

CINV ANNUAL PROGRESS REPORT – 2019

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Type (Institute or Nucleus)	Institute
Acronym	CINV
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Address	Pasaje Harrington 287, Playa Ancha Valparaíso
Stage	Continuity
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Total amount for the reported period	USD \$ 1,282,882

Contact Information	
Scientific Contact	Ramón Latorre, Director
Contact Information	<i>ramon.latorre@uv.cl</i>

<i>Institute / Nucleus Director Name</i>	<i>Institute / Nucleus Alternate Director Name</i>
Ramón Latorre de la Cruz	Juan Carlos Sáez Carreño
<i>Director's Signature</i>	<i>Alternate Director's Signature</i>

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1.1 Executive Summary

Research at the Centro Interdisciplinario de Neurociencia de Valparaíso (CINV) is driven by the general question: ***How does the Nervous System Respond to Stimuli in Health and Disease?*** Five lines of research ranging from molecular sensors to circuit and system neuroscience tackle this question, to which we added, in 2017, a Translational Research Unit to identify potential R&D projects. **Scientific productivity and collaborative work:** During 2019, we published 47 papers. Although this number is slightly lower than that for 2018, there was notable increase in impact factor [IF: 6.4 (2019) vs. 4.2 (2018)]. We published 5 papers in high impact journals, all led by CINV members (*Nat Nanotech*, *Nat Commun*, and *Nat Protocols* from the Bezanilla's Lab, *Nat Rev Neurosci*, from the Chiu's Lab, and *PNAS* from the Whitlock's Lab). Ten publications appeared in journals with IF between 5.5-8.0, including papers in *Cancers* (Sáez's and Latorre's labs), *Front Immunol* (Calixto's and Sáez's labs); *eLife* (Latorre's lab), *Glia* (Sáez's lab); *Front Neuroendocrinol* (Whitlock's lab); *J Neurosci* (Orío's lab); *Antioxid Redox Signal* (Chávez lab). It is also important to mention some articles that appeared in other prestigious journals: *PLoS Genet* (Calixto's lab); *Neurobiol Dis* (Martínez's lab); *Sci Rep* (Latorre and Palacios' labs); *J Neurochem* (Cárdenas's lab); *J Gen Physiol* (Bezanilla's lab). From this list, we wish to single out four publications: i) A non/canonical coupling of the voltage sensor domain (VSD) with the conduction pore (PD), revealed using tandem dimers of Shaker K⁺ channels. This new near-connection between the VSD and the PD influences both voltage-dependence of C-type inactivation at the selectivity filter and the overall PD open probability (Carvalho-de-Souza & Bezanilla. *Nat Commun*). ii) Guerra et al. (*J Neurochem*) showed that the β2a subunit of the Ca²⁺ channels (CaVβ2a) is a signaling molecule that regulates cortical actin dynamics, and consequently ion channel membrane expression and exocytosis in neuroendocrine cells. iii). Studies on diapausing (akin to hibernating) *C. elegans* demonstrated that damaged neurons regenerate fully in this state of metabolic quiescence. This work also showed that regenerating touch receptor neurons follow a growth pattern identical to that of development and is error-free (Caneo et al., *PloS Genet*). iv). Plaza-Briceño et al. (*Antioxid Redox Signal*) demonstrated that modulation of NMDARs by NOX2 drives changes in synaptic plasticity and spatial memory in rats exposed pre- and postnatally to ethanol. These changes are region-specific, affecting only the CA1 area but not the dentate gyrus of the hippocampus. Importantly, 23 of our graduate students co-authored 16 of the articles published in 2019 and were first author in 11 of them. **Strengthening and renovating our research faculty:** During 2019, we incorporated one additional Young Investigator to the CINV, reaching a total of 8 Young Investigators. Here, our policy has been to fund our best postdoctoral fellows for two years, during which they are free to develop their own projects in the laboratory of a senior investigator of the CINV. This approach has been highly successful: from the 8 postdocs that have entered this program, 4 now have faculty positions in different Faculties of the Universidad de Valparaíso and all of them have obtained grants from CONICYT or CORFO to continue their research. **Advanced training:** We continue to participate in the PhD and MSc Programs in Neuroscience and in the PhD Program in Biophysics and Computational Biology of the UV. All the programs are accredited from 5 to 7 years. The Neuroscience PhD Program currently has 41 students (26 female and 15 male) and this year recruited 9 students of which 4 are from abroad (Germany, Spain, Senegal and Venezuela). The PhD program in Biophysics and Computational Biology currently has 15 students including 4 students who were admitted in 2019. The Neuroscience MSc Program was re-

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accredited for 7 years. It graduated 13 students during 2019 and recruited 12 students for the 2020 academic year. CINV supports travel and stays abroad of students of all our Programs, in laboratories that are part of our international network of collaborators. **Networking:** The highlight of 2019 was the Joint Meeting of the Society of General Physiologists (SGP) and the Society of Latin American Biophysicists in September. This is the first time in 70 years that the meeting of the SGP was not held in Woods Hole (MA, USA). The meeting was an important opportunity for fostering new scientific collaborations between scientists from the USA and Latin America. A special highlight was a successful SGP fundraising campaign that supported fellowships for Latin American students and postdocs to attend the meeting. In 2018, EMBO and CONICYT signed a cooperation agreement, which made Chile an "EMBO co-operation partner". This agreement is aimed at strengthening the exchange and collaboration in biological sciences between Chile and Europe. In April 2019, the CINV hosted the visit of an EMBO delegation to Valparaíso. The visit included scientific talks by EMBO member scientists, a meeting with the EMBO Director, Dr. Maria Leptin, and a workshop on scientific writing led by Dr. Karin Dumstrei, Senior Editor of EMBO Journal. This visit strengthened the relationship between the CINV and this important scientific organization. In January 2019, we carried out the 5th Latin-American Summer School in Computational Neuroscience (LACONEU). During three weeks, 27 students (15 Chilean, 7 from other Latin-American countries and 5 from Europe) attended lectures and hands-on training from 19 speakers (11 from US, Europe and Australia) on cutting-edge topics on computational analysis of brain activity, with emphasis on the dynamics of large-scale neural networks. This school also included a 1-day Workshop "Large Scale Network Dynamics" open to the public. The successful practical and lecture "Small Brains, Big Ideas" EMBO Global Exchange Course was held for the 5th time. **Outreach:** The book "*De Mente*", a compilation of NeuroNews articles published in the virtual newspaper "El Mostrador", was published by Catalonia publishing house in June 2019, and distributed to the main bookstores in the country. A second edition was published in September 2019. Ranked as one of the most interesting cultural events in Valparaíso, the *Tertulias Porteñas* attracted almost 800 people in 2019. With the participation of leading scientists, humanists, and artists, the 3 *Tertulias* we organized in 2019 dealt with topics of high general interest and included artificial intelligence, aging, and water and human life. The first season of "*Neuropolis*", a television series created by the CINV and Puerto Visual, was broadcast throughout Chile in the Chilean National Television channel. With more than 200,000 viewers for each chapter, it is the first television series in Chile of scientific diffusion for open television created by a research center. We continue to develop our regular programs of scientific dissemination aimed at all types of audiences, such as *NeuroNews* (General Public), *Ciencia al Tiro* (primary school students), and *Falling Walls* (Young Innovators). In 2019, we put forward the *Neuroscience at your fingertips* workshop that attracted students from different high schools of the region. **Awards:** The research excellence performed by Juan C. Sáez, our Deputy Director, and Francisco Bezanilla was recognized by the US National Academy of Sciences and the American Academy of Art and Sciences, respectively.

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1.2 Resumen Ejecutivo

La investigación en el Centro Interdisciplinario de Neurociencia de Valparaíso se centra en la pregunta general: ¿Cómo responde el Sistema Nervioso a estímulos, en salud y enfermedad? Esta pregunta la abordan cinco líneas de investigación, que abarcan desde sensores moleculares a neurociencia de sistemas y circuitos, a las cuales agregamos, en 2017, una Unidad de Investigación Traslacional para identificar posibles proyectos de I+D.

Productividad científica y trabajo colaborativo: Durante 2019 publicamos 47 artículos y, aunque este es un número levemente inferior al 2018, hubo un notable incremento en el factor de impacto [IF: 6.4 (2019) vs 4.2 (2018)]. Publicamos 5 artículos en revistas de alto impacto, liderados por miembros del CINV (*Nat Nanotechnol*, *Nat Commun* y *Nat Protocols*, Bezanilla; *Nat Rev Neurosci*, Chiu, y *PNAS USA*, Whitlock). Diez publicaciones aparecieron en revistas con IF entre 5.5 y 8, incluyendo artículos en *Cancer* (Sáez y Latorre), *eLife* (Latorre), *Glia* (Sáez), *Front Neuroendocrinol* (Whitlock), *Front Immunol* (Calixto y Sáez), *J Neurosci* (Orio), *Antiox Redox Signal* (Chávez). También publicamos artículos en prestigiosas revistas: *PLoS Genet* (Calixto), *Neurobiol Dis* (Martínez), *Sci Rep* (Latorre y Palacios), *J Neurochem* (Cárdenas), *J Gen Physiol* (Bezanilla). De esta lista, destacamos 4 publicaciones: i) Un acoplamiento no-canónico del dominio sensor de voltaje (VSD) con el poro de conducción (PD), revelado con el uso de dímeros en tándem de canales de K^+ *Shaker*. Esta nueva conexión cercana entre el VSD y el PD influye tanto la dependencia de voltaje de la inactivación tipo C en el filtro de selectividad y la probabilidad de apertura del PD (Carvalho-de-Souza y Bezanilla, *Nat Commun*). ii) Guerra y cols. (*J Neurochem*) mostraron que la subunidad $\beta 2a$ de los canales de Ca^{2+} ($CaV\beta 2a$) es una molécula señalizadora que regula la dinámica de actina cortical, y en consecuencia también regula la expresión de canales de iones y la exocitosis en células neuroendocrinas. iii) Estudios en *C. elegans* en diapausa (similar a la hibernación) muestran que neuronas dañadas se regeneran completamente en este estado de quiescencia metabólica, y que las neuronas receptoras del tacto regeneradas siguen un patrón de crecimiento idéntico al que ocurre durante el desarrollo y sin errores (Caneo y cols. *PLoS Genet*). iv) Plaza-Briceño y cols. (*Antioxid Redox Signal*) mostraron que la modulación de NMDARs por NOX2 produce cambios en la plasticidad sináptica y memoria espacial de ratas con exposición pre-natal a etanol. Estos cambios son espacialmente específicos, afectando solo el área CA1, pero no el giro dentado del Hipocampo. Veintitres de nuestros estudiantes de postgrado fueron co-autores de 16 de los artículos publicados en 2019 y primeros autores en 11 de ellos.

Fortalecimiento y renovación de nuestro claustro: En 2019 incorporamos 1 nuevo Investigador Joven, llegando así a un total de 8. Nuestra política ha sido financiar a nuestros mejores investigadores post-doctorales por dos años, durante los cuales tienen la libertad para llevar adelante sus propios proyectos de investigación en el laboratorio de un científico *senior* del CINV. Esta estrategia ha sido exitosa: de los 8 postdocs que han entrado en este programa, 4 ya tienen cargos académicos en diferentes facultades de la Universidad de Valparaíso (UV) y todos se han adjudicado proyectos de FONDECYT o CORFO para continuar su investigación.

Capital Humano Avanzado: Seguimos participando en los programas de Magíster y Doctorado en Neurociencia y el Doctorado en Biofísica y Biología Computacional de la UV. Todos estos programas están acreditados por 5 a 7 años. El Doctorado en Neurociencia tiene 41 estudiantes (26 mujeres) y este año incorporó a 9 estudiantes de los cuales 4 son extranjeros (Alemania, España, Senegal, Venezuela). El doctorado en Biofísica y Biología Computacional tiene 15 estudiantes incluyendo 4

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incorporados en 2019. El Magíster en Neurociencia fue acreditado por un período de 7 años, graduó a 13 estudiantes durante 2019 y el reclutamiento fue exitoso, con 12 estudiantes aceptados de 25 postulaciones. El CINV apoya viajes y estadías de los estudiantes de todos los programas en laboratorios que son parte de nuestra red internacional de colaboradores.

Redes: Lo más destacado del 2019 fue la Reunión Conjunta de la Society of General Physiologists (SGP) y la Sociedad de Biofísicos Latinoamericanos en septiembre. Fue la primera vez en 70 años que la SGP no se reunió en Woods Hole (MA, USA). La reunión fue una importante oportunidad para fomentar nuevas colaboraciones entre científicos de USA y Latinoamérica. Un punto que es necesario resaltar fue la exitosa recolección de fondos de parte de la SGP para otorgar becas que permitieron la asistencia a la reunión a estudiantes y postdoctorantes latinoamericanos. En 2018, EMBO y CONICYT firmaron un acuerdo de cooperación, haciendo de Chile un “EMBO cooperation partner”. Este acuerdo apunta a fortalecer el intercambio y colaboración en Ciencias Biológicas entre Europa y Chile. En abril de 2019 el CINV recibió la visita de una delegación de EMBO a Valparaíso. La visita incluyó charlas científicas de miembros de EMBO, una reunión con la directora de EMBO, Dra. Maria Leptin, y un workshop sobre escritura científica dirigido por la Dra. Karin Dumstrei, Senior Editor del EMBO Journal. Esta productiva visita fortaleció la relación entre el CINV y esta organización científica. En enero de 2019, realizamos la 5ª Escuela de Verano Latinoamericana de Neurociencia Computacional LACONEU. Durante 3 semanas, 27 estudiantes (15 chilenos, 7 de otros países latinoamericanos y 5 de Europa) asistieron a charlas y sesiones prácticas de 19 expositores (11 de USA, Europa y Australia) en temas de vanguardia en Neurociencia Computacional, con énfasis en la dinámica de redes neuronales a gran escala. La escuela incluyó también un workshop de 1 día, “*Large Scale Network Dynamics*”, abierto al público. También se realizó por 5ª vez el curso teórico-práctico “*Small Brains, Big Ideas*” (EMBO Global Exchange Course).

Difusión: La Editorial Catalonia publicó el libro “*De Mente*”, una compilación de artículos de *NeuroNews* publicados en el diario electrónico *El Mostrador*. El libro fue distribuido en las principales librerías del país. Se publicó una segunda edición en septiembre de 2019. Las *Tertulias Porteñas*, uno de los eventos culturales más importantes en Valparaíso, atrajeron cerca de 800 personas en 2019. Con la participación de destacados científicos, humanistas y artistas, las 3 Tertulias organizadas en 2019 trataron temas de gran interés público: Inteligencia Artificial, Envejecimiento y el Agua. La primera temporada de *Neurópolis*, una serie de TV creada por el CINV y Puerto Visual se transmitió en todo Chile a través de TVN. Con más de 200.000 televidentes en cada capítulo, es la primera serie de televisión en Chile creada por un centro de investigación para la televisión abierta. Continuamos desarrollando nuestros programas regulares de difusión científica dirigidos a todo público, tales como *NeuroNews* (Público General), *Ciencia al Tiro* (estudiantes de Educación Básica) y *Falling Walls* (jóvenes innovadores). En 2019 implementamos el taller *Neuroscience at your fingertips* que atrajo estudiantes de Educación Media de diferentes liceos de la región.

Premios: La excelencia de las investigaciones realizadas por nuestro Director Alterno Juan Carlos Sáez, y de Francisco Bezanilla, fue reconocida por la Academia Nacional de Ciencias y por la Academia de Artes y Ciencias de los Estados Unidos, respectivamente.

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1.3. Outstanding Achievements

The highlight of 2019 was the Joint Meeting of the Society of General Physiologists (SGP) and the Society of Latin American Biophysicists in September. This is the first time in 70 years that the SGP was not held in Woods Hole (MA, USA). What follows was extracted from the Society of General Physiologists' page. "The symposium was an important platform fostering new scientific collaboration between scientists from the USA and Latin America. Scientists and trainees from both US and Latin America exchanged professional and cultural experiences that help us to create a better and trusted global scientific community. All of this was enabled by years of dreaming and planning by the organizers, Jorge Contreras, Miguel Holmgren, Ramon Latorre, and Brad Rothberg who worked steadfastly to pull off this extraordinary event. Three cheers for the organizers!".

Juan Carlos Sáez was elected to the National Academy of Sciences (USA) in recognition of his achievements in the field of gap junctions and hemichannels, These include the demonstration of electrical synapsis between cells of the immune system as well as the progress on the existence and functional role of connexin hemichannels, particularly under inflammatory conditions. In addition, he was recognized for discovering potent and selective connexin blockers that led to the generation of a spin off called CONNECTOMICA SpA of which CINV owns about 3% of the shares. Currently, patients suffering of diseases that did not have therapeutic treatment, such as Duchenne and Becker muscular dystrophies as well as dysferlinopathies, are reporting progressive improvements of their health condition to physicians specialized in neuromuscular diseases. Francisco Bezanilla was elected to the American Academy of Arts and Sciences for his important contributions to the field of ion channel biophysics.

With more than 2000 copies sold, the book "*De Mente*", a compilation of translations to Spanish of important scientific publications done by PhD students and Postdocs in a language reachable by the general public, was the outstanding achievement of the CINV in the area of outreach.

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2. Introduction

a) Description of the Institute/Nucleus:

The CINV is composed of multidisciplinary groups of researchers in areas that range from molecular modeling and biophysics to the physiology of brain circuitries. It is organized along different lines of research; however, this grouping is mostly administrative as there is plenty of collaborative work both within as well as between lines. In 2018, we created a program called “Strategic Projects” aimed at actively encouraging further intra-CINV collaborations by providing seed funding for new projects between investigators. For example, during 2019 the group working on connexins proposed to use *Drosophila* to identify genes involved in connexin 26 (Cx26) and Cx43 intracellular traffic. Similarly, *C. elegans* experts collaborated with neuroscientists who specialize in neuronal imaging to study neuronal regeneration under diapause (akin to hibernation) in the worm. This program has been highly successful, and most teams are now writing grants and producing co-authored manuscripts as a result. In addition, and to secure our future, we have consolidated our Young Investigator program in which our best postdocs can perform independent research for two years in the lab of a Senior CINV Scientist. There are currently 8 Young Investigators, and most of them are now professors in different faculties of the Universidad de Valparaíso. CINV scientists are being recognized abroad: during 2019, our Deputy Director, Juan C. Sáez, was elected to the National Academy of Sciences (NAS) and Francisco Bezanilla (already a NAS member) became a member of the American Academy of Arts and Sciences. We are proud to mention here that with the incorporation of Juan C. Sáez to NAS, the CINV currently has three NAS members. As in other years, the involvement of PhD students and Young Investigators has been important for our research. For example, Lorenzo-Ceballos et al. determined the strength of interaction between Ca^{2+} binding and the voltage sensor in BK channels (*eLife* 2019). Of note, our Max Planck Leader, Chiayu Chiu, analyzed diverse forms of long-term GABAergic synaptic plasticity (*Nat Rev Neurosci* 2019). Amongst our noteworthy findings for 2019 we highlight research relevant to pathological conditions. For example, using a lysolecithin-induced demyelination mouse model of multiple sclerosis, Li et al. (*Glia* 2019) demonstrated that astrocyte-specific Cx43 KO accelerates the remyelination process, increases the number of mature oligodendrocytes, and reduces glial activation and deposition of myelin debris. The CINV has continued to strengthen its networking capabilities by organizing important meetings and courses. In 2019, the Society of General Physiologists (SGP) joined forces with the Society of Latin American Biophysicists and held its annual meeting in Valparaíso, organized by the CINV. This was a historical event for the SGP as the meeting left its traditional location, the MBL (Woods Hole, Mass), for the first time in 73 years. This year was also very rich in international teaching activities, and included the Southern School on Biophysics, which is aimed at Latin American students; the 5th Latin-American Summer School in Computational Neuroscience (LACONEU) in which students from Latin America and Europe attended lectures and hands-on training on cutting-edge topics about computational analysis of brain activity; the successful Small Brains, Big Ideas: Insights from Invertebrates course (EMBO Global Exchange Lecture Course), aimed at Latin American students, whose objective is to expose students to the use of invertebrate model systems for basic and applied research in neurosciences and biomedicine.

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b) Research Lines and Organization of researcher's team.

Line 1. Structure and Function of Molecular Sensors. (R. Latorre, A. Neely, C. González, O. Alvarez, F. Bezanilla, M. Holmgren; and young investigators: J.A. Gárate, K. Castillo and I. García). We made progress in understanding the allosteric coupling between Ca^{2+} and voltage sensors in BK channels (Lorenzo-Ceballos et al. *eLife*. 2019) and identified the estrogen binding site in its β subunit (Granados et al. *Sci Rep*. 2019). We made progress in our understanding of the molecular basis of gating currents in voltage-gated K^+ channels and in the coupling between the voltage sensor domain and the pore opening (Carvalho-de-Souza and Bezanilla. *Nat Commun*. 2019). We also showed that when subject to a strong electric field, an ion-conducting pathway opens within the aquaporin tetramer (Bernardi et al. *Phys Chem Chem Phys*. 2019).

Line 2. Cell Signaling. (A.M. Cárdenas, J. C. Sáez, A.D. Martínez; and young investigator: H. Sánchez and A. González). Our most significant finding was the demonstration that pannexin1 channels play a critical role in the degranulation response of mast cells induced by antigen recognition during Type I hypersensitivity reactions. We demonstrated that Panx1 channels contribute to the sustained Ca^{2+} signal increase by releasing ATP, which then activates P2 receptors, allowing Ca^{2+} influx. We also demonstrated that Panx1 channels are Ca^{2+} -impermeable, refuting the long-held dogma that these channels are permeable to this ion (Harcha et al. *Front Immunol*. 2019). Thus, the role Panx1 channels under diverse physiological and pathophysiological conditions will now need to be re-evaluated.

Line 3. Genetic and Developmental Neuroscience. (K. Whitlock, A. Calixto and J. Ewer). In a collaborative work, we showed that zebrafish have lost the gene encoding gonadotropin-releasing hormone 1 (GnRH1), the highly conserved and essential peptide controlling reproduction in vertebrates. We also showed that this gene loss is not a result of inadvertent selection in the lab as the wild-type populations of zebrafish also lack this gene (Whitlock et al. *Front Neuroendocrinol*. 2019). Our findings raise the question of which peptide carries out the critical functions normally subserved by GnRH1, since the likely candidates have been shown to not be essential for reproductive functions.

Line 4. Integrative and Circuits Neuroscience. (A. Palacios, A. Chávez, P. Moya, O. Schmachtenberg; and young investigators: C. Chiu, A. Ardiles). We demonstrated that modulation of NMDARs by NOX2 drives changes in synaptic plasticity and spatial memory in rats exposed pre- and postnatally to ethanol (PAE). These changes are region-specific, affecting only the CA1 area but not the dentate gyrus of the hippocampus. More importantly, adolescent PAE rats orally fed the antioxidant and free radical scavenger apocynin exhibited significantly improved spatial memory acquisition providing important advance to our current understanding of the cellular mechanisms underlying PAE-dependent defective hippocampal function.

Line 5. Crosscutting: Computational Biology and Bioinformatics. (F.D. González, T. Pérez-Acle and P. Orió). We added the implementation of two collective variables into the Colvars module used in molecular simulation packages, NAMD and LAMMPS. This will provide thermodynamic insights into the structural conformation and stability of biomolecules (Gárate et al. *J Phys Chem B*. 2019). In a collaboration with the Millennium Nucleus MiNICAD, we showed that altered corneal sensitivity to cold after surgery is better explained by an increased expression of TRPM8 channels rather than to a decrease of K^+ channels (Piña et al. *J Neurosci*. 2019).

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3. Scientific and technological research:

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*; and young investigators: *J.A. Gárate, K. Castillo and I. García*). In recent years, we have witnessed an exponential increase in the number of medium and high resolution structures of ion channels, which is aiding us in achieving our goal of understanding, at the atomic scale, the molecular mechanisms of how conformational changes in structural domains specialized in sensing temperature, voltage or a ligand, drive the structural rearrangements underlying the gating of ion fluxes mediated by the pore domain of ion channels. However, as there is no clear assignment of the state of the channel protein in the snapshot revealed by structural studies, we often find ourselves contrasting the results of these studies with the experimental evidence obtained from functional studies. For example, structural data predicted a large degree of interaction between Ca^{2+} and voltage sensors (VSD) in Ca^{2+} - and voltage-activated K^+ (BK) channels. However, the electrophysiological data indicated that the coupling between Ca^{2+} binding and VSDs domains was poor. By investigating the effects of varying internal Ca^{2+} concentration on BK channel gating currents we found that Ca^{2+} sensor occupancy has a strong impact on VSD activation through a coordinated interaction mechanism in which Ca^{2+} binding to a single α -subunit affects all VSDs equally. Moreover, the two distinct high-affinity Ca^{2+} binding sites, RCK1 and RCK2, contained in the C-terminus domains, contribute equally to decrease the free energy necessary to activate the VSD. Thus, the voltage-dependent gating and pore opening in BK channels is, to a great extent, modulated by the interaction between Ca^{2+} sensors and VSDs (Lorenzo-Ceballos et al. *eLife*. 2019).

We also revisited the long-standing issue of 17β -estradiol (E2) binding to BK channels, which we reported many years ago (Valverde et al. 1999. *Science* 285:1929-1931). Although this study documented the direct interaction of the hormone with a voltage-gated channel and revealed the mechanism for the modulation of vascular smooth muscle BK channels by estrogens, it was still unclear whether E2 binds the BK $\beta 1$ subunit or the $\alpha/\beta 1$ complex. In collaboration with Line 5 and the Pontificia Universidad Javeriana (Colombia), we used molecular modeling, bioinformatics, mutagenesis, and electrophysiology, to identify a cluster of hydrophobic residues in the second transmembrane domain of the $\beta 1$ subunit, including the residues W163 and F166, as the binding site for E2. Since $\beta 1$ is a key molecular player in vasoregulation, our findings are important for the design of drugs that could modulate BK channels (Granados et al. *Sci Rep*. 2019).

In our research of the non-canonical coupling of the VSD with the conduction pore (PD) we constructed tandem dimers of Shaker K^+ channel to separate the normal coupling of the VSD with the opening of the pore from the direct interaction between the S4 segment of the VSD and the S5 segment of the PD (Carvalho-de-Souza & Bezanilla. *Nat Commun*. 2019). Relevant to this question was to clarify if the transmembrane segment carrying the gating charges (S4) changes its secondary structure as it moves with respect to the other segments that cross the so-called hydrophobic plug. Structural studies indicate that S4 is an alpha helix. Using metal bridges, we were able to show that the S4 segment changes to a 3-10 helix when it goes from the resting to the active state (Bassetto et al. *Biophys J*. 2019).

We also published technical and methods papers with our collaborator Bozhi Tian describing in detail different strategies used to stimulate excitable tissues with light using nanostructures that can produce electrochemical depolarizations or using thermal increases in capacitance

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(optocapacitance) (Jiang et al. *Nat Protoc.* 2019; Acaron-Ledesma et al. *Nat Nanotechnol.* 2019).

In collaboration with the group of Domenico Tricarico of the University of Bari, Italy, we found that nanomolar concentrations of bisphosphonate zoledronic acid could activate the TRPV1 channels present in osteoblasts (Scala R et al. *Cancers.* 2019). This activation mediates cell proliferation and mineralization of osteoblasts. In the field of transient receptor potential (TRP) channels we determined precisely the absolute open probability of the TRPM8 channel expressed in *Xenopus* oocytes.

In a chapter by Alvarez et al. (*Methods Mol Biol.* 2019), we used our practical experience to describe the animal care protocols, patch-clamp pipette preparation, temperature control methods, and analysis of ionic currents, needed in order to obtain reliable absolute open channel probabilities. We also developed two alternative methods to increase the levels of melanin, which is used to shield cytoplasmic fluorescence and increase the resolving power of voltage-clamp fluorescent techniques that report voltage-dependent conformational changes (Lee & Bezanilla. *J Gen Physiol.* 2019).

This year, with the arrival of J.A. Gárate, a young investigator expert in molecular dynamic and statistical thermodynamics, we added aquaporin, a channel that conducts water and which is a real challenge for electrophysiologists, to our inventory. Using non-equilibrium molecular dynamics, we joined efforts with researchers from Italy and Ireland to show that, when subject to a strong electric field, an ion-conducting pathway opens at the center of the aquaporin tetramer (Bernardi et al. *Phys Chem Chem Phys.* 2019). And in collaboration with line 5, we implemented new methods to manipulate the orientation and magnitude of the electric dipole moment to help study the effects of membrane potential on channel proteins (Gárate et al. *J Phys Chem B.* 2019). Isaac García, another of our young investigators, continued investigating the molecular mechanisms underlying the phenotype of connexin 26 mutations that causes Keratitis-ichthyosis deafness (KID) syndrome and characterized the molecular mechanism underlying the KID defects caused by mutation Cx26N14K, showing that it affects the voltage- and Ca^{2+} -dependent closure of hemichannels.

Taking advantage of our tools and expertise in the biophysics of ion channels, we contributed to work in Line 2 on excitation-secretion coupling, and showed that the Ca^{2+} channel $\beta 2\alpha$ subunit down-regulates voltage-activated ion current densities by disrupting actin-dependent traffic in chromaffin cells (Guerra et al. *J Neurochem.* 2019).

Finally, a paper that recounts the story of the Laboratorio de Fisiología Celular in Montemar from F. Bezanilla's perspective was published in *the Journal of General Physiology* as part of the Influences series (Bezanilla F. *J Gen Physiol.* 2019).

Research Line 2. Cell signaling. (J.C. Sáez, A.M. Cardenas, A.D. Martínez; and young investigators: H. Sánchez and A. González). Chemical and electrical synapses are the major communication systems used for cell-to-cell communication within the nervous system. We investigate the mechanism that regulate neurosecretion, electrical, and metabolic cell-to-cell coupling, as well as autocrine and paracrine cell-cell communication mediated by hemichannels under physiological and pathophysiological conditions of the CNS and PNS.

The pineal gland has limited independent axonal innervation and not every cell is contacted by nerve terminals. JC Sáez and A Martínez, in collaboration, demonstrated that gap junctions between cells of the pineal gland allow cell-to-cell propagation of norepinephrine-induced signals that promote glycogenolysis throughout the entire gland. Thus, the interplay

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between chemical and electrical synapses is essential for coordinating glycogen metabolism in this gland (Eugenin et al. *J Neurochem.* 2019).

Using an animal model of Alzheimer's disease, we have previously shown that mast cells are the first cells activated in the neuroinflammatory response associated with this disease (Harcha et al. *J Neurosci.* 2015). Mast cells (MCs) release pro-inflammatory mediators through the degranulation response, which can be induced by antigen recognition through immunoglobulin E (IgE) or "cross-linking," classically associated with Type I hypersensitivity reactions. Early in this reaction, Ca^{2+} influx and subsequent increase of intracellular free Ca^{2+} concentration is essential for MC degranulation. JC Sáez and A Martínez, in collaboration, demonstrated the contribution of Panx1 Chs in the degranulation response using MCs from wild type (WT) and Panx1 knock out (Panx1^{-/-}) mice after anti-ovalbumin (OVA) IgE sensitization. This work shows that Panx1 Chs play a critical role in the sequential events that lead to the degranulation response during Type I hypersensitivity reactions that could affect brain functions (Harcha et al. *Front Immunol.* 2019).

We also investigated the role of astroglial connexin43 (Cx43) in remyelination using astrocyte-specific Cx43 conditional knockout (Cx43 cKO) mice, which were the progeny of mice bearing a hGFAP promoter-driven cre and mice carrying a floxed Cx43 allele. After lecithin-induced demyelination, the remyelination process in Cx43 cKO mice was accelerated and the number of mature oligodendrocytes was increased, suggesting that depletion of Cx43 facilitates oligodendrocyte precursor cells differentiation. Thus, inhibiting Cx43 HC may be a potential therapeutic approach for treating demyelinating CNS diseases (Li et al. *Glia.* 2019).

We studied the role of de novo expression of Cxs in muscle dysfunction induced by bacterial endotoxin (LPS), by comparing the skeletal myofibers of control (Cx43^{fl/fl}Cx45^{fl/fl}) and Cx43/Cx45 expression-deficient (Cx43^{fl/fl}Cx45^{fl/fl}; Myo-Cre) mice. Myofibers of control mice undergoing endotoxemia present functional Cx HCs, largely explaining their increase in sarcolemma permeability. We propose that current therapy options for individuals undergoing endotoxic shock could be improved using Cx HC inhibitors (Cea et al. *Biochim Biophys Acta Mol Basis Dis.* 2019). A critical protein for sarcolemma integrity is dysferlin, and mutations in the dysferlin gene cause muscle dystrophy. AM Cárdenas' group demonstrated a role for dysferlin in cytoskeletal actin dynamics, which is impaired in myoblasts derived from dysferlinopathy patients. Both N-terminal and C-terminal regions of dysferlin are implicated in this mechanism (Báez-Matus et al. *Int J Mol Sci.* 2019).

Voltage-dependent Ca^{2+} channels (VDCC) play a crucial role in the exocytotic release of transmitters from neuroendocrine chromaffin cells. Through a collaboration between AM Cárdenas, A Martínez, and A Neely (Line-1), we demonstrated that the β 2a subunit of the Ca^{2+} channels (Cav β 2a) down-regulates the forward traffic of ion channels by a mechanism dependent on cortical actin dynamic, suggesting that Cav β 2a plays a role in regulating the expression of ion channels, and consequently, also exocytosis (Guerra et al. *J Neurochem.* 2019). In a collaboration with Dr. Marengo (U. Buenos Aires) AM Cárdenas discovered that a Ca^{2+} -independent and voltage-dependent exocytosis component in chromaffin cells; the mechanism implies a coupling between P/Q-type VDCC and the exocytotic machinery (Moya-Díaz et al. *Acta Physiol (Oxf).* 2019).

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by motor neuron death. In collaboration with colleagues from the Universidad de Concepción and the Biomedical Neuroscience Institute (a Millennium Institute, Santiago), we reported that in a

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model of ALS, motor neuron β -catenin displays increased association with Cx43. These findings correlate with impaired intercellular adhesion and increased cell coupling (Pinto et al. *Neurobiol Dis.* 2019) in ALS motor neurons.

We also published a review article on direct intercellular communication mediated by Cxs in prostate cancer (Asencio-Barría et al. *Cancers (Basel).* 2019). Finally, we demonstrated a close correlation between a RhoA/ROCK-dependent pathway and renal Cx43 regulation in the angiotensin II-induced renal damage (Gómez et al. *Int J Mol Sci.* 2019).

Research Line 3. Genetic and Developmental Neuroscience. (K. Whitlock, J. Ewer, and A. Calixto). We have 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 are generated in the olfactory sensory system and GnRH neuroendocrine system: 1. *Analysis of proliferative cell populations of the olfactory sensory system.* Previously, we have shown that a continuous sheet of neurectoderm gives rise to the peripheral (olfactory organs) and central (olfactory bulbs) nervous system thus presenting a new model for nervous system development (Torres-Paz and Whitlock, 2014). Further analysis (Torres-Paz et al. *Int J Dev Biol.* in press) has shown that a gradient of *distal-less* genes (Dlx) 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 discovered that the meninges of the brain are continuous with the OE and are associated with a neural-immune interface 2. *Control of GnRH cell differentiation in the adult hypothalamus.* Surprisingly, we confirmed GnRH gene loss in a specific syntenic region of the genome that is not related to domestication effects on the genome (collaboration: Dr. John Ewer and Dr. John Postlethwait, USA), and is supported by loss of GnRH proteins as shown by MALDITOF and Orbitrap analysis (collaboration: Dr. Christian Wegener, Germany) (Whitlock et al. *Front Neuroendocrinol.* 2019; Whitlock. *PNAS.* 2019). We are currently investigating whether the hypothalamic peptide Phoenixin (ligand for orphaned receptor GPR173) can 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. We have continued: 1- *Investigating how the key neuropeptides, Ecdysis Hormone (EH) and Ecdysis Triggering Hormone (ETH), control ecdysis behavior.* For this we use genetic tools we have developed in collaboration with Ben White (NIH, USA), null mutants we have isolated, and calcium imaging using GCaMP, to investigate how EH and ETH cause the sequential expression of ecdysis behaviors (Scott et al. In press). 2- *Investigating 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 (Flaven-Pouchon et al. *BMC Biol.* In press). We will continue ongoing research to understand how these processes are triggered shortly after ecdysis. 3- *Investigating 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

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with Christian Wegener (U. Würzburg, Germany) we identified the pathway through which the brain clock is coupled to the PG clock (Selcho et al, *Nat Commun.* 2017). 4- As part of a cross-line collaboration, we are continuing a project with AD Martínez (Line 2) that uses *Drosophila* to identify genes involved in connexin (Cx) function. Although Cxs are not present in flies, there are successful precedents for using this type of approach to identify novel players involved in specific cellular processes. 5- We are also continuing work with Dr. Maria Rita Passos Bueno (U. Sao Paulo, Brazil) characterizing the behavioral and anatomical defects in *Drosophila* bearing mutations in genes associated with autism in humans.

Using genomics and systems biology approaches to understand the impact of environment and microbiota on behavior and neuronal survival. 1- *Use of C. elegans as surrogate for 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 (TrN, Calixto et al, 2012). Using such model, we ask how microbiota affects the dynamics of neurodegeneration and function of TRNs. We showed that while degeneration of TRNs proceeds steadily during development and is completed at adulthood when fed *Escherichia coli* OP50, the strain routinely used for *C. elegans* maintenance, it was significantly reduced when fed *E. coli* strain HT115. We also found two bacterial metabolites responsible for neuroprotection, GABA and lactate (Urrutia et al. accepted in *PLoS Biology*). 2- *Use of the diapause state for pathogen avoidance.* We showed that when animals are exposed to environmental bacteria with pathogenic potential, they make the decision to exit development and enter diapause as a form of pathogen avoidance. This decision is transgenerationally transmitted to the progeny and depends on the RNAi machinery (Palominos et al. 2017). We proposed that small RNAs produced by intestinal bacteria are the molecular triggers for this response (Legue and Calixto, *Curr Opin Syst Biol.* 2019).

Research Line 4. Integrative and Circuits Neuroscience (A. Palacios, A. Chávez, P. Moya, O. Schmatenberg; and young investigators: C. Chiu and A. Ardiles). Members of this line continue investigating how different neuronal circuits at the synaptic levels (i.e. brain and retinal circuits) work under normal and pathological conditions including aging, neurodegenerative, and neuropsychiatric disorders, as some of these processes are known to induce alterations in both cognitive and sensory performance. Using a variety of cellular and molecular tools, combined with electrophysiology, optogenetic and behavioral analysis, research from multiple labs are revealing distinct functional changes in both excitatory and inhibitory neurons. First, we have found that modulation of NMDARs by NOX2 drives changes in synaptic plasticity and spatial memory in rats exposed pre- and post-natally to ethanol. These changes are region-specific, affecting only the CA1 area but not the dentate gyrus of the hippocampus (Plaza et al. *Antioxid Redox Signal.* 2019). In addition, we also provided physiological and behavioral evidence that, during adolescence, the function of inhibitory synaptic function in the medial prefrontal cortex (mPFC) is more susceptible than the hippocampus or auditory cortex to NMDAR hypofunction, showing apparent structure specificity (Pérez et al. *Front Cell Neurosci.* 2019). In a broader context, the impairment of inhibitory circuitry observed in the mPFC by ketamine-treatment in the adolescent could be a convergent primary site of schizophrenia (SZ)-like behavior during the adulthood. As neuroinflammatory processes have been suggested to contribute to the development of SZ and one component that has been linked to this disorder is interleukin-6 (IL-6), we examined the association between the IL6 and treatment resistance in Chilean SZ Patients and found a

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lack of association (Cavieres et al. *Schizophr Res Treatment*. 2019). Work continues on the role of inhibitory transmission in regulating activity-dependent synaptic plasticity (Chiu et al. *Nat Rev Neurosci*. 2019), and its modulation by endogenous neuromodulators such as cannabinoids at the level of the retina (Vielma et al. *Invest Ophthalmol Vis Sci*. 2020). Collaborative work within this line is also uncovering the potential role of neurotransmitter transporters in neuropsychiatric diseases. We recently demonstrated that overexpression of neuronal glutamate transporter EAAT3 at excitatory synapses in the brain recapitulates behavioral and synaptic alterations in NMDA receptor relevant to obsessive-compulsive disorder. These results provide further support for the glutamatergic hypothesis in the pathogenesis of OCD (Escobar et al. *Front Pharmacol*. 2019) and provide a valuable animal model that may open novel therapeutic approaches to treat this devastating disorder.

Using retinal circuits, we demonstrated significant physiological differences between control and high glucose conditions that mimic diabetes. While changes were evident in calcium signals and in the time course of responses to glutamate, the voltage-gated current profiles of retinal bipolar cells displayed minor variations. We also demonstrated that cannabinoid type 1 receptor (CB1R) activation shapes the responses of type 2, 3a, and 3b, OFF bipolar cells by selectively regulating GABAergic feedback inhibition at their axon terminals, and thus cannabinoid signaling might play an important role in fine-tuning signal processing in the mammalian inner retina (Vielma et al. *Invest Ophthalmol Vis Sci*. 2020). Further, we revealed that the visual response at the level of retinal ganglion cells is modulated by the naturalness of the stimulus - in particular for motion - which suggests that the tuning to the statistics of natural images already emerges at the level of the retina (Ravello et al. *Sci Rep*. 2019). We also characterized the pupillary light reflex in *Octodon degus*, a natural rodent model for the study of Alzheimer's disease, as pupillary reflex is used as a biomarker to detect early signs of central nervous system deterioration (Palanca et al. *Exp Eye Res*. 2019). We extended our sensory studies by generating an update on the anatomy and function of the teleost olfactory system (Olivares and Schmachtenberg. *PeerJ*. 2019). Finally, we characterized the visual spectral sensitivity of the Chilean recluse spider, *Loxosceles laeta*, a synanthropic species that poses a significant threat to humans and found that this species has monochromatic vision (Tapia F et al. *J Exp Biol*. 2020).

Research Line 5. Crosscutting: Computational Biology and Bioinformatics. (P. Orio, F.D. González and T. Pérez-Acle). We continue to work with models of neural excitability in order to understand the dynamics of neural networks. In 2019, we have extended this work to the study of the human connectome and how connectivity patterns can give rise to complex dynamics. Using a mean field model for large-scale brain activity, we simulated the resting-state dynamics of mean-field whole-brain models and assessed how dynamic multi-stability and ignition differ between a realistic human connectome and a variety of randomized connectomes. We found that the strength of global excitation needed to first trigger ignition in a subset of regions is smaller for the model embedding the empirical human connectome and that the propagation of ignition outside of the initial core is more gradual than for any of the randomized connectomes, allowing for graded control of the number of ignited regions. We explain these assets in terms of the exceptional weighed core-shell organization of the empirical connectome, which may be tuned to support an enhanced ignition dynamic (Castro S et al. *PLOS Comp Biol*. in press).

In collaboration with Dr. Jesús Cortes (Biocruces, Biskaia, Spain) and Dr Rodrigo Cofré (Universidad de Valparaíso), we are analyzing fMRI data from healthy participants, applying

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information theory tools. Our results show that older subjects (age ranging from 60 to 80 years) exhibit a higher predominance of redundant interactions than younger subjects (Gatica et al. *Neurocomputing*. submitted). Additionally, we are using our models to study how the neuromodulation of inhibitory activity modulates the switching between segregation and integration in the brain. Our models also help understand how the altered corneal sensitivity to cold after surgery is better explained by an increased expression of TRPM8 channels rather than a decrease of K^+ channels (Piña et al. *J Neurosci*. 2019). This result is connected to the regulation of tearing and eye dryness after surgery.

We continue collaborating with Dr. R. Latorre's team working on multiples projects, such as identifying the binding site of estradiol in BK (Granados et al. *Sci Reps*. 2019). We have also investigated the implementation of multiples molecular simulation methods applied to TRPV1, and explored the integration with Target Discovery, Drug Discovery, and Drug Delivery (Duarte et al. *Wiley Interdiscip Rev Nanomed Nanobiotechnol*. 2019). Finally, we also performed the *in vivo* test of 4 novel TRPV1 agonists obtained after virtual screening through Docking simulations using the ZING database (over 100,000 compounds). Through this approach we found a new and more potent analogue of capsaicin, with a faster onset and slower decay of analgesia (Submitted to *Pain*).

In collaboration with J.A. Gárate, a young investigator of the CINV (Line 1), we implemented two collective variables (CVs), the so-called reaction coordinates, to manipulate the orientation (i.e., angle) (μ^{\rightarrow}_a) and magnitude ($|\mu^{\rightarrow}|$) of the electric dipole moment. To this end, we studied the thermodynamics of water orientation under the application of external voltages and the folding of two polypeptides at zero-field conditions. The projection of the free-energy [potential of mean force (PMF)] along water orientation defined an upper limit of around 0.3 V for irrelevant thermodynamic effects. On the other hand, sufficiently strong μ^{\rightarrow}_a restraints applied on alanine-12 (Ala₁₂) triggered structural effects because of the alignment of local dipoles; for lower restraints, a full-body rotation is achieved. The manipulation of $|\mu^{\rightarrow}|$ produced strong perturbations on the secondary structure of Ala₁₂, promoting an enhanced sampling to its configurational space. Rigorous free-energy calculations in the form of 2-D PMFs for deca-alanine showed the utility of $|\mu^{\rightarrow}|$ as a reaction coordinate to study folding in small α helices. As a whole, we propose that the manipulation of both components of the dipole moment, μ^{\rightarrow}_a and $|\mu^{\rightarrow}|$, provides thermodynamics insights into the structural conformation and stability of biomolecules. These new CVs are implemented in the Colvars module, available for NAMD and LAMMPS (Gárate et al. *J Phys Chem B*. 2019).

Unit of Translational Science. (A. Muñoz, F.D. González, T. Pérez-Acle, J.C. Sáez and C. González). In September 2019, we hired Ms. Andrea Muñoz, who is in charge of identifying and coordinating emerging Research + Development (R + D) projects among the CINV scientists. Ms. Muñoz already identified potential R + D projects and at least 3 will be presented in the next national call for R + D grant applications (FONDEF).

Members of the Institute and members of a Chilean spin-off called Connectomica SPA prepared a grant application, which was submitted to CORFO agency (R + D project called Technological Contracts). 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 grant was awarded and is led by T. Pérez-Acle (Line 5) and A. Martínez (Line 2). The CINV will develop the specific aims of the project, including the

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toxicological analysis of a selective and potent connexin hemichannel blocker, called D4. The unit of Translational Science continues supporting a FONIS project (to the National Funds for Research in Health). This project is led by H.A Sánchez, a young investigator of the Institute, which also includes the participation of two CINV investigators, A.D. Martínez (Line 2) and P. Moya (Line 4). The main aim of this project is to determine the frequency of mutations in the Cx26 gene in congenital deafness in the Chilean population.

b) Productivity: Productivity of the Center during 2019 in terms of total publications was slightly lower than that for 2018, with 47 articles. However, there was a remarkable increase in the average impact factor of the journals [IF: 6.4 (2019) vs. 4.2 (2018)]. Five articles led by CINV members were published in high impact journals, such as (*Nat Nanotechnology*, *Nat Commun.*, *Nat Protocols*, *Nat Rev Neurosci* and *PNAS*), and ten publications in journals with IF between 5.5-8.0, including papers in *Cancers*, *eLife*, *Glia*, *Front Neuroendocrinol*, *J Neurosci* and *Antioxid Redox Signal*. The rest of our publications appear in other prestigious journals, like *PLoS Genet*, *Front Immunol*, *Neurobiol Dis*, *Sci Rep*, *J Neurochem* and *J Gen Physiol*. Fourteen articles were product of collaboration between members of the center, representing 30% of total publications. Most of them correspond to intra research line collaborations and two represent collaboration between different lines. Young investigators produced 8 articles, and postdocs co-authored nine research articles. Twenty two Doctoral and Master students coauthored 16 research articles, of which 3 have more that one student as co-author, as result of our effort to stimulate the collaborative work between students as a mentoring strategy. A description of the productivity by research line is given below.

Line 1. The strength of the allosteric coupling between Ca^{2+} sensors and voltage sensors in BK channels was determined using gating current measurements and mutagenesis (Lorenzo-Ceballos et al. *eLife*) and the estrogen binding site in its β subunit was identified (Granados et al. *Sci Rep*). Graduate Students as well as Young Investigators participate in these studies. The paper of Granados et al. shows a high degree of collaboration inside Line 1 and with Line 5. In addition, we present a mathematical model for gating currents in voltage-gated K^+ channels (Horng et al. *Biophys. J*) and found a non-canonical mechanism of coupling between the voltage sensor and pore domains (Carvalho-de-Souza and Bezanilla. *Nat Commun*). Young Investigator, J. Gárate, using non-equilibrium molecular dynamics showed that when subject to a strong electric field, an ion-conducting pathway opens at the center of the aquaporin tetramer (Bernardi et al. *Phys Chem Chem Phys*).

Line2. We unraveled the functional role of Panx1 channels in the degranulation response of mast cells (Harcha et al. *Front Immunol*). Two post-doctoral fellows of CINV, P. Harcha (First author) did most of the experiments, and Iván Barría, who demonstrated that open Panx1 channels are permeable to ATP but not to Ca^{2+} . This work was also co-authored by two investigators of Line 2 (A.D. Martínez and J.C. Sáez).

Line3. In a collaborative work between the Whitlock and Ewer labs we have shown that zebrafish have lost the gene encoding gonadotropin-releasing hormone 1, the highly conserved and essential peptide controlling reproduction in vertebrates. Furthermore, we showed that this gene loss is not a result of inadvertent selection in the lab as the wild-type populations of zebrafish also lack this gene. (Whitlock et al. *Front Neuroendocrinol*. 2019). The Calixto lab has shown that *C. elegans* during diapausing (or hibernating) damaged neurons fully regenerate, both morphological and functionally. (Caneo et al. *Plos Genet*. 2019).

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Line 4. In 2019, we demonstrated that modulation of NMDARs by NOX2 drives changes in hippocampal synaptic plasticity and spatial memory in rats exposed pre- and postnatally to ethanol (PAE). Moreover, adolescent PAE rats orally fed the antioxidant and free radical scavenger apocynin exhibited significantly improved spatial memory acquisition (Plaza-Briceno et al. *Antioxid Redox Signal.* 2019). This work was the collaborative effort of Master and PhD students in Chávez's lab. Another collaborative work, provided physiological and behavioral evidence that, during adolescence, the function of inhibitory synaptic function in the medial prefrontal cortex (mPFC) is more susceptible than the hippocampus or auditory cortex to NMDAR hypofunction, showing apparent structure specificity (Pérez et al. *Front Cell Neurosci.* 2019).

Line 5. With participation of the Young Investigator J.A. Gárate (Line 1), we implemented two collective variables Colvars module, available for NAMD and LAMMPS that provide thermodynamics insights into the structural conformation and stability of biomolecules. (Gárate et al. *J Phys Chem B.* 2019). Our models of neural excitability helped to understand how the altered corneal sensitivity to cold after surgery is better explained by an increased expression of TRPM8 channels rather than a decrease of K⁺ channels (Piña et al. *J Neurosci.* 2019). In collaboration with Line 1 and using molecular modeling and bioinformatics, we identify a cluster of hydrophobic residues in the second transmembrane domain of the $\beta 1$ subunit of the BK channel as the binding site for estrogens (Granados et al. *Sci Reps.* 2019).

c) Outstanding publications:

1. A non/canonical coupling of the voltage sensor domain (VSD) with the conduction pore (PD), revealed using tandem dimers of Shaker K⁺ channels. This new near-connection between the VSD and the PD influences both voltage-dependence of C-type inactivation at the selectivity filter and the overall PD open probability (Carvalho-de-Souza & Bezanilla. *Nat Commun*).
2. Astrocytic connexin43 hemichannels were identified as novel molecular target to favor remyelination in a model multiple sclerosis of mice treated with lyssolecithin to induce demyelination. Either silencing Cx43 expression or blocking Cx43 hemichannels speed up remyelination (Li et al. *Glia.* 2019).
3. We unravel the effects of pre- and postnatal alcohol consumption (PAE) on NMDAR function, synaptic transmission and hippocampal memory formation. We also showed that PAE rats orally fed the antioxidant and free radical scavenger apocynin exhibited significantly improved spatial memory acquisition (Plaza-Briceno et al. *Antioxid Redox Signal.* 2019).
4. In a collaborative work between the Whitlock and Ewer labs we showed that zebrafish lost the gene encoding gonadotropin-releasing hormone 1, the highly conserved and essential peptide controlling reproduction in vertebrates. We also showed that this gene loss is not a result of inadvertent selection in the lab as the wild-type populations of zebrafish also lack this gene (Whitlock et al. *Front Neuroendocrinol.* 2019).
5. Diapause induces axonal regeneration after necrotic insults in *C. elegans*. We showed that diapausing (akin to hibernating) *C. elegans* damaged neurons fully regenerate, both morphological and functionally. This work also shows that regenerating touch receptor neurons follow a growth pattern identical to that of development and is error-free (Caneo et al. *Plos Genet.* 2019).

Summary table

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<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/WOS Publications or Similar to ISI/WOS Standard	Associate Researchers	11	23
	Other Researchers	3	19
SCOPUS Publications or Similar to SCOPUS Standard	Associate Researchers	0	0
	Other Researchers	0	0
SCIELO Publications or Similar to SCIELO Standard	Associate Researchers	0	0
	Other Researchers		1
Scientific Books and chapters	Associate Researchers	1	2
	Other Researchers	0	1
Other Scientific Publications	Associate Researchers	0	0
	Other Researchers	1	1
<u>Total of Publications</u>		16	47

d) Congress Presentations:

Dr. Whitlock was chosen as a Speaker in the Plenary Session, **International Strategic Conference of Zebrafish Investigators, Pacific Grove, California, USA, January 2019**. Her talk was entitled “Neural Immune Interactions in the Olfactory Epithelia: Implications for Olfactory Imprinting and Immune Response”. Dr. Whitlock was awarded a talk because of their novel findings that the olfactory epithelia have many characteristics of immune tissue. Over 200 Principal Investigators working on zebrafish attended this meeting.

Dr. Calixto was invited as a Speaker in the “**Molecular Biosystems Conference on Eukaryotic Gene Regulation and Functional Genomics**”, in **Puerto Varas, Chile, September 30-October 4, 2019**. Her talk was entitled: RNA language in *Caenorhabditis elegans* and bacteria interspecies communication and transgenerational memory. This is the first report describing a bacterial molecule capable of transiting through the germline and to the next generations. Importantly, this information is maintained even in the absence of the bacteria that triggered it, establishing a memory of the first bacterial encounter. 120 people attended including recognized scientists.

Dr. Pablo Moya was invited to speak at the **4th biennial conference "Brain in Flux: Genetic, Physiologic, and Therapeutic Perspectives on Transporters in the Nervous System" (ISN satellite meeting), August 2019, Quebec, Canada**. In his talk Dr. Moya presented their novel findings on the role of neuronal glutamate transporter EAAT3 in obsessive compulsive disorder. “OCD relevant behaviors and synaptic alterations in a mouse model with increased neuronal glutamate transporter EAAT3 expression”.

Nicole Sanguinetti, a graduate student in the Neuroscience program of UV was selected to talk about her thesis work directed by Dr. Chiu (Line 4) at the “**Cerebral Cortex: from Progenitors to Functional Circuits**” at the **Cajal Club, a neuroscience institution based**

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in the USA that hosted an international scientific meeting in Puerto Varas, Chile. November 24-25, 2019. This event featured some of the leading neuroscientists throughout the world, focusing on new findings in the field of cerebral cortex structure and function. Nicole was awarded a talk because of their novel findings showing that serotonin is able to regulate plasticity of GABAergic synapses in the cortex by interacting with the endocannabinoid signal.

Summary Table

Type of presentation	Type of presentation	National Events [Number]	International Events [Number]
Associate Researchers	Conferences, oral communications, poster communications, others.	38	32
	Invited presentations (not included in above row)	1	3
Other researchers (Adjunct Researchers, Senior Researchers, Young Researchers, Postdoctoral Researchers)	Conferences, oral communications, poster communications, others.	26	13
	Invited presentations (not included in above row)	0	2
Students	Conferences, oral communications, poster communications, others.	32	2
	Invited presentations (not included in above row)	0	0

Other achievements:

- **Patents:** N/A
- **Intellectual property:** N/A
- **Organization of Scientific Events:** A number of national and international scientific events were organized by the CINV during 2019 and they are described in detail in Networking in terms of their aims and relevance. Here, we detail their relationships with the different research lines.

International

1. *EMBO – Chile Partnership symposia*. This activity was held at the CINV and was a joint effort between Line 1 and 3. R. Latorre and J. Ewer acted as hosts.
2. *Small Brains, Big Ideas EMBO Global Exchange practical course*. This is a joint activity of two Millennium Institutes, the BNI (Santiago) and the CINV (represented by J. Ewer and A. Calixto, Line 3).
3. *SGP 73rd Annual Symposium / SoBLA Annual Meeting*. Organized for the first time in Chile, by R. Latorre and M. Holmgren of Line 1.
4. Latin-American Summer School in Computational Neuroscience, (LACONEU). Activity organized by A. Palacios and P. Orio of Lines 4 and 5, respectively.
5. Southern School of Biophysics. An effort of Line 1 organized by C. González, R. Latorre and A. Neely.

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National

1. A joint meeting with the Advanced Center for Electric and Electronic Engineering, AC3E, a Basal Research Center (PIA, ANID) hosted by the Universidad Federico Santa María in Valparaíso. Its mission is to train advanced human capital and to develop scientifically-based technological innovations in different areas of the engineering science. Organizer: P. Orio, Research Line 5.
2. CINV Annual Meeting. Organized by CINV PhD students and Postdocs, this is a one-day activity in which the CINV Director gives an Annual Report on the center's activities and the students present their research in Symposia and posters.

▪ Scientific Editorial Boards:

Ramón Latorre: *Journal of General Physiology, Frontiers in Pharmacological Sciences; Temperature; Channels; European Biophysics Journal; Current Opinion in Neurobiology; Biological Research.*

Juan C Sáez: *"Involvement of Tancytes in the Neuroendocrine Control of Energy Homeostasis"; Frontiers in Endocrinology; special issue on "Pannexin and Connexin channels in Physiology and Pathophysiology"; Guest editor in the International Journal of Molecular Science.*

John Ewer: *Journal of Insect Science; Current Opinions Insect Science; Insect Biochemistry and Molecular Biology; PLoS Genetics (Associate Editor).*

Adrián Palacios: *Scientific Report; Biological Research; Revue Intellectica de l'Association pour la Recherche sur la Cognition (ARCo).*

Tomás Pérez-Acle: *PeerJ Computer Sciences; PeerJ.*

Carlos González: *Revista Habanera de Ciencias Médicas; Journal of Biological Chemistry; AnFaMed; Human Frontiers Physiology.*

- **Awards:** During 2019, several investigators were granted research projects from national funding agencies that should boost their productivity in areas related to the aims of CINV. For instance, Pablo Moya was granted a Regular FONDECYT project (1190833) (M\$ 234 for 4 years) entitled "Molecular and functional evaluation of a mouse model of Obsessive-Compulsive Disorder with increased EAAT3 expression". Juan C. Sáez was granted a Regular FONDECYT project (1191329) (M\$ 230 for 4 years) entitled: "Diverse cell types present pannexin1-based gap junction channels with distinct regulatory, functional and pharmacological properties". Ramón Latorre was granted a Regular FONDECYT project (1190203) (M\$ 220 for 4 years) entitled: "Voltage-sensing and coupling between voltage and Ca²⁺ sensors in voltage- and Ca²⁺-activated (BK) channels". Danilo González (as Deputy Director for the grant) was granted an R+D project from IDeA I+D FONDEF, entitled: "FageCapsuleS, bacteriófagos de Salmonella micro-encapsulados con tecnología de liberación intestino grueso y delgado" (ID18I0235) (M\$ 188 for two years).

In 2019, Kathleen Whitlock was elected to the Board of Directors of the International Zebrafish Society 2019-2022 (www.izfs.org/about-us/board-of-directors). Juan C. Sáez became a Foreign Member of the National Academy of Sciences (USA), and Francisco Bezanilla, already a NAS member, was elected to the American Academy of Arts and Sciences (USA). John Ewer was invited to be a member of DANA Alliance for Brain Initiatives (DABI).

International grants. Andrea Calixto was awarded a grant under the "Proyecto Apoyo Redes Formacion de Centros" Program (REDES180138; 2 years) entitled "Discovery of

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Neuroprotective bacterial metabolites and their mechanism of action in *C. elegans*, and a CYTED grant (P918PTE 3 years) entitled “Desarrollo de Consorcios Bacterianos para el tratamiento de enfermedades neurodegenerativas.”.

Open Access publications. We have been asked to give our opinion about Open Access publications. This is a not a trivial matter since although the Open Access system provides access to scientific information upon publication, the publication charges in the high impact factor journals that are open access, are, with few exceptions, immoral. For example, *Neuron*, *Cell Reports* and *Nature Communication* are presently charging about US \$5,000 per paper. Thus, today it is not enough to have an excellent idea and to demonstrate it experimentally, you also need substantial funding to pay for the resulting article.

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4. Education and Capacity Building

a) Education, Training and Capacity Building:

The PhD Program in Neuroscience (Director: Ana M. Cárdenas, Line 2). This Program is designed to train researchers interested in the field of development, structure, and function of the nervous system. Its strengths are in the areas of molecular physiology, biophysics, sensory neuroscience, neuronal plasticity, neuropathology, development, 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 (Web page: www.dnuv.cl).

PhD program in Biophysics and Computational Biology (Director: Patricio Orio, Line 5). This Program was started in 2015 and is one of our main achievements in education and training. Its main goal is to train scientists to understand biological processes through their physical-mathematical formalization. We receive students with diverse undergraduate training, from mathematics and physics to biology. A flexible curriculum allows each student to quickly obtain the knowledge and abilities they need most for their thesis work, which is complemented with essential background courses 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 research thesis (Web page: dbbc.uv.cl).

The Master Program in Neuroscience (Director: Agustin Martínez, Line 2). This program is characterized by a high content of basic Neuroscience and Mechanism of Neuropathology and Psychiatric Disorders in a multidisciplinary environment. Its students are from various disciplines: Biologists and Biochemists as well as Health Professionals, Engineers, and Mathematicians (Web page: www.magisterneurociencia.cl).

b) Achievements and results:

The **Neuroscience PhD Program** has been accredited continuously since 2004 by the Chilean National Committee for Accreditation (CNA). In 2017, it was re-accredited for a record 7 years. As the external reviewers indicated, the presence of the CINV within the Universidad de Valparaíso was fundamental for the significant extension of its accreditation. Fifty students have graduated (15 female; 35 male) since the Program started in 2002, of which 3 graduated in 2019. The Program currently has 41 students (26 female, 15 male). This included 9 first year students, who were selected and accepted to join the Program, of which 4 are from abroad (Germany, Spain, Senegal, and Venezuela). Twenty-eight of 41 students of this Program were granted fellowships from the Government funding agency (CONICYT); the remaining students received a fellowship from the Universidad de Valparaíso or the CINV (2 fellowships). Eight students (4 female and 4 male) from a pool of 24 applicants were accepted for the 2020 academic year.

The **PhD Program in Biophysics and Computational Biology** was accredited by the CNA from 2018 to 2023. It currently has 15 students (2 female), including 4 new students who were selected to join the Program for the 2020 academic year. Five students qualified to begin their thesis during 2019, and now a total of 11 are doing their thesis work. Eleven of the currently enrolled students were granted a PhD fellowship from CONICYT; the rest hold fellowships from the UV and/or receive subsidies from the Program.

The **Master Program in Neuroscience** was recently re-accredited by the CNA for 7 years, extending it until 2026. Since its foundation in 1999, 94 students have graduated, of which 13 students did so in 2019. Seven of these did their thesis with researchers from the CINV.

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During this year's recruitment period the program was very successful, accepting 12 students from a pool of 25 applicants. During the interview process several applicants mentioned the existence of the CINV as part of the reasons for choosing our program, suggesting that the CINV has given more visibility to this program.

c) Destination of students:

Most of the graduates of our PhD Programs currently have faculty or postdoctoral positions in Chile, USA or Europe. The first graduate of the program in Biophysics and Computational Biology (graduated at the end of year 2017) holds a Post-Doctoral research position in Dr. Francisco Bezanilla's lab at the University of Chicago. In the Master's program, about half of our students return to their professional practice after graduating, and the other half follows a scientific/academic pathway, entering diverse PhD programs in Chile and abroad, including our own PhD in Neuroscience. Some of them are academics in Chile or abroad.

Main achievements of our PhD. and Master Programs during this period:

Graduations of students working in laboratories of the CINV.

PhD Program in Neuroscience

1. Ricardo Ceriani. "GnRH and testosterone treatment generate GnRH neurons in hypothalamus of adult Zebrafish (*Danio rerio*). Advisor: K. Whitlock.
2. Yenisleidy Lorenzo-Ceballos. "Characterization of allosteric between the specialized-sensory modules of BK channels by calcium-driven regulation of voltage-sensing domains". Advisor: R. Latorre.
3. Jesús Olivares. "Study of olfactory responses in the telencephalon of rainbow trout (*Oncorhynchus mykiss*)". Advisor: O. Schmachtenberg.

Master's Program in Neuroscience. (9 out of 13 graduated students did their thesis at CINV).

1. Tito Castillo. "Study of polymorphisms in the genes of dopa decarboxylase (DDC), dopamine D2 receptor (DRD2) and endocannabinoid receptor (CNR1) in patients with refractory schizophrenia diagnosis in treatment with clozapamine". Advisor: P. Moya.
2. Francisca Henríquez. "Evaluation of the effect of over-exposure of the EAAT3 glutamate transporter on inhibitory synaptic transmission in the mouse hippocampus". Advisor: P. Moya / A. Chávez.
3. Camila Quiroz Cid. Title: "Neuromodulation of the inhibitory synaptic transmission in the retina". Advisor: A. Chávez.
4. Sebastian Estay. "Mechanisms underlying the development of reciprocal GABAergic feedback onto rod bipolar cells in mouse retina". Advisor: A. Chávez.
5. Sebastián Gallegos. "Motor effects of non-invasive electrical stimulation of the spinal cord in animal model of Parkinson's disease". Advisor: P. Moya.
6. Hugo Almarza. Title: "Changes in exocytosis in cellular lines of dyspherlinopathy carrying patients". Advisor: A.M. Cárdenas.
7. Pedro Espinoza Ahumada. Title: "Neuromodulation of the inhibitory synaptic transmission in the ventral pallidum". Advisor: A. Chávez.
8. Nicole Sanguinetti. Title: "CBI receptor located in Gabaergic neurons expressing somatostatin regulates synaptic transmission in the prefrontal cortex" Advisor: Ch. Chiu.
9. Carlos Ancatén González: "Role of BK channels in the induction of long term synaptic depression in the neonatal hippocampus". Advisor: A. Chávez.

Approval of Thesis Project and Qualifying exams of students working in CINV labs:

PhD Program in Neuroscience.

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1. Víctor Calbiague. “A lactate-shuttle in the retina? Analysis of cellular and molecular organization and possible role”. Advisors: O. Schmachtenberg and F. Paquet-Durand (U. Tuebingen).
2. Francisca Henríquez. “Evaluación de cambios moleculares y electrofisiológicos en la vía vmPFC-BLA de animales EAAT3^{glo}/CaMKII”. Advisors: P. Moya and A. Chávez.
3. Javier Cavieres. “Cellular basis of coupling between the central and the peripheral prothoracic gland clock in *Drosophila melanogaster*”. Advisor: J. Ewer.
4. Catalina Berrios. “Bases neurobiológicas de los cambios en el comportamiento de ecdisis”. Advisor: J. Ewer.
5. Paula Mujica. “Impact of chronic inhibition of Pannexin 1 channels in the structural and functional synaptic defects and spatial memory impairments in a mouse model of Alzheimer’s Disease”. Advisors: Á. Ardiles and A. González.
6. Sebastián Estay. “Developmental remodeling of AMPA and NMDA subunit composition at the Rod Bipolar Cell dyad synapse in the mouse retina”. Advisor: A. Chávez.
7. Claudia DiBerardino: Title: Role of serotonin in regulating synaptic function in the mouse retina. Advisor: A. Chávez.

PhD program in Biophysics and Computational Biology. (5 out of 6 students that approved their thesis are doing their thesis at CINV).

1. Marilyn Gatica. “High-order brain interactions and multi-scale structure in the aging”. Advisors: P. Orio and R. Cofré.
2. Carlos Coronel. “The neuromodulatory influence over the integration and segregation in the brain: insights from realistic neural mass models.” Advisor: P. Orio.
3. Rubén Herzog. “Psychedelics reconfigure the information-processing capacities of the brain: A study from whole-brain mathematical models”. Advisors: P. Orio and R. Cofré.
4. Antonio Peña. “Identificación, clonaje y caracterización biofísica de isoformas novedosas del gen HVCN1 de células mieloides supresoras”. Advisor: C. González.
5. Guido Mellado: “Gating modifier spider toxin SNX-482 partition in the charged membrane and bind to one of the voltage sensor domains of Cav2.3 channels guided by electrostatic interaction”. Advisors: A. Neely and J. A. Gárate.

Master Program in Neuroscience:

1. Macarena Churrua. “Evaluation of compulsive type behaviors in mouse EAAT3^{glo} / CMKII”. Advisor: P. Moya.
2. Lorena Prado. “Impact of a causing mutation of centronuclear myopathy on the function of dynamin-2 in neuronal and traffic morphology of AMPA receptors in excitatory synapses”. Advisor: A. Ardiles and A. González.
3. Juan José Alvear. “Functional coupling between channel HV1, and the NADPH oxidase enzymatic complex in *Mus musculus* myeloid origin suppressor cells”. Advisor: C. González.
4. Bárbara Cadiz. “Comparative analysis of nitrosative stress and survival markers / cell death in retina organization crops normal and high concentrations in glucose”. Advisor: O. Schmachtenberg.
5. Javier Palma. “Influences of structural connectivity in the dynamical functional connectivity in a network of biophysically-inspired neuronal oscillators”. Advisor: P. Orio.
6. Daniel González. “Glutamatergic influence in the regulation of the GABAergic synapsis” Advisor: Ch. Chiu.

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7. Raúl Figueroa. “Sensory and motor systems interaction reflected in shoulder motor control enhancement by the application of kinesiology tape” Advisors: Ch. Chiu and Ch. Glazebrook.

Publications of PhD and Master Students from our programs on 2019: (23 students who did their thesis at CINV co-authored 16 articles, of which 11 were first authors).

Students visiting laboratories abroad. We continued supporting the travel and stay of many of our students in the laboratories our international collaborators. Students who conducted research stay during this period include:

- Emerson Carmona: Research stay at Luis Cuello Laboratory, Texas Tech U, Texas, USA. August 2019-January 2020.
- Rubén Herzog: Research stay at Enzo Tagliacuzzi Laboratory, Universidad de Buenos Aires, Argentina. September-October 2019.
- Rubén Herzog: Research stay at Henrik J Jensen Laboratory, Imperial College London, London, England. December 2019.
- Raúl Figueroa: Visit laboratory of Dr. Cheryl Glazebrook, Faculty of Kinesiology and Recreation Management, University of Manitoba (Canada).
- Valeska Cid: Research stay at Dr. Rodrigo España lab, Drexel University College of Medicine (DUCOM), Pennsylvania, USA. November 2019 to February 2020.
- Sebastian Estay: Attend to the Neuroscience “Advanced Techniques for Synapse Biology” organized by FENS in Bourdoux, France. October 13 to November 1, 2019.

Students from abroad visiting CINV laboratories.

- Lucas Bayones, PhD student at Universidad de Buenos Aires, Argentina, visited Dr. A. M. Cárdenas’ lab. August to September, 2019.
- David Ballesterro, Undergraduate student at Universidad Nacional de Colombia, Colombia, Visited Dr. A. Palacios’ lab from August 2019 to February 2020.
- Chloe Gómez, Undergraduate student at Université de Strasbourg, Francia, visited Dr. A. Palacios’ Lab from March to August 2019.

Organization of National and International courses and workshops:

1. Southern School of Biophysical. January 7th-19th, 2019.
2. Latin-American Summer School in Computational Neuroscience, January 7-25, 2019.
3. Small Brains, Big Ideas EMBO Global Exchange Lecture Course, April 5-13, 2019.
4. Workshop on “Octodon degus: A natural model from cellular biology to behavioral ecology” in Puerto Williams (Chile). March from 28 to 3, 2019.

Strategies to hire and incorporate young investigators in 2019. CINV hired a new young investigator, Dr. Arlek González-Jamett. She obtained a 2018 FONDECYT first award grant (“Proyecto de iniciación”). She will strengthen Lines 2 and 3.

5. Networking and other collaborative work

a) Networking:

The following activities were part of our networks in **Biophysics, Computational Neuroscience and Genetic and Development**. ***International activities.*** 1. “Latin-American Summer School in Computational Neuroscience (LACONEU)” (see

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cinv.uv.cl/evento/laconeu-2019/). For three weeks, students from Chile, Latin-America and Europe) attended lectures and hands-on training from US, Europe and Australia speakers on cutting-edge topics about computational analysis of the brain activity. This school also included a 1-day Workshop “Large Scale Network Dynamics” open to the public. 2. “Southern School of Biophysics” cinv.uv.cl/ssb/). Experts from the CINV, Germany, and the USA, in different areas of biophysics ranging from structure to cell biology, gave a twelve-day intensive hands-on international workshop on modern techniques used to investigate the biophysics of ion channels. 3. The CINV hosted in Valparaíso the *Joint Society of General Physiologist (SGP)/Society of Latin American Biophysicists (SOBLA) meeting*. The topic was “Structural Basis of Electrical Signaling in the Heart and the Nervous System”. This was the 73rd SGP meeting and was held outside of the Marine Biological Laboratory in Woods Hole for the first time in its long history (72 years). With the participation of 150 scientists students and postdocs, the SGP/SOBLA symposium was designed to encourage small-group discussions and foster cross-disciplinary collaborations that tackle the increasingly complex problems in channel/transporter physiology. 4. “*Small Brains, Big Ideas*” EMBO Global Exchange practical course was offered April 5th – 13th, 2019. The primary objective of the course is to expose students from Latin America to the use of invertebrate preparations for basic and applied research in neurosciences and biomedicine. Students (27) came from Chile, Argentina, Brazil, Colombia, Ecuador, Perú, and Uruguay. The course includes a large number of lab exercises and lectures in neuroscience, ranging from the cellular to the behavioral. **National activities.** 1. *Joint meeting with the Advanced Center for Electric and Electronic Engineering, AC3E* (www.ac3e.cl) a Basal Research Center (PIA, ANID) hosted at the Universidad Federico Santa María in the City of Valparaíso. Its mission is to develop scientifically based technological innovations in different areas of the engineering science. The one-day meeting finalized with a discussion table about doing translational science in Chile, with the participation of the Minister of Science, Technology, Knowledge and Innovation, Andrés Couve (see: cinv.uv.cl/cinv-ac3e/). 2. In collaboration with Chilean Neuroscience Research Centers in Chile, we organized the Symposium in the XV Annual Meeting of the Chilean Society for Neuroscience, “*Perspectives in Neuroscience*” with four international speakers. 3. Francisco Bezanilla, Miguel Holmgren (NIH, USA) and Ramón Latorre inaugurated a new laboratory in the Faculty of Marine Sciences of the Universidad de Valparaíso. In a country with about 5,000 km of coastal waters, the lab has the goal of spearheading the study of the nervous system of marine animals.

b) Other collaborative activities:

Internal collaborations: We highlight here new internal collaborative efforts. We sought to strengthen this type of relationship by creating a “Strategic Projects” funding category, aimed specifically at providing seed funding for projects between CINV investigators. For 2019 these projects were; **1)** Andrea Calixto and Chiayu Chiu, “*Neuronal regeneration under diapause in C elegans*”; included co-mentoring a PhD student from the Neuroscience program (Scarlett Delgado). **2)** Agustín Martínez and Juan C. Sáez, “*Microglia HCs contribute to cochlea damage observed in high glucose or Gram-negative bacterial infections*”; included co-mentoring of a post-doctoral fellow. **3)** Adrián Palacios and Tomás Pérez-Acle, “*Retinal Computation.*”; included co-mentoring of post-doctoral fellow. **4)** Ramón Latorre, Francisco Bezanilla, Fernando González, Karen Castillo and Ignacio Díaz-Franulic (post-doc), “*Ion channels involved in heat and pain sensing: How they detect temperature?*” **5)** Chiayu Chiu and Pablo Moya “*The role of EAAT3 in ventromedial*

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prefrontal cortex neurotransmission and function”, included co-mentoring of a postdoctoral fellow. To date, several papers co-authored by at least two members of CINV have been published as a result of this initiative: Sáez and Martínez (in *J Neurochem*, 2019 and *Front Immunol*, 2019), and Moya and Chávez, (in *Front Pharmacol*, 2019).

Collaborations with other investigators in Chile:

In *Line 3*, Andrea Calixto collaborated with M. Hermoso’s lab (U. de Chile). See: Dubois-Camacho *et al.*, (2019). Inhibition of miR-378a-3p by Inflammation Enhances IL-33 Levels: A Novel Mechanism of Alarmin Modulation in Ulcerative Colitis. *Front Immunol.* **10**: 2449 doi: 10.3389/fimmu.2019.02449. In *Line 4*, Pablo Moya collaborated with M. Reyes (U. de Santiago), P. Iturriaga (U. de la Frontera), and G. Nuñez (U. Talca) in the design and characterization of novel, multi-target molecules as antidepressants; with E. Pérez and A. Fierro (P.U. Católica) on the pharmacological profiling of novel ligands acting at the serotonin transporter; and with J. Eugénin and K. Bravo (U. Santiago), on the neurodevelopmental effects of serotonin in brainstem respiratory network. Andrés Chávez established a new collaboration with P. Haeger (U. Católica del Norte) to unravel the effects of pre- and postnatal alcohol consumption on memory formation, and with R. Vidal (U. Mayor) to understand the functional role of IGF2, a well-known growth factor, in the modulation of synaptic function. Adrian Palacios collaborated with C. Hetz, C. Durán, G. Martínez, (U. Chile, BNI) in: “Protein Response in Retinal Neural Circuits during Aging and Neurodegeneration” and “Proteostaser-1: A gene therapy focused on decreasing neurodegeneration and increasing cognitive function in Alzheimer's disease”. Alvaro Ardiles established collaborations with C. Escudero (U. BioBio) and J.C. Tapia (U. Talca) to study the role of promigratory activation of VEGFR2 in the brain angiogenesis and its potential implication in learning and memory of offspring born to preeclampsia. He also continues his collaboration with I. Alfaro (Fundación Ciencia y Vida).

International collaborations:

CINV investigators visited or hosted the following collaborators: A. Neely visited the lab of collaborator R. Olcese (UCLA, USA); his student, D. De Giorgis (Graduate student in the Neuroscience PhD Program) spent 3 months in R. Olcese’s lab. AM. Cárdenas has an ongoing collaboration with F. Marengo (Universidad de Buenos Aires, Argentina), which resulted in the publication “Ca²⁺-independent and voltage-dependent exocytosis in mouse chromaffin cells” *Acta Physiol (Oxf)* 228: e13417. L. Bayones, a PhD student in F. Marengo’s lab, completed a month stay in her lab. Ana M. Cárdenas is also collaborating with V. Mouly (U. Sorbonne, France) and this year published “Defects in G-Actin Incorporation into Filaments in Myoblasts Derived from Dysferlinopathy Patients Are Restored by Dysferlin C2 Domains” *Int J Mol Sci* 21. pii: E37. This collaboration also includes P. Caviedes (U. de Chile). J.C. Sáez. has an ongoing collaboration on the role of hemichannels in neurodegeneration in diverse human diseases. In collaboration with G. Lau (City U. of Hong Kong) they study the role of glial hemichannels in the epilepsy model induced with pilocarpine. In addition, he studies the role of glial hemichannel in epilepsy induced with PTZ or kainic acid in collaboration with L. Barrio (Ramón y Cajal Hospital, Spain). As a result of ~10 years of collaboration, C. Giaume, Paris (France), C. Naus, Vancouver (Canada), L. Leybaert, Ghent (Belgium) and J.C. Sáez (Chile) wrote a review on the role of glial hemichannels in neurodegeneration (*Physiol Rev*; currently under revision). A. Calixto collaborated with the labs of P. Burdisso and D. de Mendoza (Argentina) to publish Urrutia *et al.* (2019). Bacterially produced metabolites protect neurons from

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degeneration. PLoS Biology 18(3): e3000638. She also collaborated with the lab of L. Reis Silveira (Universidade de Campinas, Brazil) to publish Lima *et al.* (2019). Opposing action of NCoR1 and PGC-1 α in mitochondrial redox homeostasis. *Free Radic Biol Med.* doi: 143:203-208. John Ewer continued fruitful collaborative work with B. White (NIH, USA) (Scott *et al.*, *iScience*, In press). P. Moya was invited to the U. de Antioquia (Colombia) to participate as external reviewer on a PhD thesis, to give a seminar on the role of SLC1A1/neuronal glutamate transporter 3 gene in Obsessive-Compulsive Disorder, and to evaluate a potential alliance between our PhD program in Neuroscience and the PhD program at the U. de Antioquia. He also strengthened his international collaboration with A. Holmes (NIAAA, USA) on the behavioral characterization of mouse models of anxiety and compulsivity. Oliver Schmachtenberg strengthened his collaborations with F. Paquet-Durand (U. Tuebingen, Germany) on retinal metabolism and diabetic retinopathy. A. Palacios continued his collaborations with A. Kirkwood (Johns Hopkins, USA) on the study of neural Plasticity in aging *Octodon degus*, and with B. Cessac (INRIA, France) and M.J. Escobar (U. Santa Maria, Chile) in Neural and Computational models. He also recently established a collaboration with S.X. Zhang (U. Buffalo, USA), on the role of XBP1s in a rodent model of retina during aging and diabetes. A. Palacios maintains an ongoing collaboration with P. Mombaert (Max Planck Society, Germany), studying the genetic variants of APOE in *Octodon degus* and its implications for learning and memory during aging and neurodegeneration. In 2019 they organized the first international Workshop on “*Octodon degus*: A natural models from cellular biology to behavioral ecology” in Puerto Williams (Chile). This workshop supported by the Max Planck Society and the CINV, was an opportunity to discuss novel results in genetics, sensory physiology, brain function, and neurodegeneration in this natural animal model of Alzheimer’s disease. Chiayu Chiu (Max Plank Leader) continued her collaboration with M. Higley (Yale U., USA) to elucidate the cellular mechanisms by which incoming excitatory and inhibitory synaptic signals are transformed to generate a neuronal output. A. Chávez continued his international collaboration with P. Castillo (Albert Einstein College of Medicine, USA) in order to understand the mechanism underlying synaptic transmission and plasticity in the hippocampus. Patricio Orio collaborated with Dr. Demian Battaglia, studying the dynamics of large-scale brain models. Dr. Battaglia was invited to LACONEU 2019, and a manuscript was submitted to PLoS Comp Biol (DOI: 10.1101/2020.01.28.922708). He also visited the Imperial College London, to work with Pedro Mediano and Fernando Rosas (Henrik Jensen lab) to work in the synergy in neural circuits.

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6. Outreach and connections with other sectors

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. Since 2018, the CINV decided to actively participate in the public debates of Chilean society, contributing its scientific knowledge through open discussions. After the social crisis that erupted on October 18th, the CINV participated in current debates, for example, through a “Tertulia Porteña” centered on the Chilean Water Law. CINV outreach activities have maintained a significant presence in national and regional media, including newspapers, TV programs, radio, and internet. In this regard, more researchers from the CINV are recognized spokespeople for authorities and the press. R. Latorre has kept his position as a national reference of the CINV regarding science policies. The importance of Sáez’s discoveries on the treatment of muscular dystrophy with boldine, the primary alkaloid present in the boldo tree (an endemic plant from Chile), have been widely disseminated through the press. JC. Sáez has progressively positioned himself as an institutional spokesperson for the CINV, complementing R. Latorre. K. Whitlock is a recognized spokeswoman on climate change; A. Calixto and K. Castillo actively participate in promoting the role of women in science; J. Ewer, the author of a law that may establish the time zone for Chile, is a national reference on the impact of the time zone on students and shift workers; T. Pérez-Acle, participates actively in forums, debates, and press releases on the challenges and advances of artificial intelligence, and how can help to solve the problems posed by the pandemic that is presently affecting our society; and P. Moya regularly participates in public discussions regarding neurobiological disorders.

We have also promoted the active participation of our young researchers in the press and other scientific dissemination platforms. Ch.Chiu, A. Palacios, A. Ardiles, and H. Sánchez, have all been able to disseminate their work to different interest groups, also increasing their experience in communicating to the non-scientific media remarkable neuroscience results.

The most relevant CINV outreach activities during this funding period were:

De Mente: A collection of the best NeuroNews stories of the last years was compiled, professionally edited by two experienced journalists and a scientific committee, to create a scientific book entitled "DeMente". The book was published in June 2019 by Editorial Catalonia and distributed through the main libraries of the country. Presentations in Santiago and Valparaíso, extensive coverage of national press, and excellent reviews, gave this book much visibility. More than 2000 copies sold in 2019 prompted to issue a second edition in September 2019. As it is one of the first publications in Latin America that makes important scientific publications reachable to all audiences, there is interest in the Editorial Catalonia to work on new releases in the future. (More information at cinv.uv.cl/publicaciones/#libro-de-mente)

Neuropolis: In 2019, "Neuropolis", a TV series created by the CINV and Puerto Visual, set in Valparaíso and aimed at the general audience, was broadcast throughout Chile through the TVN channel (public television channel). Based on the idea of our “Tertulias Porteñas” (How knowledge is built by the interaction of different disciplines), it is the first television series in Chile created by a research center that disseminates scientific knowledge in open television. The first season had 8 chapters, in which various experts participated in addition to carrying out entertaining "experiments" on the street that help make the understanding of

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each topic easier. The chapters were entitled "The world of addictions", "Pleasure and pain", "Intelligence and learning", "The vision and the colors", "The memory and the memories", "The sound", "Smells and flavors", "Clocks and time". As a result of the excellent public reception of the series (there were over 200.000 viewers per chapter), we are currently working on an international version of the series, to be distributed in Latin America. (More information at cinv.uv.cl/neuropolis).

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. They aim to captivate the audience 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 fourth consecutive year. Given the prestige that this activity has reached in the region, this year the TV channel UCV-TV decided to broadcast the Tertulias on television throughout the country, significantly expanding its audience. Prominent Chilean writers and communicators moderate the Tertulias. Since 2018 they have been moderated by Patricio Fernández, a Chilean journalist and writer, founder and former director of the weekly newspaper, *The Clinic*, and a panelist on various national media programs. This year the Tertulias were centered on artificial intelligence ("Artificial Intelligence. Benefit or condemnation?"), with the participation of Tomás Pérez-Acle, PhD in Biotechnology and CINV Researcher; Andrés Claro, PhD in Philosophy and Literature, and María F. Pérez, PhD in Biological Sciences; the aging ("The brain and eternal youth") with the neuroscientist Claudio Hetz, actress Paulina Urrutia, who works actively sharing her experience of living with an Alzheimer's patient, and José L. Dinamarca, Surgeon and PhD in Social Gerontology. For our last Tertulia, and in the spirit of collaborating with the global debate on climate change, the hosting of COP 25 by Chile (which had to move to Madrid after the social crisis erupted in our country), and this social crisis, we decided to make it different from the previous ones, centering it on the unique water laws of Chile ("Water, Climate Change and the Future of the Human Species"). We had an estimated audience of almost 800 people in the three Tertulias. (More information at cinv.uv.cl/tertulias-portenas)

Ciencia Al Tiro: One of the greatest challenges in Chilean society is to communicate the value of science to the general public. In 2017, *Ciencia Al Tiro* produced 10 videos based on their popular book "La Alegría de la Ciencia" (The Joy of Science). In 2018 the videos were shown on UCV-TV and the TV channel of the Cámara de Diputados (House of Representatives), where they continued to be shown in 2019. During 2019 the outlines of ten chapters for our next book of workshops "La Alegría de los Sentidos" (The Joy of the Senses) were finalized and they are now looking for financing.

In 2019, *Ciencia Al Tiro* participated in "La Ruta de Ciencia", a traveling scientific fair, developed by the Faculty of Sciences of the University of Valparaíso aimed mainly at seventh and eighth grade students. The project toured for several months different cities within the Valparaíso Region (Valparaíso, Quillota, Petorca, La Ligua, and San Felipe). *Ciencia Al Tiro*, with the participation of mainly graduate students, implemented two practical workshops "Neurons and Noses: How climate change affects the nervous system" and "Aquaponics, a technology for the future". A stand was presented where the effects of ocean

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acidification were reproduced and this change was related to the effects of increased atmospheric CO₂ on the olfactory system of marine animals.

As a result, 4 short videos of all the science workshops presented by Ruta de Ciencia were produced. This project was funded by the University of Valparaíso, the Chilean Ministry of Education and Ciencia Que Pesca. (More information at cinv.uv.cl/ciencia-al-tiro – www.cienciaaltiro.cl – www.cienciaquepesca.cl)

NeuroNews: This program continued its successful formula in which graduate students of Neuroscience select a recent high-impact publication in a neuroscience-related topic of their interest and converts it into an accessible and entertaining news story for the general public. In total, 21 NeuroNews articles were generated in 2019. Most of them have been published in the online newspaper El Mostrador, which has an international scope, reaching 251,336 effective visits throughout Latin America, with an average of 20,945 readings per article. A trademark of NeuroNews is the great variety of topics covered. For 2019, they included: the creation of the first bionic eye with a circuit similar to the retina made by 3D printing; the influence of a parasite that control the minds of humans hosts to make them take risks; the biological effects of eclipses; the explanation of human empathy may be in the mirror neurons; how was briefly revived a pig brain; the discovery of what kind of psychoactive plants used a culture that lived in Chile a thousand years ago; the sophisticated brain of octopuses and the similarities with the human brain. (More information at cinv.uv.cl/category/neuronews/)

Other activities. In 2019, 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. The documentary was exhibited during the closure of the joint meeting of the Society of General Physiologists of the United States and The Society of Latin American Biophysicists (see Networking). A copy of the documentary was distributed to the attendees to be exhibited in universities around the world. Also, YouTube has broadcasted this documentary, where it has already exceeded 10,500 views, a very significant number for this type of production. (More information at cinv.uv.cl/series-y-documentales/#montemar)

The Congress of the Future (the most important scientific dissemination activity in the country) was jointly organized in Valparaíso by the CINV. T. Pérez-Acle participated in the panel on Technology and Society and, together with the University of Valparaíso, we organized a panel on Gender (“Challenges for Chile of the XXI Century”), which featured the presentation of Dr. Anna Nagurney, director of the Virtual Center for Supernetworks. The panel was composed of the political scientist, Javiera Arce; the President of the Chilean Academy of Sciences, Cecilia Hidalgo; the Deputy and Marine Biologist, Daniella Cicardini; and the Dean of the Faculty of Sciences of the University of Valparaíso, Dr. Juan Kuznar. (More information at cinv.uv.cl/congreso-futuro-2019/)

During the course of the year, PhD students and young researchers of the CINV often gave talks on neuroscience in primary and high schools in the region. At the same time, we actively participated in scientific fairs aimed at elementary and middle schoolchildren, with presentations on the world of spiders, and how they help us understand our nervous system. (More information at cinv.uv.cl/escuelas-charlas-y-ferias/)

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b) Connections with other sectors:

Neuroscience at your fingertips: During the year 2019, we worked in collaboration with the Future Education Foundation to create a scientific experience for students from the last year of school, and to establish a permanent program of the CINV and Future Education that promotes the scientific career of students from the Valparaíso region. During its first offering, which took place between August and October, we received a group of female students who carried out a theoretical-practical internship at the CINV, During the workshop, the girls attended classes on various topics in neuroscience and carried out experiments in our laboratories, assisted by postgraduate students and teachers from our center.

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 of activities organized in Valparaíso by both institutions.

c) Other achievements:

Juán Ignacio Molina Building (formerly Severín Building): A crucial step for the new CINV science building in Valparaíso was the beginning of its construction. Initially, it was estimated that the building would be occupied in 2020. However, the work suffered delays due to the discovery of 1000 year-old archaeological remains, which reflect the long history of this site. The archaeological rescue process, carried out by State agencies, has been disseminated by the CINV through the main national press media, to strengthen the meaning of this Science Building for the city and the country, recognized as one of the most critical projects in Valparaíso.

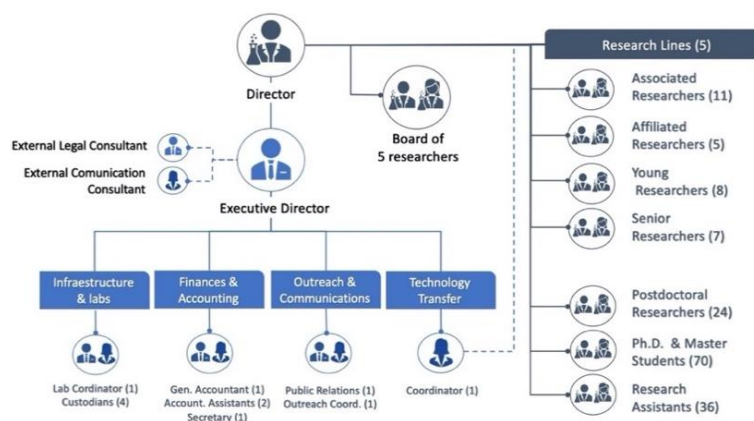
Neuroscience and companies: Following the press coverage of Dr Ewer's proposal to base the choice of a time zone for Chile on biological criteria, some companies became interested in understanding the details of the project. Recalling that most mining work is done in shifts, the interest resided in the possibility of decreasing the health problems associated with night shifts. This activity was complemented with talks to its managers and security officers about the workings of our nervous system. We are currently preparing proposals to secure funding in order to implement strategies that will alleviate the negative consequences of shift-work.

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7. Administration and Financial Status

a) Organization and administration:

An Executive Director supervises and coordinates all administrative tasks according to the needs of the CINV Director, its Board, and the Investigators. This includes: managing the Millennium Institute Grant and all other CINV researcher projects (about 17 projects per year); coordinating outreach activities and communications; networking with the private sector and with national and regional leaders; leading efforts related to the construction of the building that will house the CINV. The Executive Director's team includes an Accounting and Finance Unit, in charge of managing the administration of projects and personal contracts, among others; an Infrastructure and Laboratory team that helps in the purchase of laboratory equipment and maintenance; an Outreach and Communications team, which coordinates the carrying out of outreach activities, the organization of scientific activities (symposia, congresses), and information on the web and social media; and a Technology Transfer Unit that supports researchers in formulating projects and liaising with private companies. The University of Valparaíso provides the operating space for the CINV and has established an institutional grant to help with operating expenses. The base salary for researchers is covered by the corresponding host institutions.



Category	Female	Male	TOTAL
Assistant & Technicians	16	7	23
Administrative Staff	7	6	13
TOTAL	23	13	36

b) Financial Status:

During 2019, the CINV had a total income of CLP \$ 2,549 million (USD 3,626,636.- E/R 703), of which the Millennium Science Initiative (ICM) contributed 36%. The contribution of the Millennium Science Initiative (ICM) has varied from 55.7% (2012), 35.4% (2013), 42% (2014), 44% (2015), 43% (2016), 38% (2017) and 36% (2018). Other sources of income come from CONICYT (31%) and the University of Valparaíso (23%). The remaining 10% corresponds to other national and foreign projects.

With regard to the funds contributed by the Millennium Scientific Initiative (ICM), the greatest single expense category corresponds to "Responsible Investigator, Scientific and Additional Personnel Fees" (55% of the budget) and is devoted to funding for scholarships, post doctorates, young researchers, and to the strengthening of research teams. Sixteen percent of the budget was invested in the purchase of 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.	1
Alan Neely Delgueil	Structure and function of molecular sensors	Chilean	M	04-15-1956	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1
Ana María Cárdenas Díaz	Cellular signaling	Chilean	F	04-01-1960	Pharmacist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1
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	1
John Ewer Lothian	Genetics and developmental neuroscience	Chilean	M	02-23-1961	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1

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Juán Carlos Sáez Carreño	Cellular signaling	Chilean	M	02-02-1956	Biochemist	D	Universidad de Valparaiso	Professor UV CINV Researcher	1
Kathleen Whitlock Leaning	Genetics and developmental neuroscience	USA	F	08-27-1963	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1
Ramón Rogelio Latorre De la Cruz	Structure and function of molecular sensors	Chilean	M	10-29-1941	Biochemist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1
Tomás Pérez Acle	Molecular simulation and computational biology	Chilean	M	09-09-1970	Biologist	D	Fundación Ciencia y Vida	F. Ciencia y Vida and CINV Researcher	1
Andrés Eduardo Chávez Navarrete	System and circuits neuroscience	Chilean	M	01-10-1977	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1
Pablo Ricardo Moya Vera	System and circuits neuroscience	Chilean	M	09-09-1975	Biochemist	D	Universidad de Valparaiso	Professor UV CINV Researcher	1

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1.2 Young Researcher

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Alvaro Ardiles Araya	System and Circuits Neuroscience	Chilean	M	02-12-1977	Biochemist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1
Chiayu Chiu	System and Circuits Neuroscience	USA	F	03-21-1974	Neuroscientist	D	Universidad de Valparaíso	CINV - Max Planck Tandem Research Leader	1
Helmuth Sánchez 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 Valparaíso	Professor UV CINV Young Researcher	1
José Antonio Gárate	Molecular simulation and computational biology	Chilean	M	07-29-1983	Molecular Biotechnology Engineer	D	Universidad de Valparaíso	Professor UV CINV Young Researcher	1
Karen Castillo Huera	Structure and Function of Molecular Sensors	Chilean	F	07-23-1979	Biochemist	D	CINV	CINV Young Researcher	1

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Arlek González Jamett	Cellular Signaling	Chilean	F	11-07-1981	Biochemist	D	Universidad de Valparaíso	CINV Young Researcher	1
Daniel Aguayo Villegas	Molecular simulation and computational biology	Chilean	M	08-08-1978	Computer Civil Engineer	D	Universidad Andrés Bello	Professor U. Andrés Bello CINV Young Researcher	1

1.3 Senior Researchers

Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Alfredo Kirkwood	System and circuits neuroscience	Chilean	M	03-05-1958	Biologist	D	John Hopkins University	Professor	2
Francisco Bezanilla	Structure and function of molecular sensors	Chilean	M	05-17-1944	Biochemist	D	Chicago University	Senior Investigator	2
Gonzalo Ferreira	Structure and function of molecular sensors	Uruguayan	M	20-01-1964	Physician	D	Universidad de la República	Professor	2
Miguel Holmgren	Structure and function of	Chilean	M	05-03-1962	Biophysicist	D	NIH-NINDS	Senior Investigator	2

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	molecular sensors						Molecular Neurophysiology section. Porter Neuroscience Research Center		
Oswaldo 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

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1.4 Postdoctoral Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Justin Arthur Hugo Flaven Pouchon	Genetics and developmental neuroscience	French	M	08-29-1987	Biologist	D	Universidad de Valparaíso	Postdoctoral	1
Javier Vicente Alvarez Zepeda	Genetics and developmental neuroscience	Chilean	M	01-29-1971	Aquaculture Engineer	D	Universidad de Valparaíso	Postdoctoral	1
Felipe Alberto Villanelo Lizana	Molecular simulation and computational biology	Chilean	M	16-05-1983	Biochemist	D	Fundación Ciencia y Vida	Postdoctoral	1
Kesheng Xu	Molecular simulation and computational biology	Chinese	M	02-10-1983	Physicist	D	Universidad de Valparaíso	Postdoctoral	1
Rosalba Escamilla Hernández	Cellular signaling	Mexican	F	06-02-1971	Biochemical Engineer	D	CINV	Postdoctoral	1

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Alex Harry Vielma Zamora	System and circuits neuroscience	Chilean	M	01-05-1979	Biochemist	D	Universidad de Valparaíso	Postdoctoral	1
Angelina del Carmen Palacios Muñoz	Genetics and developmental neuroscience	Chilean	F	07-12-1981	Biochemist	D	Universidad de Valparaíso	Postdoctoral	1
Ignacio Antonio Díaz Franulic	Structure and function of molecular sensors	Chilean	M	04-02-1981	Biochemist	D	Universidad Andrés Bello	Postdoctoral	1
Nicolás Palacios Prado	Cellular signaling	Chilean	M	30-06-1981	Bachelor in Biomedical Sciences	D	Pontificia Universidad Católica de Chile	Postdoctoral	1
Nicolás Palanca Castán	System and circuits neuroscience	Spanish	M	14-05-1987	Bachelor in Biology	D	CINV	Postdoctoral	1
María Constanza Maldifassi Gatica	Cellular signaling	Chilean	F	07-11-1979	Biochemist	D	Universidad de Valparaíso	Postdoctoral	1

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Angélica del Pilar Escobar Maldonado	System and circuits neuroscience	Chilean	F	07-15-1985	Chemistry and Pharmacy	D	Universidad de Valparaíso	Postdoctoral	1
Paloma Andrea Harcha Suazo	System and circuits neuroscience	Chilean	F	06-22-1985	Bachelor in Biology	D	Universidad de Valparaíso	Postdoctoral	1
Cristián Alfonso Calfún Medina	Genetics and developmental neuroscience	Chilean	M	23-05-1983	Biochemist	D	Universidad de Valparaíso	Postdoctoral	1
Rodrigo Alexis Meza Cárdenas	System and circuits neuroscience	Chilean	M	23-10-1985	Biochemist	D	Universidad de Valparaíso	Postdoctoral	1
Iván Alejandro Barría Oñate	Cellular signaling	Chilean	M	12-05-1988	Medical Technologist	D	Universidad de Valparaíso	Postdoctoral	1
Iván Dario Bravo Tobar	Cellular signaling	Venezuelan	M	26-09-1976	Doctor	D	CINV	Postdoctoral	1

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Ricardo Honorato Zimmer	Structure and function of molecular sensors	Chilean	M	27-06-1985	Biochemist	D	CINV	Postdoctoral	1
Cesar Rodrigo Ravello Serrano	Molecular simulation and computational biology	Chilean	M	10-02-1981	Biologist	D	Fundación Ciencia y Vida	Postdoctoral	2
Alejandro Javier Martínez Ulloa	Molecular simulation and computational biology	Chilean	M	23-05-1983	Bachelor in Science	D	Universidad Andrés Bello	Postdoctoral	1
Sebastián Eduardo Gutiérrez Maldonado	Molecular simulation and computational biology	Chilean	M	06-10-1985	Biochemist	D	Fundación Ciencia y Vida	Postdoctoral	1
Alvaro Rodrigo Ruiz Fernández	Molecular simulation and computational biology	Chilean	M	03-12-1983	Biotechnology Engineer	D	Fundación Ciencia y Vida	Postdoctoral	1

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Mauricio Alejandro Aspé Sánchez	Molecular simulation and computational biology	Chilean	M	26-10-1982	Psychologist	D	Universidad de Valparaíso	Postdoctoral	1
Yorley Duarte Ayala	Molecular simulation and computational biology	Colombian	F	10-10-1982	Chemist	D	Universidad Andrés Bello	Postdoctoral	2

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1.5 Others

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Agustín Demetrio Martínez Carrasco	Cellular signaling	Chilean	M	03-18-1968	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1
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 Valparaíso	Professor UV CINV Researcher	1
Oliver Schmachtenberg	System and circuits neuroscience	Chilean	M	12-12-1970	Biologist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1
Patricio Rodrigo Orio Alvarez	Molecular simulation and computational biology	Chilean	M	12-03-1973	Biochemist	D	Universidad de Valparaíso	Professor UV CINV Researcher	1

<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	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. Milesi F. Bezanilla G. Ferreira M. Holmgren C. González K. Castillo I. García A. Neely I. Díaz R. Honorato R. Olcese J.A. Gárate	Physiology and Biophysics	08-08-11	
2	Cellular signaling	To 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. Sánchez B. Cisterna R. Escamilla A. Cárdenas M. Maldifassi I. Barria A. González N. Palacios	Cell Biology	08-08-11	

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3	Genetics and developmental neuroscience	To understand 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 C. Calfún	Developmental Biology, Genetics and Evolution	08-08-11	
4	System and circuits neuroscience	To investigate the mechanisms of neuronal encoding the visual, olfactory and cerebral physiological and pathological conditions.	Using different animal models, including Degu, a natural model for studying AD. The molecules identified by Group 2 as regulators of neurosecretion will be tested in the context of neuronal plasticity.	A. Kirkwood O. Schmachtenberg A. Chávez P. Moya A. Escobar A. Vielma Ch. Chiu A. Ardiles P. Harcha R. Meza N. Palanca	Cell Biology, Physiology and Biophysics	08-08-11	
5	Molecular simulation and computational biology	To use 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-Nilo D. Aguayo P. Orio M. Aspé T. Pérez-Acle K. Xu C. Ravello Y. Duarte A. Martínez A. Ruiz S. Gutiérrez	Numerical Methods and Computational Biophysics	08-08-11	

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		biological networks.		F. Villanelo			
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Annex 3.- Publications (Total or partially financed by MSI)

3.1.- ISI/WOS Publications or Similar to ISI/WOS Standard

3.1.1 *Associate Researchers:* The highlights correspond to the associate researchers, the participation of author (s) student (s) are underlining in each publication.

N°	1	2	3	4	5
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS
Otra Categoría					
Quartile	1	1	2	1	1
Author	Catalina Asencio-Barría, Norah Defamie, Juan C. Sáez , Marc Mesnil, Alejandro S. Godoy	<u>Báez-Matus X</u> , <u>Figueroa-Cares C</u> , <u>González-Jamett AM</u> , <u>Almarza-Salazar H</u> , Arriagada C, Maldifassi MC, Guerra MJ, Mouly V, Bigot A, Caviedes P, Cárdenas AM	Cavieres A, Campos-Estrada C, Moya Y, Maldonado R, González-Vargas R, Bustamante ML, Moya PR	Cea L, Balboa E, <u>Aníbal A</u> . Vargas, Puebla C, María C. Brañes, Escamilla R, Regueira T, Juan C. Sáez	Duarte Y, Márquez-Miranda V, Miossec MJ, González-Nilo F
Associative Researcher	Juan Carlos Sáez	Ana María Cárdenas	Pablo Moya	Juan C. Sáez	González-Nilo F
Título	Direct Intercellular Communications And Cancer: A Snapshot Of The Biological Roles Of Connexins In Prostate Cancer	Defects In G-Actin Incorporation Into Filaments In Myoblasts Derived From Dysferlinopathy Patients Are Restored By Dysferlin C2 Domains.	Lack Of Association Between The IL6R Gene Asp358Ala Variant (Rs2228145), IL-6 Plasma Levels, And Treatment Resistance In Chilean Schizophrenic Patients Treated With Clozapine	De Novo Expression Of Functional Connexins 43 And 45 Hemichannels Increases Sarcolemmal Permeability Of Skeletal Myofibers During Endotoxemia	Integration Of Target Discovery, Drug Discovery And Drug Delivery: A Review On Computational Strategies.

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Source	Cancers	Int J Mol Sci	Schizophrenia Research and Treatment	Biochimica et Biophysica Acta - Molecular Basis of Disease	Wiley Interdiscip Rev Nanomed Nanobiotechnol
Vol.	11				11
N°	1370	21			4
Inicial Page		21			
ISSN	2072-6694	1422-0067	2090-2085		1939-5116
DOI	10.3390/cancers11091370	10.3390/ijms21010037	10.1155/2019/5601249	10.1016/j.bbadis.2019.06.014	10.1002/wnan.1554
Research Line	Cellular Signaling.	Cellular Signaling.	System And Circuits Neuroscience	Cellular Signaling.	Molecular Simulation And Computational Biology
N° Associative Researcher of the Center	1	1	1	1	1
N° Investigator of the Center other Category	0	2	0	0	0
N° Students	0	3	0	1	0
Publiation Date	14-09-2019	19-12-2019	25-06-2019	01-10-2019	01-04-2019

CINV ANNUAL PROGRESS REPORT – 2019

N°	6	7	8	9	10
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS
Otra Categoría					
Quartile	1	1	1	2	1
Author	Escobar AP, Wendland JR, Chávez AE, Moya PR.	Scala R, Maqoud F, Angelelli M, Latorre R , Perrone MG, Scilimati A, Tricarico D.	Eliseo A. Eugenin, Valdebenito S, A. Gorska, Martínez A, Bitran M, Juan C. Sáez	Gárate JA, <u>Bernardin A</u> , Escalona Y, Yanez C, English NJ, Pérez-Acle T	Gómez GI, Velarde V, Sáez JC.
Associative Researcher	Chávez AE, Moya PR.	Latorre. R	Juan C. Sáez	Pérez-Acle T	Sáez JC.
Titulo	The Neuronal Glutamate Transporter EAAT3 In Obsessive-Compulsive Disorder	Zoledronic Acid Modulation Of TRPV1 Channel Currents In Osteoblast Cell Line And Native Rat And Mouse Bone Marrow-Derived Osteoblasts: Cell Proliferation And Mineralization Effect	Gap Junctions Coordinate The Propagation Of Glycogenolysis Induced By Norepinephrine In The Pineal Gland	Orientalional And Folding Thermodynamics Via Electric Dipole Moment Restraining	Role Of A Rhoa/Rock-Dependent Pathway On Renal Connexin43 Regulation In The Angiotensin Ii-Induced Renal Damage.
Source	Front Pharmacol	Cancer	Journal of Neurochemistry	Journal of Physical Chemistry B	International Journal of Molecular Sciences
Vol.	10	11		123	20
N°	1362	2		12	4408
Inicial Page				2599	
ISSN	1663-9812	2072-6694	0022-3042	1520-6106	1661-6596
DOI	10.3389/fphar.2019.01362	10.3390/cancers11020206	10.1111/jnc.14846	10.1021/acs.jpbc.8b09374	10.3390/ijms20184408.

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Research Line	System And Circuits Neuroscience	Structure And Function Of Molecular Sensors	Cellular Signaling.	Molecular Simulation And Computational Biology/ Structure And Function Of Molecular Sensors	Cellular Signaling.
N° Associative Researcher of the Center	2	1	1	1	1
N° Investigator of the Center other Category	1	0	1	1	0
N° Students	0	0	0	2	0
Publication Date	15-11-2019	11-02-2019	05-08-2019	04-03-2019	07-09-2019

CINV ANNUAL PROGRESS REPORT – 2019

N°	11	12	13	14	15
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS
Otra Categoría					
Quartile	1	1	2		1
Author	<u>Granados ST</u> , Castillo K, <u>Bravo-Moraga F</u> , Sepúlveda RV, Carrasquel-Ursulaez W, Rojas M, <u>Carmona E</u> , <u>Lorenzo-Ceballos Y</u> , González-Nilo F , González C, Latorre R , Torres YP	<u>Guerra MJ</u> , González-Jamett AM, Báez-Matus X, Navarro-Quezada N, Martínez AD, Neely A , Cárdenas AM	<u>Harcha PA</u> , <u>López X</u> , <u>Sáez PJ</u> , Fernández P, Barriá I, Martínez AD, Sáez JC	Li T, Niu J, Yu G, Ezan P, Yi C, Wang X, Koulakoff A, Gao X, Chen X, Sáez JC , Giaume C, Xiao L	Moya-Díaz J, Bayonés L, Montenegro M, Cárdenas AM , Koch H, Doi A, Marengo FD
Associative Researcher	González-Nilo F , Latorre R	AD , Neely A , Cárdenas AM	Sáez JC	Sáez JC	Cárdenas AM ,
Titulo	The Molecular Nature Of The 17β-Estradiol Binding Site In The Voltage- And Ca2+-Activated K+ (BK) Channel B1 Subunit.	The Ca2+ Channel Subunit Cav B2a Down-Regulates Voltage-Activated Ion Current Densities By Disrupting Actin-Dependent Traffic In Chromaffin Cells	Pannexin-1 Channels Are Essential For Mast Cell Degranulation Triggered During Type I Hypersensitivity Reactions	Connexin 43 Deletion In Astrocytes Promotes CNS Remyelination By Modulating Local Inflammation.	Ca2+-Independent And Voltage-Dependent Exocytosis In Mouse Chromaffin Cells
Source	Scientific Reports	Journal of Neurochemistry	Frontiers In Immunology	GLIA	Acta Physiologica
Vol.	9		10		
N°	1		2703		
Inicial Page					
ISSN	2045-2322	0022-3042	1664-3224	0894-1491	1748-1708

CINV ANNUAL PROGRESS REPORT – 2019

DOI	10.1038/s41598-019-45942-1	10.1111/jnc.14851	10.3389/fimmu.2019.02703	10.1002/glia.23770	10.1111/apha.13417
Research Line	Molecular Simulation And Computational Biology/ Structure And Function Of Molecular Sensors	Structure And Function Of Molecular Sensors / Cellular Signaling	Cellular Signaling.	Cellular Signaling.	Cellular Signaling.
N° Associative Researcher of the Center	2	2	1	1	1
N° Investigator of the Center other Category	2	2	2	0	0
N° Students	4	1	3	0	0
Publication Date	10-07-2019	16-08-2019	29-11-2019	10-12-2019	26-11-2019

CINV ANNUAL PROGRESS REPORT – 2019

N°	16	17	18	19	20
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS
Otra Categoría					
Quartile	1	1	2	1	1
Author	Osorio MI, Cabrera MA, González-Nilo F , Pérez-Donoso JM	Palanca-Castan N, Harcha PA, Neira D, Palacios AG	<u>Pérez MÁ</u> , Morales C, Santander O, <u>García F</u> , <u>Gómez I</u> , Peñaloza-Sancho V, Fuentealba P, Dagnino-Subiabre A, Moya PR. , Fuenzalida M.	Plaza W, <u>Estay Vizcarra SF</u> , de la Fuente-Ortega E, Gutierrez C, Sanchez G, Hidalgo C, Chávez AE , Haeger P	<u>Ravello CR</u> , Perrinet LU, Escobar MJ, Palacios AG
Associative Researcher	González-Nilo F	Palacios AG	Moya PR,	Chávez AE	Palacios AG
Titulo	The Odd Loop Regions Of Xena And Xenb Enzymes Modulate Their Interaction With Nitro-Explosives And Provide Structural Support For Their Regioselectivity.	Chromatic Pupillometry For The Characterization Of The Pupillary Light Reflex In Octodon Degus.	Ketamine-Treatment During Late Adolescence Impairs Inhibitory Synaptic Transmission In The Prefrontal Cortex And Working Memory In Adult Rats.	NMDA Receptor Modulation By NOX2 Drives Synaptic Plasticity And Spatial Memory Impairments In Rats Exposed Pre And Postnatally To Ethanol.	Speed-Selectivity In Retinal Ganglion Cells Is Sharpened By Broad Spatial Frequency, Naturalistic Stimuli.
Source	Journal Of Chemical Information And Modeling	Experimental Eye Research	Frontiers in Cellular Neuroscience	Antioxidants and Redox Signaling	Scientific Reports
Vol.	50		13		9
N°	9		372		456
Inicial Page	3860				

CINV ANNUAL PROGRESS REPORT – 2019

ISSN	1549-9596	0014-4835	1662-5102	1523-0864	2045-2322
DOI	10.1021/acs.jcim.9b00357	10.1016/j.exer.2019.107866	10.3389/fncel.2019.00372	10.1089/ars.2019.7787	10.1038/s41598-018-36861-8
Research Line	Molecular Simulation And Computational Biology	System And Circuits Neuroscience	System And Circuits Neuroscience	System And Circuits Neuroscience	System And Circuits Neuroscience
N° Associative Researcher of the Center	1	1	2	1	1
N° Investigator of the Center other Category	0	2	0	0	0
N° Students	0	0	3	1	1
Publication Date	27-08-2019	02-11-2019	20-08-2019	28-12-2019	24-01-2019

CINV ANNUAL PROGRESS REPORT – 2019

N°	21	22	23
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS
Otra Categoría			
Quartile	1		1
Author	Whitlock K.	Whitlock KE, Postlethwait J, Ewer J.	<u>Lorenzo-Ceballos Y,</u> Willy Carrasquel-Ursulaez, Castillo K Castillo, Alvarez O, Ramón Latorre
Associative Researcher	Whitlock K	Whitlock KE, Ewer J.	Latorre R
Titulo	Evolutionarily Conserved Peptides Coordinate Lunar Phase And Metabolism.	Neuroendocrinology Of Reproduction: Is Gonadotropin-Releasing Hormone (Gnrh) Dispensable?	Calcium-Driven Regulation Of Voltagesensing Domains In BK Channels
Source	Proceeding of the National Academy of Sciences of the United States of America	Frontiers In Neuroendocrinology	Elife
Vol.	117	53	8
N°	2 805-807	UNSP 100738	e44934
Inicial Page	805		
ISSN	0027-8424	0091-3022	2050-084X
DOI	10.1073/pnas.1920432117	10.1016/j.yfrne.2019.02.002	10.7554/eLife.44934
Research Line	Genetics And Developmental Neuroscience	Genetics And Developmental Neuroscience	Structure And Function Of Molecular Sensors

CINV ANNUAL PROGRESS REPORT – 2019

N° Associative Researcher of the Center	1	2	1
N° Investigator of the Center other Category	0	0	2
N° Students	0	0	1
Publication Date	30-12-2019	22-02-2019	11-02-2019

3.2.- SCOPUS Publications or Similar to SCOPUS Standard

3.2.1 Associate Researchers:

None

3.3.- SCIELO Publications or Similar to SCIELO Standard

3.3.1 Associate Researchers:

None

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3.4.- Scientific Books and Chapters

3.4.1 *Associate Researcher*: The highlights correspond to the associate researchers, the participation of author (s) student (s) are underlining in each publication.

N°	1	2
Publication Category	Scientific Books and Chapters	Scientific Books and Chapters
Otra Categoría		
Quartile		
Author	Álvarez O, Castillo K, <u>Carmona E</u> , González C, Ramón Latorre	Escobar MJ, Alexandre F, Viéville T, Palacios AG.
Associative Researcher	Ramón Latorre	Palacios AG
Título	Methods for Investigating TRP Channel Gating, TRP Channel Gating.	Rapid Prototyping for Bio-Inspired Robots.
Source	Methods in Molecular Biology	Springer International Publishing
Vol.	1987	
N°		
Inicial Page		
ISSN	1064-3745	
DOI	10.1007/978-1-4939- 9446-5_11	
Research Line	Structure And Function Of Molecular Sensors	System And Circuits Neuroscience
N° Associative Researcher of the Center	1	1
N° Investigator of the Center other Category	3	0
N° Students	1	0
Publication Date	27-04-2019	01-01-2019

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3.5.- Other Publications

3.5.1 Associate Researchers:

None

3.6.- “ISI/WOS Publications or Similar to ISI/WOS Standard”, “SCOPUS Publications or Similar to SCOPUS Standard” “SCIELO Publications or Similar to SCIELO Standard”, “Books and chapters in books” and “Other Publications [Other Researchers]”

3.6.1 Other researchers: The highlights correspond to the others researchers, the participation of author (s) student (s) are underlining in each Publication.

N°	1	2	3	4	5
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS
Otra Categoría					
Quartile	1	2	1		1
Author	Acarón Ledesma H, Li X, Carvalho-de-Souza JL, Wei W, Bezanilla F , Tian B	Bassetto CAZ Jr, Carvalho-de-Souza JL, Bezanilla F	Bernardi M, Marracino P, Liberti M, Gárate JA , Burnham CJ, Apollonio F, English NJ	<u>Calbiague V</u> , Vielma AH, <u>Cadiz B</u> , Paquet-Durand F, Schmachtenberg O	Caneo M, Julian V, Byrne AB, Alkema MJ, Calixto A .
Title	An Atlas Of Nano-Enabled Neural Interfaces	Metal Bridge In S4 Segment Supports Helix Transition In Shaker Channel	Controlling Ionic Conductivity Through Transprotein Electropores In Human Aquaporin 4: A Non-Equilibrium Molecular-Dynamics Study	Physiological Assessment Of High Glucose Neurotoxicity In Mouse And Rat Retinal Explants	Diapause Induces Functional Axonal Regeneration After Necrotic Insult In C. Elegans.
Source	Nature Nanotechnology	Biophysical Journal	Physical Chemistry Chemical Physics	The Journal of Comparative Neurology	PLOS Genetics

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Vol.	14				15
N°	7				1
Inicial Page	645				
ISSN	1748-3387	0006-3495	1463-9076	1550-7130	1553-7390
DOI	10.1038/s41565-019-0487-x	10.1016/j.bpj.2019.08.035	10.1039/c8cp06643d	10.1002/cne.24805	10.1371/journal.pgen.1007863
Research Line	Structure And Function Of Molecular Sensors	Structure And Function Of Molecular Sensors	Structure And Function Of Molecular Sensors	System And Circuits Neuroscience	Genetics And Developmental Neuroscience
N° Researcher of the center other category	1	1	1	1	1
N° Students	0	0	0	2	0
Publication date	03-07-2019	17-12-2019	28-01-2019	31-10-2019	14-01-2019

CINV ANNUAL PROGRESS REPORT – 2019

N°	6	7	8	9	10
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS ISI/WOS PUBLICATIONS
Otra Categoría					
Quartile	1	2	1	2	1
Author	Carvalho-de-Souza JL, Bezanilla F	Carvalho-de-Souza JL, Nag OK, Oh E, Huston AL, Vurgaftman I, Pepperberg DR, Bezanilla F , Delehanty JB	Chiu CQ , Barberis A, Higley MJ.	Dubois-Camacho K, Diaz-Jimenez D, De la Fuente M, Quera R, Simian D, Martínez M, Landskron G, Olivares-Morales M, Cidlowski JA, Xu X, Gao G, Xie J, Chnaiderman J, Soto-Rifo R, González MJ, Calixto A , Hermoso MA.	Holder MJ, Wright HJ, Couve E , Milward MR, Cooper PR.
Title	Noncanonical Mechanism Of Voltage Sensor Coupling To Pore Revealed By Tandem Dimers Of Shaker	Cholesterol Functionalization Of Gold Nanoparticles Enhances Photoactivation Of Neural Activity	Preserving The Balance: Diverse Forms Of Long-Term Gabaergic Synaptic Plasticity.	Inhibition Of Mir-378a-3p By Inflammation Enhances IL-33 Levels: A Novel Mechanism Of Alarmin Modulation In Ulcerative Colitis.	Neutrophil Extracellular Traps Exert Potential Cytotoxic And Proinflammatory Effects In The Dental Pulp.
Source	Nature Communications	ACS Chemical Neuroscience	Nature Reviews Neuroscience	Frontiers In Immunology	Journal of Endodontics
Vol.	10	10	20	10	45
N°	1		5	2449	5
Inicial Page		1478	272		513

CINV ANNUAL PROGRESS REPORT – 2019

ISSN	2041-1723	1948-7193	1471-003x	1664-3224	0099-2399
DOI	10.1038/s41467-019-11545-7	10.1021/acscemneuro.8b00486	10.1038/s41583-019-0141-5	10.3389/fimmu.2019.02449	10.1016/j.joen.2019.02.014
Research Line	Structure And Function Of Molecular Sensors	Structure And Function Of Molecular Sensors	System And Circuits Neuroscience	Genetics And Developmental Neuroscience	System And Circuits Neuroscience
N° Researcher of the center other category	1	1	1	1	1
N° Students	0	0	0	0	0
Publication date	08-08-2019	27-12-2019	05-03-2019	20-11-2019	01-05-2019

CINV ANNUAL PROGRESS REPORT – 2019

N°	11	12	13	14	15
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS
Otra Categoría					
Quartile	1	1	1	1	1
Author	Jiang Y, Parameswaran R, Li X, Carvalho-de-Souza JL, Gao X, Meng L, Bezanilla F , Shepherd GMG, Tian B	Lee EEL, Bezanilla F	<u>Legue M</u> and Calixto. A	Lima TI, Guimarães DSPSF, Oliveira AG, Araujo H, Sponton CHG, Souza-Pinto NC, Saito Â, Figueira ACM, Palameta S, Bajgelman MC, Calixto A , Pinto S, Mori MA, Orofino J, Perissi V, Mottis A, Auwerx J, Silveira LR.	Manríquez R, Peterson SD, Prado P, Orio P , Galindo GE, Zañartu M
Title	Nongenetic Optical Neuromodulation With Silicon-Based Materials.	Methodological Improvements For Fluorescence Recordings In <i>Xenopus Laevis</i> Oocytes.	RNA Language In Caenorhabditis Elegans And Bacteria Interspecies Communication And Memory	Opposing Action Of Ncor1 And PGC-1 α In Mitochondrial Redox Homeostasis	Neurophysiological Muscle Activation Scheme For Controlling Vocal Fold Models.
Source	Nature Protocols	Journal of General Physiology	Current Opinion in Systems Biology	Free Radical Biology and Medicine	Neurophysiological Muscle Activation Scheme for Controlling Vocal Fold Models
Vol.	14	151	13	143	27
N°		2			5

CINV ANNUAL PROGRESS REPORT – 2019

Inicial Page	1339	264	16	203	1043
ISSN	1754-2189	0022-1295	2452-3100	0891-5849	1534-4320
DOI	10.1038/s41596-019-0135-9	10.1085/jgp.201812189	10.1016/j.coisb.2018.08.005	10.1016/j.freeradbiomed.2019.08.006	10.1109/TNSRE.2019.2906030
Research Line	Structure And Function Of Molecular Sensors	Structure And Function Of Molecular Sensors	Genetics And Developmental Neuroscience	Genetics And Developmental Neuroscience	System And Circuits Neuroscience
N° Researcher of the center other category	1	1	1	1	1
N° Students	0	0	1	0	0
Publication date	12-04-2019	03-01-2019	01-02-2019	06-08-2019	18-03-2019

CINV ANNUAL PROGRESS REPORT – 2019

N°	16	17	18	19	20
Publication Category	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	ISI/WOS PUBLICATIONS	SCIELO Publications or Similar to SCIELO Standard
Otra Categoría					
Quartile	2	1	1	3	4
Author	Olivares J and Schmachtenberg O	Pinto C, Medinas DB, Fuentes-Villalobos F, Maripillán J, Castro AF, Martínez AD, Osses N, Hetz C, Henríquez JP.	Piña R, Ugarte G, Campos M, Íñigo-Portugués A, Olivares E, Orio P, Belmonte C, Bacigalupo J, Madrid R.	Poch A, Villanelo F, Henríquez S, Kohen P, Muñoz A, Strauss JF 3rd, Devoto L.	Scarlett E. Delgado, Camila González-Arancibia
Title	An Update On Anatomy And Function Of The Teleost Olfactory System.	B-Catenin Aggregation In Models Of ALS Motor Neurons: GSK3β Inhibition Effect And Neuronal Differentiation	Role Of TRPM8 Channels In Altered Cold Sensitivity Of Corneal Primary Sensory Neurons Induced By Axonal Damage.	Molecular Modelling Predicts That 2-Methoxyestradiol Disrupts HIF Function By Binding To The PAS-B Domain.	“Polizones Aéreos”: Vida Microbiana Sobre Y A Través De Las Olas
Source	Peer J the Journal of Life and Environmental Sciences	Neurobiology Of Disease	Journal Of Neuroscience	Steroids	Anales del Museo de Historia Natural de Valparaíso
Vol.	7	130	39	144	31
N°	e7808	104497	41		
Inicial Page			8177	21	107
ISSN	2167-8359	0969-9961	0270-6474	0039-128X	0716-0178
DOI	10.7717/peerj.7808	10.1016/j.nbd.2019.104497	10.1523/JNEUROSCI.0654-19.2019	10.1016/j.steroids.2019.02.004	

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Research Line	System And Circuits Neuroscience	Cellular Signaling	System And Circuits Neuroscience	Molecular Simulation And Computational Biology	Genetics And Developmental Neuroscience
N° Researcher of the center other category	1	1	1	1	0
N° Students	1	0	0	0	2
Publication date	27-09-2019	07-06-2019	09-10-2019	01-04-2019	01-01-2019

CINV ANNUAL PROGRESS REPORT – 2019

N°	21	22
Publication Category	Books & Chapters of Books	Other Publications
Otra Categoría		
Quartile		
Author	Chávez. F.P and Andrea Calixto	<u>Gabaldon C</u> , Andrea Calixto
Title	Use Of C. Elegans Diapause To Study Transgenerational Responses To Pathogen Infection	Worm Corpses Affect Quantification Of Dauer Recovery
Source	Methods in molecular biology (Clifton, N.J.)	microPublication Biology
Vol.	1918	
N°		
Inicial Page	191	
ISSN		2579-9430
DOI	10.1007/978-1-4939-9000-9_16	10.17912/micropub.biology.000121
Research Line	Genetics And Developmental Neuroscience	Genetics And Developmental Neuroscience

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N° Researcher of the center other category	1	1
N° Students	0	1
Publication date	01-01-2019	11-06-2019

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3.7. - Collaborative publications:

Category of Publication	1 researcher		2 researchers		3 researchers		4 or more researchers	
	Nº	%	Nº	%	Nº	%	Nº	%
<i>ISI/WOS Publications or Similar to ISI/WOS Standard</i>	30	63,82%	7	14,89%	3	6,38%	3	6,38%
<i>SCOPUS Publications or Similar to SCOPUS Standard</i>	0	0,00%	0	0,00%	0	0,00%	0	0,00%
<i>SCIELO Publications or Similar to SCIELO Standard</i>	0	0,00%	0	0,00%	0	0,00%	0	0,00%
<i>Books and chapters</i>	2	4,26%	0	0,00%	0	0,00%	1	2,13%
<i>Other Publications</i>	1	2,13%	0	0,00%	0	0,00%	0	0,00%
<u>Total of publications</u>	33	65,96%	7	14,89%	3	8,51%	4	8,51%

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Annex 4.- Organization of Scientific Events

Title of the Event	Type of Event	Date	City	Country	Scope	Number of Attendants	Number of MSI Expositors	Number of Foreign Expositors Non-MSI	National Number of Expositors Non-MSI	Duration (Days)	Target Audience	Responsible Researcher
EMBO – Chile Partnership symposia	Symposium	02-04-2019	Valparaíso	Chile	International	80	0	0	0	1	Scientific Community Students Undergraduate Professor	Ramón Rogelio Latorre De la Cruz
Small Brain Big Ideas	Workshop	05-04-2019	Santiago / Valparaíso / Las Cruces	Chile	International	68	2	14	1	8	Scientific Community	John Ewer Lothian
Meeting CINV-AC3E	Symposium	22-08-2019	Valparaíso	Chile	National	180	6	0	12	1	Scientific Community	Ramón Rogelio Latorre De la Cruz
SOBLA Annual Meeting 2019	Symposium / Meeting	04-09-2019	Valparaíso	Chile	International	150	6	40	20	4	Scientific Community	Ramón Rogelio Latorre De la Cruz
	Workshop	07-01-2019	Valparaíso	Chile	National	20	6	10	12	14		

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Southern School of Biophysics											Phd Students/ Scientific Community	Ramón Rogelio Latorre De la Cruz
Latin-American Summer School in Computational Neuroscience, LACONEU	Workshop	07-01-2019	Valparaíso	Chile	International	135	3	12	6	19	Scientific Community	Patricio Rodrigo Orio Alvarez
“O. degus: A natural model from cellular biology to behavioral ecology”.	Workshop	28/31-03-2019	Puerto Williams	Chile	National	30	3	4	11	4	Scientific Community	Adrián Palacios
Meeting CINV "Ciencias en tiempos de crisis"	Meeting	18-12-2019	Valparaíso	Chile	National	200	15	3	8	1	Scientific Community	Ramón Rogelio Latorre De la Cruz

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Annex 5.- Education and capacity building

5.1 Capacity Building inside MSI Center

MSI RESEARCHER	NUMBER						TOTAL NUMBER PER MSI RESEARCHER
	Undergraduate students		Graduate students				
			Masters		Doctoral		
	F	M	F	M	F	M	TOTAL
Fernando Danilo González Nilo	0	0	0	0	1	0	1
Carlos González Leon	0	0	0	0	0	6	6
Alan Neely Delgueil	0	0	0	0	1	2	3
Juan Carlos Sáez Carreño	0	0	0	0	2	1	3
Patricio Rodrigo Orio Álvarez	0	0	0	2	1	6	9
Ramón Rogelio Latorre De la Cruz	0	2	0	0	1	0	3
Oliver Schmachtenberg	0	0	2	0	0	3	5
John Ewer Lothian	0	0	0	1	2	2	5
Agustín Demetrio Martínez Carrasco	0	1	1	1	1	1	5
Ana María Cárdenas Díaz	0	0	2	1	0	0	3
Andrea Leonor Calixto Mohor	0	1	0	0	4	0	5
Pablo Ricardo Moya Vera	0	0	3	0	1	3	7
Adrián Palacios Vargas	0	1	0	2	0	3	6
Álvaro Oscar Ardiles Araya	1	0	0	0	2	0	3
Andrés Eduardo Chávez Navarrete	0	1	1	2	1	2	7
José Antonio Gárate Chateau	0	0	0	0	0	1	1
Kathleen Whitlock Leaning	1	0	0	0	3	2	6
Tomás Pérez Acle	0	0	0	2	0	6	8
Chiayu Chiu	0	0	1	1	1	1	4
Isaac García	0	0	0	0	0	0	0
Arlek González Jamett	5	1	1	1	0	0	8
Helmuth Sánchez	0	0	0	0	1	0	1
Karen Castillo	0	1	0	0	1	0	2
Daniel Aguayo	0	0	0	0	0	0	0
Total	7	8	11	13	23	39	101

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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	INS– Institut de Neurosciences des Systèmes - Aix Marseille Université	Marsella y Estrasburgo, France	Demian Battaglia.	Visit to the laboratory to advance the manuscript	06-22-2019	07-20-2019
Daniela De Georgis	UCLA	Los Angeles, California USA	Riccardo Olcese	Regulation of Voltage Sensing Structures of CaV1.2 Calcium channel by the Auxiliary β -subunit	03-12-2018	05-04-2019
Arles Urrutia	Universidad de Buenos Aires	Buenos Aires, Argentina	Diego de Mendoza	Metabonomic analysis of the neuroprotective bacterial diet in an axonal damage model in <i>Caenorhabditis elegans</i> ICM-MINECON P09-022 CINV, Andrea Calixto	03-18-2019	03-31-2019

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Javier Palma	Universidad de los Andes	Leticia, (Amazonas Bogotá) Colombia	Jorge Molina	2nd Andean school on neuroethology. “This school invites postgraduate Latin American students to gain first-hand experience in approaching neuropathological model systems and to interact and network with leaders in neuroethological research”	10-13-2019	10-26-2019
Emerson Carmona	Texas Tech	Lubbock, Texas, USA	Luis Cuello	Purification and Structural Studies in Hv1 Channel	07-30-2019	01-28-2020
Sebastián Urquiza	IBR Conicet UNR Instituto de Biología Molecular y Celular de Rosario	Rosario, Argentina	Diego de Mendoza	The internship was aimed at metabolizing samples of bacteria isolated from the environment in a nuclear magnetic resonance spectrum	08-26-2019	09-18-2019

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Sebastián Felipe Estay Vizcarra	Federación Europea de Sociedades de Neurociencia (FENS)	France	Camin Dean/ Keimpe Weirda	Advanced Techniques for Synapse Biology	13-10-2019	11-01-2019
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Traineeships external

Student name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Enrique García Gen	Universidad CEU Cardenal Herrera	Spain	Oliver Schmachtenberg	Lens induction myopia project in Oliver Smachtemberg's laboratory	08-06-2019	01-25-2020
David Ballesteros	Universidad Nacional de Colombia	Colombia	Adrian Palacios	To evaluate how the knock out of the protein IREK1 in the ganglion cells of the retina in mouse, affects its electrical properties and its response to electrical stimulation. A study that pretends to complement the MEA study that is currently being carried out	08-24-2019	01-31-2020
Chloe Mari Gómez	Telecom Physique Strasbourg, University of Strasbourg	France	María José Escobar, Adrián Palacios	Convolutional Neural Network (CNN) model of the retina	03-18-2019	08-23-2019
Lucas Bayones	Universidad de Buenos Aires	Argentina	Ana María Cárdenas	He studied the effects of centronuclear myopathy-dynamin 2 mutations on exocytosis.	12-08-2019	13-09-2019

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Annex 6.- Networking and other collaborative work

6.1 Formal Collaboration networks

NOMENCLATURE:

[Network Scope]

[N] National [I] International [LA] Latin American

Network Name	Network Scope	Researchers				Institutions
		From the Center		External		
		Researchers	Postdocs/ Students	Researchers	Postdocs/ Students	
Genetic and development	I	5	5	14	3	Universidad de Valparaíso
						Universidad Mayor
						Universidad de Chile
Biophysics / Physiology	I	8	4	63	18	Lewis Katz School of Medicine, Temple University, USA
						Rutgers New Jersey Medical School, USA
						National Institute of Neurological Disorders and Stroke, NIH, USA
						Universidad de Valparaíso
						University of Chicago

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6.2.- Collaboration Networks

Activity Name	Objective	Description	Co-Participants Institutions	Number of Research from the Center	Number of Postdocs /Students from the Center	Number of External Research	Number of External Postdocs/ Students	Product	Name of the Center Associate Researchers Participating in the activity
First AC3E-CINV meeting Workshop / Seminar	In order to promote mutual knowledge between CINV and AC3E	The first scientific-academic meeting to create new collaborations between both Institutions	Universidad Técnica Federico Santa María	13	9	16	5		AC3E Centro Avanzado de Ingeniería Eléctrica y Electrónica

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Annex 7. - Outreach

7.1.- Outreach activities throughout the period

Event Title	Type of Event	Scope	Target Audience	Date	Region	N° of Student from the Center	N° of Attendees	Duration in days	Participating Researchers	Responsible for the activity
Seminars of CINV										
<i>"Transgenerational memory formation elicited by bacterial RNA in interspecies communication"</i>	Seminar	Local	Universidad de Valparaíso	08-03-2019	Valparaíso	32	65	1	Andrea Calixto, Universidad Mayor- CINV	CINV Ana María Cárdenas
<i>"Modafinil affects social play behaviour and dopamine transmission in young rats"</i>	Seminar	Local	Universidad de Valparaíso	15-03-2019	Valparaíso	38	62	1	Valeska Cid, PhD student CINV- Universidad de Valparaíso	CINV Ana María Cárdenas
<i>"La construcción de la realidad en el cerebro"</i>	Seminar	Local	General community	11-04-2019	Valparaíso	25	78	1	Ranulfo Romo, Universidad Nacional Autónoma de México	CINV Ramón Latorre

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<i>“Péptidos antimicrobianos de invertebrados marinos”</i>	Seminar	Local	Universidad de Valparaíso	17-04-2019	Valparaíso	50	62	1	Anselmo Otero, University of Havana	CINV Carlos González
<i>"Making and moving synaptic vesicles in neurons"</i>	Seminar	Local	Universidad de Valparaíso	22-04-2019	Valparaíso	46	52	1	Sandhya Koushika, Tata Institute of Fundamental Research. Mumbai	CINV John Ewer
<i>“Genetic epidemiology of Tourette Disorder: a potential role of cell polarity”</i>	Seminar	Local	Universidad de Valparaíso	04-26-2019	Valparaíso	35	53	1	Gary Heiman, Dept. of Genetics, Rutgers University	CINV Pablo Moya
<i>“Injury-induced compensatory plasticity: Variations on form and function in the adult cricket nervous system”</i>	Seminar	Local	Universidad de Valparaíso	03-05-2019	Valparaíso	39	48	1	Hadley Horch, Bowdoin College	CINV Kathleen Whitlock
<i>“La producción de</i>	Seminar	Local	Universidad de Valparaíso	31-05-2019	Valparaíso	33	58	1	Juan Manuel Garrido,	CINV

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<i>conocimiento útil en la era de crecimiento económico. Una mirada desde Chile”</i>			General community						Director PhD in Philosophy Univ. Alberto Hurtado	Ramón Latorre
<i>“Proteins fragments are regulatory molecules”</i>	Seminar	Local	Universidad de Valparaíso	07-06-2019	Valparaíso	40	52	1	Alexander Zamyatnin, Institute of Biochemistry, Russian Academy of Science	CINV John Ewer /Ramón Latorre
<i>“Dissolving proteins with continuous models: electrostatics and border methods”</i>	Seminar	Local	Universidad de Valparaíso	06-07-2019	Valparaíso	40	55	1	Christopher Cooper, Universidad Técnica Federico Santa María	CINV José Antonio Gárate
<i>“Studying the mechanical properties of protein translocation”</i>	Seminar	Local	Universidad de Valparaíso	07-26-2019	Valparaíso	46	56	1	Christian Wilson, Universidad de Chile	CINV Ramón Latorre
<i>“Transcriptomic and functional</i>	Seminar	Local	Universidad de Valparaíso	09-08-2019	Valparaíso	45	65	1	Scarlett Delgado, PhD student	CINV

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<i>analysis of a neuronal pro-regenerative condition in Caenorhabditis elegans</i>									CINV- Universidad de Valparaíso	Andrés Chávez/ Ramón Latorre/ John Ewer
<i>“Ectopic expression of connexins in Drosophila clock neurons and non-neuronal tissues”</i>	Seminar	Local	Universidad de Valparaíso	09-08-2019	Valparaíso	45	65	1	Theodor Höpcke, PhD student CINV- Universidad de Valparaíso	CINV Andrés Chávez/ Agustín Martínez/ John Ewer
<i>“Human connectome boosts dynamic cortical ignition”</i>	Seminar	Local	Universidad de Valparaíso	23-08-2019	Valparaíso	47	60	1	Samy Castro, PhD student CINV- Universidad de Valparaíso	CINV Andrés Chávez
<i>“Fear memory and brain oscillations in the medial prefrontal cortex of stressed rats”</i>	Seminar	Local	Universidad de Valparaíso	30-08-2019	Valparaíso	47	60	1	Mauricio Ramirez, PhD student CINV- Universidad de Valparaíso	CINV Andrés Chávez

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<i>"Alterations on glutamatergic system in depressive-like behavior in mice"</i>	Seminar	Local	Universidad de Valparaíso	13-09-2019	Valparaíso	46	54	1	Nicolás Ardiles, PhD student CINV-Universidad de Valparaíso	CINV Andrés Chávez
<i>"Regulation of Voltage Sensing Structures of Cav1.2 Calcium Channel by the Auxiliary β-subunit"</i>	Seminar	Local	Universidad de Valparaíso	27-09-2019	Valparaíso	43	50	1	Daniela De Giorgis, PhD student CINV-Universidad de Valparaíso	CINV Alan Neely
<i>"mGluR-dependent plasticity process (LTP) to survey impairment cognitive in aging Degus"</i>	Seminar	Local	Universidad de Valparaíso	11-10-2019	Valparaíso	40	58	1	Cristobal Ibaceta, PhD student CINV-Universidad de Valparaíso	CINV Andrés Chávez
<i>"Circadian control of the daily rhythm of adult emergence by regulation of the timing of ecdysone action in Drosophila melanogaster"</i>	Seminar	Local	Universidad de Valparaíso	18-10-2019	Valparaíso	44	55	1	Liliana Bustos, PhD student CINV-Universidad de Valparaíso	CINV John Ewer

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<i>“Por qué necesitamos una nueva constitución”?</i> <i>(“Why do we need a new constitution?”)</i>	Seminar	Local	Universidad de Valparaíso General community	15-10-2019	Valparaíso	47	60	1	Luis Villavicencio, Facultad de Derecho - Universidad de Valparaíso	CINV Ramón Latorre
Workshops and general talks										
<i>“Genetic Counseling: A bridge between clinics and laboratories”</i>	Workshop	Local	Universidad de Valparaíso	22-04-2019	Valparaíso	43	58	1	Maki Kaneko, Center for Personalized Medicine at Children’s Hospital. Los Angeles, USA	CINV John Ewer
<i>“Neurociencia a tu alcance”</i> <i>(“Neuroscience at your fingertips”)</i>	Workshop	Regional	School community	08-10-2019	Valparaíso	3	3	3	Oliver Schmachtenberg CINV- Universidad de Valparaíso	CINV Fundación Educación Futuro
<i>“Uso de drogas en la adolescencia y neuroprotección”</i> <i>(“Drug use in adolescence and</i>	General talk	Local	Antilhue school community	11-04-2019	Santiago	30	60	1	Andrés Chávez, PhD CINV- Universidad de Valparaíso	CINV Fundación Educación Futuro

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<i>neuroprotection</i> ")										
<i>"Uso de drogas en la adolescencia y neuroprotección"</i> <i>("Drug use in adolescence and neuroprotection")</i>	General talk	Local	Raimpu school community	29-05-2019	Santiago	38	42	1	Andrés Chávez, PhD CINV- Universidad de Valparaíso	Raimpu highschool
<i>"Uso de drogas en la adolescencia y neuroprotección"</i> <i>("Drug use in adolescence and neuroprotection")</i>	General talk	Local	San Ignacio school community	09-10-2019	Viña del Mar	34	53	1	Andrés Chávez CINV- Universidad de Valparaíso	San Ignacio highschool
<i>"Día de la Astronomía"</i> <i>("Astronomy Day")</i>	General talk	Regional	General community	20-03-2019	Santiago		54	1	John Ewer CINV- Universidad de Valparaíso	Explora CONICYT
<i>"Día de la Cronobiología"</i> <i>("Chronobiology Day")</i>	General talk	Regional	General community	12-09-2019	Santiago		45	1	John Ewer CINV- Universidad de Valparaíso	Explora CONICYT

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<i>“La ruta de la ciencia”</i> (<i>“The science route”</i>)	General talk	Regional	General community	29-08-2019	Valparaiso	8	100	1	Kathleen Whitlock CINV- Universidad de Valparaíso	Universidad de Valparaíso
<i>“Congreso del Futuro”</i> (<i>“Congress of the future”</i>)	General talk / Round table	National	General community	General community	Valparaiso	47	600	1	Tomás Pérez - Acle, PhD CINV- Fundación Ciencia y Vida	CINV Universidad de Valparaíso Congreso del Futuro
<i>“Falling Walls Chile”</i> 14 talks of pre-selected Chilean candidates	Conference	National	General community	09-08-2019	Santiago	-	120	1	Tomás Pérez - Acle, PhD CINV- Fundación Ciencia y Vida Andrés Couve Minister of science, technology and innovation	CINV Fundación Ciencia Joven DAAD
Practical Activities										

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<i>Festival de la ciencia “El secreto de las arañas” (Science Festival "The secrets of spiders")</i>	Practical activity / Interactive Talk	Natio nal	General community	12-10- 2019	Santiago	-	1000	1	Jesús Olivares, PhD student CINV- Universidades de Valparaíso	CINV Explora - CONICYT
<i>Simón Bolívar de Quillota School: “Neurociencia y el camino a ser investigadores” (“Neuroscience and the way to be researchers”)</i>	Practical activity / Interactive Talk	Local	School community	04-10- 2019	Quillota	3	60	1	Juan José Alvear, PhD student Naileth González, PhD student CINV- Universidad de Valparaíso	Colegio Simón Bolívar de Quillota
<i>Leonardo Da Vinci School: “School of Neurosciencie at CINV” labs”</i>	Practical activity / Interactive Talk	Local	School community	10 to 11-10- 2019	Valparaíso	7	10	1	Ramón Latorre, Carlos González, Andrés Chávez, CINV- Universidad de Valparaíso	CINV Colegio Leonardo Da Vinci
Tertulias Porteñas										
	General talk		General community	23-05- 2019	Valparaiso	25	210	1	Tomás Pérez- Acle,	Ramón Latorre

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<p><i>“Inteligencia artificial ¿Beneficio o condena?” (“Artificial intelligence, benefit or condemnation?”)</i></p>									<p>CINV-Fundación Ciencia y Vida</p> <p>Andrés Claro, PhD in Philosophy, Oxford University</p> <p>Fernanda Pérez, PhD in Biological Sciences, Universidad Católica de Chile.</p>	
<p><i>“El cerebro y la eterna juventud” (“The brain and eternal youth”)</i></p>	<p>General talk</p>	<p>Regional</p>	<p>General community</p>	<p>01-08-2019</p>	<p>Valparaiso</p>	<p>58</p>	<p>250</p>	<p>1</p>	<p>Claudio Hetz, Director BNI-U. de Chile</p> <p>Paulina Urrutia, Actress</p> <p>José Luis Dinamarca, Geriatrician, U. de Valparaíso</p>	<p>Ramón Latorre</p>

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<p><i>“Agua, cambio climático y el futuro de la especie humana”</i> <i>("Water, climate change and the future of the human species")</i></p>	<p>General talk</p>	<p>30-11-2019</p>	<p>Valparaíso</p>	<p>General community</p>	<p>Valparaíso</p>	<p>42</p>	<p>250</p>	<p>1</p>	<p>Claudio Latorre, PhD in Biological Sciences Universidad Católica de Chile Gino Casassa, Civil Hydraulic Engineer Rodrigo Mundaca, Agricultural engineer and social leader</p>	<p>Ramón Latorre</p>
<p>Book and TV Series presentations</p>										
<p><i>“DeMente: El Cerebro, un hueso duro de roer”</i> Valparaíso Natural History Museum</p>	<p>Book presentation</p>	<p>Regional</p>	<p>General community</p>	<p>11-07-2018</p>	<p>Valparaíso</p>	<p>20</p>	<p>120</p>	<p>1</p>	<p>Chantal Signorio, Festival Puerto de Ideas’ Director Héctor Cossio, El Mostrador web journal’s general editor</p>	<p>CINV</p>

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									Virginia Garretón Ministry of Sciences Advisor	
<i>“DeMente: El Cerebro, un hueso duro de roer”</i> Festival de Autores de Santiago.	Book presentation	Regional	General community	28-09-2019	Santiago	30	80	1	Oliver Schmachtenberg, Jesús Olivares, CINV-Universidad de Valparaíso María Paz Bertoggia, Immunologist and scientific communicator Lucía López, journalist Macarena Rojas-Abalos, journalist	Catalonia Editions Gabriela Mistral Cultural Center
<i>“Neuropolis”</i>	Presentation	National	General community	26-09-2019	Valparaíso	10	300	1	Jaime Boetsch, Programming	CINV-Universidad de Valparaíso

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									Director of National Television of Chile, Ramón Latorre, CINV Director Andrés Couve, Minister of Science, Technology, Knowledge and Innovation.	National Television of Chile National Television Council Puerto Visual
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7.2.- 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	9	2	49	18	1	0	79
Internet	2	0	16	7	15	17	57
Audiovisual	3	0	29	1	7	0	40
Total	14	2	94	26	23	17	176

7.3. - Products of outreach

Product Type	Quantity	Target Audience	Scope
<i>“Falling Walls Lab Chile”</i> Video registration available on the CINV website with 14 talks of pre-selected Chilean candidates Presentation in Berlin of the contest winner	15	General Community	National
<i>Tertulias Porteñas</i> Event broadcast across the country on UCV-TV Video registration	3	General Community	National
<i>NeuroNews</i> 21 Articles published on the El Mostrador news website. Available on the CINV website	21	General Community	International
<i>“DeMente. El cerebro, un hueso duro de roer”</i> Two editions of the book edited and published. 2000 books sold in the year	1	General Community	National
<i>Neuropolis</i> TV series broadcast throughout the country in prime time on Chilean national television (TVN). 8 chapters available on the TVN and CINV website.	8	General Community	International

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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
Neurociencia a tu alcance (Neuroscience at your fingertips)	Create a scientific experience for the final year of school to establish a permanent CINV and Fundación Educación Futuro program.	Theoretical-practical internship	3	3	Fundación Educación Futuro	Valparaíso.	3	Education
Fundación Puerto Ideas	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)	Fundación Puerto de Ideas	Valparaíso, Antofagasta	2	Business activities
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)	National ministry of public works Regional government of Valparaíso	Valparaíso, Chile	2	Government

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Neuroscience and companies	Possibility of decreasing the health problems associated with night shifts.	Talks to its managers and security officers.	2	7 (Talks to different companies)	Mining enterprises	Valparaíso, Chile	1	Business activities
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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 [\$]	2019 Incomes		Total incomes to 2019 [\$]
		Amount [\$]	Percentage of resources used by the Center [%]	
ICM (CINV, Redes y PME)	9,378,510	1,292,839	100%	1,292,839
CONICYT (Anillo, Mincyt, Explora, Fondecup, Redes y Neuromantes)	5,448,398	1,115,026	95%	1,115,026
UV (Neuroscience Institute and Others)	5,311,329	817,923	100%	817,923
Corporación CINV	116,086	97,352	81%	97,352
CNTV, FNDR	73,301	0	0%	0
Others (CAT; N62909-13-N251-; N62909-16-1-2227; AFOSR; N62909-14-1-N121)	635,543	303,496	70%	303,496
TOTAL	20,963,168	3,626,636		3,626,636

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Annex 10.- Outstanding Activities

Name of the activity relevant in your discipline	Type of activity relevant in your discipline carried out	Description of the relevant activity in your discipline	Importance in your discipline of the activity	Possibility to maintain or replicate this activity
<p>Cerebral Cortex: from Progenitors to Functional Circuits, at the Cajal Club meeting. November 24-25, Pto Varas, Chile.</p>	<p>Scientific Symposium</p>	<p>The Cajal Club, a Neuroscience Society based in the USA, hosted an international scientific meeting in Puerto Varas, Chile. This event featured leading neuroscientists from the USA, focusing on new findings in the field of cerebral cortex structure and function. (https://cajalclub.org/cajal-at-fens/)</p>	<p>In addition to being an important networking event, the meeting contributed to the scientific development of students in latin America. Nicole Sanguinetti, a graduate student in the Neuroscience program of UV was selected to talk about her thesis work in an oral presentation.</p>	<p>None</p>
<p>4th biennial conference "Brain in Flux: Genetic, Physiologic, and Therapeutic Perspectives on Transporters in the Nervous System" (ISN satellite meeting), August 2019, Saint Paulin-Quebec, Canada</p>	<p>Scientific Symposium</p>	<p>This event featured some of the leading neuroscientists throughout the world, focusing on new findings in the field of neuronal and glia transporters and its relevance for brain function.</p>	<p>This international meeting is not only relevant for networking event, but also for Dr. Moya present his findings to the neuroscience community involved in neuronal and glial transporter function.</p>	<p>None</p>
<p>Lecture Invited to SOIBIO Montevideo,</p>	<p>Scientific Symposium</p>	<p>The annual meeting of the IberoAmerican Society for</p>	<p>Dr. González-Nilo's lecture was oriented to the integration of</p>	<p>Yes</p>

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October 28-30, 2019		Bioinformatics is organized each year in different countries of Latin America.	Bioinformatics with Molecular Simulations, showing some of the lines of research developed in CINV.	
Workshop Molecular Simulations: AMBER, May 27-30, 2019	Training Workshop	AMBER is one of the most popular software for molecular simulations. More than 30 PhD students from different Universities of Chile attended the training.	As the main lecture of the workshop, Dr. Adrian Roitberg from the University of Florida, USA was invited	Yes
“Drivers of Multi-stability in Neuronal Networks: A modelling approach” in the Workshop “Emergent Phenomena in Macroscopic Neural Networks	Scientific Symposium	The workshop was part of the 28th Annual Computational Neuroscience Meeting. (Barcelona, Spain, July 2019).	The Computational Neuroscience Meeting is the Annual meeting of the Organization for Computational Neurosciences. This is one of the most important yearly held meetings in the field.	Dr. Orio was invited to a new workshop in the 2020 meeting.
Plenary Session, International Strategic Conference of Zebrafish Investigators (SCZI), Pacific Grove, California, USA.	Scientific Symposium	Dr. Whitlock’s talk was entitled “Neural Immune Interactions in the Olfactory Epithelia: Implications for Olfactory Imprinting and Immune Response”.	This meeting is for Principal Investigators from around the world working in Zebrafish	Dr. Whitlock usually is accepted to this bi-annual international meeting
Speaker in the Molecular Biosystems" Conference on Eukaryotic Gene Regulation and	Scientific Symposium	Dr. Calixto’s talk was entitled: RNA language in <i>Caenorhabditis elegans</i> and bacteria interspecies	This is the first report describing a bacterial molecule capable of transiting through the germline and to the next generations.	None

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Functional Genomics",missing details		communication and transgenerational memory		
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