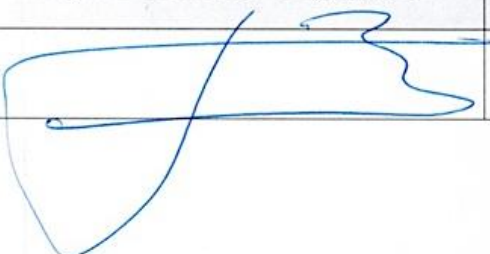
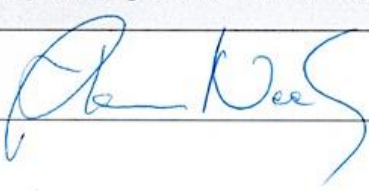


Name of the Center:	
Acronym	CINV
Code	P09-022-F
Reported period	January 1 to December 31, 2015
Starting date of the Center	08-08-2011
Address	Pasaje Harrington 287, Playa Ancha
Telephone(s)	056-032-2508040
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Host Institution(s)	Centro Interdisciplinario de Neurociencia de Valparaíso, Universidad de Valparaíso, Pontificia Universidad Católica de Chile, Universidad Nacional Andrés Bello, Universidad de Chile.
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1.1 Executive Summary

We created the **Centro Interdisciplinario de Neurociencia de Valparaíso (CINV)** with the goal of building the most important center for Neuroscience research in Chile. As a Millennium Institute (MI), during the first five years of the project, we have accomplished this aim to a great extent as evidenced by the quality and productivity of our science. This includes publications in high impact journals such as *Nature*, *Nature Communications*, *Neuron* and *PNAS*. We have strengthened our team with two internationally renowned scientists: Carlos González, an expert in ion channels, and Andrés Chavez, an expert in the field of endocannabinoids. Notably, we created the first two Chilean Max Planck Research Tandem Groups (MPRTGs) selected by a committee composed of Max Planck Institute Directors and CINV scientists. Our PhD and Masters Programs in Neuroscience are flourishing with the enrollment of excellent students, and have been enhanced by our new Ph.D. Program in Biophysics and Computational Biology initiated in March, 2015. We also increased the number of postdoctoral fellows from an average of 4 before becoming an MI to 25 in 2015. In addition to our training programs, international collaborations with different universities and centers in Europe, North, and South America, have been very productive. This year we are proud to report that our productivity was particularly high in 2015 and about 3-fold larger than when we started the MI in 2011. From a total of 54 articles published 38 correspond to papers completely made by CINV members and of those 38, CINV members were first or corresponding authors in 27. Most importantly, we added quality to quantity by publishing 5 articles in high impact factor journals such as *Journal of Neuroscience*, *Cell Reports*, *Nature Communications* and *PNAS*. During 2015 we started several adventurous and successful scientific endeavors as MI. i) **A new CINV**. Authorized by our University President, the CINV will become a *bona fide* Center, independent from the Faculty of Science and reporting directly to the University President. In this Center, CINV members will be selected on the basis of the quality of their science. A center with these characteristics has no precedent in Chile and will set an excellence standard. ii) **Advanced Training**. We would like to emphasize that in 2015, 39 publications were co-authored by students and that our postdocs are urged to develop an early independence by publishing alone (see **Miño-Galaz. *J. Phys Chem.* 2015**). Also in 2015 we started conversations with the Director of the Department of Neuroscience and the President of the University of Göttingen to create a joint PhD program in Neuroscience. iii) **Strengthening our scientific capacities**. a) **Team**. As described above, two young, scientists will be occupying the MPRTL positions in 2016. In order to implement this program, in November of 2015 we had a Symposium in which ten of the potential MPTRG Leaders participated, from which two were selected: Chiayu Chiu from Yale University, who will add optogenetics and two photon microscopy to study the development of the brain cortex, and Rodrigo Suárez at present in the University of Queensland, Australia and an expert in brain development and evolution. iv) **Networking**. Organized by the CINV and held for the first time outside USA, in March-April, 2015 we hosted the International Gap Junction Conference. It was attended by more than 170 investigators and was considered a great success by the experts in the field. It also worth mentioning that we were recognized by nature index as a highly collaborative research centers in Chile, one among of four, and the only one outside Santiago. v) **Outreach**. Since its birth as a MI the CINV has sought innovative ways of bringing science to society. The programs Tertulias Porteñas and Ciencia al Tiro have been described in detail in previous progress reports. Here, we would like to mention only one of our most renowned successes. We were able to convince the editor of the electronic newspaper “El Mostrador” to publish neuroscience articles written for the

general public by our PhD students. In total those articles have received about 86.700 visits. vi. **Science.** The CINV deals with several aspects of a fundamental scientific question: ***How does the Nervous System respond to Stimuli in Health and Disease?*** We are addressing this question along four research lines and one cross-cutting theme. a) *Structure and Function of Molecular Sensors.* b) *Cellular Signaling.* c) *Genetic and Developmental Neuroscience* d) *System and Circuits Neuroscience.* e) *Cross-cutting: Bioinformatics and Computational Biology.*

1.2 Resumen Ejecutivo.

Creamos el Centro Interdisciplinario de Neurociencia de Valparaíso (CINV) con el objetivo de construir el Centro más importante para la investigación de la Neurociencia en Chile. Como Instituto Milenio (IM), durante los primeros cinco años de proyecto, hemos logrado este objetivo en gran medida como se evidencia por la calidad y la productividad de nuestra ciencia. Esto incluye publicaciones en revistas de alto impacto como *Nature*, *Nature Communications*, *Neuron* y *PNAS*. Hemos fortalecido nuestro equipo con dos científicos de renombre internacional: Carlos González, un experto en canales iónicos, y Andrés Chávez, un experto en el campo de los endocannabinoides. En particular, hemos creado los primeros dos Max Planck Research Tandem Groups (MPRTGs) chilenos seleccionados por un comité compuesto por Directores de Institutos Max Planck y Científicos del CINV. Nuestros Programas de Magister y Doctorado están floreciendo con la incorporación de excelentes estudiantes, y se han reforzado con la creación del Programa de Doctorado en Biofísica y Biología Computacional iniciado en Marzo, 2015. También aumentamos el número de becarios postdoctorantes de un promedio de 4 antes de convertirnos en un IM a 25 en el año 2015. Además de nuestros programas de formación, colaboraciones internacionales con diferentes Universidades y centros en Europa, Norte y Sudamérica, han sido muy productivas, resultando en artículos publicados este año reportando que nuestra productividad fue particularmente alta, 3 veces mayor que cuando partimos con el IM en 2011. De un total de 54 artículos publicados el 2015, 38 corresponden a publicaciones hechas completamente por miembros del CINV, y de esas 38, en 27 miembros del CINV fueron primeros o correspondientes autores. Lo más importante, añadimos calidad a la cantidad al publicar 5 artículos en revistas de alto factor de impacto como *Journal of Neuroscience*, *Cell Reports*, *Nature Communications* y *PNAS*. Durante el 2015 partimos varias aventuras y esfuerzos científicos exitosos como IM. i) **Un Nuevo CINV**. Autorizado por nuestro Rector, el CINV se convertirá en un Centro *bona fide*, independiente de la Facultad de Ciencias, que reportará sus actividades directamente al Rector de la Universidad y cuyos miembros serán seleccionados sobre la base de su calidad como científicos. Un centro con estas características no tiene precedentes en Chile y esperamos que se transforme en un estándar a seguir. ii) **Entrenamiento avanzado**. Nos gustaría enfatizar aquí que en el 2015, 39 publicaciones nuestras tuvieron como co-autores a nuestros estudiantes, además, nuestros postdoctorantes son incentivados para desarrollar tempranamente una carrera independiente y publicar por sí solos (ver **Miño-Galaz. J. Phys Chem. 2015**). También en el 2015 partimos conversaciones con el Director de Departamento de Neurociencia y el Rector de la Universidad de Göttingen para crear un programa conjunto de Doctorado en Neurociencia. iii) **Fortaleciendo nuestras capacidades científicas**. a) **Equipo**. Como se describió anteriormente, dos científicos jóvenes ocuparán los cargos de MPTL a partir del 2016. Con la finalidad de poner en marcha este programa, en Noviembre 2015 realizamos un Simposio en el que 10 postulantes a los cargos de MPRTG, y de esos diez, dos fueron seleccionados: Chiayu Chiu de la Universidad de Yale, quien añadirá la optogenética y microscopía de dos fotones al estudio del desarrollo de la corteza cerebral, y Rodrigo Suárez, en la actualidad en la Universidad de Queensland en Australia que es un experto en el desarrollo y evolución del cerebro. iv) **Redes**. En Marzo-Abril 2015 organizamos la principal conferencia mundial sobre las Uniones en Hendidura (International Gap Junction Conference). Esta fue la primera vez que esta conferencia internacional se realiza fuera de EEUU y Europa. La conferencia fue un completo éxito con más de 170 participantes extranjeros. v) **Proyección al Medio Externo**. Desde su nacimiento como IM el CINV ha buscado formas innovadoras de acercar la ciencia a la sociedad. El programa Tertulias Porteñas y Ciencia al Tiro

han sido descritos en detalles en Memorias anteriores, por lo que ahora mencionaremos solo uno de nuestros más reconocidos éxitos del 2015. Fuimos capaces de convencer al editor del diario electrónico “El Mostrador” para publicar artículos de neurociencias escritos por nuestros estudiantes de Doctorado para el público en general. En total estos artículos han recibido cerca de 86.700 visitas. vi. **Ciencia.** El CINV trata con diversos aspectos de una pregunta científica fundamental: *¿Cómo responde el Sistema Nervioso a estímulos en Salud y Enfermedad?* Estamos abordando esta pregunta a través de cuatro líneas de investigación y un tema transversal. a) Sensores Moleculares b) Señalización Celular c) Genética y Desarrollo del Sistema Nervioso. d) Fisiología Sináptica y de Circuitos. e) Bioinformática y Biología Computacional.

2. Introduction

a) *Description of the Institute:* The Centro Interdisciplinario de Neurociencia de Valparaíso (CINV) was created with the purpose of expanding the boundaries of science in Chile outside of the gravitational pull of its omnipresent capital, Santiago. Our vision was to assemble a multidisciplinary and collaborative community of scientists by bringing together neuroscientists from diverse backgrounds such as biophysics, chemistry, mathematics, and computer science. We also thought that it was important for our researchers to be relatively free from the many constraints that plague our public institutions and to provide them with an environment that would allow them to devote most of their time to research. The goals we proposed when we were granted the Millennium Institute (MI) in 2010 were: (1) To become a multidisciplinary interregional center; (2) To build a new home for the CINV; (3) To create a PhD Program in Biophysics and Computational Biology; And (4) To create a program that would provide an opportunity for young scientists to collaborate on long-term multidisciplinary research in an independent manner and with access to state of the art facilities. The challenge for the CINV is to develop in Chile a core of faculty that can carry out integrated multidisciplinary collaborative research and training programs.

As an interregional science center, the CINV is already well known to the Chilean scientific community; it has also become known to the general public of the region of Valparaíso through its many outreach programs (Goal 1). By securing the funds to build a new home for the CINV in a historical neighborhood of Valparaíso (Goal 2), we will have a unique center where scientists can work collaboratively to create the best neuroscience possible and exploit new concepts and technologies. This new home will also greatly help the development and recovery of a Valparaíso heritage site. The building will include laboratories, offices, animal facilities, conference rooms, an interactive neuroscience museum, cafeteria, and administration; it will be ready by the end 2016. The PhD program in Biophysics and Computational Biology (Goal 3) was approved by the University governing bodies at the beginning of 2014 and the first cohort of students were selected in December 2014. Courses in this PhD program will in general be short, intensive, and hands-on, with the main purpose of transmitting to the student concepts and techniques rather than just information. Additionally, with the incorporation of two Max Planck Research groups into the CINV, we will provide the best young scientists with a space where they can work for a period of several years, be well-funded from the beginning, and work in an absolutely independent manner while taking advantage of the whole CINV infrastructure (Goal 4). The general idea is that very good young scientists, able to generate some of the most original research in neuroscience, will be able to work full time as research scientists without the constraints of teaching, committee work, and the need to rapidly obtain funding and secure tenure

b) Research Lines:

1. Structure and Function of Molecular Sensors. This line aims to understand the molecular workings of ion channels and pumps. Highlights of our research include: **1)** Identification of the N terminal of $\beta 1$ as the region responsible for the modulation of the voltage sensors of the pore-forming α (BK) subunit (**Castillo et al., PNAS., 2015**); **2)** Identification of the binding site for PI(4,5)P₂ in the TRPV1 channel (**Poblete et al., JBC, 2015**); **3)** Demonstration that Cav_{2.1} calcium channels are better tailored than Cav_{2.2} for fast synchronous neuromuscular transmission (**Naranjo et al., Biophys. J., 2015**. Commented in the issue's *News and Notable*); **4)** Direct detection of the electrical signal arising from the entrance of external potassium ions into Na⁺/K⁺-ATPase K⁺ binding sites (**Castillo et al. Nat. Comm., 2015**).

2. Cellular Signaling. This research line has as main objective to unveil the molecular mechanisms that govern the processes of neurotransmitter release by exocytosis, and the cellular communication mediated by connexins (Cxs) and pannexins (Panxs) channels. We have incorporated new technical approaches, taken advantage of current collaboration with other CINV research lines, including transgenic animal models (with line 4), biophysics (with lines 1), and molecular modeling of proteins (with lines 1 and 5). The main highlights of our scientific findings are that: **1)** Connexin43 hemichannels (HC) mediate secondary cellular damage spread in astrocyte monolayers (**Rovegno et al. *Glia*, 2015**) **2)** Cx26 mutations associated to syndromic deafness Keratitis-ichthyosis-deafness result in the formation of aberrant hetero-oligomers of wild-type Cx43 and mutant Cx26 mutants that yield hyperactive HC (**Garcia et al. *J. Invest. Dermatol.*, 2015**) **3)** HCs opening are required for amyloid β -peptide-induced degranulation of brain mast cells (MCs) (**Harcha et al. *J. of Neuroscience*, 2015**).

3. Genetic and Developmental Neuroscience. This line of research uses modern molecular-genetic tools to dissect the mechanisms underlying development and behavior in intact animals. Its most significant accomplishments are: **1)** The development of a new model showing that both the peripheral and central nervous system develop from a continuous field of cells; **2)** The ability to visualize patterns of neuronal activity induced by neuropeptides as they elicit specific behaviors in the animal and **3)** To build on our existing strengths in imaging and genetics to assay neuronal activity in whole animals by expanding our work with genetically encoded Ca^{2+} (zebrafish) and luciferase reporters (*Drosophila*).

4. System and Circuits Neuroscience. This line aims is to understand how neuronal circuits work (i.e. hippocampus and retina) under normal conditions and how they change with aging or following neurodegeneration as these processes could induce critical alterations in both cognitive and sensory performance. The milestones for this line are: We have shown the relevance of *O. degus* as a natural model to study the first signs of Alzheimer diseases (AD), including the presence and accumulation of $\text{A}\beta$ and cognitive impairment during aging. Remarkably, degus retina also presents the main biomarkers of AD, and may be a useful tool for the early non-invasive detection of AD (**Du LY et al., *PlosOne*, 2015**). Our team is also studying the role of endocannabinoid (eCB) in the modulation off a wide range of neural functions in the retina.

5. Cross-cutting: Theoretical, mathematical, and computational modeling, have made pivotal contributions to the CINV. These include: **1)** The study of the pore region of K^+ channels (**Carrasquel-Ursuláez et al. *J. Gen. Physiol.*, 2015**); **2)** Elucidation of the molecular determinants of PIP2 binding to the TRPV1 channel (**Poblete et al. *J. Biol. Chem.*, 2015**); **3)** The study of the pore region of K^+ channels (**Díaz-Franulic et al. *J. Gen. Physiol.*, 2015**); **4)** Mathematical models of the cold-activated TRPM8 receptor (**Olivares et al. *PLoS One*, 2015**). **5)** The study of conservation and function of the IC pocket in Cx32 (**Brennan et al. *J. Biol. Chem.*, 2015**); **6)** The influence of potential differences over simple dual-membrane systems resembling gap junction channels (**Escalona et al. *BMC Bioinformatics*, 2015**).

c) Organization of researcher's team

1. **Structure and Function of Molecular Sensors** (R. Latorre, A. Neely, C. González, D. Naranjo, O. Alvarez, F. Bezanilla and M. Holmgren).
2. **Cellular Signaling** (J. C. Sáez, A. M. Cárdenas and A.D. Martínez).
3. **Genetic and Developmental Neuroscience.** (J. Ewer and K. Whitlock).
4. **System and Circuits Neuroscience.** (A. Palacios, O. Schmachtenberg, A. Chávez, A. Kirkwood).
5. **Cross-cutting - Computational Biology.** (F. González-Nilo, T. Pérez-Acle, P. Orio).

3. Scientific and technological research

a) Current status of research lines:

1. Structure and Function of Molecular Sensors (*R. Latorre, A. Neely, C. González, O. Alvarez, F. Bezanilla and M. Holmgren*).

Voltage- and Ca^{2+} -activated K^+ (BK) channel. **1.** *Molecular mechanism of $\beta 1$ regulation in BK channel.* Several gating processes, allosterically coupled to each other, control the activity of BK channels and are potential targets for the regulation by auxiliary β subunits that are expressed together with the α (BK) pore-forming subunit in a tissue specific pattern. By measuring gating currents in BK channels co-expressed with chimeras between $\beta 1$ and $\beta 3$ auxiliary subunits, we were able to identify the N terminal of $\beta 1$ as the region responsible for the modulation of the voltage sensors. In addition, we narrowed down the structural determinants to two lysine residues, K3 and K4, which upon substitution virtually abolished the effects of $\beta 1$ on charge movement (**Castillo et. al., PNAS, 2015**). **2.** We identified an aromatic residue near the internal gate of BK channels that pairs with a residue from a different subunit to forms a hydrophobic ring important in determining the open-closed equilibrium and appears to uncouple Ca^{2+} binding from voltage sensor activation, as well as voltage sensor activation from channel opening. (**Carrasquel-Ursuláez et al JGP, 2015**) **3.** With the development of the lanthanide resonance energy transfer (LRET) technique in our laboratory, we were able to determine the extracellular position of transmembrane segments S0-S2 with and without the auxiliary $\beta 1$ subunit and the position of the two transmembrane segments of the $\beta 1$ subunit in the $\alpha/\beta 1$ subunit complex. These measurements allowed us to show that $\beta 1$ produces rearrangements of the BK voltage sensor domain (**Castillo et al, PNAS. In press**).

TRP channels. **1.** *Gating of Thermally Activated Channels.* Thermal TRP channels are polymodal receptors, that is, they can be activated by temperature, voltage, pH, lipids, and agonists. **2.** *Molecular Determinants of Phosphatidylinositol 4,5Bisphosphate (PI(4,5)P2) Binding to Transient Receptor Potential V1 (TRPV1) Channels.* By using electrophysiology, mutagenesis and by performing atomistic molecular dynamics (MD) and docking simulations in collaboration with Line 5, we observed that PI(4,5)P2 behaves as a channel agonist and we were able to identify the binding site for PI(4,5)P2 in the TRPV1 channel. The molecular simulations also allowed us to determine the structural rearrangements caused by PI(4,5)P2 binding. (**Poblete et. al., J. Biol. Chem., 2015**).

CaV channel. **1.** *Modulation of voltage sensors of Cav1 by auxiliary subunits.* Having shown that in calcium channels each voltages sensor (VSD) displays divergent voltage and time-dependencies and also how much they influence channel opening, it was pertinent to ask whether their behavior is affected/modulated by auxiliary subunits. We found that, without the $\alpha 2\delta$ -1 subunit, the human L-type Cav1.2 channel complex displays a right-shifted voltage dependence so that channel currents mainly develop at non-physiological membrane potentials, due to very weak VSD-pore interactions (**Savalli et al JGP, submitted**). We also investigated the impact of removing of the β subunit and discovered that the first VSD of Cav1.2 channels lacking this subunit, tends to remain in relaxed state commonly associated with inactive channels, an observation that may help untangle a long-sought answer to the molecular mechanism by which the β subunit promote channel opening (**Di Giorgis et al, in preparation**). **2.** *Cav2 and synchronous neuromuscular transmission.* The Cav2.2 (N-type) and Cav2.1 (P/Q-type) mediate synaptic transmission throughout nervous system. Recordings of calcium current in response to a command waveform shaped on the motoneuron action potential (AP) show ~fourfold greater open probability (P_o) for Cav2.1 than for Cav2.2 and we proposed that efficient activation of Cav2.1 channels during APs

contribute to a highly reliable transmission at the zebrafish neuromuscular junction (**Naranjo et al. *Biophys J.*, 2015**). This work was commented in News and Notable section of the same issue.

Voltage-gated proton channel. 1. Proton channel models: Filling the gap between experimental data and the structural rationale. Voltage-gated proton channels are integral membrane proteins with the capacity to permeate these elementary particles in a voltage and pH-dependent manner. One of the major challenges in the field is to understand how proton, which in solution do not exist as free cations can be transported with high efficiency and selectivity. Inspired in our recent review of existing proton channel models (**Pupo et al. *Channels*, 2014**) we combined electrophysiological and fluorescent experiments with molecular and quantum dynamic modeling to address this issue. The main finding is that contrary to the prevalent view that proton channels encompass a water filled path where protons can hop between adjacent water molecules, there is a water-free domain within the channel conduction pathway through which protons pass by hopping between two aspartate residues (**Pupo et al., *Nat. Comm.* submitted**).

Shaker K⁺ Channel: 1. Closing the gap between low and high conductance K-channels. The extremely conserved signature sequence in the residues forming the pore selectivity filter allows exquisite K⁺ selectivity. However, closely related K-channels with identical pore selectivity filter display differences of up to ~100-fold in unitary conductance, which is topped by BK channels with about 300 pS in symmetrical 100 mM K⁺. Can we approach BK-like conductance by increasing channel ion occupancy along the pore in channels of low conductance like Shaker? We found that substitution Pro475Asp at the internal entrance, and away from the selectivity filter, of the low conductance Shaker K-channel, increases unitary conductance from 20 pS to 160 pS. However, moving this negatively charged residue along the inner wall of the channel failed to increase single channel conductance any further. Now we tested for differences in pore architecture by measuring diffusion-limited outward currents and found that Shaker's internal pore is narrower than that of BK channels. MD simulations with the help of line 5 showed that this narrow pore imposes diffusion limit and additional dehydration steps in Shaker-derived channels that impede increasing the conductance of this channel (**Díaz-Franulic et al., *JGP.*, 2015**). Cover and Comment in the same issue.

Na⁺/K⁺ Pump. The Na⁺/K⁺ pump is a membrane protein that plays a fundamental role in maintaining the Na⁺ and K⁺ electrochemical gradients in animal cells. When Na⁺ is absent the pump can only perform K⁺ translocation reactions. If K⁺ travels a fraction of the membrane's electric field in at least one of these reactions, the K⁺ binding-unbinding equilibrium become voltage-dependent and sudden changes in voltage will shift this equilibrium generating a transient current signal. We measured K⁺ translocation currents by using H2DTG, a reversible inhibitor of the squid Na⁺/K⁺ pump. Kinetics of these transient currents shows two main components, which, in contrast to their Na⁺ counterpart, appeared to be uncoupled. We also found that only the slow component kinetics and charge distribution are dependent on the external K⁺ concentration, revealing that the two K⁺ reach their binding site before their occlusion takes place (**Castillo et al. *Nat. Comm.*, 2015**).

2. Cellular Signaling (*J. C. Sáez, A. M. Cárdenas and A.D. Martínez*):

Role of HCs made by Cxs and Panxs in neurons, glia and other cells of the Central Nervous System. 1. Connexin43 hemichannels mediate secondary cellular damage spread from the trauma zone to distal zones in astrocyte monolayers (**Rovegno et al. *Glia*, 2015**). After Brain trauma there is a secondary damage that is distal from the original injured zone, yet the mechanism of the secondary damage was unknown. Using an *in vitro* trauma model of cultured astrocytes, we found

that there is a strong induction of hemichannel (HC) activity in regions distal from the injury zone, which was inhibited by HC blockers, and was absent in astrocyte of Cx43 KO animals. The HCs hyperactivity was prevented by inhibition of P2 purinergic receptors, suggesting that the HC activity was induced by ATP released from damaged areas. The increase in HC activity was associated with an increment in apoptotic cells that was completely prevented by inhibition or absence of HCs. These findings suggest that Cx43 HCs may be a useful new therapeutic target to prevent secondary brain damage. **2. Neural progenitor cells (NPCs) isolated from the subventricular zone (SVZ) present HC activity and form functional gap junctions with glial cells (Talaverón et al. *Front. Cell. Neurosci.*, 2015).** Communication via gap junctions is required for normal NPC proliferation and for neuroblast migration towards the olfactory bulb. Previously, we found that neurosphere-derived NPCs form heterocellular gap junctions with host glial cells after mechanical injury, but the mechanism was unknown. Now, we found that neurosphere-derived cells expressed mRNA for Cx26, Cx43, Cx45 and Panx1. Our results indicate the existence of functional HCs and gap junction channels in postnatal SVZ neurospheres. In addition, we demonstrated that SVZ-derived NPCs can establish functional gap junctions with astrocytes or microglia. Therefore, cell-cell communication via gap junctions and HCs with host glial cells might subserve a role in the functional integration of NPCs after implantation in the damaged brain. **3. Restraint stress increases hemichannel activity in hippocampal glial cells and neurons (Orellana et al. *Front. Cell. Neurosci.*, 2015).** Chronic Stress induces cognitive deficits associated with major depression, glial cell activation and causes changes in neuronal plasticity and neuronal death. We previously published that neuro-inflammatory conditions activate glial cells that release ATP and glutamate via HCs inducing neuronal death due to activation of neuronal NMDA/P2X₇ receptors and Panx1 channels. In this study we found enhanced Panx1 HC activity in microglia and neurons after acute/chronic stress. Moreover, inhibition of NMDA/P2X₇ receptors reduced the chronic stress-induced HC opening, whereas blockade of Cx43 HCs and Panx1 channels fully reduced ATP and glutamate release in hippocampal slices from stressed mice. Thus, we propose that glio-transmitter release through HCs may participate in the pathogenesis of stress-associated psychiatric disorders such as depression.

Pathogenic mechanism of sensorineural deafness associated to Cxs. **1. Aberrant heteromeric HCs in syndromic deafness.** During this period, we discovered a possible pathologic mechanism of syndromic deafness, called Keratitis-ichthyosis-deafness (KID). Cx mutations associated to KID allow the formation of aberrant of heteromeric HCs between Cx43 and Cx26 bearing syndromic mutations in their amino-terminal domain (García et al. *J. Invest. Dermatol.*, 2015). We demonstrated that these heteromeric HCs are hyperactive under resting conditions because they allow the cellular uptake of different fluorescent molecules at normal extracellular Ca²⁺ concentration, a condition that normally causes the closure of HCs, and produce large HCs currents in *Xenopus* oocytes (García et al. *J. Invest. Dermatol.*, 2015). Moreover, the expression of hyperactive HCs increases the basal intracellular Ca²⁺ concentration and allows the release of ATP (García et al. *J. Invest. Dermatol.*, 2015). Finally, our work and previous reports strongly indicate that formation of hyperactive HCs is a common mechanism in several genetic and acquired diseases, like KID, ischemia and other inflammatory conditions (Retamal et al. *Front. Cell. Neurosci.*, 2015).

Regulation of HCs by signaling factors. **1. Role of serine-threonine specific protein kinase (Akt) and Ca²⁺ on cell permeabilization via Cx43 HCs induced by metabolic inhibition.** Akt plays important roles in the cell cycle and metabolism. We investigated the role of Akt on Cx43 HCs in response to metabolic inhibition. Metabolic inhibition induced a transient Akt activation, which

was necessary to increase Cx43 expression. This increase in expression was also found to depend on an intracellular increase in Ca^{2+} that was partially mediated by Akt activation. The Akt-dependent increases in Cx43 HC activity in HeLa cells also occurred after oxygen-glucose deprivation, and in cultured cortical astrocytes under metabolic inhibition. Since opening of HCs has been shown to accelerate cell death, inhibition of Akt-dependent phosphorylation of Cx43 HCs could reduce cell death induced by ischemia/reperfusion (**Salas et al. *Biochim. Biophys. Acta.*, 2015**). **2. Possible role of carbon monoxide (CO) in the redox regulation of Cx HCs.** Carbon monoxide is a gaseous transmitter that is known to be involved in several physiological processes, and recently it has been used for the treatment of several pathologies including stroke and cancer. An increase in the cGMP concentration and protein carbonylation may be the cellular mechanism that mediates CO effects. Recently, we proposed that that CO can modulate Cxs HCs (**Retamal et al. *IUBMB Life*, 2015**).

Functional Roles and regulation of plasma membrane channels made by pannexins. **1. HCs are required for amyloid β -peptide-induced degranulation of brain mast cells (MCs)** (**Harcha et al. *J. Neurosci.*, 2015**). MCs store proinflammatory mediators in secretory granules that are released upon activation with amyloid beta ($\text{A}\beta$) peptides present in brains affected by Alzheimer's disease (AD). We found a rapid degranulation of cultured MCs induced by $\text{A}\beta_{25-35}$ peptide that depends on Panx1 HCs. Moreover, $\text{A}\beta_{25-35}$ peptide also increased membrane current and permeability, as well as intracellular Ca^{2+} signal through Panx1 HCs activity. Similar findings were obtained in acute coronal brain slices of control mice. MCs are found close to amyloid plaques of patients with AD. Accordingly, in APP^{swe}/PS1^{dE9} mice, a murine model of AD, we found a drastic increase in the number of MCs located in hippocampal and cortical areas before amyloid plaque deposits became evident. Therefore, MCs might act as early sensors of amyloid peptide and recruit other cells to the neuroinflammatory response, thus playing a critical role in the onset and progression of AD. **2. Pannexin channels mediate the acquisition of myogenic commitment in C_2C_{12} reserve cells (RCs) promoted by P2 receptor activation** (**Riquelme et al. *Front. Cell. Dev. Biol.*, 2015**). The acquisition of myoblast commitment to the myogenic lineage is controlled by intracellular Ca^{2+} , which may depend on the activity of P2 receptors as well as on channels made by Cxs or Panxs. We found that extracellular ATP increases $[\text{Ca}^{2+}]_i$ via P2Rs in RCs. Moreover, ATP increases the plasma membrane permeability to small molecules and a non-selective membrane current, both of which were inhibited by chemical blockers of Cx HCs and Panx channels. In addition, exogenous ATP induced the expression of myogenic commitment and increased MyoD levels, which was prevented by the inhibition of P2Rs or knockdown of Panx1 channels. Similarly, increases in MyoD levels induced by ATP released by RCs were inhibited by Panx channel blockers. Thus, we postulate that myogenic commitment requires a feed-forward mechanism mediated by extracellular ATP, P2Rs, and Panx channels.

Regulation of vesicle transport and exocytosis by actin polymerization during physiological and pathological conditions. **1. Cortactin.** The actin binding protein cortactin defines the kinetics of single exocytotic events in neuroendocrine chromaffin cells. **2. Ca^{2+} channel.** The β subunit of the Ca^{2+} channel regulates the channel recycling at the cell surface by a mechanism that involves actin polymerization and dynamin-2. **3. Dynamin-2.** Dynamin-2 mutations that cause centronuclear myopathy impair actin dynamics and GLUT4 trafficking in myocytes (González-Jamett et al *J. of Neurochem.*, 2014).

3. Genetic and Developmental Neuroscience. (*J. Ewer and K. Whitlock*)

Neurogenesis and Behavior in Zebrafish. Notably, we have successfully generated neurospheres

(neural stem cells), shown that they give rise to the gonadotropin-releasing hormone neuroendocrine cells, and that hormone treatment can increase the number of GnRH cells. This cell type is essential for puberty where defects in the development of these cells underlie Kallmann Syndrome in humans (**Cortés-Campo et al, *Biology Open*, 2015; Letelier et al, in preparation**). In order to develop our collaboration with Dr. Bill Crowley (Harvard Medical School) to analyze Rare Sequence Variants (RSVs) that underlie Kallmann Syndrome in humans using zebrafish as a model system to knock-out (using CRISPR) or knock-down (using morpholinos) sequences identified by the RSV analysis in humans and determine the GnRH endocrine phenotype. In collaboration with Dr. John Ewer and Prof. Dr. Christian Wegener (Neurobiology and Genetics, University of Würzburg), we are using direct MALDI-TOF mass spectrometric peptide profiling to confirm GnRH1 isoforms in the hypothalamus of the adult zebrafish. By taking advantage of our previous finding and new model for olfactory sensory system development (Torres-Paz & Whitlock, *Dev. Dyn.*, 2014), we are analyzing the genetic basis for differentiation of the peripheral versus central olfactory targets by gene knock-down and knock-out techniques (**Torres-Paz & Whitlock in preparation**).

Our previous characterization of different olfactory behaviors (Stephenson et al., *Zebrafish*, 2012) has allowed us to study the correlation between neuronal differentiation as measured by activity and olfactory behaviors in zebrafish. We are using recently available lines of zebrafish expressing genetically encoded calcium indicators (GCaMP 7 /GCaMP3) in different cell types to better understand the onset of activity and plasticity in the peripheral olfactory sensory system. Currently we are using the HuC:GCaMP7 line to image activity in the developing nervous system. We are the first group to analyze the activity of olfactory sensory neurons in conjunction with the developing olfactory bulb. Strikingly, we have found that there is a synchronous pattern of activity that reflects the early neuroectodermal patterning of the olfactory bulb and epithelium (see above Torres-Paz & Whitlock 2014). Once differentiated, this pattern shifts to an asynchronous odor-inducible pattern of activity. We continue to collaborate with the Orio lab (Line 5) to analyze calcium signaling in living embryos to discern different patterns of covariance underlying organization and activation of neural (**submitted** work with Perez Acle lab, Line 5). Subsequent post-analysis of the RNAseq data (collaboration with Dr. Hazel Sive, Whitehead Institute, MIT Boston USA) had revealed an unexpected link with the immune system that we are currently investigating.

Ecdysis Behavior in Drosophila. In order to grow, insects must replace their exoskeleton. The last step in this process is the shedding of the remains of the old exoskeleton, which is accomplished through a complex sequential behavior called ecdysis. Ecdysis is triggered by the release of the neuropeptide ETH (ecdysis triggering hormone), which acts on targets in the CNS that express the A and/or B form of its receptor (ETHR). Targets expressing ETHR-A are peptidergic neurons, which are activated sequentially. We have used mutants null for genes encoding specific neuropeptides that we have isolated and targeted RNAi expression coupled with GCaMP imaging to understand how ecdysis behavior is controlled. We find that the neuropeptides downstream of ETH themselves, in combination with inhibition mediated by GABA, play a critical role in determining the CNS's sequential response to ETH and that of the ensuing ecdysis behavior. These findings have important implications for understanding how neuropeptides modulate the activity of a neuronal network, and how they regulate behavior in all animals (**Mena W and Ewer J, Manuscript in preparation**). Our recent review with Dr. White highlights recent progress in this area (White BH and Ewer J., *Annu. Rev. Entomol.*, 2014). Dr. White's and our lab are currently carrying out collaborative work. In particular, his lab has created lines that allow us to drive gene

expression in ETHR-A and –B neurons, which we are using to image the activity and genetically manipulate these 2 subsets of ETH targets, in order to understand how this peptide hormone controls ecdysis behavior.

Circadian Clocks. We have continued to investigate how the circadian clock causes a daily rhythm of emergence of the adult fly, which is known to depend on the activity of a circadian clock in the brain and one in the Prothoracic Gland (PG). We investigated how these clocks are coupled by interfering genetically with the brain and PG clock and their interaction (**Selcho M et al., Manuscript in preparation**). We have also investigated how Ca^{2+} and cAMP affect the rhythmicity of the circadian clock (Ph.D. Thesis, Angelina Palacios). Our results show that these second messengers affect the periodicity of the clock, suggesting that they may represent a route through which homeostatic signals can influence circadian function. We are now using an extremely high sensitivity camera, which allows us to monitor the activity of the circadian clock *in vitro* using flies bearing a clock gene-luciferase transgene. This equipment is currently being used to determine how the brain and PG clocks interact *in vivo* and the role of Ca^{2+} and cAMP in clock function. Thus we have made great strides in developing tools and a knowledge base necessary for unraveling the link between neuronal differentiation and activity underlying the onset and modulation of behaviors essential for survival. Some of these tools promise to make gene knockouts and gene expression drivers (GAL4) simpler to produce and more versatile (**Diao et al., Cell Reports, 2015**). We continue to collaborate with Line 4, assisting with the identification in the Chilean rodent, *Octodon degus*, of homologs of genes that have been implicated in Alzheimer disease. This rodent is a natural model for this important human disease, and we aim to correlate the occurrence of specific variants with the severity of the disease.

4). System and Circuits Neuroscience. (A. Palacios, O. Schmachtenberg, A. Chávez, A. Kirkwood)

This line aim is to understand how neuronal circuits in the hippocampus and the retina function under normal conditions and how they change with aging or under neurodegeneration since these processes induce critical alterations in both cognitive and sensory performance. At present, we have reported on the presence of the main hallmarks of Alzheimer disease (AD) in the brains of a natural AD animal model (*O. degus*): decreases in synaptic plasticity and memory processes, expression of key synaptic proteins (PSD-95, GluR2-AMPA, NR2B-NMDAR) as well as the increase of soluble A β oligomers and phosphorylated Tau proteins (*PNAS*109(34):13835-13840, 2012). More recently, we extended our observation and obtained a similar result by analyzing the retina of degus during aging, which opens the possibility of developing tools for an early optical *in-vivo* detection of AD (**Du LY et al., PlosOne, 2015**, see also *Alzheimer & Dementia*, 10(2):251-261, 2014). In collaboration with Dr. Kirkwood (Hopkins University), we have described the role of G_s and $G_{q/11}$ G-protein coupled receptors in determining the switch between LTP and LTD (Huang S et al., *Neuron*, 2012). Neuromodulation also caught our attention and we have shown a critical role of nitric oxide (NO) in the responses to glutamate in OFF bipolar cells of the retina, affecting the temporal response properties of the retina (Vielma AH et al., *PLoS One*, 2014). We also described a new mechanism for the regulation of low-light vision by acetylcholine (**Elgueta C et al., Front. Cell. Neurosci., 2015**). Work continues on the role of NO in retinal circuit modulation in the healthy and diseased retina, specifically in diabetic retinopathy. Recently, Dr. Andrés Chávez has joined our team to study the role of endocannabinoid (eCB) signaling in retinal synaptic function. These lipid messengers modulate a wide range of neural functions primarily by activating type 1 cannabinoid receptors (CB1R), which are widely expressed in the brain. In the

retinal circuit, activation of CB1R seems to modulate the temporal properties of visual signal by regulating RBC-A17 amacrine cell synapses (Chávez, unpublished observation). In addition, he is also investigating a potential interaction between 5-HT_{2R}, a subtype of serotonergic receptor, and TRPV1, a non-selective cationic channel known to be modulated by eCB, in regulating synaptic transmission and plasticity under normal and pathological conditions. Work continues on olfactory system using the rainbow trout as a biological model. In a pioneering study, we showed that rainbow trout are able to detect B-vitamins at nanomolar concentrations as well as other food-related substances previously not considered odorants for fishes such as lactic and pyruvic acid (Valdés J et al., *Fish Physiol. Biochem.*, 2015).

5). Cross-cutting - Bioinformatics and Computational Biology. (F. González-Nilo, T. Pérez-Acle, P. Orio).

This crosscutting line of research integrates experimental evidence with advanced mathematics, physics and thermodynamics to develop computational models to study biological phenomena ranging from the atomic scale to the population level. During this period, we proposed the first mathematical models of cold thermoreceptors that includes the cold-activated TRPM8 channel. In contrast to previous models, now we are able to mathematically reproduce and study the exquisite sensibility of cold-sensitive channels to *changes* in temperature. In doing so, we showed that calcium-dependent desensitization of the TRPM8 currents explains many features of this response (Olivares E et al., *PLoS One*, 2015). This model is now being applied to the interpretation of neuropathic pain conditions. We have also explored the application of new statistical distributions to the modeling of interspike intervals from spontaneously spiking sensory neurons. Thus, by considering the generation of action potentials as a cumulative damage process, we could validate the use of Birnbaum-Saunders and Inverse Gaussian distributions to model these data (Leiva V et al., *Biol Cyber*, 2015). On the other hand, we have explored from the atomic point of view structural features of the TRP, BK and Shaker channels. In collaboration with Line 1, we proposed a novel binding pocket for phosphatidylinositol 4,5-bisphosphate (PIP₂) in the transient receptor potential V1 (TRPV1) channels. Interestingly, the hydrophobic core accommodating the aliphatic tails of PIP₂ is shared with the binding pocket of capsaicin, thereby suggesting the mechanism through which capsaicin and PIP₂ activates TRPV1 (Poblete et al., *J Biol Chem*, 2015). Further elaborating on the role of the novel water pocket (IC pocket) we discovered in 2014 in the crystal structure of human connexin 26 hemichannel (hCx26), we studied its conservation and function in Cx32, demonstrating that mutations affecting the homologous tryptophan residue within the IC pocket of Cx32, hinder channel currents (Brennan MJ et al., *J. Biol. Chem.*, 2015). Moreover, by studying the influence of a potential difference over simple dual-membrane systems resembling gap junction channels, we proposed a role for charge distribution along the channel pore over ion-selectivity of gap junction channels (Escalona Y et al., *BMC Bioinformatics*, 2015).

b) Publications:

Summary table

<u>Category of Publication</u>	<u>MSI Center Members</u>	<u>Number of Publications coauthored by students</u>	<u>Total Number of Publications</u>
ISI Publications or Similar to ISI Standard	Associate Researchers	21	38
	Other Researchers	1	4

SCIELO Publications or Similar to SCIELO Standard	Associate Researchers	0	0
	Other Researchers	1	1
Scientific Books and chapters	Associate Researchers	1	2
	Other Researchers	0	0
Other Scientific Publications	Associate Researchers	0	0
	Other Researchers	0	0
Total of Publications		24	45

c) Other achievements:

i. Patents: (Annex 3.6 with full description)

1. PCT/CL2015/050033 Ultra-thin and Self-hydrating Interface Comprising a Biopolymer
2. PCT/CL2010/00744 Substituted Sulfonyl Fenil derived compound calpain inhibitors; Pharmaceutical compositions useful in the treatment of calpain activity associated diseases such as male infertility, testicular torsion, Varicocele, oligospermia, Alzheimer's, Parkinson's, Huntington, AIDS.
3. PCT/CL2015/050012 Specific Modulators of Connexin Hemichannels
4. US 9173384 B2 Surgically implanted micro-platforms and microsystems in arthropods and methods based thereon

ii. Intellectual property:

NONE

iii. Congress Presentations:

Summary Table

Type of presentation	National Events [Number]	International Events [Number]
A. Associate Researchers		
Conferences, oral communications, poster communications, others (specify)	59	34
Invited presentations (not included in above row)	8	13
B. Other researchers (Adjunct Researchers, Senior Researchers, Young Researchers, Postdoctoral Researchers and Students)		
Conferences, oral communications, poster communications, others (specify)	26	11
Invited presentations (not included in above row)	6	1

iv. Organization of Scientific Events:

International Gap Junction Conference (Valparaíso, March 28 – April 2) The leading international Scientific meeting on gap junctions was held for the first time and in the southern hemisphere. More than 250 people attended the conferences, ranging from Researchers and PhD students to the general public. This conference was organized by A. Martínez and JC. Sáez (CINV)

International Workshop: Biophysics of hemichannels and gap junction channels: A theoretical and practical training (Santiago, March 24 – 27) This workshop has been designed to give students theoretical and practical training in the most recent and relevant progress in the study of the hemichannels and gap junctions made by connexins and pannexins, including a brief historical perspective.

International Spring School Applied Statistical Thermodynamics: from theory to molecular dynamics simulation (Santiago, November 16 – 27) This BootCamp International School was aimed for graduate students, young researchers and experts in the field who wish to acquire knowledge about the fundamentals and molecular simulation techniques. The school included broad and solid theoretical bases in classical mechanics, thermodynamics and statistical mechanics, as well as practical knowledge on the main techniques of molecular simulation and free energy calculations.

International Workshop: Modeling ionic currents in Molecular Dynamics Simulations. (Valparaíso, November 16).

4th CINV-Max Plank Meeting 2015 covered different subjects of neuroscience, including neural network, neurogenetics, sensory biology, computational neuroscience and brain science. These periodic meetings have laid the groundwork to create the first two Max Planck Research Groups in Chile.

International Workshop: Biochemical, Spectroscopic and Crystallographic approaches used to study the functional-structural correlations of membrane proteins (Valparaíso, July 25 - 29) This workshop was organized by C. Gonzalez (CINV). Dr. Luis Cuello and Beatriz Velez from Texas Tech University attended.

CINV Meeting 2015 (Valparaíso, July 30) This symposium was held in the Naval Museum. Most of the members of the CINV presented their accomplishments as a talk or a poster session.

Spring Symposium in TRP Channels (Santiago, September 28) This symposium was organized by P. Orio.

Integrating Hedgehog signaling in stem cell, developmental & cancer biology. Practical course: Students were taught cellular mechanisms of Hedgehog signaling and the potential applications to stem cell, developmental and cancer biology in mouse, *Drosophila*, and zebrafish. Doctorate students Ricardo Ceriani and Pablo González (line 3) participated as teaching assistants for the zebrafish module. Santiago, Chile. Practical Course *October 17 – 20 2015*: http://www.cgrcongress.cl/gen_infor_stgo.php#: Co-organizer: Dr. Whitlock

v. Scientific Editorial Boards:

John Ewer: Journal of Insect Science, Current Opinions Insect Science, Insect Biochemistry and Molecular Biology, Journal of Comparative Physiology – A.

Carlos Gonzalez: Journal of Biological Chemistry.

F. Danilo González: Current Opinion in Structural Biology, Proceedings of the National Academy of Sciences, Journal of Physical Chemistry, Journal of Molecular Modeling, Journal of Physical Organic Chemistry, Biological Research.

Ramon Latorre: Biological Research, Proceedings of the National Academy of Sciences, Journal of General Physiology, Channels, Temperature, Frontier in Pharmacological Research.

David Naranjo: Frontiers in Physiology.

Tomas Perez-Acle: PeerJ, PeerJ Computer Sciences.

Adrian Palacios: Biological Research, Membre Correspondant International de la revue intellectica, Journal on Policy and Complex Systems.

Juan Carlos Sáez: Frontiers in Neuroscience-Neurogenetics.

vi. Awards

During this period the following regular FONDECYT were awarded to CINV investigators as P.I

1. Extrinsic and intrinsic factors controlling neural developments in vertebrates (1160076). PI: **K. Whitlock**, Co-PI: **J. Ewer**
2. Role of dysferlin in cytoskeletal actin remodeling and its impact on vesicle trafficking and membrane repair in muscular dystrophy linked to dysferlin mutations (1160495) PI: **AM. Cárdenas**.
3. Differential Regulation of Voltage-Sensors in High Voltage Activated Calcium Channels (Fondecyt 1161672) PI: **A. Neely**
4. (Fondecyt 1160261) PI: **C. Gonzalez**

R. Latorre was and invited in speakers is several international meetings:

- Plenary Lecture “Voltage and temperature coupling in transient receptor potential channels” at the Summer Symposium in Biophysics and Neurobiology, Universidad Austral de Chile, Valdivia CiSNe.
- Keynote Lecture “Temperature-sensitive little machines: TRP channels as temperature and pain sensors at the 5th Panamerican Plant Membrane Biology Workshop.
- Osvaldo Coru Mouilly lecture for the 70th year celebration of the school of Biochemistry U. de Chile: “Pequeñas máquinas sensibles a la temperatura: Canales TRP como sensores de temperatura y dolor”.
- Special lecture at the minisimposia “Fisiología y Biofísica de Canales Iónicos” at the Pontificia Universidad Javeriana Bogotá, Colombia “Función y estructura de los canales de potasio activados por calcio”.
- Conference “Allosterism and structure in the thermally –activaterd transient receptor potential channels” at Marie Curie – PRBB Scientific sessions of PRBB centres sponsored by the Centre of Genomic Regulation (CRG) and the Barcelona Biomedical Research Park.
- Special lectures Centro de Investigaciones Biomédicas de Canarias, Universidad de La Laguna, España “Modulación por subunidades accesorias de canales iónicos de potasio dependientes de calcio” o “El canal iónico que usted siempre quiso tener

R. Latorre was invited as a member of Advisory Board of the Centro de Investigaciones Biomédicas de Canarias, Universidad de La Laguna, España. He is also a member of Comision futuro, a senate sponsored committee that promotes science in Chile. He was interviewed in National Television in the show TVN conectados with the title “el cerebro”.

K. Whitlock was awarded a grant from CORFO: Innovación en Productos y Procesos (PROTOTIPO) #15ITE1-57257 named “Introducción de Sistema de acuaponía altamente eficiente en el uso de energía removable” and a grant from Fundación Chileno-Americana, USA to fund

Ciencia Al Tiro: “Proyecto Talleres de Ciencia en escuelas vulnerables de Valparaíso and Proyecto Capacitación de Profesores en Escuelas Públicas de Valparaíso”. Her continued contribution to Science Education was recognized by this year prize in “Innovación en Educación Científica: Educación Científica No Formal” from Fundación Ciencia Joven / UNESCO. She also received the “Premio Ciudad” from Fundación Futuro for her work in; Ciencia al Tiro.

K Whitlock was also invited speaker in several meeting and symposia:

- Nexos Chile-USA, David Rockefeller Center for Latin American Studies (DRCLAS), Harvard University, USA www.nexoschileusa.org, Nov 6-7
- Invited Speaker Conversaciones Sobre Neuromedicina, BNI, Facultad de Medicina, Universidad de Chile, Nov. 4.
- Invited Speaker: 8th Meeting of the Latin American Society for Developmental Biology, Santos, Brazil, October 20-23.
- Co-organizer /Invited Speaker: Integrating Hedgehog signaling in stem cell, developmental & cancer biology. October 17 – 20, 2015
- Invited Speaker, What are the model systems of our future? 34th International Ethological Conference, Cairns, Australia 9-14 August.
- Co-Organizer of the Midwest Zebrafish Meeting, Bi-annual Midwest Zebrafish Conference, Washington University School of Medicine USA, June.
- Chair Educational Workshop, Bi-annual Midwest Zebrafish Conference, Washington University School of Medicine USA, June.

T. Perez-Acle has been named Executive secretary for the South American Initiative in Molecular Simulations (SAIMS). He was invited as a Keynote Speaker at the International Gap Junction Conference and continues his work at the advisory board for the national program in scientific outreach Explora.

JC Saez was selected for the Luis Izquierdo lecture of the Annual Meeting of the Chilean Cell Biology Society with the title “Connexin and pannexin-based channels in different biological systems: from fundamental to applied science”. He was also selected as a plenary lecturer at the joint meeting of the Chilean Neuroscience-Pharmacology-Physiology Societies. Coquimbo, Chile with the title: “Connexin and pannexin hemichannels as molecular targets for chronic inflammatory responses”.

A. Chavez, was awarded the Early Career Scientific award from the TWAS foundation. This honor is given to developing-nation researchers with at least 10 international publications who show potential for a high-impact career.

A Palacios was awarded a grant from CORFO “Consolidación de la Oficina de Transferencia y Licenciamiento de la Universidad de Valparaíso” Director (15COTL-47469) and C.I in the grant “Coding and prediction at early times of the movements”. ANR-TRAYECTORIA PI Frederic Chavane. Equipe Associe Universidad de Valparaiso.

4. Education and Capacity Building

a) Education and Capacity Building:

The PhD Program in Neuroscience was created in 2002 by CINV members and is accredited through 2017. Its Director is currently Dr. John Ewer (CINV, Research line 3). It is designed to train researchers interested in the development, the structure, and the function of the nervous system. Its strengths are the areas of molecular physiology and biophysics, computational neuroscience, sensory neuroscience, neuronal plasticity and neuropathology, and development and neurogenetics.

This is the oldest Ph.D. program in Neuroscience of Chile. The impact of the CINV Millennium Institute is evident from the quality of the students accepted into the program despite the creation of 2 new Ph.D. programs in Neuroscience in Santiago. Most significantly, the proportion of students we have admitted from Santiago has been increasing. Thus, the program has matured and can compete effectively with programs in Santiago, despite the draw of the capital.

Our Program ensures funding for 4 years to all students it accepts, thereby allowing students to devote full time to their Ph.D. work. Funding is provided by governmental grants (CONICYT and MECESUP), as well as by grants offered by the University of Valparaíso. In addition, the CINV-ICM also provides graduate fellowships (8 during this period). Agreements with other graduate programs allow students to take elective courses at other universities in Chile and abroad, as well to carry out research internships. Our Program has a double Ph.D. agreement with the Scuola Internazionale Superiore di Studi Avanzati (SISSA) of Trieste, Italy (www.sissa.it), which has expanded the range of thesis topics. We are also in the process of making a similar agreement with the University of Sao Paulo, Brazil, and the University of Göttingen, Germany.

Requirements and application to enter the program were explained in first CINV-Report. Web pages: www.uv.cl and www.dnuv.cl.

The new Ph.D. program in Biophysics and Computational Biology (Program Director: Dr. Carlos Gonzalez): This Program was proposed in the original grant. The University Board approved its creation during 2014 to start its activities in March 2015. In 2015, the program accepted 4 students from Valparaíso and Santiago, who are funded through the fellowships of the University of Valparaíso. These students participated in world-class international courses as part of the program. During the recruitment period of 2015 we selected 2 students out of 5 applicants to begin their studies in 2016. Also during 2015 we prepared the documentation to submit in March 2016 an application to accredit the program by the National Commission on Accreditation.

The Masters Program in Neuroscience was founded in 1999 and is currently directed by Dr. Agustin Martinez (CINV research Line 2). The program was reaccredited for 8 years in 2011 (through 2018), becoming the longest accredited program of the University of Valparaíso. The program is characterized by a high content of basic Neuroscience as well as for its multidisciplinary nature. Its students are from various disciplines: biologists and biochemists as well as health professionals, engineers, and mathematicians, eager to understand the biological basis of the functioning of the nervous system.

Requirements and application to enter the program were explained in the first CINV-Report Web pages: www.uv.cl and www.magisterneurociencia.cl.

b) Achievements and results:

In the Neuroscience **PhD Program**, 28 students have graduated since 2002 (9 female; 19 male), of which 2 graduated during this period (see list below). The Program currently has 31 students (7 female, 24 male). During this year's recruitment period 11 applicants were considered admissible and were interviewed. Of these, 4 were selected and accepted to join the Program. Two received fellowships from CONICYT, and the rest received fellowships from the University of Valparaiso and CINV. We believe that our recruitment strategy has become more effective as we now receive enough applications to be able to select the very best. All current students typically attend one national or international conference in their area of study per year; funding is provided through their fellowship, through their advisor's grants, or through fellowships offered by the University of Valparaiso.

In the **Master Program**, 47 students have graduate since 1999 (25 females; 22 male), of which 4 graduated during this period; two of them did their thesis with researchers from our center (see list below). During this year's recruitment period, the program was very successful, receiving 33 applications of which 18 were accepted, being close to the maximum number of students we are able accept every year. Of these, 6 received fellowships from CONICYT. During the interview process several applicants mentioned the existence of the CINV as part of the reasons for choosing our program, suggesting that the CINV has given more visibility to this program.

c) Destination of Students:

PhD Program: 28 students have graduated since 2002, starting with Dr. A. Chavez in 2007. The majority of graduates of our Program are currently carrying out postdoctoral work (with the exception of a few graduates from 2015 who are either looking for postdoctoral positions or are completing experiments and preparing their thesis work for publication).

Master program: 47 have graduated since 1999, starting with Dr. Chavez in 2000. About half of our graduates have gone back to their professional practice, and the other half have followed the scientific academic pathway, entering to diverse Ph.D. programs in Chile and abroad, including our PhD in Neuroscience. Some of them are academics in Chile or abroad.

d) Main achievements of Ph.D. and Master Students from our programs during the period:

Graduations of Ph.D. students (Jan-Dec 2015):

1. Jorge Torres; Title: Coordinated development of the peripheral and central olfactory system in the zebrafish, *Danio rerio*; Advisor: Kathleen Whitlock

Graduations of Master students (Jan-Dec 2015):

1. Adolfo Agurto. Thesis: Síntesis de óxido nítrico en células bipolares de la retina de rata. Advisor: Oliver Schmachtenberg.
2. Daniela De Giorgis. Title: Regulation of Voltage sensing structures of CaV1.2 Calcium Channel by the Auxiliary β -subunit ($\beta 3$). Advisor: Dr. Alan Neely and Ricardo Olcese.

Ph.D. Thesis Project Approvals and Qualifying exams (January - December 2015):

1. Ana Abbott; Project title: Adult neurogenesis in the zebrafish hypothalamus: investigating relationship between food intake and reproduction. Advisor: Kathleen Whitlock

2. Samy Castro; Project title: Fluctuaciones Espontáneas en Actividad Neuronal Sostenida: Dinámica Multi-Estable en Modelo de Masas Neuronales”. Advisor: Patricio Orio and Wael El-Deredy.
3. Pablo González; Project title: Role and identity of glia during the development of the olfactory sensory system of the Zebrafish (*Danio rerio*); Advisor: Kathleen Whitlock
4. Yenisleidy Lorenzo; Project title: Modulación del sensor de potencial del canal BK por las subunidades auxiliares β en presencia de Ca^{2+} . Advisor: Ramon Latorre; co-advisor: Carlos Gonzalez.
5. Koyam Morales; Project title: Cambios en la eficacia sináptica generados por activación de receptores para serotonina en corteza prefrontal. Advisor: Marco Fuenzalida
6. Amaury Pupo; Project title: Mecanismo de conducción de protones en el canal H_v1. Advisor: Carlos Gonzalez; co-advisor: Ramon Latorre.:

Master Thesis Project Approvals and Qualifying exams of CINV students (January - December 2015):

1. Juan Pablo Córdova. "Modulación y Caracterización Electrofisiológica de las respuestas evocadas por luz de células Amacrinas". Advisor: Oliver Schmachtenberg
3. Nicolás Andrés Figueroa. "Vias de Entrada de Señal Lumínica Sincronizadora del Ritmo Circadiano en Araña *Euophrys Rusticana*". Advisor: John Ewer
4. Macarena Gárate. "Efecto de la Corticosterona y DHA en la Corteza Prelimbica de ratas Durante un Paradigma de Toma de Decisiones y Atención".Advisor: Alexis Dagnino
5. Marco Lovera Cabello. "Envejecimiento del Complejo Dentino-Pulpar en dientes humanos: Cambios en los componentes Neuro Inmunológico".Advisor: Eduardo Couve
7. Marcela Navarrete. "Variación en amplitud de la emision Otoacústica Producto de Distorsión en pruebas de Atención Auditiva como Resultado de la Acción del Filtro Auditivo en sujetos Normoyentes".Advisor: Paul Délano
10. Bernardo Pinto. Advisor: “Charged residues at the first transmembrane region mediate the voltage dependence of connexins slow gate”. Carlos González
11. Jacqueline Alejandra Vásquez. "Exocitosis de Vesículas Secretoras en Neuronas Corticales Derivadas de la Corteza de Un Ratón con Trisomía 16, un Modelo Del Síndrome de Down. Advisor: Ana Cárdenas.

a) Students visiting laboratories abroad. We continued supporting the travel and stay of many of our students in the laboratories of members of our international network to do research that cannot be done in Chile because lack of equipment or experience. Students who conducted research stay during this period include.

1. Sammy Castro (Ph. Student) April-May 2015. Attended Neuro-informatics course (<http://www.incf.ni.uos.de/>), then spent 12 days in lab of co-advisor, Wael el-Deredy, Ph.D. (University of Manchester, Manchester, UK)
2. Fernando Hinostroza (PhD Student). January – April 2015; visit to laboratory of Eva Alés. Ph.D. (University of Seville. Spain).
3. Cesar Ravello (PhD Student) May 2015; visit to lab of Frederic Alexander, Ph.D. (INRIA, France; Computational Neuroscience).

4. Jaime Maripillán (Master Student); Visit to laboratory of Jorge Contreras, Ph.D. (Rutgers University, NJ, USA).
5. Jorge Torres-Paz (Ph.D. Student). June 6 - July 19, 2015. Attended “Embryology: Concepts & Techniques in Modern Developmental Biology” course at Marine Biological Laboratories (MBL; Woods Hole MA USA).
6. Ruben Herzog (Ms Student) May 2015; visit to lab of Bruno Cessac, Ph.D. (INRIA, France; Computational Neuroscience)
7. Joaquin Valdes Bize (Biology graduate), January - March 2015, internship at the lab of Prof. Dr. rer. nat. F. Paquet-Durand, Cell Death Mechanism Group. Institute for Ophthalmic Research, University of Tuebingen. Research on a retinal explant model of diabetic retinopathy.

b) Organization of National and International courses and workshops:

Courses

1. International Spring School Applied Statistical Thermodynamics: from theory to molecular dynamics simulation. Organized by Tomás Pérez-Acle
2. Integrating *hedgehog* signaling in stem cell, developmental & cancer biology. Practical Course October 17 – 20, 2015 Santiago Chile. Co-organizer: Kathleen Whitlock.

Workshops

1. International Workshop: Biophysics of hemichannels and gap junction channels: A theoretical and practical training. Organizers: Agustín Martínez and Juan Carlos Sáez.
2. International Workshop: Biochemical, Spectroscopic and Crystallographic approaches used to study the functional-structural correlations of membrane proteins. Organizer: Carlos González.
3. International Workshop: Molecular dynamics simulations: From theory to applications. Organizer: Tomás Pérez-Acle
4. Educational Workshop, Bi-annual Midwest Zebrafish Conference, Washington University School of Medicine USA. Chair: Kathleen Whitlock.

Strategies to hire young investigators. In 2015 we carried out an international search to hire 2 Max Planck Tandem Research Leaders. Thirty-six young investigators applied, from which 10 were selected by a committee composed of 4 CINV investigators and 4 Max Planck investigators and invited to visit Valparaiso and participate in a symposium. Based on the symposium and an interview conducted by the selection committee, two candidates were chosen: Chiayu Chiu from Yale University who will add optogenetics and two photon microscopy to study the development of the brain cortex, and Rodrigo Suárez, presently at the University of Queensland, Australia, who is an expert in brain development and evolution. These investigators are expected to join the CINV in 2016 and 2017, respectively.

5. Networking and other collaborative work

a) Networking:

The creation, maintenance, and strengthening of scientific networks is at the core of CINV's mission. These initiatives are grouped into three main networks of scientific collaboration, depending on the CINV's scientific areas: The **Biophysics and Computational Neurosciences Network**, the **Genetic and Development Network**, and the **Intercellular Communication in the Nervous System Network**.

During 2015, these networks organized an international congress, workshops, and symposia, which are briefly outlined below.

5.1. International Workshop; Biophysical properties of hemichannels and gap junction channels: A theoretical and practical training. March 24 – 27, 2015. This workshop was designed to provide students with theoretical and practical training in the most recent developments within the field of connexin and pannexin hemichannels, including a brief historical overview. Gap junctions and connexin/pannexin hemichannels are central to many physiological and pathological aspects of neuroscience and biology in general. A total of 14 renowned Chilean and foreign scientists of our “Intercellular Communication in the Nervous System Network” met in this activity to discuss key aspects of connexin and pannexin function with 20 selected students. Part of the activities took place in Santiago and others in Valparaíso.

5.2. International Gap Junction Conference 2015, IGJC. March 28 – April 2, 2015.

IGJCs are unique interdisciplinary scientific conferences that cover all aspects of intercellular communication mediated by connexins, pannexins and innexins. This is a dynamic and multidisciplinary field that spans from molecular biology via biophysics to clinical investigation. Within this congress, young emerging researchers interacted with the most important scientists of the gap junction field, during symposia, poster sessions, and informal after hour meetings. The IGJC, the most important congress in the field, took place for the first time in South America since its initial organization in 1983. More than 180 researchers from Europe, America, Asia and Africa participated in this scientific event. 43 students were awarded travel grants by the CINV and the ICM among others, to present their work. This congress positioned the CINV as a key player in the gap junction field, allowed the generation of new international collaborations and increased the size and relevance of our “Intercellular Communication in the Nervous System Network”.

5.3. International Workshop: Biochemical, Spectroscopic and Crystallographic approaches used to study the functional-structural correlations of membrane proteins. July 25 – 29, 2015.

In this workshop, Drs. Luis Cuello and Beatriz Velez from Texas Tech University demonstrated recent advances in state-of-the-art biophysical methods to study ion channels, membrane transporters and other membrane proteins. The topics covered in the workshop included 1) Membrane protein biochemistry; 2) assessment of the structural dynamic of membrane proteins by Continuous Wave Electron Paramagnetic Resonance Spectroscopy (CW-EPRs) and Fluorescence Spectroscopy; and 3) X-ray solution structure of membrane proteins.

5.4. Spring symposium in TRP Channels. September 28-29, 2015. The Spring Symposium in TRP Channels brought together 13 outstanding researchers in the field of TRP channels biophysics, function and physiology. It aimed to generate a local forum for scientists working in different aspects of TRP channels function, and to provide a new space to share their work with students and postdocs in this field. Around 60 people attended the meeting, which also included a poster session for students and young researchers.

5.5. International Spring School Applied Statistical Thermodynamics: from theory to molecular dynamics simulation. November 16 to 27, 2015. This international spring school is a 2 week long international biannual intensive graduate school dedicated to introduce to the students on the mathematical and physical aspects of statistical thermodynamics. Defined as a bootcamp, students were exposed to two weeks of intensive lectures and hands-on work. This school was held in Fundación Ciencia para la Vida and was supported and co-organized by the CINV. Using funding from the networking project of CINV, we provided 20 full scholarships to Latin-American students. In total, 32 PhD students coming from different PhD programs attended the school. Invited lecturers included Prof. Wilfred van Gusteren from the ETH, Zurich, Prof. Chris Oostenbrink from BOKU, Vienna, and Prof. Maria Reif from TUM, Heidelberg.

5.6. Meeting CINV-Max Planck Research Leaders 2015. November 18 - 19, 2015. In the presence of several distinguished directors of Max Planck Institutes from Germany and the United States, the CINV-Max Planck Research Leader competition was celebrated in the Naval Museum of Valparaíso. Ten pre-selected outstanding young scientists presented their work from different areas of neuroscience to the audience, which included most of CINV's 120 members. This competition forms part of a formal agreement between the Max Planck Society, the CINV and the University of Valparaíso, to create a platform for research and innovation in biomedical science and precision medicine. The two winners of the competition, Rodrigo Suarez and Chiayu Chiu, will form part of a CINV-Max Planck Tandem Group in Neuroscience Research, and receive each 150.000 USD per year for five years, to conduct their research in complete freedom from University administrative or academic obligations. The competition was closed by an outdoor lunch held in the Botanical Garden of Viña del Mar, led by Ramón Latorre and Reinhard Jahn, Director of the Max Planck Institute of Biophysics in Göttingen, Germany.

b) Other collaborative activities:

Genetics and Development Network: Collaboration between lines has resulted in several publications including a primary research paper (Boric et al., *PLOS One*, 2013; line 5) and a review (Ardiles et al, *Cold Spring Harb Protoc.*, 2013). Our work with the cross-cutting line using bioinformatics tools to identify potential regulatory regions for olfactory receptors has come to fruition (**Calfun et al., *Chemical Senses*, 2016**). External to Chile we have collaborations in the area of neural and hormonal control of postecdysial behaviors in insects (White, B. H. and J. Ewer, 2014; Dr. Benjamin White, NIH; Diao *et al.* 2015), clock control of behavior (C. Wegener and J. Ewer; Dr. Christian Wegener, University of Würzburg, Germany), genetic control of Kallmann Syndrome in humans (R. Ceriani, K. Whitlock, Dr. William Crowley, Harvard Medical School).

6. Outreach and connections with other sectors

a) *Outreach:*

After four years as a Millennium Institute, we have established the CINV as an excellence research center in Valparaíso with a direct impact on the society at large and playing a fundamental role in fostering the country's scientific development. CINV's outreach strategy keep searching for new and imaginative ways of disseminating science, putting it in the eyes of the people as an activity present in everyday life. We want basic science to be valued by the society in a friendly and creative manner. With this in mind, we have carried out interdisciplinary activities linking the concerns of the scientific world with those of the society.

We have employed diverse means to reach our audience, including talks open to all public (*Tertulias Porteñas*), books, audiovisual productions (*Neuromantes and Neuronews*), and workshops with students (*Ciencia al Tiro*). The media coverage of CINV has been approached in three ways: coverage of scientific research at CINV, coverage of outreach activities and coverage of activities (Symposia, Congresses), as well as discussion about current public policies that are relevant to researchers of the CINV. In this way, CINV maintains a permanent and growing presence in local, regional and national media. Media presence of CINV since 2014 has been estimated to be worth around USD 370,000. In this regard, one milestone was the presence of Dr. John Ewer in national media (Television and newspapers) with the discussion about the policy implemented by the Ministry of Energy on not applying daylight saving time change during winter, which affects health and alertness, especially of children and adolescents. This year is the second season of our series “*NeuroNews*”, a joint venture between CINV and the main Chilean news media in Internet the online newspaper “*El Mostrador*” (7.5 million visits/month). This agreement – unprecedented in Chile– consists on the periodic delivery of articles, prepared by PhD and Master students, under the supervision of Dr. O. Schmachtenberg, that ‘translate’ into a common language research articles published in world-class scientific journals and that are of interest to the general audience. Thirteen articles were published in 2015 and received 86,700 visits (20% more than last year). (<http://cinv.uv.cl/category/neuronews/>).

Since 2011, CINV has increased its outreach activities –independently and in alliances with other institutions–, being now a widely recognized institution throughout the city and the country. Its most relevant outreach activities are:

Tertulias Porteñas. Since the year 2012 we bring together high-level scientists, artists and intellectuals, to discuss neuroscience-related topics with an interdisciplinary approach. Tertulias are open to all audiences, and aim to improve the understanding of science by society and to captivate the public with the creative inspiration that moves scientists. During 2015 the Tertulias were chaired by the prominent psychiatrist and playwright Marco Antonio de la Parra and sponsored by Universidad de Valparaíso, Consejo Nacional de la Cultura y las Artes, Radio Valentín Letelier, Iniciativa Científica Milenio, Mercurio de Valparaíso (newspaper), Hotel Cirilo Armstrong, and the Altamira Brewery. **2015 Tertulias were** “What do we know about the language?”, “What do we know about emotions?”, and “What do we know about flavors?” Estimated audience: 220 people in each Tertulia. (<http://cinv.uv.cl/tertulias-portenas/>)

¿Qué tienes en mente? Neuroscience talks series given by CINV researchers to school students in all the Valparaíso Region. Activities were focused on small groups of 16-17 years old students, in order to increase the interaction between researchers and the students. Partner Institutions: Faculty of Sciences Universidad de Valparaíso.

2015 talks: five, in different cities of the Valparaíso region and an estimated audience of 250 students in total. It is one of the most recognized activities by the regional authorities. Participants

could apply for the Summer School in Neuroscience, organized by Andres Chavez and the Millennium Nucleus Nu-MIND in January 2016. (<http://cinv.uv.cl/que-tenes-en-mente/>)

“What we know about our brain?”. Dr. A. Chavez. Viña del Mar

“Senses, our window to the world”. Dr. O. Schmachtenberg. Viña del Mar.

“Neuroscience sense”. Dr. P. Orio. Quilpué.

“We are a living battery”. C. González. Quillota.

“Brain Chemistry”. Dr. A. M. Cárdenas. Zapallar.

Festival Puerto de Ideas: Valparaiso hosted *Puerto de Ideas*, the first festival of cultural reflection in South America, and Antofagasta hosts the science version of the festival. This Festival includes presentations and activities from prominent national and foreign participants, which range from scientists to all kinds of artists. Dr. R. Latorre is part of the Advisory Board of the Festival, inviting recognized neuroscientist to participate with talks for open public. During the Festival the documentary “Montemar and the labyrinths of memory”, produced by CINV and Cábala Producciones, was shown to the public with a presentation by its Director, Gonzalo Argandoña.

Ciencia al Tiro (www.cienciaaltiro.cl). Program created in 2008 by the CINV researcher K. Whitlock. The program works with students from public schools in Valparaíso to enhance knowledge of science through workshops and long-term research projects at the same time strengthening the links with the community. In 2014 long-term research projects were initiated at the “Edificio Verde” (*Green Building*) including studies of electricity and energy efficient light bulbs, the use of restaurant waste as food for fish, and study of circadian rhythm in the hedgehog. Additionally we use the Aquaponics system to study water pH and the nitrogen cycle.

Other outreach activities in 2015:

April of 2015: As part of Earth Day and to prepare the way for the Second Conference Our Ocean, the US ambassador, Michael Hammer, together with students painted a large mural in Valparaíso.

In May 2015: Launch of the book "The Joy of Science" at the Museum of Natural History of Valparaiso, at a ceremony with the Director of Ciencia al Tiro, Dr. K. Whitlock, the President of the University of Valparaiso, A. Valle, and the Director of CINV, Dr. R. Latorre. The book includes twelve workshops of the Ciencia al Tiro program. Cata, the protagonist, asks how the world works as she tours cities like Valparaiso and San Pedro de Atacama. On this trip we develop experiments that teach manufacturing compasses, thermometers, electric motors, solar ovens and cook biscuits in them, and also teach how the brain works.

October 2015: The Ciencia al Tiro program was selected to be part of “Cambio Global” (Global Change) by Cabala Productions and broadcast by National television of Chile. Cambio Global is a series of documentaries in which the story of people committed to their community is discussed, promoting lifestyles in harmony with the environment, fighting against pollution, climate change, waste or greenhouse gases, and finding a new meaning for their lives in activities related to ecology and the environment.

November 2015: Fundación Futuro recognizes every year individuals, institutions, NGOs, government agencies, and social organizations that have made the city a human, entertaining, democratic, ecological, informed, supportive, or more beautiful worship space. This year, the Ciencia al Tiro program was awarded the prize in recognition of its contribution to the development of the city of Valparaiso.

December 2015: In the third edition of the Prize for Innovation in Science Education, organized by the Fundación Ciencia Joven (Young Science Foundation), and the support of UNESCO,

Ciencia al Tiro was selected in the category of non-formal education, where children from vulnerable schools carry out hands-on scientific experiments.

Audiovisual Production CINV. Each year, CINV develops or takes part in some audiovisual product related to science outreach. In 2012 we participated in publishing the book “*Francisco Varela, la ciencia del ser*” (“Francisco Varela, the science of being”), in 2013 the TV series “*Neuromantes*” was produced and there was participation in different programs (“*Vida Conciencia*”, “*Chile Innova*”). In 2015 the CINV decided, in partnership with Cábala Producciones to make a new audiovisual production, on the basis of “Neuromantes” oriented to network television, so as to reach a larger audience. In September “Neuropolis” (the new production) won a grant from the National Television Council for production in 2016, and transmission on national TV in 2017.

b) Connections with other sectors:

Juan Ignacio Molina Building (formerly Severín Building): A crucial step for the new CINV building in a historical district of Valparaíso was the start of the bidding process for its construction. Financing will come from the Chilean State, who will provide 70% of the funds (USD 5,460,000) from national and regional funds, and from the Universidad de Valparaíso, who will provide the remaining 30% (USD 2,340,000). The building should be completed by 2018 and seeks to be a reference for national scientific infrastructure, which will also aid with the revival of the historic district.

Progress in financing and planning for the construction of the building has been possible thanks to the positioning of CINV at the regional and national levels, given by the media campaigns and by meetings with political authorities, local institutions, and opinion leaders.

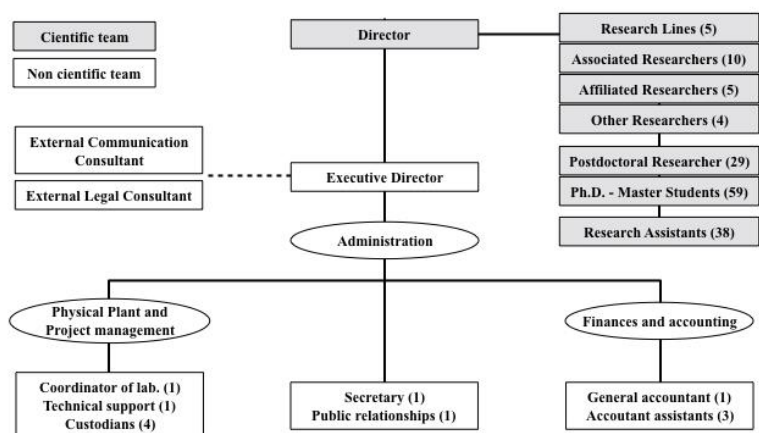
Fundación Puerto de Ideas: Dr. Ramón Latorre, as CINV Director, is a permanent member of the Scientific Committee of Puerto de Ideas Foundation, which organizes the yearly Festivals in Antofagasta and Valparaíso. This alliance will ensure the presence of renowned scientists in the Festival, including researchers of CINV.

Local Institutions: The CINV is an active guest in different institutions concerned with the development of the city and the Region. Currently, CINV cooperates with the Corporación La Matriz and the Instituto de Sistemas Complejos de Valparaíso. In 2015 an agreement was signed with Fundación Ciencia Joven to work together in creative and high impact ways to popularize science. It has positioned itself as a relevant entity for the discussion of local public policies, and is a reference for the attraction of advanced human resources, regionalization and development.

7 Administration and Financial Status (1Página)

a) Organization and administration:

An Executive Director supervises and coordinates all the administrative duties according to the needs of the Director and of other Researchers. These include the management of the Millennium Institute Grant and of all other grants of CINV researchers (almost 15 grants per year), He also coordinates outreach and networking activities with the private sector and with community leaders, together with



all efforts aimed at securing funds and the construction of the new building to house the CINV, and the communication strategy of CINV. The organization includes the Accounting Team, which manages the different grants and human resources, and a Physical Plant and Project Support team that assists researchers in the purchasing of equipment and computer maintenance, and provides support for the development and submission of grants. The support for scientific (Symposia, Congress) and outreach activities is coordinated by a Public Relations coordinator, with the support of the entire management team. Each host institution provides office and laboratory space to individual investigators holding faculty positions. Base salaries for investigators are provided by the corresponding host institution. The Universidad de Valparaíso has set up an institutional grant to help with operational expenses.

Category	Female	Male	TOTAL
Assistant & Technicians	18	20	38
Administrative Staff	12	5	17
TOTAL	30	25	55

b) Financial Status:

During 2015, the CINV had a total income of \$1.891.363.783, of which the Millennium Institute (MI) contributed 44%. The contribution from the MI has varied from 55,7% (2012), 35,4% (2013), and 42,0% (2014). The other sources of income came from CONICYT (24% in 2015) and the Universidad de Valparaíso (30% in 2015). There was an increase in the **goods category and equipment** of 15.24% due to the acquisition of new equipment for laboratories, according to the incorporation of new researchers (A. Chávez). The category "**Honorarios**" also increased due to the incorporation of new Postdoctoral fellows, and the creation of a special scholarship for students of the new Ph.D. in Biophysics and Computational Biology of the Universidad de Valparaíso, created and led by CINV.

8 Annexes:

Annex 1.- Institute / Nucleus Researchers

1.1 Associate Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Adrian Palacios	SENSORY AND SYSTEMS.	Chilean	M	18/03/1958	Psychologist	D	Universidad de Valparaíso	Professor	2
Alan Neely	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Chilean	M	15/04/1956	Biologist	D	Universidad de Valparaíso	Professor	2
Ana Maria Cardenas	CELL SIGNALING.	Chilean	F	1/4/1969	Pharmacist	D	Universidad de Valparaíso	Professor	2
Carlos González	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Cuban	M	13/12/1965	Biophysicist	D	Universidad de Valparaíso	Professor	2
Danilo González Nilo	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION .	Chilean	M	9/12/1968	Chemist	D	Universidad Andrés Bello	Professor	2
John Ewer	DEVELOPMENTAL GENETICS AND BEHAVIOR.	Chilean	M	23/02/1961	Biologist	D	Universidad de Valparaíso	Professor	2
Juan Sáez	CELL SIGNALING.	Chilean	M	2/2/1956	Biochemist	D	Universidad Católica de Chile	Professor	2
Kathleen Whitlock	DEVELOPMENTAL GENETICS AND BEHAVIOR.	American	F	27/08/1963	Biologist	D	Universidad de Valparaíso	Professor	2
Ramón Latorre	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Chilean	M	29/10/1941	Biochemist	D	Universidad de Valparaíso	Professor	2
Tomás PérezAcle	COMPUTATIONAL BIOLOGYAND MOLECULAR SIMULATION.	Chilean	M	9/9/70	Biologist	D	Fundación Ciencia & Vida	Assoc. Inv.	2

1.2 Young Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Daniel Almonacid	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION .	Chilean	M	28/03/1981	Biochemist	D	Universidad Andrés Bello	Researcher	2
José Pérez	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION .	Chilean	M	23/11/1978	Biochemist	D	Universidad Andrés Bello	Professor	2
Karen Castillo	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Chilean	F	23/07/1979	Biochemist	D	Universidad de Valparaíso	Researcher	1
Alvaro Ardiles	CELL SIGNALING	Chilean	M	2/12/1977	Biochemist	D	Universidad de Valparaíso	Researcher	1

1.3 Senior Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Alfredo Kirkwood	SENSORY AND SYSTEMS.	Chilean	M	5/3/58	Biologist	D	John Hopkins University	Professor	2
Francisco Bezanilla	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Chilean	M	17/05/1944	Biochemist	D	Chicago University	Professor	2
Gonzalo Ferreira	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Uruguayan	M	20/01/1964	Physician	D	Universidad de la República	Professor	2
Miguel Holmgren	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Chilean	M	3/5/1962	Biophysicist	D	NIH-NINDS	Senior Investigator	2
Oswaldo Alvarez	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Chilean	M	19/10/1942	Biochemist	D	Universidad de Chile	Professor	2
Ralph Greenspan	DEVELOPMENTAL GENETICS AND BEHAVIOR.	American	M	23/03/1950	Biologist	D	Kavli Institute for Mind and Brain	Professor	2
Verónica Milessi	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Argentinian	F	2/12/1962	Pharmacist	D	Universidad Nacional de La Plata	Professor	2

1.4 Others

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Agustín Martínez	CELL SIGNALING.	Chilean	M	14/08/1968	Biologist	D	Universidad de Valparaíso	Professor	2
Andrés Chávez	SENSORY AND SYSTEMS.	Chilean	M	10/1/1977	Biologist	D	Universidad de Valparaíso	Profesor	2
Daniel Aguayo	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION .	Chilean	M	8/8/1978	Biochemist	D	Universidad Andrés Bello	Professor	2
David Naranjo	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS.	Chilean	M	17/10/1957	Biologist	D	Universidad de Valparaíso	Professor	2
Oliver Schmachtenberg	SENSORY AND SYSTEMS.	Chilean	M	12/12/1970	Biologist	D	Universidad de Valparaíso	Professor	2
Patricio Orio	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION .	Chilean	M	3/12/1973	Biochemist	D	Universidad de Valparaíso	Professor	2
Hans Moldenhauer*	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS	Chilean	M	22/2/1983	Biochemist	D	Universidad de Valparaíso	Researcher	1
Ignacio Díaz*	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION	Chilean	M	2/4/1981	Biochemist	D	Universidad Andrés Bello	Researcher	1
Angelina Palacios*	DEVELOPMENTAL GENETICS AND BEHAVIOUR	Chilean	F	12/7/1981	Biochemist	D	Universidad de Valparaíso	Researcher	1
Juan Castillo*	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS	Chilean	M	22/7/1985	Biologist	D	Universidad de Valparaíso	Researcher	1

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David Báez*	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS	Chilean	M	18/1/1983	Biochemist	D	Universidad de Valparaíso	Researcher	1
German Miño*	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS	Chilean	M	29/5/1971	Biochemist	D	Universidad de Valparaíso	Researcher	1
Gustavo Contreras*	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS	Chilean	M	15/9/1982	Biochemist	D	Universidad de Valparaíso	Researcher	1
Pavel Prado*	CELL SIGNALING	Cuban	M	22/3/1976	Biologist	D	Universidad de Valparaíso	Researcher	1
Arlek González*	CELL SIGNALING	Chilean	F	7/11/1981	Biochemist	D	Universidad de Valparaíso	Researcher	1
Rosalba Escamilla*	CELL SIGNALING	Mexican	F	2/6/1971	Biochemist Engineer	D	Pontificia Universidad Católica de Chile	Researcher	1
Adam Aguirre*	CELL SIGNALING	Chilean	M	22/7/1967	Veterinarian	D	Pontificia Universidad Católica de Chile	Researcher	1
Carlos Puebla*	CELL SIGNALING	Chilean	M	7/4/1981	Biochemist	D	Pontificia Universidad Católica de Valparaíso	Researcher	1
Justin Flaven*	DEVELOPMENTAL GENETICS AND BEHAVIOUR	French	M	29/8/1987	Biologist	D	Universidad de Valparaíso	Researcher	1
Isabel Benjumeda*	SENSORY AND SYSTEMS	Spanish	F	5/12/1980	Psicologist	D	Universidad de Valparaíso	Researcher	1
Alex Vielma*	SENSORY AND SYSTEMS	Chilean	M	5/1/1979	Biochemist	D	Universidad de Valparaíso	Researcher	1
Alberto Martin*	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION	Spanish	M	6/8/1980	Biologist	D	Universidad de Valparaíso	Researcher	1

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José Garate*	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION	Chilean	M	29/7/1983	Molecular Biotechnology Engineer	D	Fundación Ciencia & Vida	Researcher	1
Calixto Domínguez*	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION	Chilean	M	28/3/1973	Microbiologist	D	Fundación Ciencia & Vida	Researcher	1
Erick Olivares*	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION	Chilean	M	11/11/1976	Biologist	D	Universidad de Valparaíso	Researcher	1
Isaac García*	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS	Chilean	M	20/4/1978	Medical Technologist	D	Universidad de Valparaíso	Researcher	1
Diana Rojas*	CELL SIGNALING	Colombian	F	15/1/1974	Nutritionist	D	Universidad de Valparaíso	Researcher	1
Wilson Mena*	DEVELOPMENTAL GENETICS AND BEHAVIOUR	Chilean	M	29/9/1980	Biologist	D	Universidad de Valparaíso	Researcher	1
Carolina Soto*	CELL SIGNALING	Chilean	F	3/1/1979	Biochemist	D	Universidad de Valparaíso	Researcher	1
Fanny Momboisse*	CELL SIGNALING	French	F	6/3/1981	Biologist	D	Universidad de Valparaíso	Researcher	1
Kesheng Xu*	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION	Chinese	M	2/10/1982	Physist	D	Universidad de Valparaíso	Researcher	1
Carla Alvarez*	SENSORY AND SYSTEMS	Spanish	F	22/6/1985	Biologist	D	Universidad de Valparaíso	Researcher	1
Audry Fernandez*	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS	Cuban	F	18/9/1981	Biochemist	D	Universidad de Valparaíso	Researcher	1
Alvaro Ardiles *	CELL SIGNALING	Chilean	M	12/2/1977	Biochemist	D	Universidad de Valparaíso	Researcher	1

Annex 2.- Research Lines

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date [dd/mm/yy]	Ending Date [dd/mm/yy]
1	STRUCTURE AND FUNCTION OF MOLECULAR SENSORS	We try to understand how ion channels and pumps can respond to a variety of stimuli.	It is a combination of molecular biology, electrophysiology, modern fluorescence techniques, simulations and molecular modeling.	D. Naranjo, R. Latorre, A. Neely, O. Alvarez, F. Bezanilla, M. Holmgren, V. Milesi, C. González & G. Ferreira, K. Castillo.	73	08-08-2011	
2	CELL SIGNALING	Investigate how protein-protein interactions and covalent modifications of dynamin control neurosecretion and trafficking of ion channels.	Using patch clamp amperometry and total internal reflection fluorescence microscopy the handling by the cell of vesicles containing neurotransmitters is characterized.	JC. Sáez, AM Cárdenas & A. Matínez.	61	08-08-2011	
3	DEVELOPMENTAL GENETICS AND BEHAVIOR	Understanding how the nervous system develops and produces complex behaviors.	Using zebrafish and <i>Drosophila</i> as biological models, the development of the olfactory system and the genetic pathways controlling behavior are studied.	K. Whitlock, J. Ewer & R. Greenspan.	63 y 74	08-08-2011	
4	SENSORY AND SYSTEMS	To investigate the mechanisms of neuronal encoding the visual, olfactory and cerebral physiological and pathological conditions.	Using different animal models, including Degu, a natural model for studying AD. The molecules identified by Group 2 as regulators of neurosecretion will be tested in the context of neuronal plasticity.	A. Palacios, A. Kirkwood, A. Chávez & O. Schmachtenberg.	61 y 73	08-08-2011	
5	COMPUTATIONAL BIOLOGY AND MOLECULAR SIMULATION	Using high performance computing for molecular modeling of membrane proteins, drug design assisted by computer, and inference and dynamics of biological networks.	Interaction between theoretical and experimental biologist to create new methods, models and hypothesis suitable to be tested by the experimental groups.	FD. González, T. Pérez-Acle, P. Orió, D. Aguayo, J. Pérez & D. Almonacid.	6, 59 y 73	08-08-2011	

Annex 3.- Publications

(Totally or partially financed by ICM). Students co-authoring a paper are underlined and CINV investigators shown in **bold face**

3.1.- ISI Publications or Similar to ISI

vii) 3.1.1 Associate Researchers:

1. **Aguayo D**, Pacheco N, Morales EH Collao B, Luraschi R, Cabezas C, Calderón P, **Gonzalez-Nilo F**, Gil F, Calderón IL Saavedra CP (2015) Hydrogen peroxide and hypochlorous acid influx through the major S. Typhimurium porin OmpD is affected by substitution of key residues of the channel. *Arch biochem Biophys.* 568: 38-45.
2. Brennan MJ, Karcz J, Vaughn NR, Woolwine-Cunningham Y, DePriest AD, **Escalona Y**, **Pérez-Acle T**, Skerrett IM (2015) Tryptophan Scanning Reveals Dense Packing of Connexin Transmembrane Domains in Gap Junction Channels Composed of Connexin 32. *J Biol Chem.* 290 (28): 17074-84.
3. Camarada MB, Márquez-miranda V, Araya-Durán I, Yévenes A, **Gonzalez-Nilo F**. (2015) PAMAM G4 dendrimers as inhibitors of the iron storage properties of human L-chain ferritin. *Phys Chem Chem Phys.* 17(29):19001-11.
4. **Carrasquel-Ursulaez W**, **Contreras GF**, **Sepúlveda R**, **Aguayo D**, **Gonzalez-Nilo F**, **Gonzalez C and Latorre R**. (2015) Hydrophobic interaction between contiguous residues in the S6 transmembrane segment acts as a stimuli integration node in the BK channel. *J Gen Physiol.* 145(1):61-74.
5. **Carrasquel-Ursulaez W**, **Moldenhauer H**, **Castillo JP**, **Latorre R** & Alvarez O. (2015) Biophysical analysis of thermosensitive TRP channels with a special focus on the cold receptor TRPM8. *Temperature.* 2(2):188-200.
6. **Castillo JP**, Rui H, Basilio D, Das A, Roux B, **Latorre R**, Bezanilla F, Holmgren M. Mechanism of potassium ion uptake by the Na(+)/K(+)-ATPase. *Nat Commun.* 2015 Jul24;6:7622. doi: 10.1038/ncomms8622.
7. **Castillo K**, **Contreras GF**, **Pupo A**, **Torres Y**, **Neely A**, **Gonzalez C** and **Latorre R**. (2015) Molecular mechanism of $\beta 1$ regulation in BK channel. *Proc Nat | Acad Sci USA.* 112(15): 4809-14.
8. **Castillo K**, **Pupo A**, **Baez-Nieto D**, **Contreras GF**, **Morera FJ**, **Neely A**, **Latorre R** and **Gonzalez C** (2015) Voltage-gated proton (Hv1) channels, a singular voltage sensing domain. *FEBS Letters* 589(2015): 3471-3478.
9. Cortés-Campos C, Letelier J, **Cerani R**, **Whitlock KE**. (2015) Zebrafish adult-derived hypothalamic neurospheres generate gonadotropin-releasing hormone (GnRH) neurons. *Biol Open.* 4(9):1077-86.
10. Diao F, Ironfield H, Diao F, Luan H, Shropshire W, **Ewer J**, marr E, Potter CJ, Landgraf M and White BH (2015) "Plug-and-Play Genetic Access to Drosophila Cell Types Using Exchangeable Exon Cassettes" *Cell Reports.* 10(8):1410-21.
11. **Díaz-Franulic, I.**, **Sepúlveda R**, **Navarro-Quezada N**, **Gonzalez-Nilo FD** and **Naranjo D**. (2015) Pore dimensions and the role of occupancy in unitary conductance of shaker K-channels. *J Gen Physiol* 146:133-146.

12. Du LY, Chang LY, Ardiles AO, Tapia-Rojas C, Araya J, Inestrosa NC, **Palacios AG**, Acosta ML. (2015) Alzheimer's disease-related protein expression in the retina of *Octodon degus*. *PLoS One*. 2015 Aug 12; 10(8):e0135499.
13. Elgueta C, Vielma AH, **Palacios AG**, **Schmachtenberg O**. (2015) Acetylcholine induces GABA release onto rod bipolar cells through heteromeric nicotinic receptors expressed in A17 amacrine cells. *Front. Cell. Neurosci.* 9:6.
14. García IE, Maripillán J, Jara O, Cerani R, Palacios-Muñoz A, Ramachandran J, Olivero P, **Pérez-Acle T**, **Gonzalez C**, **Sáez JC**, Contreras JE, **Martínez AD**. (2015) Keratitis-Ichthyosis-Deafness syndrome-associated Cx26 mutants produce non-functional gap junctions but hyperactive hemichannels when co-expressed with wild type Cx43 *J Invest Dermatol.* 135(5): 1338-47.
15. Garcia-Elias A, Berna-Erro A, Rubio-Moscardo F, Pardo-Pastor C, Mrkonjić S, Sepúlveda RV, Vicente R, **Gonzalez-Nilo F**, Valverde MA. (2015) Interaction between the linker, Pre-S1, and TRP Domains Determines Folding, Assembly and Trafficking of TRPV Channels. *Structure* 23(8):1404-13.
16. Harcha PA, Vargas A, Yi C, Koulakoff AA, Giaume C, **Sáez JC**. (2015) Hemichannels Are Required for Amyloid β -Peptide-Induced Degranulation and Are Activated in Brain Mast Cells of APP^{swe}/PS1^{dE9} Mice. *J Neurosci.* 2015 Jun 24;35(25):9526-38.
17. Inestrosa NC, Rios JA, Cisternas P, Tapia-Rojas C, Rivera D, Braidy N, Zolezzi JM, Godoy JA, Carvajal FJ, Ardiles AO, Bozinovic F, **Palacios AG**, Sachdev PS. (2015). Age progression of neuropathological markers in the brain of the Chilean rodent *Octodon degus*, a natural model of Alzheimer's disease. *Brain Pathology.* 25 (2015) 679-691.
18. Krüger E, Mena W, Lahr EC, Johnson EC, and **Ewer J**. (2015). Genetic analysis of Eclosion Hormone action during *Drosophila* larval ecdysis. *Development.* 2015 Sep 22. pii: dev.126995. Dec 15;142(24):4279-87.
19. Langenhan T, Barr MM, Bruchas MR, **Ewer J**, Griffith LC, Maiellaro I, Taghert PH, White BH, Monk KR (2015) Model Organisms in GPCR Research. *Mol pharmacol.* 88(3):596-603.
20. Leiva, V., Tejo, M., Guiraud, P., **Schmachtenberg O**, **Orio P** and Marmolejo-Ramos, F. Modeling neural activity with cumulative damage distributions. *Biological Cybernetics.* 109(4-5):421-33.
21. Márquez-Miranda V, Camarada MB, Araya-Durán I, Varas-Concha I, **Almonacid DE**, **Gonzalez-Nilo F**. (2015) Biomimetics: From Bioinformatics to Rational Design of Dendrimers as Gene Carriers. *PLoS One.* 10(9):e0138392.
22. Morera FJ, Baez-Nieto D, Lorenzo Y, **Castillo K**, Pupo A, Vargas-Chacoff L and **Gonzalez C** (2015) Role of ion channels in salt secretion by atlantic salmon gills during acclimation to seawater. *Physiological Mini Reviews*, 8(1):1-10.
23. Morera FJ, Saravia J, Pontigo JP, Vargas-Chacoff L, Contreras GF, Pupo A, Lorenzo Y, **Castillo K**, Tilegenova C, Cuello LG, **Gonzalez C**. (2015) Voltage-dependent BK and Hvl channels expressed in non-excitable tissues: new therapeutics opportunities as targets in human diseases. *Pharmacol Res.* 2015 Aug 21. pii: S1043-6618(15)00179-6. doi: 10.1016/j.phrs.2015.08.011. Nov;101:56-64. Review.
24. **Naranjo D**, Wen H and Brehm P (2015). Zebrafish CaV2.1 Calcium Channels Are Tailored for Fast Synchronous neuromuscular Transmission. *Biophysical journal.* 108(3):578-84.

25. Olivares E, Salgado S, Maidana JP, Herrera G, Campos M, Madrid R and Orio P (2015). TRPM8-dependent dynamic response in a mathematical model of cold thermoreceptor. *PLoS One* 588(Pt 17):3141-8.
26. Orellana JA, Moraga-Amaro R, Díaz-Galarce R, Rojas S, Maturana CJ, Stehberg J, Sáez JC. (2015) restraint stress increases hemichannel activity in hippocampal glial cells and neurons. *Front Cell Neurosci.* 9:102.
27. Poblete H, Oyarzún I, Olivero P, Comer J, Zuñiga M, Sepúlveda RV, Báez-Nieto D, Gonzalez Leon C, Gonzalez-Nilo F, Latorre R. (2015) Molecular Determinants of Phosphatidylinositol 4,5Bisphosphate (PI(4,5)P2) Binding to Transient Receptor Potential VI (TRPV1) Channels. *J Biol Chem.* 290(4):2086-98.
28. Prado-Gutierrez P, Castro-Fariñas A, Morgado-Rodriguez L, Velarde-Reyes E, Martínez AD, Martínez-Montes E. Habituation of auditory steady state responses evoked by amplitude-modulated acoustic signals in rats. *Audiology Research.* 5(113):21-28
29. Retamal MA, Leon-Paravic CG, Ezquer M, Ezquer F, Del Rio R, Pupo A, Martínez AD, Gonzalez C (2015) Carbon Monoxide: A New Player in the Redox Regulation of Connexin Hemichannels. *IUBMB Life.* 67(6):428-37.
30. Retamal MA., Reyes EP., García IE., Pinto B., Martínez AD, Gonzalez C (2015) Diseases associated with leaky hemichannels. *Frontiers in Cellular Neuroscience.* 9:267.
31. Riquelme MA, Cea LA, Vega JL, Puebla C, Vargas AA, Shoji KF, Subiabre M, Sáez JC. (2015) Pannexin channels mediate the acquisition of myogenic commitment in C2C12 reserve cells promoted by P2 receptor activation. *Front Cell Dev Biol.* 3:25.
32. Rovegno M, Soto PA, Sáez PJ, Naus CC, Sáez JC and Von Bernhardt R. (2015) Connexin 43 hemichannels mediate secondary cellular damage spread from the trauma zone to distal zones in astrocytes monolayers. *Glia* 63(7):1185-99.
33. Sáez JC, Cisterna BA, Vargas A, Cardozo CP. (2015) Regulation of pannexin and connexin channels and their functional role in skeletal muscles. *Cell Mol Life Sci.* 72(15):2929-35.
34. Salas D, Puebla C, Lampe PD, Lavandero S, Sáez JC. (2015) Role of Akt and Ca²⁺ on cell permeabilization via connexin43 hemichannels induced by metabolic inhibition. *Biochem Biophys Acta.* 1852(7):1268-1277.
35. Suzuki, K., Lovera, M., Schmachtenberg O. and Couve, E. Axonal Degeneration in Dental Pulp precedes Primary Teeth Exfoliation. *J Dental* 94(10):1446-53.
36. Talaverón R, Fernández P, Escamilla R, Pastor AM, Matarredona ER, Sáez JC (2015) Neural progenitor cells isolated from the subventricular zone present hemichannel activity and form functional gap junctions with glial cells. *Front Cell Neuroscience* Oct 13; 9:411.
37. Valdés, J., Olivares, J., Ponce, D., and Schmachtenberg O (2015) Analysis of olfactory sensitivity in rainbow trout (*Oncorhynchus mykiss*) reveals their ability to detect lactic acid, pyruvic acid and four B-vitamins. *Fish Physiol. Biochem.*, 41(4):879-85.
38. Whitlock KE. (2015) The loss of scents: Do defects in olfactory sensory neuron development underlie human disease? *Birth Defects Res C Embryo Today.* 105(2):114-25.

viii) 3.1.2 Other researchers:

1. Arias-Darrz L, Cabezas D, Colenso CK, Alegría-Arcos M, Bravo-Moraga F, Varas-Concha I, Almonacid DE, Madrid R, Brauchi S. (2015) A transient receptor potential ion channel in

- Chlamydomonas* shares key features with sensory transduction-associated TRP channels in mammals. *Plant Cell* jan;27(1):177-88 doi: 10.1105/tpc.114.131862.
2. García-Puente Y, **Prado P**, Martínez E. (2015) Time-frequency methods for studying non-stationary auditory responses. *IFMBE Proceedings* 49:540-543.
 3. **Miño-Galaz GA**, Gutierrez G (2015) Hydrogen bonds and asymmetrical heat diffusion in alpha helices. A computational analysis *Chemical Physics Letters* 635:16-22.
 4. **Miño-Galaz GA**. (2015) Allosteric Communication Pathways and Thermal Rectification in PDZ-2 Protein: A Computational Study *J. Phys Chem B*. 119(20):6179-89.

3.2.- SCIELO Publications or Similar to SCIELO

ix) 3.2.1 Other researchers:

1. Cerquera A, Muñoz J, Araya J, Gómez O (2015) Registro de actividad eléctrica en la retina de una rata albina empleando una matriz de microelectrodos. *Acta Biológica Colombiana*. 20(3):37-46.

3.3.- Scientific Books and Chapters

x) 3.3.1 Associate Researchers:

1. Ferreira G, **Raddatz N**, **Lorenzo Y**, **Gonzalez C**, and **Latorre R**(2015) Biophysical and Molecular Features of thermosensitive TRP Channels involved in Sensory Transduction. Chapter in: *TRP Channels in Sensory transduction*, R. Madrid, J. Bacigalupo (eds.), Springer International Publishing Switzerland.
2. **Olivares, E**; **Orio P**. (2015) Mathematical Modeling of TRPM8 and the Cold Thermoreceptors. In: *TRP Channels in Sensory Transduction*. Madrid, R.; Bacigalupo, J., editors. Springer International Publishing, 209-223

3.4.- Other Publications

NONE

3.5.- Collaborative publications:

Category of Publication	1 researcher		2 researchers		3 researchers		4 or more	
	N°	%	N°	%	N°	%	N°	%
ISI Publications or Similar to ISI Standard	28	62,22%	5	11,11%	4	8,89%	1	2,22%
SCIELO Publications or Similar to SCIELO Standard	0	0,00%	0	0,00%	0	0,00%	0	0,00%
Books and chapters	1	2,22%	1	2,22%	0	0,00%	0	0,00%
Other Publications	0	0,00%	0	0,00%	0	0,00%	0	0,00%
Total of publications	29	64,44%	6	13,33%	4	8,89%	1	2,22%

3.6 Patents

Title	Description	Económico Sector	Number	Country	Submission Date	Award Date	Status	Benefit
Ultra-thin and Self-hydrating Interface Comprisin a Biopolimer	The invention relates to an ultra-thin self-hydrating interface comprising a first support or substrate layer of a metal or semiconductor; a layer of hydrating biopolymer, having a thickness of between 10 and 200 Angstrom; and a layer of lipids capable of forming a lipid bi-layer, having a thickness of between 40 and 160 Angstrom. Second, mention is made of the method for obtaining the interface, which comprises the steps of depositing on a layer of metal or semiconductor a thin layer of the hydrating biopolymer having a thickness of between 10 and 200 Angstrom using high-vacuum physical vapour deposition; and on the resulting structure depositing a layer of lipids capable of forming a lipid bi-layer having a thickness of between 40 and 160 Angstrom using high-vacuum vapour deposition; wherein the thickness of each layer during the deposition process is controlled by high-resolution ellipsometry (VHRE). In addition, use of the interface to obtain a biosensor.	Industry, Medicine, Biotechnology and, Nanotechnology	PCT/CL 2015/050 033	Chile	13/8/2015		Being reviewed	0
Substituted Sulfonyl Fenil derived compound calpain inhibitors; Pharmaceutical compositions useful in the treatment of calpain activity associated diseases such	Phenyl sulfonyl derivative compounds substituted amines; pharmaceutical composition of these compounds; and their use in treating pathologies associated with inhibition of calpain, such as male infertility, testicular torsion, varicocele, oligospermia, Alzheimer's Disease, Parkinson's and AIDS among others.	Pharma	PCT/CL 2010/007 44	Chile	10-12-10	25-6-15	Being reviewed	\$352.550

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<p>as male infertility, testicular torsion, Varicocele, oligospermia, Alzheimer's, Parkinson's, Hungtintong, AIDS.</p>								
<p>Specific Modulators of Connexin Hemichannels</p>	<p>The invention relates to methods for identifying specific modulators of hemichannels formed by connexins, using structural bioinformatics methods for calculating the interaction energy with ligands and compositions for selectively modulating the activity of hemichannels formed by connexins. The invention describes, inter alia, a computer-assisted method that can be used to estimate the interaction energy between ligands belonging to a database of chemical compounds, with a binding pocket defined by the region comprising residues 3-10 (NTH), 29-40 (TM1), 74-93 (TM2) of a protomer and residues 29-40 (TM1) of an adjacent protomer in connexin 26 or equivalent residues in other connexins. In particular, the invention provides compounds that specifically inhibit the activation/opening of connexin hemichannels, identified with the aforementioned method, which can be used for the treatment of inflammatory diseases, vascular diseases, cardiac arrhythmias, chronic wounds, retinal neuroprotection, pain treatment, denervation of skeletal muscles, muscular dystrophies, spinal cord damage and genetic diseases characterised by an increase in the activity of hemichannels formed by connexins.</p>	<p>Pharma.</p>	<p>PCT/CL 2015/050 012</p>	<p>Chile</p>	<p>14-4-2015</p>		<p>Being reviewed</p>	<p>0</p>
<p>SURGICAL Y IMPLANTED MICRO-PLATFORMS</p>	<p>A method is provided for producing an arthropod comprising introducing a microsystem such as a MEMS device into an immature arthropod under conditions that result in producing an adult arthropod with a functional microsystem permanently attached</p>	<p>Biotechnology</p>	<p>PCT/US 2007/025 437</p>	<p>USA</p>		<p>3-11-2015</p>	<p>Being reviewed</p>	<p>0</p>

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<p>AND MICROSYST EMS IN ARTHROPO DS AND METHODS BASED THEREON</p>	<p>to its body. A method is also provided for producing a robotic apparatus. The method can comprise introducing a microsystem such as a MEMS device into an immature arthropod under conditions that result in producing a robotic apparatus with the microsystem permanently attached to the body of the adult arthropod.</p>							
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Annex 4.- Organization of Scientific Events

Scope	Title	Type of Event	City	Country	Responsible Researcher
International	International Gap Junction Conference	Conference	Valparaíso	Chile	Agustín Demetrio Martínez Carrasco
International	International Workshop: Biophysics of hemichannels and gap junction channels: A theoretical and practical training	Workshop	Santiago, Valparaíso	Chile	Juan Carlos Sáez Carreño
International	International Spring School Applied Statical Thermodynamics: from theory to molecular dynamics simulation	Conference	Santiago	Chile	Tomás Pérez Acle
International	Meeting CINV-Max Planck Research Leaders 2015	Symposia	Valparaíso	Chile	Ramón Rogelio Latorre De la Cruz
International	International Workshop: Biochemical, Spectroscopic and Crystallographic approaches used to study the functional-structural correlations of membrane proteins	Workshop	Valparaíso	Chile	Carlos González Leon
International	Modeling ionic currents in Molecular Dynamics Simulations	Workshop	Valparaíso	Chile	Tomás Pérez Acle
National	CINV Meeting 2015	Symposia	Valparaíso	Chile	Ramón Rogelio Latorre De la Cruz
National	Spring symposium in TRP Channels	Symposia	Santiago	Chile	Patricio Rodrigo Orio Alvarez

Annex 5.- Education and capacity building

5.1.Capacity Building inside MSI Centers

MSI RESEARCHER	NUMBER												TOTAL NUMBER PER MSI RESEARCHER		
	Undergraduated Students			Graduated Students						Postdoctoral Researchers					
				Master			Doctoral								
	F	M	T	F	M	T	F	M	T	F	M	T			
Adrián Palacios	1	1	2	1	1	2	0	1	1	1	0	1	3	3	6
Agustín Martínez	1	0	1	2	3	5	0	1	1	2	2	4	5	6	11
Alan Neely	0	1	1	2	0	2	0	1	1	0	0	0	2	2	4
Ana María Cárdenas	0	0	0	3	0	3	0	1	1	1	1	2	4	2	6
Andrés Chávez	1	0	1	1	0	1	0	0	0	1	0	1	3	0	3
Carlos González	0	0	0	0	1	1	0	2	2	1	2	3	1	5	6
David Naranjo	0	0	0	0	0	0	0	1	1	0	1	1	0	2	2
F. Danilo González	3	2	5	2	1	3	2	0	2	0	0	0	7	3	10
John Ewer	1	0	1	0	2	2	0	2	2	1	2	3	2	6	8
Juan Carlos Sáez	3	1	4	0	0	0	5	5	10	1	3	4	8	10	19
Kathleen Whitlock	0	0	0	0	0	0	2	4	4	0	1	1	2	5	7
Oliver Schmachtenberg	4	1	5	0	2	2	0	1	1	1	1	2	5	5	10
Patricio Orio	0	2	2	0	0	0	1	3	4	0	2	3	2	6	9
Ramón Latorre	0	0	0	0	0	0	1	1	1	0	2	2	1	3	4
Tomás Pérez - Acle	0	2	2	0	1	1	0	2	2	0	3	3	0	8	8
TOTAL	14	10	24	11	11	22	11	25	37	9	20	29	46	66	112

5.2.- Short-term Traineeships of MSI students (Include postdoctoral trainees)

Student Name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Gonzalo Valdivia	Johns Hopkins University	United States of America	Alfredo Kirkwood	It was studied through field potential electrophysiology technic the mGluR dependent - LTD and LTP plasticity process in old and young mice. Measurements were made in Hippocampus (CA1 specifically). The model used was transgenic mouse APP/PS1 representing related to Alzheimer's disease mutations. The study is part of the thesis project and was aimed at collecting data for comparison with the natural model of alzheimer Octodon Degus.	10/12/2014	15/01/2015
Jaime Maripillán	University of Rutgers	United States of America	Jorge Contreras	Conduct research into gating and regulation Cx26 hemichannels and mutants	20/08/2015	15/02/2016
Joaquín Valdés	University of Tuebingen	Germany	Francois Paquet-Durand	The aim of the intern was to develop an in vitro model to simulate diabetic retinopathy in organotypic cultures (retinal explants) of retinas from healthy mice and altering the composition of the culture medium to mimic diabetes (remove insulin and / or glucose) to study the mechanism of cell death in these conditions.	01/02/2015	15/04/2015
Sammy Castro	University of Manchester	England	Wael El-Deredy	Training in Neural Mass Models	11/05/2015	26/05/2015
Fernando Hinojosa	Universidad de Sevilla	Spain	Eva Alex	To study the impact of R465W dynamin-2 mutation kinetics of the ssion process in mast cells using capacitance measurments.	05/01/2015	03/04/2015
Alejandro Bernardín	Mcmaster University	Canadá	Jonathan Dushoff	Establecer una colaboraciión con el profesor Dushoff para la utilizacion de la herramienta PISKA en el modelamiento de enfermedades infecciosa	28-12-2015	31-03-2016
José Gárate	University for Natural Resources	Austria	Martin Wilckens	Modelamiento	1/7/15	27-07-2015
Alberto Martin	University College of Dublin	Alemania	Dr. Gianluca Pollastri	Bioinformatica	9/7/15	15-07-2015

Annex 6.- Networking and other collaborative work

6.1 Networking

NOMENCLATURE:
[Network Scope]
 [N] National [I] International [LA] Latin American

Network Name	Network Scope	Network Participants				Institutions
		From the Center		External		
		Researchers	Postdocs / Students	Researchers	Postdocs / Students	
Intercellular Communication in Nervous System Network	Internacional	4	0	6	0	Pontificia Universidad Catolica de Chile, ECOS-CONICYT
Biophysics and Computational Neurosciences Network	International	6	3	7	0	CINV Fundación Ciencia para la Vida
Convenio entre la Universidad Federal del Sur de la Bahía y la Universidad de Valparaíso	Internacional	1	0	1	0	Universidad Federal del Sur de la Bahía
Convenio entre la Universidad de la República y el Centro Interdisciplinario de Neurociencia de Valparaíso	Internacional					CINV y la Universidad de la República de Uruguay
Convenio entre la Universidad de la Plata y la Universidad de Valparaíso	Internacional	2	0	1	0	Universidad de La Plata, Universidad de Valparaíso y CINV
Max Planck – CINV Research Leaders Programm	Internacional	4	0	36	0	CINV y Max Plank Society for the advancement of science

6.2.- Other collaborative activities

Activity Name	Co-Participant Institution(s)	Participants [Number]				Products [Type & Number]
		MSI center		External		
		Researchers	Postdocs/Students	Researchers	Postdocs/Students	
ACT1121 "Molecular and cellular mechanism of muscular dystrophy related to mutations of dysferlin"	Facultad de Medicina, Universidad de Chile	2	1	4	5	1 Simposio Jornada Chilena de Miología 5 Abstract
ACT1113 "Study the physiological role of TRP channels in The Termotransuction And Synaptic Plasticity"	Universidad de Santiago de Chile	1	0	5	8	1 Simposio
ACT1104 " Censor Voltage Ion Channels: Structure to Function"	Universidad del Desarrollo, Universidad de Talca	7	4	2	1	17 Papers 1 Congreso 1 Curso 1 Workshop
ACT 1107 "Integration of structural biology to the development of Biotechnology"	Universidad Nacional Andrés Bello, Universidad de Talca, Universidad de Chile, Fundación Ciencia para la Vida	12	5	14	13	2 Patents 20 Papers 2 workshop
CONICYT / REDES 140241 Theoretical and experimental identification of novel chemical compounds targeting the lipopolysaccharide (LPS) of clinically relevant Bacterial Pathogens.	Centro de Bioinformática y Biología Integrativa (CBIB), Centre for Infection and Immunity, Queen's University of Belfast	2	0	1	0	1 Scientific Exchange
NC130011 Nucleo Milenio de Enfermedades Neuropsiquiátricas	Universidad Nacional Andrés Bello, Universidad de Chile	1	3	4	30	1 Paper

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Proyecto Mecesus UVA 0604 Desarrollo de una plataforma interdisciplinaria en salud, Un referente internacional en el desarrollo de la medicina de precisión	Universidad de Valparaíso	1	0	0	0	1 Plataform
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Annex 7.- Outreach**7.1.- Outreach activities throughout the period.***(The language of the seminar titles were kept as announced)*

Description of activity	Type of Event	Date	Location Region	Target audience
I Jornada Invernal de Neurociencia	Conference	24/7/15	Universidad de Valparaíso	Secondary students
Pecados y virtudes de la Ciencia Moderna	Conference	18/11/15	Fundación Ciencia para la Vida, Santiago	General Community
Tertulias Porteñas: “¿Qué sabemos del lenguaje?”	Other	27/7/15	Centro de Extensión del Consejo Nacional de la Cultura y las Artes	General Community
Tertulias Porteñas: “¿Qué sabemos de las emociones?”	Other	15/10/15	Centro de Extensión del Consejo Nacional de la Cultura y las Artes	General Community
Tertulias Porteñas: “¿Qué sabemos de los sabores?”	Other	26/11/15	Centro de Extensión del Consejo Nacional de la Cultura y las Artes	General Community
Cocina de Vanguardia con Chris Chipot	Other	27/11/15	El Internado, Valparaíso	General Community
¿Qué tienes en mente?: “¿Qué sabemos de nuestro cerebro?” Andrés Chávez (CINV-UV)	Other	8/5/15	Viña del Mar, V Región	Secondary students
¿Qué tienes en mente?: “Los Sentidos, nuestra ventana al mundo” Oliver Schmachtenberg (CINV-UV)	Other	25/5/15	Viña del Mar, V Región	Secondary students
¿Qué tienes en mente?: “Neurociencia de los sentidos” Patricio Orio (CINV-UV)	Other	24/6/15	Quilpué, V Región	Secondary students
¿Qué tienes en mente?: “Charla Conexinas” Agustín Martínez (CINV-UV)	Other	7/3/15	Huechuraba, Región Metropolitana	Secondary students

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¿Qué tienes en mente?: “Somos una pila o una batería viviente” Carlos Gonzalez (CINV-UV)	Other	19/8/15	Quillota, V Región	Secondary students
¿Qué tienes en mente?: “La Química del Cerebro” Ana María Cárdenas (CINV-UV)	Other	24/9/15	Zapallar, V Región	Secondary students
¿Qué tienes en mente?: “Ciclo Circadiano” John Ewer (CINV-UV)	Other	15/10/15	Valparaíso, V Región	Secondary students
Segunda Charla 70 años Carrera de Bioquímica en honor a “Osvaldo Cori Mouilly”: “Pequeñas máquinas sensibles a la temperatura. Canales TRP como sensores de temperatura y dolor” Dr. Ramón Latorre	Conference	15/7/15	Santiago, XIII Región	Universitary Students
“Altered Spontaneous ans Activity Dependent Synaptic Vesicle Recycling at Complexin null” Dr. Ramon Jorquera	Seminar	22/1/15	Universidad de Valparaíso	University studens
“Rol de la quinasa Cdk5 durante el dolor inflamatorio facial” Dr. Elías Utreras	Seminar	5/6/15	Universidad de Valparaíso	University studens
“Endo y Fitocannabinoides como herramientas biomédica” Dr. Fernando Sepúlveda	Seminar	20/3/15	Universidad de Valparaíso	University Students. Academics. General public
“Desat1, a swiss army knife for Drosophila reproduction” Dr. Jean-Francois Ferveur	Seminar	2/4/15	Universidad de Valparaíso	University Students. Academics. General public
“Biomarkers and cell replacement therapy at early Parkinson's disease: From human electrophysiology to cell grafting in a non-human primate model” Dr. René Quilodrán	Seminar	8/5/15	Universidad de Valparaíso	University students
“Molecular and preclinical studies of novel positive allosteric modulators of $\alpha 7$ nicotinic receptors” Dr. Hugo Arias	Seminar	12/5/15	Universidad de Valparaíso	University students
“Where do you find the time? The Neural Basis of Circadian Timekeeping in Drosophila” Dr. Orié T. Shafer	Seminar	15/5/15	Universidad de Valparaíso	University students

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“Structural Bioinformatics Approaches for the Discovery and Design of Novel Drugs” Dr. Carlos F. Lagos	Seminar	26/6/15	Universidad de Valparaíso	University students
“Brainstorming the Brain: Unveiling the brain oscillations and synchrony as predictors of a neurological state” Dr. Carolina Oliva	Seminar	3/7/15	Universidad de Valparaíso	University students
“Function, plasticity and development of specific brain synapses” Dr. Ralph Schneggenburger	Seminar	7/7/15	Universidad de Valparaíso	University students
“Role of RCAN1 isoforms on calcineurin activity, mitochondrial morphology and oxidative stress” Dr. Cristian Zambrano	Seminar	10/7/15	Universidad de Valparaíso	University students
“Organización funcional de actividad cerebral para la cognición humana” Dr. Juan R. Vidal	Seminar	14/7/15	Universidad de Valparaíso	University students
“¿Son superpotentes los N-BOMes? Estudios en nuevos ligandos serotoninérgicos” Dr Bruce Cassels (Universidad de Chile)	Seminar	23/7/15	Universidad de Valparaíso	University students
“Esquizofrenia: de lo cognitivo a lo social” Dr. Francisco Aboitiz	Seminar	4/8/15	Universidad de Valparaíso	University students
“ROS and ryanodine receptor-mediated Ca ²⁺ signals are key components of BDNF-induced synaptic plasticity” Dra. Tatiana Adasme Rocha	Seminar	7/8/15	Universidad de Valparaíso	University students
“Cortical resonance frequencies emerge from network size and connectivity” Dr. Wael El-Deredy	Seminar	14/8/15	Universidad de Valparaíso	University students
“Extracellular nucleotides: key regulators for musculoskeletal system remodeling” Dra. Sonja Buvinic Radic	Seminar	21/8/15	Universidad de Valparaíso	University students
“New mechanisms on insulin action: role of calcium in the skeletal muscle bioenergetics” Dr. Ariel Contreras-Ferrat	Seminar	28/8/15	Universidad de Valparaíso	University students
“Neural mechanisms of social interaction: From perception to inter-	Seminar	21/9/15	Universidad de Valparaíso	University students

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subjetivity” Dr. José Luis Ulloa (Brain & Spine Institute, Francia)				
“Evolution of structural and functional properties in TRP Channels” Dr. Sebastián Brauchi (Universidad Austral)	Seminar	25/9/15	Universidad de Valparaíso	University students
“Mecanismos moleculares implicados en la regulación de TRPM4 en la migración celular” Dr. Oscar Cerda (ICBM, Universidad de Chile)	Seminar	9/10/15	Universidad de Valparaíso	University students
“Hemicanales y su posible papel en la muerte neuronal inducida por procesos inflamatorios” Dr. Juan Andrés Orellana	Seminar	16/10/15	Universidad de Valparaíso	University students
“Impact of diet on neuroprotection and behavior” Dra. Andrea Calixto (Universidad Mayor)	Seminar	23/10/15	Universidad de Valparaíso	University students
“Bases Moleculares de la Disfunción Neuronal en la Enfermedad de Alzheimer” Dra. Andrea Paula-Lima (Universidad de Chile)	Seminar	30/10/15	Universidad de Valparaíso	University students
“Obesidad asociada a defectos en la vasculatura linfática” Dra. Noelia Escobedo (St Jude Children’s Research Hospital, USA)	Seminar	6/11/15	Universidad de Valparaíso	University students
“Acetilcolina y la regulación de comportamientos mediados por el sistema olfatorio Dr. Araneda(University of Maryland)	Seminar	2/9/15	Universidad de Valparaíso	University students
“Parkinson Disease: New Therapeutic Strategies” Dra. Gabriela Mercado (ICBM, Universidad de Chile)	Seminar	4/9/15	Universidad de Valparaíso	University studens
“Establishing the boundaries between memories encoding, retrieval and forgetting” Dr. Pedro Bekinschtein (Universidad de Buenos Aires)	Seminar	10/11/15	Universidad de Valparaíso	University students
“Past and future of bio-molecular simulations” Dr. Willem F van Gunsteren (Swiss Institute of Technology (ETH), Suiza)	Seminar	16/11/15	Universidad de Valparaíso	University students

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“Ions in computer simulatios” Dra. María Reif (Technische Universität München (TUM), Germany)	Seminar	16/11/15	Universidad de Valparaíso	University students
“The dynamics of perception during looming, receding and focusing” Dr. Andre Longtin	Seminar	23/11/15	Universidad de Valparaíso	University students
“Biophysical discoveries with a computational calorimeter” Dr. Chris Chipot	Seminar	23/11/15	Universidad de Valparaíso	University students
“El rol de la percepción auditiva en el desarrollo de las patologías de la voz” Dr. Matías Zañartu (Universidad Técnica Federico Santa María)	Seminar	27/11/15	Universidad de Valparaíso	University students
“Visualizing lipid metabolism and signaling using zebrafish as a model system” Dr. Steve Farber(Johns Hopkins University)	Seminar	2/9/15	Universidad de Valparaíso	University Students
“TRP channels everywhere: from the oregano taste to the oocyte maturation (and fertulization!)” Dra. Ingrid Carvacho	Seminar	7/3/15	Universidad de Valparaíso	University studens
“Los psicoestimulantes como agentes despolarizantes: activación de canales de calcio por anfetaminas” Dr. José M. Eltit	Seminar	29/5/15	Universidad de Valparaíso	University studens
Postdoc Seminar: Diana Rojas, “On the opposite role of angiotensin II and angiotensin 1-7 during adipogenic differentiation: a possible mechanism by differential regulation of Connexin 43”	Seminar	21/7/15	Universidad de Valparaíso	University students
Student Seminar: Paula Mujica, “Mechanism of dominant negative effect of deafness-associated EL1 mutants of Cx26 on Cx43 Gap Junction Channels”	Seminar	11/8/15	Universidad de Valparaíso	University students
Student Seminar: Carolina Flores, “Pannexin and Purinergic Signaling in Fibroblast Migration and Dermal Regeneration”	Seminar	18/8/15	Universidad de Valparaíso	University students

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Student Seminar: Cesar Ravello, “Motion Processing in the Early Visual System of a Diurnal Rodent”	Seminar	18/8/15	Universidad de Valparaíso	University students
Student Seminar: Juan Ahumada, “Prostaglandin E2 decreases inhibitory synaptic transmission in hippocampus”	Seminar	25/8/15	Universidad de Valparaíso	University students
Student Seminar: Fernando Hinojosa, “Molecular dynamics simulations of the dynamin-2 mutation R465W: impact on dynamin-2 monomer structure and dimer interactions”	Seminar	25/8/15	Universidad de Valparaíso	University students
Postdoc Seminar: Arlek Gonzalez, “Dynamin-2, a Centronuclear Myopathy-associated GTP-Ase, is required for Actin-Dependent Vesicle Trafficking in Muscle Cells”	Seminar	1/9/15	Universidad de Valparaíso	University students
Student Seminar: Pablo Gonzalez, “Identity of glial progenitors during the development of the olfactory sensory system”	Seminar	8/9/15	Universidad de Valparaíso	University students
Student Seminar: Koyam Morales, “Serotonin induces inhibitory long-lasting depression in Prefrontal Cortex”	Seminar	8/9/15	Universidad de Valparaíso	University students
Postdoc Seminar: Hans Moldenhauer; “Effective pore size and radius of capture for K ⁺ ions in K-Channels”	Seminar	13/10/15	Universidad de Valparaíso	University students
Student Seminar: Juan Morales, “The effect of a reduced sAHP-conductance on the glutamatergic synaptic plasticity of kindled rats”	Seminar	20/10/15	Universidad de Valparaíso	University students
Student Seminar: Claudia Salazar, “La exposición neonatal a hormonas sexuales afecta a largo plazo areas dopaminérgicas cerebrales involucradas en motivacion y locomocion”	Seminar	3/11/15	Universidad de Valparaíso	University students
Student Seminar: Pedro Espinoza, “Evaluación de Conductas asociadas a trastornos obsesivo compulsivo en modelos animales, a través de cambios	Seminar	3/11/15	Universidad de Valparaíso	University students

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en la expresión de EEAT3 en Neuronas GABAérgicas”				
“Similitud Estructural entre receptores de serotonina y acetilcolina: una oportunidad para la polifarmacología” Dr. Miguel Reyes-Parada (USACH)	Seminar	9/11/15	Universidad de Valparaíso	University students
Postdoc Seminar: Justin Flaven-Pouchon, “Neuropeptide in Drosophila development: the tanning hormone bursicon revisited”	Seminar	11/12/15	Universidad de Valparaíso	University students
Student Seminar: Bernardo Pinto, “Charged residues at the first transmembrane region mediate the voltage dependence of connexins slow gate”	Seminar	15/12/15	Universidad de Valparaíso	University students
“Mitral cell response are strongly dependent on trial-to-trial anticipatory variability in the basal firing rate” Dr. Diego Restrepo (University of Colorado, USA)	Seminar	13/11/15	Universidad de Valparaíso	University students
“Intrinsic and extrinsic mechanisms that shape granule cell-driven synchronous activity in the olfactory bulb” Dr. Nathan E. Schoppa (University of Colorado, USA)	Seminar	13/11/15	Universidad de Valparaíso	University students
“Reconstruction of their multilevel dynamics from 3D+time imaging of developing embryos” Dr. Nadine Peyriéras (CNRS, Francia)	Seminar	18/12/15	Universidad de Valparaíso	University students
“Análisis y diseño de circuitos genéticos para control metabólico” Dr. Diego Oyarzún (Imperial College, London)	Seminar	1/12/2015	Universidad de Valparaíso	University students
“The oocyte to embryo transition: Rescued from the dark side, the oocyte awakens” Dr. Ricardo Fuentes (University of Pennsylvania, USA)	Seminar	4/12/15	Universidad de Valparaíso	University students

7.2.- Products of outreach

Name of Product	Product Objective	Target Public	Type of Product	Scope
Second Record of Tertulia Porteña (Las Emociones)	Tertulias seek to bring neuroscience to society through the holding of meetings between scientists, artists and intellectuals. They talk around a topic of common interest to all of them, generating discussion spaces that promote interdisciplinary knowledge.	General Community.	Other	National
Third Record Tertulia Porteña (Los Sabores)	Tertulias seek to bring neuroscience to society through the holding of meetings between scientists, artists and intellectuals. They talk around a topic of common interest to all of them, generating discussion spaces that promote interdisciplinary knowledge.	General Community.	Other	National
First Record of Tertulia Porteña (El Lenguaje)	Tertulias seek to bring neuroscience to society through the holding of meetings between scientists, artists and intellectuals. They talk around a topic of common interest to all of them, generating discussion spaces that promote interdisciplinary knowledge.	General Community.	Other	National
Tertulias Flyers	Tertulias seek to bring neuroscience to society through the holding of meetings between scientists, artists and intellectuals. They talk around a topic of common interest to all of them, generating discussion spaces	General Community.	Poster	National

	that promote interdisciplinary knowledge.			
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7.3.- Articles and Interviews

Type of Media and Scoupe	Local / Regional		National		International		Total
	N° Interviews	N° Articles	N° Interviews	N° Articles	N° Interviews	N° Articles	
Written	0	14	1	29	0	0	44
Internet	0	0	2	30	0	2	34
Audiovisual	0	0	10	0	3	0	13
Total	0	14	13	59	3	2	91

Annex 8.- Connections with other sectors

Activity	Type of Connection	Type of Activity	Institution Country	Agent Type	Economic Sector
Construction of the new CINV Building in Valparaíso	3	7 (Building scientific and outreach infrastructure)	Chile	2	Government
Fundación Ciencia Joven Agreement	2	7 (Bring Science to Society)	Chile	2	Biotechnology
Fundación Puerto Ideas Scientific Committee	3	7 (Puerto Ideas Festival)	Chile	2	Business activities

NOMENCLATURE:

[Type of Connection] [1] Services Contract [2] Cooperation Agreement

[Type of Activity] [1] Development of Studies [2] Project Implementation [3] Training [4] Prospective Activity [5] Scientific Training
[6] Installation of Scientists [7] Others (specify at the table foot other type of activity)
[Agent Type] [1] Industry and Services [2] Organizations and Public Services [3] Educational Sector

Annex 9

9.1 Total incomes:

Exchange rate: US\$ 1 = \$ 500

Funds	Accumulated incomes to last year [\$]	2015 Incomes		Total incomes to 2015 [\$]
		Amount [\$]	Percentage of resources used by the Center [%]	
ICM (CINV, Redes y PME)	6.539.706	832.965.000	91%	832.965.000
CONICYT (Anillo, Mincyt, Redes y Neuromantes)	2.698.701	459.473.674	100%	459.473.674
UV (Depto. Neuro y Direc. Invest.)	3.153.592	573.980.236	100%	573.980.236
Corporación CINV	37.585	20.888.715	69%	20.888.715
CNTV, FNDR	103.061	0	0%	0
Others (N62909-13-N251)	337.106	4.056.158	828%	4.056.158
TOTAL	12.869.751,47	1.891.363.783		1.891.363.783

9.2 Outcome structure:

ITEM	Accumulated expenses to last year [\$]	2015 Expenses [\$]				Total expenses to 2015 [\$]	%
		Operative	Networking	Outreach	Total		
Honoraria Researchers	570.408.025	270.258.095	0	0	270.258.095	840.666.120	25,85%
Honoraria students and other personnel	626.036.688	139.343.354	0	0	139.343.354	765.380.042	23,53%
Tickets and travel expenses	223.944.674	49.230.385	2.439.240	8.965.410	60.635.035	284.579.709	8,75%
Materials/supplies	124.700.915	45.769.285	1.095.760	34.590	46.899.635	171.600.550	5,28%
Goods and equipment	465.913.715	159.986.154	0	0	159.986.154	625.899.869	19,24%
Infrastructure	17.080.682	0	0	0	0	17.080.682	0,53%
Administrative expenses	180.225.050	43.420.517	0	0	43.420.517	223.645.567	6,88%
Publications and subscriptions	13.288.758	4.619.417	0	0	4.619.417	17.908.175	0,55%
Consultancies	170.169.463	49.627.589	3.810.000	0	53.437.589	223.607.052	6,87%
Overhead	60.377.116	7.800.000	0	0	7.800.000	68.177.116	2,10%
Insurance costs	6.907.865	3.561.079	0	0	3.561.079	10.468.944	0,32%
Legal personality expenses	0	0	0	0	0	0	0,00%
Others	3.155.171	445.417	0	0	445.417	3.600.588	0,11%
Total Expenses (\$)	2.462.208.122	774.061.292	7.345.000	9.000.000	790.406.292	3.252.614.414	100,00%

9.3 Financial accounting

ITEM	2015 [\$]				TOTAL TO 2015
	Operative	Networking	Outreach	Total [\$]	
Income	\$ 816.620.000	\$ 7.345.000	\$ 9.000.000	\$ 832.965.000	\$ 3.190.867.663
Outcome	\$ 774.061.292	\$ 7.345.000	\$ 9.000.000	\$ 790.406.292	\$ 3.124.660.195
Annual balance	\$ 42.558.708	\$ -	\$ -	\$42.558.708	\$ 66.207.468

9.4 Intercambio

Tipo Investigador	Nombre	Tipo de actividad realizada	Duración de la estadía	País al que viajó	Entidad que financia (Milenio/Externo/Mixto)
Asociado	<i>Ramón Latorre de la Cruz</i>	<i>Estadía de Investigación</i>	<i>13 días</i>	<i>EEUU</i>	<i>Externo</i>
Asociado	<i>Ana María Cárdenas Díaz</i>	<i>Meeting of the French Neuroscience Society</i>	<i>8 días</i>	<i>Francia</i>	<i>Externo</i>
Asociado	<i>Ramón Latorre de la Cruz</i>	<i>Colaboración</i>	<i>9 días</i>	<i>España</i>	<i>Externo</i>
Asociado	<i>Kathleen Whitlock</i>	<i>Latin American Society fir Developmental Biology</i>	<i>5 días</i>	<i>Brasil</i>	<i>Externo</i>
Adjunto	<i>Andrés Chávez Navarrete</i>	<i>TWAS 13th General Conference & 26th General Meeting</i>	<i>6 Días</i>	<i>Austria</i>	<i>Externo</i>
Adjunto	<i>Oliver Schmachtenberg</i>	<i>European Retina Meeting 2015</i>	<i>4 días</i>	<i>Inglaterra</i>	<i>Externo</i>
Asociado	<i>Kathleen Whitlock</i>	<i>34th International Ethological Conference, Behaviour 2015</i>	<i>6 días</i>	<i>Australia</i>	<i>Externo</i>
Asociado	<i>John Ewer Lothian</i>	<i>34th International Ethological Conference, Behaviour 2015</i>	<i>6 días</i>	<i>Australia</i>	<i>Externo</i>
Asociado	<i>Carlos González León</i>	<i>Estadía de investigación, Laboratorio Dr. Luis Cuello</i>	<i>10 Días</i>	<i>EEUU</i>	<i>Externo</i>
Adjunto	<i>Oliver Schmachtenberg</i>	<i>9th World Congrers of the Internarional Brain Research Organization</i>	<i>5 Días</i>	<i>Brasil</i>	<i>Externo</i>
Asociado	<i>Ramón Latorre de la Cruz</i>	<i>Mechanosm of Membrane Transport Integrating Structure, Function and Dynamics. Gordon Research Conference</i>	<i>6 días</i>	<i>EEUU</i>	<i>Externo</i>
Asociado	<i>Kathleen Whitlock</i>	<i>Seminar Washington University</i>	<i>7 días</i>	<i>EEUU</i>	<i>Externo</i>
Adjunto	<i>Patricio Orio Alvarez</i>	<i>Estadía de investigación en laboratorios</i>	<i>10 Días</i>	<i>Francia, Alemania</i>	<i>Externo</i>
Asociado	<i>Alan Neely Delgueil</i>	<i>Estadía de investigación en laboratorio Dr. Ricardo Olcese UCLA</i>	<i>19 Días</i>	<i>EEUU</i>	<i>Externo</i>
Asociado	<i>Carlos González León</i>	<i>Estadía de investigación en laboratorio del Centro de Formación en Ciencias Ambientales</i>	<i>7 Días</i>	<i>Brasil</i>	<i>Externo</i>

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<i>Asociado</i>	<i>Adrián Galo Palacios Vargas</i>	<i>Visita a los laboratorios de Dr. Guillaume Masson y Dr. Bruno Cessac</i>	<i>14 Días</i>	<i>Francia</i>	<i>Externo</i>
<i>Asociado</i>	<i>Adrián Galo Palacios Vargas</i>	<i>ONR Computational Neuroscience Program Review scheduled 18-19 June 2015. Arlington. Washington. A. Palacios Expositor.</i>	<i>4 Días</i>	<i>USA</i>	<i>Externo</i>
<i>Asociado</i>	<i>Fernando Danilo González Nilo</i>	<i>Mision Bioteecnologica Faiser Boston</i>	<i>7 Días</i>	<i>USA</i>	<i>Externo</i>
<i>Asociado</i>	<i>Fernando Danilo González Nilo</i>	<i>Visita FDA Arkansas</i>	<i>10 Días</i>	<i>USA</i>	<i>Externo</i>
<i>Asociado</i>	<i>Fernando Danilo González Nilo</i>	<i>Misión Tecnologica Aleitat Barcelona</i>	<i>7 Días</i>	<i>España</i>	<i>Externo</i>
<i>Asociado</i>	<i>Fernando Danilo González Nilo</i>	<i>GCRS Global Sumit on regulatory Sciences</i>	<i>7 Días</i>	<i>Italia</i>	<i>Externo</i>
<i>Asociado</i>	<i>Fernando Danilo González Nilo</i>	<i>US Army</i>	<i>7 Días</i>	<i>USA</i>	<i>Externo</i>
<i>Asociado</i>	<i>Fernando Danilo González Nilo</i>	<i>Albert Einstein</i>	<i>18 Días</i>	<i>USA</i>	<i>Externo</i>
<i>Asociado</i>	<i>Fernando Danilo González Nilo</i>	<i>Bethan Administration hospital New York</i>	<i>18 Días</i>	<i>USA</i>	<i>Externo</i>

Nombre Investigador	Nacionalidad	Tipo de actividad realizada	Duración de la estadía	País desde el que viajó	Entidad que financia (Milenio/Externo/Mixto)
<i>Mihail Rocco</i>	<i>Norteamericano</i>	<i>Seminarios</i>	<i>7 Días</i>	<i>USA</i>	<i>Externo</i>
<i>Raul Araya</i>	<i>Chileno</i>	<i>Seminario y estadía Investigación</i>	<i>14 Días</i>	<i>USA</i>	<i>Externo</i>
<i>María Reif</i>	<i>Alemana</i>	<i>Escuela Internacional de Postgrado</i>	<i>14 días</i>	<i>Alemania</i>	<i>Mixto</i>
<i>Chris Oostembrink</i>	<i>Suizo</i>	<i>Escuela Internacional de Postgrado</i>	<i>14</i>	<i>Austria</i>	<i>Mixto</i>

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<i>Wilfred van Gunsteren</i>	<i>Holandés</i>	<i>Escuela Internacional de Postgrado</i>	<i>14</i>	<i>Suiza</i>	<i>Mixto</i>
<i>Rocío Talaveron</i>	<i>Española</i>	<i>Pasantía Investigación</i>	<i>60 días</i>	<i>España</i>	<i>Externo</i>
<i>Fernando Marengo</i>	<i>Argentino</i>	<i>Implementar técnica en laboratorio</i>	<i>7 días</i>	<i>Argentina</i>	<i>Externo</i>
<i>Alberto Pereda</i>	<i>Argentino</i>	<i>IGJC</i>	<i>5 Días</i>	<i>EEUU</i>	<i>Milenio</i>
<i>Luis Cuello</i>	<i>Norteamericano</i>	<i>Curso Cristalografía</i>	<i>9 Días</i>	<i>EEUU</i>	<i>Mixto</i>
<i>Beatriz Veles</i>	<i>Norteamericano</i>	<i>Curso Cristalografía</i>	<i>9 Días</i>	<i>EEUU</i>	<i>Mixto</i>
<i>Ignacio Cancino</i>		<i>Research leaders</i>	<i>5 Días</i>	<i>Canada</i>	<i>Mixto</i>
<i>Ricardo Olcese</i>	<i>Italiano</i>	<i>Defensa Tesis</i>	<i>3 días</i>	<i>EEUU</i>	<i>Externo</i>
<i>Cris Chipot</i>	<i>Francés</i>	<i>Meeting Línea 5</i>	<i>5 días</i>	<i>Francia</i>	<i>Milenio</i>
<i>Andre Longtin</i>	<i>Canaliense</i>	<i>Meeting Línea 5</i>	<i>5 días</i>	<i>Canada</i>	<i>Milenio</i>
<i>Chiayu Chiu</i>	<i>Norteamericana</i>	<i>Research Leaders</i>	<i>6 días</i>	<i>EEUU</i>	<i>Mixto</i>
<i>Alisson Gontijo</i>	<i>Brasilero</i>	<i>Research Leaders</i>	<i>6 días</i>	<i>Portugal</i>	<i>Mixto</i>
<i>Francisco Rivera</i>	<i>Chileno / Español</i>	<i>Research Leaders</i>	<i>5 días</i>	<i>Sao Paulo</i>	<i>Mixto</i>
<i>Giovanni González</i>	<i>Norteamericano</i>	<i>Research Leaders</i>	<i>6 Días</i>	<i>EEUU</i>	<i>Mixto</i>
<i>Karen Pérez de Arce</i>	<i>Chilena</i>	<i>Research Leaders</i>	<i>6 Días</i>	<i>EEUU</i>	<i>Mixto</i>
<i>Eric Beyer</i>	<i>Norteamericano</i>	<i>IGJC</i>	<i>5 días</i>	<i>EEUU</i>	<i>Milenio</i>
<i>Eduardo Macagno</i>	<i>Norteamericano</i>	<i>IGJC</i>	<i>5 días</i>	<i>EEUU</i>	<i>Milenio</i>
<i>Akio Suzumura</i>	<i>Japonés</i>	<i>IGJC</i>	<i>5 días</i>	<i>Japón</i>	<i>Milenio</i>
<i>Rob F. Jackson</i>	<i>Norteamericano</i>	<i>Pasantía</i>		<i>EEUU</i>	<i>Externo</i>

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<i>Ximena Nelson</i>	<i>Neozelandés</i>	<i>Pasantía</i>		<i>Nueva Zelanda</i>	<i>Externo</i>
<i>Jean-Francois Ferveur</i>	<i>Francés</i>	<i>Pasantía</i>		<i>Francia</i>	<i>Externo</i>
<i>Miguel Holmgren</i>	<i>Chileno</i>	<i>Pasantía</i>	<i>19 Días</i>	<i>EEUU</i>	<i>Externo</i>
<i>Francisco Bezanilla</i>	<i>Chileno</i>	<i>Pasantía</i>	<i>19 Días</i>	<i>EEUU</i>	<i>Externo</i>
<i>Gonzalo Ferreira</i>	<i>Uruguayo</i>	<i>Pasantía</i>	<i>20 Días</i>	<i>Uruguay</i>	<i>Externo</i>