features on visual attention during scene viewing in 18- and 24-month-olds

Helo Andrea Veronica[1], Aygun Oytun[2], Rukoz Yumisay[2], Rämä Pia[2,3]. [1]Departamento de Fonoaudiología, Facultad de Medicina, Universidad de Chile. [2]Laboratoire Psychologie de la Perception (UMR 8242), Université Paris Descartes. [3]CNRS.

Visual attention and gaze allocation during the exploration of our visual environment are influenced by an interaction between top-down (i.e. cognitive control) and bottom-up (i.e. perceptual features) mechanisms. For instance, objects that are either salient or semantically inconsistent with the visual context attract our attention. While visual attention has been extensively studied in adults, less has been investigated in developing populations. It is known that visual exploration of real-world-scene develops during early childhood. However, little is known about the interaction between bottom-up and top-down mechanisms. Here, we investigated the influence of perceptual features and semantic inconsistencies on attention allocation in 18- and 24-month-olds. We measured gaze allocation while children explored visual scenes, which contained either an inconsistent (e.g., slippers on a stove) or consistent (e.g., pan on a stove) object either in a high-saliency or low-saliency condition. The results showed that both age groups looked longer to salient than non-salient objects. Interestingly, the 24-month-old children looked longer to inconsistent objects only when these objects were highly salient while semantic consistency did not affect gaze allocation at 18-months. Our findings indicate that bottom-up guidance is dominant over top-down guidance before the age of 2-years. It is possible that before this age, children have not yet acquired enough semantic scene knowledge to guide their visual attention. Later, at 24-month-olds, the ability to detect semantic inconsistencies emerges, but it is still strongly affected by perceptual features. These findings further suggest that the top-down control of visual attention increases with age during early childhood.

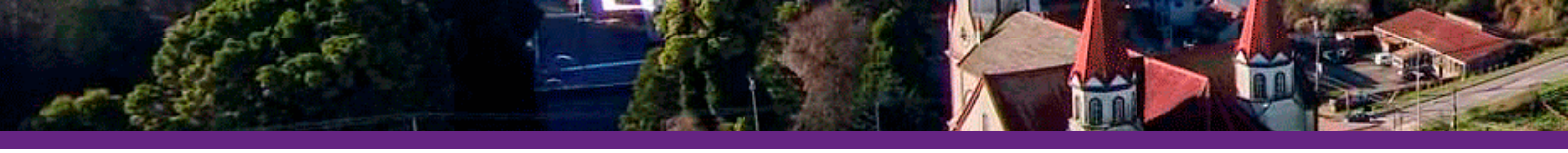


17) Pupil diameter signals workload level induced by environmental noise during reading in high school students

Montefusco-Siegmund Rodrigo[1,4], Diaz Diego[2], Frez Danixa[3], Fuentes-Carrasco Francisco[2], Madariaga Samuel[5,4], Ulloa-Sánchez Felipe[2], Couve Andrés[4]. [1]Escuela de Kinesiología, Medicina, Universidad Austral de Chile. [2]N/A, Instituto Nacional. [3]N/A, Liceo Javiera Carrera. [4]Biomedical Neurocience Institute, Facultad de Medicina, Universidad de Chile. [5]Departamento de Neurociencia, Facultad de Medicina, Universidad de Chile.

Although sometimes we are able to generate an expected behavior, the adaptation to the environment conditions may increase the difficulty needed to achieve the goal. This is especially critical in the educational context where children are commonly exposed to many distractors inside and outside the class room. In urban schools one of the main distractors is auditory noise, represented by traffic, conversations, screams, sirens, honks, among others. While this environmental noise has the potential to distract the students, they can actively disengage from this distractor to keep attention on achieving an expected performance. In this study we used pupil diameter as a proxy for mental workload while students from high school level were performing a reading comprehension task in the presence or absence of environmental noise. Our results show that while the subjects are able to keep a sustained performance through text related questions, the increment on pupil diameter reveals a sustained increase in cognitive workload.

Iniciativa Científica Milenio, ICM P09-015-F



18) Influence of phase and frecuency of a periodic stimuli in the entrainment of alpha oscillations in the brain

Otero Ferreiro Mónica[1], Escobar-Silva María José[1,2], El-Deredy Wael[2,3]. [1]Ingeniería Electrónica, Universidad Técnica Federico Santa María. [2]Sistemas Biomédicos, Advanced Center for Electrical and Electronic Engineering. [3]Escuela de Ingeniería Civil Biomédica, Universidad de Valparaíso. (Sponsored by Wael El-Deredy)

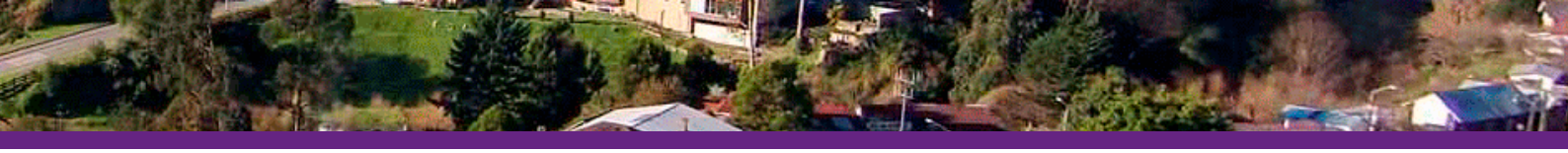
Oscillations are prevalent features of brain activity. Neural oscillations have been suggested to be basic mechanisms which allow the synchronization of neural activity within and across brain regions and, contribute to the accurate temporal codification of neural processes underlying perception, attention, cognition, and behavior among others. Several mathematical methods and theoretical approaches have been used to analyze the dynamics of brain oscillations. The mechanisms of persistence and propagation of an entrained signal between neural areas are investigated in this research using EEG recordings. Entrainment of the EEG alpha band (8-14Hz) has been used to influence expected perceptual discrimination of subsequent stimuli, such that, low power alpha (or waxing alpha phase) at the time of presentation facilitates perceptual discrimination, while high power alpha (or waning alpha phase) will impede discrimination.The capacity to entrain the brain to a range of frequencies with an external continuous periodic input is assessed. It is also characterized the conditions in which we are able to observe the persistence of the entrained signal after the removal of the external driving frequency. Moreover, it is examined the effect of the phase in which the entrainer signal is finished over the persistence of the entrained alpha brainwave. Besides, it is studied how the entrained signals in the alpha band range modulates the perceptual response to a near threshold discrimination task.

1. CONICYT-PFCHA/Doctorado Nacional/2017- 21171741_Mónica Otero Ferreiro

2. FONDECYT REGULAR 1161378 a cargo del profesor Wael El-Deredy

3. UTFSM: Universidad Técnica Federico Santa María

4. AC3E : Advanced Center for Electrical and Electronic Engineering

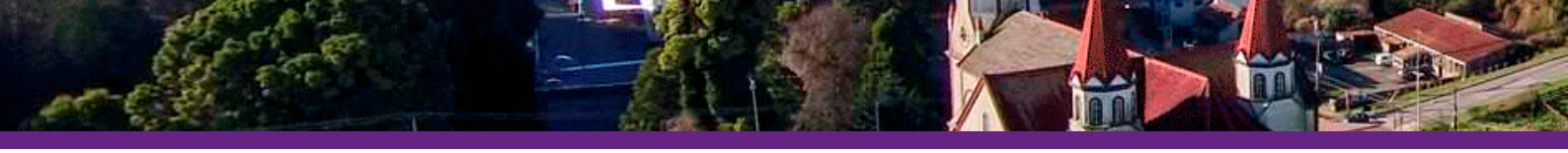


19) Cortical activation of healthy volunteers and muscle tension dysphonia (MTD) patients during Lombard Effect: an EEG study.

Prado Pavel[1], Castro Christian[2], Weinstein Alejandro[3], Zepeda Lucía[1], Zañartu Matías[4]. [1]AC3E, Universidad Técnica Federico Santa María. [2]Department of Speech, Language and Hearing Sciences, Universidad de Valparaíso. [3]Biomedical Engineering School, Universidad de Valparaíso. [4]Department of Electronic, Universidad Técnica Federico Santa María.

The cortical mechanisms controlling the voice production during the Lombard Effect (LE, the involuntary tendency of speaking louder in noisy environments) have not been completely described. We tested whether the cortical activation associated to LE is disrupted in patients with primary muscle tension dysphonia (MTD); a voice pathology characterized by the high levels of stiffness and tension of the vocal folds in absence of known structural disorders. Both patients and healthy volunteers (N=20) were asked to utter series of syllables in three experimental conditions: quiet, Lombard (elicited by speech noise at 80 dB HL) and recovery (quiet, 5 minutes after the end of LE conditions). Electroencephalogram (EEG) was recorded from 64 scalp-electrodes (10/20 system). The event related potentials (ERP) elicited by the auditory feedback of one's own voices were computed to analyze the amplitude and the neural generators of the N1-P2 complex. Cortical activations were estimated using standardized low-resolution brain electromagnetic tomopraphy (sLORETA). In both groups, increased N1-P2 amplitudes were obtained in the Lombard condition in comparison with that obtained in quiet. The response amplitude decreased in the recovery condition but did not return to its basal level in MTD patients. The auditory feedback of one´s own voice induced the activation of left temporal and frontal areas, including the Broca´s and Wernicke´s areas, primary auditory cortex, primary motor cortex and temporal language areas. Statistically significant activations (permutations test, 5000 permutations) were obtained between groups, suggesting disrupted auditory-motor integration mechanisms in MTD patients.

This work was supported by the Advanced Center for Electrical and Electronic Engineering, AC3E, Basal Project FB0008, CONICYT



20) Effect of acute psychosocial stress on auditory and visual processing

Rojas-Thomas Felipe[1]. [1]Metropolitana, Psicologia, Pontificia Universidad Católica de Chile.

An EEG-compatible adaptation of the Montreal Imaging Stress Task (MIST) was developed to induce psychosocial stress in healthy subjects. With this adaptation, we analyzed their auditory processing of attended sounds, pupillary dilatation, heart rate, subjective levels of stress-anxiety, and salivary levels of the stress hormone (cortisol). ERPs components associated with sensitivity (N1) and more elaborated processing (P3) were assessed using an auditory paradigm oddball. The results showed that the psychological stress decreases the amplitude of P3, as well as the phasic pupil dilation response towards objective tones decreases after psychological stress. Finally, we detected that MITS induces an increment in subjective levels of stress-anxiety, heart rate, and salivary levels of the stress hormone cortisol.

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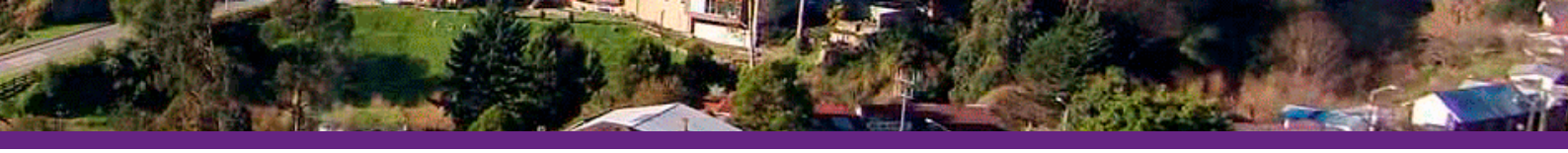


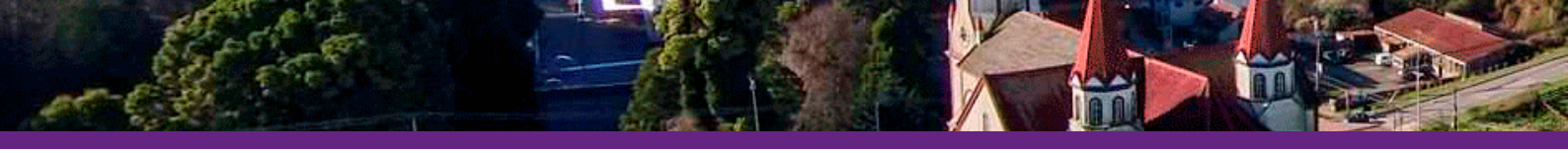
21) Neural signatures of visuo-spatial working memory in medicated and unmedicated ADHD children

Valdés Joaquín[1], Medel Vicente[1], Ihnen Josefina[1], Irani Martín[2], Ossandón Tomás[1]. [1]Neurodynamics of Cognition Lab, Departamento de Psiquiatría, Facultad de Medicina, Pontificia Universidad Católica de Chile. [2]Laboratory for Brain-Machine Interfaces and Neuromodulation, Facultad de Medicina, Pontificia Universidad Católica de Chile.

Deficits in visuo-spatial working memory (VSWM) are one of the most common impairments in subjects with ADHD. Specifically, modulations of the P3a and P3b event-related potentials, and both the power of fronto-central theta (3-7 Hz) and posterior alpha (8-12 Hz) components have been shown to occur in dependence of working memory load. In this study, ADHD patients (9-13 yo) performed a VSWM task in two separate sessions, on- and off-medication (MPH-ON and MPH-OFF), which in all cases was methylphenidate, while being monitored using scalp EEG.

Whole session behavioral data indicate that MPH-OFF children had worst performance than controls in the task. Preliminary data shows increase in amplitude of the P3a and decreases in the P3b component in ADHD children, which could be related to increased orienting to novel stimuli and with the deficits in the task. The time-frequency analysis shows that in the encoding and recognition phase MPH-OFF children present lower power in theta in central electrodes and lower alpha in the encoding phase in posterior electrodes. ICA analysis of the theta component reveals decreased power in MPH-OFF children in the encoding and recognition phase. An analysis of the power spectral density slope, as a marker of neuronal variability, revealed increased variability in ADHD compared to controls, indicating that this neuromodulatory disorder might impede the brain from reaching a optimal sensory encoding state where above criterion performance is achieved. Overall, these results suggest that behavioral impairments in VSWM task in ADHD children might be due to abnormalities in neural activity.

Supported by Anillo ACT1414 and Fondecyt 1180932.



22) Behavioral flexibility in dominant mice, an interplay between physiology and social behavior

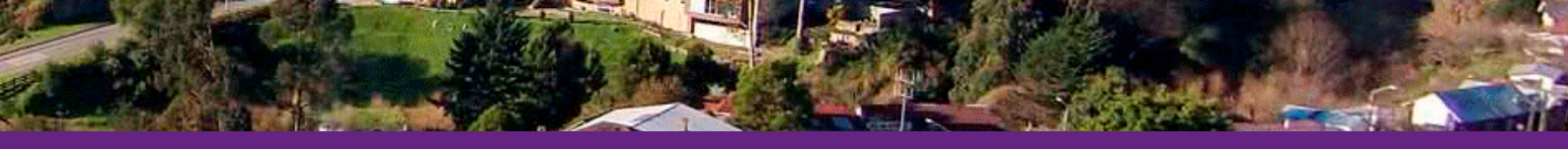
Lara-Vasquez Ariel [1], Morán Constanza[1], Morales Cristian[1], Fuentealba Pablo[1]
(1) Centro Interdisciplinario de Neurocienica, Departamento de Psiquistria, Medicina, Pontificia Universidad Católica de Chile, Centro Interdisciplinario de Neurociencia

Behavioral flexibility refers to the adaptive changes in the behavior of an animal, in response to changes in the internal or external environment like social context. Prefrontal cortex (PFC) and hippocampus are two regions of the brain of mammals that comprise multiple circuits that mediate functions related to behavioral flexibility and dominance hierarchy related behaviors.

Here we report ,in different litters mice group, the social behaviour in modified T-maze task and correlate its performance with the basal functional connectivity between PFC and hippocampus in the anesthetized mice.

In behavioral experiments we found that dominant mice were the only social group that present an increase in their latencies in the collective T-maze task. In physiological experiments we found that the firing rate of PFC neurons discharged at high levels and have more activity during post hippocampal ripple (a characteristic oscillation of Hippocampus) compared with other subordinate mice.
Thus, these results suggest that the cognitive processes in dominant mice present differences in behavior in a T-maze task and basal physiology. In addition, the higher activity in PFC could be related with more connectivity in this areas for process information about the behavior of others to detect, remember, and process information about social stimuli in the T-maze task.

Current understanding of the neural mechanisms associated with behaviour flexibility and social hierarchy as well as related behavioural in a social context is limited. These data show new evidence about behaviour and cerebral circuits in relation to behavioural flexibility and social rank.



23) Investigating the functional network topology of attention and mental effort using fMRI, graph theory and pupillometry

Wainstein Gabriel[1], Shine James M.[2], Alnæs Dag[3], Poldrak Russell[4], Ossandon Tomas[4], Matar Elie[5]. [1]Psiquiatria, Medicina, Pontificia Universidad Católica De Chile. [2]brain and mind center, medicine, Sydney university. [3]Department of Psychology, Oslo university. [4]Department of Psychology, Standford University. [5]Brain and Mind center, Sydney University.

There is now evidence that the noradrenergic system provides important effects over cognitive functions. For instance, it has been shown that the functional network architecture of the brain and the amount of integration is sensitive to concentrations of noradrenaline, modulating the sensitivity of regions to ongoing activity from across the broader network, thus facilitating cognitive performance through the integration of specialist brain regions as a function of cognitive tasks. Although a connection between arousal, mental effort and attention has long been hypothesized, there is currently a lack of direct empirical evidence for this link. To study this relationship, we used a multiple object tracking task, with 4 level of attentional load, in 17 subjects, using fMRI and an eye-tracker to measure the pupil size. By means of a data driving approach we found a group of brain regions that follows the same pattern of effort related processes as the pupil diameter in terms of BOLD signals and large-scale integration. Hence, as pupil size is reflecting the LC-NE dynamics and its modulation of several cortical networks, the variation on its activity affects the neural gain of widespread brain regions facilitating integration between them. This effect is adaptatively modulated according to task demands, learning and attentional effort required in the ongoing activity. Here, we provide mechanistic evidence for the instantiation of mental effort through the parametric engagement of the ascending arousal system and its role in large-scale system dynamics and cortical communication

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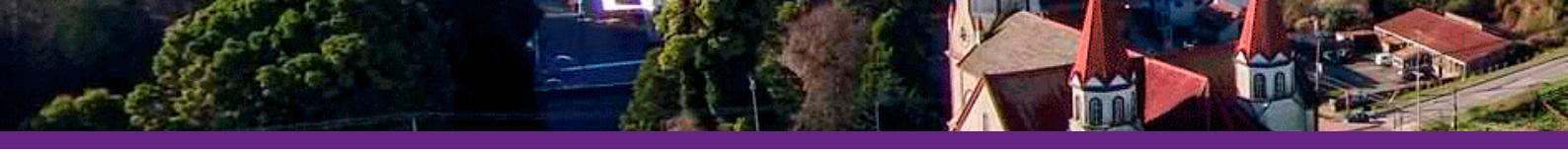

24) The visual context on web pages defines ocular behavior.

Madariaga Samuel [1], Muñoz Kristofher[1], Maldonado Pedro[1]. [1]Departamento de Neurociencia, Facultad de Medicina, Universidad de Chile.

One of the most important and natural aspects of human visual perception is the segmentation and the capture of objects within a visual scene. Despite great efforts in computer science, the simulation of the ocular behavior that characterizes this acquisition process in a specific task is still an open problem. In the present study, we evaluated the models of visual saliency and objects segmentation in different web pages. We recorded 80 healthy subjects (38 females and 42 males) who were shown 14 web pages with 5 subpages. Each image was shown for 6 seconds and their ocular behavior was recorded while they looked freely at the screen. We found that in visual saliency, there is a spatial bias which is not characterized by the current models related to the specific behavior on websites. Furthermore, the models of visual objects segmentation were deficient compared with the areas of interest generated by the clustering of fixations on the image. With these results, we can be observed that the visual behavior besides being related to the task are strongly subject to the cognitive context, and even more, this variability between contexts seems to be previously trained by experience and are consistently independent of sex and age.

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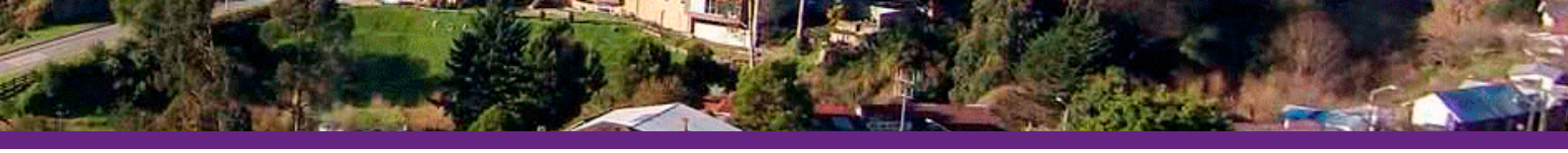

25) Dynamic complexity and aperiodicity of human local field potential activity during a visuospatial working memory task

Medel Vicente[1], Irani Martín[2], Castro Samy[3], Valdés Joaquín[1], Brice Follet[1], Lachaux Jean-Philippe[4], Ossandón Tomás[1]. [1]Laboratory Neurodynamics of Cognition, Medicina, Pontificia Universidad Católica De Chile. [2]Laboratory for Brain-Machine Interfaces and Neuromodulation, Medicina, Pontificia Universidad Católica De Chile. [3]Laboratorio de Neurociencia Computacional, Centro Interdisciplinario de Neurociencia de Valparaíso, Universidad de Valparaíso. [4]INSERM U1028, CNRS UMR5292, Lyon University.

The neural internal dynamics and responsiveness to external stimuli fluctuate rapidly in the awake brain (Harris & Thiele, 2011). These fluctuations related to arousal and attentional processes can be indexed by variations in both periodic activity (e.g. band limited power changes) representing neural oscillations, and underlying aperiodic background activity, corresponding to spontaneous "noise" activity of cortical neural networks (McGinley et al., 2015). As Local Field Potentials (LFP) have been proposed to represent, on the one hand, collective behavior of a large set of independent oscillators (Engel et al., 2001) and, on the other, arise from complex asynchronous patterns (Alvarez and Destexhe, 2004), here we show a preliminary LFP characterization in intracranial recordings during a visuospatial working memory task (VWM) (Wainstein et al., 2017) in terms of aperiodic and complexity features of the brain signal. The data was obtained from five neurosurgical patients with intractable epilepsy at the Epilepsy Department of the Grenoble Neurological Hospital (Grenoble, France). Complexity in brain activity can be measured by both Power Spectral Density (PSD) slope (Voytek et al., 2015), which is thought to acknowledge the desynchronization and aperiodicity of the neural network as a product of asynchronous neural firing activity (Podvalny et al., 2015), and entropy measures, which describe the amount information in the signal. We will show a functional and spatial characterization of the dynamic variations of PSD slope and entropy during VWM task. Our preliminary approach introduces a novel relation between aperiodic neural activity and signal complexity involved in VWM.

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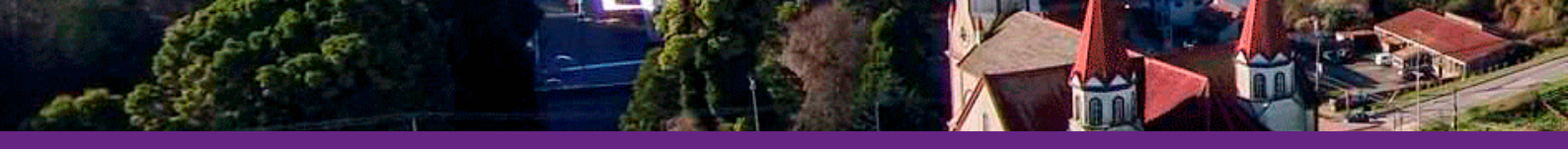
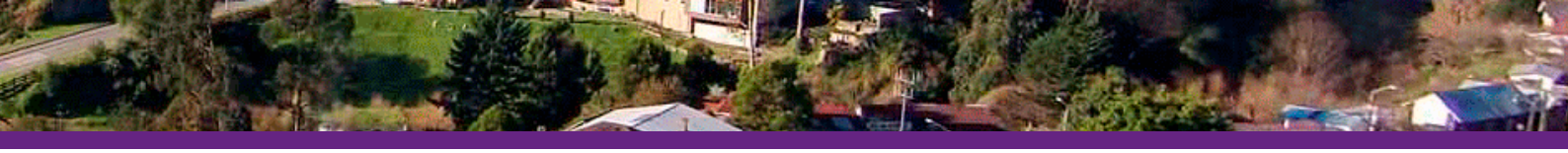


26) Diversity of neuronal activity is provided by mixed (chemical plus electrical) synapses

Xu Kesheng[1], Patricio Orio[2]. [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, University of Valparaíso, Chile. [2]Centro Interdisciplinario de Neurociencia de Valparaso, Facultad de Ciencias, Universidad de Valparaso.

Many experiments have evidenced that electrical and chemical synapses(mixed synapse) coexist in most organisms and brain structures. The role of electrical and chemical synapse connection in diversity of neural activity generation has been investigated separately in networks of varying complexities. Nevertheless, theoretical understanding of mixed synapses in diverse dynamical states of neural networks for self-organization and robustness still has not been fully studied yet. To understand its underlying mechanism, we here present a model of neural network built with mixed synapse connections to investigate the emergence of global and collective dynamics states. This neural networks consists of excitatory and inhibitory populations interacting together. The excitatory population is connected by excitatory synapses in small world topology and adjacent neurons are also connected by gap junctions. The inhibitory population is only connected by chemical inhibitory synapses with all-to-all interaction. We numerically show that in the networks with weak electrical coupling, the synchrony states generated by this architecture are mainly controlled by heterogeneity among neurons and the balanced of its excitatory and inhibitory inputs. More importantly, we show that the boundary between subthreshold regime and firing regimes of excitatory populations is linear. In networks with strong electrical coupling, diverse dynamical states arise from different combinations of excitatory and inhibitory weights. We show that the synchronous firing, cluster synchrony, and various ripples events (such as traveling waves) emerge by slight modification of chemical coupling weights. For large enough electrical synapse coupling, the whole neural networks become synchronized. Our results pave a theoretical way in the study of the dynamical mechanisms and computational significance of the contribution of mixed synapse in the neural functions.Fondecyt projects 3170342 (KX) and 1181076 (PO) from CONICYT, Chile. ICM-MINECON, Proyecto P09-022-F, CINV, Chile.



27) Increased expression of serine racemase in the brain induced by aging and systemic inflammation

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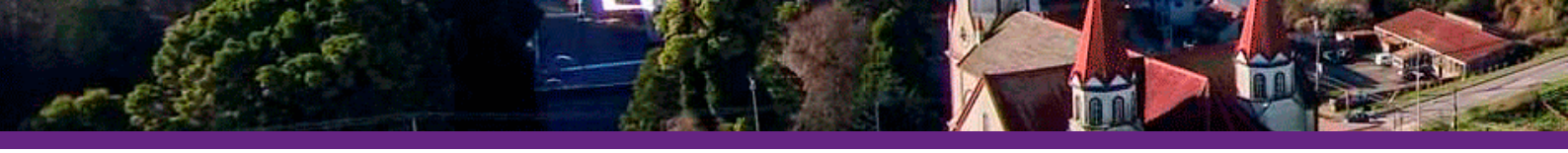
D-serine is a Dextro aminoacid and an endogenous co-agonist of the glutamate N-methyl-D-aspartate receptor (NMDAR). Synthesis of D-serine by serine-racemase (SR), and its release, are increased in inflammation, potentiating excitatory transmission by glutamate, but also potentially facilitating excitotoxicity. Similarly, whereas a mild chronic inflammatory response may facilitate a robust activation of astrocytes and microglia in response to stressors, overactivation may lead to abnormally increased levels of D-serine, potentiating further NMDAR-mediated neurotoxicity. Thus, we postulate the existence of aging-dependent changes on SR expression, probably associated with impairment in the inflammatory response. Juvenile and adults mice (3 and 12 months old C57/BL6/j mice, respectively) received a single i.p. injection of vehicle (PBS) or 0.5 mg kg-1 LPS to induce systemic inflammation. After 24 h, mice were perfused with Hank's buffer to obtain brain lysates, or with PBS and fixative for morphological studies. Serine racemase content was measured by western blot, and its presence in microglia and astrocyte was evaluated by triple SR-IBA1-GFAP immunofluorescence in 20 µm sections of brain cortex and hippocampus. We observed that SR expression in the brain was increased in adults compared with juvenile mice. In addition, LPS induced a robust increase in the number of reactive astrocytes and microglia in the cortex and hippocampus, and a mild increase in SR expression, observed mainly in astrocytes of adult mice. Our data supports the existence of aging-dependent changes on SR expression associated with inflammatory activation, suggesting the existence of an unexplored role of D-serine during systemic inflammation.

Funded by Grant FONDECYT 1171645 (RvB) & FONDECYT Postdoctoral Grant 3180553 (SBC)



28) c-Abl tyrosine kinase regulates autophagy in models of Alzheimer´s disease

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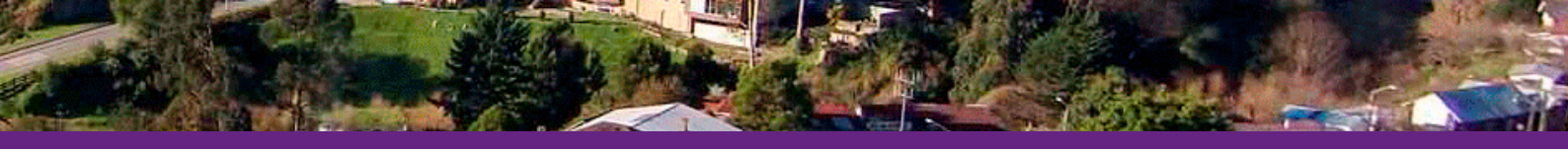
Introduction:
Alzheimer´s disease (AD), the most common form of dementia, is characterized by progressive accumulation and aggregation of two types of proteins in the brain; the β-amyloid peptide (Aβ) andthe hyper phosphorylated tau protein. Autophagy is a cellular process by which cytosolic components and organelles are recycled. It has been proposed that autophagy has a key protective role in neurodegenerative diseases, preventing the accumulation of toxic proteins. The tyrosine kinase c-Abl is activated in AD and recently it has been shown that its inhibition promotes autophagy. Here we studied whether c-Abl could be regulating the process of autophagy in AD models.

Materials and methods:
We used three AD models: i) *in vitro,*the CHO cell line stably expressing the human β-amyloid precursor protein (APP) with the Swedish mutation, ii) *in vivo,*the AD transgenic mice (APPswe/PSEN1Δ9) and iii) the AD transgenic mice with genetic deletion of tyrosine kinase c-Abl. In the first two models, treated with c-Abl inhibitors, and in the AD model with genetic deletion of the c-Abl, we evaluated autophagy markers.

Results:
In AD models, we observed an autophagic flux reduction with an accumulation of the proteins p62 and LC3-II. The autophagic flux was restored in presence of c-Abl inhibitors and its genetic absence.

Discussion:
Our results suggest that c-Abl activation in AD models could be inhibiting the autophagy process, contributing to the AD pathology.

FONDECYT 1161065 to AA, CARE-Chile-UC AFB170005 and FONDEF D10E1077.



29) Evaluation of alterations in the excitation-inhibition equilibrium in an animal model of autism induced by VPA

Lara Marcelo[1], Rodríguez Valentina[1], Morales Bernardo[1], Rojas Patricio[1]. [1]Biología , Química y Biología, Universidad de Santiago de Chile.

Autism is the most common Autism Spectrum Disorder affecting approximately 1% of the world population. The etiology of this disorder is still unknown, however, environmental factors such as prenatal exposure to valproic acid (VPA) are involved in the generation of this disorder. Studies in humans and animals have show alterations in the action of certain neurotransmitters in areas such as the cortex and the hippocampus. About 50% of patients with autism have epilepsy in adult stages. Evidence has shown that both disorders have a series of mechanisms in common, such as alteration in the excitation-inhibition equilibrium, changes in the morphology of temporal structures and changes in brain electrical activity. The main evidence has identified changes in the level of expression of GABAA receptor subunits and chloride co-transporters. This is why the objective of this work focuses on studying the glutamatergic and GABAergic alterations in the dentate gyrus in an animal model of autism and how these increase the probability of generating seizures. Through the generation of behavioral tests of social interaction and anxiety, the animal model induced by VPA was validated. On the other hand, extracellular field recordings in VPA animals identified GABAergic and glutamatergic alterations in the dentate gyrus, where an increase in excitation in VPA animals was observed. This laid the foundations for understanding the mechanisms by which the comorbidity of autism and epilepsy in humans is generated.

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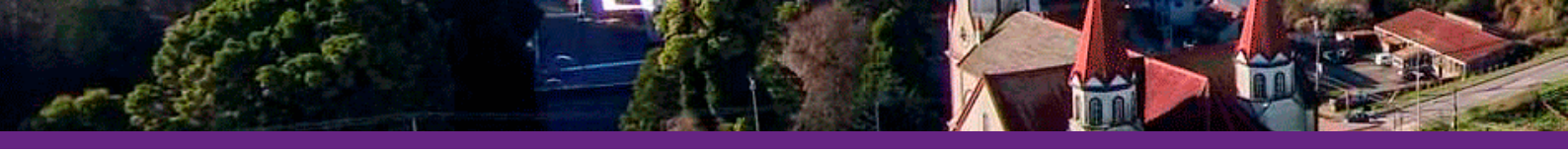
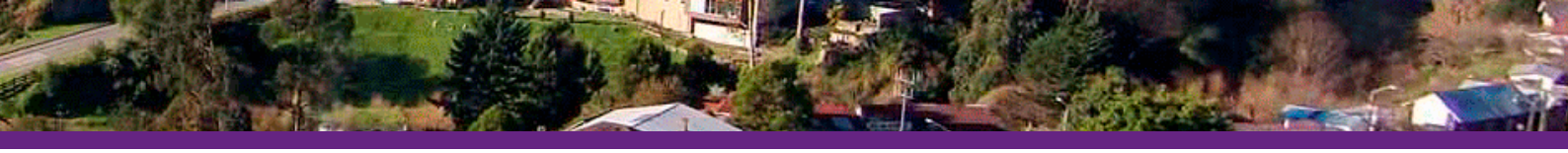


30) 5-HT2 and TRPV1 channels interaction in anxiety-like behaviors

Haro-Acuña V[1,2], Estay S.F[2], Meza R[2], Chávez A.E[2], Moya P.R[1,2]. [1]Laboratorio de Neurogenética, Instituto de Fisiología, Facultad de Ciencias, Universidad de Valparaíso. [2]Centro Interdisciplinario de Neurociencias de Valparaíso, CINV, Universidad de Valparaíso.

Serotonin (5-HT) system has a key role in the pathogenesis of anxiety disorders and it is known that activation of 5-HT2 type receptor (5-HT2R) induces anxiety-like behaviors in mice. Interestingly, the same outcome is observed following activation of the vanilloid receptor TRPV1, a nonselective ligand-gated cation channel well-known to regulate synaptic transmission and neuronal function associated with pain sensation, but that is also expressed in the brain. As 5HT2Rs are G coupled receptors (Gq11) which activation produce a variety of lipid mediators including the endovanilloids/endocannabinoid anandamide, it is possible to suggest that 5-HT2Rs and TRPV1R might interact to regulates anxiety-like behavior. To test this idea, first we evaluated the effect of 5-HT2R activation and found that the agonist mCPP produce anxiogenic effect in mice. Such effect was eliminated by co-administration with the TRPV1-R antagonist CPZ. Importantly, the anxiogenic effect of mCPP was completely eliminated in TRPV1 -/- mice. Moreover, we found that administration of CPZ, the antagonist of TRPV1, reverses anxiety-like behaviors in SERT -/- mice, a well-known model of anxiety. Together the data suggest that TRPV1-R is necessary for both, 5-HT2Rs-mediated anxiety-like behaviors and for the anxious phenotype of SERT-deficient mice. Currently, we are investigating the potential interaction between 5-HT2/TRPV1 to regulate synaptic function in both the prefrontal cortex and the hippocampus.

Supported by Nucleo Milenio NuMIND (NC130011) and the Millenniun Institute CINV (P09- 022F).

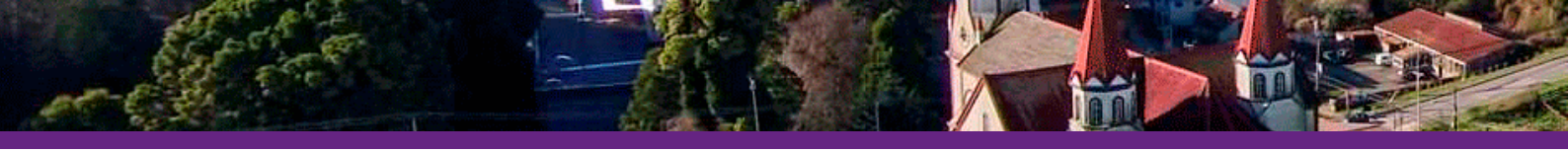


31) Role and regulation of hemichannels and pannexons in the neuropathic form of Gaucher´s disease

Rojas-Vidal Consuelo[1,2], Oyarzún Juan-Esteban[1], Yañez María-José[2], Zanlungo Silvana [2], Orellana Juan-Andrés [1]. [1]Neurología, Medicina, Pontificia Universidad Católica de Chile. [2]Gastroenterología, Medicina, Pontificia Universidad Católica de Chile. (Sponsored by Juan Andrés Orellana)

Gaucher´s disease (GD) is a neurodegenerative condition characterized by the accumulation of glucocerebroside in lysosomes as result of mutations in the β-glucocerebrosidase gene. Although the neuropathic form of GD involves RIPK3-mediated necroptosis, the cellular mechanisms associated to neuronal death remain unknown. Recent evidence indicates that plasma membrane hemichannels and pannexons may constitute a signalling pathway involved in neuroinflammation. Here, we evaluate whether the function and expression of hemichannels/pannexons as well as intracellular Ca2+ dynamics ($[Ca^{2+}]_i$) are affected by the neuropathic form of GD. SHSY5Y neuroblastoma cells were chronically treated with conduritol-β-epoxide (CBE), a β-glucocerebrosidase inhibitor, which constitute a pharmacological model of neuropathic GD. The activity and expression/distribution of hemichannels and pannexons were measured by ethidium uptake and western blotting/immunofluorescence, respectively, whereas changes in basal and ATP-mediated $[Ca^{2+}]_i$ dynamics were recorded with FURA-2. Cellular viability was measured by automatic counter cells and uptake of ethidium homodimer-1. SHSY5Y cells treated for 12-72 h with CBE exhibited a progressive increase in ethidium uptake that was accompanied with increased levels of pannexin-1 (Panx1) and connexin-43 (Cx43). Etd uptake was reverted by different blockers of Cx43 hemichannels and Panx1 channels, whereas CBE also evoked strong alterations in $[Ca^{2+}]_i$ dynamics that were partially associated to the activity of these channels. The viability was slightly affected by CBE and blockers of hemichannels and pannexons prevented this response. The CBE-mediated alterations in Cx43 and Panx1 channel function and $[Ca^{2+}]_i$ dynamics might constitute a novel mechanism underlying the pathogenesis of neuropathic GD.

FONDECYT 1160710 (JAO), Anillo ACT1411 (JAO) and FONDECYT 1150186 (SZ)

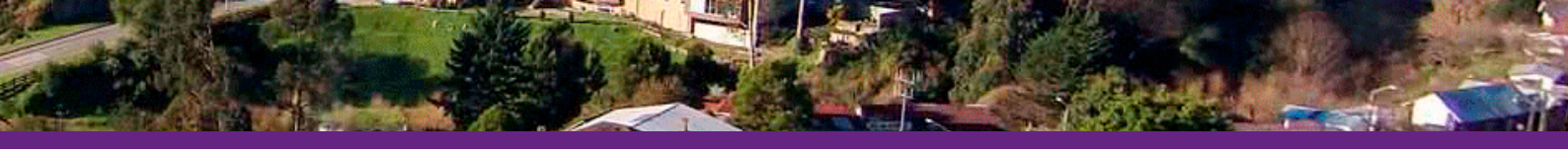


32) Abnormal neurodevelopmental progression of tonic and phasic GABAergic neurotransmission in the somatosensory cortex of a murine model of Fragile X Syndrome

Zúñiga Nolberto[1,2], Abarca Diego[1,3], Pino Gabriela[1], Cea-del Río Christian[1]. [1]CIBAP, Escuela de Medicina, Facultad de Ciencias Médicas, Universidad de Santiago de Chile. [2]Programa de Doctorado en Neurociencia, Facultad de Química y Biología, Universidad de Santiago de Chile. [3] Química y Farmacia, Facultad de Química y Biología, Universidad de Santiago de Chile.

Fragile X syndrome (FXS) is a neurodevelopmental disorder caused by the mutation of the *Fmr1* gene that silences the expression of the FMRP Protein. FMRP regulate the mobilization and translation of different synaptic mRNAs through critical periods of synaptic plasticity and adulthood. During early postnatal developmental stages, GABAA receptors (GABAARs) mediating phasic and tonic responses transition from one dominated by those containing α2/α3 and α5 subunits, respectively, in young animals, to α1- and δ-containing GABAARs in the adult. In this study, we hypothesize that inhibitory neurotransmission develops abnormally in FXS affecting the excitatory/inhibitory (E/I) balance of the network which could determine the hyperexcitability phenotype seen in the syndrome. Using a combination of immunodetection and electrophysiological techniques we analyzed the expression profiles of α1, α2, α5 and δ GABAARs subunits and their role in phasic and tonic inhibitory postsynaptic responses in P10, P14 and P21 control and FXS mice. Our results indicate that both phasic and tonic GABAA-mediate inhibition follow abnormal trajectories of neurodevelopment in somatosensory cortex of the FXS animal model. Moreover, expression profiles of α1 and δ GABAA subunits fit closely to their physiological counterpart properties. These results suggest an abnormal progression of maturation of the inhibitory drive in the somatosensory cortex of the FXS mice. Furthermore, these alterations could account for an inadequate maturation of the synaptic connectivity and E/I balance of this network, determining an inability to properly process the somatosensory stimuli.

This work was supported by FONDECYT #11150816 and the RETURN TO HOME Fellowship of the International Brain Organization (IBRO).



33) Histological description of CB-1 receptor in medulla oblongata

Cáceres-Vergara Daniela [1], Ochoa Martin [1], Irribarra Estefanía [1], Eugenín Jaime [1]. [1]Biología, Química y Biología, Universidad de Santiago de Chile.

The cannabinoid type 1 receptor (CB-1R) is widely distributed in the central nervous system, including the brainstem. This receptor modulates several functions, including breathing. The activation of this receptor depresses breathing *in vivo* and *in vitro*, however, the mechanism that generates this breathing depression is unclear. The distribution of CB-1R on the respiratory network has not been studied yet. In this work, we show the immunolabeling through immunohistochemistry and immunofluorescence for the CB-1R, in 20 µm thick cross sections of the CF1 mice brainstem. We found CB-1R-positive cells in nucleus of the solitary tract, hypoglossum and raphe nucleus. These results show that CB-1Rs are expressed in several respiratory-related nuclei of the mouse medulla, where cannabinoid activation can induce a respiratory rhythm depression.

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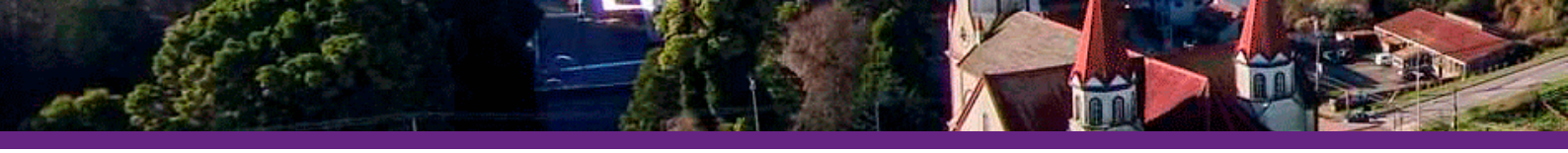
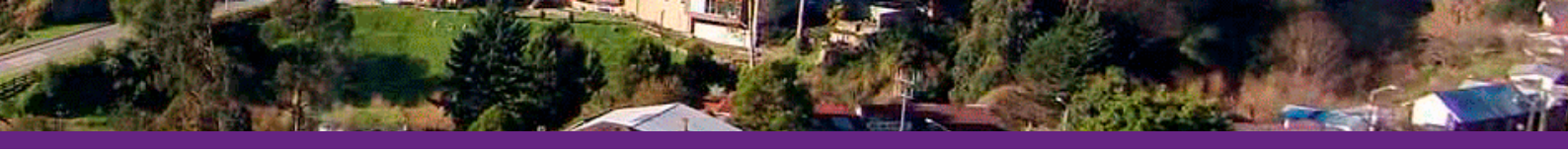


34) Glycine receptor beta subunit is related with interleukin 1B central pain sensitization

Alvarez Roberto, Solorza Jocelyn[2], Sepulveda Nicolas, **Mariqueo Trinidad** [1]. [1]Escuela de Medicina, Escuela de Medicina, Universidad de Talca. [2]Centro de Bioinformática y Simulación Molecular/Escuela de Medicina, Escuela de Medicina, Universidad de Talca. (Sponsored by FONDECYT 3170690 T.MARIQUEO Tmariqueo@utalca.cl)

The glycine receptors (GlyRs) are membrane proteins that belong to Ligand Gated ion Channels family (Cys-loop) whose function is mediate rapid inhibitory synaptic transmission in the spinal cord and brainstem. The GlyRs are constructed by five different subunits α1-4 (functional) and a βauxiliary subunit (βGlyR) assembled as homomeric receptors or as heteromeric receptors containing α and β subunits. Impairment in GlyRs mediated inhibitory neurotransmission is thought to play a critical role in central pain hypersensitivity. We evaluated the expression of βGlyR subunit in neuropathic (Chronic Constriction Injury, CCI) and inflammatory (Zymosan injected) models of chronic pain. RT-qPCR analysis of spinal cord samples showed increased βGlyR gene expression after 3 days of CCI surgery and similar results were obtained by Western blot analysis. Inflammatory pain model showed increased level of βGlyR gene expression after 4 hours. A homology model of homopentameric (5α2) and heteropentameric GlyRs (composed by 2α2 and 3β subunits) was developed and used to obtain interfaces of interaction between GlyRs and interleukin IL-1β. Our results showed that sites of interaction of IL-1β with GlyR is associated with residues belonging of the back of the loop C, Cys-loop and Pre-M1 regions of the βGlyR subunit. This binding modes involves mainly hydrogen bonds between Glu1-Asn53 (IL-1β) with Thr158 (βGlyR), Glu50-Glu51 (IL-1β) with Arg160 (βGlyR), Ala1-Val3 (IL-1β) with Tyr204 (βGlyR) and Asn53-Asp54 (IL-1β) with Arg227 (βGlyR). Taking together, these findings suggest an important, albeit underappreciated role of auxiliary βGlyR in the establishing of chronic pain sensitization.

FONDECYT 3170690 T.MARIQUEO

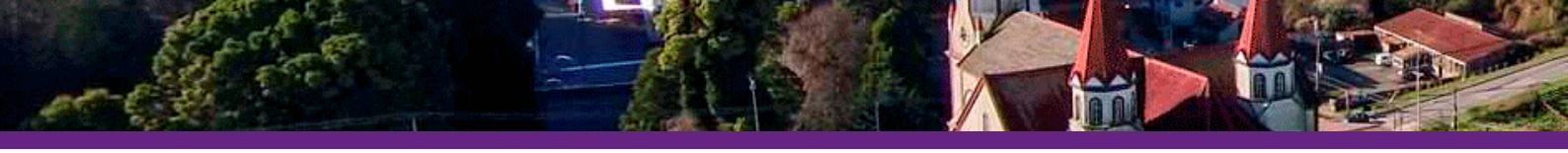


35) Learning memories, coming back in the cockroach steps

Fernández Germán Leonardo[1]. [1]Instituto de Ciencias Naturales, Universidad de Las Américas.

Learning can be understood as an internal adaptation to environmental changes, reflected as a behavior modification. This internal process involves changes in the organization and synaptic activity. One of the first experimental demonstrations of this relationship came from the experiments of Dr. Joaquín Luco during the 60´s. In those experiments, Dr. Luco amputated the front legs of cockroaches, legs used to clean the antennae. In this new condition, the cockroach must learn to stand on three of the four remaining legs to perform the task. Electrophysiological recordings of the nerves that control the hind legs of the amputated insects, showed an increase in the probability of discharge compared with the non-amputated ones. More than 50 years have passed since those experiments, and cockroaches are still used as a model of insect walk. The knowledge generated in this years, has been used, not only to understand how the cockroach is able to run and coordinate six legs without stumbling, also to develop new machine control algorithms. Despite of these researches, the plasticity of motor control circuits continues to be subject of intense debate. In our experiments, we return to the open questions of Dr. Luco using new approaches. Trying to elucidate if the changes in the response of the axons in cockroaches are due a change in connectivity or the incorporation of new neurons. These observations could give important information about the plasticity of motor control circuits and their importance in learning.

proyecto 0172017, Dirección de Investigación Universidad de las Américas.

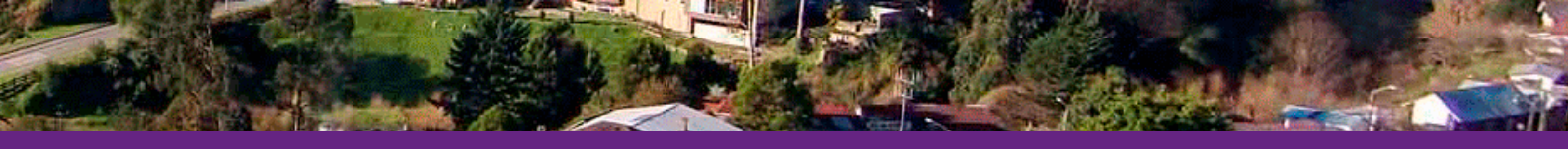


36) The blockade of Pannexin 1 channels mitigates synaptic plasticity deficits in Alzheimer´s disease model

Gajardo Ivana[1], Estay Carolina[1], Ponce Daniela[1], Lopez-Espíndola Daniela[3,2], García-Rojas Francisca[1], Silva-Villanueva Gabriel[1], Gómez Bárbara[1,3], Mery Elena[1,3], Muñoz Pablo[4,1,2], Ardiles Álvaro O.[6,1,5]. [1]Departamento de Patología y Fisiología, Facultad de Medicina, Universidad de Valparaíso. [2]Centro de Investigaciones Biomédicas, Facultad de Medicina, Universidad de Valparaíso. [3]Escuela Tecnología Médica, Facultad de Medicina, Universidad de Valparaíso. [4]Center for Applied Neurological Sciences, Facultad de Medicina, Universidad de Valparaíso. [5]Centro Interdisciplinario de Neurociencias de Valparaíso, Universidad de Valparaíso. [6]Centro Interdisciplinario de Estudios en Salud, Facultad de Medicina, Universidad de Valparaíso. (Sponsored by Álvaro O. Ardiles Araya)

Glutamate receptors are key elements for essentials brain functions including synaptic plasticity and cell survival. Their dysfunction activates of signaling pathways leading to disruptions in synaptic structure and function as commonly observed in diverse synaptopathies such as Alzheimer's disease (AD). AD is a degenerative condition characterized by an early accumulation of soluble oligomeric forms of amyloid β peptide (sAβos) that induces synaptic loss and later cognitive deficits and dementia. Emerging evidence suggests that the deleterious effects of soAβs may be mediated by ionotropic NMDARs, particularly by activation of GluN2B-containing NMDARs, metabotropic glutamate receptor mGluR5 and downstream signaling involved in the induction of Long-term depression (LTD) and dendritic spines retraction. Recently, we have reported that Pannexin 1 (Panx1), a protein forming non-selective channels, modulates glutamatergic neurotransmission and NMDAR-dependent synaptic plasticity. Indeed, we showed that the absence of Panx1 channels increase long-term potentiation (LTP) meanwhile prevent LTD. We hypothesized that the blockade of Panx1 channels in a transgenic mouse model of AD reverts the deleterious effects of sAβos on excitatory synaptic plasticity. Interestingly we found that the incubation of hippocampal slices obtained from a transgenic mouse with probenecid (PBN), a Panx1 channel blocker, increased LTP and decreased LTD, showing the opposed effects of sAβos on the threshold for the induction of NMDAR-dependent synaptic plasticity. Such effects were accompanying by a reduction in p38 MAPK activation and GluN2B mediated fEPSP, suggesting that Panx1 channels blockade interfere with sAβos signaling and could restore NMDAR function and synapse integrity.

FONDECYT #1115076, PAI #79150045 and ICM P09-022-F

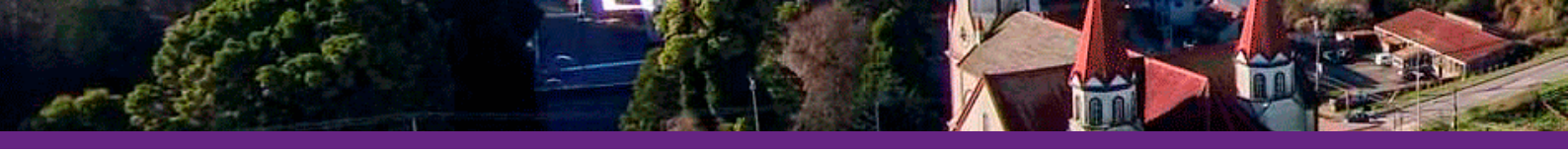


37) Changes in AMPA receptors composition regulate the development of reciprocal GABAergic Feedback onto Rod Bipolar Cells in mouse Retina

Estay Sebastián [1], Chávez Andrés[1]. [1]Centro Interdisciplinario de Neurociencia de Valparaíso, Facultad de Ciencias, Universidad de Valparaíso.

In the mammalian retina, GABAergic A17 amacrine cells provide reciprocal inhibitory feedback to rod bipolar cells (RBCs), thereby shaping the time course of visual signaling *in vivo*. Previous results have indicated that A17 feedback require both $GABA_A$ and $GABA_C$ receptors activation at the axon terminal of RBCs, whereas GABA release from A17 amacrine cells can be triggered by Ca^{2+} influx through Ca^{2+}-permeable AMPA receptors (CP-AMPA). Interestingly, this feedback inhibition is completely absent prior the eye opening (postnatal ~P15), but how reciprocal inhibitory synapses develop and are maintained remains unclear. Here, using mouse retinal slices, electrophysiology and pharmacology, we evaluated the functional properties of reciprocal feedback before and after eye opening in order to examine the role of visual information on the formation and maintenance of this reciprocal synapse. Our data suggest that before and after eye opening there were no significant differences in GABA and glutamate-evoked inhibitory postsynaptic currents (IPSCs) recorded in RBC. In contrast, we found that CP-AMPAR-mediated excitatory postsynaptic currents (EPSCs) were absent in A17 amacrine cells before the eye opening, suggesting that AMPARs with distinct subunit composition and/or function allows for selective expression of reciprocal GABAergic feedback onto RBCs after eye opening. Currently, we are investigating light-dependent changes in AMPAR subunit composition in A17 amacrine cells.

FONDECYT #1151091 (AEC), PMI UVA 1402 (SE), and Millennium Institute CINV (P09-022-F)

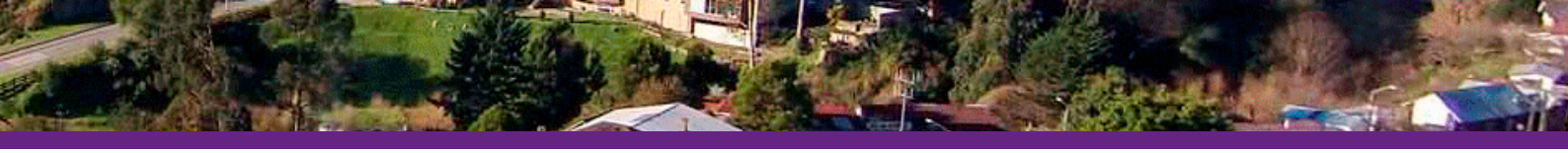


38) Neuronal glutamate transporter EAAT3 and its functional role at GABAergic inhibitory synapses

Henríquez Francisca P[2,1], Estay Sebastian F[3,2], Meza Rodrigo C[3], Moya Pablo R[1,2,3], Chavez Andrés E[2,3]. [1]Instituto de Fisiología, ciencias, Universidad de Valparaíso. [2]Núcleo Milenio Nu-MIND Biology of Neuropsychiatric Disorders, Ciencias, Universidad de Valparaíso. [3]Centro Interdisciplinario de Neurociencias de Valparaíso, Ciencias, Universidad de Valparaíso. (Sponsored by Andrés Chavez Navarrete)

EAAT3 is a neuronal glutamate transporter expressed in the postsynaptic region of glutamatergic synapses, where its activation regulates the activation of the NMDA type and mGluR1 receptors by controlling the diffusion of glutamate towards neighbor synapses (spillover). EAAT3 is also expressed at GABAergic synapses, where a lower expression of EAAT3 produces an increase in neuronal excitability and a decrease in GABA synthesis, probably by a decrease in the income of glutamate (GABA precursor) into the GABAergic cell. However, the physiological role of EAAT3 to regulate GABAergic synaptic function remains unclear. Using pharmacology, electrophysiology and an animal model with conditional overexpression of EAAT3 at GABAergic interneurons (EAAT3glo/GAD65), we evaluated the functional impact of EAAT3 at inhibitory synaptic transmission in the CA1 area of the hippocampus. Bath application of the EAAT3 specific inhibitor reduces the amplitude of GABAergic inhibitory potentials (fIPSPs) and currents (IPSCs) and decreases the input/output relationship, suggesting that under physiological conditions EAAT3 might play an important role in regulating inhibitory synapse. Next, we evaluated the functional properties of GABAergic synapse in EAAT3glo/GAD65 mice and found that while EAAT3 are, indeed, increased in the hippocampus, no changes in the excitatory/inhibitory ratio, paired pulse ratio, short-term depression and spontaneous GABA release were found, strongly suggesting that overexpression of EAAT3 at inhibitory synapses does not alter basal synaptic transmission. Currently, we are investigating the role of EAAT3 in regulating activity-dependent changes of GABAergic transmission as well as neuronal excitability in order to understand the functional role of EAAT3 in regulating inhibitory synapses.

FONDECYT #1141272(P.R.M.), #1151091 (A.E.C) , Millennium Nucleus NU-MIND MINECOM NC-130011 (P.R.M, A.E.C.), CINV Institute (P09-022-F) and CONICYT PAI/INDUSTRIA 79090016

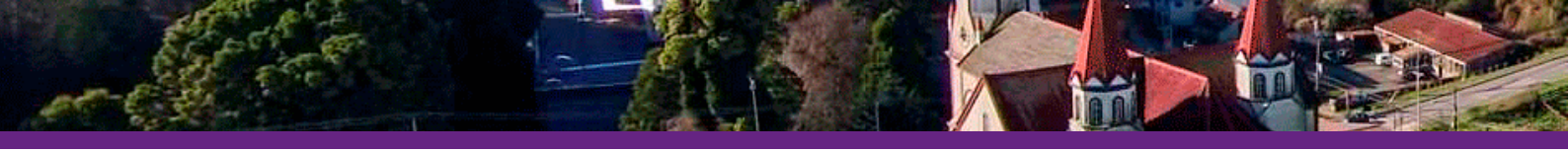


39) Effect of astrocyte activity on axon-oligodendroglia glutamatergic transmission

Vejar Sebastián Russelsh [1], Pulgar-Sepúlveda Raul [1], Varas Rodrigo[1], Ortiz Fernando C.[1] (1) Instituto de Ciencias Biomédicas, Ciencias de la Salud, Universidad Autónoma de Chile

Oligodendrocytes precursors cells (OPCs) receive glutamatergic synaptic inputs from axons in the corpus callosum (CC). It has been shown that astrocytes activation evoked OPC-intracellular calcium increases in the optic nerve, a major white matter tract. Since one of the most distinctive roles play for astrocytes is to modulate glutamatergic synapses (i.e. tripartite synapse), an astrocyte-axon-OPC interaction it is likely to occur. However, there are no studies exploring a putative modulatory role of astrocytes on axon-OPC glutamatergic signaling. To test whether astrocytes activation modifies glutamatergic synaptic inputs on OPCs we are recording callosal OPC spontaneous excitatory post-synaptic currents (sEPSC) during the pharmacological ablation of astrocytes. We have validated our approach with a proof of concept experiment where we applied fluorocitrate (FC) 3 mM (a glial cell metabolic 'poison') in order to kill astrocytes during the sEPSC recording of OPCs. Our data indicate that after ~ 15 min of FC bath application astrocytes die but no effect was found in the characteristic I-V curve of surrounded OPCs or Oligodendrocytes. Likewise, neurons were not affected by the treatment. We are currently evaluating OPC sEPSC and miniature properties before and during astrocytes ablation. Additionally, we are currently performing stereotaxic injections of the AAV-GFAP-ChR2-mCherry adenovirus in the corpus callosum of adult mice. By using this tool we project to record OPC synaptic activity during astrocyte photo-activation. This project will contribute to the understanding of the complex glia-neuron and glia-glia relationships present in the central nervous system.

FONDECYT 11160616, REDI170037 and DIUA127-2018



40) Intraoperative Alpha Relative Power Predicts Subsyndromal Postoperative Delirium In Elderly Patients Undergoing Major Abdominal

Gutierrez Rodrigo[2,1], **Egaña José Ignacio[2,3]**, Reyes Fernando[2], Briceño Consatanza[4], Penna Antonello[2]. [1]Centro de Investigación Clínica Avanzada (CICA), Medicina, Universidad de Chile. [2]Anestesiología y Reanimación, Medicina, Universidad De Chile. [3]Biomedical Neuroscience Institute, Medicina, Universidad de Chile. [4]Escuela de Terapia Ocupacional, Medicina, Universidad de Chile.

Background:
Postoperative delirium (POD) or subsyndromal delirium (POSSD) iare frequent complications, specially in elderly patients. It is associated with adverse outcomes, such as mortality. The intraoperative electroencephalographic (EEG) signal could be a promissory tool to detect patients at risk to develop POD or POSSD. The aim of this study was to determine the role of the EEG spectral analysis in the prediction of POD.

Patients and methods:
We conducted an observational study with 28 patients older than 60 years, scheduled for elective major abdominal surgery. Intraoperative EEG data was obtained with a 16 channels EEG. POD was detected with the application of the cognitive assessment method twice a day. Spectrograms were built both, before and 60 minutes after anaesthesia induction. The relative power of delta (1-4 Hz), theta (5-8 Hz) and alpha (9-12 Hz) bands were calculated.

Results:
28 patients were analysed. Two patients presented POD and 12 patients presented POSSD. There were no differences in the spectral analysis between the groups in basal state. However, 60 minutes after anaesthesia induction, patients who develop POD or POSSD have a lower alpha relative power in the spectrogram. This difference is even more marked in the occipital electrodes. Patients who develop POD or POSSD are also older and with a lower preoperative cognitive performance, evaluated with Montreal cognitive assessment.

Discussion:
A lower intraoperative alpha relative power is associated with an increased risk to develop POD or PODSS. This is only evident after the induction of general anaesthesia.

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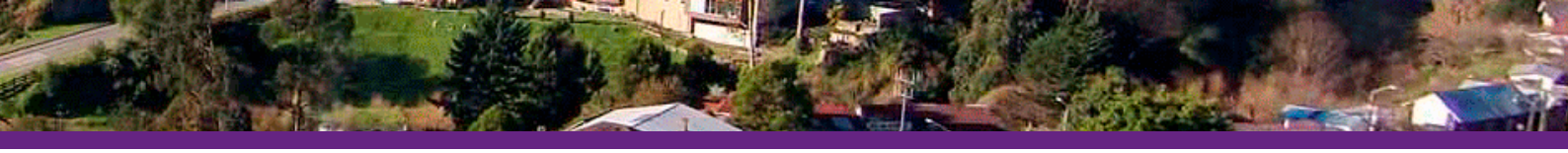


41) Contribution of Kv1.6 channels to spontaneous activity modulation on damaged sensory myelinated axons

Gonzalez Luis Martin[1], Ugarte Gonzalo[2], Díaz Paula[1], Espinoza Fernanda[1], Madrid Rodolfo[2], Calvo Margarita[1]. [1]Fisiología, Ciencias Biológicas, Pontificia Universidad Católica de Chile. [2]Biología, Quimica y Biología, Universidad de Santiago de Chile.

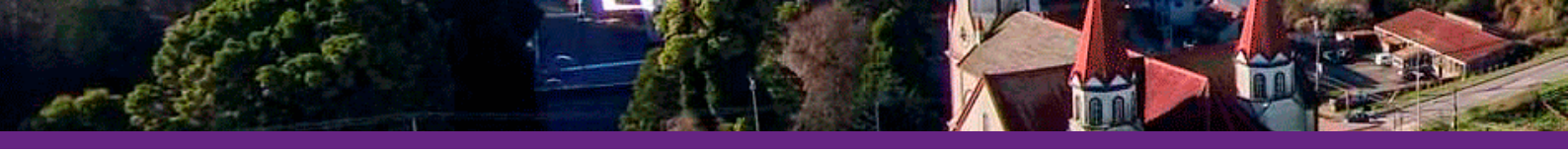
Background:
Neuropathic pain following peripheral nerve injury is associated with hyperexcitability in damaged myelinated sensory axons, which begins to normalize overtime. We have previously shown that following nerve injury, axonal Kv1 channels switches the expression of its α-subunits and are relocated, invading the paranode, which coincides with a marked reduction in spontaneous activity recorded in spinal nerves, and diminished pain behavior. Blocking Kv1 channels with αDTX reinstates hyperexcitability, but whether Kv1.6 participates in this phenomenon remains unclear.

Aim:
To describe changes in spontaneous electric activity in axons of DRG cultured explants dependent of Kv1.6 channels in vitro.

Methods:
We myelinated DRG explant cultures from d16 Sprague Dawley rat embryos. We recorded intracellular calcium changes in axons in response to 30 mM KCl. Spontaneous currents in axons were recorded in cell-attached voltage clamp configuration at 0 mV, using 10-12 MΩ sodium gluconate intracellular solution-filled glass pipettes.

Results:
DRG explant cultures showed consistent calcium responses on 44% of axons upon KCl stimulation (25,57 ± 1,07 nM 1st peak, 20,26 ± 3,48 nM 2nd peak). Recording of calcium-positive healthy axons showed that 40% presented spontaneous action potential firing, with a very low firing rate (0,013 AP/s, maximum amplitude of 195,9±47,7 pA, n=5). We would expect an increase in the firing rate on axotomized axons, as previous findings have shown on rat injured nerves. Application of αDTX on healthy axons should also increase this firing rate, whereas application of CPY-Fe1 (Kv1.6 blocker) should only affect injured axons.

Fondecyt 1161019



42) Decreased expression of NGF in skin of patients with Recessive Distrophic Epidermolysis Bullosa diminish the regeneration of nerve fibers promoting neuropathic pain

Muñoz Daniela[1], Sandoval Mauricio[2], Calvo Margarita[1]. [1]Fisiología, Ciencias Biológicas, Pontificia Universidad Católica de Chile. [2]Dermatología, Medicina, Pontificia Universidad Católica de Chile.

Chronic pain in Recessive Distrophic Epidermolysis Bullosa (RDEB) patients is a common and weakening problem. This pain can be secondary to inflammation, musculoskeletal or neuropathic. Neuropathic pain (NP) is due to a lesion or disease affecting the somatosensory system. Only unmyelinated sensory nerve fibres (peptidergic and non-peptidergic C-fibres) can cross the dermoepidermal limit and can be found in the epidermis. RDEB patients have a high rate of NP due to damage of unmyelinated and thinly-myelinated fibres that innervate the skin in a length-dependent pattern, suggesting that neuropathy is caused by recurring episodes of skin blistering and regeneration. Sensory nervous system regeneration is dependent on the production of neurotrophic factors (NFs) by innervation targets such as the skin. NGF binds to TrkA receptor and stimulates peptidergic C-fibres regeneration, whereas GDNF binds to GFRα1 receptor and stimulates non-peptidergic C-fibres regeneration. NFs expression in adult healthy skin is very low, but it increases significantly after skin injury. We postulate that this NFs expression response after nerve injury is diminished in RDEB patients and therefore present a lack of skin fibre regeneration. We have created a "skin injury model" to compare with healthy control patients. 2 skin biopsies were obtained from the same spot (day 0 and day 10 after first injury), and GDNF, NGF and BDNF expression in the skin was evaluated by qPCR. The results showed that NGF was significantly reduced in RDEB patients in this skin injury model.

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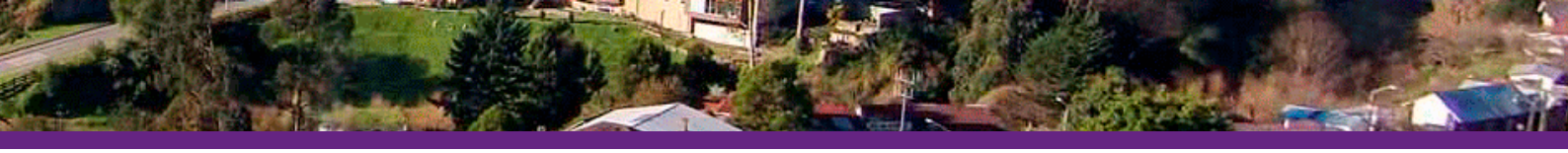


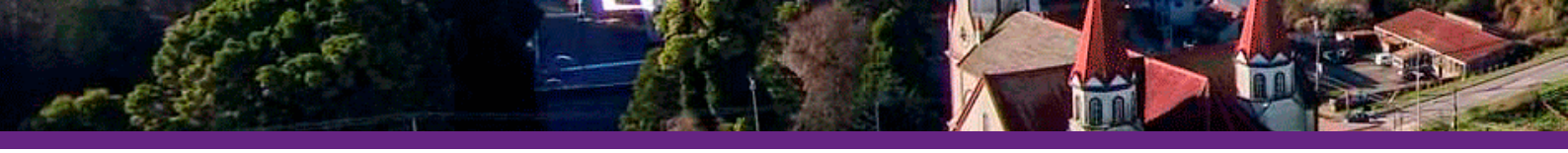
43) Effects of astrocyte activity on myelin regeneration

Pulgar Raúl[1], García-Blanes María [2], Vejar Sebastián [2], Suarez Benjamín [2], Varas Rodrigo [2], Ortiz Fernando C.[2]. [1]instituto de ciencias biomedicas, ciencias de la salud, Universidad Autónoma de Chile. [2]Mechanisms of myelin formation and repair lab, Ciencias de la Salud, Universidad Autónoma de Chile.

Demyelinating diseases, such as multiple sclerosis (MS),are characterized by the presence of demyelinated lesions in the white matter tracts of the central nervous system. Although a conservative hallmark of these lesions is the massive recruitment of reactive astrocyte, to date, their role on the demyelination/ remyelination process is not completely understood.

After a demyelination insult, there is a spontaneous repair process (remyelination) characterized by the migration, proliferation, and differentiation of oligodendrocyte precursor cells (OPC) that originate remyelinating oligodendrocytes (OL). Astrocytes release several molecules that modify OPC proliferation and differentiation, potentially affecting OL production and the consequent myelin synthesis. To answer whether astrocytes can promote remyelination we manipulate astrocyte activity in lysolecithin (LPC)-induced demyelinated lesions to test their effects at the time window that correspond to the remyelination process. To inhibit astrocyte function, we are inducing either astrocyte metabolic ablation or their genetic inactivation in lesion. Optogenetic stimulation is being performed as a gain-of-function experiment. The effect of these manipulations on the oligodendroglia population is being analyzed by the quantification of OPCs and OLs using conventional immunohistochemistry and confocal microscopy.Likewise, compound action potential (CAP) recordings and electron microscopy are being currently conducted to evaluate myelin functional recovery after astrocyte manipulation. So far, we have confirmed our experimental models and we are currently conducting cellular counting analysis. Our results will shed light on the possible glia-glia interactions involved in myelin disorders such as MS.

FONDECYT 11160616, REDI170037 and DIUA127-2018.



44) Multisensory stimuli coding in the hippocampus during a non-spatial goal-directed task

Tiznado Vicente[1]. [1]Psiquiatría, Medicina, Pontificia Universidad Católica de Chile.

The hippocampus has been at the center of neuroscience contemporary research due to its involvement in both episodic memory and spatial navigation, related to CA1 place cells' activity. However, recent findings have reported that CA1 neurons can also encode a wide variety of non-spatial, behaviorally-relevant features of the environment. In parallel, it was recently established a causal role of stimulus-related hippocampal field potential signals in the execution of goal-directed behaviors, which are key processes needed for survival. Due to the multisensory nature of experience, accomplishing these behaviors requires the association of sensory information arising from different sensory modalities related to environmental events. Nevertheless, it remains unclear how the hippocampus encodes multisensory information at the single unit level during a goal-oriented task, and the importance of this activity for behavioral performance. Here, we recorded CA1 activity while animals performed a non-spatial goal-directed task, which required learning associations of uni/bimodal stimuli with different outcomes. We found that 41% of recorded neurons exhibited stimulus encoding, which included representations of individual sensory modalities, but also their conjunctive representation. Interestingly, the proportions of neurons responding to different sensory modalities correlated with performance. Moreover, for neurons that responded conjunctively, the firing patterns for the different encoded sensory modalities also correlated with performance. These neurons were also differentially reactivated during ripples, which are relevant for functional communication between different brain areas. Taking together, these results contribute to a better understanding of how the hippocampus encodes non-spatial information and how this coding could be relevant for goal-oriented behaviors.

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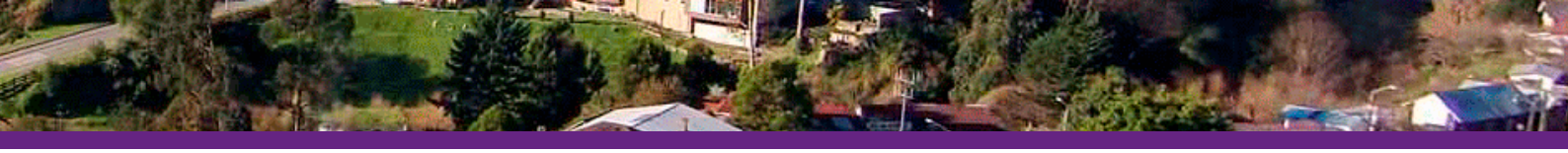

45) On the organization of habenular network in the brain of bichir, Polypterus senegalus

Ahumada-Galleguillos Patricio[1,2], Weiss Camila[1,2], Concha Miguel[1,2,3]. [1]Institute of Biomedical Sciences, Faculty of Medicine, Universidad de Chile. [2]Biomedical Neuroscience Institute, Faculty of Medicine, Universidad de Chile. [3]Center for Geroscience, Brain Health and Metabolism, Faculty of Medicine, Universidad de Chile. (Sponsored by Miguel Luis Concha Nordemann)

The bichir, *Polypterus senegalus*, belongs to basal non-teleost actinopterigeans lineages. Given its phylogenetic position, the understanding of brain organization in this fish has primary relevance to address brain evolution in vertebrates and, specially, in more derived groups, as teleostei. The habenula (Hb) is part of an extended brain network involving forebrain, midbrain and hindbrain. At evolutionary level, the conservation of the afferent circuitry of Hb differs from the shift on its efferents, from sensorial (i.e. lampreys and teleostei) to limbic (i.e. mammals). This observation suggests a change in the contextual information that is used by different species to activate habenular circuits. In this context, there is few antecedent regarding the organization of habenular network in bichir. Furthermore, it is unknown if the remarkable asymmetry between the left and right Hb of bichir could be coded into the afferent and/or efferent connectivity pattern of habenular system of this fish. To address this issues we focus on description of the organization of habenular network of *Polypterus senegalus*. Methodologically, we have used anterograde and retrograde neuronal tracers, histology and immunohistochemestry.

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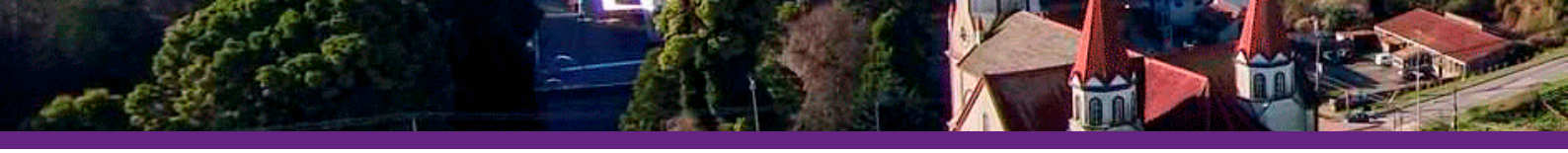
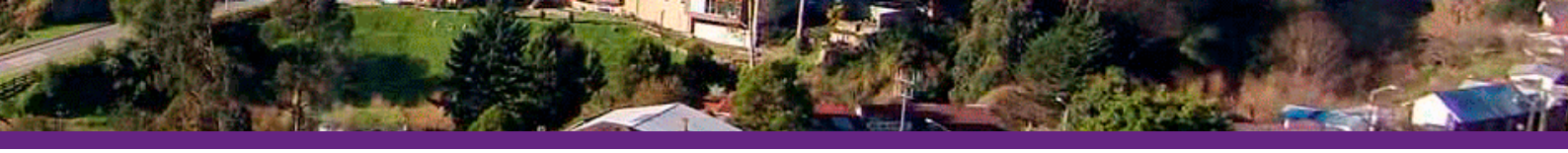


46) P2X7 receptors in the rat nodose ganglion neurons and their role in sensory modulation

Alcayaga Julio[1], Del Rio Rodrigo[2,4,3], Vera Jorge[1], Retamal Mauricio A.[5]. [1]Departamento de Biología, Facultad de Ciencias, Universidad de Chile. [2]Centro de Excelencia en Biomedicina de Magallanes (CEBIMA), Unversidad de Magallanes. [3]Departamento de Ciencias Fisiológicas, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile. [4]Centro de Envejecimiento y Regeneración (CARE), Pontificia Universidad Católica de Chile. [5]Centro de Fisiología Celular e Integrativa, Facultad de Medicina, Clinica Alemana Universidad del Desarrollo.

Nodose ganglion (NG) sensory neurons express ionotropic nucleotide receptors (P2X), which activation depolarizes and increases discharge frequency of NG neurons. Although most evidences indicate that $P2X_2$ and $P2X_3$ are the most conspicuous subunits in NG, $P2X_7$ receptor agonists have been reported to increase NG activity. Thus, we studied the effects of $P2X_7$ receptor agonists and antagonists, and the cellular distribution of this receptor in the rat NG. The NG and vagus nerve (n=20) were excised from anesthetized (pentobarbitone 60 mg/kg) adult male rats, superfused *in vitro* with Hanks' saline at constant flow (1.2 mL/min), temperature (38±0.5 °C) and pH (7.43). The NG was placed in a chamber and the vagus nerve recorded using a differential AC amplifier; the signal was amplified, band pass filtered (0.1-1000 Hz), recorded, and the discharge frequency (f_{VN}) assessed (in Hz) with a spike discriminator and counter. For immunohistochemistry, the ganglia were immersed in cold buffered 4% paraformaldehyde, permeabilized, processed, stained with a mouse anti-$P2X_7$ monoclonal antibody and visualized using confocal laser microscopy. $P2X_7$ agonist (benzoyl-ATP; 0.05-2 mM) produced brief, dose-dependent increases of f_{VN}, which mean maximal magnitude was 60% of that induced by 500 µg of ATP (261±35 Hz); a $P2X_7$ antagonist (A-804598; 1µM) reduced the responses induced by benzoyl-ATP and ATP. $P2X_7$ immunoreactivity was localized mostly in NG neurons and some axonal process, with no positive staining of glial-like structures. Our results indicate that NG neurons constitutively express $P2X_7$ receptors and that they may participate in the generation or modulation of afferent activity.

FONDECYT 1130177 (JA), 1180172 (RDR) and 1160227 (MAR)

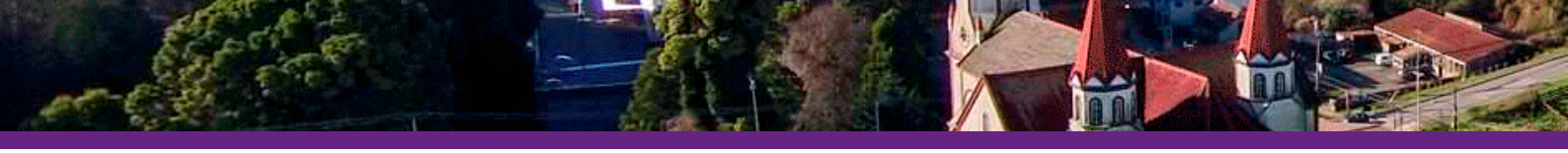


47) Comparative Electrophysiological Assessment of Bipolar Cell Properties in Organotypic Retinal Culture of Mouse and Rat

Calbiague Víctor Manuel[1], Cádiz Bárbara[1], Pires Ronakarina[1], Vielma Alex H.[1], Schmachtenberg Oliver[1].
[1]CINV, Ciencias, Universidad de Valparaíso.

One of the CNS tissues most sensitive to chronic high glucose levels is the retina. Despite our increasing knowledge about the biochemical processes involved in glucoseneurotoxicity, little is known about the electrophysiological consequences of chronic high glucoseon individual neurons and neuronal circuits. Rodent retinal explants cultured for up to three weeks allow to investigate early morphological and functional alterations caused by elevated glucose. Specifically, electrophysiological antecedents including the electroretinogram suggest that retinal bipolar cells, which transmit and filter information from the outer to the inner retina, may serve as sensitive early biomarkers forincipient neuronal damage caused chronic high glucose conditions.Here, we compared the electrophysiological profiles of specific bipolar cell types with data from ex-vivo retinas of mouse and rat organotypic retinal explants after 1 to 3 weeks in culture under high glucose conditions (25 and 30 mM equivalent to 450 and 540 mg/dL, respectively). Our results indicate that electrophysiological recordings of different BC types from rat and mouse retinal explants cultured under high glucose concentrations are readily obtained for up to three weeks in culture. Although the retinal layers display a progressively reduced thickness in culture, bipolar cells retain their electrophysiological fingerprints and remain morphologically identifiable for up to two weeks. Furthermore, responses to glutamate and endogenous inhibitory responses are routinely observed, indicating that the retinal circuitry remains intact during this period. In conclusion, both rat and mouse retinal explants are useful for the study of high glucose neurotoxicity in retinal explants trough the analysis of their electrophysiological properties.

FONDECYT REGULAR No. 1171228, Millennium Institutive CINV, and CONICYT PhD scholarship 2018.

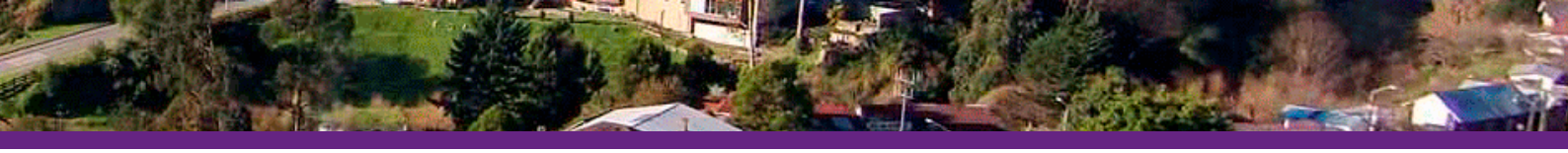


48) Subdomains of the Accessory Olfactory Bulb exhibits steady differences at Granular Cell Layer along ontogeny

Delgado Scarlett Elizabeth[1], Fernández-Aburto Pedro[1], Mpodozis Jorge[1]. [1]Biología, Ciencias, Universidad de Chile.

The mammalian Vomeronasal System (VNS) is a pheromone-sensitive olfactory system associated with modulation of socio-sexual behaviors. In most mammals it is constituted by two subdomains, anatomically segregated at the Accessory Olfactory Bulb (AOB): anterior (aAOB) and posterior (pAOB). AOB is also one of the brain areas where neurogenesis takes place during whole lifespan. These cells, mostly Granular (Gr) interneurons, form dendrodendritic synapse with secondary projection cells, affecting learning processes associated with semiochemicals. Some species of caviomorph rodents exhibit specie-specific morphometric differences between the AOB subdomains. These differences are not innate, but develop during early post-natal stages. In the social rodent Octodon degus, the aAOB has twice the volume of pBOA, along with more glomeruli and secondary projection neurons. At present, is not known whether cells of the Granular Cell Layer (GrCL) associated to each of the AOB subdomains exhibit morphometric differences, nor it is known whether these presumptive differences are innate or dynamic during ontogeny. We estimate in *Octodon degus* the volume and the number of cells of the GrCL in both AOB subdomains at different postnatal stages, performing unbiased stereological measurements on sagittal AOB sections stained with Nissl. We found that the volume and the number of cells at the GrCL were in all stages two or three times larger in the aAOB than in the pAOB. At the aAOB these values undergo minimal postnatal changes, while at the pAOB they decrease from P30. This ontogenic dynamic agree closely with the developmental course of maturity of the AOB

FONDECYT #1170027



49) Do you see what I am saying? Electrophysiological correlates of visual speech perception and automatic mimicry

Michon Maëva[1], Boncompte Gonzalo[2], López Hernández Vladimir[1]. [1]Psicología, Ciencias Sociales, Pontificia Universidad Católica de Chile. [2]Laboratorio de Neurodinámicas de la Cognición, Medicina, Pontificia Universidad Católica de Chile. (Sponsored by Comisión Nacional de Investigación Científica y Tecnológica)

The role of visual and motor systems have long been undervalued by traditional theories of speech perception. As a consequence, it remains unclear if the articulatory information carried by visual speech perception can activate motor systems and to what extent its activation can be interfered by restricting the orofacial effectors of the observer. To elucidate this, 34 participants were recorded with a 64-Channel EEG device (BioSemi) while they attentionally observed or imitated short videos displaying 4 types of orofacial movements (i.e., still mouth, syllables, backward-played syllables and non-linguistic mouth movements) and non-biological movements. The experiment consisted in 2 blocks, one where participants freely observed the videos and another where participants were asked to hold an effector depressor horizontally between their teeth during the observation of the videos. The blocks were counterbalanced between subjects. The time-frequency analysis of the signal revealed a significant difference between the syllables and backward-syllables conditions in Mu and Beta frequency bands. Mu rhythm has been reported to be a good candidate to appreciate mirror neuron system activity as Mu power consistently decreases during the execution or the observation of an action. Interestingly, when participants were holding the effector depressor the Mu suppression between syllables and backward syllables was no longer significant. The results are discussed in line with a trimodal repertoire for speech proposed by the authors that very likely emerge from imitation and social cognition skills.

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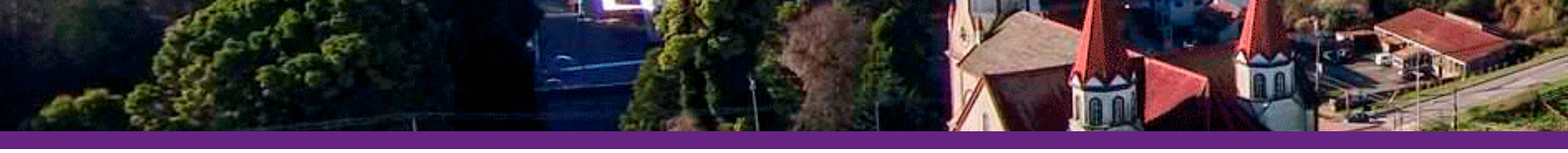

50) The Beta nature of olfactory oscillations in rainbow trout (Oncorhynchus mykiss)

Olivares Jesus[1], Orio Patricio[1], Schmachtenberg Oliver [1]. [1]Neurociencia, Ciencias, Universidad de Valparaiso.

Although the role of neural oscillations evoked by odors in the olfactory system of vertebrates is not yet understood, there is evidence that synchronization of neural networks in specific frequencies may allow to isolate transient communication pathways between distant brain regions that, even with weak synaptic connections, remain temporally connected, allowing several separate analysis processes in parallel. Beta rhythms have been recorded in different structures of the olfactory system and in many species of mammals including mouse, rat, cat, dog, rabbit and vole, and it has been demonstrated that these oscillations emerge and are modulated by olfactory tasks like odor learning and odor sensitization. Beta oscillations have never been observed in absence of odor stimulation. Here, we stimulate and record, electrophysiological activity from four olfactory areas of the olfactory system in parallel, in anesthetized rainbow trout (*Oncorhynchus mykiss*), by electroolfactogram recording from the olfactory epithelium (OE), and LFP oscillation recordings of olfactory bulb (OB), and two olfactory regions from the telencephalon: ventral nucleus from ventral telencephalon (Vv), and dorsal posterior area (Dp). Our results show prominent oscillations with a dominant frequency between 6.7 – 8.1 Hz in the three recorded regions, with a high degree of coherence (over 0.6) between them. These oscillations disappear if OB-telencephalon connections are mechanically ablated, suggesting the "beta" nature of this oscillations.

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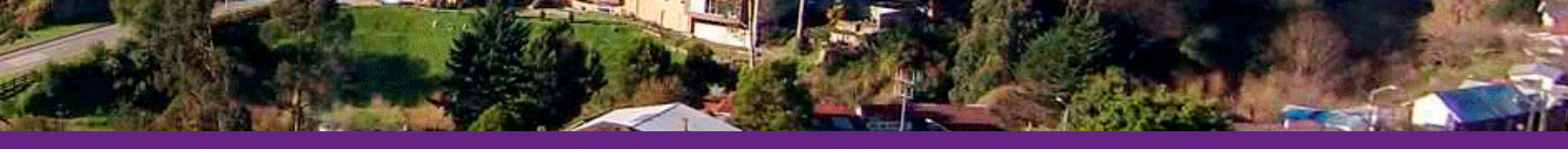

51) Dopaminergic modulation of inhibitory signaling in the mouse retina

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Retinal dopamine (DA) is an important neuromodulator that participates in light adaptation, contrast sensitivity and visual acuity. It is widely accepted that DA synthesis is induced by light in specialized amacrine cells (DAC), whose processes extend across both plexiform layers of the retina. It has been reported that DA participates in the regulation of electrical coupling and the excitability of different retinal cells types by regulating voltage-activated sodium, potassium and calcium channels. Moreover, DA can inhibit GABA release from amacrine cells. However, how these dopamine actions affect inhibitory transmission onto bipolar cells and signal input to ganglion cells is unclear. Here, using electrophysiological recordings, we analyzed the role of the dopaminergic system in the control of basal inhibitory activity in bipolar and ganglion cells of light and dark adapted mouse retinal slices. Our results indicate that in dark adapted conditions, bath application of DA (50 mM) increased the frequency and amplitude of inhibitory activity in ON bipolar cells, whereas it decreased frequency but not amplitude of inhibitory activity in ON ganglion cells. In contrast, inhibitory activity in OFF bipolar and ganglion cells remains unchanged. In photopic conditions, frequency but not amplitude of inhibitory activity was decreased by DA in ON cone bipolar cells, but increased in OFF ganglion cells. Currently, we are studying the contribution of different DA receptors to unravel this complex modulation circuit, whose importance is fundamental to understand the development of retinal pathologies like myopia, in which dopamine signaling is involved.

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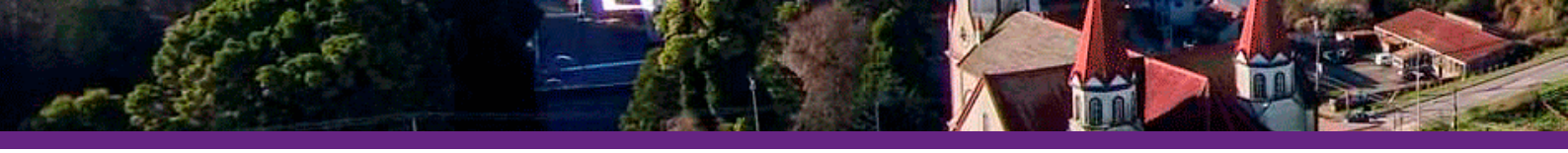
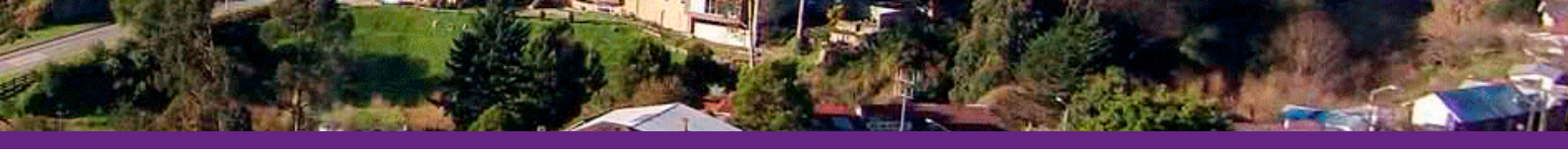


52) Inhibitory role of corticotrophin releasing factor receptor type-2 in the basolateral amigdalar-medial prefrontal cortex transmission of the rat

Yarur Hector Eduardo [1], Vega-Quiroga Ignacio[1], González Marcela[1], Noches Verónica[1], Ciruela Francisco[2], Andrés Maria E.[1], Gysling Katia[1], [1]Cell and Molecular Biology, Biological sciences, Pontificia Universidad Catolica de Chile, [2]Unitat de Farmacologia, Universitat de Barcelona

Basolateral amygdala (BLA) excitatory projections to the medial prefrontal cortex (mPFC) play a key role within the circuitry controlling stress behaviors, pain and fear. Stressful events block synaptic plasticity between BLA and mPFC. Interestingly, in stress responses, corticotrophin releasing factor (CRF) is a key component acting through type 1 and type 2 CRF receptors (CRF1 and CRF2). Importantly, while CRF1 has been involved in mPFC functioning, the participation of CRF2 in BLA-mPFC synaptic transmission still is unclear. Here, we provide direct evidence of the presynaptic expression of CRF2 mRNA and protein in mPFC nerve terminals originated in BLA. We also show that dopamine D1 receptors (D1R) colocalize with CRF2 in these mPFC nerve terminals. Intra mPFC infusion of antisauvagine-30 (aSvg-30), a CRF2 antagonist, increased glutamate levels induced by BLA activation. Interestingly, the increase in glutamate release observed in the presence of aSvg-30 was significantly inhibited in the presence of SCH23390, a D1R antagonist. These findings show that CRF2 is expressed in BLA nerve terminals in mPFC and that it exerts an inhibitory role in the synaptic transmission between BLA and mPFC. In addition, our results also show that the inhibition of mPFC CRF2 unmasks the effect of D1R over the connectivity between the BLA and mPFC. Overall, CRF2 emerges as a new modulator of the BLA-mPFC connection that it has been shown to play a critical role in emotional disorders.



53) Effects of human conditioned serum and electric pulse stimulation on TLR4 signaling on human primary myotubes

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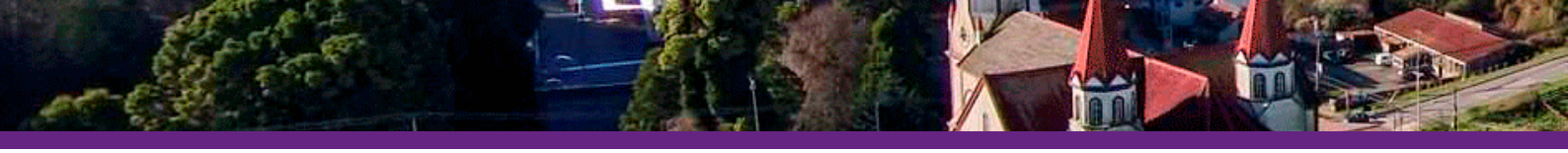
Background:
Obesity has become a global health challenge that leads to insulin resistance, low-grade chronic inflammation and ultimately to Type 2 Diabetes. Exercise has demonstrated anti-inflammatory effects. The mechanisms involved are still unknown but probably includes Toll-like Receptor (TLR) signalling. Exposure to low-doses of exogenous ligands including LPS, NEFA as well as heat shock protein (HSP70) may reduce TLR4 expression.

Aim:
To determine the effect of electrical stimulation (EPS) (endurance exercise mimetic) incubated with human serum collected at rest or post-exercise on TLR4 expression and signalling in lean subjects in primary cell culture.

Methods:
Human myoblast were obtained from muscle biopsies of 3 different healthy sedentary volunteers. Cells were differentiated for 7 days in conditioned serum collected at basal and immediately after exercise from Normal and Diabetic blood donors. Afterwards, myotubes were EPS for 8hr.

Results:
8hr-EPS activated AMPK, which indicates an in vitro exercise-like effect. Normal exercise-conditioned serum significantly reduced phosphorylation of TAK1 and P38MAPK ($p < 0.05$), with no change on TLR4 protein. An EPS effect was observed on TAK1 and ERK1/2 MAPK phosphorylation, with no changes in others proteins of the TLR4 signaling. In contrast, an increased effect was observed in normal myotubes differentiated in diabetes-conditioned serum. Findings showed increased phosphorylation of TAK1, and NFκβ-p65, increased protein content but both decreased phosphorylation of ERK1/2 and P38-MAPK, and a serum/EPS interaction effect on TLR4 protein, NFκβ-p65 and ERK1/2. **Conclusion:** *EPS and pooled serum obtained from individuals undergoing the prolonged endurance exercise modified TLR signalling in human primary cells.*

This study was funding by FONDECYT iniciation 11150576 (HZ)



54) **Somatostatin containing interneurons of dentate gyrus participate in pattern separation mechanism**

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Pattern separation is the process that ensures that similar memories will be stored in different way. For this process is important to keep a low excitability of granule cells, a principal neuron of dentate gyrus (DG). To understand the mechanism of pattern separation, we studied in transgenics mice the physiological and behavioural effect of optogenetic inhibition of somatostatin containing interneurons of dentate gyrus (SOM). In electrophysiological experiments we found that inhibition of SOM produces an increase inthe firing rate of units that have longer duration and higher burst index, two characteristics of excitatory neurons of DG, within which are the granule cells. Next, in behavioral experiments, we tested if this change in firing rate of granule cells could affect pattern separation process. For that we measured the performance in discriminate two similar spatial configurations in mice that were implanted bilaterally in DG with optical fiber. We found that inhibition of SOM in encoding phase of the test affect the discrimination of two similar contextual-spatial configurations. According with our results, we propose that pattern separation mechanism involve activation of SOM, while memories are being encoded, ensuring low excitability of granule cell. For other hand, loss of SOM (which happens in epileptic and aged mice) would implicate problems in pattern separation mechanism.

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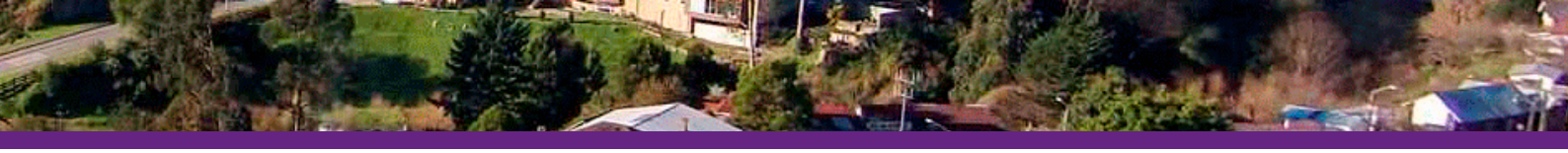

55) Protective effect generated by social interaction in a murine model of psoriatic dermatitis

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Psoriasis is one of the most common chronic inflammatory diseases that affects 2-3% of the adult world population. From the histological point of view, it is characterized by an aberrant proliferation of keratinocytes produced by the activation of T cells, triggered by various stimuli, such as: skin traumas, microbial infections, stress, ultraviolet light, as well as genetic predisposition. Among the factors that trigger the recurrence of the disease, previous stress events have been identified that increase the severity of the injuries or trigger a new cycle of the same. There is no empirical evidence of a possible protective effect that testosterone would generate in psoriatic patients, producing a decrease in histological manifestations and the severity of the disease. This study evaluated the protective effect generated by social interaction in a murine model (Mus musculus BALB / c) of psoriasiform dermatitis, by analyzing the response of adult males to exposure to congeners and females, prior to the induction of dermatitis. psoriasiform, by applying imiquimod to 5%. The results of the histological analysis of the skin and of proinflammatory cytokines suggest that the social interaction in the studied model exerts a protective effect decreasing the severity of the clinical manifestations of psoriasiform dermatitis. The results are discussed in the light of the possibility of providing more information on the mechanism by which social interaction and testosterone secretion modify the progression of the disease in a murine model

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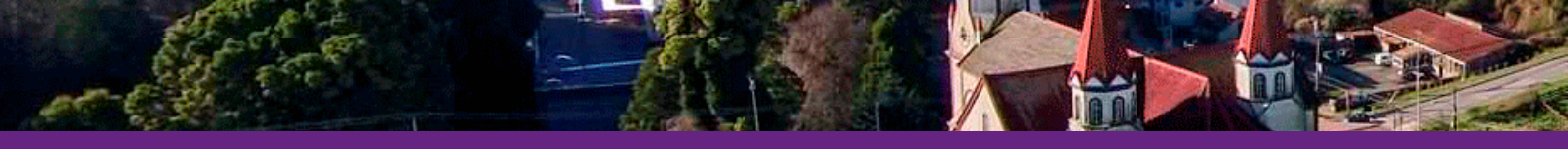

56)Contribution of NMDA receptors to the acquisition of hippocampal neuronal polarity

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Glutamate is the main excitatory neurotransmitter in the central nervous system. NMDA receptors (NMDARs) are Ca^{2+} channels activated by glutamate participating in neuronal maturation and synaptic plasticity, playing essential roles in the development and functionality of the nervous system. However, the contribution of NMDARs to neuronal polarity and axonal specification in young hippocampal neurons has not been explored. In this work, we studied the contribution of the NMDARs to the establishment of neuronal polarity. Our immunoblotting and immunocytochemical data showed that NMDARs are expressed during neuronal polarity acquisition and are functional due to the fact that agonist treatments increased calcium influx, which was blocked by specific antagonists. Although NMDARs classically act at postsynaptic membrane, we found that endogenous and transfected NMDARs were distributed also in the axonal compartment early in development, suggesting new roles in the early neuronal development. Moreover, NMDARs loss- and gain-of-function altered neuronal polarization and axonal elongation by a mechanism that involves Ca^{2+} release from endoplasmic reticulum (Ca^{2+}-induced Ca^{2+} release, *CICR*), Rac1 activity and actin cytoskeleton dynamics. Finally, we found that NMDARs activity also regulates Reactive Oxygen Species (ROS) production, signalling molecules that are instrumental to support neuronal development. Together, our results suggest that early physiological glutamate presence activates NMDARs to support early neuronal development previous to synapse formation, supporting the notion that glutamate is not only necessary for neurotransmission but also for early neuronal development and axonal growth.

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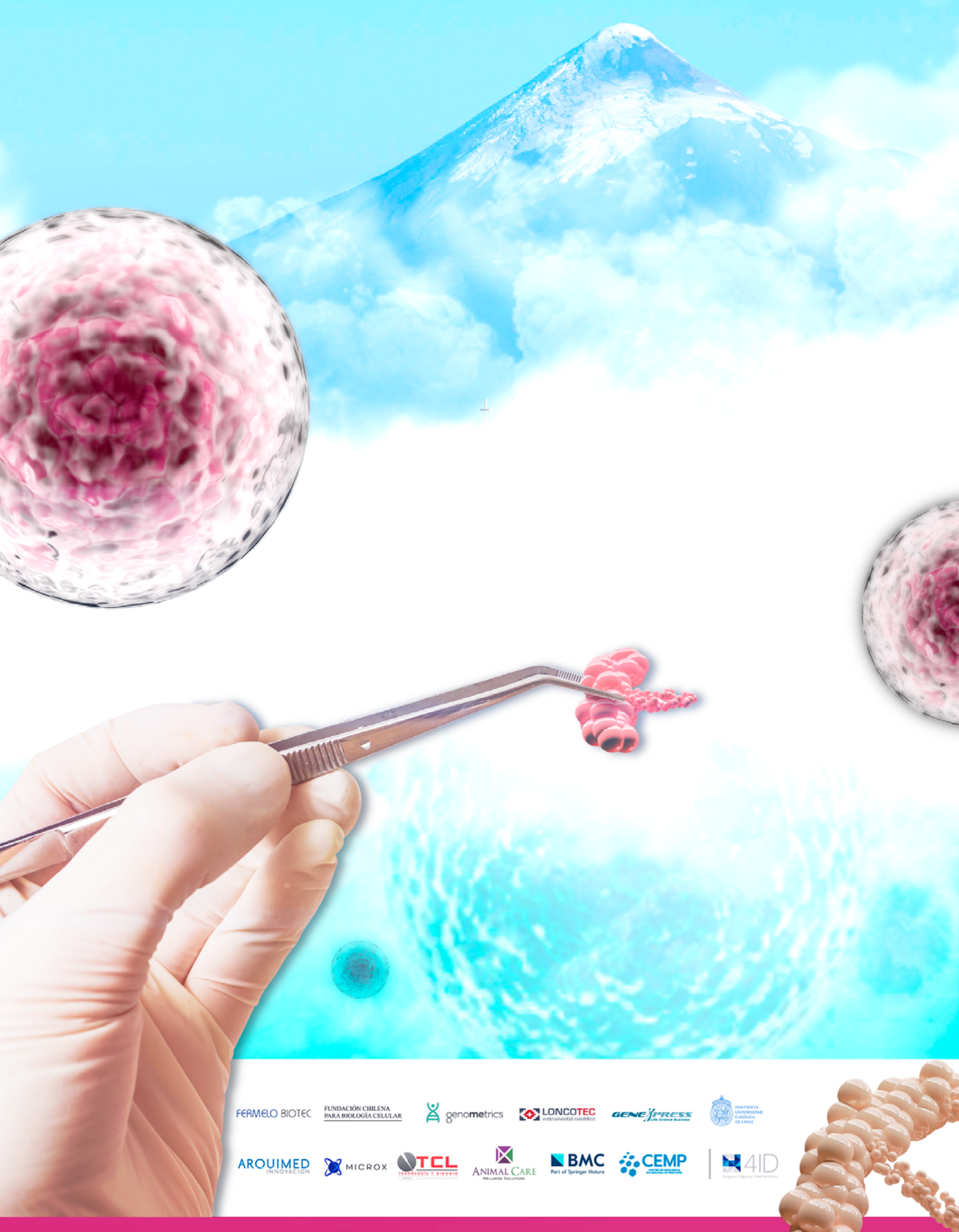
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