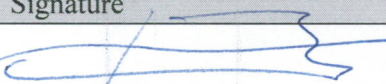
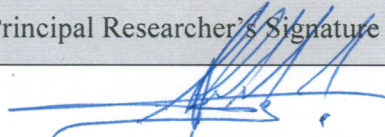


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|---|--|
| Name of the Center: Centro Interdisciplinario de Neurociencia de Valparaiso | |
| Acronym | CINV |
| Code | P09-022-F |
| Reported period | January 1 st to December 31 st , 2018 |
| Starting date of the Center | 08-08-2011 |
| Address | Pasaje Harrington 287, Playa Ancha Valparaiso |
| Telephone(s) | 322-508040 |
| Web Page | www.cinv.cl |
| Host Institution(s) | Corporación Centro Interdisciplinario de Neurociencia de Valparaiso, Universidad de Valparaiso, Pontificia Universidad Católica de Chile, Universidad Nacional Andrés Bello, Fundación Ciencia & Vida. |
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| Ramón Latorre de la Cruz | Juan Carlos Sáez Carreño |
| Principal Researcher's Signature | Deputy Principal Researcher's Signature |
|  |  |

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1.1 Executive Summary (2 páginas)

Since its birth, the “Centro Interdisciplinario de Neurociencia de Valparaíso” (CINV) has dealt with the scientific question: ***How does the Nervous System Respond to Stimuli in Health and Disease?*** We have addressed this question through different lines of research that go from Molecular Sensors to System and Circuit Neuroscience, which are supported by a Cross-cutting line, the Bioinformatic and Computational Biology line. We have recently added an additional Translational Research Unit. **Scientific productivity and collaborative work.** During 2018 we produced 55 publications with an average impact factor of 4.2. We published 2 papers in high impact journals led by CINV members (*PNAS*, from González’s and Latorre’s Labs, and *Neuron* from Chiu’s Lab). Notably, Ignacio Díaz-Franulic, a postdoctoral Fellow, was corresponding author of a *PNAS* paper. We also published 4 articles in prestigious journals with IF between 5.5 and 8.0, including one in *Curr. Op. Immunol.* (Sáez’s Lab), one in *PLoS Genetics* (Ewer’s lab), one in *Neuropsychopharmacol.* (Chávez’s and Moya’s Labs), and one in *Front Immunol.* (Sáez’s Lab). We also wish to highlight our articles published in journals that are prominent in their respective fields including *J. Physiol (Lond)* (1), *J. Gen. Physiol.* (3), *Biophys J* (4), *Sci. Rep.* (3). Finally, we single out the following publications: 1- A report on the allosteric communication between fast and slow gating in connexin 26 hemichannel, which revealed a possible mechanism for the gain-of-function phenotype of the G12R syndromic deaf mutation (García et al. *J Gen Physiol.* 150:697, 2018). This paper received a commentary from the journals’ editors in the same issue. 2- The Sáez laboratory established that hemichannels play a critical role in endothelial insulin resistance induced by pro-inflammatory cytokines and high glucose concentration, which precedes a diabetic condition known to lead to neurodegeneration (Sáez et al., *Front. Immunol.* 9:1899, 2018). 3- Reflecting the tight link between the regulation of inhibitory circuits and their function, our Max Planck leader, Chiayu Chiu, found that inhibitory synapses from dendrite-targeting somatostatin-expressing interneurons in the cortex are selectively potentiated by glutamatergic activity (Chiu et al., *Neuron*, 97:368, 2018). Our graduate students contributed strongly to our productivity. Indeed, 39 students co-authored 23 articles published in 2018, and were first author in 11 of them. **Strengthening and renovation of our faculty.** J.C. Sáez, our Deputy Director, became a Professor at the University of Valparaíso (UV), and his laboratory has been fully functional since September 2018. Also, Francisco Bezanilla became an Honorary Professor of the UV and a good-standing member of the CINV during 2018. In response to the agreement between the Max Planck Society, the UV and CINV acquired a 2-photon microscope that is currently fully functional and helping the research of Chiayu Chiu, Andrés Chávez, Karen Castillo, and Helmuth Sánchez. Castillo and Sánchez are CINV young investigators, both of which are independently funded (by a FONDECYT grant and a FONIS Award from CONICYT, respectively). **Advanced training.** We continue to actively participate in the PhD and MSc Programs in Neuroscience and in the PhD Program in Biophysics and Computational Biology of the UV. The Neuroscience PhD Program was accredited for a record of 7 years in 2017 and 9 students were recruited for the 2019 academic year (7 female, 2 male), of which 4 are from abroad (Germany, Spain, Senegal, and Venezuela). The PhD program in Biophysics and Computational Biology has 12 students, and 4 more were selected for 2019. In 2018, this program was re-accredited for 5 years by the Chilean National Committee on Accreditation, an outstanding accomplishment for such a young program, in recognition of its design and its faculty. The Neuroscience MSc Program received 32 applications of which 16 were accepted. This program is currently in the process of re-

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accreditation. **Networking.** For 15 days in October 2018, our PhD students and Postdocs had the opportunity to attend a Chemical Biology course offered by Prof. William Kobertz (University of Massachusetts Medical School). Fluorescence, engineering proteins using unnatural amino acids, and chemical genetics, were some of the topics of the course, which included both theoretical and practical sessions. In August 2018, the CINV organized the first Chilean conference on Computational Neuroscience, headed by P. Orio. Its main objective was to bring together the neuroscientific community interested in using computational approaches to solve complex problems in neuroscience. The CINV Deputy Director, J.C. Sáez, led the Latin American Training Program (LATP) “From molecules to behavior – the quest for new treatments of neuropathologies”. This is the first time that a LATP course was held in Chile, and set a record for the most applicants in the program’s history (150). R. Latorre, in his capacity as Member of the Council of the Latin American Academy of Sciences (ACAL), organized the Council meeting of the ACAL and a Symposium that took place at the headquarters of the Chilean Academy of Sciences. It consisted of talks by ACAL members elected in 2018, and dealt with topics ranging from climate change and biodiversity to the control of tumor cell growth. The CINV, in partnership with the Young Science Foundation, organized the 3rd “Falling Walls Lab” competition in Valparaíso. Young innovators from all over the country were invited to compete. The winner was the designer of a robotic hand designed to help with the rehabilitation of stroke patients, and will represent Chile at the global competition in Berlin. Together with the Max Planck Society, the CINV organized the Symposium “Understanding Brain Function and Dysfunction: from Synapses to Circuits”. The 3-day symposium was organized by C. Chiu and consisted of presentations by Max Planck Institute Directors and Max Planck Leaders, and discussed the latest advances in neuroscience. The CINV participated in the organization and teaching of the EMBO Practical Course on Developmental Biology, which attracted students from all over Latin America. **Outreach.** The De Mente book, which is the compilation of NeuroNews articles published in the virtual newspaper “El Mostrador”, was edited by Editorial Catalonia and will be published at 2019, and will allow this initiative to reach a wider audience including readers abroad. *NeuroNews*, which started as an exercise for our PhD students in translating scientific articles into articles suitable for the general public, has reached more than 300,000 readers. Ranked as one of the most interesting cultural events in Valparaíso, the *Tertulias Porteñas* attracted more than 400 people in 2018. The 3 events that were offered in 2018 were moderated by Patricio Fernández, a well-known Chilean journalist, and concluded with a *Tertulia* entitled “What make us express solidarity?”, which caused a lively discussion between economists, philosophers, and scientists. Based on the book “*La Alegría de la Ciencia*” (The Joy of Science), 10 video documentaries will be shown through the National Television open station. Each video describes, in a playful manner accessible to young children, the ways an electric motor or a compass work, how to build a thermometer, amongst others. Finally, a crucial step for the new CINV science building in Valparaíso was the beginning of the contract for the construction of the building in April, 2018.

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1.2 Resumen Ejecutivo (2 páginas)

Desde su nacimiento, el “Centro Interdisciplinario de Neurociencia de Valparaíso” (CINV) ha abordado la pregunta sobre **¿cómo responde el sistema nervioso a los estímulos en la salud y la enfermedad?** a través de diferentes líneas de investigación que van desde los sensores moleculares a la neurociencia de sistemas y redes neuronales, respaldadas por una línea transversal, la línea de Bioinformática y Biología Computacional. Recientemente hemos agregado una Unidad de Investigación Traslacional. **Productividad científica colaborativa.** Durante 2018 produjimos 55 publicaciones con un factor de impacto promedio de 4,2. Publicamos 2 artículos en revistas de alto impacto que fueron dirigidos por miembros del CINV (*PNAS*, Laboratorios de González y Latorre, y *Neuron*, del Laboratorio de Chiu). Cabe destacar que Ignacio Díaz-Franulic, becario postdoctoral, fue el autor correspondiente de un artículo de *PNAS*. También publicamos 4 artículos en revistas de prestigio con IF entre 5,5 y 8,0, incluido uno en *Curr. Opin. Immunol.* (Laboratorio de Sáez), uno en *PLoS Genetics* (laboratorio de Ewer), uno en *Neuropsychopharmacol.* (Laboratorios de Chávez y Moya), y uno en *Front. Immunol.* (Laboratorio de Sáez). También deseamos destacar nuestros artículos publicados en revistas destacadas en sus respectivos campos, como *J. Physiol* (Lond) (1), *JGP.* (3), *Biophys J* (4), *Sci. Rep.* (3). Finalmente, destacamos las siguientes publicaciones: **1-** Un artículo que reveló un posible mecanismo para el fenotipo de ganancia de función de los hemicanales formados por la mutante de Cx26G12R, que produce un tipo de sordera sindrómica (*JGP.* 150: 697, 2018). Este artículo recibió un comentario de los editores de las revistas en el mismo número. **2-** El laboratorio de Sáez estableció que los hemicanales desempeñan un papel crítico en la resistencia a la insulina endotelial inducida por citoquinas proinflamatorias y alta concentración de glucosa, lo que precede a una condición diabética que conduce a la neurodegeneración (*Front. Immunol.* 9: 1899, 2018). **3-** Nuestra líder de Max Planck, Chiayu Chiu, descubrió que las sinapsis inhibitorias de las interneuronas que expresan somatostatina en la corteza son potenciadas selectivamente por la actividad glutamatérgica (*Neuron*, 97: 368, 2018). Nuestros estudiantes graduados contribuyeron fuertemente a nuestra productividad. De hecho, 39 estudiantes fueron coautores de 23 artículos publicados en 2018, y fueron los primeros autores en 11 de ellos. **Refuerzo y renovación de nuestros investigadores.** J.C. Sáez, nuestro Director Alterno, se convirtió en profesor de la Universidad de Valparaíso (UV), y su laboratorio ha estado en pleno funcionamiento desde septiembre de 2018. Además, Francisco Bezanilla se convirtió en profesor honorario de la Universidad de Valparaíso (UV) y miembro destacado del CINV durante 2018. En respuesta al acuerdo entre la Sociedad Max Planck, la UV y el CINV se adquirió un microscopio de 2 fotones, que actualmente está en funcionamiento y ayuda a la investigación de C. Chiu, K. Castillo, A. Chávez y H. Sánchez. Tanto Castillo como Sánchez son parte de nuestros Jóvenes Investigadores, y en la actualidad son financiados de forma independiente (FONDECYT y FONIS de CONICYT, respectivamente). **Formación de Capital Humano.** El programa de doctorado en neurociencias fue acreditado por 7 años en 2017 y fueron reclutados 9 estudiantes para el año académico 2019 (7 mujeres y 2 hombres), de los cuales 4 son extranjeros (Alemania, España, Senegal y Venezuela). El programa de doctorado en biofísica y biología computacional ahora tiene 12 estudiantes, y se seleccionaron 4 más para 2019. En 2018, este programa fue acreditado nuevamente por 5 años por el Comité Nacional de Acreditación de Chile, un logro excepcional para un programa tan joven. El programa de maestría en neurociencias recibió 32 solicitudes de ingreso, de las cuales 16 fueron aceptadas. Este programa se encuentra actualmente en proceso de re-acreditación. **Redes.** Durante 15 días en Septiembre

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de 2018, nuestros estudiantes de doctorado y postdoctorados tuvieron la oportunidad de asistir a un curso de biología química ofrecido por el profesor William Kobertz (Universidad de Massachusetts). Fluorescencia, ingeniería de proteínas que utilizan aminoácidos no naturales y genética química, fueron algunos de los temas del curso, que incluyeron sesiones teóricas y prácticas. En agosto de 2018, el CINV organizó la primera conferencia chilena sobre neurociencia computacional, dirigida por P. Orio. Su objetivo era reunir a la comunidad neurocientífica interesada en la utilización de enfoques computacionales para resolver problemas complejos en neurociencia. J.C. Sáez, dirigió el Programa de Capacitación para América Latina (LATP) "De las moléculas al comportamiento: búsqueda de nuevos tratamientos para las neuropatologías". Esta es la primera vez que se realiza un curso de LATP en Chile y se establece un récord histórico de solicitudes para participar (150). R. Latorre, en su calidad de Miembro del Consejo de la Academia Latinoamericana de Ciencias (ACAL), organizó la reunión del Consejo de la ACAL y un Simposio que tuvo lugar en la sede de la Academia Chilena de Ciencias. Consistió en charlas de miembros de ACAL elegidos en 2018, y trató temas que van desde el cambio climático y la biodiversidad hasta el control del crecimiento de células tumorales. El CINV, en colaboración con la Fundación Ciencia Joven, organizó el 3er concurso "Falling Walls Lab" en Valparaíso. Jóvenes innovadores de todo el país fueron invitados a competir. El ganador fue el diseñador de una mano robótica que se utilizará para ayudar en la rehabilitación de pacientes con accidente cerebrovascular y representará a Chile en la competencia mundial en Berlín. Junto con la Sociedad Max Planck, el CINV organizó el Simposio "Entendiendo la función y la disfunción cerebral: de las sinapsis a los circuitos". El simposio de 3 días fue organizado por C. Chiu y consistió en presentaciones de los directores del Instituto Max Planck y los líderes de Max Planck, y se discutió los últimos avances en neurociencia. El CINV participó en la organización y enseñanza del "Curso práctico de EMBO sobre biología del desarrollo", que atrajo a estudiantes de toda América Latina. **Difusión al medio.** El libro "*De Mente*", que es la compilación de artículos de Neuro News publicados en el periódico virtual "El Mostrador", fue editado por Editorial Catalonia y se publicará el 2019, permitiendo que esta iniciativa llegue a un público más amplio, incluida gente en el extranjero. Neuro News, que comenzó como un ejercicio para Nuestros estudiantes de doctorado y de magister en el traspaso de información de artículos científicos a lenguaje apto para el público en general, ha alcanzado más de 300.000 lecturas. Clasificado como uno de los eventos culturales más interesantes en Valparaíso, las Tertulias Porteñas celebradas en 2018 atrajeron a más de 400 personas. Los 3 eventos que se ofrecieron en 2018 fueron moderados por Patricio Fernández, un conocido periodista chileno, y concluyeron con una Tertulia titulada "¿Que nos hace solidarios?", que provocó una animada discusión entre economistas, filósofos y científicos. Basado en el libro "La Alegría de la Ciencia", se exhibieron 10 videos documentales en TVN. Cada video describe, de una manera lúdica y accesible para niños pequeños, las formas en que funciona un motor eléctrico o una brújula, cómo construir un termómetro, entre otros. Finalmente, un paso crucial para el nuevo edificio de ciencia del CINV en Valparaíso fue el comienzo del contrato para la construcción del edificio en abril de 2018.

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2. Introduction (2 páginas)

A) Description of the Institute and highlights of 2018

Since its birth, the principal aim of the CINV has been to understand the workings of the nervous system through a multidisciplinary approach that spans from molecules to neural networks. Structured along five different lines of research and one translational unit, CINV biophysicists, neuroscientists, and computer modelers collaborate to produce neuroscience that goes beyond the limits of their specialized fields of research. An important driving force that guides our scientific endeavors is the creation of a space for regional science of excellence in a centralized country, by offering creative neuroscientist an environment free of the constraints that limit their abilities to do cutting-edge research. With only two more years of support from the Millenium Initiative, we think that the CINV is in good standing to face the future. During 2018, the construction of the new building that will host the Center started, and is expected to be completed by the middle of 2020. Young and very talented scientists have been incorporated as young investigators, three of them have positions in different faculties of the University of Valparaiso, and two more have secured funds from CONICYT and CORFO. Moreover, these young investigators, which include our Max Planck Leader, C. Chiu, are producing some of the CINV's best science. We mention here a *J. Gen. Physiol.* (150:697, 2018) paper by I. García that received praise from the journal's editorial board, and a *Neuron* paper from the laboratory of C. Chiu. Graduate education is strong at the CINV. In 2015, the CINV put forward the first PhD program in Biophysics in Chile, which, only two years after its creation, was accredited for 5 years. With a flexible study plan, this PhD Program has attracted excellent students with a most diverse backgrounds ranging from biologists to mathematicians. During 2018 the CINV was very active in strengthening its networking capacities. J.C. Sáez organized for the first time in Chile the Latin American Training Program (LATP) ("From molecules to behavior—the quest for new treatments of neuropathologies."), R. Latorre organized the Council Meeting of the Academy of Science of Latin America (ACAL), which was accompanied by a Symposium with the participation of recently elected ACAL members. C. Chiu put together a CINV-Max Planck Meeting "Understanding Brain Function and Dysfunction: from Synapses to Circuits" in which Max Planck Research Leaders and Max Planck Institute Directors participated.

B) Research Lines

Line1. *Structure and Function of Molecular Sensors.* (R. Latorre, A. Neely, C. González, O. Alvarez, F. Bezanilla, M. Holmgren, J.A. Gárate, K. Castillo and I. García). This year we highlight the paper by García et al. (*J. Gen. Physiol.* 2018). This paper gives a coherent mechanism that accounts for the gain-of-function keratitis-ichthyosis-deafness syndrome produced by a point mutation (G12R) in the hemichannel formed by connexin 26. We devised a method to determine the stoichiometry between two Ca^{2+} -activated channel subunit using lanthanide resonance energy transfer measurements. The method is general and can be applied to different protein complexes (Carrasquel-Ursulaez et al. *Biophys. J.*, 2018). Notably, and for the first time, we were able to measure and characterize the gating current generated by the proton channel Hv1 (Carmona et al. *PNAS*, 2018).

Line 2. *Cell Signaling.* (A.M. Cárdenas, J. C. Sáez, H. Sánchez and A.D. Martínez). The most relevant findings for 2018 are: Panx1 hemichannels play a critical role in ATP release required for Ca^{2+} waves propagation in a model of epilepsy (Wellmann et al. *Front. Cell. Neurosci.*,

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2018). Hemichannels play a critical role in endothelial insulin resistance, which precedes neurodegeneration (Sáez et al. *Front. Immunol.* 2018). With young investigator, A. Ardiles, we found that Panx1 deficiency affects the reversion of a previously acquired spatial memory capability (Gajardo et al., *Front. Mol. Neurosci.* 2018). In collaboration with lines 1 and 5, we discovered that the mutation in human Cx26 that causes syndromic deafness (G12R) produces hemichannel hyperactivity (García et al. *J. Gen. Physiol.* 2018). We also found a mechanism involved in Down syndrome by showing that the regulator of calcineurin 1 (RCAN1) contributes to the impairment of exocytosis (Vásquez-Navarrete et al. *Front. Cell. Neurosci.*, 2018).

Line 3. Genetic and Developmental Neuroscience. (J. Ewer, K. Whitlock and A. Calixto). We have continued to investigate how neuropeptides and the circadian clock (Palacios-Muñoz & Ewer, *PLoS Genet.*, 2018) regulate *Drosophila* behavior. Our work in zebrafish led to the startling discovery of the evolutionary loss of the gene encoding the essential reproductive peptide, GnRH1 (Whitlock et al. *Front. Neuroendocrinol.*, 2019), which may have caused the coopting of a novel peptide, Phoenixin. We also uncovered a surprising neural immune interface in the olfactory epithelia of developing and adult zebrafish. In *C. elegans* we discovered that diapause promotes axonal regrowth on axonal regeneration (Caneo, M. et al. *PLoS Genet.* 2019) and that bacterial diets can provide protective metabolites against neurodegenerative decline. In both zebrafish and *C. elegans*, there appears to be a neural-immune interface involved in chemosensory memories of relevant odors.

Line 4. Integrative and Circuits Neuroscience. (A. Palacios, A. Chávez, P. Moya, Alvaro Ardiles C. Chiu, and O. Schmachtenberg). During 2018, we advanced our understanding of the role of different classes of inhibitory neurons in the control of glutamatergic activity at the synaptic level (Chiu et al. *Neuron*, 2018), and in controlling cortical operations at the circuit level (Espinosa et al. *Cereb. Cortex*, 2018). We uncovered the functional role of neuronal glutamate transporters in neuropsychiatric diseases by demonstrating that overexpression of EAAT3 at excitatory synapses in the brain recapitulates behavioral and synaptic alterations in NMDA receptor activity relevant to obsessive-compulsive disorder (Delgado-Acevedo et al. *Neuropsychopharmacology*, 2018). These results also provided a valuable animal model that may open novel therapeutic approaches to treat this devastating disorder.

Line 5. Crosscutting: Computational Biology and Bioinformatics. (F. D. González, T. Pérez-Acle, and P. Orio). This year, we highlight the work of Orio et al., (*Chaos*, 2018) showing how both chaotic and stochastic neuronal dynamics interact to shape the multistable behavior of the brain. Moreover, we demonstrated the capabilities of PISKaS, a modeling platform suitable for conducting a stochastic simulation of complex multiscale systems using an agent and rule-based approach (Bustos et al. *Methods Mol. Biol.* 2018). In collaboration with Lines 1 and 2, we demonstrated that both fast and slow gating processes of connexin26 hemichannels are impaired by the G12R mutation (García et al. *J. Gen Physiol.* 2018). We highlight the continuity of our joint efforts with Line 1 to explore the thermal activation pathway of TRPV1 (Castillo et al. *Phys Biol.* 2018). Also, we explored nano-scale delivery systems (Camarada et al. *Langmuir*, 2018; Elizondo-García et al. *Molecules*, 2018).

Line 6. Translational Research Unit. (J. C. Sáez, C. González, T. Pérez-Acle, F. D. González). At the end of 2017, we hired a coordinator of the activities of this section. During 2018 emerging Research + Development projects were identified. Three applications are in preparation, and two others were presented and awarded. One corresponds to a technological contract from

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Connectomica SPA awarded by CORFO. The other project was funded by FONIS and is led by the young investigator, H. Sánchez.

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3. Scientific and Technological Research (12 páginas para Institutos)

a) Current status of research lines:

Research Line 1: Structure and Function of Molecular Sensors (R. Latorre, A. Neely, C. González, O. Alvarez, F. Bezanilla, M. Holmgren, J.A. Gárate, K. Castillo and I. García).

Ion channels are unique molecular sensors that allow ion fluxes across the cell membrane and cause changes in membrane potential in response to different physical stimuli such as temperature and voltage, as well as chemical stimuli. The long-term goal of this research line is to identify and characterize the different structural domains involved in sensing temperature, voltage or Ca^{2+} and how they regulate the ion-conducting machinery. We continue to expand the scope of our research in the realm of molecular modeling and the involvement of mutant channels in different kind of pathologies, known as channelopathies.

The collaboration with Line 2 and 5 have contributed significantly to these new avenues. One example is the most recent contribution to our understanding of the molecular mechanisms responsible for the devastating Keratitis-ichthyosis-deafness (KID) syndrome, which is caused by a mutation in connexin 26 (García et al., *J. Invest. Dermatol.* **2015** *135*(5):1338-47 and **2016**, *136*(3):574-83). Combining single-channel measurements and molecular dynamics simulations, we discovered that the G12R mutation causes a displacement of the N-terminus that allows the interaction of R12 with R99, preventing the channel from closing. This persistently conducting state defines the molecular mechanism for the gain-of-function effect of this mutation in KID syndrome (García et al., **2018**, *J. Gen. Physiol.* **150**:697-711).

Continuing with our work combining high-resolution electrophysiological and optical methods, we gained new insights into the structure-function of voltage- and Ca^{2+} -activated K^+ (BK) channels. The paper by Carrasquel-Ursulaez et al., **2018**, *Biophys. J.* **114**:2493-2497 revealed the association stoichiometry between the γ and β subunits of BK channels by lanthanide resonance energy transfer (LRET) measurements. A book chapter was also published that focuses on the role of the Slo channel family in neurons under both physiological and pathological conditions (Carrasquel-Ursulaez et al., **2018**, *The Oxford Handbook of Neuronal Ion Channels*). Particularly exciting are our recent results on the allosteric coupling between Ca^{2+} and voltage sensors in BK channels. By recording gating currents at different Ca^{2+} concentrations, a feat achieved by one of our most gifted students **Yenisleidy Lorenzo-Ceballos**, we measured a -140 mV leftward shift in the gating-charge (Q-V) curve when inside out patches were exposed to Ca^{2+} concentrations known to saturate high-affinity Ca^{2+} -binding sites. This large shift indicates that Ca^{2+} binding greatly decreases the energy necessary to activate the channel voltage sensors, facilitating pore opening.

On the other hand, reducing the number of Ca^{2+} -binding sites using site-directed mutagenesis decreases to about one half the leftward shift of the Q-V curve produced by high intracellular Ca^{2+} , regardless on which Ca^{2+} binding site was ablated. Thus, the high-affinity Ca^{2+} -binding sites appear to contribute equally to decrease the free energy necessary to activate the VSD. These results reveal separate and additive allosteric interactions between Ca^{2+} -sensors and the voltage sensors in BK channels.

Voltage-gated proton channel (Hv1) monomers share the same general architecture of the VSDs of voltage-gated K^+ 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 in the

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field is the direct measurement of gating currents in Hv1 channels. Last year we successfully measured the gating currents emerging from the movement of gating charges of Hv1. The features of the isolated gating currents suggest that the voltage sensor undergoes several voltage-dependent conformational changes during activation before opening. However, most of the charge is displaced in a single central transition (**Carmona et al., 2018, PNAS 115:9240-9245**). One caveat of the experimental strategy used to eliminate proton conduction was the introduction of the N264R mutation, which traps the voltage-sensor in a near fully active conformation, as inferred by the very slow recovery of the gating charge upon membrane repolarization. This year we explored new mutations that interfered with conductance but do not induce charge trapping. C. González was invited to write a commentary about proton permeation in proton channels in a Cross Talk hosted by the *Journal of Physiology* (**Comments on Cross Talk 33: Alvarez et al., J. Physiol. Pp 1-4**). The comment contrasts two opposing views on proton conduction: Grotthuss proton wire or ionization of at least one amino acid (*A Glimpse into the Permeation Pathway of the Voltage-Dependent Proton Channel*).

Our efforts to understand cold sensing by TRP melastatin receptor type 8 (TRPM8) involved in innocuous cold sensing was summarized in a review (**Castillo et al., 2018, Phys Biol. 15 021001**). In collaboration with line 5, we built a molecular model of the TRPM8 coiled-coils based on a cryo-EM structure of a bird TRPM8 channel, and discovered that in addition to the hydrophobic interactions typical of coiled-coil assemblies, a cluster of polar residues that populate the central region appears to participate in temperature sensitivity as confirmed by anisotropic the thermal diffusion method (ATD). Interestingly, by constructing chimeric channels between TRPM8 and TRPM7 (insensitive to temperature), we were able to confer temperature sensitivity to TRPM7 when it expresses the coiled-coil domain of TRPM8 and cold sensitivity is obliterated in TRPM8 when the channel expresses the coiled-coil domain of TRPM7 (TRPM8/cc-TRPM7). Our findings strongly support a role for the coiled-coil domain as a highly temperature sensitive module in TRPM8 channels. With our ongoing investigations, we hope to define the allosteric pathway(s) that connects cold sensing with channel opening.

During the last year, and with the incorporation of the young scientist, José Antonio Gárate, an expert in molecular dynamics, the aquaporin channel was brought to our attention. This channel conducts water instead of ions, and thus there is no electrical reporting of the transport process. In this case, molecular dynamics simulations is a critical tool to further our understanding of water permeation through these ubiquitous proteins. Using classical molecular dynamics simulations, and in collaboration with international collaborators from Rome and Dublin, we showed how external electrical fields alter the dynamics of the selectivity filter in human aquaporin 4 (**Bernardi et al., 2018, J. Chem. Phys. 149:24; 245102**). We discovered that several residues within the pore are substantially affected by axially applied electric fields influencing water permeation. We also investigated the impact of applying strong fields to a membrane containing aquaporin and found that they promote the formation and stabilization of a trans-protein electropore lying at the center of symmetry of the tetramer formed by the aquaporin subunits called the fifth middle pore (**Marracino et al 2018, ACS Omega, 3(11), 15361–15369**). This finding is particularly important as it may explain ion currents reported in aquaporins by some authors. In collaboration with line 5, we also contributed to the development of new software that simplifies the study of residue interaction network (RIN) from molecular dynamics simulations using graph theory (**Contreras-Riquelme, et al., 2018, Peer. J. 6; e5998**). Profiting from in-house skills and resources and in collaborations with organic chemists from Vienna, we

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have developed novel antagonists of the main component of lipopolysaccharide that underlies the inflammation caused by Gram-negative bacteria, which is the main cause for septic shock (Borio et al., 2018, *Chem. Med. Chem. Phys. Lett.*, 13 2317-233).

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

We focus on the mechanisms underlying changes in cell-cell communication mediated by connexin and pannexin hemichannels, and on the mechanisms of neurosecretion. We proposed them as useful molecular targets to treat and prevent the progression of neurological diseases (i.e, epilepsy, infections, Alzheimer disease and muscular dystrophies). We also studied the assembly of these channels as well as their gating mechanism, which provide critical information on the relevance of hemichannels as membrane components of autocrine and paracrine cell-cell communication mechanisms of inflammation with particular attention to neuroinflammation. We found that pannexin1 hemichannels play a critical role in the migration of dendritic cells (Sáez et al., 2018 *Current Opin. Immunol* 52:74-80) and in Ca^{2+} waves propagation, in a model of epilepsy (Wellmann et al., 2018, *Front Cell Neurosci.*12:446.). We also demonstrated that hemichannels play a relevant role in angiotensin II-induced cell damage (Gómez et al., 2018, *Int. J. Mol. Sci.* 19(4). pii: E957) and in two infectious diseases: 1) sepsis (i.e., P2X₇ receptors and TRPV2 channels) (Balboa et al., 2018, *Shock* 49(2):221-228); and 2) trypanosomiasis (Barría et al., 2018, *Am. J. Trop. Med. Hyg.* 1860(1):91-95). In addition, we demonstrated that connexin hemichannels play a critical role in endothelial insulin resistance induced by pro-inflammatory cytokines and high glucose concentration, which precedes a diabetic condition known to lead to neurodegeneration (Sáez et al., 2018, *Front. Immunol.* 9:1899). In addition, we participated in inter-line collaborative research. In association with young investigator, Alvaro Ardiles of line 3, we found that the absence of pannexin1 affects the reversion of a previously acquired spatial memory (Gajardo et al., 2018, *Front. Mol. Neurosci.* 11:114.), revealing an important role for pannexin1 channels in learning and memory. Finally, together with lines 1 and 5, we found that mutations in human Cx26 (G12R), which cause syndromic deafness, produce hemichannel hyperactivity by impairing the fast gate mechanism that is required to close the hemichannels (García et al., 2018, *J Gen. Physiol.* 150:697-711), providing a molecular mechanism for this disease. Regarding other relevant mechanisms involved in neurological diseases, we showed that the regulator of calcineurin 1 (RCAN1), a gene present in the Down syndrome critical region, contributes to the impaired exocytosis observed in the trisomic condition (Vásquez-Navarrete et al., 2018, *Front Cell Neurosci.* 12:189). We were also invited to write reviews in some of the topics of our expertise including exocytosis, spreading depression, Alzheimer disease, inflammation, redox-mediated regulation of connexin channels, and involvement of Ca^{2+} in cell migration (Marengo and Cárdenas, 2018, *Pflügers Arch.* 470:155-167; Guiza et al., 2018, *Front Physiol.*9:1414; Giaume et al., 2018, *Neurosci Lett.* 695:100-105; Rovegno and Sáez, 2018, *Biochim Biophys Acta Biomembr.* 1860(1):216-223; Sáez and Green, 2018, *Int J Mol Sci.* Aug 21;19(9)).

Research Line 3. Genetic and Developmental Neuroscience. (*K. Whitlock, J. Ewer, and A. Calixto*)

We continued using 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

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are generated in the olfactory sensory system and GnRH neuroendocrine system: **1. Analysis of proliferative cell populations of the olfactory sensory system.** We have previously 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 has shown that a gradient of *distal-less* (Dlx) 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. Parallel to this analysis, we have discovered that the meninges of the brain are continuous with the OE and are associated with a neural-immune interface (see below) **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 neutrophil migration to the OE via the blood vasculature. In further analysis of the adult brain we show that the OE is unique: the principal population of neutrophils reside in the OE suggesting it is also an immune tissue. In collaboration with Pablo Moya (Line 4), Dr. C. Calfún (CINV postdoc) is testing a novel viral delivery system of CRISPR/Cas9 via the OE to mutagenize 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 of neural precursors in the adult, we have discovered hormone-inducible progenitor populations in the hypothalamus. 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 with Dr. J. Ewer, also Line 3) that is not related to domestication effects on the genome, and is supported by loss of GnRH proteins as shown by MADITOF and Orbitrap analysis (Whitlock, Postlethwait, and Ewer, *Front. Neuroendocrinol.*, 2019). We have discovered a hypothalamic peptide that may replace GnRH function in zebrafish. **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. **1- We investigate how the key neuropeptides, Eclosion Hormone (EH) and Ecdysis Triggering Hormone (ETH), control ecdysis behavior.** Specifically, we investigate how EH and ETH cause the sequential expression of ecdysis behaviors. 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. **2- We investigate how EH and ETH cause peripheral actions.** In addition to triggering the ecdysial behavioral sequence, the release of EH and ETH causes changes in peripheral tissues that are critical to insect survival. These include the clearing of molting fluid from the trachea (the network of tubes that provides air directly to each tissue), as well as the rapid hardening (sclerotization) and pigmentation (melanization) of the new exoskeleton, collectively referred to as sclerotization. **3- We determine 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 previously identified the pathway through which the brain clock is coupled to the PG clock. We continue these investigations, aimed at determining how the circadian clock imposes daily rhythmicity to adult emergence (Palacios-Muñoz & Ewer, 2018, *PLoS Genet.* 14(6):e1007433). In particular, we investigate whether genes involved in the synthesis and/or the release of the molting hormone, ecdysone, and/or its actions via its nuclear receptor, EcR, are

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regulated by the clock. **4-** *As part of a cross-line collaboration, we are continuing a project with A. 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. **5-** *We are also continuing a collaboration with Dr. Maria Rita Bueno (U. Sao Paulo, Brazil) characterizing the behavioral and anatomical defects in Drosophila bearing mutations in genes associated with autism in humans.* **Using genetic analysis and genomics approaches to understand the impact of cellular and environmental stress on neuronal and organismal survival.** **1.** *A number of C. elegans models have been used to study neurodegeneration.* One of these is a *C. elegans* strain expressing a neurotoxic allele of the MEC-4(d) DEG/ENaC channel that causes the progressive degeneration of the touch receptor neurons. Using such model, we evaluated the effect of various dietary bacteria on neurodegeneration dynamics and touch receptor neuron (TRN) function. While degeneration of TRNs occurs gradually and is completed at adulthood, when worms are raised on *Escherichia coli* OP50, the strain routinely used for *C. elegans* maintenance, it was significantly reduced when raised on the *E. coli* HT115 strain. HT115 protection is long-lasting and not restricted to the touch receptor neurons. Comparative genomics, transcriptomics, and metabolomics approaches pinpointed the neurotransmitter γ -aminobutyric acid (GABA) as the metabolite differentially produced between OP50 and HT115. HT115 mutants lacking glutamate decarboxylase enzyme genes (Gad), which catalyze the conversion of GABA from glutamate, lost the ability to produce GABA and also fail to stop neurodegeneration. Moreover, *in situ* GABA supplementation or heterologous expression of Gad in *E. coli* OP50 conferred neuroprotective activity to this strain. **2.** *We discovered that diapause formation strongly induces the regrowth of broken axons and functional regeneration from a neuronal soma alone (Caneo et al., 2019, PLoS Genet, 15(1):e1007863).* Diapause entry is triggered by food deprivation and can be used as a new model for the genetic analysis of requirements for neuronal regrowth. We showed that a key regulator of this process is the insulin pathway and DLK-1, both of which are strongly conserved in most animals. **3.** *We also showed that animals confronted with pathogenic bacteria 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. We proposed that this response is triggered by bacteria residing in the worm intestine, which communicates to the animal via small RNAs (Legue and Calixto, 2019, Curr. Opin. Systems Biol. 13: 16-22). Recently, we identified bacterial RNAs that are key triggers of the response and their molecular contributions are in the process of being validated *in vivo*. Another important piece of evidence points at specific miRNAs from *C. elegans* involved in response to pathogens. We built interacting gene networks formed by transcription factors and miRNAs in the worm 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.

Research line 4. Integrative and Circuits Neuroscience (A. Palacios, A. Chávez, P. Moya, Alvaro Ardiles C. Chiu, and O. Schmachtenberg)

This group focuses on understanding how different brain and retinal neuronal circuits work at the synaptic level under normal and pathological conditions, including aging, neurodegeneration, and neuropsychiatric disorders, as some of these processes induce critical alterations in both cognitive and sensory performance. Using a variety of cellular and molecular tools, combined

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with electrophysiology, optogenetic, and behavioral analysis, our research is revealing the roles of different classes of inhibitory neurons. First, we have found that inhibitory synapses from dendrite-targeting somatostatin-expressing (SOM-) interneurons in the cortex are selectively potentiated by excitatory glutamatergic activity (Chiu et al., 2018, *Neuron*, 97:368-377). In a broader context, this work suggests a tight link between the regulations of inhibitory circuits and their function. Whereas perisomatic inhibition from parvalbumin interneurons shapes and is shaped by principal cell firing (cell output), dendritic inhibition from SOM-interneurons modulates and is modulated by synaptic activity (cell input). In addition, we provide physiological and behavioral evidence that SOM-interneurons play an important role in gating the synaptic output of the basal forebrain, controlling cortical operations (Espinosa et al., 2019, *Cerebral Cortex* 29:42-53). Collaborative work within this line is also uncovering the potential role of neurotransmitter transporters in neuropsychiatric diseases. We recently demonstrated that overexpression of the neuronal glutamate transporter, EAAT3, at excitatory synapses in the brain recapitulates behavioral and synaptic alterations in NMDA receptors relevant to obsessive-compulsive disorder (OCD) (Delgado-Acevedo et al., 2018, *Neuropsychopharmacol.* 44(6):1163-1173). These results provide further support for the glutamatergic hypothesis in the pathogenesis of OCD, and also provide a valuable animal model that may open novel therapeutic approaches to treat this devastating disorder.

Collaborative work continued with Line 2. We demonstrated that pannexin 1 channels play an important role in the induction of synaptic plasticity and in the learning and memory processes (Gajardo et al., 2018, *Front Mol Neurosci.* 11:114). We also extended our collaborative work to understand the role of neonatal exposure to estradiol in the modulation of dopaminergic transmission in the nucleus accumbens, which may be associated with increased reinforcing effects of drugs of abuse (Bonansco et al., 2018, *J. Neuroendocrinol.* 30(7):e12574). Work continues in this area by demonstrating the existence of similarities among the binding sites of the monoaminergic serotonin (SERT) and dopamine (DAT) transporter, proteins that have been implicated in several psychiatric and neurological disorders. Beyond their functional implications, our findings are valuable for the design of novel selective and non-selective ligands for these transporters (Núñez-Vivanco et al., 2018, *PLoS One.* 13(7):e0200637). At the level of sensory systems, we concentrated our efforts in understanding the role of inhibitory synapses in regulating visual processing in the inner retina. We found that electrical coupling between GABAergic A17 amacrine cells could enhance reciprocal inhibitory feedback to rod bipolar cells, and thus regulate the temporal properties of visual responses (Elgueta et al., 2018, *Sci Rep.* 8(1):3123). In addition, we found that retinal ganglion cells (RGCs) with peripheral receptive fields are larger, faster, and have shorter transient responses. This translates into higher sensitivity at high temporal frequencies when compared to RGCs with more central receptive fields in a diurnal retina, which highlights the complexity of the computational strategies implemented in the early stages of visual processing (Escobar et al., 2018, *Front Cell Neurosci.* (12) 444). We have extended our research at the level of sensory systems by showing that Schwann cells, a class of glial cells of the peripheral nervous system, change their phenotype following nerve injuries and also display long-term changes during aging (Couve et al., 2018, *J. Dental Res.* 97(3):347-355 and *Front. Cell. Neurosci.* 12:299).

Research Line 5. Crosscutting: Computational Biology and Bioinformatics. (D.F. González T. Pérez-Acle and P. Orio,). By combining experimental evidence with advanced mathematics,

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physics, and thermodynamics, we develop computational models to study diverse biological systems. Our efforts are organized in: **I.** Theoretical & Computational Neuroscience (TCN), **II.** Theoretical Biophysics (TBs), and **III.** Target Discovery, Drug Discovery and Drug Delivery (TD5). In **TCN**, using numerical simulations, we have advanced our knowledge about how complex behavior emerges in neuronal networks. We showed how chaotic and stochastic interact in shaping the multistable brain operation (Orio P et al., 2018, *Chaos* 28(10), 106321) and how long-range dependency can arise from rather simple -but noisy- neuronal adaptation mechanisms (Richard et al., 2018, *J Comput Neurosci* 44(3):297-312). In collaboration with Line 4, this research has provided analysis techniques that are now being used in the study of synchrony of oscillations in sensory systems. We also developed a novel simulation platform (PISKaS) suitable for conducting stochastic simulations of complex multiscale systems using an agent and rule-based approach. We demonstrated the multiscale modeling capabilities of PISKaS by applying it to the study of the Sigma factor transcriptional network of *E. coli*. We have also applied PISKaS to the effect of information on the dispersion of the Ebola fever and on the role of trust as a proxy for the creation of economic capital in human societies (Pérez-Acle et al., 2018, *Biochem Biophys Res Commun.* 498(2):342-351.; Bustos et al., 2018, *Methods Mol Biol.* 1819:3-32). Working with our collaborators from Lines 1 and 2, in **TBs**, by relying on a transdisciplinary approach including molecular modeling and simulations together with mutagenesis and biophysical techniques, we demonstrated that the G12R mutation in human connexin (Cx) 26 hemichannels, which causes syndromic deafness, impairs both the fast and slow gating processes (García et al., 2018, *J. Gen Physiol.* 150(5):697-711). To support these findings, we developed a set of novel methods that use network theory to analyze the structure and dynamics of Cx-based channels discovering a very uncommon interaction between arginine in position 12 of the amino-terminal and arginine 99 located in the intracellular loop of Cx26 (Contreras-Riquelme et al., 2018, *PeerJ*, 6:e5998). In **TB** we have also investigated the thermal pathway of TRPV1 to identify the residues involved in the thermal activation process (Castillo et al., 2018, *Phys Biol.* 15(2):021001). To date, we have 4 new mutants with different temperature sensitivities that validate the thermal pathway observed in our simulations. In the same context, we have developed a more precise theoretical method that describes 3 kinds of residues that are involved in the modulation of the thermal activation of TRPV1. During 2019 we will explore in detail the thermodynamic process through ITC and DSC using TRPV1 self-ensembled in micelles and nano-discs. The overexpression of TRPV1 and its reconstitution in lipid vesicles is ongoing through the collaboration with Dr Eleonora Zakharian, University of Illinois College of Medicine. In **TD5**, we have continued exploring different drug-delivery systems, including gold nanoparticles (Camarada et al, 2018, *Langmuir.* 34(34):10063-10072) and dendrimers (Elizondo-García et al, 2018, *Molecules.* 23(4)).

Of note, by relying on strategic funding from the CINV, we hired a new postdoctoral researcher who will conduct research in Neuromorphic Computing, fostering a new collaborative effort with A. Palacios from Line 3.

Research Line 6. Unit of Translational Science (D. González, T. Pérez Acle, J.C. Sáez and C. González).

In July 2018 we hired Mr Javier Ramírez, who was in charge of identifying and coordinating emerging Research + Development (R + D) project among the CINV scientists. Mr Ramírez met with each scientist of CINV to identify potential R + D projects and at least three were identified,

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which are currently in preparation to be presented in future national calls for R + D grant applications.

Members of this Unit and members of a Chilean spin-off called Connectomica SPA coordinated the preparation of a grant application, which was submitted to and later awarded by CORFO (R + D project called Technologic Contracts)(CORFO :Corporación de Fomento de la Producción). The “Contrato Tecnológico” project is entitled: “Evaluación ADME/Tox D4: Un fármaco candidato para el tratamiento de la distrofia muscular de Duchenne” (*Evaluation of ADME/Tox D4: a candidate drug for the treatment of Duchenne muscular dystrophy*). The project is led by T. Pérez-Acle (Line 5) and A. Martínez (Line 2). The CINV is charged with developing the main aims of the project, including the toxicological analysis of a selective and potent connexin hemichannel blocker, called D4. Also, the CINV representative, A. Martínez, will determine the EC50 for Cx43 and Cx45 hemichannels using fluorescence and electrophysiology techniques. Line 6 also aided in the presentation of a FONIS project (Fondo de Investigación Nacional en Salud = National Funds for Research in Health). The main aim is to determine the frequency of mutation in the Cx26 gene in congenital deafness in the Chilean population. The Director of this project is the young investigator, Helmuth Sánchez; the project also includes CINV investigators, A. Martínez and P. Moya.

b) Publications

Summary table

| <u>Category of Publication</u> | <u>MSI Center Members</u> | <u>Number of Publications coauthored by students</u> | <u>Total Number of Publications</u> |
|---|---------------------------|--|-------------------------------------|
| ISI Publications or Similar to ISI Standard | Associate Researchers | 15 | 31 |
| | Other Researchers | 5 | 17 |
| SCIELO Publications or Similar to SCIELO Standard | Associate Researchers | 0 | 0 |
| | Other Researchers | 0 | 0 |
| Scientific Books and chapters | Associate Researchers | 2 | 5 |
| | Other Researchers | 0 | 0 |
| Other Scientific Publications | Associate Researchers | 0 | 1 |
| | Other Researchers | 1 | 1 |
| <u>Total of Publications</u> | | 23 | 55 |

b) Other achievements

Patents:

NONE

Intellectual property:

Dra. Kathleen Whitlock;

1. 333912018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Compost.
2. 333922018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Biogas.

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3. 333932018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Energía Solar Eléctrica.
4. 333942018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Hornos Solares.
5. 333952018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Manos Sucias.
6. 333962018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Acuaponía.
7. 335362018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Un Motor Simple.
8. 335372018 Obra De Creación Artística Obra Artística (Videograma) Titulada: El Termómetro.
9. 335382018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Una Brújula.
10. 335502018 Obra De Creación Artística Obra Artística (Videograma) Titulada: Guateros Mágicos.

Congress Presentations:

Summary Table

| Type of presentation | National Events [Number] | International Events [Number] |
|---|-----------------------------|----------------------------------|
| A. Associate Researchers | | |
| Conferences, oral communications, poster communications, others (specify) | 19 | 18 |
| Invited presentations (not included in above row) | 8 | 6 |
| B. Other researchers (Adjunct Researchers, Senior Researchers, Young Researchers, Postdoctoral Researchers and Students) | | |
| Conferences, oral communications, poster communications, others (specify) | 6 | 8 |
| Invited presentations (not included in above row) | 2 | 2 |

Organization of Scientific Events:

- **Symposia Two Photons organized by Dr. Andrés Chávez and Dr. Chiayu Chiu.**

The two-photon microscope was inaugurated on May 25th. It is the only one of its kind in the country, and allows the study of neurons in real time and in three dimensions. This activity was attended by the President of the University of Valparaíso, Dr. Aldo Valle, Dr. Ramón Latorre, Director of the CINV, and the President of CONICYT, Dr. Mario Hamuy

- **1st Chilean Conference on Computational Neuroscience, by Dr. Patricio Orio.**

This first meeting of computational neuroscience in Chile, organized by researcher of the CINV, Dr. Patricio Orio, was held at the CIAE, center of the University of Valparaíso (August 9 and 20) and was attended by researchers, postdocs, and students, with backgrounds as diverse as biology,

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physics, mathematics, and informatics. The assistants shared their latest results and work in progress, establishing links and fostering interdisciplinary interactions.

- **Latin American Training Program 2018, Organized by Dr. Juan Carlos Sáez.**

A group of graduate and postgraduate students from leading universities and research centers throughout Latin America and the Caribbean participated in the Latin American Training Program 2018 (LATP Chile), which took place at the Universidad de Valparaíso. The course, which was held for the first time in Chile, brought together leading scientists throughout the region and the world, who provided young scientists with training in the field of theoretical and experimental neuroscience. The course lasted three weeks (from August 26 to September 15), had an intense program of activities and involved nearly forty national and foreign researchers.

- **Symposia Academia de Ciencias de America Latina (ACAL 2018) Organized by Dr. Ramón Latorre.**

This meeting was organized by Dr. Ramón Latorre, Director of CINV, with support from the Allende Connelly Foundation and the Chilean Academy of Sciences. The "Academia de Ciencias de América Latina" (ACAL) is a regional alliance that brings together 250 Latin American researchers. On this occasion, the need was expressed to provide support for science in countries in crisis, including Nicaragua and Venezuela.

- **Meeting Max Planck, Valparaíso “Understanding Brain Function and Dysfunction: from Synapses to Circuits. Organized by Dr. Chiayu Chiu.**

This activity was organized by Dr. Chiayu Chiu, who is also one of the two "Max Planck Leader Group" investigators hired through the alliance between the CINV and the Max Planck. It brought together world experts in Valparaíso and allowed scientists from the CINV to interact with Max Planck groups from Germany, Argentina, and the United States, and share novel findings about brain function.

- **Symposia organized for the IX Annual Meeting of the Chilean Society of Neuroscience.**

CINV researchers organized and participated in two symposia held during the 2018 Meeting of the Chilean Society of Neuroscience Meeting (November 20-22, Puerto Varas): "From neural connectivity to network dynamics", organized by Patricio Orio; "From the retina to the CNS: Role of neuromodulatory systems", organized by Oliver Schmachtenberg and "Recent progress on the mechanism of neurological dysfunction in epilepsy", organized by Juan C. Sáez. These events included presentations from other national and international scientists and attracted an audience of about 40 scientists each.

- **CINV Meeting 2018. “Science that makes changes”.**

Organized by CINV graduate students, this year's name for the annual CINV meeting was “**Science that Makes Changes**”. The meeting was held at the Naval Museum where most members of the CINV presented their accomplishments for 2018 as a talk or a poster.

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Scientific Editorial Boards

John Ewer: PLoS Genetics, J. Insect Sci., Current Op. Insect Sci., Insect Biochem. Mol. Biol., J. Comp. Physiol. A

Carlos González: J. Biol. Chem., AnFaMed, Revista Habanera de Ciencias Médicas, Front. Physiol.

Ramón Latorre: Biol. Res., Proc. Nat. Acad. Sci., J. Gen. Physiol., Channels, Temperature, Front. Pharmacol. Sci., Eur. Biophys. J..

Tomás Pérez-Acle: PeerJ, PeerJ Computer Sciences.

Adrián Palacios: Biol. Res., Membre Correspondant International de la revue intellectuelle, Journal on Policy and Complex Systems.

Juan Carlos Sáez: Invited Ed. special edition magazine Int. J. Mol. Sci., Involvement of Connexin Hemichannels in the Inflammatory Response of Chronic Diseases.

Andrés Chávez: Revista ReCISAM. Universidad de Tarapaca, Chile, Review Editor in Frontiers in Cellular Neuroscience.

Awards: During this period the following Fondecyt grants were awarded to CINV investigators as P.I

- Role of connexin hemichannels in the crosstalk between odontoblast and dental primary afferents in cariogenic conditions (11180531). **PI: Isaac García.**
- Role of dynamin-2 in central nervous system synapses: potential impact of centronuclear myopathy-causing mutations on ampa-receptor trafficking and excitatory synaptic transmission (11180731). **PI: Arlek González.**
- Chaos vs. noise as drivers of multistability in neural networks (1181076). **PI: Patricio Orio.**
- Molecular mechanisms at the nanobio interfase: applications and biohazard (1180987). **PI: José Antonio Gárate.**
- The cold-receptor TRPM8 channel contains a temperature sensor at coiled-coil domain located at C-terminus end (1180999). **PI: Karen Castillo.**
- Functional coupling between voltage sensor and permeation pathway in hv1 channels (1180464). **PI: Carlos González**

Other Awards

1. Project support Networks Training Centers (REDES180138). **PI. Andrea Calixto.**
2. Development of computational methods for the determination of causal-condition specific gene regulatory networks. **PI. Andrea Calixto.**
3. The best researcher UNAB. **PI. Danilo González Nilo.**
4. Member of the World Academy of Science o TWAS. **YR Karen Castillo.**
5. Member of the Chile-USA Council on Science, Technology and Innovation. US Embassy in Chile. **PIs. Tomás Pérez Acle and John Ewer**
6. FONIS Grant, Research associate. Identification of Mutations Causing Congenital Deafness in Chile, Directors Helmuth Snchez (CINV-UV) and Elvira Cortese (Fac. Medicine). **PI. Agustín Martínez.**
7. CORFO. Technological Contract Project. Conectomica-CINV. Scientific Coordinator. **PI. Agustín Martínez.**

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4. **Education and Capacity Building** (4 páginas para Institutos)

The CINV participates in 3 Graduate programs: the Master's Program in Neuroscience, the PhD. Program in Neuroscience, and the PhD. Program in Biophysics and Computational Biology

A) Masters Program in Neuroscience.

This program is directed by Dr. Agustín Martínez (CINV research Line 2). This program has been accredited by the CNA since 2006, and is currently being re-accredited. It 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. For requirements to apply to the program see www.magisterneurociencia.cl

a) *Achievements and results:*

Eighty-one students have graduated since its creation in 1999 (44 females; 37 male). This year the program received 32 applications of which 16 were accepted, being close to the maximum number of students we can accept every year. Of these, 2 received fellowships from CONICYT. During the interview process, several applicants mentioned the existence of the CINV as one of the reasons for choosing our program. All students typically attend one national or international scientific meeting in their area of study per year; funding is provided through their fellowship, their advisor's grants, or by fellowships offered by the University of Valparaíso.

b) *Graduations of students:*

Last year we graduated 10 students of which 6 did their thesis in laboratories of the CINV, listed below.

1. Jaime Maripillan Sobarzo. Title: "Papel del citoesqueleto en el tráfico de hemicanales y en la formación de uniones en hendidura". Advisor: Dr. A. Martínez (Line 2).
2. Mauricio Javier Segura Del Rio. Title: "Ritmos circadianos y actividad locomotora anticipatoria en *Octodon degus*." Advisor: Dr. J. Ewer (Line 3).
3. Ana Becerra Ibáñez. Bibliographic Revision. Title: "Posibles mecanismos implicados en el efecto de la música de Mozart en los daños por estrés crónico en la función emocional, cognitiva y plasticidad límbica". Advisor: Dr. A. Martínez (Line 2).
4. Jorge Luis Castex Páez. Title: "Papel del carboxilo terminal de la conexina 43 en la permeabilidad de la membrana plasmática mediada por hemicanales.". Advisor: Dr. A. Martínez (Line 2).
5. Luis Manríquez Cockbaine. Title: "Alteraciones en paradigmas de memoria y aprendizaje producidas en ratones". Advisor: Dr. P. Moya. (Line 4).
6. Kiyoko Nelida Suzuki Barrera. Title: "Respuesta neurovascular en pulpa dental durante reabsorción radicular fisiológica de dientes temporales humanos". Advisors: Drs. E. Couve and O. Schmachtenberg (Line 4).

c) *Thesis Project Approvals and Qualifying exams:*

Last year 10 thesis projects were approved, of which 5 are advised by CINV members:

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1. Francisca Henríquez Belmar. Title: “Evaluación de la transmisión sináptica inhibitoria en el hipocampo de un modelo con sobreexpresión del transportador de glutamato EAAT3” Advisor: Dr. Dr. Pablo Moya (Line 4).
2. Camila Quiroz Cid. Title: Neuromodulación de la transmisión sináptica inhibitoria en la retina de mamíferos”. Advisor: Dr. A. Chávez (Line 4).
3. Hugo Almarza Salazar. Title: “Alteraciones en el tráfico vesicular en líneas celulares de pacientes portadores de disferlinopatía”. Advisor: Dr. A.M. Cárdenas (Line 2).
4. Alejandra Dominique Díaz Valdivia. Title: “Sensibilidad espectral de las células rabdoméricas de la retina proximal de *argopecten purpuratus*”. Advisor: Dr. O. Schmachtenberg (Line 4).
5. Carlos Ancaten. Title: “Regulación de la excitabilidad neuronal mediada por TRPV1 en el giro dentado”. Advisor: Dr. A. Chávez (Line 4).

d) Destination of Students:

About half of our graduates have gone back to their professional practice, and the other half have followed the academic pathway, entering diverse Ph.D. programs in Chile and abroad, including our PhD in Neuroscience. Some of them are academics in Chile or abroad.

B) PhD Program in Neuroscience (Program Director Dr. Ana M. Cárdenas, line 2).

This program was created in 2002, and is designed to train researchers interested in the field of development, structure, and function of the nervous system. Its strengths are the areas of molecular physiology and biophysics, sensory neuroscience, neuronal plasticity and neuropathology, development and neurogenetics, and computational neuroscience. 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.

a) Achievements and results:

This program has been accredited continuously since 2004 by the Chilean National Committee on Accreditation (CNA). In recognition for its high-quality, in 2017 it was re-accredited for a record 7 years through 2025. The proportion of students originating from other countries has been increasing. Thus, the program has matured and can compete effectively with programs in Santiago, despite the draw from the capital. Our program ensures funding for 4 years to all accepted students, allowing students to devote full time to their PhD. In addition to fellowships from the Government funding agency (CONICYT, available only to accredited graduate programs), the Universidad de Valparaíso and the CINV provides graduate fellowships (12 and 1 fellowships in 2018, respectively). Currently, the Program has 34 students (20 females, 14 males). In 2018 9 students (7 female; 2 male) were selected and accepted to join the Program. Of these, 4 are from abroad (Germany, Spain, Senegal and Venezuela). Four students received fellowships from CONICYT.

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b) Graduations of students (2018 academic year):

In 2018, we graduated 7 students of which 4 did their thesis in laboratories of the CINV, listed below.

1. Fernando Hinostroza. Title: “Impact of dynamin-2 R465W mutation linked to centronuclear myopathy on dynamin interactions, helix dimer, and helix structure: a study using molecular dynamics simulations”. Advisor: Dr. Ana M. Cárdenas.
2. Cesar Ravello. Title “Motion coding in rodent retina under stimulation with complex images”. Advisor: Adrian Palacios.
3. Miguel Piñeiro. Title: “Study of CCAP regulatory mechanism of ecdysis behavioral sequence in *Drosophila* through mathematical and computational model”. Advisor: Patricio Orio.

c) Thesis Project Approvals and Qualifying exams (2018 academic year):

Last year 5 students approved their thesis projects and qualifying exams of which 5 are doing the thesis in laboratories of the CINV, listed below.

1. Cristobal Ibaceta. Title “mGluR dependent plasticity process (LTP and LTD) to survey impairment cognitive in aging degus, as well as voluntary exercise”. Advisor: Dr. Adrian Palacios.
2. Liliana Bustos. Title “Circadian control of the daily rhythm of adult emergence by regulation of the timing of ecdysone action in *Drosophila melanogaster*”. Advisor: Dr. John Ewer.
3. Carolina Flores. Title “Pannexin-1 regulates dendrite branching and dendritic spine formation by modulating actin polymerization by Rac1 and Cdc42 small Rho-GTPase”. Advisors: Dr. Álvaro Ardiles and Dr. Agustín Martínez
4. Scarlett Delgado. Title: “Transcriptomic and functional analysis of a neuronal pro-regenerative condition in *Caenorhabditis elegans*”. Advisors: Dr. Andrea Calixto and Dr. Chiayu Chiu.
5. Felipe Tapia. Title “Rol de la modulación colinérgica en la secreción de factores de crecimiento por epitelio pigmentario de la retina y sus implicaciones en el desarrollo de la miopía”. Advisors: Dr. Oliver Schmachtenberg and Dr. Andrés Chávez.

d) Destination of Students:

The majority of graduates of our Program currently have faculty or postdoctoral positions in Chile, USA or Europe, with the exception of a few graduates from 2018 who are either looking for postdoctoral positions or are completing experiments and preparing their thesis work for publication.

C) PhD. program in Biophysics and Computational Biology (Program Director: Dr. Patricio Orio, Line 5).

This Program is one of the main achievements of the CINV in terms of 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. It receives students with diverse undergraduate

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training, from mathematics and physics to biology. A flexible study plan allows each student to quickly obtain the knowledge and abilities most relevant to their thesis, plus a common background in Biophysics of Excitability and Computational Biology. Computational Neuroscience, Ion channel Biophysics and Molecular Modeling of Macromolecules are some of the topics that the students can develop in their thesis.

a) Achievements and results:

During 2018, this program was re-accredited for 5 years by the CNA, an outstanding period for a second-time accreditation, which reflects the quality of its study plan and its faculty. Currently it has 12 students (2 females), and 4 more were selected for the 2019 year. Two students qualified to begin their thesis during 2018 (see list below), and now a total of 5 are carrying out their thesis work. Eleven of the currently enrolled students were granted a PhD fellowship from CONICYT. Our students participate regularly in different international courses and Congresses and travel abroad for international stays to carry out work relevant to their thesis.

b) Destination of Students:

The only graduate of the program (graduated at the end of year 2017) holds a Post-Doctoral research position in Dr. Francisco Bezanilla's laboratory at University of Chicago.

c) Thesis Project Approvals and Qualifying exams (2018 academic year):

Last year, two students approved their thesis projects and qualifying exams of which one is doing the thesis in laboratories of the CINV,

1. Emerson Carmona. Title: "Corrientes de compuerta del canal de protones dependiente de voltaje Hv1". Advisors: Dr. Carlos González and Dr. Ramón Latorre.

Students visiting laboratories abroad.

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

- Samy Castro: Techniques for the analysis of brain connectivity at Dr. Bratislav Misić's lab, Montreal Neurological Institute Canada. September 4th to 29th, 2018.
- Daniela Di Georgis: Regulation of voltage sensing structures of CaV1.2 calcium channel by the auxiliary β -subunit at Dr. Ricardo Olcese's lab, UCLA. USA. December 12th 2018 to April 4th, 2019.

Students from abroad visiting CINV laboratories.

- Alejandro Herrera Delgado, PhD student at Universidad de Sevilla, Spain, visited Dr. Juan Carlos Sáez's lab. August 21st to November 21st, 2018.
- Maximiliano Zuluaga, undergraduate student at Universidad Nacional de Colombia, visited Dr. Oliver Schmachtenberg's lab. July 30th to December 12th, 2018.
- Lucas Bayones, PhD student at Universidad de Buenos Aires, Argentina, visited Dr. Ana M. Cárdenas' lab. September 23 to October 6th, 2018.

Organization of National and International courses and workshops:

1. 1st Jornada Chilena de Neurociencia Computacional. August 9th to 10th, 2018.
2. Latin American Training Program 2018. August 27th to September 15th.

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3. Max Planck meets Valparaiso Microscopy Course. December 3st, 2018.
4. Symposium: Understanding Brain Function and Dysfunction: from Synapses to Circuits. December 4th, 2018.
5. CINV Meeting 2018. “Science that makes changes”. December 20th, 2018.
6. Course: “Learn and Build your Own Chemical Tools for Biomedical Research” October 8th-19th, 2018.
7. Council meeting of the ACAL and a Symposium, November 14th 2018.
8. EMBO Practical Course on Developmental Biology, January 9th – 21st, 2018.

Strategies to hire and incorporate young investigators.

In 2018, our center hired a new young investigator, Dr. Isaac García. He was awarded a CONICYT grant for “Insertion of Advanced Human Capital in the Academy” in 2017, and a FONDECYT grant for “Initiation to Research” in 2018. Currently, Dr. García has an academic position at the Dentistry School of Universidad de Valparaiso. He will greatly strengthen Line 1 and our PhD programs.

5. Networking and other collaborative work (3 páginas para Institutos)

a) Networking

In 2018, the CINV consolidated both its national and international alliances and collaborations by organizing activities such as Symposia and International Meetings in Valparaiso. Under the direction of J.C. Sáez, the Latin American Training Program (LATP) was held for the first time in Chile and was sponsored by the CINV and the Society for Neuroscience (SfN), with the support of IBRO (August 22th to September 14th; entitled “From molecules to behavior – the quest for new treatments of neuropathologies”). From 150 applicants 15 students were selected (10 women and 5 men; 4 from Argentina, 3 from Brazil, 4 from Colombia, 2 from Mexico, 1 from Perú and 1 from Chile) to participate with all expenses covered by the organization. CINV researchers played a key role in the course, with the participation of 13 senior investigators and 3 young investigators (H. Sánchez I. García, K. Castillo). In addition, 20 national and international speakers were invited to teach in the course. The program included lectures, workshops, laboratories, etc. More information is available at: cinv.uv.cl/evento/latin-american-training-program/ and www.sfn.org/Initiatives/Diversity-Programs/Latin-American-Training-Program

In France, the State designated 10 Universities to increase their development. One focus is to expand their horizon by interacting with institutions around the globe. The CINV was chosen as the Chilean Institution with complementary research features that would potentiate their teaching and research. During the academic 2018 year Prof. Laurent Counillon, Vice-Dean Faculty of Sciences, and Prof Jeanick Brisswalter, Vice Président Recherche, both from University Côte d’Azur, Nice, France, visited the CINV and, together with R. Latorre and J.C Sáez, discussed the best way to establish a solid teaching collaboration. Dr Counillon already contributed with several lectures in the LATP 2018. R. Latorre and J.C Sáez were invited to contribute with lectures in graduate courses at the University Côte d’Azur in 2019. These events will also serve to define efficient collaborative research between members of both institutions.

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The CINV and the Chilean Academy of Science, with the support of the Allende Connelly Foundation, organized the Meeting of the Council of the Academy of Science of Latin American (ACAL), and a Symposia. The Symposium aimed to strengthen the bonds of Latin American science, in particular with Venezuelan scientists who are experiencing very difficult times in terms of adequate conditions to develop their research and teaching. The activity was led by Dr. R. Latorre and included the participation of the Council of ACAL, composed of Claudio Bifano (Venezuela), President; Rafael Apitz (Venezuela), Chancellor; and María Luisa Izaguirre (Venezuela), Co-Chancellor; and the council members Gerhard Malnic (Brazil), Ramón Latorre (Chile), and Jorge Allende (Chile). Some of the recently-elected ACAL members also participated. More information is available at cinv.uv.cl/simposio-acal/

As part of the **Genetic and Development Network**, the CINV participated in the organization and teaching of the “EMBO Practical Course on Developmental Biology”. This international course is offered every 2 years since 2010 and attracts students from all over Latin America. It is an intensive 13 day laboratory and lecture course for advanced graduate students and postdoctoral fellows who seek a broad view of the modern issues of Developmental Biology. The animal models used for the practical work included zebrafish, *Drosophila*, *Xenopus*, chick, and planarians. In 2018 it was organized by Dr. Roberto Mayor (UCL, London, UK), Dr. Carmen Feijoo (UNAB, Chile) and Dr. John Ewer (CINV, line 3). Faculty for 2018 were John Ewer, Ray Keller, Roberto Mayor, Nipam Patel, Alejandro Sanchez-Alvarado, Andrea Streit, Claudio Stern, and Kathleen Whitlock. The course also included a one-day symposium open to the Chilean scientific community. For more information, see biodesarrollo.unab.cl. Dr. Whitlock participated as an instructor and symposium speaker in the V Latin American Zebrafish Network (LAZEN) Course and Symposium was held from May 4th -12th, 2018 at the Institute of Biotechnology of the National Autonomous University of Mexico. The purpose of LAZEN is to promote the use of zebrafish as a research model, the exchange of material and experiences, and to foster advanced training of young scientists in the region. A group of 19 students (undergraduate, graduate and post-doctoral researchers) from 8 different countries took part in the course and symposium.

As part of our network in **Biophysics and Computational Neuroscience**, the CINV organized in August 2018 the first Chilean conference on Computational Neuroscience, headed by Dr P. Orio. The main objective of this two-day workshop was to bring together the largest neuroscientific community with computing interests, to get to know each other and exchange different points of view among national researchers working in this discipline, to strengthen the networks and scientific collaboration. It was attended by 75 researchers, postdocs, and students with backgrounds as diverse as biology, physics, mathematics, and computing. More information is available at cinv.uv.cl/1-jornada-de-neurociencia-computacional/.

Working together with the Max Planck Society, the CINV hosted the 2nd CINV-Max Planck Symposium, “Understanding Brain Function and Dysfunction: from Synapses to Circuits” from December 2nd to 5th, 2018. Prominent neuroscientists from Max Planck Institutes in Germany, the United States, and Argentina participated in the meeting, including 8 past and current institute directors. The event was organized by Dr. Chiu, a CINV-Max Planck Group Leader, to disseminate knowledge and facilitate collaborations among researchers locally within the CINV,

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nationally in Chile, and internationally in the Americas. Symposium speakers covered topics ranging from neurodevelopment, synaptic physiology, neuronal excitability, sensory processing, circadian rhythm, social behavior, and stress, which are all active areas of research in the CINV and at the Universidad de Valparaíso. In fact, 8 of the 22 speakers were faculty within the CINV (R. Latorre, J.C. Sáez, A. Martínez, A. Chávez, J. Ewer, K. Whitlock, A. Calixto, C. Chiu and R. Suárez). In conjunction with the symposium, the CINV also held an imaging workshop in which 6 local students were selected to participate in a practical laboratory course for two afternoons. These students received hands-on training in advanced fluorescence microscopy techniques such as the spinning disk and 2-photon microscopes. More information is available at cinv.uv.cl/mpsymposium/

b) Other collaborative activities.

Juan Carlos Sáez and Christian Steinhäuser from Bonn University applied for a binational research grant.

John Ewer continued long-term collaborative work with Benjamin White (NIH, USA) and Christian Wegener (University of Würzburg, Germany).

Andrea Calixto was awarded a collaborative strategic research grant from CYTED-Conicyt, together with Diego de Mendoza (IBR, Argentina) and Ernesto Perez Rueda (Instituto de Biotecnología, UNAM, Mexico) to identify bacterial consortia that offer neuroprotection. Scientist Chiayu Chiu is also part of the research group. Additionally, Dr. Calixto was awarded a Networking grant (REDES, PCI) to support the collaborative research initiative with Max Planck in Dresden, Germany (Teymuraz Kurzchalia) and the IBR in Argentina (Alejandro Vila). This grant aims to discover neuroprotective bacterial metabolites and their mechanism of action in *C. elegans*.

Andrés Chávez is collaborating with Dr Pablo Castillo from Albert Einstein College of Medicine and Dr. Marco Fuenzalida from Universidad de Valparaíso to unravel the role of serotonin receptors in the modulation of excitatory and inhibitory synaptic plasticity. In addition, Dr. Chávez is collaborating with Dr. Paola Haeger, Universidad Católica del Norte, Chile, in order to understand the mechanism underlying changes in NMDA receptor mediated transmission after early and postnatal alcohol consumption and their effect on memory process in offspring.

Pablo Moya continued collaborations with scientists Andrew Holmes (NIAAA) and Ashok B. Kulkarni (NIDCR) on the generation and characterization of a novel genetic model to study OCD neurobiology, resulting in a publication in *Neuropsychopharmacology* on Dec 2018. As part of his duties as member of the Latin American Board of the American College of Neuropsychopharmacology (ACNP), Dr. Moya organized the visit of Dr. Carlos Zárate from NIMH to give plenary talks both at UV as well as at the meeting of the Chilean Society of Neurology, Neuropsychiatry and Neurosurgery (SONEPSYN), and to foster basic-clinical collaborations in future.

Agustín Martínez has a longstanding collaboration with colleagues from the University of Chicago, Drs. Eric Beyer and Viviana M. Berthoud. This collaboration is centered on the study on the structural mechanism of opening of Cx50 hemichannels. He also collaborates with Dr. Jorge Contreras (Rutgers University) on the biophysical consequences of mutations in Cx26 and Cx30 associated with human disease. Finally, a national collaboration with Juan Pablo Henríquez (Universidad de Concepción), resulted in the discovery that motoneurons develop electrical synapses in ALS patients (work currently under revision).

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Dr. Christophe Chipot has been constant collaborator of the CINV, working with Dr. Danilo F. González on Theoretical Biophysics. Dr. Chipot is a prominent researcher from the CNRS. During his stays in Chile he has organized more than 7 workshops aimed at PhD and undergraduate students.

A successful collaboration started between Dr. Danilo F. González and Dr. Zakharian from the University of Illinois College of Medicine, Illinois, USA in the field of over-expression and purification of transmembrane proteins, specifically, TRPV1 and TRPM8.

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6. Outreach and connections with other sectors (3 páginas para Institutos)

a) Outreach:

During this second period as a Millennium Institute, the outreach activities of CINV were aimed at conveying to citizens the notion that an adequate development of science is essential if Chile is to become a developed country, and to show how science could help with the implementation of public policies. In particular, this year the CINV decided to actively participate in public debates of the Chilean society, contributing its scientific knowledge to the public discussions. The result of CINV outreach activities amounted to an important number of newspapers articles, appearances in radio, TV, and internet, throughout the country. In this regard, different researchers of the CINV are recognized spokespersons for authorities and for the press. Dr. R. Latorre is a national reference regarding science policies. In the national press and Congressional Commissions he provides an important role in explaining the importance of science for the adequate development of knowledge in the country. In particular, dissemination of science in regions outside Santiago (capital of Chile) is crucial in an extremely centralized country, and is becoming more important than ever given the recent creation of the Ministry of Science. The CINV has also participated in public activities promoting the role of women in science, with the participation of Drs. K. Whitlock, A. Calixto and K. Castillo. The acceptance of Dr. K. Castillo as the only Chilean member of TWAS Young Member was an important achievement in that sense. Dr. J. Ewer continues his presence in national media explaining how the daylight-saving time system can have important consequences for the health of children and adolescents in Chile and has authored a law that may establish the time zone for Chile. Dr. T. Pérez-Acle had an active role in communicating how artificial intelligence can help solve the problems and challenges of our society, and Dr. Moya appeared in newspapers and radio interviews disseminating research on the neurobiological basis of Obsessive-Compulsive Disorder. In addition, Dr. J.C. Sáez disseminated his discoveries on the treatment of muscular dystrophy with boldine, the main alkaloid present in the boldo tree (an endemic plant present in the central region of Chile) in various media, public talks, and medical groups of the Teleton Foundation. This earned him the recognition from Las Últimas Noticias, one of the most important newspapers in the country, as one of the 5 most important discoveries of the year made by Chilean scientists. Since 2015, Dr O. Schmachtenberg's laboratory has developed a research line on the sensory systems of the Chilean recluse spider, being able to demonstrate the olfactory abilities of these animals, and becoming a spokesperson on this issue of relevance to public health, generating multiple press articles and participating in documentaries of national and international distribution.

The most relevant CINV outreach activities were:

Tertulias Porteñas. Since 2011 we bring together high-level scientists, artists, and intellectuals, to discuss neuroscience-related topics with an interdisciplinary approach. The *Tertulias* are open to the general public and aim to captivate the public with the creative inspiration that moves science, the humanities, and the arts, with the ultimate goal of showing that science always leads us to unknown territories that are worth exploring. The *Tertulias* are consolidating the alliance between science and culture that the CINV has promoted since its beginnings. In particular, a partnership with the National Council of Arts and Culture has allowed us to use the central hall of this institution for the third consecutive year. The *Tertulias* are moderated by prominent Chilean writers and communicators. This year, with the aim of including the discussions presently taking place in our society, we invited Patricio Fernández to moderate them. He is a

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Chilean journalist and writer, founder and former director of the weekly *The Clinic*, and a panelist on various national media programs. This year the *Tertulias* were centered around nutrition (“We are what we eat?”), with the participation of Andrea Calixto, neurobiologist of CINV, and Sofía Bustos, nutritionist and advisor of the Ministry of Health of Chile; human gender (“What do we know about gender?”) with Kathleen Whitlock, neuroscientist of CINV, Alessia Injoke, engineer and transgender activist, and Agustín Squella, lawyer, writer and National Humanities Award recipient; and solidarity and altruism (“What makes us express solidarity?”) with Carlos Rodríguez-Sickert, PhD in Economics, Sasha Mudd, PhD in History and Philosophy of Science, and Álvaro Fischer, engineer in Mathematics, businessman and writer. We had an estimated audience of more than 400 in the three *Tertulias*.

Falling Walls Chile: In partnership with the Fundación Ciencia Joven (Young Science Foundation) and the German Academic Exchange Service (DAAD), the CINV brought the Falling Wall Lab contest to Chile for the third time. This event seeks to identify the young innovator who will represent Chile at the global Falling Walls event in Germany in 2018, organized by the Falling Walls Foundation, where about 100 young people from all around the world will present their innovative projects in 3 minutes. The winner in the final satge in Valparaíso, Martín Serey, a 25-year-old engineer, designed a low-cost robotic device that helps with cerebrovascular rehabilitation by sending signals to the nervous system that allow the recovery of hand motor control. With national and regional press coverage, with the participation of national authorities of CORFO and a jury led by the Deputy Director of CINV, Dr. J.C. Sáez, this activity continues to position Valparaíso as a lighthouse of science in Chile.

Ciencia Al Tiro: One of the greatest challenges in Chilean society is to communicate the value of science to the general public. In 2016, this outreach program 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 to 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 we can capture solar energy, etc. The videos were evaluated by teachers from the Regions of Valparaíso, Antofagasta, and Bio Bio and received excellent ratings. The videos are currently being shown on UCV-TV (www.ucv3.cl) and the TV channel of the Chamber of Deputies. Now is interested in airing the program nationally. The characters (PhD Students) pass through Valparaíso asking questions about how things work and use science to find the answers. This project was financed by CONICYT/Explora, CINV, Universidad de Valparaíso, Fundación Chileno-Americana (chileusfoundation.org) and Ciencia Que Pesca (www.cienciaquepesca.cl). During 2018 we continued to develop and implement new science workshops on the theme of Sensory Systems.

NeuroNews: This program 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, 17 NeuroNews articles were produced in 2018, all of them published in the online newspaper *El Mostrador*, which has an international scope, reaching a total of 308.497 effective reading throughout Latin America with an average of 18.147 readings per article. A trademark of NeuroNews is the great variety of topics covered. In 2018, we would like to highlight: phobias in humans and the effects of sad music on them, cerebral activity during orgasms in women, the time zone that correspond to our country and the effects of the seasonal change, the mechanisms involved in contagious itching, and the use of artificial intelligence to diagnose and predict the

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effectiveness of the treatment for schizophrenia (cinv.uv.cl/category/neuronews/). In parallel, a collection of the best NeuroNews stories of the last years was compiled, professionally edited by two external journalists and a scientific committee, and illustrated to create a scientific book entitled “DeMente”. It will be published by Editorial Catalonia in 2019 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 2018, 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 Biophysics in Chile. This production participated in the 2018 scientific film program of the “Congress of the future”, the main scientific dissemination activity in the country. In addition, Youtube has broadcasted this documentary, and has already exceeded 9,400 views, a very significant number for this type of production. At the beginning of 2018, the Netflix Series “72 animales peligrosos de Latinoamérica” (“72 dangerous animals from Latin America”) was launched, with the participation of Jesús Olivares, a PhD graduate from our center who explained different aspects of the biology of two different Chilean spider species. This series was produced by NatGeo and has an international scope. Finally, the CINV participated in a chapter of the TV Serie “Experimenta”, which presents the concerns of children who ask interesting questions and carry out experiments together with Chilean scientists. Angelina Palacios-Muñoz, a young researcher of our center, discussed how the biological clock works in nature and the important role of *Drosophila* in scientific research.

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 start of construction of the building in the month of April 2018, which is estimated to be occupied in 2020. The support of national and regional authorities, who have become aware of the importance of the CINV in national science and regional development, made possible the funding of this unique project that will recover a historical Valparaíso neighborhood. This building, named Edificio de la Ciencia (The building of science) is recognized as one of the most important projects in this area in the country.

Fundación Puerto de Ideas: Dr. R. Latorre is a permanent member of the Scientific Committee of the Puerto de Ideas Foundation, which organizes the yearly “Puerto de Ideas” Festivals in Antofagasta and Valparaíso. This alliance ensures the presence of renowned scientists at the Festival, including researchers of the CINV, and activities organized in Valparaíso for both institutions.

Congreso Nacional: During 2018 the CINV presented a bill to the Chilean Government that establishes a time zone for Chile taking into account the functioning of our biological clock. This initiative is authored by Dr. John Ewer with the support of Senator Guido Girardi, President of the Senate Health Committee, who has been an important promoter of scientific policies and creator of the Congreso del Futuro. So far the bill has been unanimously approved by the Senate Health Committee and will next be discussed in the Senate. This bill is the fruit of work done in previous years, which allowed the issue to be understood by the senators, and includes the visit of Michael Rosbash, Nobel Laureate 2017 for his work on biological clocks, as well as extensive presence in national media.

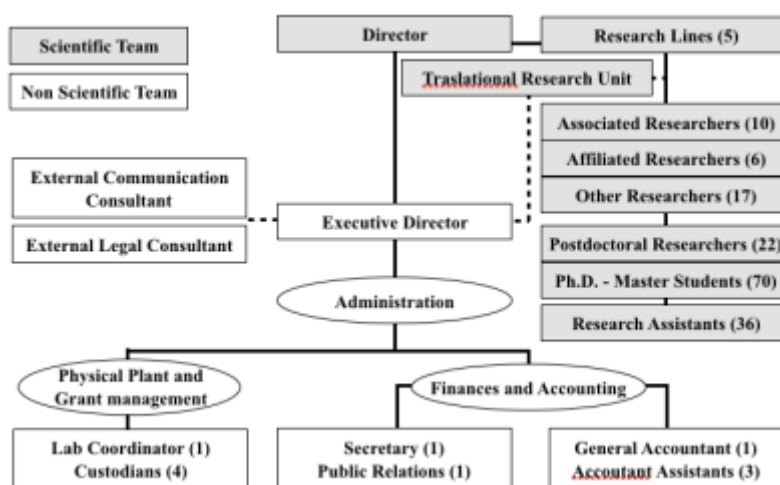
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7. Administration and Financial Status

a) *Organization and administration:*

An Executive Director and his team supervise and coordinate all administrative duties according to the needs of the Director and of other Researchers. This includes managing the Millennium Institute Grant and all other grants of CINV researchers (about 17 grants per year); the outreach and networking activities; as well as all efforts related to the new building to house the CINV and the communication strategy of the CINV. The work 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. The new Translational Research Unit, which is

responsible for establishing contacts between scientists, companies, and institutions, and coordinates applied projects. It depends on a scientific directory and the coordination of the Executive Director of CINV. 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. In the case of Universidad de Valparaíso, where most of the researchers belong, the institution has set up a grant to help with operational expenses.



| Category | Female | Male | TOTAL |
|-------------------------|--------|------|-------|
| Assistant & Technicians | 22 | 9 | 31 |
| Administrative Staff | 7 | 5 | 12 |
| TOTAL | 29 | 15 | 44 |

b) *Financial Status:*

During 2018, the CINV had a total income of CLP\$2.388.225.268.- (USD\$3.725.780), to which the Millennium Scientific Initiative (ICM) contributed 36%. The historic contribution of the ICM to the total income was 55.7% in 2012, 35.4 % in 2013, 42.0% in 2014, 44% in 2015, 43% in 2016, and 38% in 2017. Other sources of income for CINV come from CONICYT (35%) and the Universidad de Valparaíso (25%), as well as foreign grants (4%).

The greatest share (58%) of ICM funds go to towards honoraria of scientific and additional personnel, including postdocs, and young researchers, and towards the strengthening of research teams. Approximately 12% was invested in scientific equipment.

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8. Annexes

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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 María Cárdenas Díaz | 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 | Professor UV CINV | 2 |

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| | | | | | | | Chile | Researcher | |
|----------------------------------|---|------------|---|------------|------------|---|--------------------------------|---------------------------------------|---|
| Kathleen Whitlock Leaning | Genetics and developmental neuroscience. | US Citizen | F | 08-27-1963 | Biologist | D | Universidad de Valparaiso | 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 Valparaiso | 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 |
| Andrés Eduardo Chávez Navarrete | System and circuits neuroscience. | Chilean | M | 01-10-1977 | Biologist | D | Universidad de Valparaiso | 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 |

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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 Valparaiso | Professor or 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 | 2 |

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| | | | | | | | | | |
|----------------------------------|--|---------|---|------------|------------|---|--------------------------|---------------------------|---|
| | | | | | | | | Young Researcher | |
| Karen Castillo Huera | Structure and Function of Molecular Sensors. | Chilean | F | 07-23-1979 | Biochemist | D | CINV | CINV Young Researcher | 1 |
| Daniel Aguayo Villegas | Molecular simulation and computational biology. | Chilean | M | 08-08-1978 | Biochemist | D | Universidad Andrés Bello | Professor U. Andrés Bello | 2 |
| Marlene Natalia Arismendi Macuer | Molecular Simulation And Computational Biology . | Chilena | F | 10-08-1980 | Biochemist | D | Universidad Andrés Bello | Young Researcher | 2 |

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 | Uruguayan | M | 20-01-1964 | Physician | D | Universidad de la República | Professor | 2 |

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|------------------|--|-------------|---|------------|--------------|---|--|---------------------|---|
| | sensors. | | | | | | | | |
| 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 | 10-14-1942 | 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 | Nationality | Gender | Date of birth | Profession | Academic Degree | Affiliation | Current Position | Relation with Center |
|------------------|---------------------|-------------|--------|---------------|------------|-----------------|---------------------------|------------------|----------------------|
| Agustín Demetrio | Cellular signaling. | Chilean | M | 03-18-1958 | Biologist | D | Universidad de Valparaiso | Professor UV | 2 |

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| | | | | | | | | | |
|---|--|--------------|---|------------|-----------------------|---|---------------------------|------------------------------------|---|
| Martínez Carrasco | | | | | | | | CINV Researcher | |
| Andrea Leonor Calixto Mohor | Genetics and developmental neuroscience. | Chilean | F | 09-04-1974 | Biologist | D | Universidad Mayor | Professor U. Mayor CINV Researcher | 2 |
| Carlos González León | Structure and function of molecular sensors. | Cuban | M | 12-13-1965 | Biophysicist | D | Universidad de Valparaiso | Professor UV CINV Researcher | 2 |
| Oliver Schmachtenberg Carlos González León | System and circuits neuroscience. Structure and function of molecular sensors. | ChileanCuban | M | 12-12-1970 | BiologistBiophysicist | 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 Valparaiso | Professor UV CINV Researcher | 2 |

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1.5 Postdoctoral

| Full Name | Research Line | Nacionali ty | Gender | Date of birth | Profession | Academic Degree | Affiliation | Current Position | Relati on with Center |
|--|--|-----------------|--------|------------------|-------------------------|--------------------|---|---------------------|--------------------------------|
| Florence Anne Laure Gutzwiller | Genetics And Developmental Neuroscience. | Chilean | F | 03-26-1987 | Biochemist | D | Pontificia Universidad Católica de Chile | Postdoctoral | 1 |
| Arlek Marion González Jamett | Cellular Signaling. | Chilean | F | 11-07-1981 | Biochemist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Justin Arthur Hugo Flaven Pouchon | Genetics And Developmental Neuroscience. | French | M | 08-29-1987 | Biologist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Javier Vicente Alvarez Zepeda | Genetics And Developmental Neuroscience. | Chilean | M | 01-29-1971 | Aquaculture Engineer | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Felipe Alberto Villanelo Lizana | Molecular Simulation And Computational Biology. | Chilean | M | 05-16-1982 | Biochemist | D | Fundación Ciencia y Vida | Postdoctoral | 1 |
| Kesheng Xu | Molecular Simulation And Computational Biology. | Chinese | M | 10-02-1983 | Physical | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Bruno Alejandro Cisterna | Cellular Signaling. | Chilean | M | 11-13-1982 | Medical technology | D | Pontificia Universidad Católica de | Postdoctoral | 1 |

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|------------------------------------|---|---------|---|------------|---------------------------------|-----------|--|--------------|---|
| Irrazabal | | | | | | | Chile | | |
| Rosalba Escamilla Hernández | Cellular Signaling. | Chilean | F | 02-06-1971 | Biochemist | D | Pontificia Universidad Católica de Chile | Postdoctoral | 1 |
| Alex Harry Vielma Zamora | System And Circuits Neuroscience. | Chilean | M | 01-05-1979 | Biochemist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Angelina del Carmen Palacios Muñoz | Genetics And Developmental Neuroscience. | Chilean | F | 07-12-1981 | Biochemist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Alberto Jesus Martin Martin | Molecular Simulation And Computational Biology. | Spanish | M | 06-08-1980 | Biologist | D | Fundación Ciencia y Vida | Postdoctoral | 1 |
| Hans Joseph Moldenhauer Barrientos | Structure And Function Of Molecular Sensors. | Chilean | M | 02-22-1983 | Biochemist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Ignacio Antonio Díaz Franulic | Structure And Function Of Molecular Sensors. | Chilean | M | 04-02-1981 | Biochemist | Doctorado | Universidad Andrés Bello | Postdoctoral | 1 |
| Nicolas Palacios Prado | System And Circuits Neuroscience. | Chilean | M | 06-30-1981 | Bachelor in Biomedical Sciences | D | Pontificia Universidad Católica de Chile | Postdoctoral | 1 |
| Nicolas | System And | Spanish | M | 05-14-1987 | Bachelor in | D | Centro | Postdoctoral | 1 |

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|--------------------------------------|--|-------------|---|------------|-------------------------------|---|---|--------------|---|
| Palanca Castan | Circuits Neuroscience. | | | | Biology | | Interdisciplina rio de Neurociencia | | |
| María Constanza Maldifassi Gatica | Cellular Signaling. | Chilean | F | 11-07-1979 | Biochemist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Leonel Eugenio Medina Daza | Molecular Simulation And Computational Biology . | Chilean | M | 08-27-1980 | Civil Engineering Electrician | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Maria Guadalupe Cascallares | Genetics And Developmental Neuroscience. | Argentinian | F | 01-18-1988 | Physical | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Angélica del Pilar Escobar Maldonado | System And Circuits Neuroscience. | Chilean | F | 07-15-1985 | Chemistry and Pharmacy | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Marlene Natalia Arismendi Macuer | Molecular Simulation And Computational Biology . | Chilean | F | 08-10-1980 | Biochemist | D | Universidad Andrés Bello | Postdoctoral | 1 |
| Estefanía Andrea Hugo Caselli | Molecular Simulation And Computational Biology. | Chilean | F | 06-09-1987 | Chemist | D | Universidad de Valparaiso | Postdoctoral | 2 |
| Willy Reinaldo Carrasquel Urzulaez | Structure And Function Of Molecular Sensors. | Venezuelan | M | 06-01-1986 | Biologist | D | Universidad de Valparaiso | Postdoctoral | 1 |

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|---|--|------------|---|------------|---|---|-------------------------------------|--------------|---|
| | | | | | | | | | |
| Yorley Andrea Duarte Ayala | Molecular Simulation And Computational Biology. | Colombian | F | 10-10-1982 | Chemical Engineering for the Food Industry | D | Universidad Andrés Bello | Postdoctoral | 2 |
| Bernardo Ismael Pinto Anwandter | Structure And Function Of Molecular Sensors. | Chilean | M | 11-27-1987 | Biochemist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Paloma Andrea Harcha Suazo | System And Circuits Neuroscience. | Chilean | F | 06-22-1985 | Bachelor in Biology | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Cristián Alfonso Calfún Medina | Genetics And Developmental Neuroscience. | Chilean | M | 05-23-1983 | Biochemist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Rodrigo Alexis Meza Cardenas | System And Circuits Neuroscience. | Chilean | M | 10-23-1985 | Biochemist | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Fernando Andrés Hinostroza Balmaceda | System And Circuits Neuroscience. | Chilean | M | 01-09-1988 | Bachelor in Biological Sciences | D | Universidad de Valparaiso | Postdoctoral | 1 |
| Ivan Alejandro Barria Oñate | Cellular Signaling. | Chilean | M | 12-05-1988 | Medical technology | D | Universidad de Antofagasta | Postdoctoral | 1 |
| Ivan Dario Bravo Tobar | Cellular Signaling. | Venezuelan | M | 09-26-1976 | Medicine | D | Universidad Centro Occidental | Postdoctoral | 1 |

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|-------------------------------|--|---------|---|------------|------------|---|----------------------|--------------|---|
| | | | | | | | (ucla) | | |
| Ricardo Honorato Zimmer | Structure And Function Of Molecular Sensors. Molecular Simulation And Computational Biology. | Chilean | M | 06-27-1985 | Literature | D | Universidad de Chile | Postdoctoral | 1 |
| Cesar Rodrigo Ravello Serrano | Molecular Simulation And Computational Biology. | Chilean | M | 02-10-1981 | Literature | D | Ciencia y Vida | Postdoctoral | 2 |

| <u>NOMENCLATURE:</u> | | |
|--|--|--|
| [Gender] [M] Male [F] Female | [Academic Degree] [U] Undergraduate [M] Master [D] Doctoral | [Relation with Center] [1] Full time [2] Part time |

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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 I. Díaz R. Honorato H. Moldenhauer R. Olcese B. Pinto J.A. Gárate R. Honorato | 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 I. Bravo H. Sanchez P. Gutierrez B. Cisterna R. Escamilla A. Cárdenas A. González | Cell Biology | 08-08-11 | |

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| | | | | | | | |
|---|--|---|---|--|--|----------|--|
| | | | | M. Maldifassi I. Barria | | | |
| 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 C. Calfún | Biology of development Genetics and evolution | 08-08-11 | |
| 4 | <i>Integrative and circuits neuroscience</i> | 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. Vielma Ch. Chiu A. Ardiles N. Palacios P. Harcha R. Meza F. Hinostroza | 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 | 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 T. Pérez F. Villanelo E. Hugo L. Medina K. Xu | Numerical methods and computation Biophysics | 08-08-11 | |

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| | | | | | | | |
|---|---------------------------------------|---|---|--|---|--------------|---|
| | | biological networks. | | C. Ravello M. Arismendi Yorley Duarte | | | |
| 6 | Technological Transference Unit | Increase our portfolio of R+D+i projects and network of strategic alliances with public and private sector actors to finance research initiatives, supporting contracting and management of research and technologies developed for subsequent transfer. | Responsible for identifying opportunities for integration between the research carried out at CINV and the public and private sector, generating and transferring knowledge to positively impact society | Juan Carlos Sáez Tomás Pérez-Acle Danilo González Nilo Carlos González | Biomedicine Agriculture Ecosystem and environment | 07-01- 17 | Pending on funding availabi- lity |

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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. Acevedo W, Capitaine C, Rodríguez R, Araya-Durán I, **Gonzalez-Nilo F**, Pérez-Correa JR, Agosin E (2018) Selecting optimal mixtures of natural sweeteners for carbonated soft drinks through multi-objective decision modeling and sensory validation. *Journal of Sensory Studies*. 33(6): e12466. doi: 10.1111/joss.12466.
2. **Alvarez O**, Carmona E, **Latorre R**, **Gonzalez C**. (2018) A Glimpse into the Permeation Pathway of the Voltage-Dependent Proton Channel (Hv1). Comments on CrossTalk 33: Proton permeation through HV1 requires/does not require transient protonation of a conserved aspartate in the S1 transmembrane helix. *Journal of Physiology*. doi: 10.1113/JP275101.
3. Balboa E, Saavedra F, Cea LA, Vargas AA, Ramírez V, Escamilla R, **Sáez JC**, Regueira T. (2018) Sepsis-Induced Channelopathy in Skeletal Muscles is Associated with Expression of Non-Selective Channels. *Shock*. 49(2):221-228. doi: 10.1097/SHK.0000000000000916.
4. Barría I, Güiza J, Cifuentes F, Zamorano P, **Sáez JC**, González J, Vega JL. (2018) Trypanosoma cruzi Infection Induces Pannexin-1 Channel Opening in Cardiac Myocytes. *Am J Trop Med Hyg*. 1860(1):91-95. doi: 10.1016/j.bbamem.2017.10.006.
5. Bonansco C, Martínez-Pinto J, Silva RA, Velásquez VB, Martorell A, Selva MV, Espinosa P, **Moya P**, Cruz G, Andrés ME, Sotomayor-Zárate R. (2018) Neonatal exposure to estradiol increases dopaminergic transmission in Nucleus Accumbens and morphine-induced conditioned place preference in adult female rats. *J Neuroendocrinol*. 30(7):e12574. Doi: 10.1111/jne.1257.
6. Camarada MB, Comer J, Poblete H, Azhagiya Singam ER, Marquez-Miranda V, Morales-Verdejo C, **González-Nilo FD** (2018) Experimental and Computational Characterization of the Interaction between Gold Nanoparticles and Polyamidoamine Dendrimers. *Langmuir*. 34(34):10063-10072. doi: 10.1021/acs.langmuir.8b01809.
7. Carmona EM, Larsson HP, Neely A, **Alvarez O**, **Latorre R**, **Gonzalez C**. (2018) Gating charge displacement in a monomeric voltage-gated proton (Hv1) channel. *Proc Natl Acad Sci USA*. 115(37):9240-9245. doi: 10.1073/pnas.1809705115.
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1. Bernardi M, Marracino P, Ghaani MR, Liberti M, Del Signore F, Burnham CJ, **Gárate J.A.**, Apollonio F, English NJ. (2018) Human aquaporin 4 gating dynamics under axially oriented electric-field impulses: A non-equilibrium molecular-dynamics study. *J Chem Phys.* 2018 Dec 28;149(24):245102. doi: 10.1063/1.5044665.
2. **Bezanilla F** (2018) Influences: The Cell Physiology Laboratory in Montemar, Chile. *J Gen Physiol.* 150(11):1464-1468. doi: 10.1085/jgp.201812157.
3. Borio A, Holgado A, **Garate JA**, Beyaert R, Heine H, Zamyatina A. (2018) Disaccharide-Based Anionic Amphiphiles as Potent Inhibitors of Lipopolysaccharide-Induced Inflammation. *ChemMedChem.* 13(21):2317-2331 doi: 10.1002/cmdc.201800505.
4. Couve E and **Schmachtenberg O** (2018) Schwann Cell Responses and Plasticity in Different Dental Pulp Scenarios. *Front Cell Neurosci.* 12:299. doi: 10.3389/fncel.2018.00299.
5. Carvalho-de-Souza JL, Pinto BI, Pepperberg DR, **Bezanilla F**. (2018) Optocapacitive Generation of Action Potentials by Microsecond Laser Pulses of Nanojoule Energy. *Biophys J.* 114(2):283-288. doi: 10.1016/j.bpj.2017.11.018.
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8. Gajardo I, Salazar CS, Lopez-Espíndola D, Estay C, Flores-Muñoz C, Elgueta C, Gonzalez-Jamett AM, **Martínez AD**, Muñoz P, **Ardiles ÁO** (2018) Lack of Pannexin 1 Alters Synaptic GluN2 Subunit Composition and Spatial Reversal Learning in Mice. *Front Mol Neurosci.* 11:114. doi: 10.3389/fnmol.2018.00114.

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9. García IE, Sánchez HA, **Martínez AD**, Retamal MA. (2018) Redox-mediated regulation of connexin proteins; focus on nitric oxide. *Biochim Biophys Acta*. 1860(1):91-95. doi: 10.1016/j.bbamem.2017.10.006.
10. Horng TL, Eisenberg RS, Liu C, **Bezanilla F**. (2018) Continuum Gating Current Models Computed with Consistent Interactions. *Biophys J*. 2018 Dec 14. pii: S0006-3495(18)34501-6. doi: 10.1016/j.bpj.2018.11.3140. [Epub ahead of print].
11. López-Jury L, **Meza RC**, Brown MTC, Henny P, Canavier CC. (2018) Morphological and biophysical determinants of the intracellular and extracellular waveforms in nigral dopaminergic neurons: A computational study. *J Neurosci*. 38(38):8295-8310. doi: 10.1523/JNEUROSCI.0651-18.201.
12. Miramontes-Sequeiros LC, **Palanca-Castán N**, Caamaño-Chinchilla L, Palanca-Soler A. (2018) The phenotypic variability in *Rana temporaria* decreases in response to drying habitats. *Sci Total Environ*. 612:538-543. doi: 10.1016/j.scitotenv.2017.08.261.
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14. Richard A, **Orio P**, Tanré E (2018) An Integrate-and-fire Model To Generate Spike Trains With Long-range Dependence. *Journal Of Computational Neuroscience* 44(3):297-312. Doi: 10.1007/s10827-018-0680-1.
15. Rimkute L, Kraujalis T, Snipas M, **Palacios-Prado N**, Jotautis V, Skeberdis VA and Bukauskas FF. (2018) Modulation of Connexin-36 Gap Junction Channels by Intracellular pH and Magnesium Ions. *Front. Physiol*. 9:362. doi: 10.3389/fphys.2018.00362.
16. Valdez Capuccino JM, Chatterjee P, **García IE**, Botello-Smith WM, Zhang H, Harris AL, Luo Y, Contreras JE. (2018) The connexin26 human mutation N14K disrupts cytosolic intersubunit interactions and promotes channel opening. *J Gen Physiol*. 2018 Dec 7. pii: jgp.201812219. Doi: 10.1085/jgp.201812219. [Epub ahead of print].
17. Xu K, Maidana JP, Castro S and **Orio P** (2018) Synchronization transition in neuronal networks composed of chaotic or non-chaotic oscillators. *Scientific Reports*. 8(1):8370. doi: 10.1038/s41598-018-26730-9.

3.2.- SCIELO Publications or Similar to SCIELO

NONE

3.2.1 Associate Researchers:

NONE

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3.2.2 Other researchers

NONE

3.3.- Scientific Books and Chapters

3.3.1 Associate Researchers:

1. Bustos Á, Fuenzalida I, Santibáñez R, **Pérez-Acle T**, Martin AJM. (2018) Rule-Based Models and Applications in Biology. Chapter in: Computational Cell Biology: Methods and Protocols, Methods in Molecular Biology, Louise von Stechow and Alberto Santos Delgado (eds.), Methods Mol Biol. 1819:3-32. doi: 10.1007/978-1-4939-8618-7_1.
2. Carrasquel-Ursulaez W, Lorenzo Y, Echeverria F and **Latorre R** (2018). Large conductance potassium channels in the nervous system. In: The Oxford Handbook of Neuronal Ion Channels, Oxford Handbooks Online, UK. Online publication date: April 2018. DOI: 10.1093/oxfordhb/9780190669164.013.11.
3. González-Jamett AM, Bevilacqua JA and **Cárdenas, AM** (2018) "Hereditary Myopathies". In Muscle Cell and Tissue. Edited by Kunihiro Sakuma; Ed. InTechOpen, Chapter 6, pages 81-114. DOI: 10.5772/intechopen.76076
4. **Latorre R**, **Castillo K**, and Díaz-Franulic I (2018) Sensing Pain and Temperature. In: The Proceedings of the Workshop on Cell Biology and Genetics. Edward M. De Robertis (editor). Libreria Editrice Vaticana. Vatican City. Chapter. pag 44-63
5. **Sáez JC**. (2018) Does Inflammatory Response Cause Tissue Dysfunction in Chronic Diseases?. In: The Proceedings of the Workshop on Cell Biology and Genetics. Edward M. De Robertis (editor). Libreria Editrice Vaticana. Vatican City. Chapter. pag 64-72

3.3.2 Other researchers:

NONE

3.4.- Other Publications

3.4.1 Associate Researchers

1. Moreno M, Zacarias A, Velasquez L, Gonzalez G, Alegría-Arcos M, **González-Nilo FD**, Gross EKV. (2018) Experimental and theoretical structural/spectroscopical correlation of enterobactin and catecholamide Data Brief. 20:2054-2064. doi: 10.1016/j.dib.2018.08.114.

3.4.2 Other researchers:

1. Marracino P, Bernardi M, Liberti M, Del Signore F, Trapani E, **Gárate JA**, Burnham CJ, Apollonio F, English NJ. (2018) Transprotein-Electropore Characterization: A Molecular

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Dynamics Investigation on Human AQP4. ACS Omega. 3(11):15361-15369. doi: 10.1021/acsomega.8b02230.

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 | 34 | 61,81 % | 6 | 10,9% | 2 | 3,64% | 2 | 3,64% |
| SCIELO Publications or Similar to SCIELO Standard | 0 | 0,00% | 0 | 0,00% | 0 | 0,00% | 0 | 0,00% |
| Books and chapters | 5 | 9,09% | 0 | 0,00% | 0 | 0,00% | 0 | 0,00% |
| Other Publications | 2 | 1,364 % | 0 | 0,00% | 0 | 0,00% | 0 | 0,00% |
| Total of publications | 41 | 74,55 % | 6 | 10,9% | 2 | 3,64% | 2 | 3,64% |

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Annex 4.- Organization of Scientific Events

| Scope | Title | Type of Event | City | Country | Responsible Researcher |
|---------------|---|---------------|------------|---------|-------------------------------|
| National | Symposia Two Fotons Microscope | Symposium | Valparaiso | Chile | Andrés Chávez / Chiayu Chiu |
| Nacional | 1st Chilean Conference on Computational Neuroscience | Symposium | Valparaiso | Chile | Patricio Rodrigo Orio Alvarez |
| Internacional | Latin American Trainig Program 2018 | Workshop | Valparaiso | Chile | Juan Carlos Sáez |
| Nacional | Symposia Academia de Cienicas de America Latina (ACAL) | Symposiun | Santiago | Chile | Ramón Latorre |
| International | Meeting Max Planck, Valparaiso “Understanding Brain Function and Dysfunction: from Synapses to Circuits | Symposium | Valparaiso | Chile | Chiayu Chiu |
| National | CINV Meeting 2018. “Science that makes changes” | Symposiun | Valparaiso | Chile | Ramón Latorre |
| National | Learn and Build your Own Chemical Tools for Biomedical Research | Workshop | Valparaiso | Chile | Ramón Latorre |

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Annex 5.- Education and capacity building

5.1 Capacity Building inside MSI Center

| Tutor | Undergraduated Student | | Graduated Students | | | | Total |
|------------------------------------|------------------------|----|--------------------|----|----------|----|-------|
| | | | Master | | Doctoral | | |
| | F | M | F | M | F | M | |
| Fernando Danilo González Nilo | 1 | 0 | 0 | 0 | 2 | 0 | 3 |
| Carlos González Leon | 0 | 0 | 0 | 0 | 0 | 5 | 5 |
| Alan Neely Delgueil | 0 | 1 | 1 | 0 | 1 | 1 | 4 |
| Juan Carlos Sáez Carreño | 1 | 0 | 0 | 0 | 3 | 2 | 6 |
| Patricio Rodrigo Orio Alvarez | 0 | 0 | 0 | 1 | 0 | 7 | 8 |
| Ramón Rogelio Latorre De la Cruz | 0 | 1 | 0 | 0 | 2 | 0 | 3 |
| Oliver Schmachtenberg | 1 | 1 | 2 | 0 | 0 | 2 | 6 |
| John Ewer Lothian | 0 | 0 | 0 | 2 | 3 | 2 | 7 |
| Agustín Demetrio Martínez Carrasco | 0 | 2 | 2 | 3 | 1 | 0 | 8 |
| Ana Maria Cárdenas Díaz | 0 | 0 | 3 | 1 | 1 | 1 | 6 |
| David Oliver Naranjo Donoso | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| Andrea Leonor Calixto Mohor | 0 | 1 | 0 | 1 | 4 | 0 | 6 |
| Pablo Ricardo Moya Vera | 0 | 0 | 4 | 3 | 1 | 3 | 11 |
| Adrián Palacios Vargas | 0 | 0 | 0 | 1 | 0 | 3 | 4 |
| Alvaro Oscar Ardiles Araya | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| Andrés Eduardo Chávez Navarrete | 0 | 2 | 1 | 2 | 0 | 0 | 5 |
| José Antonio Gárate Chateau | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| Kathleen Whitlock Leaning | 1 | 0 | 0 | 0 | 1 | 3 | 5 |
| Tomás Pérez Acle | 0 | 2 | 0 | 1 | 1 | 5 | 9 |
| Chiayu Chiu | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| Total | 4 | 11 | 14 | 15 | 20 | 35 | 100 |

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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 |
|--------------------|---------------------------------|-----------|-------------------|--|---------------|-------------|
| Samy Castro | Montreal Neurological Institute | Canada | Bratislava Mistic | Techniques for the Analysis of Brain Connectivity | 04-09-2018 | 29-09-2018 |
| Daniela Di Georgis | UCLA | USA | Ricardo Olcese | “Regulation of Voltage Sensing Structures of CaV1.2 Calcium channel by the Auxiliary β -subunit” | 12/03/2018 | 04/05/2019 |
| Arles Urrutia | Universidad de Buenos Aires | Argentina | Diego Mendoza | Analysis of neuroprotective bacterial metabolites by Nuclear Magnetic Resonance. | 08-01-2018 | 08/30/2018 |

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Traineeships external

| Student name | Institution | Country | Advisor | Project Description | Starting Date | Ending Date |
|---------------------------|----------------------------------|-----------|-----------------------|--|---------------|-------------|
| Lucas Bayones | Universidad de Buenos Aires | Argentina | Ana María Cárdenas | He studied the effects of centronuclear myopathy-dynamin 2 mutations on exocytosis | 09-16-2018 | 10-04-2018 |
| Alejandro Herrera Delgado | Universidad de Sevilla | Spain | Juan Carlos Sáez | Conexine | 08-21-2018 | 11-21-2018 |
| Maximiliano Zuluaga | Universidad Nacional de Colombia | Colombia | Oliver Schmachtenberg | Electrophysiological characterization of retinal amacrine cells | 30-07-2018 | 28-12-2018 |

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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 development | 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) |

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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 | |
| 1 st <i>C. elegans</i> Latin American meeting | Pasteur Institute | 1 | 3 | 2 | x | I Scielo publication |

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Annex 7. - Outreach

7.1. - Outreach activities throughout the period

| Description of activity | Type of Event | Date | Location Region | Target audience |
|---|---------------|------------|-----------------|-------------------------------------|
| Seminars of CINV | | | | |
| “Atomic force microscopy” Tomás Corrales Universidad Técnico Federico Santa María | Seminar | 04-13-2018 | Valparaiso | Universidad de Valparaiso community |
| "ICAN" modulate neuronal excitability and synaptic transmission” Elias Leiva Universidad de Santiago de Chile | Seminar | 05-11-2018 | Valparaiso | Universidad de Valparaiso community |
| “ <i>Nutrición en Plantas: De las moléculas al ecosistema</i> ” Rodrigo Gutierrez Pontificia Universidad Católica de Chile | Seminar | 05-11-2018 | Valparaiso | Universidad de Valparaiso community |
| “ Bases celulares y moleculares del autismo: Via de señalización Wnt/beta- catenina”. Giancarlo De Ferrari Centro de Investigaciones Biomédicas Universidad Andrés Bello | Seminar | 06-08-2018 | Valparaiso | Universidad de Valparaiso community |
| <i>Modelado termodinámico: lenguajes basados en reglas para estudiar procesos termodinámicos ”</i> Ricardo Honorato CINV | Seminar | 06-15-2018 | Valparaiso | Universidad de Valparaiso community |

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| | | | | |
|--|---------|------------|------------|-------------------------------------|
| <p><i>“Understanding the function of the tyrosine phosphatase PTPRD in neural stem cell biology and its role in autism”</i></p> <p>Gonzalo Cancino Universidad Mayor</p> | Seminar | 06-22-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>"Connectivity structures drive multistability of global brain activity"</i></p> <p>Samy Castro, PhD Student Doctorado en Ciencias Mención Neurociencias Universidad de Valparaiso - CINV</p> | Seminar | 06-29-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>"Activation of 5-HT2 receptors regulate TRPV1 receptor activity: role on anxiety-like behaviors"</i></p> <p>Valentina Haro, PhD Student Doctorado en Ciencias Mención Neurociencias Universidad de Valparaiso - CINV</p> | Seminar | 06-29-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>“The Touch That Matters Most”</i></p> <p>Francis McGlone Professor of Neuroscience Liverpool John Moores University</p> | Seminar | 07-08-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>“Neuroplasticity and Epigenetics in Health and Disease”</i></p> <p>Brigitte Van Zundert Universidad Andres Bello</p> | Seminar | 08-03-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>“El mundo de la industria”</i></p> <p>Romina Hidalgo Pfizer</p> | Seminar | 08-10-2018 | Valparaiso | Universidad de Valparaiso community |

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| | | | | |
|---|---------|------------|------------|-------------------------------------|
| <p><i>"Prefrontal-Hippocampal functional connectivity during memory acquisition "</i> Ignacio Negrón Universidad de Valparaiso</p> | Seminar | 08-24-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>"Formation of heteromeric Cx26S17F/Cx30 channels in syndromic deafness and its functional consequences on channel function and purinergic responses"</i> Ana Abott, PhD Student Doctorado en Ciencias Mención Neurociencia Universidad de Valparaiso - CINV</p> | Seminar | 10-05-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>"Enhanced innate immune response in the olfactory sensory system of developing zebrafish"</i> María F. Palominos, PhD Student Doctorado en Ciencias Mención Neurociencia Universidad de Valparaiso - CINV</p> | Seminar | 10-12-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>"Seeing What's Out There: Fluorescent Visualization of Cellular Efflux"</i> William Kobertz University of Massachusetts Medical School</p> | Seminar | 10-18-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>"Mecanismo neurobiológicos de las interacciones sociales basadas en la negociación y sus implicancias en enfermedades neuropsiquiátricas"</i> Pablo Billeke Universidad del Desarrollo</p> | Seminar | 10-19-2018 | Valparaiso | Universidad de Valparaiso community |

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| <p><i>“Pannexin-1 regulates dendrite branching and dendritic spines formation in hippocampal neurons by modulating actin polymerization”</i></p> <p>Carolina Flores, PhD Student Doctorado en Ciencias Mención Neurociencia Universidad de Valparaiso - CINV</p> | Seminar | 10-26-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>“The biotechnology and informatics era and how it is changing our daily lives”</i></p> <p>Erik Bongcam-Rudloff The Swedish University for Agricultural Sciences</p> | Seminar | 11-06-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>“Glutamatergic Plasticity and Homeostatic Regulation in the Mechanism of Ketamine’s Rapid Antidepressant Response”</i></p> <p>Carlos Zarate National Institute of Mental Health</p> | Seminar | 11-07-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>“Efectos de las prácticas e instituciones socioculturales en la compatimentalización de la diversidad biológica humana”</i></p> <p>Nicolás Montalva Universidad Mayor</p> | Seminar | 11-09-2018 | Valparaiso | Universidad de Valparaiso community |
| <p><i>“Genetic and cellular mechanisms in Autism Spectrum disorders”</i></p> <p>Maria Rita Passos Bueno Universidade de São Paulo, Brasil</p> | Seminar | 11-16-2018 | Valparaiso | Universidad de Valparaiso community |

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| <i>“Estandares de Calidad de investigación en la industria”</i> Romina Hidalgo Pfizer | Seminar | 11-16-2018 | Valparaiso | Universidad de Valparaiso community |
| <i>“Estandares de Calidad de investigación en la industria”</i> Edwin Castillo Pfizer | Seminar | 11-16-2018 | Valparaiso | Universidad de Valparaiso community |
| <i>“New insights into Alzheimer's disease synaptotoxicity: the potential involvement of Pannexin 1 channels”</i> Álvaro Ardiles Universidad de Valparaiso – CINV | Seminar | 11-30-2018 | Valparaiso | Universidad de Valparaiso community |
| <i>“Transporte de Péptidos y Nanopartículas a través de Biomembranas”</i> Fernando González Nilo CINV Associate Investigator | Seminar | 03-21-2018 | Valparaiso | Universidad Andrés Bello |
| <i>“Bionanotecnología”</i> Fernando González Nilo Investigador Asociado CINV | Seminar | 11-20-2018 | Santiago | Universidad Andrés Bello |
| Tertulias Porteñas | | | | |
| <i>¿Somos lo que comemos?</i> Andrea Calixto CINV Researcher | “Fireside chat” | 05-05-2018 | Valparaiso | General community |
| <i>¿Qué sabemos de género?</i> Kathleen Whitlock CINV Researcher | “Fireside chat” | 02-08-2018 | Valparaiso | General community |
| <i>¿Qué nos hace solidarios?</i> | “Fireside chat” | 22-11-2018 | Valparaiso | General community |
| Falling Walls | | | | |
| <i>Falling Walls Lab Valparaiso</i> 13 talks of pre-selected Chilean candidates | Conference | 08-08-2018 | Valparaiso | General community |

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|---|-----------------|------------|------------|------------------------------|
| Book presentation | | | | |
| <i>“Cuba: viaje al fin de la revolución”</i> Patricio Fernandez, CINV Tertulias Porteñas moderator | Launching | 12-12-2018 | Valparaiso | General community |
| Penta UC Program Visit to CINV | | | | |
| <i>Penta UC Program Visit to CINV</i> Angelina Palacios CINV Postdoctoral researcher | Talks and visit | 10-05-2018 | Valparaiso | Penta UC Program Students |
| TV Series | | | | |
| <i>“Experimenta: Neurociencia, que no te de sueño!”</i> Angelina Palacios CINV Postdoctoral researcher | TV Series | 09-03-2018 | Valparaiso | General community |
| <i>“72 animales peligrosos de Latinoamérica”</i> Produced by NatGeo and distributed by NetFlix Jesús Olivares CINV | TV Series | 01-01-2018 | Valparaiso | General community |
| <i>Ciencia Altiro: TV series Presentation</i> <i>“La Alegría de la Ciencia”</i> María Fernanda Palominos Doctorado en Ciencias Mención Neurociencia Universidad de Valparaiso - CINV | TV Series | 07-28-2018 | Valparaiso | General community |

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7.2. - Products of outreach

| Product Type | Quantity | Target Audience | Scope |
|---|----------|-------------------|---------------|
| “Falling Walls Lab Chile” - Video recording of all presentations. | 8 | General Community | National |
| Tertulias Porteñas- Video recording of all topics | 3 | General Community | National |
| Ciencia Altiro: TV series Presentation “ La Alegría de la Ciencia” | 10 | General Community | National |
| NeuroNews | 17 | General Community | International |
| DeMente | 1 | General Community | National |

7.3.- Articles and Interviews

| Type of Media and Scoupe | Local / Regional | | National | | International | | Total |
|--------------------------|------------------|-------------|---------------|-------------|---------------|-------------|------------|
| | N° Interviews | N° Articles | N° Interviews | N° Articles | N° Interviews | N° Articles | |
| Written | 19 | 2 | 39 | 6 | 0 | 0 | 66 |
| Internet | 0 | 0 | 28 | 6 | 10 | 21 | 65 |
| Audiovisual | 0 | 0 | 11 | 0 | 0 | 0 | 11 |
| Total | 19 | 2 | 78 | 12 | 10 | 21 | 142 |

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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 | Valparaiso Chile | 2 | Government |
| Fundación Puerto Ideas Scientific Committee | Bringing science of excellence to the community in different regions of the country | Talks to the general public on recent scientific discoveries | 2 | 7 (Talks open to the community) | Chile | Valparaiso Antofagasta | 2 | Business activities |
| Falling Walls Lab | Promote the innovation and creativity of young | Second meeting held in Chile to select a representative | 2 | 7 | Chile | Valparaiso, Chile | 2 | Other |

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|---------------------|---|--|---|------------|-------|--------------------|---|-------|
| | students and professionals | of the country for the Falling Walls Lab meeting in Berlin | | | | | | |
| Congreso del Futuro | The talks on scientific topics of great social relevance that were in charge of leading international Speakers. | Eighth version of this event, which was held for the first time in regions, the CINV participated in the organization of the day that brought more than a thousand people. | 2 | 1 (Talks) | Chile | Valparaiso , Chile | 2 | Other |
| Congreso Nacional | Legislative Law | Legislative Law | 2 | 1 (Law) | Chile | Valparaiso , 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

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Annex 9.- Total incomes:

| Funds | Accumulated incomes to last year [\$] | 2018 Incomes | | Total incomes to 2018 [\$] |
|--|--|----------------------|--|----------------------------|
| | | Amount [\$] | Percentage of resources used by the Center [%] | |
| ICM (CINV, Redes y PME) | 5.684.226.794 | 853.908.000 | 117% | 853.908.000 |
| CONICYT (Anillo, Mincyt, Explora, Fondecup, Redes y Neuromantes) | 2.988.573.861 | 841.650.002 | 98% | 841.650.002 |
| UV (Depto. Neuro y Direc. Invest.) | 3.132.203.086 | 601.661.247 | 94% | 601.661.247 |
| Corporación CINV | 76.608.352 | 5.000.000 | 70% | 5.000.000 |
| CNTV, FNDR | 51.530.500 | 0 | 0% | 0 |
| Others (CAT; N62909-13-N251-; N62909-16-1-2227; AFOSR; N62909-14-1-N121) | 360.780.992 | 86.006.019 | 30% | 86.006.019 |
| TOTAL | 12.293.923.585 | 2.388.225.268 | | 2.388.225.268 |

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Annex 10.- Exchange:

| Type of researcher | Name | Type of activity | Length of stay | Destination Country | Financial entity (Millennium/External/Multiple sources) |
|--------------------|-----------------------|--|----------------|---------------------|---|
| Adjunct | Carlos González | Workshop of Postgraduate and PhD, Acuatorinas Structure and function | 5 days | Argentina | External |
| Adjunct | Carlos González | 90 Aniversay Chile Biology Society in Puerto Varas | 5 days | Chile | External |
| Adjunct | Oliver Schmachtenberg | 90 Aniversay Chile Biology Society in Puerto Varas | 5 days | Chile | Multiple Sources |
| Adjunct | Patricio Orio | XIV Annual Reunion of Neuroscience Chilean Society | 5 days | Chile | Multiple Sources |
| Associate | Alan Neely | 90 Aniversay Chile Biology Society in Puerto Varas | 5 days | Chile | External |
| Associate | Andrés Chávez | 90 Aniversay Chile Biology Society in Puerto Varas | 3 days | Chile | External |
| Associate | John Ewer | X Congress Argentinian of Entomology | 4 days | Argentina | External |
| Associate | John Ewer | 17th European Drosophila | 5 days | Poland | External |

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|-----------|-----------------------|--|---------|-----------------|-----------|
| | | Neurobiology Conference 2018 | | | |
| Associate | Pablo Moya | LXXIII Congress of the Society of Neurology, Psychiatry and Neurosurgery of Chile SONEPSYN | 3 days | Chile | External |
| Associate | Pablo Moya | ACNP American College of Neuropsychopharmacology | 5 days | USA | Millenium |
| Adjunt | Patricio Orio | 4 th International Conference on Mathematical Neuroscience ICMNS 2018 | 8 days | Antibes, France | External |
| Associate | Juan Carlos Sáez | ASCB-EMBO 2018 Meeting | 5 Days | San Diego | External |
| Associate | Juan Carlos Sáez | Albert Einstein College of Medicine | 1 Day | New York | External |
| Associate | Juan Carlos Sáez | National Center for the Medical Consequences of SCI, James J. Peters VA | 1 Day | New York | External |
| Adjunct | Oliver Schmachtenberg | 11th Fens Forum of Neuroscience | 11 Days | Berlin | External |
| Adjunct | Oliver Schmachtenberg | 90 Chilean Society of Biology Annual Meeting 2018 | 11 Days | Berlin | External |
| Associate | Tomás Pérez Aclé | XXXII Annual Meeting Chilean Society for Cell Biology | 5 Days | Chile | External |
| Associate | Tomás Pérez Aclé | SAIMS 2018 | 3 Days | Chile | External |
| Associate | Tomás Pérez Aclé | 7th European Conference on | 5 Days | Chile | |

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|-----------|----------------------|---|--------|--------------|-----------|
| | | Computational Biology | | | External |
| Associate | Danilo González Nilo | BIO International Convention | 4 Days | Boston | External |
| Associate | Danilo González Nilo | XXVII International Materials Research Congress | 5 Days | Cancun | External |
| Associate | Danilo González Nilo | ISCB-Sol Bio-EMBnet joint Latin American Conference | 5 Days | Viña del Mar | External |
| Associate | Kathleen Whitlock | International Zebrafish Meeting | 4 Days | USA | External |
| Associate | Kathleen Whitlock | 13th International Congress on the Biology of Fish | 5 Days | Canada | External |
| Associate | Ramon Latorre | 62th Annual Meeting Biophysical Society | 5 Days | USA | External |
| Associate | Ramon Latorre | ACAL Meeting | 2 Days | Chile | Millenium |
| Associate | Alan Neely | 62th Annual Meeting Biophysical Society | 5 Days | USA | External |
| Associate | Agustín Martínez | 90 Aniversay Chile Biology Society in Puerto Varas | 5 days | Chile | External |
| Associate | Agustín Martínez | Congreso Nacional de la Sociedad de Fisiología | 3 days | Chile | External |

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| Researcher Name | Nationality | Type of activity | Length of stay | Country of Origin | Financial entity (Millennium / External / Multiple sources) |
|-------------------------|--------------------|-------------------------|-----------------------|--------------------------|--|
| Romina Hidalgo | Argentinian | Seminar | 1 day | Argentina | Millennium |
| Edwin Castillo | Argentinian | Seminar | 1 day | Argentina | Millennium |
| Maria Rita Passos Bueno | Brazilian | Seminar | 2 days | Brasil | Multiple Sources |
| Carlos Zarate | American | Seminar | 2 days | USA | Multiple Sources |
| Erik Bongcam-Rudloff | Swedish | Seminar | 2 days | SWEDEN | Multiple sources |
| William Kobertz | American | Seminar/ Workshop | 10 days | USA | Millennium |
| Francis McGlone | British | Seminar | 1 day | UK | External |
| Marcelo Ozu | Argentinian | Colaboration | 30 days | Argentina | Multiple Sources |