CINV ANNUAL PROGRESS REPORT – 2017

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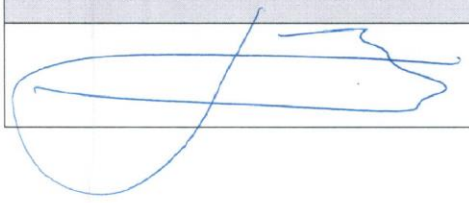	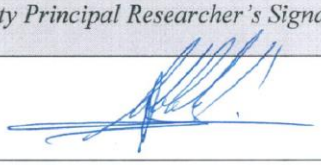

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1.1 Executive Summary

The Centro Interdisciplinario de Neurociencia de Valparaiso (CINV) deals with several aspects of a fundamental scientific question: ***How does the Nervous System respond to Stimuli in Health and Disease?*** We address this question along five research lines: *a) Function of Molecular Sensors. b) Cellular Signaling. c) Genetic and Developmental Neuroscience. d) System and Circuits Neuroscience.* e) *Cross-cutting: Bioinformatics and Computational Biology*. In 2017, the *Translational Research unit* was implemented to facilitate the creation of translational projects. **Scientific productivity and collaborative work.** This year we produced 53 publications. This is the same number as we published last year, but in this case we improved their average impact factor (IF) (2017: 4.8 vs 2016: 4.5). Four papers were published in journals with IF >12, two of which were led by CINV members (*Nature Communications* from Ewer´s Lab, and *Physiological Review*s from Latorre's Lab). In addition, a total of 5 articles appeared in well-positioned journals (e.g., *Journal of Neuroscience, Glia, Science Signaling and mBio*). Forty eight students co-authored 26 articles published in 2017 and were the first author in 8 of them. Moreover, Dr. Angélica Escobar, one of our postdoctoral recruits during 2017, was selected to contribute a commentary in the highly competitive Journal Club of the *Journal of Neuroscience* (Escobar A. 2017. *J. Neurosci*). Among the scientific contributions, we can highlight three of them. The first, spearheaded by our first graduate from the PhD Program in Biophysics and Computational Biology (Pinto BI et al, 2017. *Sci Rep* **7**:15851), proposes a novel allosteric model to explain the modulatory effects of Ca^{2+} and voltage in connexin hemichannels. A second breakthrough is the demonstration of localized protein translation in the axon, accomplished by taking advantage of the large axon size of the Humboldt squid found in the coast of Valparaiso (Mathur C et al. 2018, *Sci Rep* 8:2207). Lastly, the coordination between central and peripheral pacemakers is known to be essential for the function of circadian clocks, but little is still known about the mechanism involved in such coordination. In a *Nature Communication* paper, we show that in *Drosophila*, the ticking of the central clock is transmitted via a specific neuropeptide, sNPF, to non-clock neurons that then release another neuropeptide (PTTH) that feeds forward onto steroid hormone-producing cells in the prothoracic gland. This coupling between two clocks could serve as a paradigm to understand how daily rhythms in steroid hormone are generated in animals. **Strengthening and renovation of our faculty.** In 2016, Dr Juan C. Sáez became Deputy Director of the CINV and this year (2017) the Universidad de Valparaíso (UV) offered him a Full Professorship, effective starting during the first semester of 2018, and once his laboratory is ready. His incorporation into the CINV as an in-house member will strengthen the *Cellular Signaling* line of research, allowing the CINV to strengthen its leadership in the field of gap-junction channels and hemichannels formed by connexins and pannexins. To fulfill our plans to recruit an outstanding senior researcher, the UV and CINV sustained conversations with Dr Francisco Bezanilla, Lillian Eichelberger Cannon Professor in the Department of Biochemistry and Molecular Biology in the University of Chicago and member of the National Academy of Sciences, USA. Dr. Bezanilla is a leading figure in the field of biophysics of ion channels and transport proteins as well as a long-standing collaborator of the CINV. As a result of those conversations, Dr. Bezanilla will be a part-time member of CINV (6 months per year) starting in 2018 and he will become an Honorary Professor at the Universidad de Valparaíso. Last year we have acquired a two-photon microscope, with CINV and CONICYT funds, ,a critical equipment for the research of Dr. Chiu,

our CINV-Max Planck Tandem Group Leader, Also, in 2017 our Young Investigators have been successful in obtaining research funds through FONDECYT grants. Young Investigators, García and Garate, became associate professors at the UV through the CONICYT Advanced Human Capital (AHC) program, a highly competitive award that secures funds for salary, supplies, and small equipment for a 3-year period. **Advanced training.** We continue to actively participate in the PhD and Masters Programs in Neuroscience of the Universidad de Valparaíso, which continues to attract students from Chile and abroad. This year, 9 students were admitted to the PhD Program in Neuroscience for the 2018 academic year, one of the highest numbers to date. Last year this program was re-accredited for a record 7 years by the national accreditation agency (CNA). The Masters Program in Neuroscience have graduated 11 students of which six did their thesis in laboratories of the CINV. Also last year, 8 students associated with CINV labs approved their Master thesis project, which corresponds to 73% of all thesis projects of this Program. The PhD program in Biophysics and Computational Biology had 10 regular students during 2017, four of which were carrying out thesis, and one of which graduated (B. Pinto), becoming our first graduate of this Program. **Networking.** During 2017, the CINV organized important international meetings, strengthening existing collaborations. The highlight of the year was the Latin American Symposium on Chronobiology (LASC), which is organized every 2 years in a different Latin American country and was held for the first time in Chile (Valparaíso; November 2-7, 2017). The leading organizer was Dr. John Ewer. An important highlight was the participation of Dr. Michael Rosbash (Brandeis Univ., USA), co-recipient of the 2017 Nobel Prize in Physiology or Medicine for his work on the circadian clock of *Drosophila*. As part of our network in Biophysics and Computational Neuroscience, we carried out the 4th Latin-American Summer School in Computational Neuroscience (LACONEU) in January 2017. From November 20 to December 2, 2017, and led by Dr. José Gárate and Dr. Tomas Pérez-Acle, the CINV co-organized together with Fundación Ciencia & Vida (Santiago, Chile) the second version of the International Spring School of Applied Statistical Thermodynamics 2017 (AST2017). **Outreach.** The highlights for 2017 in this area was the airing of "*The Joy of Science*", a television series based on the book of the same name published by Dr. K. Whitlock, which seeks to explain scientific phenomena to children through entertaining experiments. In partnership with the Young Science Foundation, the 2nd "Falling Walls Lab" competition was held, inviting young innovators from all over the country to represent Chile in the global competition in Berlin. The winner proposed a software that allows diseases of the visual system to be rapidly detected. Dr. Michael Rosbash, also helped transmit to society, through a well-covered press conference, the importance of biological clocks in health and disease. He also gave a talk for the general public, which covered historical as well as recent advances in the field of circadian rhythms in a most entertaining manner. The documentary "Montemar and the labyrinths of memory" (2015), which describes the development of biophysics in Chile, was broadcasted on public television with a high rating for this type of program. Under the general title of "NeuroNews", articles published in top international journals are translated by PhD and Master students in a language accessible to the general public and are published periodically in the very-visited online newspaper "El Mostrador". A book containing most of these articles will be published in 2018. During the second semester of 2017, the new building for the CINV was tendered and awarded to a prestigious building company. Construction will start during the first semester of 2018.

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1.2 Resumen Ejecutivo

El Centro Interdisciplinario de Neurociencias de Valparaíso (CINV) se relaciona con diversos aspectos de una pregunta científica fundamental: ***Cómo Responde el Sistema Nervioso a los Estímulos en Condiciones de Salud y Enfermedad?*** Abordamos esta pregunta en cinco líneas de investigación: *a) Función de Sensores Moleculares. b*) *Señalización Celular*. *c) Aspectos Genéticos y del Desarrollo en Neurociencias d*) *Neurociencia de Sistemas y Circuitos* e) *Línea Transversal: Bioinformática y Biología Computacional*. El 2016 se estableció una *unidad de Investigación Traslacional* para facilitar la creación de proyectos traslacionales. **Productividad Científica y trabajo en colaboración.** Este año produjimos 53 publicaciones. Aunque es el mismo número que el año pasado, ahora mejoramos su factor de impacto promedio (IF) (2017: 4.8 vs 2016: 4.5). Cuatro manuscritos fueron publicados en revista con IF >12, dos de los cuales fueron liderados por miembros del CINV (*Nature Comm* (Lab., Ewer), y *Physiol Review*s (Lab., Latorre)). Además, 5 artículos aparecieron en revistas bien posicionadas (e.g., *Journal of Neuroscience, Glia, Science Signaling y mBio*). Los estudiantes (48) son co-autores de 27 artículos y de éstos, fueron primeros autores en 8. Más aún, la Dra. Angélica Escobar, uno de nuestros post doctorantes reclutados durante el 2017, contribuyó con un comentario en la competitiva sección "Journal Club" del *J. Neurosci.* (Escobar A. 2017 *J. Neurosci*). Entre las contribuciones científicas, destacamos tres de ellas. La primera, liderada por nuestro primer graduado del Programa de Doctorado en Biofísica y Biología Computacional (Pinto BI y cols., 2017. *Sci Rep* **7**:15851), propone un nuevo modelo alostérico para explicar los efectos del Ca^{2+} y del voltaje en hemicanales formados por conexinas. Una segunda es la demostración de la síntesis de proteínas localizada en el axón haciendo uso del gran tamaño del axón de la jibia de Humboldt, que se ubica en la costa de Valparaíso (Mathur C y cols., 2018, *Sci Rep* **8**:2207). Por último, se sabe que la coordinación entre los marcapasos centrales y periféricos es esencial para la función de los relojes circadianos, pero poco se conoce acerca del mecanismo involucrado en dicha coordinación. Nosotros mostramos en una publicación en "*Nature Communication"*, que en *Drosophila*, el tictac del reloj central es transmitido a través de un neuropéptido específico, sNPF, a neuronas que no pertenecen al reloj que luego liberan otro neuropéptido (PTTH), que alimenta río abajo a las células productoras de hormonas esteroidales en la glándula protorácica. Este acoplamiento entre dos relojes podría servir de paradigma para comprender cómo se generan los ritmos hormonales diarios en animales. **Reforzamiento y renovación de nuestros académicos.** Durante el 2016, el Dr Juan C. Sáez fue nombrado Sub Director del CINV y este año (2017), la Universidad de Valparaíso (UV) le otorgó el cargo de Profesor Titular, que se hará efectivo durante el primer semestre 2018, una vez que su laboratorio esté habilitado. Su incorporación al CINV como miembro interino, reforzará la línea de investigación de Señalización Celular, permitiendo al CINV incrementar su liderazgo en el campo de los canales de uniones en hendidura y de hemicanales formados por conexinas y panexinas. Para lograr nuestros planes de reclutar un destacado investigador de acabada experiencia, la UV y el CINV sostuvieron conversaciones con el Dr Francisco Bezanilla, Profesor Titular Lillian Eichelberger Cannon del Departamento de Bioquímica y Biología Molecular en la Universidad de Chicago y miembro de la Academia Nacional de Ciencias de EEUU. El Dr. Bezanilla es un líder en el campo de la biofísica de canales iónicos como también un antiguo colaborador del CINV. Fruto de dichas conversaciones, el Dr. Bezanilla se convertirá en un miembro del CINV como Profesor Titular Honorario en la Universidad de Valparaíso comenzando en el 2018. Las investigaciones de la Dra. Chiu, un líder del "CINV-Max Planck Tandem Group", se verán enriquecidas con la

adquisición de un microscopio de dos fotones, con fondos provenientes del CINV y de CONICYT, que se encontrará habilitado en Marzo 2018. En el 2017 nuestros Investigadores Jóvenes fueron galárdonados con proyectos FONDECYT y los Investigadores Jóvenes García y Gárate ingresaron como profesores asociados a la UV a través del programa CONICYT de Capital Humano Avanzado (AHC), una distinción que asegura financiamiento para honorarios, fungibles y equipamiento menor por un período de 3 años. **Entrenamiento avanzado.** Se continúa participando activamente en los Programas de Doctorado y Maestría en Neurociencia de la Universidad de Valparaíso. Estos siguen atrayendo estudiantes de Chile y el extranjero. Este año, se admitieron 9 estudiantes al Programa de Doctorado en Neurociencia para el año académico 2018, uno de los números más altos a la fecha y el programa fue re acreditado por un período récord de 7 años por la agencia nacional de acreditación. En el año 2017, el programa de Maestría en Neurociencia admitió 11 estudiantes, 6 de los cuales trabajan con miembros del CINV. También el último año, 6 estudiantes asociados a laboratorios del CINV aprobaron su proyecto de tesis de Maestría, lo que corresponde al 60% de todos los proyectos de tesis de este Programa. El programa de Doctorado en Biofísica y Biología Computacional matriculó 10 alumnos durante 2017, cuatro están realizando sus tesis y uno de ellos se graduó (B. Pinto), convirtiéndose en el primer graduado de este Programa. **Red de Colaboraciones.** Reforzando las colaboraciones, durante el 2017 el CINV organizó importantes reuniones internacionales. Lo más destacado fue el Simposio Latino Americano de Cronobiología (LASC), organizado cada dos años en un país diferente de Latino América llevándose a cabo por primera vez en Chile y liderado por el Dr. John Ewer. El LASC contó con la importante participación del Dr. Michael Rosbash, Premio Nobel 2017 en Fisiología y Medicina por su trabajo en el reloj circadiano de la *Drosophila*. Nuestra red de trabajo en Biofísica y Neurociencia Computacional, llevó a cabo la 4ª Escuela de Verano Latino-Americana en Neurociencia Computacional (LACONEU) en Enero del 2017. El CINV co-organizó junto con la Fundación Ciencia & Vida (Santiago, Chile) la segunda versión de la Escuela de Primavera Internacional de Termodinámica Estadística Aplicada 2017. Directores: Dr. José Gárate y el Dr. T. Pérez-Acle,). **Extensión.** El lanzamiento de "*La Alegría de la Ciencia*" fue lo destacado del 2017. Este es un programa de series televisión basados en el libro del mismo nombre de la Dra. K. Whitlock. En el se intenta explicar los fenómenos científicos a niños a través de experimentos entretenidos. En asociación con la Fundación Ciencia Joven, se llevó acabo la 2a competencia de "Falling Walls Lab". Jóvenes innovadores de todo el país compitieron para representar a Chile en la competencia mundial en Berlín. El ganador propuso un programa computacional que detecta rápidamente enfermedades del sistema visual. Porotra parte, Dr. Michael Rosbash, transmitió a la comunidad a través de una conferencia de prensa la importancia de los relojes biológicos en la salud y la enfermedad. Dr. Rosbach dio también una conferencia dirigida a público general, cubriendo los avances en el campo de los ritmos circadianos de manera muy entretenida. , y dirigido por el Dr. José Gárate y el Dr. T. Pérez-Acle, Con un alto "rating" se transmitió en televisión abierta el documental "Montemar y los laberintos de la memoria" que describe el desarrollo de la biofísica en Chile. El exitoso diario electrónico "El Mostrador" y bajo el título "NeuroNews", ha seguido publicando los artículos publicados en revistas internacionales traducidos por estudiantes de Doctorado y Maestría a un lenguaje comprensible por el público general. Un libro que contiene la mayoría de estos artículos será publicado el 2018. Durante el segundo semestre del 2017, se licitó y se otorgó la construcción del nuevo edificio para el CINV a un prestigiosa empresa constructora. La construcción comenzará durante el primer semestre del 2018.

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2. Introduction

a) Description of the Institute and highlights of year 2017.

The general aim of the CINV is the development and potentiation in Chile of the Neuroscience through a multidisciplinary approach that covers from molecules to behavior. Our long-term objective is to offer creative neuroscientists freedom from constraints that limit their ability to do cutting-edge research. In this regard, the CINV is the first and only Chilean Institute, that through collaboration with the Max Planck Institutes, created and *ad-hoc* program able to attract young, creative and adventuresome neuroscientists. This program, the Max Planck Research Groups incorporated its first member in December of 2016, Dr Chiayu Chiu. To accomplish her goals, Dr Chiu needed state-of-the-art imaging and engineering. During 2017, the CINV in conjunction with the Nucleus led by Dr Chavez, made an effort to put at her disposition a two-photon microscope, unique in Chile, that will allow her to visualize electrical and biochemical signals at the level of single synapses. On the other hand, the need of engineering that enables us to develop new research tools for studying the intricacies of the nervous system will be accomplished by Dr Francisco Bezanilla, hired by the Univ. of Valparaíso and the CINV during 2017. Dr Bezanilla has single-handed developed new microscopes and fluorescent techniques and in his own words regarding our incomplete understanding of excitability has stated that to have a better grasp of the problem "we *will require to develop new equipment to follow in-time transitions of single molecules and new analytical tools to predict their path, and I hope to contribute to that in the future*." It is important to mention here and representing the future of the CINV, during 2017, our Young Investigators were successful in securing funds for their research and two of them (Drs. García and Gárate) obtained a position at the Univ. of Valparaíso.

b) Research Lines

1. *Structure and Function of Molecular Sensors*. We should highlight two major scientific contributions of this group, both published in *Scientific Reports*. One reflects the effort of our first graduate from the PhD program on Biophysics and Computational Biology (Pinto et al., 2017, *Sci Rep* **7**:15851; jointly with Line 2) that helps to unravel the mechanisms of Ca^{2+}-dependent gating of connexin hemichannels. This finding is likely to have a significant impact in future research on the field. The other contribution is a breakthrough that demonstrates localized axonal membrane protein translation taking advantage from axon size of the Humboldt squid found in the coast of Valparaíso (Mathur et al., 2018, *Sci Rep* 8:2207). The leadership of our research team in electrophysiology was recognized in two invited reviews. One in Physiological Review (an effort that put together Line 1 & 5), the most cited journal in physiology entitled "Molecular Determinants of BK Channel Functional Diversity and Functioning". The second review was an invitation revisit the most relevant discoveries reported in the first 100 years of the *Journal of General Physiology*. In this special issue, R. Latorre and O. Alvarez took us back to the constant-field equation in membrane ion transport developed by David Goldmann and used to these days to explain cell's membrane potential from the ionic gradients. **2.** *Cell Signaling*. Our discovery of new molecular target to treat and prevent progression of neurological diseases (i.e., Alzheimer disease, depression, epilepsy, muscular dystrophies and infectious diseases) based on inhibition of hemichannels required different *in vitro* and *in vivo* methods in central and peripheral tissues. These approaches provided critical information on the relevance and efficacy of new anti-inflammatory agents discovered by us (i.e., Maturana et al.,

2017, *Develop Neurobiol.* 77:625; Sáez et al., 2017, *Sci Signal* 10(506) and Yi et al., 2017, *Glia* 65:1607). We also reported new insight on the gating mechanism of hemichannels (i.e., Vargas et al., 2017, *Frontiers in Physiol*. 8:38; Pinto et al., 2017, *Sci Re*p. 7:15851) and the role Dynamin-2 mutations linked to centronuclear myopathy (González-Jamett et al., 2017, *Sci Rep*. 7:4580). The leadership of our research team neuroinflammation and muscle dystrophies was recognized in 7 invited reviews (e.g., *Physiol. Rev., for p*ublication in 2018). **3**. *Genetic and Developmental Neuroscience*. In 2017, Line 3 published a hard-fought article that shows that *Caenorhabditis elegans* living on pathogenic bacteria can avoid bacterial infection by entering diapause through a transgenerational, RNAi pathway-dependent, mechanism (Palominos et al., *2017 MBio.* 8(5). pii: e01234-17). We also contributed to our understanding of how *Drosophila* central and peripheral circadian clocks are coordinated to produce a circadian rhythm of adult emergence (Selcho et al., *Nature Comm* 8:15563. doi: 10.1038/ncomms15563). **4.** *Integrative and circuits Neuroscience*. This year, Line 4 wants to highlight the collaborative work of our young and postdoctoral investigators. Using a variety of cellular and molecular tools, combined with electrophysiology, we advanced in the understanding of the role of neuromodulatory systems like nitric oxide (NO) and cannabinoid signaling. We demonstrated specific bipolar cell types as NO sources in the inner retina and its role in physiological processes (Agurto et al., 2017, *Exp Eye Res.* 161:30). These finding will have a significant impact in our current understanding of how retinal circuit works to generated vision. Work continues to understand how different neuronal circuits work under normal and pathological conditions including aging, neurodegenerative and neuropsychiatric disorders. We helped to increase our understanding of the functional roles of connexin hemichannels under physiological and pathological conditions (Vargas et al., 2017, *Frontier Physiol* 8:38) and the role of IRE1 in protecting against Alzheimer disease (Ardiles et al., 2017, *Acta Neuropathol*. 134:489). **5.** *Crosscutting: Molecular Simulation and Computational Biology. a)* In 2017, as collaboration with Line 3, we applied a novel method based on graphlets to compare the topology of gene regulatory networks in the zebrafish olfactory system (Martin et al. 2017. *PeerJ* 5:e3052). We applied our conductance-based model of cold thermotransduction to understand how hypersensitivity to cold can arise from the down-regulation of the I_{Kd} K^+ currents. *b) Theoretical Biophysics*. 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. 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.

c) Organization of researcher's team:

We are organized in 5 research lines, and one translational research unit that was created in 2016 and implemented last year. This new unit supports the translational research efforts of the Research Lines, to aid in the generation of spin-offs. To this purpose, we hired a manager with experience in generating R & D grant applications (e.g., CORFO) and in intellectual property protection.

To stimulate collaborative research inside CINV, we have implemented several strategies: 1.- Regular meetings between students, postdocs and young investigators, to discuses their projects. 2.- Postdoctoral fellowship award for collaborative research. 3.-CINV annual meeting, in which students and PIs presents their work. 4.- Special funding exclusively for collaborative research between CINV members.

3. Scientific and Technological Research

a) Current status of research lines

Structure and Function of Molecular Sensors

(*R. Latorre, A. Neely, C. González, O. Alvarez, F. Bezanilla, M. Holmgren, K. Castillo and I. García***).**

Ion channels are modular proteins in which the ligand binding sites, the voltage sensors and the conduction machinery are all contained in different structural domains of the same protein. The long-term goal of this research line is to better understand how these different structural domains interact with each other in regulating ionic currents. In addition, the scope of our research has recently expanded to understanding the roles of these channels in health and disease.

An important finding during this period has been the demonstration that protein translation and trafficking to the membrane can occur in axons, even in the absence of the soma. To this end, we took advantage of our previous experience with giant axons that can be isolated from the Humboldt squid found in the coast of Valparaiso. We injected isolated axon with *in vitro* transcribed RNA encoding fast inactivating *Drosophila* Shaker K_V channels, and after few hours of voltage-clamp recording, a strong inactivating component of the axon K^+ current emerged. This result provides definitive evidence that isolated axons can use their resident machinery to synthesize fully functional membrane proteins such as ion channels (**Mathur et al. 2018, *Sci Rep* 8:2207**). A couple of years ago we joined forces with our resident experts on connexin hemichannels (Line 2 and in molecular modeling (Line 5). The purpose of this alliance was to unravel the molecular mechanisms responsible for the phenotype of the mutation (G12R) in Connexin 26 (Cx26), which causes Keratitis-ichthyosis deafness (KID) syndrome (García et al., *J.Invest. Dermatol*. 2015 and 2016). Combining single-channel measurements and molecular dynamic simulations this year we were able to elucidate the structural changes caused by mutation that lead to the disruption of a process known as fast gating. We found that the G12R mutation causes a displacement of the N terminus that allows the interaction of R12 with R99, which keeps the channel open, thereby providing a molecular mechanism for the gain-of-function effect of this mutation (**García et al., *J. Gen. Physiol*. In Press).** As we gained experience in connexin hemichannel structure and function, together with Line 2 we undertook the challenge of deciphering the mechanisms of Ca^{+2}-mediated inhibition. This research was carried out by the first graduate from the PhD. Program on Biophysics and Computational Biology ***(*Pinto et al., 2017, *Sci Rep* 7:15851**), who discovered that, contrary to the prevailing view, Ca^{+2} does not block the channel, but instead stabilizes the closed states through an allosteric mechanism in which voltage and Ca^{2+} sensors interact allosterically.Two invited reviews recognized the leadership of our research team in electrophysiology. One in *Physiological Reviews,* the most cited journal in physiology, was entitled "Molecular Determinants of BK Channel Functional Diversity and Functioning" and was a joined effort of Line 1 and 5 (**Latorre et al., *Physiol Rev*. 2017;97:39-87**). The second review was an invitation to join an exclusive group of researchers to revisit the most relevant discoveries reported in the first 100 years of the Journal of General Physiology. In this special issue R. Latorre and O. Alvarez took us back to the constant-field equation in membrane ion transport developed by David Goldman, and which is still used today to explain a cell's membrane potential on the basis of the ionic gradients present across the membrane (***J Gen Physiol*. 2017; 149:911-920**). Our expertise in high resolution electrophysiological and optical methods has allowed us to gain

important new insights into the structure-function of voltage- and Ca^{2+}-activated K^+ (BK) channels in which four voltage sensor domain (VSD) and eight intracellular high-affinity Ca^{2+}-binding sites functionally converge to facilitate channel opening. Two families of accessory proteins, β and γ, modulate BK channel gating and pharmacology. Notably, in the absence of internal Ca^{2+}, the γ1 subunit promotes a large shift of the BK conductance-voltage curve to more negative potentials. However, very little is known about how α and γ1 subunits interact. In particular, the association stoichiometry between both subunits is unknown. We designed a method to answer this question using lanthanide resonance energy transfer (LRET). The method assumes that the kinetics of LRET sensitized emission (SE) of the donor double-labeled α/γ1 complex is the linear combination of the kinetics of the SE in single-labeled complexes. We used a lanthanide binding tag (LBT) engineered into either the α or the γ1 subunits to bind Tb^{3+} as the donor. The acceptor (BODIPY) was attached to the BK pore blocker, iberiotoxin. We determined that γ1 associates with the α subunit with a maximal 1:1 stoichiometry. This method could be applied to determine the stoichiometry of association between proteins within heteromultimeric complexes. (**Carrasquel-Ursulaez et al *Biophys. J.* In press**). Voltage-gated proton channel (Hv1) monomers share the same architecture with VSDs of voltage-gated channels, but in Hv1 the four transmembrane segments play the double role of voltage-sensing and proton conduction. A key piece of information that was missing is the direct measurement of gating currents. We report here that one of our most gifted graduate students from the PhD Program in Biophysics and computational biology succeeded in isolating the currents emerging from the movement of gating charges of Hv1, a feat that was highly appreciated at the Biophysical Meeting in February 2018 **(Carmona et al. ms. In prep)**. A particularity of permeation through Hv1 is that, in contrast to other cations, protons are always sharing an electron with either water or an organic molecule. For this reason the permeation pathway is unlikely to be that of typical ion channels; its exact mechanism is still a matter of debate (**Alvarez et al *J. Physiol.* In press)**.Taking advantage of our ability to express and record from calcium channels in the absence of auxiliary subunits, we addressed the still controversial question of the role of auxiliary subunit on the downregulation of calcium current induced by certain small GTPases and found that Cav2.3 mediated current is indeed inhibited by the small GTPase GEM, but not by REM. We have a high expectation that the interaction between Cav2.3 and GEM will help us dissect out the different interaction involved in the regulation of calcium channels.Continuing with our efforts to understand cold sensing by TRPM8 channels, recently reviewed in **Castillo et al., *Phys Biol.* 2018**. This year we investigated the role of a coiled-coil domain at the end of the C-terminus and found that its progressive shortening decreased cold sensitivity. In collaboration with line 5, we constructed a molecular model of the TRPM8 coiled-coils and discovered that in addition to hydrophobic interactions typical of coiled coil, a cluster of polar residues that populated the central region appears to participate in temperature sensitivity as corroborated by anisotropic thermal diffusion and site-directed mutagenesis. A complete characterization of temperature- and voltage-activated TRP channel gating requires a precise determination of the absolute probability of opening over a wide range of voltages, temperatures, and agonist concentrations. We have achieved this in the case of the TRPM8 channel expressed in *Xenopus laevis* oocytes, where we were able to cover an extensive range of probabilities and applied voltages, up to an unprecedented 500 mV. Finally, our team published a book chapter describing animal care protocols, patch clamp pipette preparation, methods of temperature control, and of methods for the analysis of ionic currents to obtain reliable absolute

open channel probabilities (**Alvarez et al, *Methods in Molecular Biology*. Chapter Book, In press**)**CellSignaling.***(J.C. Sáez A.M. Cárdenas, A. Martínez and H. Sánchez)* During 2017, we studied the mechanism by which the cortical actin cytoskeleton controls exocytosis of proteins and transmitters. We reported that the F-actin binding protein cortactin regulates the dynamics of the exocytotic fusion pore by a mechanism that depends on cortactin phosphorylation by ERK1/2 and Src kinases and on the availability of monomeric actin **(González-Jamett et al., 2017 *Front Cell Neurosci* 11:130)**. With regard to F-actin's function in neurological diseases, we demonstrated that an altered actin dynamics underlies myopathies caused by mutations in dynamin-2. This actin dysfunction impairs the exocytosis of the glucose transporter GLUT4 **(González-Jamett et al., 2017 *Sci Rep* 7:4580)**. In collaboration with Pablo Caviedes (Univ. Chile), we continued studying how different genes that are overexpressed in Down's syndrome contribute to altered cellular signaling found in the trisomic condition. This year we reported that the overexpression of the Na^+/myo-inositol cotransporter (SMIT1) promotes abnormal cholinergic and glutamatergic Ca^{2+} signals in trisomic CTb cells **(Cárdenas et al., 2017. *Neurotox Res* 32:614-623)**. We recently reviewed our efforts to understand the mechanisms that regulate exocytosis in neuroendocrine cells **(Marengo and Cárdenas, 2018. *Pflügers Arch* 470: 155-167)**. In addition, and consistent with our long-term interest in understanding the functional consequences of heteromeric gap junction channel formation, we found, in a collaborative study, that co-expression of Cx45 and Cx43 enables the formation of heteromeric hemichannels with greatly reduced permeability, unitary conductance, and with asymmetric voltage gating properties that favor asymmetric flux of molecules across gap junction channels **(Zhong et al., 2007. *Front Physiol.* 2017 May 29;8:346).** For these studies we used double whole cell voltage clamp and diffusion of fluorescent tracers to measure electrical coupling and single gap junction channels currents, respectively. Our interest in the regulation of connexin-based channels was described in a recently published review **(García et al., 2018. *Biochim Biophys Acta.* 1860:91-95)**.We continue studying the role of hemichannels and other non-selective channels in neurological diseases and muscle dystrophies. We demonstrated that boldine, which is extracted from a Chilean endemic tree called boldo, inhibits connexin and pannexin hemichannels but does not affect gap junction channels. We also found that a daily dose of boldine protects neurons from Aβ amyloid peptide *in vivo* using the app/sp1 mouse model of Alzheimer's disease **(Yi et al., 2017. *Glia* 65:1607-1625)**. In addition, we demonstrated that boldine as well as D4, a selective connexin hemichannel blocker that we identified using bioinformatics, revert the skeletal muscle to normal conditions in the mdx mouse model of Duchenne's disease **(Cisterna et al., in preparation)**. We also studied the role of hemichannels in dendritic cell migration using microfabricated channels that facilitate cell migration by mimicking the confined environment of tissues and allow the quantitative analysis of cell speed and cytoskeletal organization. We found that ATP, which is released upon damage and is a dangerous molecule when unregulated, stimulated fast dendritic cell motility through an autocrine signaling loop, which was initiated by the activation of $P2X_7$ receptors and further amplified by pannexin 1 (Panx1) channels **(Sáez et al., 2017. *Sci Signal*. 21;10(506)**. We also found that gestational stress induces drastic permeabilization of hippocampal astrocytes and microglia, which is mediated by connexin hemichannels and is characteristic of neuroinflammation, was reverted by connexin hemichannel blockers **(Maturana et al., 2017. *Dev. Neurobiol.* 77(5):625-642)**. We found similar neuroinflammation in Balb/c mice treated with single epileptogenic dose of pentilentetrazol (PTZ) or kainate as well as in PTZ kindling mice. In these mice, treatment with a

single dose of boldine or D4 prevented or stopped the epilepsy and the increase in hemichannels of glial cells **(Sáez et al., In preparation)**. Moreover, we found that the neuroinflammatory response activated by β-amyloid peptide is completely inhibited by cannabinoids **(Gajardo-Gómez et al., 2017. *Glia* 65:122-137)**. In collaboration with T. Pérez-Acle from Line 5 and O. Schmachtenberg from Line 4, we found no expression of gap junction channels in HeLa cells transfected with Cx39. Instead, using whole cell path-clamp, we identified functional hemichannels of about 75 pS, with peculiar permeability to small molecules but impermeable to Ca^{2+} and resistant to octanol and heptanol, two classic inhibitors of connexin-based channels **(Vargas et l., 2017. *Front Physiol.* 2017;8:38)**. As result of our progress in neuroinflammation and muscular dystrophies we were invited to write several reviews **(Plotkin et al., 2017. *Curr Osteoporos Rep.* 15:326-334; Puebla et al., *Front Physiol.* 2017;8:11; Giaume et al., *Neurosci Lett.* Sep 8. pii: S0304-3940(17)30740-1.; Rovegno et al., 2017. *Biochim Biophys Acta*. 1860:216-223; Charvèriat et al., 2017. *Front Cell Neurosci.*;11:174; Sáez, 2017. *J. Physiol.* 595:2411-2412; Puebla et al., 2017. *Front Physiol.* 2017;8:11).** In a new collaboration with José L. Vega from Universidad de Antofagasta we found that infection of cardiac myocytes with pathologic *T. cruzi* induces the opening of pannexin 1 channels that appear to be critical for initiating Ca^{2+} transients needed for *T. cruzi* infection **(Vega et al., 2018. *Am J Trop Med Hyg*. 98:105-112)**. Since T. *cruzi* also infect astrocytes and leptomeningeal cells in the CNS, these findings open a new opportunity to understand whether hemichannels participate in the neuroinflammation caused by unicellular parasites.**Genetic and Developmental Neuroscience.***(K. Whitlock, J. Ewer and A. Calixto).* We have continued 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 proliferative cell populations of the olfactory sensory system.* We have shown that a continuous sheet of neurectoderm gives rise to the peripheral (olfactory organs) and central (olfactory bulbs) nervous system thus presenting a new model for nervous system development. Further analysis **(Torres-Paz, J., Tine, EM., and Whitlock, KE. in preparation)** has shown that a gradient of *distal-less* genes subdivides the anterior neurectoderm where high Dlx expression drives cells into the peripheral olfactory epithelia (OE) pathway and lower expression drives cells into the central olfactory bulb pathway. As part of this analysis we have made the surprising discovery that oligodendrocyte specific markers are expressed in the OE and olfactory nerve of developing and adult zebrafish **(González, P. et al., in preparation)**. Thus glia characteristic of the central nervous system may also populate the peripheral OE. ***2.*** *Neuroimmune interaction in the olfactory sensory system.* We have discovered a novel damage induced neuro-immune response in the OE. This response is not present in other sensory systems and involves calcium signaling that initiates neutrofil migration to the OE via the blood vasculature **(Palominos, M. F. and Whitlock, K. E., in preparation)**. As part of a cross-line collaboration with Pablo Moya (Line 4), Dr. C. Calfún has been awarded a CINV postdoc to develop an OE mediated pathway for mutagenesis by CRISPR/Cas9 system to study immune system function in the olfactory sensory system of zebrafish and mouse. ***3.*** *Control of GnRH cell differentiation in the adult hypothalamus*. Through our characterization neural precursors in the adult fish we have discovered hormone-inducible progenitor populations in the hypothalamus **(Ceriani, R., Brown, D. and Whitlock, K. E., in preparation)**. These data support a model where patients with GnRH deficiencies "revert" and become fertile via

activation of quiescent neural progenitor pools in the hypothalamus. Surprisingly, we confirmed GnRH gene loss in a specific syntenic region of the genome (collaboration: Dr. John Ewer) that is not related to domestication effects on the genome (collaboration: Dr. John Postlethwait, USA), and is supported by loss of GnRH proteins as shown by MADI-TOF and Orbitrap analysis (collaboration: Dr. Christian Wegener, Germany) **(Whitlock, Ewer, Wegner and Cerani in preparation)**. Currently we are investigating alternate peptide pathways in the hypothalamus. ***Using genetic analysis and genomics approaches to understand the impact of cellular and environmental stress on neuronal and organismal survival.*** **1.** We have discovered that diapause formation strongly induces the regeneration of broken axons **(Caneo et al., under review)**, and established that the silencing of the insulin receptor is a key effector of the process. Diapause entry is triggered by food deprivation, and can be used as a new model for genetic analysis of requirements for neuronal regrowth. ***2-*** *Using the same degenerative model we previously observed a differential response to neurodegeneration depending on the bacterial food animals eat*. We dissected the differences in gene expression between the most and the least protective bacteria and found that an enzyme required for adapting to acidic stress (GAD) is key for neuroprotection. Currently, we are examining the contribution of specific metabolites resulting from GAD activity in neuronal protection **(Urrutia et al., in preparation)**; ***3.*** *We also showed that animals confronted with pathogenic bacteria as the sole source of food make the decision to exit development and enter diapause as a form of pathogen avoidance*. This decision is transmitted to the progeny in a transgenerational manner, and depends on the RNAi machinery **(Palominos et al., 2017. *mBio 8:5*)**. We proposed that this response is triggered by bacteria residing in the worm intestine, which is communicating to the animal in the form of small RNAs. Currently, we have identified bacterial RNAs that are key triggers of this response and are in the process of validating their molecular contributions *in vivo* **(Legue et al., in preparation)**. We also have other important evidence that points to specific miRNAs from *C. elegans* being involved in the worm's response to pathogens **(Gabaldon et al, in preparation)**. We built gene interacting networks formed by transcription factors and miRNAs in the worms as well as bacterial RNAs with worm effectors. These networks will be validated in the coming years to establish a full picture of the interspecies communication between bacteria and their worm host. ***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. We are currently: ***1.*** *Investigating how the key neuropeptides, Eclosion Hormone (EH) and Ecdysis Triggering Hormone (ETH), control ecdysis behavior*. For this we use genetic tools we have developed in collaboration with Ben White (NIH, USA), null mutants we have isolated, and calcium imaging using GCaMP, to continue ongoing work that investigates how EH and ETH cause the sequential expression of ecdysis behaviors. ***2.*** *Investigating how EH and ETH control tracheal air-filling*. In addition to triggering the ecdysial behavioral sequence, the release of EH and ETH causes the rapid clearing of molting fluid from the trachea, the network of tubes that provides air directly to each tissue. The lining of the main tracheal trunks is replaced during the molt, and at ecdysis the cuticular lining from the previous stage is shed and remaining molting fluid immediately resorbed; failure to do so leads rapidly to death due to anoxia. We are currently carrying out functional and molecular screens to identify the genes involved in causing rapid air-filling **(Alvarez & Ewer, unpublished)**. ***3.*** *Investigating how EH and ETH cause rapid cuticle melanization*. Following ecdysis the new exoskeleton is rapidly hardened (sclerotization)

and pigmented (melanization); failure to do so immediately after ecdysis rapidly leads death due to desiccation. We have previously identified the neurohormone, bursicon that is responsible for sclerotization in all insects. It has been assumed that the epidermis is the direct target of bursicon, yet our recent genetic analysis indicates that this long-held assumption is incorrect **(Flaven-Pouchon & Ewer, unpublished)**. ***4.*** *Determining 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 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, 2017. *Nat Commun 8: 15563. doi: 10.1038/ncomms15563*)**. We are currently continuing this work by investigating whether genes involved in the synthesis and/or the release of the molting hormone, ecdysone, are regulated by the clock. **5.** As part of a cross-line collaboration, we are starting a project with Agustín Martínez (Line 2) that uses *Drosophila* to identify genes involved in connexin function. Although these proteins are not present in flies, there are many successful precedents for using this type of approach to identify novel players involved in specific cellular processes.**System and Circuits Neuroscience.***(A. Chávez, P. Moya, O. Schmachtenberg, A Palacios, C. Chiu and A. Ardiles).*Our research focuses on understanding how neuronal circuits work (i.e., brain and retinal circuits) under normal and some pathological conditions including aging, neurodegenerative and neuropsychiatric disorders as some of these processes can induce critical alterations in both cognitive and sensory performance. Using a variety of cellular and molecular tools, combined with electrophysiological and behavioral tests, we found that the endoplasmic reticulum triggers the activation of proteins involved in the unfolded protein response, such as IRE1, which may be important to protect against Alzheimer´s disease **(Ardiles et al., 2017. *Acta Neuropathol.* 134:489-506)**. We also provided physiological and behavioral evidence indicating that somatostatin interneurons in the CNS are critical for gating the synaptic output of the basal forebrain controlling cortical operations **(Espinosa et al., 2017. *Cereb Cortex.* 17:1-12.)**. Collaborative work continues with other CINV lines. Together with Line 2 we demonstrated that Cx39 forms functional hemichannels, thereby increasing our understanding of the functional roles of connexin hemichannels under physiological and pathological conditions **(Vargas et al., 2017 *Front Physiol.* 8:38)**. We also continued our collaborative efforts to understand the role of neuromodulatory systems in regulating neuronal circuits, including nitric oxide (NO) and cannabinoid signaling. We demonstrated that specific bipolar cells have NO sources in the inner retina and play critical roles in physiological processes of the retinal circuit **(Agurto et al., 2017. *Exp Eye Res*. 161:30-35)**. We found that cannabinoid signaling play an important role in regulating visual signaling processing by selectively controlling GABAergic but not glycinergic inhibitory signals onto different types of bipolar cells in the inner retina **(Vielma et al. *J Neuroscience* JN-RM-0733-18)**. Ongoing work focused on the potential interaction between NO and cannabinoid signaling to regulate retinal function. Moreover, we found that electrical coupling between GABAergic A17 amacrine cells occurs in the retina to regulate inhibitory feedback onto RBCs, by synchronizing and facilitating GABA release onto rod bipolar cells **(Elgueta et al., *Scientific Report* in press)**. Additional collaborative work focused on the neuromodulatory function of serotonin in regulating retinal circuits. We have found that activation of 5-HT1 receptors regulates excitatory synaptic inputs onto ganglion cells under normal conditions. In contrast, using the 5-HT transporter knockout mouse we found that increased levels of serotonin impaired 5-HT1 receptor localization and excitatory synaptic

function. It also produced a decrease in the global retinal activity and action potential firing rates, indicating that serotonin might play an important role in regulate retinal synaptic function. A manuscript including some of these results is in preparation **(Quiroz et al.)**. We extended our analysis on the functional specialization of sensory system in rodents and spiders, and found that a subterranean rodent exhibit, paradoxically, diurnal instead of nocturnal visual specializations **(Vega-Zuñiga et al., 2017. *J. Sci Rep*. 2;7:41704)** and that the spider, *Loxosceles laeta*, presents a specific olfactory system for the detection of conspecifics **(Calbiague et al., 2017. *J Med Entomol.* 2017;54(5):1435-1439)**. We extended our collaborative work to understand the functional role of the EAAT3 neuronal glutamate transporter to regulate neuronal circuits and behavior **(González et al., 2017. *Biol Res.* 50:29)**, and found that overexpressing EAAT3 induces anxiety and compulsive-like behavior together with changes in NMDA receptor mediated synaptic function at the cortico-striatal synapses **(Delgado-Acevedo et al., *Mol Psychiatric* BPS-D-17-01818)**. In addition, we are analyzing the role of EAAT3 in regulating retinal visual processing and found that, in ganglion cells, excitatory synaptic function is reduced, likely by regulating glutamate diffusion from bipolar cells and through the activation of NMDA receptor in the overexpressing EAAT3 mouse. We also contributed to the demonstration that the modulatory effects of amphetamine on the sex-specific expression of vasopressin manner could be responsible for sex-dependent vulnerability to addiction **(Ahumada et al., 2017. *J Neuroendocrinol.* Apr;29(4))**. International scientific collaborations also forms part of our effort to understand how neuronal circuits work. We demonstrated that by increasing the excitation/inhibition balance, long term potentiation enhances granule cells output in the dentate gyrus, an observation that may contribute to dentate-dependent forms of learning and epilepsy **(Hashimotyodani et al., 2017. *Neuron.* 95:928-943.e3)**. We also contributed to the international discussion about our current understanding of the mechanisms underlying synaptopathies **(Ardiles et al., 2017. *Neural Plast.* 2017:2643943)**. During this period, we have made important progress to contribute to the integral development of CINV human resources to successfully perform as independent researchers in the future. Highlights of our commitment to support training are individual Journal club publications from one of our postdoctoral fellows **(Escobar, 2017. *J Neurosci.* 37:11072-11073)**. Moreover, both formally and in practice, strategies are in process (i.e. grant collaborations, sharing students and postdoctoral fellows) to increase our internal collaborative work, which will be reflected in the number of collaborative publications among line 4 PIs during 2018. **Crosscutting: Computational Biology and Bioinformatics.** *(Tomás Pérez-Acle, Danilo González and P. Orio)*. By combining experimental evidence with advanced mathematics, physics, and thermodynamics we develop computational models to study diverse biological phenomena. Our transdisciplinary efforts are organized in three areas: **I**. Theoretical & Computational Neuroscience **(TCN)**, **II**. Theoretical Biophysics **(TBs),** and **III**. Target Discovery, Drug Discovery and Drug Delivery **(TD5)**. In **TCN,** we develop and analyze mathematical models describing the behavior of biological systems at multiple spatial and temporal scales. Our approaches include dynamical system analysis, numerical simulations of both deterministic and stochastic nature, parameter sweeping, rule-based modeling, and the application of artificial intelligence methods. Our models of neural excitability are aimed at understanding how the interplay of different ion channels produce complex neural behavior, as occurs in sensory systems and their neuropathies. In doing so, our models helped us understand how an imbalance of the expression of K^+ channels underlie different forms of neuropathic pain related to cold perception **(González et al, 2017. *J Neurosci***

37:3109-3126; González et al., 2017. *Adv. Exp. Med. Biol.* 1015:265-277). Based on neuronal-based dynamical models, we are studying how chaotic dynamics and the stochastic opening of ion channels may shape the dynamics of neuronal networks. Of note, we described the emergence of chaotic behavior in a biophysically-inspired mathematical model of oscillatory neurons **(Xu et al., 2017. *Front. Comput. Neurosci.* 11:12)**. We then used this model to investigate how chaotic regimes may affect the way in which neurons become synchronized within a network. We propose that chaotic oscillators promote *multistability* resembling the dynamics of EEG and fMRI recorded without stimulation **(Xu et al., *Sci. Rep.* under revision)**. Relying on a stochastic modeling approach based on the Kinetic Montecarlo Algorithm (also known as the Guillespie's Algorithm), we proposed the use of agent-based simulations as a suitable framework to study diverse multiscale biological phenomena, ranging from the set of gene regulatory events related to Sigma factors in *E. coli*, the role of information as a potential prophylactic measure to modulate the dispersion of the Ebola virus among human populations, and up to the study of the role of trust between people as a proxy for the creation of social capital and therefore, the economic growth in human societies **(Perez-Acle et al. *BBRC* 2017 498(2).)**. In **TBs,** we use a set of molecular modeling and molecular dynamics (MD) simulation techniques to provide hypotheses and/or atomic-level descriptions of molecular phenomena, or to generate the theoretical basis for understanding the fundamental laws behind molecular biophysics. Of note, the interaction with colleagues from other research lines allowed us to increase the impact of our research by nurturing a virtuous cycle of knowledge creation between experimental and theoretical approaches. In collaboration with Line 1 researchers, by using novel approaches in MD simulations such as Anisotropic Thermal Diffusion, we expanded our understanding on the microscopic mechanisms related to temperature sensing by TRPV1 channels **(Catillo et al., 2017. *Phys Biol.* 2018 Jan 24;15(2):021001; Pinto et al., 2017. *Sci Rep.* Sep 5;7(1):10522)**. Similarly, by using near-to-equilibrium MD simulations we continue expanding our understanding of the molecular determinants related to the functional diversity of BK channels **(Latorre et al., 2017. *Physiol Rev.* 97:39-87)**. In collaboration with Line 2, and by using a mixed approach between molecular modeling, MD simulations, and artificial intelligence methods, we studied structure/function relationships in connexin-based channels, proposing that charge, molecular flexibility, and valence are the main molecular properties that could explain the action of Gap Junction channels blockers **(Villanelo et al., 2017. *BMC Cell Biology* 18:5; Vargas et al., 2017. *Front. Physiol.* 8:38)**. By further exploring the use of inorganic surfaces as substrates for the creation of bio-silicon interfaces, we proposed that electrostatic interactions are the main contributors to the stability of absorbed biological molecules interacting with SiO_2 surfaces **(Gutierrez-Maldonado et al., 2017. *Chemical Physics Letter.* 674, 64–70)**. In **TD5**, by combining molecular modeling and molecular simulations with cellular and molecular biology, and electrophysiological approaches, we continue exploring new drug nano-carriers based on functionalized dendrimers, nano-bubbles and other transfectant agents. We also further explored the biological effects of selective and specific hemichannel blockers as a chronic treatment for both muscular dystrophy and epilepsy using *in vivo* models. Finally, we expanded our efforts to understand the effect of three novel TRPV1 channel agonists that could be used to the treatment of chronic pain.

Translational Research Unit

The main role of the CINV is to produce science driven by curiosity. Nevertheless, we recognize that our researchers have a wide range of expertise, which could be capitalized upon to solve

problems that are of interest to industry. For this reason, we created a Translational Research Unit in 2017 to aid in finding and developing applied research opportunities (science-based innovation)[1].During this first year we explored several initiatives aimed at testing different approaches to innovation for the CINV. As a result of these efforts, two research contracts with the industry crystallized. The first of these is headed by Dr. Danilo González, and is a partnership between the CINV and Neobiotec S.A., with the purpose of modifying enzymes for the food industry, using protein engineering and bioinformatic tools. The second one is between Dr. Oliver Schmachtenberg (CINV) and Tecnova SpA. and seeks to test the efficacy of new traps for the poisonous spider, *Loxoceles Laeta*. In both cases, the collaborations were successful, and the companies were satisfied with the results. For the CINV the outcomes were also very educational: the researchers worked in close collaboration with industry, learning a different work culture and environment. Moreover, these collaborations allowed the CINV to create the administrative procedures and protocols needed to become a reliable provider for the industry, as in intermediate step to becoming a reliable partner for joint research initiatives.

All this experience will be fully exploited in 2018, when the CINV will apply, along with industry, to several applied research grants. But more importantly, the CINV will expand its industry network and will use its input to re-align the CINV research capabilities to create several "industry driven research initiatives" (***without distorting the current basic research lines***). By doing this, we expect our research to contribute to science-based innovation, and also strengthen the collaboration between researcher from different CINV research lines (as well as with other institutions).This Translational Research Unit has also helped us apply for two FONDEF grants aimed at: a) the development of an antidote against *Loxosceles Laeta´*s venom (Oliver Schmachtenberg, deputy director, Line 4); and b) the use of new proton channels blockers for cancer therapy (Carlos Gonzalez, Director, Line 1; Agustín Martínez, Deputy Director, Line 2). In addition, we made significant progress in pre-clinical studies of a new hemichannel blocker (D4) to treat many inflammatory diseases. In parallel, we are investigating the molecular mechanism of action of the D4 molecule (Lines 1, 2 and 5), basic research which is needed in order to continue with the clinical studies (for which we need to obtain new funds).

The development of a new generation of proton channels blockers for treatment of cancer, including the one affecting nervous system, has opened a significant new technological research line. The proposed therapy is based in the functional role of Hv1 proton channel in tumor-supporting myeloid-derived suppressor cells (MDSC)**.** We have shown that the Hv1 proton channel is expressed in MDSC and its activity is required for MDSC-mediated suppression of T cells, as well as for maintaining MDSC in an undifferentiated state. These elements could establish the Hv1 proton channel as an important molecule for tumor-induced immunosuppression, which has not been previously shown. Thus, this work could lead to a future research project aimed at finding effective Hv1 inhibitors with therapeutic and commercial applications. To achieve these new strategic goals, the CINV shifted the professional profile of the person responsible of the Translational Unit from a "technology transfer coordinator" to "Innovation Advisor".

[1] There is a technology licensing office (TLO) in every partner research institutions of the CINV, including of course the University of Valparaiso. These TLOs are in charge (among other duties) to actively scout for research outcomes in order to protect the intellectual property and try to transfer those results. Unlike the TLO, the CINV Translational Research Unit goal is to detect society and industry needs and to orientate/align the CINV research

capabilities in order to promote and facilitate collaborative research initiatives with external institutions (mainly the industry). On the innovation value chain, this Unit is working "upstream", managing the research capabilities of the CINV (instead of managing the portfolio of research outcomes, which is responsibility of the TLOs).

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	18	34
	Other Researchers	8	19
SCIELO Publications or Similar to SCIELO Standard	Associate Researchers	0	0
	Other Researchers	0	0
Scientific Books and chapters	Associate Researchers	0	0
	Other Researchers	0	0
Other Scientific Publications	Associate Researchers	0	3
	Other Researchers	0	0
Total of Publications		26	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)	15	27
Invited presentations (not included in above row)	1	4
B. Other researchers (Adjunct Researchers, Senior Researchers, Young Researchers, Postdoctoral Researchers and Students)		
Conferences, oral communications, poster communications, others (specify)	21	12

Invited presentations (not included in above row)	1	0

iv. **Organization of Scientific Events:**

II International Spring School Applied Statistical Thermodynamics 2017: from theory to molecular dynamics simulation (AST2017).

This International Spring School uses a BootCamp format to expose the students to intensive two weeks all-day of theoretical and practical knowledge acquisition. It is especially intended for PhD students, as well as for young Researchers or Professionals in the field, who wish to acquire state-of-the-art knowledge about the Statistical Thermodynamics foundations of Molecular Dynamic Simulations, including advanced techniques and protocols. General topics covered include classical mechanics, thermodynamics and statistical mechanics, as well as advanced simulation techniques. Students are encouraged to bring their own projects in which the acquired knowledge will be applied.

LACONEU 2017: 4th Latin-American Summer School in Computational Neuroscience. The principal aim of **LACONEU** is to promote in Latin America the field of Computational Neuroscience through cutting edge mathematical and computational science tools and its applications in Biomedical Research and Clinical Application. The multidisciplinary study of brain function using neuroscience, mathematics and computational approaches helps to a better understanding of brain functionalities under normal or pathological states, as well as, to enhance important advances in education, theoretical frameworks, brain imaging, and biomedical therapies.

LASC 2017: XIV Latin American Symposium on Chronobiology.

This International Symposium is held every two years in a different Latin American country; it was held for the first time in Chile, The symposium was an opportunity to discuss concepts and recent results related to the circadian clock and sleep in a variety of systems and was organized around the following general topics: human circadian rhythms, sleep, circadian clock networks, and molecular clocks.

Symposia organized for the XIII Annual Meeting of the Chilean Society of Neuroscience.

CINV researchers organized and participated in two symposia held in the 2017 Meeting of the Chilean Society of Neuroscience Meeting (October 1-3, Castro): "From neural connectivity to network dynamics", organized by Patricio Orio, and "From the retina to the CNS: Role of neuromodulatory systems", organized by Oliver Schmachtenberg with the participation of Andrés Chavez and Chiayu Chiu. The events included presentations from other national and international scientists in the respective field, and gathered an audience of about 40 people each.

CINV Meeting 2017. Every Brain Matters: Strengthening an Inclusive Science.

This symposium called “Every Brain Matters: Strengthening an Inclusive Science” was held in the Naval Museum, most of the members of the CINV presented their accomplishments as a talk or a poster session. This activity was organized by students of the Millennium Institute.

v. Scientific Editorial Boards

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

Carlos González: Journal of Biological Chemistry, 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 Biophysics Journal.

Tomás Pérez-Acle: PeerJ, PeerJ Computer Sciences.

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

vi. Awards *During this period the following regular Fondecyt were awarded to CINV invetigators 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, Eduardo Couve, Alex Vielma.***
3. Glutamatergic regulation of distinct gabaergic synapses and its impact on neuronal function in the cortex (1171840) ***PI: Chiayu Chiu.***

vii. Other Awards

1. Molecular Basis of excitability and neuronal homeostasis. Air Force Office of Scientific Research under award number FA9550-16-1-0384 to R. Latorre
2. Renewal of Transmission Electronic Microscope, to ensure the continuation of ultrastructural research Universidad de Valparaíso. FONDEQUIP EQM170027, PI: Oliver Schmachtenberg.
3. Outstanding accomplishment in translation of research results, Dirección de Transferencia y Desarrollo de la Vicerrectoria de Investigaciones, Pontificia Universidad Católica de Chile, PI: Juan Carlos Sáez.
4. Top Chile Santander-UC. Grant to visit diferents Universities in Hong Kong during an entire month, PI: Juan Carlos Sáez.
5. Member of the Latin American Academy of Science (ACAL), PI: Juan Carlos Sáez.
6. The publication, "ATP promotes the fast migration of dendritic cells through the activity of pannexin 1 channels and P2X7 receptors", that was publish in Sci Signal. (Sáez et al., 2017) was awarded with the cover page of the journal issue.
7. Isaac Garcia was awarded with the highly competitive PAI-CONICYT program, a national competition for advanced human capital insertion into the academy. This grant will allow him to obtain an academic position in the Faculty of Odontology of the Universidad de Valparaíso. The proposal was granted to study the role of hemichannels in the mechanism of dental pain.
8. Juan Carlos Sáez won an open competition for an academic full position in the Universidad de Valparaíso. The competition was open to national and international applicants with the level of senior scientist and full professor.

4. Education and Capacity Building

a) Education and Capacity Building:

The PhD Program in Neuroscience Its Director is currently Dr. John Ewer (CINV, Research line 3). This Program is designed to train researchers interested in the development, the structure, and the function of the nervous system. Its strengths are the areas of molecular physiology and biophysics, computational neuroscience, sensory neuroscience, neuronal plasticity and neuropathology, and development and neurogenetics. This program supports the intellectual and research needs of our students, and encourages them to take elective courses at other universities in Chile and abroad, as well to carry out research internships abroad. The latter is possible through collaborative arrangements of CINV investigators. This program was founded in 2002 and has been continuously accredited since 2004. Last year it was re-accredited for a record 7 years, through 2025, which was an important recognition to the high quality of the program. As the external reviewers indicated, the presence of the CINV within the Universidad de Valparaíso was fundamental for the extension of the accreditation. We have continued admitting high quality students to the program. Most significantly, the proportion of students originating from Santiago has been increasing. Thus, the program has matured and can compete effectively with programs in Santiago, despite the draw of the capital. Our Program ensures funding for 4 years to all students it accepts, thereby allowing students to devote themselves full time to their Ph.D. In addition to fellowships from the Government funding agency (CONICYT, available only to accredited graduate programs) and from the University of Valparaiso, the CINV-ICM also provides graduate fellowships (12 during this period). *Requirements to apply to the Program were explained in first CINV-Report, and can also be found at the Program's website: www.dnuv.cl*.

Ph.D. program in Biophysics and Computational Biology (Program Director: Dr. Patricio Orio, Line 5). This Program started in March 2015 with 4 students from Valparaíso and Santiago, and is one of our main achievements in education and training. Its main goal is to train scientists to understand biological processes through their physical-mathematical formalization. This requires the integration of interdisciplinary studies, from the molecular level to mathematical modeling. We receive students with diverse undergraduate training, from mathematics and physics to biology. A flexible study plan allows each student to quickly obtain the knowledge and abilities most related to their thesis field, plus a common background in Biophysics of Excitability and Computational Biology. During 2017, the program had 10 students, one of which graduated at the end of 2017; another 3 are carrying on their thesis work. For the 2018 academic year, we accepted 5 new students. Last year all students participated in different international courses and Congresses, and 2 travelled abroad for international stays to carry out work relevant to their thesis. The Program is currently accredited (by the National Commission on Accreditation), allowing its students to apply for CONICYT Doctoral fellowships.

The Masters Program in Neuroscience currently directed by Dr. Agustin Martinez (CINV research Line 2). The program is accredited until 2018. The program is characterized by a high content of basic Neuroscience and mechanism of neuropathology and psychiatric disorders in a multidisciplinary environment. Its students are from various disciplines: biologists and biochemists as well as health professionals, engineers, and mathematicians.

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

Postdoctoral training. Twenty seven postdocs worked in our center during 2017, of which 14 were financed through CINV, 6 have postdoctoral FONDECYT grants and 7 other fundings. Most of them are working in collaborative research inside and between different research lines, for example, Isaac Garcia worked in the opening and closing mechanism of hemichannel (Lines 1 and 2), Felipe Villanelo developed molecular models of different channels (Lines 5 and 1). One of the mechanisms to improve the collaboration between lines was the establishment of a special postdoctoral fellowship award for postdoctoral trainees with a project linking two laboratories. For example, Dr. Maldifassi obtained this award to study the functional and molecular interaction between Panx1 channels and alpha7 nicotinic receptors in the nervous system, which is a collaboration between Drs. Cárdenas and Martinez of line 2. The high scientific quality of our postdocs is demonstrated by obtaining FONDECYT postdoctoral awards for 2018 contest by Drs Maldifassi, Palacios, and Flaven. Furthermore, Dr. Angélica Escobar, one of our postdoctoral candidates recruited during 2017, was selected to contribute a commentary in the competitive "Journal Club" section of the Journal of Neuroscience (Escobar A. 2017 *J. Neurosci*). We encourage our postdocs to develop their independent career. Last year Dr. Garcia obtained an academic position in the faculty of odontology, through a PAI-CONICYT grant, to study the role of hemichannels in oral pain.

b) Achievements and results:

PhD Program: 40 students have graduated since 2002 (11 female; 29 male), of which 2 graduated during this period (see list below). The Program currently has 53 students (29 female, 24 male). During this year's recruitment period 9 students were selected and accepted to join the Program. Of these, 8 received fellowships from CONICYT (a new record for the Program); the remaining student received a fellowship from the University of Valparaiso. 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 (e.g., 2015 and 2017) to 6 (2016) per year. Similarly, our success in securing fellowships from CONICYT also varies widely, from 20% to 100%, even though the applicants are qualitatively academically comparable. 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.

Master Program: 71 students have graduate since 1999 (40 females; 31 male), of which 11 graduated during this period; 6 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 35 applications of which 21 were accepted, being close to the maximum number of students we are able accept every year. Of these, 2 received fellowships from CONICYT. During the interview process several applicants mentioned the existence of the CINV as part of the reasons for choosing our program, suggesting that the CINV has given more visibility to this program.

Main achievements of Ph.D. and Master Students from our programs during the period: During this period, forty-eight students are co-authors of 27 articles and of these, eight were first authors.

CINV ANNUAL PROGRESS REPORT – 2017

Graduations of students

***PhD Program in Neuroscience*: 1.- Mauricio Aspé.** Title: Unmasking reciprocity: behavioral component and neural correlates of human trustworthiness. Advisor: J. Ewer; co-advisor: R. Rumiati (SISSA, Trieste, Italy) (Line 3). **2.- Cristián Calfún.** Title: "Genomic Plasticity in the Olfactory Epithelium mediated by Odorant Exposure in Zebrafish (*Danio rerio*)." Advisor: K. Whitlock (Line 3).

***Ph.D. program in Biophysics and Computational Biology:* 1.- Bernardo Pinto.** Title: "Role of charged amino acids in the voltage dependence and inhibition by calcium of connexin channels." Advisors: Carlos González and Ramón Latorre (Line 1).

Masters Program in Neuroscience: *Last year we have graduated 11 students of which six did their thesis in laboratories of the CINV, listed below.* **1.- Marco Lovera Cabello.** Title: "Characterization of neuro-immune components in the pulp of healthy teeth and chronic periodontitis.". Advisor: Dr. E. Couve in collaboration with O. Schmuchtenberg (Line 4). **2.- Evelyn Cordero Roldán**. Title: "Bibliographic review: genetics and behavior of attention deficit hyperactivity syndrome." Advisor: Dr. P. Moya. **3.- Elvira Cortése Saavedra.** Title: "Mechanism of gentamicin toxicity mediated by panx1." advisor: Dr. A. Martínez (Line 2). **4.- Jesús Olivares Dubart** . Title: "Spider corner (Loxosceles laeta) as a biological model in neurosciences.". Advisor: Dr. O. Schmachtenberg (Line 4). **5.- Claudia Salazar Salazar**. Title: "Octodon degus a natural model of aging and neurodegeneration: the role of voluntary exercise in memory." Advisor: Dr. A. Palacios (Line 4). **6.- Indira Lara Pattzi.** Title: "Role of the TRPV1 channel in the modulation of the transmission, excitatory synaptic during postnatal development in the hippocampus." Advisor: Dr. A. Chavez (Line 4).

Thesis Project Approvals and Qualifying exams:

***PhD Program in Neuroscience*: 1.- Daniela De Giorgis.** Title: "Regulation of voltage sensing structures of CaV1.2 Calcium channel by the auxiliary B-Subunit." Advisor: A. Neely (Line 1). **2.- Nicolás Ardiles.** Title: "Relación entre alteraciones de la expresión de EAAT3 en el núcleo accumbens y conductas tipo-depresivas." Advisor: P. Moya (Line 4). **3.- Adolfo Agurto**. Title: "Changes in 5-HT2A receptor activity in orbitofrontal cortex pyramidal neurons underlying escalated aggression." Advisor: P. Moya (Line 4). **4.- Cristofer Reyes**. Title: "Regulation of the expression of Orexins by the serotonin 5-HT1A receptor through Foxa2 factor." Advisor: P. Moya (Line 4). **5.- Valentina Haro**. Title: "Modulation of the TRPV1 channel mediated by activation of 5-HT2 receptors." Advisor: Pablo Moya (Line 4).

Masters Program in Neuroscience: Last year 11 thesis projects were approved, of which 8 are advised by CINV members: **1.- Marcela Benavides Bastías.** Title: "Methylations in the promoter of the bdnf, nr3c1 and ska2 gene are associated with suicidal events and are associated with aggressive and impulsive coping strategies." Advisor: Dr. Dr. Pablo Moya (Line 4). **2.-Tito Castillo Varas**. Title: "Study of case-control association of polymorphisms in the genes of dopa decarboxylase (ddc), dopamine d2 receptor (drd2) and endocannabinoid cr1 receptor in schizophrenia." Advisor: Dr. Dr. Pablo Moya (Line 4). **3.- Fernanda Espinosa González**. Title: "Levels of methylation in genes nr3c1, slc6a4 and fkbp5 and relation with intellectual capacity tests in adolescents belonging to a municipal establishment of secondary education, of the seventh region of the maule." Advisor: Dr. Pablo Moya (Line 4). **4.-Sebastián Estay Vizcarra.** Title: "Mechanisms that regulate the development and refinement of reciprocal gabaergic

synapses on bipolar rode cells." Advisor: Dr. Andrés Chavez (Line 4). **5.- Ricardo Illesca Matus.** Title: "Evaluation of the expression of the serotonin transporter as a mediator of the effect of voluntary exercise on episodic memory." Advisor: Dr. Pablo Moya (Line 4). **6.- Cristian Malhue Vásquez.** Title: "Mechanism of negative dominance of human mutants associated with deafness cx26g59a and cx26g59v on wild connexins." Advisor: Dr. Agustín Martínez. (Line 2). **7.- Soraya Mora Barrientos.** Title: "Detection of neuronal assemblies in ganglion cells of the retina of octodon degus." Advisor: Dr. Adrián Palacios. (Line 4). **8.- Nicole Sanguinetti González.** Title: "cb1 receptor located in gabaergic neurons expressing somatostatin regulate the synaptic transmission in the prefrontal cortex." Advisor: Dr. Chiayu Chiu (Line 4).

Students visiting laboratories abroad: **1.- Bernardo Pinto** (Ph.D. Student: advisor: Dr. Carlos González, Line 1). Visited Dr. Bezanilla's laboratory (University of Chicag, USA) to work colaborative in "Optocapacitive Generation of Action Potentials by Microsecond Laser Pulses of Nanojoule Energy". **2.- Melissa Alegría** (Ph.D student in Graduate Program in Biophysics and Computational Biology) visited the lab of Patricia Babbit (University of California, San Francisco, USA), October-December 2017.

Students graduated from other postgraduate programs with Thesis inside CINV**: 1.- Ximena Báez Matus** (Master in Cellular and Molecular Biology; UV). Title: "Role of dysferlin in the remodeling of cortical F-actin in muscle cells: Implication in in vitro models of dysferlinopathies.": Advisor: Dr. A. M. Cárdenas (Line 2).

Graduation of Undergraduate students: **1.- Victor Manuel Calbiague**, (Bachelor of Science, UV). Title: "Patch clamp analysis of bipolar cell properties in rat retinal explants compared to retina ex – vivo." Advisor: O. Schmachtenberg (Line 4). **2.- Daniela Ponce López**, (Bachelor of Science, UV). Title: "Analysis of the olfactory potency of the water-soluble fraction of crude oil by means of electroolfatogram records in rainbow trout." Advisor: Dr. O. Schmachtenberg (Line 4). **3.-Constanza Bertea Seissus** (Bachelor of Science, UV). Title: "Loxosceles laeta venom toxicity assays in human fibroblast cultures." Advisor: O. Schmachtenberg (Line 4). **4.- Cindel Figueroa Cades** (Bachelor of Science). Title: "Evaluation of the dynamics of the actin cytoskeleton in dysferlin-deficient cell lines and generation of a dysferlin-GST construct." Advisor: Dr. A. M. Cárdenas. (Line 2). **5.-Antonio Peña Pichicoi** (Professional title of biochemist PUCV). Title: "Identification of the Hv1 proton channel in mouse suppressor myeloid derived cells." Advisor: Dr. C. González (Line 1).

Organization of national and international courses: Our center has participated and / or organized many national and international scientific teaching initiatives, like courses and workshops, as part of our networking activities (see networking section).

5. Networking and other collaborative work

a) Networking

During 2017, the CINV has consolidated both its national and international collaborations, alliances that allowed the organization in Valparaíso of important Symposia and International Meetings.

As part of the **Genetic and Development Network** the highlight of 2017 was the LASC (Latin American Symposium on Chronobiology) that is held every two years in a different Latin American country; it was held for the first time in Chile, November 2-7, 2017. The lead organizer was John Ewer (Line 3); co-organizers included Carola Millán (U. Adolfo Ibáñez), Luis Larrondo (P. U. Católica) and Adrián Ocampo (U. de Chile). The symposium was an opportunity to discuss concepts and recent results related to the circadian clock and sleep in a variety of systems and was organized around the following general topics: human circadian rhythms, sleep, circadian clock networks, and molecular clocks. In addition to representing a unique opportunity to learn and discuss the latest findings in the field, this symposium provided Latin American researchers with an opportunity to identify research topics and approaches that could be addressed through international collaborative work. The complete program can be found at: http://cinv.uv.cl/lasc2017/program-2/. By all accounts, The 2017 LASC was a successful and well-organized symposium, with a good diversity of topics and participation from Latin American researchers (in addition to invitees). An important highlight was the participation of Dr. Michael Rosbash (Brandeis University, USA), co-recipient of the 2017 Nobel Prize in Physiology or Medicine for his work on the circadian clock of *Drosophila*. In total 170 persons registered for the symposium, mostly from Chile (46%), Brazil (24%), and Argentina (19%), but including Mexico (5%), Uruguay (4%), and USA (2%). Registrants included Faculty/Principal investigators (38%), postdoctoral fellows (12%) and students -mostly PhD students- (50%). Importantly, there was almost complete gender parity in all categories (students, postdocs, and faculty, and invited and plenary speakers).

As part of our network in **Biophysics and Computational Neuroscience**, four important activities were carried out. **1**. The 4th Latin-American Summer School in Computational Neuroscience (LACONEU) in January 2017 (Dr. Orio and Dr. Palacios, Line 4). During three weeks, 27 students (15 Chilean, 10 from other Latin-American countries and 2 from Europe) attended lectures and hands-on training from 16 speakers (9 from US and Europe) and 4 tutors on cutting-edge topics about the computational analysis of the brain activity, with emphasis on network dynamics. This school also included a 1-day Workshop"Computational Neurosciences: Trends and Challenges for the 2030" open to the public. LACONEU is now consolidated as a high-level training opportunity for students in Latin-America and abroad. **2.** From November 20 to December 2, 2017, we co-organized together with Fundación Ciencia & Vida (Santiago, Chile) the second version of the International Spring School Applied Statistical Thermodynamics 2017: from theory to molecular dynamics simulation (AST2017) (Dr Gárate, Line 5, Young Investigator; Dr Perez-Acle, Line 5 and Fundación Ciencia y Vida). In AST2017 participated as lecturers Professors Willem F van Gunsteren from the Swiss Institute of Technology (ETH), Zürich, Suiza; Chris Oostenbrink from the University of Natural Resources (BOKU), Vienna, Austria ; Jose Antonio Garate, from the CINV, Valparaíso, Chile; and Tomas Perez-Acle

from CINV-Fundación Ciencia & Vida, Santiago, Chile. **3**. Dr González-Nilo (Line 5, Translational Unit) organized a Workshop on integration of Target Discovery, Drug Discovery and Drug Delivery TD4, in the Universidad Nacional Andrés Bello (UNAB), Santiago, 20-24 November, 2017 with the assistance of Dr. Serge Mignani, CNRS, France as one o the main speakers. He also organized the Workshop: Beyond Kd: ITC versus Free Energy Calculations, UNAB, Santiago, 11-13 December, 2017. International Invitees: Christophe Chipot (CNRS research director, University of Lorraine, France) and Chad Brautigam (The University of Texas Southwestern Medical Center, Texas, USA).

Invited by Dr Carlos González (Line 1, Translational Unit), Dr. Anselmo Otero, Professor at University of Havana, Cuba, shared 15-day stay at the CINV in April 2017. During this period he teach immunotherapy and production of biotechnological compounds, such as polyclonal and monoclonal antibodies to our students. Together with Dr. González, he wrote a grant, to obtain specific blockers of the proton (Hv1) channel for therapeutic purposes.

The CINV has also been active outside Chile and Dr. Calixto (Line 3), in conjunction with two investigators of the Pasteur Institute in Montevideo, organized the 1st *C. elegans* Latin American meeting held in the Pasteur Institute in February 2017, in Uruguay.

Future meetings that will attract scientists from all over the world were set forward in 2017. For example, in November of 2017, Dr. Chiu was invited to attend the annual meeting of the MP Group Leaders that was hosted by MPFI in Florida. During this 2-day retreat, Dr. Chiu was introduced to fellow Max Planck Group Leaders in South America. To solidify this new relationship, Dr. Chiu, with the help of the CINV, is planning to host a conference of the Max Planck Group Leaders in Valparaiso in December 2018. Among the invited speaker are: Drs. David Fitzpatrick, Reohei Yasuda and Hyungbae Kwon from MPFI (USA), Drs. Damián Refojo, Antonia Marin Burgin and Luis G. Morelli from Biomedicine Institute of Buenos Aires - CONICET (Argentina) and Dr. Reinhard Jahn from the Max Planck Institute for Biophysical Chemistry (Germany).

b) Other collaborative activities.

Individually, CINV scientists have visited several laboratories around the world strengthening or originating new collaborations. **1.** After a productive visit to Hong Kong, Dr Sáez (Line 2) initiated new collaboration with Dr. Geoffrey Lau from City University of Hong Kong who works on epilepsy, one of the research areas of interest of Line 2. He also met two French scientists. Dr. Eric Honoré and Laurent Counillant. Dr. Honoré will visit the CINV on April 2018 and will give a seminar on stretch-activated channels and Dr. Counillon will visit the CINV on August 2018 and will give two talks in the Latin American Training Program sponsored by SfN and CINV. Both researchers have manifested their interest to establish collaborations with scientists of the CINV. **2.** Most recently, using optogenetics to activate selectively specific GABAergic interneuron subtypes, Dr. Chiu (MPTRL) showed that inhibitory synapses from dendrite-targeting somatostatin-expressing (SOM-) interneurons are selectively potentiated by excitatory glutamatergic activity (Chiu et al., Neuron, 2018). In a broader context, this work suggests a tight link between the regulation of inhibitory circuits to their function. Whereas perisomatic inhibition from parvalbumin interneurons shapes and are shaped by principal cell firing (cell output), dendritic inhibition from SOM-interneurons modulates and are modulated by synaptic activity (cell input). The completion of this project was made possible by two trips to the laboratory of her

postdoctoral mentor, Dr. Michael Higley, at Yale University in 2017 (February and October), which were supported by CINV funds. Dr. Chiu is continuing her collaboration with Dr. Higley, with two publications in preparation. **3.** Dr Moya (Line 4) was invited to become part of the American College of Neuropsychopharmacology (ACNP) Latin America Advisory Group, during the 56th Annual Meeting held on December 3-7, 2017 in Palm Springs, California. During the official session at the meeting, the ACNP Latin American Advisory Group worked in: a) to establish a structure and venue for communication to all Latin American scientists and clinicians that belong to ACNP. b) to promote and communicate the mission of ACNP across Latin American societies and universities. c)to coordinate efforts aimed at increasing participation of established investigators from Latin America to the annual ACNP meeting. d) to act as a magnet and a mentoring venue to attract/encourage the most promising young scientists and clinicians from Latin America to participate at the ACNP meeting and apply for membership. Advisory Group calls were planned for 2018 (every other month) to continue working in the mentioned tasks. **4**. Dr. Chavez lab continues its international collaboration with Dr. Pablo Castillo (Albert Einstein College of Medicine, USA) in order to understand the mechanism underlying synaptic transmission and plasticity in the hippocampus, a key brain area involved in cognitive processes such as learning and memory. He also actively collaborate with Dr. Mario Penzo (NIMH, NIH, USA) to understand the functional role of the non-selective cationic channel TRPV1, a well-known channel involved in pain sensation, to regulate anxiety and fear behavior. **5.** Dr. Latorre has continued his long-standing collaboration with Drs. Bezanilla and Holmgren and trough CINV and the Air Force Research Office of USA they have installed a well-equipped laboratory to continue their inquiries regarding the mechanism of protein synthesis in axons. On the other hand, as part of the Council of the Latin American Academy of Sciences Dr. Latorre attended a meeting of the Council in Bogota, Colombia where he established strong ties with Colombian and Venezuelan scientists and was charged to organize the next council meeting in Santiago, Chile.

6. Outreach and connections with other sectors

a) Outreach:

During its first five-year period as a Millennium Institute, the goal of the CINV was to differentiate itself from the traditional ways of communicating science to the general public in Chile. During this second period, the Outreach activities of CINV had the aim of conveying to the citizen that the adequate development of science is essential if Chile wants to become part of the developed countries. In particular, we have tried, through the research done in neuroscience at the CINV, to communicate to non-scientific public the advantages of understanding how the nervous system works and how its malfunction may lead to problems of national importance. In this regard, different researchers of the CINV are recognized spokespeople in specific areas of science for authorities and also for the press. For example, the opinions of Dr. R. Latorre are a national reference with regard to scientific policy. His presence in the national press and in Congressional Commissions is an important effort to explain the role of science for the adequate development of the country, in particular in regions outside Santiago (capital of Chile), in an extremely centralized country. In addition, Dr. T. Pérez-Acle fulfills the same role, explaining natural disasters and massive infections through the work of computer models, and their role in the future society. On the other hand, Dr. J. Ewer is recognized as the scientist able to explain how a political decision regarding the daylight saving time system, have important consequences for health of children and young people in Chile. With a permanent presence in press, including a debate with the Minister of Energy, Dr. Ewer was able to explain how knowledgeable Chilean scientists can help in the development of better public policies in our country. An important achievement was the national press coverage of the visit of the 2017 Nobel laureate Dr. M. Rosbash to the XIV Latin American Symposium on Chronobiology 2017 (LASC 2017) organized by the CINV, including a public talk and a Press conference with the main National press outlets. The product of CINV outreach actions amounted to important number of articles in newspapers, appearances in radio, TV, and internet throughout the country.
The most relevant 2017 CINV outreach activities were:

Falling Walls Chile: In partnership with the Fundación Ciencia Joven (Young Science Foundation), the CINV brought the Falling Wall Lab contest to Chile for the second time. This event seeks to identify innovative young people in all areas of knowledge, and its purpose was to select the young innovator who will represent Chile at the global Falling Walls event in Germany in 2018, where about 100 young people of all around the world will present their innovative projects. With the participation of Guido Girardi, Senator and President of the Commission "Congreso del Futuro", which promotes the adequate interaction between science and national policies, the seven candidates selected for the final stage in Valparaiso presented their innovative ideas in 3 minutes. With national and regional press coverage, and the support of institutions like Congreso del Futuro, the German cooperation agency (DAAD), and a jury lead by the Deputy Director of CINV, Dr. Juan C. Sáez, this activity of the CINV continues to position Valparaiso as a beacon of science in Chile.

Ciencia Al Tiro 2017: One of the greatest challenges in Chilean society is to communicate the value of science to the general public. In 2016, this outreach program were awarded a "Concurso Nacional de Proyectos EXPLORA de Valoración y Divulgación de la Ciencia y la Tecnología"

to produce 10 videos based on our book "La Alegría de la Ciencia". The goal of these videos is to show how science is part of everyday life and celebrate science within the context of familiar situations: the difference between the motor of a bus and of a trolley; what can we do about all the rotting garbage; how can we capture solar energy, etc. We started filming in Jan. 2017 and celebrated the release of the videos in July 2017. The videos were evaluated by teachers from the Regions of Valparaiso, Antofagasta, and Bio Bio and received excellent ratings. Currently the videos are being shown on UCV-TV (www.ucv3.cl) and the "Canal de television de la Camara de Diputados" is now interested in airing the program nationally. In the videos the main protagonist is "Cata" played by Doctorate student María Fernanda Palominos. She is accompanied by Yury (Yury Duran) and Giaco (Giacomo Silva), two students from Valparaíso´s public schools who participate in the Ciencia Al Tiro program. The three characters pass through Valparaiso asking questions about how things work and use science to find the answers. This project was financed by CONICYT/Explora, CINV, Univ. de Valparaíso, Fundacion Chileno-Americana (http://chileusfoundation.org) and Ciencia Que Pesca (www.cienciaquepesca.cl). During 2017 we continued to develop and implement new science workshops on the theme of Sensory Systems. In these workshops, we have simple experiments that explore how our nervous system processes sensory signals. These workshops will be developed into our next book: "La alegria de los Sentidos".

NeuroNews: In 2017, NeuroNews continued its successful formula permitting graduate students of Neuroscience. to select a recent high-impact publication in a neuroscience.-related topic of their interest, and convert it into an entertaining news story for the general public. In total, 16 NeuroNews articles were produced, the majority of which were published in the online newspaper El Mostrador. A trademark of NeuroNews is the great variety of topics covered. In 2017, we would like to highlight here several articles on diverse subjects including: fake news on Facebook, the consumption of Ayahuasca, depression in adolescents, evidence for altruism in ravens, phobias in humans and the effects of sad music on them, cerebral activity during orgasms in women, and the mechanisms involved in contagious itching. In parallel, a collection of the best NeuroNews stories of the last years was compiled, professionally edited by two external journalists, and illustrated to create a scientific book entitled "DeMente". It will be published by Editorial Catalonia in the course of 2018, and distributed through the best libraries of the country.

Audiovisual Productions. Each year, the CINV develops or takes part in audiovisual products related to science outreach. In 2017, the CINV continued promoting the documentary "Montemar and the labyrinths of memory" (2015), which tells the history of the laboratory of Montemar, near Valparaíso, and the scientists who started the development of Biophysics in Chile. This production of CINV in partnership with Cábala Producciones was transmitted on national television (UCV Televisión). It had a very high rating opening the possibility that UCV television broadcast other productions of our center, such as "La Alegría de la Ciencia", the TV serie created by Dr. K. Whitlock, researcher of the CINV. In addition, Youtube has broadcasted the documentary "Montemar and the labyrinths of memory" already exceeding 8,000 views. For comparison, we found that the average number of viewers of Chilean films released in cinemas in 2017 was close to 9,500, and of documentaries it was 1,750. In January 2018, the organization

of Congreso del Futuro invited us to present the documentary in four different regions of the country.
During 2017, the CINV appeared in more than one hundred different news reports, which were disseminated through television, radio, newspapers (national and regional), as well as through the Internet. The media presence of the CINV includes coverage in major national newspapers including *El Mercurio*, *La Tercera*, and*Ultimas Noticias*, the financial newspaper *Diario Financiero*, as well as various regional newspapers. We have also had continuous coverage through *El Mostrador,* one of the country's most widely read electronic newspapers. Finally, we have also attracted special press coverage through the main TV channels (*TVN*, *Chilevisión*, *Canal 13*).
The economic value of this presence in the country's mainstream press is estimated to be $ 292 million CLP (almost $ 490,000 USD). Considering that the news that emerges from regions receives less covered than does the news that originates from the capital, the strong presence of the CINV (a regional center) in different media, further attests to the importance of the news we are providing.

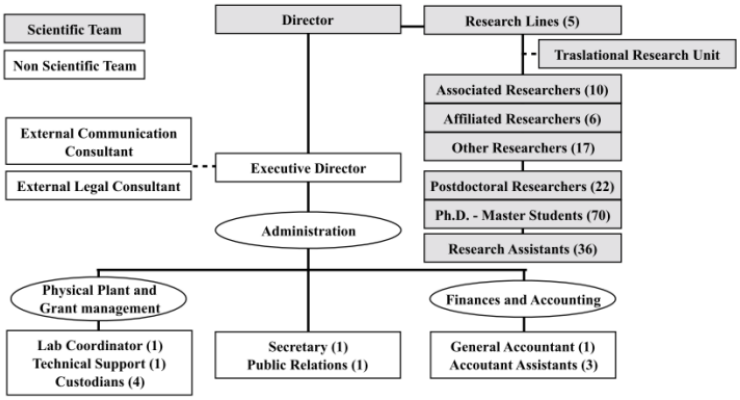
b) Connections with other sectors:

Juan Ignacio Molina Building (formerly Severín Building): A crucial step for the new CINV science building in Valparaíso was the completion of the bidding and adjudication process. The construction will begin in 2018, and the building will be operative in about 2 years. The support of authorities like the Valparaíso Mayor, Senators, and Ministries, who have become aware of the importance of CINV in national science and regional development, made possible the accomplishment of this unique project that will recover a historical Valparaíso neighborhood.

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

7. Administration and Financial Status

a) Organization and administration:



An Executive Director supervises and coordinates all administrative duties according to the needs of the Director and other Researchers. This includes managing the Millennium Institute Grant and all other grant of CINV researchers (about 17 grants per year). He also coordinates outreach and networking activities with the private sector and 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 the Accounting Team, which manages the grants and human resources; a Physical Plant and Project Support team 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 activities (Symposia, Congresses) and outreach activities. Each host institution provides office and laboratory space for the individual holding faculty positions. The base salary of individual researchers 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	14	21	35
Administrative Staff	11	5	16
TOTAL	33	28	51

b) Financial Status:

During 2017, the CINV had a total income of CLP$2.281.990.276.- (USD$3,187,129), to which the Millennium Scientific Initiative (ICM) contributed 38%. The contribution of the (ICM) was 55.7% for 2012, 35.4% 2013, 42.0% 2014, 44% for 2015 and 43% for 2016. Other sources of income for CINV come from CONICYT (34% in 2017) and the Universidad de Valparaíso (22% in 2017) and foreign grants (6% in 2017).

In relation to the contribution made by ICM, the greatest share corresponds to the category "Responsible Researcher, Scientific and Additional Personnel" with 49%, mainly due to the incorporation of a Max Planck Research Leader, Assistant investigators and their technical staff. In addition, to maintain for the third consecutive year the scholarships for PhD in Biophysics and Computational Biology of the Universidad de Valparaíso, created and directed by CINV. There was also an increase in the purchase of goods and equipment (28%) for the implementation of Dr. Chiayu Chiu's laboratory and the implementation of the two-photon microscope.

8. Annexes:

Annex 1.- Institute / Nucleus Researchers

1.1 Associate Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Adrián Palacios Vargas	System and circuits neuroscience.	Chilean	M	03-18-1958	Psychologist	D	Universidad de Valparaíso	Professor UV CINV Researcher.	2
Alan Neely Delgueil	Structure and function of molecular sensors.	Chilean	M	04-15-1956	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2
Ana Maria Cardenas Diaz	Cellular signaling.	Chilean	F	04-01-1969	Pharmacist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2
Fernando Danilo González Nilo	Molecular simulation and computational biology.	Chilean	M	12-09-1968	Chemist	D	Center for Bioinformatics and Integrative Biology (CBIB) Universidad Andrés Bello	Professor U. Andrés Bello CINV Researcher	2
John Ewer Lothian	Genetics and developmental neuroscience.	Chilean	M	02-23-1961	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 UV CINV Researcher	2

Kathleeen Whitlock Leaning	Genetics and developmental neuroscience.	US Citizen	F	08-27-1963	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2
Ramón Rogelio Latorre De la Cruz	Structure and function of molecular sensors.	Chilean	M	10-29-1941	Biochemist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2
Tomás Pérez Acle	Molecular simulation and computational biology.	Chilean	M	09-09-1970	Biologist	D	Fundación Ciencia para la Vida	F. Ciencia & Vida and CINV Researcher	2

1.2 Young Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Alvaro Ardiles Araya	Cellular Signaling.	Chilean	M	02-12-1977	Biochemist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2
Chiayu Chiu	System and Circuits Neuroscience	USA	F	03-21-1974	Neuroscientist	D	CINV	CINV - Max Planck Tandem Research Leader	1
Helmuth Sanchez Riquelme	Cellular Signaling.	Chilean	M	06-19-1978	Biologist	D	CINV	CINV Young Researcher	1
Isaac Eduardo García Carrillo	Structure and function of molecular sensors.	Chilean	M	04-20-1978	Medical Technologist	D	Universidad de Valparaiso	CINV Young Researcher	1
José Antonio Gárate	Molecular simulation and computational biology	Chilean	M	07-29-1983	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	07-23-1979	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	03-05-1958	Biologist	D	John Hopkins University	Professor	2
Francisco Bezanilla	Structure and function of molecular sensors.	Chilean	M	05-17-1944	Biochemist	D	Chicago University	Senior Investigator	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	05-03-1962	Biophysicist	D	NIH-NINDS Molecular Neurophysiology section. Porter Neuroscience Research Center	Senior Investigator	2
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	12-02-1962	Pharmacist	D	Universidad Nacional de LaPlata	Professor	2
Riccardo Olcese	Structure and function of molecular sensors.	Italian	M	05-26-1962	Physician	D	UCLA	Professor	2

1.4 Others

Full Name	Research Line		Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Agustín Demetrio Martínez Carrasco	Cellular signaling.	Chilean	M	03-18-1958	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2
Andrea Leonor Calixto Mohor	Genetics and developmental neuroscience.	Chilean	F	09-04-1974	Biologist	D	Universidad Mayor	Professor U. Mayor CINV Researcher	2
Andrés Eduardo Chávez Navarrete	System and circuits neuroscience.	Chilean	M	01-10-1977	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2
Carlos González León	Structure and function of molecular sensors.	Cuban	M	12-13-1965	Biophysicist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2

Daniel Aguayo Villegas	Molecular simulation and computational biology.	Chilean	M	08-08-1978	Biochemist	D	Universidad Andrés Bello	Professor U. Andrés Bello	2
David Oliver Naranjo Donoso	Structure and function of molecular sensors.	Chilean	M	10-17-1957	Biologist	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 Ricardo Moya Vera	System and circuits neuroscience.	Chilean	M	09-09-1975	Biochemist	D	Universidad de Valparaiso	Professor UV CINV Researcher	2
Patricio Rodrigo Orio Alvarez	Molecular simulation and computational biology .	Chilean	M	12-03-1973	Biochemist	D	Universidad de Valparaíso	Professor UV CINV Researcher	2

1.5 Postdoctoral

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Alberto Jesus Martin Martin	Molecular simulation and computational biology.	Spanish	M	06-08-1980	Biologist	D	Fundación Ciencia & Vida	Postdoctoral	2
Alex Harry Vielma Zamora	System and circuits neuroscience.	Chilean	M	01-05-1979	Biochemist	D	Universidad de Valparaiso	Postdoctoral	2
Angelica del Pilar Escobar Maldonado	System and circuits neuroscience.	Chilean	F	07-15-1985	Pharmaceutical chemist	D	Universidad de Valparaíso	Postdoctoral	2
Angelina del Carmen Palacios Muñoz	Genetics and developmental neuroscience.	Chilean	F	07-12-1981	Biochemist	D	Universidad de Valparaíso	Postdoctoral	2
Arlek Marion González Jamett	Cellular signaling.	Chilean	F	11-07-1981	Biochemist	D	Universidad de Valparaíso	Postdoctoral	2
Estefanía Andrea Hugo Caselli	Molecular simulation and computational biology.	Chilean	F	06-09-1987	Chemist	D	Universidad de Valparaíso	Postdoctoral	1
Felipe Alberto	Molecular simulation	Chilean	M	05-16-1982	Biochemist	D	Fundación Ciencia &	Postdoctoral	2

Villanelo Lizana	and computational biology.						Vida		
Florence Anne Laure Gutzwiller	Genetics and developmental neuroscience.	France	F	03-26-1987	Biologist	D	Universidad Mayor	Postdoctoral	1
Germán Andrés Miño Galaz	Molecular simulation and computational biology.	Chilean	M	05-29-1971	Biochemist	D	Universidad Andrés Bello	Postdoctoral	2
Gustavo Felipe Contreras Cáceres	Structure and function of molecular sensors.	Chilean	M	09-15-1982	Biomedical engineer	D	Universidad de Valparaíso	Postdoctoral	2
Hans Joseph Moldenhauer Barrientos	Structure and function of molecular sensors.	Chilean	M	02-22-1983	Biochemist	D	Universidad de Valparaiso	Postdoctoral	2
Ignacio Antonio Díaz Franulic	Molecular simulation and computational biology.	Chilean	M	04-02-1981	Biochemist	D	Universidad de Valparaiso	Postdoctoral	2
Javier Vicente Alvarez Zepeda	Genetics and developmental neuroscience.	Chilean	M	01-29-1971	Aquaculture engineer	D	Universidad de Valparaíso	Postdoctoral	2
Karel Mena	Structure and function of molecular sensors.	Cuban	M	09-10-1975	Biologist	D	Universidad de Valparaíso	Postdoctoral	2
Justin Arthur Hugo Flaven	Genetics and developmental	France	M	08-29-1987	Biologist	D	Universidad de Valparaíso	Postdoctoral	2

Pouchon	neuroscience.								
Kesheng Xu	Molecular simulation and computational biology.	Chinese	M	10-02-1983	Physicist	D	Universidad de Valparaíso	Postdoctoral	2
Bruno Alejandro Cisterna Irrazabal	Cellular Signaling.	Chilean	M	13-11-1982	Medical Technologist	D	Pontificia Universidad Católica de Chile	Postdoctoral	2
Leonel Eugenio Medina Daza	Molecular simulation and computational biology.	Chilean	M	08-27-1980	Civil engineer	D	Universidad de Valparaíso	Postdoctoral	2
María Constanza Maldifassi Gatica	Cellular signaling.	Chilean	F	11-07-1979	Biochemist	D	Universidad de Valparaíso	Postdoctoral	2
Maria Guadalupe Cascallares	Genetics and developmental neuroscience.	Argentinian	F	01-18-1988	Physicist	D	Universidad de Valparaíso	Postdoctoral	2
Marlene Natalia Arismendi Macuer	Molecular simulation and computational biology.	Chilean	F	10-08-1980	Biochemist	D	Universidad Nacional Andrés Bello	Postdoctoral	2
Nicolás Palacios Prado	System and circuits neuroscience.	Chilean	M	06-30-1981	Biologist	D	Pontificia Universidad Católica de Chile	Postdoctoral	2
Nicolás Palanca	System and circuits	Spanish	M	05-14-1987	Biologist	D	Centro Interdisciplina	Postdoctoral	2

Castan	neuroscience.						rio de Neurociencia de Valparaíso		
Pavel Prado Gutierrez	Cellular signaling.	Chilean	M	03-22-1976	Biologist	D	Universidad de Valparaiso	Postdoctoral	2
Rosalba Escamilla Hernández	Cellular signaling.	Chilean	F	02-06-1971	Biochemist	D	Pontificia Universidad Católica de Chile	Postdoctoral	2
Yorley Andrea Duarte Ayala	Molecular simulation and computational biology.	Colombian	F	10-10-1982	Nutritional Chemist	D	Universidad Andrés Bello	Postoctoral	1
Willy Reinaldo Carrasquel Urzulaez	Structure and function of molecular sensors.	Venezuelan	M	06-01-2018	Biologist	D	Universidad de Valparaíso	Postdoctoral	2

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 and function of molecular sensors	We try to understand how ion channels and pumps can respond to a variety of stimuli.	It is a combination of molecular biology, electrophysiology, modern fluorescence techniques, simulations and molecular modeling.	R. Latorre O.Alvarez V. Milessi F. Bezanilla G. Ferreira M.Holmgren C. González K. Castillo I. García A. Neely W. Carrasquel K. Mena G. Contreras H. Moldenhauer R. Olcese	Physiology and biophysics	08-08-11	
2	Cellular signaling	Investigate how protein-protein interactions and covalent modifications of dynamin control neurosecretion and trafficking of ion channels.	Using patch clamp amperometry and total internal reflection fluorescence microscopy the handling by the cell of vesicles containing neurotransmitters is characterized.	JC. Sáez A. Martínez H.Sanchez P. Gutierrez B. Cisterna R. Escamilla A. Cardenas A. González M. Maldifassi N. Palacios	Cell Biology	08-08-11	

3	Genetics and developmental neuroscience	Understanding how the nervous system develops and produces complex behaviors.	Using zebrafish and Drosophila as biological models, the development of the olfactory system and the genetic pathways controlling behavior are studied.	J. Ewer K Whitlock A.Calixto J. Alvarez A. Palacios J. Flaven F.Gutzwiller M. Cascallares	Biology of development Genetics and evolution	08-08-11	
4	System and circuits neuroscience	To investigate the mechanisms of neuronal encoding the visual, olfactory and cerebral physiological and pathological conditions.	Using different animal models, including Degu, a natural model for studying AD. The molecules identified by Group 2 as regulators of neurosecretion will be tested in the context of neuronal plasticity.	A. Kirkwood O.Schmachtenberg A. Chávez P.Moya N. Palanca A. Palacios A. Escobar A. Zamora Ch. Chiu A. Ardiles	Cell biology physiology Biophysics	08-08-11	
5	Molecular simulation and computational biology	Using high performance computing for molecular modeling of membrane proteins, drug design assisted by computer, and inference and dynamics of biological networks.	Interaction between theoretical and experimental biologist to create new methods, models and hypothesis suitable to be tested by the experimental groups	F. D González D. Aguayo P Orio A Martin I. Díaz T Pérez F. Villanelo E. Hugo G. Miño L. Medina K. Xu D. Naranjo M. Arismendi J. Gárate	Numerical methods and computation Biophysics	08-08-11	

Annex 3.- Publications (Total or partially financed by MSI)
Students co-authoring a paper are underlined and CINV investigators shown in **bold face**

3.1.- ISI Publications or Similar to ISI Standard

3.1.1 Associate Researchers:

1. **Alvarez O** and **Latorre R**. (2017). The enduring legacy of the "constant-field equation" in membrane ion transport. J Gen Physiol. 149(10):911-920. doi: 10.1085/jgp.201711839.
2. Berna-Erro A, Izquierdo-Serra M, Sepúlveda RV, Rubio-Moscardo F, Doñate-Macián P, Serra SA, Carrillo-Garcia J, Perálvarez-Marín A, **González-Nilo F**, Fernández-Fernández JM, Valverde MA (2017) Structural determinants of 5',6'-epoxyeicosatrienoic acid binding to and activation of TRPV4 channel. Sci Rep. 7(1):10522. doi: 10.1038/s41598-017-11274-1.
3. **Cárdenas AM**, Fernández-Olivares P, Díaz-Franulic I, **González-Jamett** AM, Shimahara T, Segura-Aguilar J, Caviedes R, Caviedes P. (2017) Knockdown of Myo-Inositol Transporter SMIT1 Normalizes Cholinergic and Glutamatergic Function in an Immortalized Cell Line Established from the Cerebral Cortex of a Trisomy 16 Fetal Mouse, an Animal Model of Human Trisomy 21 (Down Syndrome). Neurotox Res. 32(4):614-623. doi: 10.1007/s12640-017-9775-0.
4. **Castillo K**, Diaz-Franulic I, Canan J, **Gonzalez-Nilo F** and **Latorre R**. (2017) Thermally-activated TRP channels: Molecular sensors for temperature detection. Phys. Biology. doi. org /10.1088/1478-3975/aa9a6f.
5. Charvériat M, Naus CC, Leybaert L, **Sáez JC,** Giaume C. (2017) Connexin-Dependent Neuroglial Networking as a New Therapeutic Target. Front Cell Neurosci. n 26;11:174. doi: 10.3389/fncel.2017.00174.. Review.
6. Duran-Aniotz C, Cornejo V, Espinoza S, **Ardiles AO**, Medinas D, Salazar C, Foley A, Gajardo I, Thielen P, Iwawaki T, Scheper W, Soto C, **Palacios AG**, Hoozemans J, Hetz C. (2017) IRE1 Signaling exacerbates Alzheimer's disease pathogenesis. Acta Neuropathologica. Sep;134(3):489-506. doi: 10.1007/s00401-017-1694-x.
7. Gajardo-Gómez R, Labra VC, Maturana CJ, Shoji KF, Santibañez CA, **Sáez JC,** Giaume C, Orellana JA. Cannabinoids prevent the amyloid β-induced activation of astroglial hemichannels: A neuroprotective mechanism. Glia. 65(1):122-137. doi: 10.1002/glia.23080.
8. Giaume C, **Sáez JC**, Song W, Leybaert L, Naus CC. (2017) Connexins and pannexins in Alzheimer's disease. Neurosci Lett. 2017 Sep 8. pii: S0304-3940(17)30740-1. doi: 10.1016/j.neulet.2017.09.006.
9. **González-Jamett AM** , Guerra MJ , Olivares MJ , Haro-Acuña V , Baéz-Matus X , Vásquez-Navarrete J, Momboisse F , Martinez-Quiles N, **Cárdenas AM**. (2017). The F-Actin Binding

Protein Cortactin Regulates the Dynamics of the Exocytotic Fusion Pore through its SH3 Domain. Front. Cell. Neurosci., May 4;11:130 . doi: 10.3389 /fnc el.2017.00130.

10. **González-Jamett AM**, Baez-Matus X, Olivares MJ, Hinostroza F, Guerra-Fernández MJ, Vasquez-Navarrete J, Thao Bui M, Guicheney P, Romero NB, Bevilacqua JA, Bitoun M, Caviedes P, **Cárdenas AM**. (2017). Dynamin-2 mutations linked to Centronuclear Myopathy impair actin-dependent trafficking in muscle cells. Scientific Reports. 7(1):4580 doi: 10.1038/s41598-017-04418-w
11. Gutierrez-Maldonado SE, **Garate JA**, Retamal MJ, Cisternas MA, Volkmann UG, **Pérez-Acle T** (2017) Accessing the structural and thermodynamic properties of ultra-thin layers of C32 adsorbed on a SiO2 surface. Chemical Physics Letters. 674: 64–70. doi: 10.1016/j.cplett.2017.01.065
12. **Latorre R**, **Castillo K**, Carrasquel-Ursulaez W, Sepulveda RV, **Gonzalez-Nilo F**, **Gonzalez C** and **Alvarez O**. (2017). Molecular determinants of BK channel functional diversity and functioning. Physiological Reviews, 97(1):39-87. doi:10.1152/physrev.00001.2016.
13. Manzanares D, Araya-Durán I, Gallego-Yerga L, Játiva P, Márquez-Miranda V, Canan J, Jiménez Blanco JL, Mellet CO, **González-Nilo FD**, García Fernández JM, Ceña V. (2017) Molecular determinants for cyclo-oligosaccharide-based nanoparticle-mediated effective siRNA transfection. Nanomedicine (Lond). 12(13):1607-1621. doi: 10.2217/nnm-2017-0123.
14. Márquez-Miranda V, Abrigo J, Rivera JC, Araya-Durán I, Aravena J, Simon F, Pacheco N, **González-Nilo FD**, Cabello-Verrugio C. (2017) The complex of PAMAM-OH dendrimer with Angiotensin (1-7) prevented the disuse-induced skeletal muscle atrophy in mice. Int J Nanomedicine. ; 12:1985-1999. doi: 10.2147/IJN.S125521.
15. Márquez-Miranda V, Araya-Durán I, **Gonzalez-Nilo FD**. (2017). Multiscale molecular simulations applied to nucleic acid- dendrimer interactions studies. Curr Pharm Des. 23(21):3062-3075. doi: 10.2174/1381612823666170306093224.
16. Maturana CJ, **Aguirre A**, **Sáez JC.** (2017) High glucocorticoid levels during gestation activate the inflammasome in hippocampal oligodendrocytes of the offspring. Dev Neurobiol. 77(5):625-642. doi: 10.1002/dneu.22409.
17. **Martin AJ**, Contreras-Riquelme S**, Dominguez C**, **Perez-Acle T.** (2017) LoTo: a graphlet based method for the comparison of local topology between gene regulatory networks. PeerJ.5:e3052. doi: 10.7717/peerj.3052.
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3.2.- SCIELO Publications or Similar to SCIELO

NONE

3.2.1 Associate Researchers:

NONE

3.2.2 Other researchers

NONE

3.3.- Scientific Books and Chapters

3.3.1 Associate Researchers:

NONE

3.3.2 Other researchers:

NONE

3.4.- Other Publications

3.4.1 Associate Researchers

NONE

3.4.2 Other researchers:

NONE

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	36	67,9%	12	22,6%	2	3,8%	3	5,7%
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%	0	0,00%	0	0,00%	0	0,00%
Other Publications	0	0,00%	0	0,00%	0	0,00%	0	0,00%
Total of publications	36	67,9%	12	22,6%	2	3,8%	3	5,7%

Open access journals have opened a window of information that have become indispensable for the entire scientific community. One can say that open access journals have "democratized" the information coming from research laboratories around the world reducing the existing gap existing between developed and developing communities. However, it is important to note that although some publications of this type are of excellent level and strict, in their reviewing process and selection of articles, the proliferation of open access journal has led to the appearance of journals of questionable quality, even though they are indexed, a fact that goes in detriment of the dissemination of scientific knowledge of high standards.

Annex 4.- Organization of Scientific Events

Scope	Title	Type of Event	City	Country	Responsible Researcher
International	II International Spring School Applied Statistical Thermodynamics 2017: from theory to molecular dynamics simulation (AST2017).	Symposium	Santiago	Chile	Tomás Pérez-Acle
Internacional	LACONEU 2017: 4th Latin-American Summer School in Computational Neuroscience	Symposium	Valparaíso	Chile	Patricio Rodrigo Orio Alvarez
Internacional	XIV Latin American Symposium on Chronobiology 2017 LASC 2017	Conferencia	Valparaíso	Chile	John Ewer Lothian
Nacional	Symposia organized for the XIII Annual Meeting of the Chilean Society of Neuroscience.	Symposiun	Castro	Chile	Patricio Orio
Nacional	Meeting CINV 2017	Symposium	Valparaíso	Chile	Ramón Rogelio Latorre De la Cruz

Annex 5.- Education and capacity building

5.1 Capacity Building inside MSI Center

MSI RESEARCHER	Undergraduated Student		Graduated Students						Total
			Master		Doctoral		Postdoctoral		
	F	M	F	M	F	M	F	M	
Fernando Danilo González Nilo	1	0	0	0	2	0	2	0	5
Carlos González Leon	0	2	0	0	0	4	0	2	8
Alan Neely Delgueil	0	0	1	0	1	0	0	1	3
Juan Carlos Sáez Carreño	1	0	0	0	3	3	1	2	10
Patricio Rodrigo Orio Alvarez	1	0	0	0	0	5	0	2	8
Oliver Schmachtenberg	2	1	0	0	0	3	0	1	7
Adrián Galo Palacios Vargas	0	0	1	1	0	4	0	1	7
Tomás Pérez Acle	0	0	0	2	2	5	0	2	11
Ramón Rogelio Latorre De la Cruz	0	1	0	0	2	0	0	2	4
Ana María Cárdenas Díaz	1	0	2	1	1	1	2	0	8
Kathleen Elizabeth Whitlock Leaning	0	0	0	0	1	3	0	0	4
John Ewer Lothian	0	0	0	1	0	1	2	2	6
Agustín Demetrio Martínez Carrasco	0	2	2	3	0	0	0	1	8
Andrés Eduardo Chávez Navarrete	0	1	1	1	0	0	0	0	3
David Oliver Naranjo Donoso	0	0	0	0	0	1	1	1	3
Alvaro Oscar Ardiles Araya	0	1	0	0	0	0	0	0	1
Andrea Leonor Calixto Mohor	0	1	0	1	3	0	1	0	6
Pablo Ricardo Moya Vera	0	0	0	2	0	1	1	0	4
Total	**6**	**9**	**7**	**12**	**15**	**31**	**10**	**17**	**107**

5.2. - Short-term Traineeships of MSI students

Traineeships internal of MSI students (Include postdoctoral trainees)

Student name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Bernardo Pinto	The University of Chicago	USA	Francisco Bezanilla	Optocapacitive Generation of Action Potentials by Microsecond Laser Pulses of Nanojoule Energy.	19-01-2017	01-04-2017
Melissa Alegría	University of California	USA	Patricia Babbit	Theoretical and practical fundamentals of protein classification at the superfamily level using sequence similarity networks.	12-10-2017	01-12-2017

Traineeships external

Student name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Rosa Scala	Universidad Degli Studi di Bari Aldo Moro	Italy	Ramón Latorre	To develop the characterization of transient receptor potential (TRP)-ion Channel and ligand binding modulation.	08-05-2017	15-07-2017
Lucas Bayones	Universidad de Buenos Aires	Argentina	Ana María Cárdenas	To work in Dra Ana María Cardenas'Lab to understand the secretion mechanisms in cells with high stimulation frequency and functioning.	03-07-2017	04-08-2017
Jose Miguel Cuaxospa Blancas	Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional	Mexico	Ramón Latorre	Lab Internship with Dr. Ramón Latorre.	21-03-2017	18-08-2017
Sara Peña	Doctorado en Farmacología, Universidad de Chile	Chile	Ana María Cárdenas	Lab Intenship with Dra. Ana Cárdenas.	01-06 2017	30-06-2017

Annex 6.- Networking and other collaborative work

6.1 Networking

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

Network Name	Network Scope	Network Participants [Number]				Institutions
		From the Center		External		
		Researchers	Postdocs/ Students	Researchers	Postdocs/ Students	
Genetic and develpment	I	5	15	14	20	Universidad de Valparaíso
						Pontificia Universidad Católica de Chile
						Universidad de Chile
						Universidad Adolfo Ibañez
Biophysics and computational neuroscience	I	8	27	16	27	Pontificia Univeresidad Católica de Chile
						Universidad de Chile
						Universidad de Santiago
						Universidad de Valparaíso
						Fundación Ciencia & Vida
						US Air Force Office of

						Scientific Research (AFOSR)

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	
Workshop "Integration Drug Discovery and Drug Delivery:D4".	Univ. Nacional Andrés Bello (UNAB)	2	1	1	11	
Workshop "Beyond Kds: New computational and experimental methods to address challenges in drug discovery".	Univ. Nacional Andrés Bello (UNAB)	2	1	2	15	
1st *C. elegans* Latin American meeting	Pasteur Institute	1	3	2	x	I Scielo publication

Annex 7. - Outreach

7.1. - Outreach activities throughout the period

Description of activity	Type of Event	Date	Location Region	Target audience
Seminars of CINV				
"Bases celulares y moleculares de la hipersensibilidad dolorosa al frío en respuesta a daño axonal" Rodolfo Madrid, PhD Profesor Asociado Facultad de Química y Biología Universidad de Santiago	Seminar	01-20-2017	Valparaíso	Universidad de Valparaíso community
"Behavioural Neuroscience of Food" *Raffaella Rumiati, PhD.* *Director of the Neuroscience and Society Lab (iNSuLa)* SISSA, Trieste, Italy.	Seminar	03-17-2017	Valparaíso	Universidad de Valparaíso community
"How to make a blood vessel sprout". *Nathan D. Lawson, Ph.D.* *Professor in the Department of Molecular, Cell, and Cancer Biology, University of Massachusetts Medical School*	Seminar	03-24-2017	Valparaíso	Universidad de Valparaíso community
"Péptidos antimicrobianos derivados	Seminar	04-07-2017	Valparaíso	Universidad de Valparaíso

de invertebrados marinos". *Anselmo Otero, PhD* *Centros de Estudios de Proteínas,* *Facultad de Biología,* *Universidad de La Habana, Cuba.*				Community
"New insights in the molecular function of large conductance voltage and calcium gated potassium channels (BK)" *Teresa Giráldez, PhD* *Departamento de Ciencias Médicas Básicas Instituto de Tecnologías Biomédicas (ITB) y Centro de Investigaciones Biomédicas deCanarias (CIBICAN)* *Universidad de La Laguna (Tenerife) Spain.*	Seminar	04-17-2017	Valparaíso	Universidad de Valparaíso community
"How to achieve specific corticosteroid signaling using promiscuous receptors" *Diego Á*lvarez de la Rosa, PhD *Departamento de Ciencias Médicas Básicas Instituto de Tecnologías Biomédicas (ITB) y Centro de Investigaciones Biomédicas de Canarias (CIBICAN)* *Universidad de La Laguna (Tenerife)* *Spain.*	Seminar	04-17-2017	Valparaíso	Universidad de Valparaíso Community

"Timing and Prediction in Audition: From Sound to Speech". *Sonja A. Kotz, PhD* *Faculty of Psychology and Neuroscience, Dept. of Neuropsychology and Psychopharmacology, Maastricht University, Maastricht, The Netherlands* *& Max Planck Institute for Human Cognitive and Brain Sciences, Dept. of Neuropsychology, Leipzig, Germany.*	Seminar	01-28-2017	Valparaíso	Universidad de Valparaíso community
"*Ciencias de la mente y su relación con el budismo"* Wangchuk Dorjee Negi, PhD Central University of Tibetan Studies, India.	Seminar	05-26-2017	Valparaíso	Universidad de Valparaíso community
"Avances sobre comunicación intercelular mediadas por canales intercelulares y hemicanales realizados en y desde Chile" Juan Carlos Sáez, PhD Profesor Titular Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Investigador CINV.	Seminar	06-21-2017	Valparaíso	Universidad de Valparaíso Community
" Los Problemas de la conciencia"	Seminar	06-23-2017	Valparaíso	Universidad de Valparaíso Community

Pablo López Silva, PhD Profesor adjunto Escuela de Piscología , Facultad de Medicina *Universidad de Valparaíso.*				
"Proton regulation of the Na-Ca exchanger: its implications during cardiac acidosis" Michela Ottolia, PhD Associate professor Division of Molecular Medicine Departments of Anesthesiology & Perioperative Medicine David Geffen School of Medicine University of California Los Angeles	Seminar	06-27-2017	Valparaíso	Universidad de Valparaíso community
"L-type Calcium Channel Gating Modifiers: Prospective Next-generation, Antiarrhythmics" Riccardo Olcese, PhD Professor of Anesthesiology and Physiology Division of Molecular Medicine Department of Anesthesiology & Perioperative Medicine David Geffen School of Medicine University of California Los Angeles	Seminar	06-30-2017	Valparaíso	Universidad de Valparaíso Community
"Structure Emergence at the Bio-	*Seminar*	07-18-2017	Valparaíso	Universidad de Valparaíso

Nano Interface: a Multi-Scale Theoretical Approach" *José Antonio Gárate PhD* Young Investigator of Ciencia & Vida CINV.				community
"Descubrimiento de drogas contra enfermedades desatendidas: Aproximaciones preclínicas*"* Benjamín Aguilera, PhD Dpto. de Química Inorgánica y Analítica, Laboratorio de Radicales Libres y Antioxidantes, Facultad de Ciencias Químicas y Farmacéuticas *Universidad de Chile*	Seminar	07-21-2017	Valparaíso	Universidad de Valparaíso Community
"Studying the unique voltage-gated proton channel conformational transitions by gating current measurements" Emerson Carmona Student's PhD *CINV*	Seminar	08-15-2017	Valparaíso	Universidad de Valparaíso community
"Recompensas y Castigos? en la Corteza Visual " *Alfredo Kirkwood PhD* *Professor of Neuroscience Mind and Brain Institute Johns Hopkins University, USA*	Seminar	08-25-2017	Valparaíso	Universidad de Valparaíso community

"Protein folding, disorder and ultra-fast simulations" Tobin Sosnick, PhD. Chair, Dept. of Biochemistry and Molecular Biology, Institute For Biophysical Dynamics, Computation Institute, University of Chicago.	Seminar	29-08-2017	Valparaíso	Universidad de Valparaíso community
" A Computational Network Model of Major Depression: from glutamate dysfunction to EEG biomarkers " Albert Compte PhD Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) Barcelona, Spain.	Seminar	09-28-2017	Valparaíso	Universidad de Valparaíso community
"Design of new heterocyclic compounds with biological activity in GPCRs, based on 3D-QSAR studies" Jaime Mella, PhD Instituto de Química y Bioquímica Facultad de Ciencias, Universidad de Valparaíso	Seminar	10-06-2017	Valparaíso	Universidad de Valparaíso Community
"Intrinsic cortical activity : From bench to the Clinic" Jan-Marino Ramirez. PhD Director, Center for Integrative Brain, Research, Seattle Children's Research Institute.	Seminar	10-13-2017	Valparaíso	Universidad de Valparaíso Community

" Modulatory sites in GABAA receptors: relevance to anesthetic action" Dra. Constanza Maldifassi Postdoctoral CINV	Seminar	11-03-2017	Valparaíso	Universidad de Valparaíso
"Estimulación eléctrica de fibras nerviosas con señales kilohertz." Leonel Medina, PhD Investigador Postdoctoral CINV	Seminar	12-01-2017	Valparaíso	Univesity de Valparaíso
¿Qué Tienes en Mente?				
"Los secretos de la araña de rincón" Jesús Olivarez Ph.D Student	Seminar	09-08-2017	Limache	Secondary School Students
"Los sentidos, nuestra ventana al mundo" O. Schmachtenberg, CINV Researcher	Seminar	10-05-2017	Valparaíso	High School Students
"Los secretos de la araña de rincón" Jesús Olivarez Ph.D Student	Seminar	10-12-2017	Quilpué	High and Secondary School Students
"¿Puede un computador imitar a nuestro cerebro?" Patricio Orio, CINV Researcher	Seminar	10-25-2017	Valpraíso	High School Students
Ciencia Altiro				
Lanzamiento Libro de La Alegría de la Ciencia Kathleen Whitlock	Videos	07-25-2017	Valparaíso	General Community
Falling Walls Lab				

Falling Walls Lab Valparaíso 8 talks of pre-selected Chilean candidates	Conference	09-22-2017	Valparaíso	General Community

7.2. - Products of outreach

Product Type	Quantity	Target Audience	Scope
"De Mente" - Edited book based on articles from the neuronews workshop	1	General Community	Nacional
"Falling Walls Lab Chile" - Video recording of all presentations.	8	General Community	Nacional
"LASC 2017" - Video recording of Celine Vetter talk	1	General Community	Internacional
"LASC 2017" - Video recording of Nobel Prize Michael Rosbash talk and interview	1	General Community	Internacional
"La alegría de la ciencia" – Videos edited based on the book "La alegria de la Ciencia"	10	General Community	Nacional

7.3.- Articles and Interviews

Type of Media and Scoupe	Local / Regional		National		International		
	N° Interviews	N° Articles	N° Interviews	N° Articles	N° Interviews	N° Articles	Total
Written	22	28	16	26	0	0	92
Internet	0	0	1	22	1	1	25
Audiovisual	0	1	4	1	0	0	6
Total	**22**	**29**	**21**	**49**	**1**	**1**	**123**

Annex 8. - Connections with other sectors:

Activity and Objective	Expected Impact	Obtained Results	Type of Connection	Type of Activity	Institution Name	Institution City, Región & Country	Agent Type	Economic Sector
Juan Ignacio Molina Building (formerly Severín Building)	Renovation of the historical district of the city based on the construction of the new CINV building	Tender for the construction of the building	2	7 (Building scientific and outreach infrastructure)	Chile	Valparaíso Chile	2	Government
Fundación Puerto Ideas Scientific Committee	Bringing science of excellence to the	Talks to the general public on recent scientific	2	7 (Talks open to the community)	Chile	Valparaíso Antofagasta	2	Business activities

	community in different regions of the country	discoveries						
Falling Walls Lab	Promote the innovation and creativity of young students and professionals	Second meeting held in Chile to select a representative of the country for the Falling Walls Lab meeting in Berlin	2	7	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

Annex 9.- Total incomes:

Funds	Accumulated incomes to last year [$]	2017 Incomes		Total incomes to 2017 [$]
		Amount [$]	Percentage of resources used by the Center [%]	
ICM (CINV, Redes y PME)	4.826.451.751	857.775.043	139%	857.775.043
CONICYT (Anillo, Mincyt, Explora, Redes y Neuromantes)	2.212.071.861	776.502.000	75%	776.502.000
UV (Depto. Neuro y Direc. Invest.)	2.620.319.828	511.883.257	100%	511.883.257
Corporación CINV	61.649.565	14.958.787	69%	14.958.787
CNTV, FNDR	51.530.500	0	0%	0
Others (CAT; N62909-13-N251-; N62909-16-1-2227; AFOSR; N62909-14-1-N121)	239.909.803	120.871.189	99%	120.871.189
TOTAL	**10.011.933.308**	**2.281.990.276**		**2.281.990.276**

Annex 10.- Exchange:

Type of researcher	Name	Type of activity	Length of stay	Destination Country	Financial entity (Millennium/External/Multiple sources)
Associate	Adrian Palacios	IBRO-LAC. Annual Neuroscience American Congress	6 days	USA	External
Adjunt	Agustin Martinez	International Gap Junction Conference	8 days	England	External
Associate	Alan Neely	Biophysical Society 2017 Annual Meeting	7 days	USA	External
Associate	Ana María Cárdenas	Society Neuroscience Argentina Congress	4 days	Argentina	External
Adjunt	Andrea Calixto	1st Latin American C. elegans Meeting	2 days	Uruguay	Multiple sources
Adjunt	Andrea Calixto	C. elegans International Meeting.	5 days	USA	Multiple sources
Adjunt	Chiayu Chiu	Research in lab of Dr. Michael Higley, Yale University	32 days	USA	Multiple sources
Adjunt	Chiayu Chiu	Research in lab of Dr. Michael Higley, Yale University	23 days	USA	Multiple sources
Adjunt	Chiayu Chiu	SFN conference	4 days	USA	Multiple sources
Adjunt	Chiayu Chiu	Max Planck meeting of Institute Directors and	3 days	USA	Multiple sources

		Group Leaders			
Associate	John Ewer	58th Annual Drosophila Research Conference	7 days	USA	External
Associate	John Ewer	Visiting investigator, lab of Dr. Daisuke Yamamoto, Tohoku University, Sendai, Japan	30 days	Japan	Exteranl
Associate	John Ewer	Chronobiology	6 days	USA	External
Associate	Juan Carlos Sáez	International Gap Junction Conference	8 days	Scotland	Millenmium
Associate	Juan C. Sáez	Seminar	5 days	Universidad Javeriana, Colombia	External
Associate	Juan C. Sáez	Seminar	3 days	Vaticane, Rome, Italy	External
Associate	Juan C. Sáez	Seminar	1 month	Hong Kong City University	External
Associate	Juan C. Sáez	Seminar	1 month	Pasteur Research Pole, Hong Kong University	External
Associate	Juan C. Sáez	Seminar	1 month	Hong Kong University of Science and Technology	External
Associate	Juan C. Sáez	Seminar	1 month	Hong Kong Polytechnic University	External
Adjunt	Oliver Schmachtenberg	Visit Department of Optometry and Vision Sciences at	12 days	New Zealand	External

		The University of Auckland			
Adjunt	Patricio Orio	CNS 2017, 26th Annual Computacional Neuroscience Meeting	10 days	Belgic	Millenmium
Associate	Ramón Latorre	Biophysical Society 2017 Annual Meeting	8 days	USA	External
Associate	Ramón Latorre	38th World Congress of the International Union of Physiological Sciences Rhythmhms of life - Rio de Janeiro 2017	7 days	Brazil	External
Associate	Ramón Latorre	Academia de Ciencia Exactas Físcas y Naturales de Colombia	5 days	Colombia	External
Associate	Ramón Latorre	Workshop Cell Biology and Genetics Casina Po IV, Pontificia Accademia delle Scienze, The Vatican	5 days	Italia	Extenal
Associate	Tomás Pérez-Acle	International Gap Junction Conference	8 days	Scotland	Millenmium
Associate	Tomás Pérez-Acle	International Society for Computational Biology	5 days	Czech Republic	Millenmium

Type of researcher	Name	Type of activity	Length of stay	Destination Country	Financial entity (Millenmium/ External / Multiple sources)
Albert Compte	Spanish	Seminar	4 days	Spain	External
Alfredo Kirkwood	Chilean	Seminar	4 days	USA	External
Anselmo Otero	Cuban	Seminar	1 month	CUBA	External
*Diego Á*lvarez de la Rosa	Spanish	Seminar	2 days	Spain	Multiple sources
Jan-Marino Ramirez	US Citizen	Seminar	3 days	USA	External
Marcelo Ozu	Argentinian	Colaboration	39 days	Argentina	External
Michela Ottolia	Italian	Seminar	12 days	USA	External
Nathan D. Lawson	USA	Seminar	6 days	USA	External
Raffaella Rumiati	Italian	Seminar	5 days	USA	External
Riccardo Olcese	Italian	Seminar	12 days	USA	External
Sonja A. Kotz	German	Seminar	5 days	Germany	External
Teresa Giráldez	Spanish	Seminar	2 days	Spain	Multiple sources
Tobin Sosnick	US Citizen	Seminar	3 days	USA	Multiple sources
Wangchuk Dorjee Negi	Indian	Seminar	1 days	India	External