Name of the Center:	
Acronym	CINV
Code	P09-022-F
Reported period	January 1 to December 31, 2016
Starting date of the Center	08-08-2011
Address	Pasaje Harrington 287, Playa Ancha
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Host Institution(s)	Corporación Centro Interdisciplinario de Neurociencia de Valparaíso, Universidad de Valparaíso, Pontificia Universidad Católica de Chile, Universidad Nacional Andrés Bello, Universidad de Chile, Fundación Ciencia & Vida.
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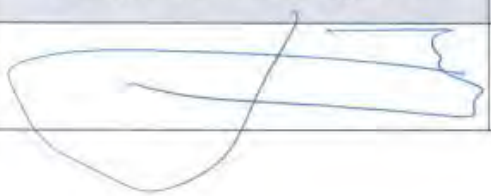	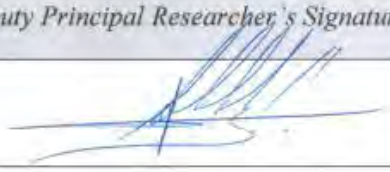

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1.1 Executive Summary

This report summarizes the advances made during the first year of the second five-year period of the **Centro Interdisciplinario de Neurociencia de Valparaíso (CINV)** as a Millennium Institute (MI).The CINV deals with several aspects of a fundamental scientific question: ***How does theNervous System respond to Stimuli in Health and Disease?*** During the first period we addressed this question along four research lines:*a) Etructure and Function of Molecular Sensors,b*) *Cellular Signaling*, *c) Genetic and Developmental Neuroscience, d*) *System and Circuits Neuroscience*; and one cross-cutting theme: e) *Bioinformatics and Computational Biology*. In 2016, we created a *Translational Research Unit* with the purpose of supporting our translational research efforts.We hope that this unit will facilitate the conception of translational projects and the generation of spin-offs. **Scientific productivity and collaborative work**. Our 2016 scientific productivity was higher than that of all previous years of the CINV as a MI. We published a total of 53 articles, including some in high impact journals such as *Neuron, eLife, Cell Reports, PNAS,* and *Journal of Neuroscience*. Importantly, 26 publications were authored by more than one CINV researcher, of which 9 resulted from collaborations across different research lines. During 2016, 29 (55%) of our publications were co-authored by students, and in 12 of them they were firstauthors. **Strengthening our faculty**. Dr. Juan C. Sáez, a leading authority on connexin function and dysfunction in health and disease, became Deputy Principal Researcher. In addition, we have included new scientists to the team: Dr. Pablo Moya, whouses genetic tools to investigate the molecular basis of mood and anxiety disorders was incorporated to the line of *System and Circuits Neuroscience*; Dr. Andrea Calixto brings to the CINV her expertise in the use of *C. Elegans* as a biological model, and strengthens the line of *Genetic and Developmental Neuroscience.* We are also proud to announce the incorporation to the CINV of Dr. Chiayu Chiu, our first Max Planck Tandem Research Leader, in November of 2016. Dr. Chiu uses optogenetics in combination with electrophysiology to investigate the local actions of synapses and decipher the complex interplay between synaptic excitation and inhibition in the mouse brain. Her research, and that of the entire CINV, will greatly benefit from a recently awarded grant to establish a state-of-the-art two-photon microscope system in Valparaiso, which will help consolidate our microscope facility as one of the most advanced in the country. **Young Investigators.** During 2016, we incorporated to the CINV four young investigators. Dr. Karen Castillo has a background in cell biology and electrophysiology and reinforces the research line on *Molecular Sensors*; Dr. Helmuth Sánchez, an expert in connexin hemichannels, adds research on channelopathy in syndromic deafness to Line 2; Dr. Alvaro Ardiles has initiated an exciting project investigating the role of pannexin channels in synaptic functions. His work combines concepts and techniques currently in use in the *Cell Signaling* and *System and Circuits Neuroscience* lines, thereby aiding to bridge these two lines of CINV research; and Dr. José A. Gárate, who uses computers to model phenomena ranging from human behavior to molecular interactions, greatly strengthens Line 5 and our PhD program in Biophysics and Computational Biology. Dr. Gárate's mastery of *in silico* tools will potentiate future collaborations across all lines of research. **Advanced training.** Our PhD and Masters Program in Neuroscience continues to attract students from Chile and abroad; for example, 9 students were admitted to the Ph.D. Program in Neuroscience for the 2017 academic year, one of the highest numbers to date. Similarly, the number of students receiving their graduate degree was also higher than usual, with 6 students

receiving a PhD degree in Neuroscience and 12 receiving Master's degrees. Notably, we created a new PhD Program in Biophysics and Computational Biology. This program has been highly successful; it was accredited for two years after only one year of existence, and has attracted excellent students from all over the country and abroad. It is worth mentioning that most of these students recently obtained PhD scholarships from a national competition, with one of them beingthe country's top applicant. **Networking.**A collaboration with D r. Miguel Holmgren (NIH, USA) and Dr. Francisco Bezanilla (University of Chicago, USA) brought about the installation of a new laboratory dedicated to the study of membrane transport and protein synthesis in the giant axon of the Humboldt squid. The arrival of Dr. Chiayu Chiuhas consolidated ties betw een the CINV and several Max Planck Institutes. In particular, Dr. Chiu will receive support and has access to resources at the Max Planck Florida Institute for Neuroscience in Florida (USA), including their state-of-the-art neuroimaging and electron microscope core facilities. During 2016, the CINV became an active partner of a University of Valparaíso institutional development project entitled "Development of an interdisciplinary platform for innovation in health".The biannual practical course and associated international symposium,"Small Brains Big Ideas", was successfully offered for a fourth time. Renowned scientists from the USA, UK, and Chile participate in this course, whose primary objective is to expose students from Latin America to the use of invertebrate preparations for basic and applied research in neurosciences and biomedicine (see www.smallbrains.org).Twenty-four students were selected this year. The course is organized by Drs. Andrea Calixto and John Ewer (CINV), and Dr. Jimena Sierralta (MI for Biomedical Neuroscience, BNI). Itwas funded by EMBO, as well as by the CINV and BNI MIs, thereby providing an example of how different Millennium Institutescan collaborate successfully.Two new avenues of partnership wereinitiated in 2016: first, members of the CINV are now actively participating in a collaborative grant called Neuromorphics, dedicated to the analysis of "Big data" in neuroscience; it includes 5 different Chilean universities and is funded by the US Air Force; and second, the CINV, the University of Valparaíso, and the National Center of Minimal Access Surgery of Cuba signed a Collaborative Agreement in the area of Medical Sciences.**Outreach.**The highlight of 2016 in this area was the hosting together withthe "Fundación Ciencia Joven", of the "Falling Walls Lab" contest, an activity that brought together 13 young innovators and took place for the first time in Chile. The winner, a young woman with expertise in industrial design, was invited to the global competition in Berlin, Germany.In addition, we helped create a new TV Series, "From atoms to the Cosmos", which was broadcastat prime timeand presented the work of different research centers in Chile. As in other years, the "Tertulias Porteñas" brought together Neuroscientists, Philosophers, and Artists to discussin a round table format what we know abouta variety of topics ranging from "Happiness" to "The use of marihuana" in front of a diverse audience. The project "Ciencia al tiro" led by Dr. Whitlock resulted in the production of videos based on the book entitled "*La alegría de la ciencia*" (*The Joy of Science*).The videos describe in an entertaining manner numerous science projects, ranging from "How to make a thermometer" to "How the information flows through the nervous system".

1.2 Resumen Ejecutivo.

Resumimos en este informe de avance los progresos hechos durante el primer año del segundo periodo del **Centro Interdisciplinario de Neurociencia de Valparaíso (CINV)** como un Instituto Milenio (IM). El CINV se preocupa de contestar los diferentes aspectos de una pregunta científica fundamental:: Cómo responde el sistema nervioso a los estímulos en salud y enfermedad_***How does the Nervous System respond to Stimuli in Health and Disease?.***Durante este periodo hemos tratado de responder a esta pregunta recurriendo a 4 líneas de investigacion:*a) Estructura y Función de Sensores Moleculares, b*) *Señalización Celular*, *c) Neurociencia Genética y del Desarrollo, d*) *Neurociencia de Sistemas y Circuitos*; y un tema transversal: *e) Biología Computacional y Bioinformática*. Durante el 2016, creamos una unidad de *Investigación Translacional*. Esperamos que esta unidad facilite la generación de proyectos translacionales y la generación de "spin-offs". **Productividad Científica y Trabajo Collaborativo.** La productividad científica en el 2016 fue más alta que en los años anterioresdel CINV como IM. Publicamos un total de 53 artículos, incluyendo algunos en revistas de alto impacto como *Neuron, eLife, Cell Reports, PNAS,* y *Journal of Neuroscience*. Destacamos que 26 publicaciones tuvieron la co-autoría de más de un investigador del CINV, 9 de las cuales resultó de colaboraciones de diferentes líneas de investigación.En el 2016, 29 (55%) de nuestras publicaciones fueron co-autorías que incluían a estudiantes y en 12 de ellas fueron primeros autores. **Reforzando Nuestro Equipo**.El Dr. Juan Carlos Sáez, una autoridad en la función de las conexinas en salud y enfermedad, fue nombrado Investigador Principal Alterno.Hemos además incluido a nuestro equipo nuevos científicos: El Dr. Pablo Moya, quien usa herramientas genéticas para investigar las bases moleculares de los desodenes del comportamiento y la ansiedad, fue incorporado a la línea de *Neurociencia de Sistemas y Circuitos*; La Dra. Andrea Calixto trajo al CINV su experiencia en el uso del C. elegans como modelo biológico y refuerza la línea de *Neurociencia del Desarrollo y Genética.* Estamos orgullosos de anunciar la incorporación al CINV de la Dra. Chiayu Chiu en Noviembre, 2016, nuestra primera Max Planck Tandem Research Leader. La Dra. Chiu usa optogenética en combinación con electrofisiología para investigar acciones locales de las sinápsis y decifrar la compleja relación que existe entre excitación e inhibición sináptica en el cerebro del ratón. Sus investigaciones y todas las del CINV se beneficiarán de gran manera gracias a un proyecto que permite la instalación de un microscopio de dos fotones. Este consolidará nuestro laboratorio de microscopía como uno de los más avanzados del país. **Investigadores Jóvenes.** Durante el 2016 hemos incorporado al CINV 4 investigadores jóvenes. Dra. Karen Castillo con experiencia en biología cellular y electrofisiología refuerza la linea de *Sensores Moleculares*; Dr. Helmuth Sánchez, un expert en hemicanales de conexinas contribuirá con sus investigaciones a la Línea 2; El Dr. Alvaro Ardiles inició un atractivo proyecto que investiga el papel de las panexinas en las funciones sinápticas. Su trabajo combina conceptos y técnicas que se usan en *Señalización Celular* y en *Neurociencia de Sistemas y Circuitos* creando de esta manera un puente entre estas dos líneas de investigación del CINV; y el Dr. José A. Gárate, quien usa computadores para modelar fenómenos que van desde el comportamiento humano hasta las interacciones moleculares, resfuerza la Línea 5 y nuestro programa de doctorado en Biofísica y Biología Computacional. La experiencia del Dr. Gárate en herramientas *in silico* potenciará todas las líneas de investigación. **Entrenamiento Avanzado.** Nuestros programas de doctorado y magister han continuado atrayendo estudiantes de Chile y el extranjero. Por ejemplo, 9

estudiantes fueron asdmitidos en el program de doctorado en Neurociencia en el 2017, uno de los números más altos hasta la fecha. De la misma manera, con 6 estudiantes que recibieron el grado de doctor y 12 el de magister el 2016, el número de estudiantes que se graduaron fue mayor que lo normal. La creación del programa en Biofísica y Biología Computacional debe destacarse. Este programa ha sido muy exitoso siendo acreditado por dos años solo después de un año de existencia, atrayendo a estudiantes de todo el país y del extranjero. Cabe destacar que la mayoría de los estudiantes han recibido becas de doctorado del Conicyt, siendo uno de ellos evaluado como uno de los mejores portulantes del país. **Redes.** Una colaboración con los Drs. Holngrem (NIH, USA) y Bezanilla (Univ. of Chicago, USA) permitió la instalación de un laboratorio dedicado a el transporte a través de membranas y a la síntesis de proteínas en el axon gigante de la jibia de Humboldt. La llegada de la Dra. Chiu ha permitido estrechar nuestra relación entre el CINV y varios Institutos Max Planck. La Dra. Chiu recibirá apoyo y tendrá acceso a las instalaciones del Instituto Max Planck Institute para la Neurociencia en Florida (USA), las que incluyen sus modernas instalaciones de neuroimagen y microscopía electrónica. Durante el 2016 el CINV llego a ser parte de un proyecto institucional de desarrollo de la U. de Valparaíso:"Desarrollo de una plataforma interdisciplinaria para la innovación en salud". Por cuarta vez se ofreció el curso práctico bianual y simposio internacional, "Small Brains Big Ideas". Este curso tiene como principal objetivo exponer a los estudiantes de América Latina al uso de preparaciones de invertebrados en la investigación básica y aplicada en neurociencia y biomedicina (verwww.smallbrains.org). Participaron en el curso renombrados científicos de USA, UK y Chile. El curso es organizado por los Drs. Andrea Calixto y John Ewer (CINV) y la Dra. Jimena Sierralta (MI for Biomedical Neuroscience, BNI). Financiado por EMBO, así como por los IMsCINV y el BNI, el curso es un ejemplo de como los Institutos Milenios pueden colaborar de manera exitosa. En el 2016 se iniciaron dos nuevas actividades: 1. Miembros del CINV están participando activamente en un proyecto colaborativo "Neuromorphics" dedicado al análisis de grandes datos en Neurociencia que incluye a 5 universidades chilenas y es financiado por la Fuerza Aérea de USA; y 2.El CINV, la U. de Valparaíso y el Centro de Cirujía de Mínimo Acceso de Cuba firmaron un acuerdo de colaboración en el área de las cienciasd médicas. **Extensión.** Lo más destacado del 2016 fue la orhganiación en conjunto con "Fundación Ciencia Joven", del concurso "Falling Walls Lab" una actividad que juntó a 13 jóvenes ionnovadores por primera vez en Chile. La ganadora, una diseñadora industrial, fue invitada a la competencia global en Berlín, Alemania. El CINVayudó a crear una nueva serie de TV "De Los Átomos al Cosmos". Esta se transmite a hora estelar y presenta el trabajo que se realiza en los diferentes Centro de Investigación de Chile.Como en otros años las "Tertulias Porteñas" juntó neurocientíficos, filósofos y artistas que frente a audiencia participaron en el renombrados científicos de USA, UK y Chile Renowned scientists from the USA, UK, and Chile muy diversa conversaron acerca de tópicos tan variados con la felicidad y el uso de la marihuana. "Ciencia al tiro" proyecto creado por la Dra. Whitlock produjo videos basados en el libro "*La alegría de la ciencia*". Diseñados para estudiantes de la enseñanza básica describen varios proyectos científicos que van desde "Como hacer un termómetro" a "Como la información fluye a través del sistema nervioso".

2. Introduction

a) Description of the Institute and highlights of 2016.

Our main aim is to create an advanced Neuroscience research center that serves as an intellectual hub for scientists from diverse disciplines working together in multidisciplinary teams to solve challenging neuroscience problems. Our goal is to finish the second period as an internationally recognized Millenium Institute (MI) science center housed in a public university and to expand the boundaries of science in our extremely centralized country. The CINV has already been recognized by the Chilean scientific community as an interregional center, and through its many outreach programs is well known to the general public of the Valparaíso region. Internationally, the CINV is also gaining ground. In a issue ofNature from November 2015, the article "Opening Borders and Barriers" dedicated to collaborative work around the world listed the CINV as one of 4 Chilean centers with the highest degree of collaborative work and the only one outside the capital, Santiago. Perhaps the most outstanding scientific event of 2016 was the incorporation of Dr. Chiayu Chu as the first Max Planck Tandem Research Leader (MPTRL) within the CINV, thus creating the first Max Planck Research Group in Chile. The agreement signed by the Max Planck Society, the University of Valparaíso, and the CINV allows the MPTRL to focus on their research, free of teaching, committee obligations, and the need to pursue funds and tenure for a period of 5 years (extendable to 7). During 2016 we incorporated young investigators whose independent research will strengthen CINV's research efforts by incorporating new concepts and techniques. In advanced training, our recently created PhD program in Biophysics and Computational Biology has now been accredited and has been extremely successful in capturing excellent students. Another highlight of 2016 was the successful fundraising to buy a two-photon microscope, which will be fully functional by June and in this regard will be unique in Chile. Part of the funds for this equipment was obtained through a 2016 CONICYT FONDEQUIP grant (~US$300,000) awarded to A. Chávez.

b) Research Lines:

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

This research line is interested in how the different types of energy contained in electrical, thermal, and chemical stimuli are transformed into mechanical energy (the pore opening). Using a variety of techniques ranging from fluorescence to electrophysiology, we made important advances in our understanding of: *a)* the mechanisms involved in the allosteric communication that exists between voltage and Ca^{2+} sensors and pore opening in the voltage- and Ca^{2+} -activated (BK) channel. *b)* The allosteric coupling between voltage and temperature sensors and the pore domain in thermoTRP channels. *c)* Direct demonstration of membrane protein synthesis in the giant axon of the Humboldt squid.

2. Cell Signaling.J. C. Sáez, A.M. Cárdenas and A.D. Martínez.

The main goals and advances of this research line are to understand: a) the role of dynamin in fast endocytosis and of the actin binding protein, cortactin, in exocytosis. *b)*The involvement of connexinhemichannels (Cx HCs) in skeletal muscle diseases includingmuscular dystrophies due to protein mutations (e.g., dysferlin or dystrophin) as well as in conditions that induce degeneration of skeletal myofibers (e.g., sepsis, inflammatory agents, glucocorticoids, spinal cord injury and denervation). *c)*The impact of mutations in connexin on their mechanism of action (e.g., gating and permeability) such as

to cause syndromic and non-syndromic deafness. *d)*The importance of glial hemichannelsin animal models of human neurodegenerative diseases.

3. Genetic and Developmental Neuroscience.J. Ewer, K. Whitlock and A. Calixto.

This research line uses molecular-genetic tools to dissect the mechanisms underlying development and behavior in intact animals.*a)* In zebrafish we identified a novel group ofpluripotent glial cells in the olfactory epithelium (OE) expressing the transcription factor *olig2*, uncovered a neural-immune interaction in the OE, and shown that GnRH progenitors in the adult brain differentiate in the absence of cell division. *b)* Used the patterns of Ca^{2+}visualized using the genetically encoded GCaMP sensor to understand how different neuropeptides control ecdysis behavior in *Drosophila.* *c)* Identified the pathway through which the activity of the central circadian clock of *Drosophila* is transmitted to a peripheral clock in order to impose a daily rhythmicity to the pattern of adult emergence. ***d)*** Used *C. elegans* to study the implications of specific dietary molecules on behavior and neurodegeneration.

4. Integrative and circuits Neuroscience. A. Chávez, P. Moya, A. Palacios and O. Schmachtenberg

Research into the mechanisms of neuromodulation at central synapses.*a)* In the retina, we found that NO modulates the OFF pathway, regulating the response of bipolar and amacrine cells. Similarly, we showed that cannabinoid signaling regulates night vision. *b)* We found that the transcription factor XBP1, Arc signaling, and BDNF are involved in synaptic plasticity in the hippocampus. *c)* Work continued on the pathogenesis of Alzheimer's disease (AD) through the use of natural and transgenic AD models. *d)* We expanded our animal toolbox to include several conditional knock out mice to better understand synaptic function in the CNS under physiological and pathological conditions. *e)* Max Planck Tanden Research Leader Chiayu Chiu was incorporated into this line; she will set up a state-of-the-art laboratory including the 2-photon microscopy.

5. Crosscutting: Computational Biology and Bioinformatics.T. Pérez-Acle, F. D. González, D. Naranjo, and P. Orio

We combine experimental evidence with mathematics, physics, and thermodynamics and develop computational models to study biological phenomena. *a)Theoretical & Computational Neuroscience*. We applied a novel method based on graphletsto compare the topology of gene regulatory networks in the zebrafish olfactory system. We also applied our conductance-based model of cold thermotransductionto understand how hypersensitivity to cold can arise from the down-regulation of the IKd potassium current.*b) Theoretical Biophysics*. All potassium channels have a highly conserved ion selectivity filters. We proposed that large conductance potassium channels are endowed of wider internal vestibules than dopotassium channels with smaller conductances. By relying on simple atomistic models for gap junction channels, we proposed that internal negative charges diminish the free energy barrier faced by cations during transport. Finally, we studied the interaction betweentheTRPV1 channel and the DkTx toxin. In *c) Target Discovery, Drug Discovery and Drug Delivery*, we continue to explore new nano-carriers, new TRPV1 channel agonists, and hemichannel blockers, using *in vitro*and *in vivo*models.

6. Translational Research.J. C. Sáez, T. Pérez-Acle, D. González

This new unit was created during the last year to support the translational research efforts of the Research Lines and to aid in the generation of spin-offs. For this we hired a manager with experience in generating R + D grant applications (e.g., CORFO) and in intellectual property protection.

3. Scientific and technological research

a) Current status of research lines:

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

Like antennas capturing the signals that arrive from the external world, ion channels transform the energy contained in different stimuli into the mechanical energy necessary to open the conductive pore. It is the dissipation of the ionic gradients through these conductive units that then causes the changes in membrane potential that are critical for nervous system function. Our research line is interested in how, from a molecular point of view, the different types of energy contained inelectrical, thermal, and chemical stimuli are transformed into mechanical energy (the pore opening). On the other hand, the dissipation of ionic gradients caused by the opening of ion channels is restored by pumps, and our group has lately been interested in the mechanism involved in the movement of Na^+ and K^+ mediated by the Na^+/K^+ ATPase of the giant axon of the Humboldt squid.

Voltage- and Ca^{2+}-activated K^+ (BK) channel. BK channels are modular proteins encompassing several modules including four peripheral voltage sensors and a large intracellular C-terminus where the Ca^{2+}binding sites reside. Voltage and Ca^{2+} sensors are allosterically coupled to the pore gate. Recognizing its significant contributionsto the field, our group was invited to write together with members of Line 5, a review in the most cited journal in physiology **(Latorre et al., *Physiol. Rev.* 2017).** This review discusses in depth the biophysics and physiological role of this channel encoded by a single gene, in particular, how association with auxiliary subunits greatly increaseschannel function diversity. By using genetically encoded lanthanide-binding tags (LBT) that bind terbium with high affinity as a LRET donor and a fluorophore-labeled iberiotoxin as the LRET acceptor we were able to determine the architecture of the external aspect of BK and how this architecture is rearranged by the auxiliary β1-subunit **(Castillo et al,*PNAS* 2016)**. We have previously found that 17β-estradiol (E2) is able to activate BK channels and that this modulatory effect of the hormone requires the presence of the β1 subunit (Valverde et al. *Science*, **285**:1929, 1999). In collaboration with the laboratory of Dr. Yolima Torres (Universidad Javeriana, Bogota, Colombia) and using mutagenesis, immunofluorescence, and gating and macroscopic current measurements we were able to determine that the E2 binding site resides in the β1-subunit.The increase in channel activity produced by estrogens is due to the stabilization of the voltage sensor in its active configuration and to an increase in the coupling between the voltage sensor and the pore opening.

TRP channels. Thermal TRP channels are polymodalreceptors activated by temperature, voltage, pH, lipids, and agonists. Two invited reviews were published during 2016. The first, in the prestigious Annual Review of Biophysics, reviewed in detail a subject that our group was the first to describe: the allosteric coupling between the temperature and voltage sensor modules and the pore domain. We also proposed, for the first time, that an anisotropic thermal diffusion model may explain the large temperature sensitivity of thermo TRP channels (**Diaz-Franulicet al.,*Ann. Rev. Biophys.* 2016**). In the second review,written in collaboration with Line 5, we gave an account of how our current knowledge regarding the structure of different TRP channels can be used to propose a structure-oriented pharmacology for this class of proteins(**Díaz-Franulic et al.,*Mol.Pharmacol.* 2016**).

CaV channel.In 2015 we reported that each voltages sensor (VSD) of the CaV channel displays divergent voltage and time-dependencies and how they influence channel opening. This year we published work showing that the auxiliary α2δ-1 subunits responsible forthe right-shifted voltage dependence appears to be a consequence of an increase in the interaction energy between VSDs and the pore and a reduction in the total number of charges coupled to channel opening (**Savalli et al.,*J.Gen. Phyisol.*2016**). During 2016, we also made progress toward estimating the number of charges necessary to open CaV channels. We have measured the voltage dependencies for channel opening at extremely low voltages where the overall Po approached 10^{-7} in giant patches encompassing several hundreds channels.

Voltage-gated proton channel* (H_V)** Contrary to the prevalent view that proton channels encompass a water filled path where protons can hop between adjacent water molecules, we combinedmutagenesis, fluctuation analysis, and molecular and quantum dynamics simulations, to show that there are water-free domains within the channel conduction pathway through which protons pass by hoping between aspartate residues (**Pupo et al., *PNAS, Submitted). This year we also spent time and effort investigating Hv channels as a potential target for cancer therapy (**Fernándezet al.,*Mol. Pharmacol*. 2016).** An initial report of this investigation shows thatinhibition of Hv (HVCN1) induces acidification of leukemic Jurkat T cells promoting cell death by apoptosis (**Asuaje et al., *Pflügers Arch.* 2016**).

Na^+/K^+ Pump.Our research of the Na^+/K^+ pump using the giant axon from the Chilean Humboldtsquid lead to the discovery and unambiguous demonstration that isolated axon have the intrinsic capability for *de novo* synthesis of functional oligomeric membrane proteins (**Mathur *et al.,J. Neurosci. submitted***).

Connexinhemichannels: A fruitful collaboration has developed which combines the strength of Line 1 in ion-channel biophysics with the expertise of line 2 in connexinhemichannelsand is complemented by the skills of line 5in molecular modeling. Following our work showing that a mutation in Cx26 linked to the Keratitis-ichthyosis-deafness (KID) syndrome produce hyperactive hemichannels when co-expressed with wild type Cx43,we revisited the subject in light of new structural modeling (**García et al.,*J.. Invest.Dermatol.2015, 2016***). To unravel the molecular mechanisms underlying this hyperactivity, we incorporated single channel measurements and molecular dynamic simulations to find that this hyperactivity is mediated by mutation-induced structural changes that modify hemichannel gating mechanism by virtually eliminating a process known as fast gating and causing an increase in the open probability. This work identified for the first time the molecular mechanism by which KID mutations in Cx26 cause gain of function changes in hemichannels (**García et al., *J. Gen. Physiol. under revision***). To further understand voltage-dependent gating of these hemichannels we carried out detailed electrophysiological characterization of several connexinhemichannels and showed that the charged residues at the end of the first transmembrane segment play a critical role in voltage sensing (**Pinto et al., . *J. Biol. Chem.2016).***

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

Control of neurotransmitter release.In collaboration with Dr. Fernando Marengo (Univ. Buenos Aires), we demonstrated that under low frequency stimulation, vesicle recycling depends on a dynamin-dependent fast endocytosis **(Moya-Díaz et al., *Front Cell Neurosci.*2016**). We also showed that the actin binding protein, cortactin, regulates the

exocytosis induced by activation of nicotinic receptors in chromaffin cells (***Front. Cell.Neurosci. U*nder revision**). Our efforts to understand the mechanisms that regulate exocytosis and vesicle recycling in neuroendocrine cells were recently reviewed **(Cárdenas and Marengo, *J. Neurochem*. 2016)**. In association with our collaborator Pablo Caviedes (Univ. Chile), we have continued studying the contribution of the different genes that are overexpressed in Down Syndrome (DS) to actin dynamics, calcium signals, and exocytosis dysfunctions using a cell line derived from brain cortex of trisomy 16 fetal mouse, an animal model of DS.We published a paper **(Pérez-Núñez et al., *Neurotox. Res.* 30:76-87**) and have a manuscript under revision in Neural Plasticity reporting these findings, and sponsored the Master's Thesis/Dissertation of Jacqueline Vásquez.

Hemichannels in skeletal muscle diseases.We explored the molecular mechanisms involved in muscular dystrophies and demonstrated that a dysfunction of actin dynamics underlies myopathies caused by mutations in dynamin-2 (***Scientific Reports* under revision)**. We also characterized the Chilean population bearing dysferlinopathies**(Díaz et al., *Muscle Nerve*2016)** and determined that hemichannels play a critical contribution to the etiopathogenesis of this disease **(Cea et al., *BMC: Cell Biology*. 2016).** Our recent findings on this issue have been reported in a recent review **(Cárdenas et al., *ExpNeurol* 2016)**.In collaboration with Dr. Luis Barrio from the Ramón y Cajal Hospital, Madrid, Spain, we found that connexinhemichannels are expressedin the skeletal muscles of patients with Duchenne and Becker muscular dystrophies (DMD and BMD). In addition, we found that*mdx* mice models of DMD and BMD, express connexinhemichannels. We generated *mdx* mice deficient in Cx43 and Cx45 specifically in skeletal muscles and found that they lackinginflammasomeactivation and apoptotic cell death **(Cea et al., *Cell. Mol. Life Sci.* 2016)**.Moreover, we found that muscle atrophy induced by glucocorticoids is the consequence of connexinhemichannels expression since Cx43 and Cx45 KO myofibers do not show activation of the inflammasome and atrophy (**Cea et al., *Biochem Biophys Acta. Molecular Basis of Disease* 2016)**, implying that the current treatment of muscles dystrophies with glucocorticoids is likely to worsen the muscular condition. In collaboration with two experts in spinal cord injury, Dr. C. Cardozo and W. Bauman (National Center for the Medical Consequences of SCI, James J. Peters VA, New York), we demonstrated that the soluble activin receptor IIB does not prevent muscle atrophy in a mouse model of spinal cord injury **(Graham et al.*J. Neurotrauma.*2016)**. In contrast, we demonstrated in a systematic study that connexinhemichannels are responsible for the ionic unbalance and negative protein balance of denervatedmyofibers (**Cisterna et al., 2016 *Biochem Biophys Acta.. Molecular Basis of Disease* 2016).**At the molecular level, we demonstrated that the activation of Cx43 hemichannels by an inflammatory unsaturated fattyacid is mediated by phosphorylation of Cx43 by AKT kinase in serine residue373 **(Puebla et al., *Biochem.; Biophys.Acta.Molec.and Cell Biol. of Lipids* 2016)**. Our experience in the gating and pharmacologyhemichannelshas resulted in collaborative work with several laboratories in the USA **(Johnson et al., *J Membr Biol.* 2016).**

Connexin hemichannels in deafness and brain diseases.We produced molecular models of mutant Cx26 and found that most mutations that cause hemichannelgain-of-function affect pore-lining residues **(García et al.,*J Invest. Dermatol*. 2016)**. Most syndromic mutations were found clustered in the amino-terminal domain and in the para-helix region of the transition zone between the first transmembrane domain and the first extracellular loop, which is a highly conserved domain in the connexin family and a critical region for channel gating and regulation. Our finding showingthat some Cx26 syndromic mutations

targeting the N-terminal domain produce highly hyperactive hemichannels when co-expressed with wild type Cx43, suggests that the Keratitis-ichthyosis-deafness (KID)disease is a consequence of aberrant connexin-connexin interactions that result in hyperactive heteromerichemichannels. This is consistent with the fact that Cx26 is co-expressed with Cx43 in the skin and cochlea during development and in adulthood.These findings plus the analysis of the literature help us to propose a general mechanism of this type of disease**(García et al.,*BMC Cell Biol*.2016)**. We also characterized the effect of the syndromic mutation G12R on voltage gating activation and the Ca^{2+} effects in the Cx26 hemichannel. This mutant shows gain of function in homomeric as well asheteromeric configurations. We found that mutation G12R produced loss of the fast voltage gating mechanism without modifying the effects of extracellular Ca^{2+}**(*García et al., J Gen. Physiol. under revision*)**. In addition, the mean open time of single G12R hemichannelsis longer than normal, which may explain the hyperactivity of this hemichannel.One of the final goals of this project is to identify the molecular consequencesof connexinhemichannelmutations. We determined the role in voltage sensing of the charged residues at the end of the first transmembrane domain ofCx26, Cx46, and Cx50. Conductance/voltage curves together with kinetic analyses reveal that the fast and slow gating of Cx26 involves the movement of two and four charges across the electric field, respectively. These results indicate that the charges at the end of the first transmembrane domain are part of the slow gate voltage sensor in connexins**(Pinto et al., *J. Biol. Chem.*2016)**.

As a continuation of our previous findings on the role of connexin and pannexinhemichannelsof glial cells in animal models of stress-induced brain diseases,we found that oligodendrocytes express the molecular elements of the inflammasome, which is activated by stress and is due to activation of connexin and pannexinhemichannels. These findings could be relevant for preventing stress-induced demyelinization and depression **(Maturana et al., *Develop. Neurobiol.*2016)**.Related to the treatment of neuroinflammatory conditions, we demonstrated that cannabinoids prevent the amyloid β-induced activation of astroglialhemichannels and consequently could serve as neuroprotective agents **(Gajardo-Gómez et al., *Glia* 2017)**

Line 3.Genetic and Developmental Neuroscience. *(K. Whitlock,J. Ewer, and A. Calixto)*
We continue to use genetic tools to understand the development of the nervous system and the resulting behaviors.

Genetic control of neural differentiation and function in the zebrafish*.**We continue to investigate how the different classes of neurons, glia, and neuroendocrine cells are generated in the olfactory sensory system and GnRH neuroendocrine system: ***1. *Analysis of regenerating and non-regenerating cell populations of the olfactory sensory system.* **a)** We have identified anew class of glial cells in the olfactory epithelium that are progenitor-like cells capable of generating neurons and glia not only during development but also in the adult animal. **b)** We have discovered a damage-induced neuro-immune response in the olfactory sensory epithelium. This response is not shared by other sensory systems and involves calcium signaling in the olfactory sensory neurons and olfactory bulb; ***2***. *Control of GnRH cell differentiation in the adult hypothalamus?* **a)** We have discovered that the neural progenitor population in our recently described neurospheres, which are capable of generating neurons, glia, and GnRH cells, correspond to a specific region of the intact hypothalamus in the adult animal. Furthermore through our characterization of

neurogenesis in the hypothalamus of the adult we have discovered that the progenitor population differentiates in the absence of cell division and this process can be enhanced by hormone treatment, thus supporting the model that patients with GnRH deficiencies (hypogonadic hypogonadism, HH) "revert" and become fertile via activation of quiescent neural progenitor pools in the hypothalamus. **b)** In collaboration with Dr. John Ewer, we have performed a bioinformatic analysis of the different isoforms of GnRH to understand GnRH loss in a specific syntenic region of the genome and its potential evolutionary significance relative to domestication effects on the genome (collaboration with Dr. John Postlethwait, USA) and alternate peptide pathways (Dr. Christian Wegener, Germany). Through collaboration with C. Wegener we are analyzing a recently described peptide Phoenixin, that is capable of activating the GnRH reproductive axis; ***3***. *Does activity control neural identity?* We have found that damage induced calcium activity plays a role in both neural-immune response and generation of new neurons in the olfactory epithelium. We are continuing our collaboration with the lab of T. Pérez-Acle (Line 5; **Calfun et al., *Chemical Senses 2016***) to analyze genetic networks controlling olfactory receptor expression.

Regulation of Drosophila behavior by neuropeptides and the circadian clock.We use insect ecdysis (the behavior used by all insects to shed the old exoskeleton at the end of every molt) to understand how neuropeptides and the circadian clock regulate animal behavior. During this period we have: ***1***- *Continued to investigate how the key neuropeptides, Eclosion Hormone (EH) and Ecdysis Triggering Hormone (ETH), control ecdysis behavior*. For this we used genetic tools we have developed in collaboration with Ben White (NIH, USA; cf., **Diao *et al*., *Genetics* 2016),** null mutants we have isolated, and calcium imaging using GCaMP, to understand how EH and ETH cause the sequential expression of ecdysis behaviors **(Mena *et al*., *eLife* 2016)** and physiological changes **(Flaven-Pouchon *et al*., *Insect Biochem. Mol. Biol*. 2016).** ***2***- *Determined how the central brain clock and the peripheral clock in the prothoracic gland (PG) are coupled*. Clock function in both the brain and the PG are necessary for a circadian pattern of adult emergence. In collaboration with Christian Wegener (U. Würzburg, Germany) we have recently identified the pathway through which the brain clock is coupled to the PG clock **(Selcho *et al., Nature Comm. In Press*)**. Finally, we are collaborating with A. Palacios (Line 4), aiding in the mining of the genome of the Chilean rodent, *Octodon degu* for genes homologous to genes associated with Alzheimer's disease in humans **(Salazar *et al*., *Biol Res.*2016)**; we also maintain an interest in the role of neuropeptides in regulating animal behavior, including that of humans **(Aspé*et al*., *Front Neurosci*2016)**.

Using genetic and genomic approaches to understand how dietary molecules regulate survival of neurons in models of neurodegeneration and regeneration. We have continuedour analysis of how cellular and environmental stress and specific food molecules impact biological systems and modify neuronal phenotype and behavior, using *C. elegans* as a model organism. We are addressing three main questions: **1.**How do metabolic changes such as diapause formation and deregulation of the insulin pathway affect neuronal degeneration and contribute to neuronal regeneration? For this we have developed a new technique to analyze neuronal regeneration in single diapausing worms. In collaboration with Mark Alkema (University of Massachusetts, USA), we performed an EMS mutagenesis screen to discover genes that are required for neurodegeneration during diapause. Fifty-eight candidate genes are in the process of cloning and characterization. **2.** Which components of food regulate the kinetics of degeneration, followed by global

analysis of transcriptome in the host to understand the changes in gene expression that trigger neuronal protection and regeneration.**3.** How do small RNA from pathogenic bacteria cause transgenerationally-transmitted changes in host behavior. We employ strategies that include functional genomics, behavioral assays, molecular and cellular techniques and RNAseq approaches.

Line 4 Circuits and systems neuroscience. (A. Chávez, P. Moya, A. Palacios, and O, Schmachtenberg)
During 2016, we have continuedour research toward understanding how the neuronal circuits in the hippocampus and retina function under normal conditions and how this functionchanges under pathological conditions including aging, neurodegenerative and neuropsychiatric disorders, whichcan cause severe alterations in both cognitive and sensory performance. Regarding cognitive process and the regulation of memory formation, we have found that the transcription factor XBP1 and Arc signaling are critically involved in synaptic plasticity in the hippocampus (**Martinez *et al., Cell Reports,* 2016*; Wang et al., J. Neurosci.*2016**). Moreover, we have found that TARP 8 is a main substrate of CaMKII, a key kinase required for synaptic plasticity and memory formation ***(*Park *et al., Neuron* 2016*)***. Work continuous in the retina, where we have found that abnormal serotonin homeostasis alters global retinal ganglion cell function using the serotonin transporter KO as a mouse model. Similarly, we found that cannabinoid signaling regulates night vision responses *in vivo*.
Ongoing data using the 5-HT transporter knockout (SERT KO) mouse as a model of anxiety and susceptibility to depression show that SERT KO mice have impairments in working memory in a manner that is dependent of working load. Moreover, *in vitro* experiments show that the mechanism of synaptic plasticity is impaired in SERT KO mice. Our findings also show that SERT KO mice express normal long-term memory and improved cognitive flexibility. Work continued on the pathogenesis of Alzheimer`s disease (AD) with the comparative study of natural and transgenic AD models ***(*Salazar *et al., Biol. Res.*2016*)***.
At the sensory system level, we have shown that nitric oxide modulates the OFF pathway by regulating the response of bipolar and amacrine cells in the inner and outer retina **(Vielma and Schmachtenberg *Science Reports.* 2016*)***. Ongoing research work at this line have found that abnormal serotonin homeostasis alters global retinal ganglion cell function using the serotonin transporter KO as a mouse model. Similarly, we found that cannabinoid signaling regulates night vision responses *in vivo*. Interestingly, in a close collaborative work, our team has preliminary evidence indicating that both the excitatory and the inhibitory function required for normal neuronal circuit function is impaired in the retina of SERT KO mice. To gain a better understanding of synaptic function in the CNS under physiological and pathological conditions, our team has expanded its collection of mice models of disease including conditional CB-1 KO (knockout), SERT KO , TRPV1 KO , and 5-FAD and APP-PC1 Δ9 mice. Of note, the Max Planck Tandem Research Leader, Dr.Chiayu Chiu has joined our research line and is currentlysetting up a state-of-the-art laboratory, which includes a 2-photon microscopy purchased with CINV funds and a FONDEQUIP grant from CONICYT awarded to A. Chávez.

Line 5. Crosscutting: *Computational Biology and Bioinformatics.* *(T. Pérez-Acle, F.D.González, D. Naranjo and P. Orio).*

By combining experimental evidence with advanced mathematics, physics, and thermodynamics we develop computational models to study biological phenomena ranging from the atomic scale to the population level. Our research efforts are organized in three main areas: *1. Theoretical & Computational Neuroscience, 2. Theoretical Biophysics and 3. Target Discovery, Drug Discovery and Drug Delivery (TD5).*

1.Theoretical & Computational Neuroscience. We proposed a novel computational method to compare the topology of gene regulatory networks **(Martin et al., *Plos One* 2016**). This method was successfully applied to recognize changes in the expression of olfactory receptors in Zebrafish during odorant exposure (in collaboration with Line 3) **(Calfún et al., *Chem. Senses.* 2016)**. We have applied our conductance-based model of cold thermotransduction **(Olivares et al., *Plos One.* 2015)** to the interpretation of experimental data showing how pathological conditions such as hypersensitivity to cold can arise from the down-regulation of the IKd potassium current **(González et al., *J. Neurosci.* 2017)**. We also analyzed the chaotic behavior in a burst generation model; our analyses showed that the hyperpolarization-activated current Ih -very common in the CNS-, induces period-doubling cascades and chaos when combined with other burst generation mechanisms **(Xu et al., *Front. Comput. Neurosci.* 2017)**.

*2.Theoretical Biophysics.*To explain the physical basis for large or small conductance in potassium channels, we proposed that large conductance channels are endowed of wider pores, where ions can be more stable that in narrower pores **(Moldenhauer et al., *Scientific Reports* 2016; Naranjo et al., *J. Gen. Physiol.* 2016)**. On the other hand, by relying on simple atomistic models akin to gap junction channels, we proposed a role for charge distribution over ion transport processes in these channels **(Escalona et al., *Biophys. J.* 2016)**. Importantly for water dynamics within proteins, we proposed that the transition from dimers to collective dipoles drives solvent loading in carbon nanotubes **(Garate et al., *J. Chem.Phys.* 2016)**. During the last year, we developed a molecular model of the BK channel by combining functional and theoretical data **(Castillo et al., *PNAS*2016; Latorre et al., *Physiol. Rev.* 2017)**. Additionally, we studied the interaction between TRPV1 channel and DkTx toxin. In the same context, we developed a model for TRPV1 channel gating which has been experimentally validated **(Díaz-Franulic et al., *Mol. Pharmacol*. 2016)**.

3.TD5.We continue to explore new nano-carriers and the biological effects of hemichannel blockers in both muscular dystrophy and epilepsy using *in vivo* models. Based on our collaboration with the US Army Research Lab, we completed a virtual screening thatidentified 3 novel TRPV1 channel agonists. Moreover, we have applied a computational method to track heat-diffusion pathways (ATD) across the TRPV1 channel **(Diaz-Franulic et al. *Ann. Rev. Biophys.* 2016)** and are implementing the experimental protocol as a proof of concept, using gold nanoparticles in a joint effort with researchers from Line 1.

b)Publications:

Summary table

Category of Publication	**MSI Center Members**	**Number of Publications coauthored by students**	**Total Number of Publications**
ISI Publications or Similar to ISI Standard	Associate Researchers	24	38
	Other Researchers	3	10
SCIELO Publications or Similar to SCIELO Standard	Associate Researchers	0	0
	Other Researchers	0	0
Scientific Books and chapters	Associate Researchers	1	1
	Other Researchers	0	0
Other Scientific Publications	Associate Researchers	0	1
	Other Researchers	1	3
Total of Publications		**29**	**53**

c) Other achievements:

i. Patents:

NONE

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)	41	38
Invited presentations (not included in above row)	4	4

B. Other researchers (Adjunct Researchers, Senior Researchers, Young Researchers, Postdoctoral Researchers and Students)		
Conferences, oral communications, poster communications, others (specify)	11	5
Invited presentations (not included in above row)	1	0

iv. Organization of Scientific Events:

International Symposiun Biology of Neuropsychiatric Disorders.Over 130 graduate students and scientists from Latin America with the support of IBRO-LARC participated in the first International Symposium organized by NuMIND with the support of CINV. World class speakers lectured on cutting-edge research in neurobiological mechanisms underlying mental illnesses including Post Traumatic Stress Disorder, Schizophrenia, Depression, Obsessive-Compulsive Disorder and Drug Addiction.

Small Brains, Big Ideas (Valparaíso, November 10-19)The "Small Brains, Big Ideas: Biomedical Insights from Invertebrates" practical course and international symposium was offered for the fourth time in November 2016. The primary objective of the course is to expose students from Latin America to the use of invertebrate preparations for basic and applied research in neurosciences. The course was again organized by Dr. Jimena Sierralta (BNI, MI), Dr. Andrea Calixto (CINV; Line 3), and Dr. John Ewer (CINV, Line 3), and remains a strong example of an important outreach activity that involves 2 MIs.

CINV Meeting 2016 (Valparaíso, July 29) 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.

v. Scientific Editorial Boards:

John Ewer: *Journal of Insect Science, Current Opinions Insect Science, Insect Biochemistry and Molecular Biology*

Carlos González: *Journal of BiologicalChemistry, AnFaMed, Revista Habanera de Ciencias Médicas.*

Ramón Latorre: *Biological Research, Proceedings of the National Academy of Sciences, Journal of General Physiology, Channels, Temperature, Frontiers in Pharmacological Sciences, European Journal of Biophysics.*

David Naranjo: *Frontiers in Physiology.*

Tomás Pérez-Acle: *PeerJ, PeerJComputer Sciences.*

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

Juan Carlos Sáez: *BMC CellBiology.*

vi. Awards

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

1. Molecular Mechanisms of Connexin Hemichannel Hyperactivity in KID (keratitis-ichthyosis-deafness) syndrome (1171240)***PI: AgustínMartínez; Co-PI: John Ewer***

2. Electrophysiological assessment of glucose neurotoxicity mediated by oxidative/nitrosative stress in bipolar cells of organotypic retinal explants*(*1171228) ***PI:Oliver Schmachtenberg; Co-PI: Adrián Palacios***

3. Ligand and Temperature Activation in TRPV1 Channels: A Thermodynamics and Molecular Simulations Analysis(1170733) ***PI: Fernando González Nilo; Co-PI: Carlos González***

4. Is There A Voltage-Controlled Hydraulic Gating In The Human Connexin 26 Hemichannel? (1160574) ***PI: Tomás Pérez-Acle; Co-PI: Agustín Martínez***

vii. Other Awards

Neuromorphic Inspired Science. Molecular Basis of Excitability and neuronal Homeostasis- ***PI: Ramón Latorre; Co-PIs: Francisco Bezanilla and Miguel Holmgren.*** Funded by the Air Force Office for Scientific Research, USA.

4. Education and Capacity Building

a) Education and Capacity Building:

The PhD Programin Neuroscience was created in 2002 by CINV members and is accredited through 2017. Its Director is currently Dr. John Ewer (CINV, Line 3). It is designed to train researchers in the development, structure, and function of the nervous system. 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.This Program ensures funding for 4 years to all students it accepts, thereby allowing students to devote full time to their PhD work. Funding is provided by governmental grants (CONICYT and MECESUP), as well as by grants offered by the University of Valparaiso. In addition, the CINV provides graduate fellowships (6 during this period). *Information, requirements, andapplication informationcan be found at*www.dnuv.cl.

Ph.D. Program in Biophysics and Computational Biology (Director: Dr. Patricio Orio, Line 5). This Program was proposed in the original grant and started its activities in March 2015 with 4 students. Two students were admitted for the 2016 academic year, and 5 more were selected for the 2017 academic period.Its students have participated in world-class international courses and congresses, and two of them travelled abroad for international stays to carry out work relevant to their thesis. Importantly, the Program was recently accredited for a period of 2 years, allowing itsstudents to apply to CONICYT Doctoral fellowships. In the 2016 application period, 9 students were granted fellowships, of which one was ranked 2nd and the other 6th for the entire country.

TheMasters Programin Neurosciencewas foundedin 1999 and is currently directed by Dr. AgustínMartínez (CINV, Line 2). The program was reaccredited for 8 years in 2011, becoming the longest accredited program of the University of Valparaíso.Itis characterized bya high content ofbasic Neuroscience as well as for itsmultidisciplinarity.Its studentsarefrom various disciplines includingbiology, biochemistry,health, engineering,andmathematics.*Requirements and application informationcan be found at* www.magisterneurociencia.cl.

b) Achievements and Results:

In the **Neuroscience PhD Program**, 38students have graduated since 2002 (11 female; 27 male), of which 6 graduated during this period (see list below). The Program currently has 34 students (15 female, 19 male). During this year's recruitment period 13out of 20 applicants were considered admissible and were interviewed. Of these, 9 were selected and accepted to join the Program. Two received fellowships from CONICYT; the rest received fellowships from the University of Valparaiso and the 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. Although each year we are able to admit good candidates from the pool of applicants, we do not understand why the number of applicants varies from year to year, sometimes significantly. As a result, the number of graduates also varies between 2 (see Report for 2015) to 6 (this Report) per year. We are exploring different strategies to attract greater number of applicants; one of these involves offering lab

technique courses to advanced undergraduate students who are majoring in biomedical areas.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 **Masters Program**, fifty students have graduated since 1999 (26females; 24male), of which 12 graduated during this period; eight 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 38 applications of which 17 were accepted, being close to the maximum number of students we are able accept every year. Of these, 1 received a fellowship from CONICYT, which is quite good considering that only 5% of applicants from the whole country were granted a fellowship. During the interview process several applicants mentioned the CINV as one of the reasons for choosing our program.***Destination of Students:*** **PhD Program**: 38 students have graduated since 2002. The majority of graduates of our Program are currently carrying out postdoctoral work (with the exception of a few graduates from 2016 who are either looking for postdoctoral positions or are completing experiments and preparing their thesis work for publication).**Masters program:**Fifty students (26 female, 24 men) have graduated since 1999. 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.

c) Main achievements of Ph.D. and Master Students from our Programs During the Period:

Graduation of students (Note: some students did their thesis work in labs outside the CINV).

PhD Program in Neuroscience

1. Oscar Jara; Title: Mecanismo de Regulación diferencial del tráfico y función de HC de Cx43 y Cx26 por el citoesqueleto de actina. Advisor: Agustín Martínez (Line 2).
2. Willy Carrasquel; Title: Estudio sobre acoplamiento alostérico entre los sensores de potencial y el poro en el canal BK. Advisor: Ramon Latorre (Line 1).
3. Amauri Pupo; Title: Mecanismo de conducción de protones en el Canal Hv1 Advisor: Carlos González (Line 1).
4. Ignacio Díaz; Title: "Turning a small into large conductance k-channel: how far can we go?" Advisor: David Naranjo (Line 5).
5. Severin Lions; Title: "Effect of visuospatial cues on multiple-choice questions reading and solving". Advisor: Marcela Peña (U Chile) (Not part of CINV).
6. Ricardo Ramírez; Title: "Steroid modulation of TRPV1 during oxidative cell death". Advisor: Pablo Olivero (Not part of CINV).

Masters Program in Neuroscience

1. Mario Wellmann; Title: "Hiperexcitabilidadastroglial en el hipocampo epiléptico: contribución de la señalización astrocito-astrocito". Advisor: Dr. Christian Bonansco (Not part of CINV)
2. Bernardo Pinto; Title: "Charged residues at the first transmembrane region mediate the voltage dependence of connexins slow gate". Advisor: Dr. Carlos González (Line 1)

3. Camila Morales; Title: "Caracterización de la Transmisión Sináptica Inhibitoria en Hipocampo y Corteza Prefrontal de Rata Tipo Ezquizofrénica Asociación con la Memoria de Trabajo". Advisor: Dr. Marco Fuenzalida (Not part of CINV).
4. Irina Galli. Title: "Desempeño de Tareas de Memoria y de Respuesta Emocional de Mujeres Jóvenes Durante el Ciclo Menstrual". Advisor: Dr. A. María Cárdenas (Line 2)
5. María José Guerra; Title: "Rol de la subunidad β de los canales de Ca^{+2} voltaje dependientes en la expresión de los canales en celulascromafines de bovino". Advisor: Dra. Ana María Cárdenas (Line 2).
6. Camilo Miguel. Title: "Temporal changes in retinal network due to patterns of oscillatory stimuli suggest an oscillatory plasticity mechanism. Advisor: Dr. Adrián Palacios (Line 4).
7. Miguel Fuentes; Title: "Papel de la comunicación intercelular mediada por uniones en hendidura y hemicanales durante el proceso de diferenciación de células madres mesenquimaticas de piel adulta hacia un linaje adipogenico". Advisor: Dr. Agustín Martínez (Line 2)
8. Ricardo Ceriani. Title; "Caracterización de la mutante cx26n14y y su efecto en la formación y funcionalidad de uniones en hendidura y hemicanales". Advisor: Dr. Agustín Martínez (Line 2).
9. Melissa Pavez. Title; "Estimulación temprana para inducir resiliencia en ratas prepúberes estresadas prenatalmente". Advisor: Dr. A.Dagnino (Not part of CINV).
10. Marcela Navarrete. Title; "Frequency-specific auditory attention changes the behavioral detection of tones and modulates the amplitudes of stimulus-frequency otoacoustic emissions". Advisor: Dr. Paul Délano (Not part of CINV).
11. Carolina Flores. Title; "Rol de panexina 1 en la formación de espinas dendríticas y la en composición de las sinapsis del hipocampo de ratón". Advisor: Dr. A. Martínez (Line 2).
12. Jacqueline Vásquez. Title; "Disfunción en la exocitosis de vesículas secretoras en un modelo celular del síndrome de Down". Advisor: Dra. Ana María Cárdenas (Line 2).

Thesis Project Approvals and Qualifying Exams

In addition to graduations, 6 students from the Neuroscience graduate program passed their qualifier exams and successfully defended their thesis project; the advisors of 4 of these students are researchers of the CINV MI. One student from the recently-created program in Biophysics and Computational Biology also passed this important milestone. Finally, 13 students from the Masters Program in Neuroscience passed their qualifier exams and successfully defended their thesis project; the advisors of 8 of these students are researchers of the CINV MI.

d) 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 of lack of specialized equipment or experience. Students who conducted research stay during this period include:

1. Daniela De Giorgis (Ph.D. Student; advisor: Dr. Alan Neely, Line 1). Visited Dr. Olcese's laboratory (UCLA School of Medicine, USA) to perfect her skill in voltage-clamp fluorometryand learn more about how the contribution of the voltage-sensing domain to the opening of calcium channels is modulated by regulatory subunits.
2. Cesar Ravello (Ph.D. Student; advisor: Dr. Adrián Palacios, Line 4) spent 2 weeks doing research in Dr. Perrinet's lab (Aix Marseille Université, France) developing new natural

stimuli (Motion Cloud) to be applied to the retina to compute the spatial and temporal proprieties of receptive field of retinal ganglion cells. This research stay took place in the context of the international project entitled "A Network for Computational Neuroscience: From Vision to Robotic" ECOS / CONICYT C13E06 (2014-2016; PI: Cesar Ravello).

3. Alejandro Bernardín (Ph.D. Student; advisor: Dr. Tomás Pérez-Acle, Line 5) visited the lab of Jonathan Dushoff (Mcmaster University, Canada) to learn the use of the PISKA tool in infectious disease modeling.
4. Jaime Maripillán (Master's student; Advisor: Dr. Agustín Martínez, Line 2) visited de lab of Jorge Contreras (Rutgers University, USA) to learn 2-electrode voltage clamp.
5. Mauricio Caneo (Master's student; Advisor: Dr. Andrea Calixto, Line 3) visited the lab of Dr. Kurzchalia (Max Planck Institute, Germany) to work on a project entitled: "Identification of bacterial metabolites contributing to neuronal protection".

e) Organization of National and International courses and workshops:

Courses.

The "Small Brains, Big Ideas: Biomedical Insights from Invertebrates" practical course and international symposium was offered for the fourth time in November 2016. The primary objective of the course is to expose students from Latin America to the use of invertebrate preparations for basic and applied research in neurosciences. The course was again organized by Dr. Jimena Sierralta (BNI, MI), Dr. Andrea Calixto (CINV; Line 3), and Dr. John Ewer (CINV, Line 3), and remains a strong example of an important outreach activity that involves 2 MIs. The course included:Lectures covering basic and also specialized knowledge about the use, genetics, development, physiology, and behavior of these genetic model organisms; laboratory exercises with Drosophila, C. elegans, and bees; faculty research talks and student presentations; one outreach talk for high school students and teachers, and the general public (given by Dr. Ulrike Heberlein, HHMI, Janelia Research Park, USA); and a one-day symposium open to the Chilean scientific community.Strategies to hire and incorporate young investigators.

In 2015 we carried out an international search to hire 2 Max Planck Tandem Research Leaders. The first of these, Dr. Chiayu Chiu, joined the CINV during 2016 and is currently setting up her lab. She will use optogenetics and two photon microscopy to study the development of the brain cortex. The second Max Planck Tandem Research Leader, Dr. Rodrigo Suárez, is presently at the University of Queensland, Australia. He is an expert in brain development and evolution and is expected to join the CINV in 2019.

We have also incorporated the category of "Young Investigators" to the CINV as a way to help outstanding young scientists transition to becoming independent scientists. During 2016, we incorporated the Young Investigators: Dr. Karen Castillo who has a background in cell biology and electrophysiology and reinforces the research line on Molecular Sensors; Dr. Helmuth Sánchez, who is an expert in connexinhemichannelsand adds research on channelopathy in syndromic deafness to Line 2; Dr. Alvaro Ardiles investigates the role of pannexin channels in synaptic function. His work combines concepts and techniques currently in use in the Cell Signaling and System and Circuits Neuroscience lines, thereby bridging these two lines of CINV research; and Dr. José A. Gárate, who uses computers to model phenomena ranging from human behavior to molecular interactions, greatly strengthens Line 5 and our PhD program in Biophysics and Computational Biology.

5. Networking and other collaborative work

a) Networking:

The creation, maintenance, and strengthening of scientific networks is at the core of CINV`s mission. All CINV investigators maintain active collaborations with national and/or international laboratories. Here we only highlight collaborations and projects that we think are of particular importance for extending the breadth of the research efforts of the CINV. These include:

- The arrival of Dr. Chiayu Chiu (Line 4) has consolidated ties between the CINV and several Max Planck Institutes. In particular, Dr. Chiu will receive support and has access to resources at the Max Planck Florida Institute for Neuroscience in Florida (USA), including their state-of-the-art neuroimaging and electron microscope core facilities.
- The CINV became an active partner of a University of Valparaíso institutional development project entitled "Development of an interdisciplinary platform for the innovation in health" (PI Dr. Adrián Palacios, Line 4).
- Five Chilean Universities are participating in a multidisciplinary grant funded by the USA Air Force Office of Scientific Research (AFOSR) entitled "Neuromorphic Inspires Science to Maximize Big Data Dynamic Problem Solving". Dr. Ramón Latorre (CINV Director, Line 1) is the PI of the University of Valparaíso's project entitled "Molecular Basis of Excitability and Neuronal Homeostasis"; Dr. Danilo González (Line 5) also participates in this project.
- The CINV, the University of Valparaíso, and the National Center of Minimal Access Surgery of Cuba signed a collaborative agreement in the area of Medical Sciences.
- Dr. Carlos González (Line 1) has established several collaborations in the field of ion channels which have been formalized though agreements between the University of Valparaíso and the corresponding foreign institutions. These include collaborations with Dr. Veronica Milesi (Universidad de La Plata, Argentina), Dr. Gonzalo Ferreira (Universidad de La República, Uruguay), and Dr. Orlando Jorquera (Universidad del Sur de Bahia, Brazil.
- The biannual practical course and associated international symposium, "Small Brains Big Ideas", was successfully offered for a fourth time. The course is organized by Drs. Andrea Calixto and John Ewer (CINV; Line 3), and Dr. Jimena Sierralta (MI for Biomedical Neuroscience, BNI). It was funded by EMBO, The Company of Biologists, as well as by the CINV and BNI MIs, thereby providing an example of how different Millennium Institutes can collaborate successfully. Renowned scientists from the USA, UK, and Chile participated in this course, whose primary objective is to expose students from Latin America to the use of invertebrate preparations for basic and applied research in neurosciences and biomedicine (see www.smallbrains.org).

b) Other collaborative activities:

- A long-standing collaboration of Dr. Ramon Latorre (Line 1) with Dr. Miguel Holmgren (NIH, USA) and Dr. Francisco Bezanilla (University of Chicago, USA) brought about the installation of a new laboratory devoted to the study of membrane transport and protein synthesis in the giant axon of the Humboldt squid.
- Dr. Alan Neely (Line 1) continues to collaborate with Dr. Olcese`s laboratory at the Division of Molecular Medicine Dept. of Anesthesiology, UCLA School of medicine.

Some of the 2016 results were published in J Gen Physiol. 148:147-59 by Savalli *et al*.: "The α2δ-1 subunit remodels CaV1.2 voltage sensors and allows Ca^{2+} influx at physiological membrane potentials."

- Dr. Ana M. Cárdenas (Line 2) has an ongoing collaboration with Fernando Marengo (Universidad de Buenos Aires). They have written three papers together, and will co-sponsor a PhD thesis.
- Dr. Ana M. Cárdenas (Line 2) is currently also collaborating with Marc Bitoun (INSERM, France). They already have a manuscript under revision in Scientific Report.
- Dr. Juan C. Sáez (Line 2) is currently collaborating with Christian Giaume (College de France, France), Christian Naus (University of British Columbia, Canada), and Luc Leybaert (Ghent University, Belgium); they are preparing a review for Physiological Reviews on connexin and pannexin channels in neurodegeneration as a result of their long lasting collaborations.
- Dr. Juan C. Sáez (Line 2) is consultant of the main project that support Dr Christopher Cardozo and Dr. William Bauman from the James J. Peters (Veterans Affairs Medical Center, USA).
- Dr. Agustín Martínez collaborates with Jorge Contreras (Rutgers University, USA) on voltage and calcium gating mechanisms in normal and disease-linked Cx-based channels. He also collaborates with Drs. Eric Beyer and Viviana M. Berthoud (University of Chicago, USA) on regulation of intercellular communication by Cx-Cx interactions, its molecular mechanisms and functional consequences.
- Dr. John Ewer has established long-standing collaborations with Dr. Ben White (NIH, USA) and Dr. Christian Wegener (Wurzburg University, Germany). These collaborations resulted in publications in 2015 and 2016.
- The month-long visit of Dr. John Ewer (Line 3) to the laboratory of Dr. Daisuke Yamamoto (Tohoku University, Japan) has created an opportunity for future collaborative work in *Drosophila* neurogenetics. They plan to apply for a CONICY MEC in 2018 grant, which would allow Dr. Yamamoto to visit the CINV for at least 2 months during 2019.
- Dr. Adrián Palacios (Line 4) continues long-term collaborative work with Dr. Alfredo Kirkwood (Johns Hopkins University, USA) on neuroplasticity in transgenic mouse and *Octodon degus*, a natural model for Alzheimer disease. In 2016, Dr. Kirkwood's stay was funded by CONICYT PAI grant "Fortalecimiento de la Investigación y Docencia en Neurociencia: Alteración de los Mecanismos de Aprendizaje y Memoria durante Neurodegeneracion."
- Dr. Adrián Palacios (Line 4) has established collaborative work with Dr. Frederic Chavane through an ANR collaborative project entitled: "Encoder et predire le movement le long de trajectoires par le systeme visual precoce." CE37 ANR-TRAYECTORY, 2016-2019. PI Dr. Frédéric Chavane (Aix-Marseille Université, France), co-PI Dr. A. Palacios.
- Since 2014, a collaboration between Dr. Chávez (Line 4) and Dr. Pablo Castillo (Albert Einstein College of Medicine, USA) aims to study the mechanisms underlying synaptic plasticity and its modulation by endogenous neuromodulators under normal and pathological conditions. In a recent visit Dr. Chávez concluded some experimental work aimed at studying the role of TARPy8 and CaMKII in synaptic plasticity (Park et al., 2016; Neuron).
- Dr. González-Nilo(Line 5) maintains a close collaboration with Dr. M. Valverde from Universitat Pompeu Fabra, Spain. The main goal is to study TRPV4 activation by epoxyeicosatrienoic acids by combining docking and molecular dynamics simulations

along with binding assays and functional studies. The results of this work were recently submitted to Scientific Reports.
- Dr. González-Nilo (Line 5) has a project with the US Army aimed at the rational design of pain Inhibitors.
- The PhD thesis defense of Mauricio Aspé (tutor: John Ewer, Line 3 and Raffaella Rumiati, SISSA) brought to Chile Raffaella Rumiati, which permitted the re-opening of interest in a joint SISSA/CINV program.

6. Outreach and connections with other sectors:

a) Outreach:

Since its inception as a Millennium Institute, CINV has sought to differentiate itself from the traditional ways of spreading science to the general public in Chile. During this period, the CINV has set itself the objective of explaining the importance of basic science for the country's development, associating the research in neuroscience done at the CINV with problems that the country is undergoing at present and with news of national contingency.In this regard, an important achievement has been the coverage of Dr. J. Ewer's work on the biological clock in newspapers, radio and television, as a result of the Government's decision to modify the daylight saving time system and its impact on the everyday day life of the Chileans, in particular on children. Another important achievement was the co-production together with others research centers of the TV program "From the atom to the cosmos", which disseminates the work of the main scientific centers of the country, showing some of our most relevant research and the impact it will have in the near future on the development of the country. Dr. Latorre presented the role of the CINV as a basic scientific center in Chile and in the regionalization of the country.In the process of disseminating science to the public in general, we also sought to show another side of our researchers, such as their personal interests and backgrounds.In addition to showing a greater diversity of CINV researchers, we have established some CINV scientist as references for current debates in the country where science can give a technical advice. For example, Dr. Whitlock has discussed the problems of education in Chile (as a result of her experience with the project "Ciencia al Tiro") and the role of women in science.Dr. Chavez provided a scientific perspectiveto the debate on the legalization of marijuana and Dr. Moya gave an overview on the complexities of depression and its treatments. The product of CINV outreach actions amounted to important number of articles in newspapers, appearances in radio, TV, and internet.

The most relevant 2016 CINV outreach activities were:

Tertulias Porteñas. Since 2012 we bring together high-level scientists, artists, and intellectuals, to discuss neuroscience-related topics with an interdisciplinary approach. Tertulias are open to the general public and their aim is to captivate the public with the creative inspiration that moves science, the humanities, and the art, with the ultimate goal of showing that science always leads us to unknown territories that are worth colonizing. The tertulias were held in emblematic places of Valparaíso. In 2015 and 2016, a partnership with the National Council of Arts and Culture allowed us to use the central hall of this institution, consolidating the alliance between science and culture that CINV has promoted since its beginnings. Tertulias in 2016 were moderated, as they were from 2011 to 2014, by the prominent Chilean writer andcommunicator, Cristián Warnken. This year, our young scientists have acted as panelists, helping them show their work to wider audiences. **2016 Tertulias: "**What do we know about the Cannabis?" Panelists: Andrés Chávez, CINV Neuroscientist; Anneliese Dörr, Psychologist; and Jorge Dahm, Lawyer and Minister of the Supreme Court."What do we know about happiness?": Panelists: Pablo Moya, CINV Neuroscientist; Ziley Mora Philosopher; Armando Roa, lawyer and translator of Shakespeare. Estimated audience: 250 people in each Tertulia. (cinv.uv.cl/tertulias-portenas/).

Falling Walls Chile: In partnership with the Fundación Ciencia Joven (Young Science Foundation), CINV brought the Falling Walls Lab contest to Chile for the first time. This

event seek to identify innovative young people in all areas of knowledge and its purpose was to select the Young innovator who should represent Chile at the global Falling Walls event in Germany where about 100 young people of all around the world will present their achievements.With the participation of the Minister of Economy, the 13 candidates selected for the final stage in Valparaiso, each had 3 minutes to present their innovative ideas.With important national press coverage, and the financial support of private companies, the CINV continues to position Valparaiso as a beacon of science in Chile(cinv.uv.cl/fwlab/).

"Que tienes mente" talks and lab visits: As it has done in the past, the CINV organized talks in different schools of Valparaiso, to bring science closer to children who do not normally know what scientists are doing. Four talks were held in 2016, with a total estimated audience of 270 students.This year the talks were directed to students interested in science and who need to choose their possible career the next two years (cinv.uv.cl/que-tienes-en-mente/). They included: "Brain Chemistry", Dr. A. M. Cárdenas, Quilpué; "Senses, our window to the world", Dr. O. Schmachtenberg, Quilpué; "From molecular randomness to the neural order", Dr. D. Naranjo, Valparaíso; "What do we know about our brain?", Dr. A. Chávez, Viña del Mar.This year, we also organized visits of students interested in science from Valparaíso and Santiago to the CINV laboratories. With participation of CINV faculty, PhD Students and Posdocs, the students heard scientific talks and received an explanation about the operation of the CINV laboratories. Total number of students: 100 over 4 visits.

Festival Puerto de Ideas: Valparaiso has been hosting *Puerto de Ideas*, the first festival in South America that "democratized" the access to cultural activities previously restricted to the academic and intellectual elites. The city of Antofagasta, on the other hand, hostsa *Puerto de Ideas*entirely dedicated to the dissemination of science. These Festivals summon prominent national and foreign speakers–ranging from scientists to all kinds of artists. CINV researchers Drs. K. Whitlock and A. Chávez participated in the*Puerto de Ideas*, Antofagasta.In addition, within the framework of the *Puerto de Ideas*Valparaíso, the CINV organized a meeting between the renowned neuroscientist, Semir Zeki, with artists and intellectuals from Valparaíso, seeking common points between science, humanities, and the arts (www.puertodeideas.cl).

Ciencia al Tiro (www.cienciaaltiro.cl).Program created in 2008 by the CINV researcher K. Whitlock, 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 Aquaponics system to study water pH and the nitrogen cycle. **Activities for 2016**:Ciencia al Tiro participated in Puerto Ideas Antofagasta 2016 through two workshops on solar energy led by Dr. Whitlock, based on the book "La alegría dela ciencia" ("The Joy of Science"), which was published in 2015 by this same program. The first one was aimed at students between 4th and 6thgrade from public schools in the Antofagasta region. The second workshop was aimed at children and families in general as part of the main program of the Puerto Ideas Festival(www.youtube.com/watch?v=K5wEM4zw7ew). Similar workshops were held in Antofagasta, and Santiago, due to the involvement of different schools and institutions. This year began the production of the video series "La alegría de la ciencia" based on the book of the Ciencia al Tiro program. It will be composed of 10 chapters of 5 minutes each,

and will be broadcast in 2017 by Novasur, CNTV's educational and cultural television network, and by VTR's "Vive Chile" network, ensuring nationwide coverage. Dr. Whitlock was also invited to participate in various activities aimed at promoting innovation in education like the UCN Diploma in Education, Creativity and Innovation, the II Congress of Education Kosmopolits, and at the InternationalFestival of Social Innovation.

Tunnel of Science: In October 2016, the University of Valparaíso, with the collaboration of the CINV, again brought the Science Tunnel to Valparaíso, Chile, a traveling exhibition of the Max Planck Society, which presents the main advances in all areas of science. During its 3 month visit (which includes the month of January 2016) the Tunnel of Science attracted almost 50 thousand visitors, aiding to position Valparaiso as a city of science. The exhibition also included the cooperation of the Max Planck Society in Latin America, highlighting the new Max Planck Research Groups in association with CINV.

Audiovisual Productions. Each year, the CINV develops or takes part in audiovisual products related to science outreach. In 2016 CINV, in partnership with Cábala Producciones, the CINV worked in a new audiovisual production aimed at internet and social networks that show the work of scientists and students of CINV. In addition, members of the CINV participated in the creation of the series "From the atom to the cosmos" transmitted by the news channel “24 Hours”, aimed at making public the work of the main scientific centers of the country. This year, we also began the recordings of the new production "Neuropolis", a scientific series set in Valparaiso that dynamically explains how our brain works. It will be presented in November 2017 on the National Television channel of Chile, with presence in Chile and abroad.

b) Connections with other sectors:

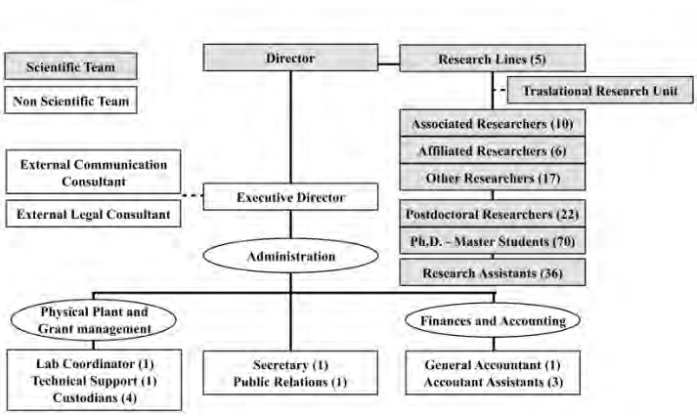
Juan Ignacio Molina Building (formerly Severín Building): A crucial step for the new CINV building in a historical district of Valparaíso was to obtain the additional funds (USD 3,000,000) needed tostart the bidding process for its construction. With the financial support of the Chilean Government, who will support 80% of the costs through national and regional funds (USD 8,800,000), and from the Universidad de Valparaíso, who will support the remaining 20% of the costs (USD 2,000,000), we estimate that the building will be in operation by the end of 2018. The building will be a reference in terms of its infrastructure and will greatly contribute to the revival of the historic district.

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

German Embassy: the CINV, as a result of the agreement signed with the Max Planck Society and the organization of events, such as the Falling Walls Lab, has become a bridge between Chile and Germany for scientific collaboration.In 2016 the CINV received in Valparaiso the President of the University of Göttingen, the Commission of Science and Technology of the German Parliament, the President of the DAAD, and the delegation of the universities of the State of Hessen.In this way the CINV is working in partnerships in conjunction with the University of Valparaiso, which allow the expansion of student training capabilities and scientific collaborations.

7. Administration and Financial Status

a) Organization and administration:



An Executive Director supervises and coordinates all the administrative duties according to the needs of the Director and of other Investigators. This includes managing the Millenium Institute Grant and all other grants of CINV researchers (around 17 grants per year). He also coordinates outreach and networking activities with the private sector and with community leaders, as well as all efforts related to the new building to house the CINV, and the communication strategy of the CINV. The team includes theAccounting Team, which manages the grants and human resources; a Physical Plant and Project Supportteam that assists in the purchase of equipment and computer maintenance, and supports the development and submission of grants; a public relations person who provides support for scientific (Symposia, Congress) and outreach activities.Each host institution provides office and laboratory space for the individual investigators holding faculty positions. The base salaryof individual investigators is covered 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	19	17	36
Administrative Staff	9	4	13
TOTAL	28	21	49

b) Financial Status:

During 2016 the CINV had a total income of CLP$1,685,693,787 (~USD$2.600.000), to which the Millennium Cientific Initiative (ICM) contributed 43%. Thecontribution of the ICMwas 7% for 2012, 35.4% for 2013, 42.0% for 2014, and44% for 2015. Other sources of income for the CINV come mainly from the University of Valparaiso (28% in 2016) and CONICYT (24% in 2016).

In relation to what was contributed by the ICM, the greatest share corresponds to the category "Responsible Researcher, Scientific and Additional Personnel", which amounts to 59%, mainly due to the incorporation of two Deputy Researchers and of their technical staff. Three Young Investigators were also incorporated; ICM also funded, for the second consecutive year, scholarships for 6 graduate students of the PhD in Biophysics and Computational Biology. There was also an increase in technical personnel for the different research lines.Another element worth mentioningare the changesinrank: during 2016 Dr. Agustín Martínez went from Adjunct Researcher to Associate Researcher, and Dr. Juan Carlos Sáez went from being Associate Researcher to Deputy Principal Researcher.

8. Annexes:

Annex 1.- Institute / Nucleus Researchers

1.1 Associate Researchers

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Adrián Palacios Vargas	System and circuits neuroscience.	Chilean	M	18-03-1958	Psychologist	D	Universidad de Valparaíso	Professor UV, CINV Researcher.	2
Agustín Martínez Carrasco	Cellular signaling.	Chilean	M	14-08-1968	Biologist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Alan Neely Delgueil	Structure and function of molecular sensors.	Chilean	M	15-04-1956	Biologist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Ana María Cárdenas Diaz	Cellular signaling.	Chilean	F	01-04-1969	Pharmacist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Carlos González León	Structure and function of molecular sensors.	Cuban	M	13-12-1965	Biophysicist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Fernando Danilo	Cross- cutting - computational	Chilean	M	9-12-1968	Chemist	D	Universidad Andrés Bello	Professor U. Andrés	2

González Nilo	biology							Bello, CINV Researcher	
John Ewer Lothian	Genetics and developmental neuroscience.	Chilean	M	23-02-1961	Biologist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Juan Carlos Sáez Carreño	Cellular signaling.	Chilean	M	02-02-1956	Biochemist	D	Pontificia Universidad Católica de Chile	Professor P. U. Católica de Chile, CINV Researcher	2
Kathleeen Whitlock Leaning	Genetics and developmental neuroscience.	US Citizen	F	27-08-1963	Biologist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Ramón Latorre De la Cruz	Structure and function of molecular sensors.	Chilean	M	29-10-1941	Biochemist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Tomás Pérez Acle	Cross- cutting - computational biology	Chilean	M	09-09-1970	Biologist	D	Fundación Ciencia & Vida	F. Ciencia & Vida and CINV Researcher	2

1.2 Young Researchers

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Alvaro Ardiles Araya	Cellular Signaling.	Chilean	M	12-02-1977	Biochemist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Chiayu Chiu	System and Circuits Neuroscience.	USA	F	21-03-1974	Neuroscientist	D	CINV	CINV Max Planck Tandem Research Leader	1
Helmuth Sanchez Riquelme	Cellular Signaling.	Chilean	M	19-06-1978	Biologist	D	CINV	CINV Young Researcher	1
José Antonio Gárate	Cross-Cutting - Computational biology	Chilean	M	29-07-1983	Molecular Biotechnology Engineer	D	Fundación Ciencia & Vida	Professor F. Ciencia &Vida, CINV Young Researcher	2

Karen Castillo Huera	Structure and Function of Molecular Sensors.	Chilean	F	23-07-1979	Biochemist	D	CINV	CINV Young Researcher	1

1.3 Senior Researchers

Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Alfredo Kirkwood	System and circuits neuroscience.	Chilean	M	05-03-1958	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	03-05-1962	Biophysicist	D	NIH-NINDS Molecular Neurophysiology section.	Senior Investigator	2

							Porter Neuroscience Research Center		
Osvaldo Alvarez	Structure and function of molecular sensors.	Chilean	M	19-19-1942	Biochemist	D	Universidad de Chile	Professor	2
Verónica Milessi	Structure and function of molecular sensors.	Argentinian	F	02-12-1962	Pharmacist	D	Universidad Nacional de LaPlata	Professor	2
Riccardo Olcese	Structure and function of molecular sensors.	Italian	M	26-5-1962	Physician	D	UCLA	Professor	2

1.4 *Others*

Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Andrea Calixto Mohor	Genetics and developmental neuroscience.	Chilean	F	04-09-1974	Biologist	D	Universidad Mayor	Professor UV, CINV Researcher	2
Andrés Chávez Navarrete	System and circuits neuroscience.	Chilean	M	10-01-1977	Biologist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
David Naranjo Donoso	Structure and function of molecular sensors.	Chilean	M	17-10-1957	Biologist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Patricio Orio Alvarez	Cross-cutting - Computational biology	Chilean	M	03-12-1973	Biochemist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Oliver Schmachtenberg	System and circuits neuroscience.	Chilean	M	12-12-1970	Biologist	D	Universidad de Valparaíso	Professor UV, CINV Researcher	2
Pablo Moya Vera	System and circuits neuroscience.	Chilean	M	09-09-1975	Biochemist	D	Universidad de Valparaíso	Profesor UV, CINV Researcher	2

Daniel Aguayo Villegas	Cross cutting – Computational biology	Chilean	M	08-08-1978	Biochemist	D	Universidad Andrés Bello	Professor U. Andrés Bello	2
Alberto Martin Martin	Cross-cutting - computational biology. Structure and function of molecular sensors.	Spanish	M	08-06-1980	Biologist	D	Fundación Ciencia & Vida	Postdoc	1
Alex Vielma Zamora **	System and circuits neuroscience.	Chilean	M	05-01-1979	Biochemist	D	Universidad de Valparaíso	Postdoc	1
Amauri Pupo Meriño	Structure and function of molecular sensors.	Cuban	M	05-08-1980	Biochemist	D	Universidad de Valparaíso	Postdoc	1
Angelina Palacios Muñoz	Genetics and developmental neuroscience.	Chilean	F	12-07-1981	Biochemist	D	Universidad de Valparaíso	Postdoc	1
Arlek González Jamett	Cellular signaling.	Chilean	F	11-07-1981	Biochemist	D	Universidad de Valparaíso	Postdoc	1
Audry Gómez Fernandez	Structure and function of molecular sensors.	Cuban	F	19-09-1981	Biochemist	D	Universidad de Valparaíso	Postdoc	1

Bruno Cisterna Irrazabal	Cellular signaling.	Chilean	M	13-11-1982	Medical Technologist	D	Universidad de Valparaíso	Postdoc	1
Carlos Puebla Aracena	Cellular signaling..	Chilean	M	04-07-1981	Biochemist	D	Pontifícia Universidad Católica de Chile	Postdoc	1
Carolina Soto Riveros	Cellular signaling.	Chilean	F	03-01-1979	Biochemist	D	Universidad de Valparaíso	Postdoc	1
Felipe Villanelo Lizana	Cross-cutting - Computational biology.	Chilean	M	16-05-1982	Biochemist	D	Fundación Ciencia & Vida	Postdoc	1
Germán Miño Galaz	Cross-cutting - Computational biology	Chilean	M	29-05-1971	Biochemist	D	Universidad Andrés Bello	Postdoc	1
Gustavo Contreras Cáceres	Structure and function of molecular sensors.	Chilean	M	15-09-1982	Bio-medical Engineer	D	Universidad de Valparaíso	Postdoc	1
Hans Moldenhauer Barrientos	Structure and function of molecular sensors.	Chilean	M	22-02-1983	Biochemist	D	Universidad de Valparaíso	Postdoc	1

Ignacio Díaz Franulic	Structure and function of molecular sensors. Cross-cutting - Computational biology.	Chilean	M	02-04-1981	Biochemist	D	Universidad Andrés Bello	Postdoc	1
Isaac García Carrillo	Structure and function of molecular sensors.	Chilean	M	20-04-1978	Medical Technologist	D	Universidad de Valparaíso	Postdoc	1
Javier Alvarez Zepeda	Genetics and developmental neuroscience.	Chilean	M	20-01-1971	Aquaculture Engineer	D	Universidad de Valparaíso	Postdoc	1
Justin Flaven Pouchon	Genetics and developmental neuroscience.	France	M	29-01-1971	Biologist	D	Universidad de Valparaíso	Postdoc	1
Karel Mena	Structure and function of molecular sensors.	Cuban	M	09-10-1975	Biologist	D	Universidad de Valparaíso	Postdoc	1
Kesheng Xu	Cross - cutting - Computational biology.	Chinese	M	02-10-193	Physical	D	Universidad de Valparaíso	Postdoc	1
Pavel Prado Gutierrez	Cellular signaling.	Cuban	M	22-03-1976	Biologist	D	Universidad de Valparaíso	Postdoc	1

Rosalba Escamilla Hernández	Cellular signaling.	Chilean	F	06-02-1971	Biochemist	D	Pontifícia Universidad Católica de Chile	Postdoc	1
Adam Aguirre Ducler	Cellular signaling.	Chilean	M	22-07-1967	Veterinary	D	Pontifícia Universidad Católica de Chile	Postdoc	1

** Postdoctoral fellow funded by CINV since Nov 2016

NOMENCLATURE:		
[Gender] [M] Male [F] Female	**[Academic Degree]** [U] Undergraduate [M] Master [D] Doctoral	**[Relation with Center]** [1] Full time [2] Part time

Annex 2.- Research Lines

Nº	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date
1	STRUCTURE ANDFUNCTION OF MOLECULAR SENSORS.	We try tounderstand howion channels andpumps canrespond to avariety of stimuli.	It is a combination of molecular biology, electrophysiology, modern fluorescence techniques, simulationsand molecular modeling.	R. Latorre,A. Neely, C. González, K. Castillo, O. Alvarez, F. Bezanilla,M. Holmgren,V. Milesi, G. Ferreira.	Physiology and biophysics	08-08-11	

2	CELLULAR SIGNALING.	Investigate howprotein-proteininteractions andcovalentmodifications ofdynamin controlneurosecretion and trafficking ofion channels.	Using patch clamp amperometry andtotal internal reflection fluorescence microscopy the handling by the cell ofvesicles containing neurotransmitters is characterized.	JC. Sáez, AM Cárdenas y A. Martínez, H Sanchez.	Cell biology.	08-08-11	
3	GENETICSAND DEVELOPMENTAL NEUROSCIENCE.	Understandinghow the nervoussystem developsand producescomplex behaviors.	Using zebrafish and Drosophila as biological models, the development of the olfactory system and the genetic pathways controlling behavior arestudied.	K. Whitlock, J. Ewer, Andrea Calixto.	Biology of development Genetics and evolution.	08-08-11	
4	SYSTEM AND CIRCUITS NEUROSCIENCE.	To investigate themechanisms ofneuronal encodingthe visual, olfactory andcerebral physiological andpathological 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, P Moya, A. Ardiles	Cell biologyPhysiology. Biophysics	08-08-11	
5	CROSS-CUTTING - COMPUTATIONAL BIOLOGY	Using highperformance computing formolecular modeling ofmembrane	Interaction between theoretical andexperimental biologist to create newmethods, models and hypothesissuitable	D. Naranjo F. González-Nilo, T. Pérez-Acle, P. Orio, J.A. Gárate, D. Aguayo, R Cabrera	Numerical methods and computation. Biophysics	08-08-11	

		proteins, drugdesign assisted bycomputer, andinference anddynamics ofbiological networks.	to be tested by theexperimental groups.				

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. *Aspé-Sánchez M, Moreno M, Rivera MI, Rossi A and **Ewer J**. (2016) "Oxytocin and vasopressin receptor gene polymorphisms: role in socialand psychiatric trait". Frontiers inNeuroscience28; 9:510. doi: 10.3389/fnins.2015.00510.*

2. *Calfún C, Domínguez C, **Pérez-Acle T**,**Whitlock KE**. (2016). "Changes in olfactory receptor expression are correlated with odor exposure during early development in the zebrafish (Danio rerio)". Chem Senses.1861 (5):439-48.*

3. ***Cárdenas AM**, **González-Jamett AM**, Cea LA, Bevilacqua JA, Caviedes P. (2016. "Dysferlin function in skeletal muscle: Possible pathological mechanisms and therapeutical targets in dysferlinopathies". Exp Neurol. 283(Pt A):246-254. doi: 10.1016/j.expneurol.2016.06.026.Review.*

4. ***Cárdenas AM**, Marengo F. (2016. "How the stimulus defines the dynamics of vesicle pool recruitment, fusion mode and vesicle recycling in neuroendocrine cells". J Neurochem. 137(6):867-79. doi: 10.1111/jnc.13565. Review*

5. *Castillo JP, Sánchez-Rodríguez JE, Clark Hyde H, Zaelzer CA, Aguayo D, Sepúlveda R, Luk LYP, Kent S,**Gonzalez-Nilo F**, **Bezanilla F,** and **Latorre R**. (2016."β1 Subunit-InducedStructuralRearrangements of the Ca^{2+} and Voltage-Activated K^{+} (BK) Channel". Proc. NatlAcadSci (USA).113(23):E3231-9. doi: 10.1073/pnas.1606381113.*

6. *Cea LA, Puebla C, Cisterna BA, **Escamilla R**, Vargas AA, Frank M, Martínez-Montero P, Prior C, Molano J, Esteban-Rodríguez I, Pascual I, Gallano P, Lorenzo G, Pian H, Barrio LC, Willecke K,**Sáez JC**. (2016). "Fast skeletal myofibers of mdx mouse, model of Duchenne muscular dystrophy, express connexinhemichannels that lead to apoptosis". Cell Mol LifeSci.73 (13):2583-99. doi: 10.1007/s00018-016-2132-2*

7. *Cea LA, Balboa E, Puebla C, Vargas AA, Cisterna BA, **Escamilla R**, Regueira T, **Sáez JC**. (2016). "Dexamethasone-induced muscular atrophy is mediated by functional expression of connexin-based hemichannels". BiochimBiophys Acta.1862 (10):1891-9. doi: 10.1016/j.bbadis.2016.07.003*

8. *Cea LA, Bevilacqua JA, Arriagada C,**Cárdenas AM**, Bigot A, Mouly V,**Sáez JC**, Caviedes P. (2016). "The absence of dysferlin induces the expression of functional connexin-based hemichannels in human myotubes". BMC Cell Biol. May 24; 17 Suppl 1:15. doi: 10.1186/s12860-016-0096-6.*

9. *Cisterna BA, Vargas AA, Puebla C,**Sáez JC**. (2016). "Connexinhemichannels explain the ionic imbalance and lead to atrophy in denervated skeletal muscles".Biochim Biophys Acta.1862(11):2168-2176. doi: 10.1016/j.bbadis .2016. 08.020*

10. *Diao, F., **Mena. W**., Shi, J., Park, D., Diao, F., Taghert, P.,**Ewer J**., and White, B.H. (2016). "Thesplice Isoforms of the Drosophila Ecdysis Triggering Hormone receptor have developmentally distinct roles". Genetics. 202(1):175-8.*

11. ***Diaz-Franulic I**, Caceres-Molina J, Sepúlveda RV, **Gonzalez-Nilo F**, and **Latorre R**(2016). "Structurally driven pharmacology of transient receptor potential vanilloid1 (TRPV1) channel".MolPharmacol Sep;90(3):300-8. doi: 10.1124/mol.116.10443.*

12. *Diaz-Franulic I, Poblete H, **Miño G**, **Gonzalez C**, and **Latorre R** (2016). "Allosterism and structure in thermally activated transient receptor potential channels". Ann. Rev. Biophys.45:371-98. doi: 10.1146/annurev-biophys-062215-011034.*

13. *Díaz J, Woudt L, Suazo L, Garrido C, Caviedes P,**Cárdenas AM**, Castiglioni C, Bevilacqua JA. (2016). "Broadening the Imaging Phenotype of Dysferlinopathy at Different Disease Stages". Muscle Nerve. 54(2):203-10. doi: 10.1002/mus.25045.*

14. *Escalona Y, **Garate JA**, Araya-Secchi R, Huynh T, Zhou R,**Pérez-Acle T**. (2016) "Exploring the membrane potential of simple dual-membrane systems as models for gap-junction channels". Biophys J. Jun 21,110(12):2678-88. doi: 10.1016/j.bpj.2016.05.005.*

15. *Fernández A, Pupo A, Mena-Ulecia K and **Gonzalez C**, (2016). "Pharmacological modulation of proton channel Hv1 in cancer therapy: Future perspectives". Mol Pharmacol Sep; 90(3):385-402. doi: 10.1124 /mol. 116. 103 804*

16. ***Flaven-Pouchon J**, Farine JP,**Ewer J**, Ferveur JF. (2016). "Regulation of cuticular hydrocarbon profile maturation by Drosophila tanning hormone, bursicon, and its interaction with desaturase activity". Insect Biochem Mol Biol. 79:87-96. doi: 10.1016/j.ibmb.2016.10.007.*

17. ***Garate JA*,*Pérez-Acle T***. *(2016). "From dimers to collective dipoles: Structure and dynamics of methanol/ethanol partition by narrow carbon nanotubes". J Chem Phys. 2016 Feb 14;144(6):064105*

18. ***García IE***, ***Prado P***, *Pupo A, Jara O, **Rojas-Gómez D**, Mujica P, Flores-Muñoz C, González-Casanova J, **Soto-Riveros** C, Pinto BI, Retamal MA,**Gonzalez C**and **Martinez AD**(2016). "Connexinopathies: a structural and functionalglimpse. BMC Cell Biology May 24; 17Suppl 1:17. doi: 10.1186/s12860-016-0092-x.*

19. ***García IE***, *Bosen F, Mujica P, Pupo A, Flores-Muñoz C, Jara O,**Gonzalez C**, Willecke K and **Martinez AD**(2016). "From Hyperactive Connexin26Hemichannels to impairments in epidermalcalcium gradient and permeability barrierin the keratitis-ichthyosis-deafnesssyndrome". J Invest Dermatol 136(3):574-83.*

20. *Graham Z, Collier L, QinW, Peng Y,**Sáez JC**, Bauman WA and Christopher Cardozo J. (2016). "A soluble activin receptor IIB fails to prevent muscle atrophy in a mouse model of spinal cord injury". J Neurotrauma. 33(12):1128-35. doi: 10.1089/neu.2015.4058*

21. *Krick S, Wang J, St-Pierre M,**Gonzalez C**, Dahl G, Salathe M. (2016). "Dual Oxidase 2 (Duox2) Regulates Pannexin 1-mediated ATP Release in Primary Human Airway Epithelial Cells via Changes in Intracellular pH and Not H_2O_2 Production". J Biol Chem. 291(12):6423-32. doi: 10.1074/jbc.M115.664854*

22. *Márquez-Miranda V, Peñaloza JP, Araya-Durán I, Reyes R, Vidaurre S, Romero V, Fuentes J, Céric F, Velásquez L,**Gonzalez-Nilo F**, Otero C. (2016) "Effect of Terminal Groups of Dendrimers in the Complexation with Antisense Oligonucleotides and Cell Uptake". Nanoscale Res Lett. 11(1):66. doi: 10.1186/s11671-016-1260-9*

23. *Márquez-Miranda V, Araya-Durán I, Camarada MB, Comer J, Valencia-Gallegos JA, **Gonzalez-Nilo F**. (2016). "Self-Assembly of Amphiphilic Dendrimers: The Role of Generation and Alkyl Chain Length in siRNA Interaction".Sci Rep. 2016 Jul 5; 6:29436. doi: 10.1038/srep29436.*

24. ***Martin AJ***, *Dominguez C, Contreras-Riquelme S, Holmes DS,**Pérez-Acle T**. (2016). "Graphlet Based Metrics for the Comparison of Gene Regulatory Networks". PLoS One. 11(10):e0163497. doi: 10.1371/journal.pone.0163497.*

25. *Martínez G, Vidal RL, Mardones P, Serrano FG, **Ardiles AO**, Wirth C, Valdés P, Thielen P, Schneider BK, Kerr B, Valdés JL,**Palacios AG**, Inestrosa NC, Glimcher LH, Hetz C. (2016). "Regulation of memory formation by the transcription factor XBP1". Cell-Report. 14(6):1382-94.*

26. *Mena W, Diegelmann S, Wegener C,**Ewer J**. (2016). "Stereotyped responses of Drosophila peptidergic neuronal ensemble depend on downstream neuromodulators. Elife. 2016 Dec 15; 5. pii: e19686. doi: 10.7554/eLife.19686.*

27. ***Moldenhauer H**, Díaz-Franulic I, **Gonzalez-Nilo F**,Naranjo D (2016)."Effective pore size and radius of capture for K^+ ions in K-channels". ScientificReports6:19893*

28. *Moya-Díaz J, Álvarez JD, Montenegro M, Bayonés L, Belingheri AV, **González-Jamett AM**,**Cárdenas AM**, Marengo FD (2016). "Sustained exocytosis after action potential-like stimulation at low frequencies in mouse chromaffin cells depends on a dynamin-dependent fast endocytotic process". Front Cell Neurosci. Jul 26; 10:184. doi: 10.3389/fncel.2016.00184*

29. *Pérez-Núñez R, Barraza N, **Gonzalez-Jamett A**,**Cárdenas AM**, Barnier JV, Caviedes P. (2016). "Overexpressed Down Syndrome Cell Adhesion Molecule (DSCAM) Deregulates P21-Activated Kinase (PAK) Activity in an In Vitro Neuronal Model of Down Syndrome: Consequences on Cell Process Formation and Extension".Neurotox Res.30 (1):76-87. doi: 10.1007/s12640-016-9613-9.*

30. *Pinto BI, **García IE**, Pupo A, Retamal MA, **Martinez AD**, **Latorre R**and**Gonzalez C** (2016) "Charged residues at the first transmembrane region contribute to the voltage dependence of connexins slow gate". J Biol Chem291 (30):15740-52. doi: 10.1074/jbc.M115.709402*

31. *Puebla C, Cisterna BA, Salas DP, Delgado-López F, Lampe PD,**Sáez JC**. (2016). "Linoleic acid permeabilizes gastric epithelial cells by increasing connexin 43 levels in the cell membrane via a GPR40- and Akt-dependent mechanism". BiochimBiophys Acta. 1861(5):439-48.*

32. *Qiu F, Chamberlin A, Watkins BM, Ionescu A, Perez ME, Barro-Soria R,**González C**, Noskov SY and Larsson HP (2016). "Molecular mechanism of Zn^{2+} inhibition of a voltage-gated proton channel". Proc Natl Acad Sci U S A. 113(40):E5962-E5971*

33. *Retamal MA, **García IE**, Pinto B, Pupo A, **Baez-Nieto D**, Stehberg J, Del Rio R,**Gonzalez C**. (2016). "Extracellularcysteine in connexins: role as redoxsensors". Front in Physiol Jan 28; 7:1. doi: 10.3389/fphys.2016.00001. e Collection 2016*

34. ***Sáez JC**. (2016). "Proceedings of the International Gap Junction Conference 2015". BMC Cell Biol. May 24; 17 Suppl 1:18. doi: 10.1186/s12860-016-0097-5*

35. *Salazar C, Valdivia G, **Ardiles AO**, **Ewer J**,**Palacios AG**. (2016). "Genetic variants associated with neurodegenerative Alzheimer disease in natural model". Biological Research. Special Issue. 26;49(1):14 doi: 10.1186/s40659-016-0072-9*

36. *Savalli N, Pantazis A, Sigg D, Weiss JN,**Neely A** and **Olcese R** (2016). "The α2δ-1 subunit remodels CaV1.2 voltage sensors and allows Ca^{2+} influx at physiological membrane potentials". J Gen Physiol. 148(2):147-59. doi: 10.1085/jgp.201611586.*

37. *Sepúlveda-Crespo D, Vacas-Córdoba E, Márquez-Miranda V, Araya-Durán I, Gómez R, Mata FJ, **Gonzalez-Nilo FD**, Muñoz-Fernández MÁ. (2016). "Effect of Several HIV Antigens Simultaneously Loaded with G2-NN16 Carbosilane Dendrimer in the Cell Uptake and Functionality of Human Dendritic Cells". Dec 21; 27(12):2844-2849. doi: 10.1021/acs.bioconjchem.6b00623.*

38. *Wang H, **Ardiles A**, Yang S, Valdivia G, Baek M, Tran T, Posada-Duque R, Chuang YA, **Palacios AG**, Gallagher M, Worley P, Kirkwood A. (2016). "Metabotropic Glutamate Receptors Induce a Form of LTP Controlled by Translation and Arc Signaling in the hippocampus". Journalof Neuroscience 3; 36(5):1723-9.*

viii) 3.1.2 Other researchers:

1. *Bousquet F, Chauvel I, **Flaven-Pouchon J**, Farine JP, Ferveur JF. (2016) "Dietary rescue of altered metabolism gene reveals unexpected Drosophila mating cues". J Lipid Res. 2016 Mar; 57(3):443-50. doi: 10.1194/jlr.M064683.*

2. *Chetty S, Bhakat S, **Martin AJ,** Soliman ME. (2016). "Multi-drug resistance profile of PR20 HIV-1 protease is attributed to distorted conformational and drug binding landscape: molecular dynamics insights. J Biomol Struct Dyn. 2016 Jan; 34(1):135-51.*

3. *English NJ and **Garate JA** (2016). "Near-microsecond human aquaporin 4 gating dynamics in static and alternating external electric elds: Non-equilibrium molecular dynamics. J Chem Phys. 145(8):085102. doi: 10.1063/1.4961072*

4. *Lions S, Peña M (2016). "Reading Comprehension in Latin America: Difficulties and Possible Interventions". New Dir Child Adolesc Dev. 2016(152):71-84. doi: 10.1002/cad.20158*

5. *Marracino P, Liberti M, Trapani E, Burnham CJ, Avena M, **Garate JA**, Apollonio F, English NJ. (2016). "Human Aquaporin 4 Gating Dynamics under*

Perpendicularly-Oriented Electric-Field Impulses": A Molecular Dynamics Study. Int J Mol Sci. 2016 Jul 14; 17(7). pii: E1133. doi: 10.3390/ijms17071133.

6. *Muñoz P, Estay C, Díaz P, Elgueta C,* ***Ardiles ÁO****, Lizana PA (2016). "Inhibition of DNA Methylation Impairs Synaptic Plasticity during an Early Time Window in Rats Neural Plast. 2016:4783836. doi: 10.1155/2016/4783836.*

7. ***Naranjo D****,* ***Moldenhauer H****, Pincuntureo M and* ***Díaz-Franulic I*** *(2016). "Pore size matters for potassium channel conductance". J. Gen. Physiol.148 (4):277-91. doi: 10.1085/jgp.201611625.*

8. *Park J,****Chávez AE****, Mineur YS, Morimoto-Tomita M, Lutzu S, Kim KS, Picciotto MR, Castillo PE, Tomita S. (2016). "CaMKII Phosphorylation of TARPγ-8 Is a Mediator of LTP and Learning and Memory". Neuron. 92(1):75-83. doi: 10.1016/j.neuron.2016.09.002*

9. *Valdés J, Trachsel-Moncho L, Sahaboglu A, Trifunovic D, Miranda M, Ueffing M, Paquet-Durand F,* ***Schmachtenberg O****(2016). "Organotypic retinal explant cultures as in vitro alternative for diabetic retinopathy studies. ALTEX. 33(4):459-464. doi: 10.14573/altex.1603111.*

10. ***Vielma, A.H****. and* ***Schmachtenberg O****. (2016). "Electrophysiological fingerprints of OFF bipolar cells in rat retina". Sci. Rep., Jul 26; 6:30259. doi: 10.1038/srep30259.*

3.2. - SCIELO Publications or Similar to SCIELO

NONE

3.3.- Scientific Books and Chapters

ix) 3.3.1 Associate Researchers:

1. ***MartínezAD****, JaraO, CerianiR, MaripillánJ, MujicaP,* ***GarcíaIE*** *(2016). "Methods to determinate formation of heteromerichemichannels. Chapter in: Gap Junction and Pannexin Channels,A Volume in the Methods in Signal Transduction Series". Bai D. and Sáez J.C. Eds. CRC Press, P239-252. Book Chapter*

3.4.- Other Publications

x) 3.2.1 Associate Researchers:

1. ***Ewer J.*** *(2016) Como elegir un horario para Chile. Anales Museo de Historia Natural de Valparaíso. Volumen 29, páginas 9-13.*

xi) 3.2.2 Other researchers:

1. ***Chávez Andrés E****. (2016) ¿Cómo afecta el color al comportamiento?: Una mirada a la visón ultravioleta en mamíferos. Anales Museo de Historia Natural de Valparaíso. Volumen 29, páginas 21-24.*

2. ***Moya Vera PR****. (2016). "Interacciones genético-ambientales en el comportamiento". Anales Museo de Historia Natural de Valparaíso. Volumen 29, páginas 28-32.*

3. *Olivares J. (2016). "Reseña bibliográfica sobre la araña de rincón (LoxoscelesLaeta, Fam. Sicariirae): Que sabemos y que necesitamos saber". Anales Museo de Historia Natural de Valparaíso. Volumen 29, páginas 53-56.*

3.5. - Collaborative publications:

Category of Publication	1 researcher		2 researchers		3 researchers		4 or more researchers	
	Nº	**%**	**Nº**	**%**	**Nº**	**%**	**Nº**	**%**
ISI Publications or Similar to ISI Standard	21	39.62 %	16	30.19%	8	15.09%	2	3.77%
SCIELO Publications or Similar to SCIELO Standard	0	0.00%	0	0.00%	0	0.00%	0	0.00%
Books and chapters	0	0.00%	1	1.89%	0	0.00%	0	0.00%
Other Publications	3	5.66%	0	0.00%	0	0.00%	0	0.00%
Total of publications	**24**	**45.28%**	**17**	**32.08%**	**8**	**15.09%**	**2**	**3.77%**

Not included in this table are 2 papers authored by students by themself (1) or with non CINV investigator (1).

3.6 Patents

NONE

Annex 4.- Organization of Scientific Events

Scope	Title	Type of Event	City	Country	Responsible Researcher
International	International Symposiun Biology of Neuropsychiatric Disorders	Symposium	Valparaíso	Chile	Andrés Chávez
International	Small Brains Big Ideas	Symposium	Valparaíso	Chile	John Ewer Lothian
National	CINV Meeting 201	Symposium	Valparaíso	Chile	Ramón Latorre

Annex 5.- Education and capacity building

5.1. Capacity Building inside MSI Centers

MSI RESEARCHER	NUMBER												TOTAL NUMBER PER MSI RESEARCHER		
	Undergraduate students			Graduate students						Postdoctoral researchers					
				Masters			Doctoral								
	F	M	T	F	M	T	F	M	T	F	M	T	F	M	T
Fernando González	0	0	**0**	0	1	**1**	2	0	**2**	0	2	**2**	2	3	**5**
Carlos González	0	1	**1**	0	0	**0**	0	3	**3**	1	4	**5**	1	8	**9**
Alan Neely	0	0	**0**	1	0	**1**	1	0	**1**	0	0	**0**	2	0	**2**
Juan Carlos Sáez	1	0	**1**	0	0	**0**	4	3	**7**	1	3	**4**	6	6	**12**
Patricio Orio	1	0	**1**	0	0	**0**	0	5	**5**	0	1	**1**	1	6	**7**

Oliver Schmachtenberg	4	0	**4**	0	1	**1**	0	2	**2**	0	1	**1**	4	4	**8**
Adrián Palacios	0	1	**1**	1	2	**3**	0	2	**2**	0	0	**0**	1	4	**5**
Tomás Pérez Acle	0	1	**1**	0	2	**2**	1	5	**6**	0	2	**2**	1	10	**11**
Ramón Latorre	0	1	**1**	0	0	**0**	2	2	**4**	0	0	**0**	2	3	**5**
David Naranjo	0	0	**0**	0	0	**0**	0	2	**2**	0	1	**1**	0	3	**3**
Ana María Cárdenas	1	0	**1**	4	0	**4**	1	1	**2**	1	0	**1**	7	1	**8**
Kathleen Whitlock	0	0	**0**	0	0	**0**	2	3	**5**	0	0	**0**	2	3	**5**
Agustín Martínez	1	3	**4**	3	3	**6**	0	1	**1**	1	1	**2**	5	8	**13**
John Ewer	0	0	**0**	0	1	**1**	0	1	**1**	1	2	**3**	1	4	**5**
Andrés Chávez	0	1	**1**	1	1	**2**	0	0	**0**	0	0	**0**	1	2	**3**
Pablo Moya	0	0	**0**	0	1	**1**	0	1	**1**	0	0	**0**	0	2	**2**
Alvaro Ardiles	0	1	**1**	0	1	**1**	0	0	**0**	0	0	**0**	0	2	**2**
Andrea Calixto	0	1	**1**	0	1	**1**	3	0	**3**	0	0	**0**	3	2	**5**
TOTAL	8	10	**18**	10	14	**24**	16	31	**47**	5	17	**22**	39	71	**110**

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

i. Traineeships internal

Student Name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Daniela De Giorgis Oliva	UCLA School of Medicine	USA	Riccardo Olcese	To perfect her skill in voltage-clamp fluorometry and learn more about how the contribution of the voltage-sensing domain to the opening of calcium channels is modulated by regulatory subunits.	01-02-2016	31-03-2016
César Ravello Serrano	CNRS Marseille	France	Adrián Palacios	To develop new natural stimuli (Motion Cloud) to be applied to the retina to compute the spatial and temporal proprieties of receptive field of retinal ganglion cells	15-11-2016	15-12-2016
Jaime Maripillán Sobarzo	Rutgers University	USA	Jorge Contreras	To learn 2-electrode voltage clamp	20-08-2015	20-02-2016
Mauricio Caneo Contreras	Max Planck Institute	Germany	Teymuras Kurzchalia	To use mass spectrometry to identify components that are present in the good versus the bad quality diets. This work complemented our experiments aimed at evaluating morphological and functional protection of neurons in vivo.	28-06-2016	28-09-2016
Alejandro Bernardín Sepúlveda	Mcmaster University	Canada	Jonathan Dushoff	Establish a collaboration with Professor Dushoff for the use of the PISKA tool in infectious disease modeling	28-12-2015	31-03-2016

ii. Traineeships external

Student name	Destination Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Ana Aquiles Reyes	Universidad de Valparaíso	Mexico	Patricio Orio	Lab internship with Dr Patricio Orio	12-12-2016	31-12-2016
Albert Pahissa Gallego	Universidad de Valparaíso	Spain	Agustín Martinez	Lab internship with Dr. Agustín Martínez	01-03-2016	31-08-2016

Annex 6.- Networking and other collaborative work

6.1 Networking

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

Network Name	Network Scope	Researchers				Institutions
		From the Center		External		
		Researchers	Postdocs / Students	Researchers	Postdocs / Students	
Genetic and Develpment Network	I	3	0	0	19	Universidad de Valparaíso, Universidad Católica de Chile, Center for Mathematical Modeling-CMM (Chile), Universidad Andrés Bello, CINV, University College London (UK), Universidad Mayor

Biophysics and Computational Neurosciences Network	I	7	10	32	46	Max Planck Institute Germany, Institut National de Recherche en Informatique et en Automatique-INRIA (France), UTFSM (Chile), Center for Mathematical Modeling-CMM (Chile), Universidad de Valparaíso, Universidad Católica de Chile, Universidad Andrés Bello, CINV

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	
Coupling of circadian clock	University of Würzburg, Germany	1	4	1	1	1, ISI publication
Mechanism of neuropeptide action	NIH, USA	1	1	1	1	1, ISI publication
Proposal of model for cellular and physiological bases of KID disease	LIMES, University of Bonn	2	5	1	1	1, ISI publication
Molecular Basis of Excitability and Neuronal Homeostasis.	University of Chicago and NINDS (National Institute of Neurological Disorders and Stroke) of (NIH), USA.	2	3	2	2	

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
Seminars of CINV				
"Aberrant Cx26 hemichannels and keratitis-ichthyosis-deafness syndrome" Helmuth A. Sánchez R. Ph.D. Associate, Dominick P. Purpura Department of Neurosciences, Albert Einstein College of Medicine, Bronx, NY	Seminar	01-04-2016	Valparaíso	University of Valparaíso community
"Multiple task-dependent asynchronous hierarchies within the visual brain's parallel processing systems" Dr. Semir Seki, Wellcome Laboratory of Neurobiology, U. College of London.	Seminar	07-04-2016	Valparaíso	University of Valparaíso community
"Genetic dissection of retinal growth in zebrafish: moving forward in revers" Leonardo Valdivia, PhD. Department of Cell and Developmental Biology. U. College London.	Seminar	06-05-2016	Valparaíso	University of Valparaíso community
"Contralateral targeting of the corpus callosum" Laura Fenlon, Queensland Brain Institute, The U. of Queensland	Seminar	11-05-2016	Valparaíso	University of Valparaíso community
"Evolution and develpment of	Seminar	13-05-2016	Valparaíso	University of Valparaíso

neocortical circuits" *D*r. Rodrigo Suárez (Max Planck Leader), Queensland Brain Institute, The U. of Queensland				community
"Obesidad materna y su impacto en la función reproductiva y metabólica de la descendencia" Gonzalo Cruz, PhD, Laboratorio de alteraciones reproductivas y metabólicas CNPC, Instituto de Fisiología, U. de Valparaíso	Seminar	10-06-2016	Valparaíso	University of Valparaíso community
"Control de reaciones químicas con óptica cuántica" Dr. Felipe Herrera. Department of Physics, U. de Santiago de Chile	Seminar	15-07-2016	Valparaíso	University of Valparaíso community
"Study of monocarboxylate transporters in Drosophila, toward the establishment of an in vivo model for the analysis of brain metabolism" Dra. Jimena Sierralta. Profesor Asociado, Programa de Fisiología y Biofísica ICBM, Facultad de Medicina, U. de Chile.	Seminar	12-08-2016	Valparaíso	University of Valparaíso community
"Canales iónicos y la regulación del metabolismo en músculo esquelético" Dr. Enrique Jaimovich. Profesor Titular, Centro de Estudios Moleculares de la célula, Facultad de Medicina, U. de Chile.	Seminar	19-08-2016	Valparaíso	University of Valparaíso community
"Comunicación en la Ezquizofrenia" Dra. María Francisca Alonso, del	Seminar	26-08-2016	Valparaíso	University of Valparaíso Community

Programa de Fonoaudiología de la Universidad de Valparaíso, y académica de la Facultad de Medicina de la U. Santo Tomás.				
"The endoplasmic reticulum and protein trafficking in axons" Dr. Andrés Couve, del Programa de Fisiología y Biofísica, Institudo de Ciencias Biomédicas (ICBM), Instituro de Neurociencias Biomédicas (BNI), Facultad de Medicina, U. de Chile.	Seminario	27-09-2016	Valparaíso	University of Valparaíso Community
"Papel del las cisteinas intra y extracelulares de la Cx46 como sensores de los cambios en el potencial redox" Dr. Mauricio Retamal, del Centro de Fisiología Celular e Integrativa, de la Facultad de Medicina, U. del Desarrollo	Seminar	30-09-2016	Valparaíso	University of Valparaíso Community
"Relojes circadianos, optogenética y biología sintética en modelos fúngicos: desafiando los conceptos de visión y memoria" Luis F. Larrondo Ph.D. Associate Professor. Departamento de Genética Molecular y Microbiología. Director of MN-FISB (Millennium Nucleus for Fungal Integrative and Synthetic Biology). Facultad de Ciencias Biológicas. Pontificia U. Católica de Chile	Seminar	14-10-2016	Valparaíso	University of Valparaíso Community
"Alimentos y nutrición para una vida	Seminar	04-11-2016	Valparaíso	University of Valparaíso

sana y un planeta saludable" Dr. Ricardo Uauy. profesor del INTA de la U de Chile y de la Facultad de Medicina, PUC.				Community
"Calcium Signaling, Cellular Oxidative Tone and Synaptic Plasticity" Cecilia Hidalgo. Biomedical Neuroscience Institute, CEMC & Physiology and Biophysics Program, ICBM, Facultad de Medicina, U. de Chile.	Seminar	18-11-2016	Valparaíso	University of Valparaíso Community
"Receptor de tipo II de BMPs en diferenciación morfológica en motoneuronas: un caso de serendipia" Nelson Osses. Laboratorio de Química Biológica, Pontificia U. Católica de Valparaíso	Seminar	25-11-2016	Valparaíso	University of Valparaíso Community
"Ca2+ transfer from endoplasmic reticulum to mitochondria; an unexpected vulnerability of cancer cells." Dr. Julio César Cárdenas. Geroscience Center for Brain Health and Metabolism. Instituto de Ciencias Biomédicas, U. de Chile. Buck Institute for Research in aging.	Seminar	12-12-2016	Valparaíso	University of Valparaíso Community
"Human-Aquaporin 4: is there a voltage-regulated gating?" José Antonio Gárate. Fundación Ciencia & Vida Researcher and CINV Young Researcher	Seminar	23-12-2016	Valparaíso	University of Valparaíso Community

Tertulias Porteñas				
¿Que sabemos de la Cannabis? Andrés Chávez, CINV Researcher	"Fireside Chat"	28-06-2016	Valparaíso	Valparaíso Community
¿Que sabemos de la Felicidad? Pablo Moya, CINV Researcher	"Fireside Chat"	27-9-2016	Valparaíso	Valparaíso Community
¿Qué Tienes en Mente?				
"La química del cerebro" A. M. Cárdenas, CINV Researcher	Seminar	17-05-2016	Quilpué	High School Students
"Los sentidos, nuestra ventana al mundo" O. Schmachtenberg, CINV Researcher	Seminar	09-08-2016	Quilpué	High School Students
"Desde el azar molecular al orden neuronal" D. Naranjo, CINV Researcher	Seminar	11-10-2016	Valparaíso	High School Students
"¿Qué sabemos sobre nuestro cerebro?" A. Chávez, CINV Researcher	Seminar	3-11-2016	Viña del Mar	High School Students
Falling Walls Lab				
Falling Walls Lab Valparaíso 13 talks of pre-selected Chilean candidates	Conference	22-09-2016	Valparaíso	General Community Universitary Students

7.2.- Products of outreach

Product Type	Quantity	Target audience	Scope
Video Recording Tertulias Porteñas	*2*	General Community	National
Video Recording Falling Walls Lab	15	General Community	International

7.3.- Articles and Interviews

Type of media and scope	Local/Regional		National		International		
	N° Interviews	N° Articles	N° Interviews	N° Articles	N° Interviews	N° Articles	**TOTAL**
Written	4	17	0	43	1	0	**65**
Internet	0	0	1	42	0	1	**44**
Audiovisual	1	0	2	3	1	0	**7**
TOTAL	**5**	**17**	**3**	**88**	**2**	**1**	**116**

Annex 8.- Connections with other sectors

Activity and Objective	Expected Impact	Obtained Results	Type of Connection [Number]	Type of Activity [Number]	Institution Name	Institution City, Región & Country	Agent Type [Number]	Economic Sector
Construction of the new CINV Building in Valparaíso		Funds for CINV building	2	7 (Building scientific and outreach infrastructure)	Chile	Valparaíso, Chile	2	Government
Fundación Puerto Ideas Scientific Committee		Talks to the general public on recent scientific discoveries	2	7 (Puerto Ideas Festival)	Chile	Valparaíso Antofagasta	2	Business activities
Falling Walls Lab		Promote innovation among young scientists in Chile	2	7	Chile	Valparaíso, Chile	2	Other
Reception of German Academic and Government Institutions		Explore the options for collaborations between Chile and Germany	2	4	Chile	Valparaíso, Chile	2	Other

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

9. Total incomes:

Funds	Accumulated incomes to last year [CLP$]	2016 Incomes		Total incomes to 2016 [CLP$]
		Amount [CLP$]	Percentage of resources used by the Center [%]	
ICM (CINV, Redes y PME)	4.102.818.000	723.633.751	101%	723.633.751
CONICYT (Anillo, Mincyt, Explora, Redes)	1.808.824.174	403.247.687	93%	403.247.687
Universidad de Valparaíso (Department, Research Direction)	2.150.776.299	469.543.529	100%	469.543.529
CINV Corporation	39.681.215	21.968.350	85%	21.968.350
CNTV, FNDR	51.530.500	0	0%	0
Others funds	172.609.333	67.300.470	59%	67.300.470
TOTAL	**8.326.239.521**	**1.685.693.787**		**1.685.693.787**

9.1 Exchange

Type of researcher	Name	Type of activity	Length of stay	Destination Country	Financial entity (Millenmium/External/ Multiple sources)
Associate	Ramón Latorre	60th Annual Meeting Biophysical Society	6 days	USA	Multiple sources
Associate	John Ewer	XII Congress International Society for Neuroethology	5 days	Uruguay	External
Associate	John Ewer	15th Biennial Meeting Society for Research on Biological Rhytms SRBR 2016	10 days	USA	External
Adjunct	Patricio Orio	Conference in Mathematical Neuroscience y trabajo colaborativo INRIA	11 days	France	Multiple sources
Associate	Ramón Latorre	Ion Channels Gordon Research Conferencia	10 days	USA	External
Associate	John Ewer	Seminar in Universidad de Sao Paulo	3 days	Brazil	External
Associate	Ramón Latorre	2nd FALAN Congress 2016	4 days	Argentina	External
Associate	John Ewer	XXV International Congress of Entomology	6 days	USA	External
Associate	Agustín Martínez	2nd FALAN Congress 2016	5 days	Argentina	External
Adjunct	Oliver Shcmachtenberg	2nd FALAN Congress 2016	5 days	Argentina	Multiple sources
Adjunct	Andrés Chávez	2nd FALAN	6 days	Argentina	External

		Congress 2016			
Adjunct	Patricio Orio	2nd FALAN Congress 2016	5 days	Argentina	Multiple sources
Associate	Alan Neely	III Latin American Federation of Biophysical Socities, IX IberoAmerican Congress of Biophysics XLV Reunión Anual SAB 2016	5 days	Argentina	External
Associate	Ramón Latorre	Congreso Sociedad de Biofísica, III LAFeBS, IX beroAmerican Congress of Biophysics XLV Reunión Anual SAB 2016	5 days	Argentina	External
Associate	Ramón Latorre	Scientific exchange in the field of Cancer, and signing of collaboration agreements with the Centro Nacional de Cirugía de Mínimo Acceso.	10 days	Cuba	Millennium
Associate	Carlos González	Scientific exchange in the field of Cancer, and signing of collaboration agreements with the Centro Nacional de Cirugía de Mínimo Acceso.	10 days	Cuba	Millennium
Associate	Ramón Latorre	Biophysical Society 2017, Annual Meeting	8 days	USA	External
Associate	Ana M Cárdenas	2nd FALAN Congress 2016	5 days	Argentina	External
Associate	Adrián Palacios	2nd FALAN Congress 2016	5 days	Argentina	External

Adjunct	Andrea Calixto	International Society for Computational Biology Latin America Bioinformatics Conference	3 days	Argentina	External
Associate	Juan Carlos Sáez	Second Latin America Chapter Conference of the Cell Stress Society International	3 days	Colombia	External
Associate	Tomás Pérez-Acle	III LAFEBS / IX IberoAmerican Congress of Biophysics / XLV Reunión Anual SAB 2016	5 days	Argentina	Extrernal
Associate	Fernando Danilo González Nilo	60th Annual Meeting Biophysical Society	6 days	USA	External
Adjunct	Pablo Moya	XXIV World congress of Psychiatric Genetic	5 days	Israel	External
Adjunct	Pablo Moya	2nd International Conference on Epilepsy and treatment	2 days	Italy	External
Adjunct	Pablo Moya	Seminar in European Brain Research Institute	1 day	Italy	External
Adjunct	Pablo Moya	Seminar in Institute di Ricerche Farmacologiche Mario Negri	1 day	Italy	External

Researcher Name	**Nationality**	**Type of activity**	**Length of stay**	**Country of origin**	**Financial entity (Millenmium/ External/Multiple sources)**
Semir Zeki	Turkey	Seminar	11 days	England	Multiple sources

Rodrigo Suarez	Chilean	Seminar	2 days	Australia	External
Laura Fenlon	US Citizen	Seminar	2 days	USA	External
Julio Cesar Cárdenas	Chilean	Seminar	3 days	USA	External
Helmuth Sánchez	Chilean	Seminar	4 days	USA	External
Leonardo Valdivia	Chilean	Seminar	2 days	USA	External
Teymuras Kurzchalia	Georgia	Symposium Small Brain Big Ideas	2 days	Germany	Mixed
Marek Mlodzik	Chzec	Symposium Small Brain Big Ideas	2 days	USA	Multiple sources
Claire Benard	Canadian	Symposium Small Brain Big Ideas	2 days	USA	Multiple sources
Brian Smith	US Citizen	Symposium Small Brain Big Ideas	2 days	USA	Multiple sources
Geraldine Wright	US Citizen	Symposium Small Brain Big Ideas	2 days	United Kingdom	Multiple sources
Mark Alkema	Duth	Symposium Small Brain Big Ideas	2 days	USA	Multiple sources
Patrick Emery	Swiss	Symposium Small Brain Big Ideas	2 days	USA	Multiple sources
Carolina Rezaval	Argentina	Symposium Small Brain Big Ideas	2 days	United Kingdom	Multiple sources
Ulrike Heberlein	Chilean	Symposium Small Brain Big Ideas	2 days	USA	Multiple sources
Scott Waddell	English	Symposium Small Brain Big Ideas	2 days	United Kingdom	Multiple sources