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Index

1.

1.1 Executive Summary

The Biomedical Neuroscience Institute (BNI) has become a reference center in Latin America that brings together a critical mass of leading neuroscientists, clinicians, mathematicians, physicists, engineers, entrepreneurs, and education and health professionals to explore the structure and function of the brain under normal physiology and disease, from cells to whole organisms, and strongly interact with the community. 2018 represents thrird year our second 5-year period. New strategies proposed in the mid-term review were consolidated during this period in addition to preparing the basis that will generate the vision for the "new institute" through the competitive renewal system. The key objectives that build upon the existing institute's achievements and currently drive BNI's activities are: (i) to further enhance the quality of BNI trademark inter-disciplinary and collaborative research; (ii) to promote translational research and interactions with the private sector; (iii) to expand the impact of training and capacity building; (iv) to strengthen education and outreach. In this period, due to the assignment of AC as Minister of Science and Technology, CHz and JS took the leadership. We have rearranged the structure to potentiate the different areas of development at BNI (science, innovation, outreach, and education) with an increased participation of BNI investigators. In addition, we started an auto evaluation process to define the areas we would like to potentiate in the next period and also evaluate the performance of all BNI researchers to identify strong and weak areas that will allow us to define future research.

According to our structure, six lines conduct research on the relationship between structure and function of the brain, following a bottom up, multi-scale approach in complementing model organisms (flies, multiple fish models, mice, rats, and humans) including clinical research. Two transversal research lines promote a highly collaborative strategy conducting research and development in biomathematics (BioMat) and neuropathology. Our *Applied Neuromedicine and Technology Platform* (*NeuroTech*) concentrates our growing capacity in technology transfer and innovation. Our outreach and education platform *Loligo* connect BNI with school-students, science teachers and the general community. BNI's research is supported by students, postdocs, young investigators, engineers, entrepreneurs, clinicians, and by a team of highly qualified and motivated staff.

The productivity of BNI includes the achievements of now five Associated Investigators, two Senior Investigators, and ten Adjunct Investigators. During 2018 almost 200 people constituted the core of the institute. Adjunct investigators, who have academic positions and independent and funded research lines have successfully fulfilled their role to bridge, strengthen and expand research areas and to build their sustainability. Additionally, Adjunct Investigators with MD-PhD degrees conduct studies in animal models and humans in the areas of neurological and psychiatric disorders providing a practical strategy to achieve one of our main aims related to translational research and the clinic. Moreover, young staff scientists have been able to develop independent research lines and to secure national and international highly competitive funding.

13 young investigators, 40 postdocs, 44 PhD, 24 Magholgister, 16 undergraduate students and a team of 80 technical and professional staff complete BNI's multidisciplinary research team. During 2018, 10 theses were co-directed by BNI Investigators. 7 students visited foreign laboratories to conduct collaborative research. BNI hosted 5 international students and postdocs from countries in South America and Europe, including Colombia, Panama, Uruguay, Germany and the Netherlands. As part of their comprehensive scientific training, 50 BNI students participated in outreach activities. Several trainees left BNI, continuing their career paths in other national institutions or abroad, while others have stayed to pursue a higher degree or a postdoctoral position. 7 postdocs continued their scientific careers elsewhere, including academic positions in Chile and USA.

During 2018 BNI Investigators published 53 articles, like 2017 (51) with an average ISI impact factor of 5.3, which compares favorably to similar centers in the developed world and maintains our excellent trend. High impact factor articles in journals such as, *Nature Cell Biology, Molecular Cell, EMBO Mol Medicine,* and reviews in prestigious journals of wide circulation such as *Molecular Cell,* and *Trends in Neuroscience,* in addition to the selection for cover image and the publication of editorial comments about our research, demonstrate the international impact of research at BNI. BNI researchers continued their strong presence in national and international meetings, with 95 posters or oral presentations during 2018.

The first license option was signed with the Australian BravoBiotech company for the technology "Method for genetic treatment using the AAV-XBP1s/GFP virus and use thereof in the prevention and treatment of amyotrophic lateral sclerosis". After a legal dispute conducted by our lawer J Diaz, BNI sucesfully registered the brand BNI in the 41 category Education. It was an important achievement because the acronym BNI is also the brand of a big finance international company.

During 2018 several national and international scientific events contributed to create an exciting multidisciplinary atmosphere at BNI. We organized 12 regular seminars, *Conversations in Neuromedicine*, in topics connecting neuroscience and medicine, which included local and internationals speakers. We continued to promote monthly internal seminars organized and executed by young investigators and postdocs with support of our professional staff. We carried out the 6th version of *NeuroSur*, which included (i) the symposium *Frontiers in Neurotechnology: A latin American perspective* (dec 5th, 2018) (ii) the *NeuroSur* business meeting, which for has started to develop a structured diagnosis of the Tech Transfer Centers in Iberoamerica. Taking advantage of the newly secured Cyted funds *NeuroSur* oriented its efforts to improve the capacities and encourage more TechTransfer initiatives in Iberoamerican countries.

In order to reinforce the identity of the Institute and to promote the interaction between teams of different laboratories we organized our annual two-day BNI retreat at Mantagua Village in Concon, Valparaiso, with a program of lectures (*Research at BNI*, *Science and Experience*), presentation and evaluation of *Seed Grants*, discussions around relevant scientific and ethical topics (for example authorship, experimentation in animals, working conditions, and research at BNI), and stimulating social excursions and recreational activities.

Testing of new ideas and attraction of young investigators continued through our successful programs of *Seed Grants* and *Bridge Fellowships*. **MC, SH** and **CHz** were recognized for their contribution to research and publishing in top rank journals at the Universidad ed Chile.

Press coverage of the institute's activities has firmly established BNI as a reference center in Chile and Latin America. BNI press appearances were valued in an outstanding $ 1.037.613 USD, with 91 appearances in newspapers, 3 in weekly magazines, 57 online, 9 on radio, and 7 on television. Press coverage has contributed to position BNI as a resource center for neuroscientists, clinical practitioners, high-school students, entrepreneurs and the general public. Rodrigo Tapia, the head of Education and outreach, continued successful presentations of the Brain Tent in different scientific events and witht the support of the HHMI-Biointeractive organized the first Chilean Meeting for Science Educators, where 160 high school teachers from all over the country participated for three days.

R. Tapia, B Cadiz, and S Reyes, who lead the Education and outreach, Communications and Technology Transfer and Innovation platfoms respectively are based in the new building. The site has consolidated as a centralized hub and an ideal setting to engage with the community. An Executive Office contributed to connect with other sectors, a Grant Management Office is responsible for the financial administration, and a Board of Directors continues to steer the Institute's strategy

1.2 Resumen Ejecutivo

El Instituto de Neurociencia Biomédica (BNI) se ha convertido en un centro de referencia en América Latina. Reúne a una masa crítica de neurocientíficos, médicos, matemáticos, físicos, ingenieros, emprendedores y profesionales de la educación y la salud para explorar la estructura y función del cerebro bajo estado fisiológio normal y en enfermedad, desde la exploración celular hasta organismos completos, interactuando fuertemente con la comunidad. 2018 representa el tercer año de nuestro segundo período de 5 años. Las nuevas estrategias propuestas en la revisión intermedia se siguen consolidando durante este período, además de preparar la base que generará la visión para el "nuevo instituto" a través del sistema de renovación competitiva. Los objetivos clave en los que se basan los logros del instituto y que actualmente impulsan las actividades de BNI son: (i) bajo el sello de marca BNI mejorar aún más la investigación y colaboración interdisciplinaria (ii) promover la investigación traslacional y las interacciones con el sector privado; (iii) expandir el impacto en formación y desarrollo de capacidades de sus estudiantes; (iv) fortalecer la educación y divulgación de la ciencia En este período, debido al nombramiento de **AC** como Ministro de Ciencia y Tecnología**, CHz** y **JS** tomaron el liderazgo del instituto. Hemos reorganizado la estructura para potenciar las diferentes áreas de desarrollo en BNI (ciencia, innovación, extensión y educación) con una mayor participación de los investigadores de BNI. Además, comenzamos un proceso de autoevaluación para definir las áreas que nos gustaría potenciar en el próximo período y también evaluar el desempeño de todos los investigadores para identificar áreas fuertes y débiles que nos permitirán definir futuras investigaciones. La ciencia que se realiza en BN está basada primeramente en seis líneas de investigación, las que siguen un enfoque de abajo hacia arriba, desde la relación entre la estructura y función del cerebro hasta escalar a organismos completos (moscas, múltiples modelos de peces, ratones, ratas y seres humanos), incluida la investigación clínica. Dos líneas de investigación transversales promueven una estrategia altamente colaborativa que conduce la investigación y el desarrollo en biomatemática (BioMat) y neuropatología. Nuestra plataforma de neuromedicina y tecnología aplicada (NeuroTech) concentra nuestra creciente capacidad de transferencia tecnológica e innovación. Nuestra plataforma de extensión y educación Loligo conecta a BNI con escolares, profesores de ciencias y con la comunidad en general. La investigación de BNI está respaldada por estudiantes, postdoctorados, jóvenes investigadores, ingenieros, emprendedores, clínicos y por un equipo de personal altamente calificado y motivado. La productividad científica de BNI incluye el trabajo de seis Investigadores Asociados, dos Investigadores Senior, y diez Investigadores Adjuntos. Durante 2018 casi 200 personas constituyeron el núcleo del instituto. Los investigadores adjuntos, quienes tienen cargos académicos y líneas de investigación independientes y con financiamiento propio, han cumplido con éxito su función de vincular, fortalecer y ampliar las áreas de investigación y construir su sostenibilidad. Además, los investigadores adjuntos con títulos de MD-PhD realizan estudios en modelos animales y humanos en las áreas de trastornos neurológicos y psiquiátricos, lo que proporciona una estrategia clara para lograr uno de nuestros principales objetivos relacionados con la investigación traslacional y la clínica. Además, científicos jóvenes han podido desarrollar líneas de investigación independientes y asegurar fondos nacionales e internacionales altamente competitivos. 13 investigadores jóvenes, 40 posdoctorados, 44 estudiantes de postdoctorado, 24 estudiantes de magíster, 16 estudiantes de pregrado y en conjunto con un equipo de 80 técnicos y profesionales forman el equipo de investigación multidisciplinario de BNI. 10 tesis fueron codirigidas por los investigadores de BNI. 7 estudiantes visitaron laboratorios extranjeros para realizar investigaciones colaborativas. BNI recibió a 5 estudiantes internacionales y posdoctorados de países de América del Sur y Europa, incluidos Colombia, Panamá, Uruguay, Alemania y los Países Bajos. Como parte de su capacitación científica integral, 50 estudiantes de BNI participaron en actividades de extensión y divulgación científica. Varios participantes dejaron BNI y continuaron su carrera en otras

instituciones nacionales o en el extranjero, mientras que otros se han quedado para obtener un título superior o una posición postdoctoral. 7 postdocs continuaron sus carreras científicas en otros lugares, incluyendo posiciones académicas en Chile y Estados Unidos.

Durante 2018, los investigadores de BNI publicaron 53 artículos, similar número al año 2017 (51 publicaciones) con un factor de impacto ISI promedio de 5.3, que se compara favorablemente con centros similares en el mundo desarrollado y mantiene nuestra excelente tendencia. Artículos de alto impacto en revistas como *Nature Cell Biology*, *Molecular Cell*, *EMBO Mol Medicine* y reseñas en prestigiosas revistas de gran circulación como *Molecular Cell y Trends in Neuroscience*, además de la selección de la imagen de portada y la publicación de comentarios editoriales sobre nuestra investigación, demuestran el impacto internacional de la investigación realizada en BNI. Los investigadores de BNI continuaron su fuerte presencia en conferencias nacionales e internacionales, con 95 poster o presentaciones orales durante el periodo informado. Se firmó la primera opción de licencia con la compañía australiana BravoBiotech para la tecnología *"Método para el tratamiento genético utilizando el virus AAV-XBP1s / GFP y su uso en la prevención y tratamiento de la esclerosis lateral amiotrófica"*. Después de una disputa legal realizada por nuestra abogada J Díaz, BNI logró registrar la marca BNI en la categoría 41 Educación. Fue un logro importante porque el acrónimo BNI es también la marca de una gran empresa internacional de finanzas. Variados eventos científicos nacionales e internacionales contribuyeron a crear un ambiente multidisciplinario en BNI. Organizamos 12 seminarios regulares, *Conversaciones en neuromedicina*, sobre temas relacionados con la neurociencia y la medicina, que incluyeron oradores locales e internacionales. Continuamos promoviendo seminarios internos mensuales organizados y ejecutados por jóvenes investigadores y postdoctorados con el apoyo de nuestro personal profesional. Llevamos a cabo la sexta versión de *NeuroSur*, que incluyó (i) el simposio *Fronteras en Neurotecnología: una perspectiva latinoamericana* (5.dic.2018) (ii) NeuroSur meeting, en las que se comenzó a desarrollar un diagnóstico estructurado sobre el estado de la transferencia tecnológica en Iberoamérica.Mediante financiamiento Cyted, NeuroSur está orientando sus esfuerzos para mejorar las capacidades y alentar más iniciativas de Transferencia tecnológica en los países iberoamericanos. Con el fin de reforzar la identidad con el Instituto y promover la interacción entre equipos de diferentes laboratorios BNI, organizamos nuestro retiro anual, con una duración de dos días en Mantagua Village en Concon, Valparaíso, con un programa de conferencias (Investigación en BNI, Ciencia y Experiencia) , presentación y evaluación de *Fondos Semilla*, discusiones sobre temas científicos y éticos relevantes (por ejemplo, autoría, experimentación en animales, condiciones de trabajo e investigación en BNI), y estimulación de excursiones sociales y actividades recreativas. Hemos continuado con nuestros exitosos programas *Beca Puente* y *Fondos Semilla* para brindar apoyo a novedosas ideas de nuestros investigadores. La Universidad de Chile entregó reconomientos a **MC, SH y CHz** por su contribución a la investigación y publicación en revistas de primer nivel. La cobertura de prensa de las actividades del instituto ha establecido a BNI como un centro de referencia en Chile y América Latina. Las apariciones en prensa se valoraron en $ 1.037.613 USD, con 91 apariciones en periódicos, 3 en revistas semanales, 57 en Internet, 9 en radio y 7 en televisión. RTapia, Director de Extención y Educación, continuó itinerancias exitosas del *Domo Cerebro* y con el apoyo del HHMI-Biointeractive organizó el primer Congreso Chileno de Educadores de Ciencias, en el que durante tres días participaron 160 docentes de secundaria de todo el país. R. Tapia, B Cádiz y S Reyes, quienes lideran las plataformas de Extensión y Educación, Cultura y Comunicaciones y Transferencia tecnológica e Innovación, respectivamente, centran sus operaciones en el nuevo edificio. El sitio se ha consolidado como un centro de encuentros y un entorno ideal para interactuar con la comunidad. Una Oficina Ejecutiva contribuyó a conectarse con otros sectores, una Oficina de Administración de Subvenciones es responsable de la administración financiera y una Junta Directiva continúa dirigiendo la estrategia del Instituto.

1.3 Outstanding Achievements

BNI has transformed into a reference center in biomedicine, life science and biotechnology in the region. The productivity and impact of our research is recognized internationally, where many PIs inside BNI are leading figures in their respective fields. BNI has been able to generate a signature of research that is based in the combination of different animal models and mathematical modeling, coupled with strong international alliances. This year, BNI researchers published in top journals like *Nature Cell Biology*, *PNAS* and *Molecular Cell*, generating a huge impact in the local press, in addition to 53 other research articles. This is an outstanding achievement for the reality in the country. We aim to do science without limits despite our scarce resources, by generating a strategy that envisions BNI as a platform to develop new collaborative networks and to rise complementary funding from national and international agencies to perform "blue sky science", in addition to innovation and clinical research. This approach combined with a solid outreach and educational platform has placed BNI in the public domain, constituting a central pillar of the Chilean scientific community to show the value of science in general and neuroscience I particular to our society. This achievement is reflected in the fact that **CH** was selected President of the National Academy of Science and **AC** as the first Minister of Science and Technology. More international students and postdocs are interested in developing their careers at BNI since they see an opportunity to receive outstanding training that will foster their independency. During 2018 focused in generating an internal culture, with the goal to educate students and young researchers in critical thinking, the social impact of science and communication skills. We believe that this project also asserts the feeling of belonging to the Institute. We believe that this commitment is central to generate union and cultivate the best of everyone to devote to science and technology with a social and collaborative vision. In terms of scientific achievements, we have been able to discover new avenues in the understanding of human disease and how it relates to cellular stress pathways, in addition to uncover new regulatory elements underlying cellular homeostasis. We also advanced research about aspects of brain and neuronal networks development and novel genes important for the brain metabolism in *Drosophila*. Mporeover novel mechanisms of modulation of attention and advances in clinical studies in Schizophrenia and Parkinson have been published by our investigators. **CHz** has been able to move forward several patents into an international phase and to license the first technology to Australia, in addition to strengthening the interactions with international pharma like Genzyme, GSK and Mounttam Biotechnology aiming to develop novel drugs and therapeutics using gene therapy to treat human brain disease. The technology platforma has secured new contracts with the special participation of eye tracking technology.

2. Introduction

a) Description of the Institute

The Biomedical Neuroscience Institute (BNI) is a reference center in Latin America that brings together a critical mass of leading neuroscientists, clinicians, mathematicians, physicists, engineers, entrepreneurs, and education and health professionals who explore the structure and function of the brain under normal physiology and disease conditions, from cells to whole organisms, and who strongly interact with the community. Four fundamental aims have remained as BNI's backbone: (i) to accomplish world-class scientific research; (ii) to train and host the new generations in a vibrant - but demanding - and unique transdisciplinary environment; (iii) to produce high-standard clinical research and transfer its impact to society; and (iv) to become a resource center for specialized clinical practitioners, teachers and the general public. The key objectives driving BNI's activities during this period were:

(i) To further enhance the quality of BNI trademark inter-disciplinary and collaborative research. This approach is based on the use of complementary animal models, mathematics to uncover

hidden biological phenomena, advanced scientific equipment and investigation at multiples scales from genes to behavior. A special focus was placed on areas that foster *in vivo* approaches, connect phenomenological scales, and promote clinical research in neurology and psychiatry. We have also promoted a strong sense of belonging, and a unique and intense scientific culture to inspire younger generations. This year we published three high impact papers combining animal models and approaches, demonstrating the efficacy our strategy and consolidated our research vision with solid outputs. We obtained the cover image of *Molecular Cell*, with an editorial comment in addition to a highlight of the biography of the students who participated in the study. This article involved collaboration with 9 labs around the globe.

(ii) To promote translational research and interactions with the private sector. A *Neuromedicine and Technology Platform*, which promotes a culture of innovation, was established in 2016 to develop internationally competitive and innovative solutions in biotechnology, neuro-systems, and data science that impact health and other areas. Technology transfer and interaction with industry grew rapidly at BNI. A fulltime specialist, institutional projects with the private sector and other collaborative applied projects with the Faculty of Physical and Mathematical Sciences at Universidad de Chile are part of our achievements. We strenghthened our relations with the Technological Office at the University of Chile and new patents were filled and we have also moved into international PCT phases. One technology to treat ALS was liscenced to Bravo Biotech in Australia where **CHz** is part of the Scientific Advisory Board. New alliances with international biotech companies such as *Mounttam Biotechnology* in the US have been stablished to test the potential of rapalogues to treat Parkinson, in addition to other interactions with *GSK* and Proteostasis therapeutics in the USA. A CORFO grant was developed to provide technological service to the Chilean biotech company *Cellus* and to improve the value of their stem cell technologies. In addition, two FONDEF grants in gene therapy were developed in partnership with *Genzyme-Sanofy* the top 4th biotech company in the world.

(iii) To expand the impact of training and capacity building. Training efforts continue to focus on attracting young talent through formal university graduate programs, and to bridge initiatives for recruiting postdocs. We promote the incorporation of young international investigatorsas well as basic and clinical researchers in biology and mathematics. BNI is also becoming a hotspot for engineers conducting applied research. We are part of the INSPIRED network funded by the European Community (800.000 EUR) which fosters collaborations by students between labs in France, Ireland, Germany and Greece. This involment generated a joint thesis between Chile and France, we received a PhD student from France and one of our postdocs spent a year in Ireland. We also established new networks to collaborate with France and Switzerland by rising funding for bidirectional interactions from ECOS Conicyt and the Swiss goverment. In addition, the CYTED grant led by **AC** was consolidated to generate a network based on innovation in South America.

(iv) To strengthen the impact of outreach activities. Interaction with school students and teachers is at the heart of BNI's scientific culture. *From motivation to education* is the thread that connects our online and onsite activities for kids with a growing focus on high school teachers through our international alliance with Howard Hughes Medical Institute / Biointeractive. To date approximately 500 science teachers have received complementary training at BNI. We were also part of two of the largest outreach activities of the country, Puerto Ideas and Congreso Futuro. Our overall structure includes six research lines that conduct studies on the relationship between the structure and function of the brain, following a bottom up, multi-scale approach in complementing model organisms including clinical studies, and two transversal research lines that explore biomathematics and neuropathology. An *Applied Neuromedicine and Technology Platform* seeks to connect the scientific knowledge produced at BNI with the growing needs of industry in the areas of biotechnology applied to human health, medical devices, brain-machine interfaces, psychology and behavior and remote health monitoring. *Loligo*, our outreach and education initiative, reaches

students and high-school teachers throughout the country. BNI's research is supported by students, postdocs, young investigators, young clinicians, and shared facilities. Approximately 30% of funds are allocated directly to individual researchers for operational expenses whereas the remaining 70% is invested in common undertakings. Millenium funding constitutes approximately 25% of the total operating costs for scientific activities (excluding salaries for Investigators, CONICYT fellowships and use of University infrastructure). Funds from 12 national and international projects, from public and private sources contribute to the overall impact of the institute. An International Advisory Board helps steer the institute's research and a Board of Directors contributes to invigorate the interactions with the F Med and with U Chile. All activities at BNI are supported by a team of 12 professionals in the areas of Education/Outreach, Technology Transfer and Innovation, Executive management, and Grant management.

b) Research Lines:

During 2018 we continued to consolidate our organizational model of research lines. To facilitate the revision process in this and other sections we have used initials to refer to BNI Associate or Senior Investigators involved in a particular project, publication or other activity: A Couve (**AC**), C Hetz (**CHz**), M Concha (**MC**), S Härtel (**SH**), C Hidalgo (**CH**), P Maldonado (**PM**), J Sierralta (**JS**), H Silva (**HS**). BNI Adjunct Investigators are indicated by bold initials and last name.

We are currently executing 8 research lines: **RL1.** Sub-cellular functional dynamics (**AC/SH/CHz/CH/JS/P Olguín**). **RL2.** Cellular identity and morphology (**AC/CHz/JS/P Olguín**). **RL3.** Supra-cellular development and circuits: (**MC/SH/M Cerda/P Olguín**). **RL4.** Plasticity and behavior (**AC/CHz/CH/A Paula-Lima/JL Valdés/P Délano**). **RL5.** Systems Neuroscience (**PM/R Fuentes/JL Valdés/P Délano**). **RL6.** Clinical studies (**CHz/PM/HS/R Fuentes/P Gaspar/JM Matamala/S Matus/A Paula-Lima/JL Valdés/R Vidal/P Délano**). **RL7.** Biomathematics (**MC/AC/SH/CH/M Cerda**). **RL8.** Neuropathology (**MC/CHz/CH/JS/R Fuentes/P Gaspar/JM Matamala/S Matus/ Paula-Lima/R Vidal/P Délano**).

c) Organization of researcher's team:

BNI consists of 6 Associated Investigators who conduct research at different biological scales or with different disciplinary approaches (**MC/AC/SH/CHz/PM/JS**). Additionally, one Senior Investigator conducts and advices in clinical studies (**HS)** and the other (**CH**) conducts research and provides internal strategic advice. 10 Adjunct Investigators bridge, complement and expand research areas in mathematics, biology and clinical studies in neurology, psychiatry and from this year also audiology (**M Cerda, R Fuentes, P Gaspar, JM Matamala**, **S Matus, P Olguín, A Paula-Lima, JL Valdés, R Vidal and the recently incorporated P Délano**). The average age of the team of 18 leading investigators is 45.8 years. 13 young investigators, 40 postdocs, 44 PhD, 24 Master, 16 undergraduate students and a group of 80 technicians and professionals complete the multidisciplinary research team. Strategies to foster interactions include: (i) leaders that coordinate platforms for collaborative research lines, technology and animal models; (ii) co-mentorship of students/postdocs/young investigators/young clinicians; (iii) monthly internal seminars, shared infrastructure including the fully operational BNI building and common facilities; (iv) organization of scientific events, theoretical/practical courses, educational activities and an annual retreat; (v) special funds to incite new ideas and collaborative research (seed grants) and postdoctoral fellowships encouraging co-mentoring that include the adjunct researchers; and (vi) weekly planning meetings and monthly *Science+Strategy* meetings with Associate, Senior and Adjunct Investigators. Funds allocated to strategic aims such as facilities, postdoctoral *Bridge Fellowships*, *Seed Grants*, infrastructure, equipment, innovation, education/outreach and administration are reviewed every year to comply with strict interaction criteria. BNI investigators are responsible for

specific tasks such as reviewing *Bridge Fellowships, Seed Grants*, networks, education/outreach, connecting with clinicians, or organization of *Science+Strategy* meetings and other scientific events.

3. Scientific and technological research:

a) **Current status of research lines:**

Each research line (RL1-8), although mainly carried out by one or two Associate researchers, it involves the interaction of multiple laboratories. We discuss publications within this section to enrich the discussion and highlight the achievements in the context of specific research lines. ***Annex 2***.

RL1. Sub-cellular functional dynamics. We have continued our studies in endoplasmic reticulum function and dynamics. Reviews have been published confirming the leading role of the group in the role of the endoplasmic reticulum in local translation and the unfolded protein response (Luarte et al., 2018, González et al., 2018 (**AC**); García-González et al., 2018, Martínez et al., 2018, Lebeaupin et al., 2018, Rojas-Rivera., 2018, Valenzuela et al., 2018, González-Quiroz et al., 2018, Gerakis and Hetz 2018, Carreras-Sureda et al., 2018, Pérez-Arancibia et al., 2018, Hetz and Papa, 2018 (**CHz**)). In this research line one of the topics is the study of the role of proteostasis in brain physiology and its role also in different neurodegenerative diseases. To feed this project with novel basic discoveries we performed two interactome studies to identify novel regulators of the pathway. This year we published the function of two of the interactors discovered using a yeast two hybrid screen using IRE1-α as bait. The role of the physical association of the UPR sensor and Filamin A in cell migration, which was the result of collaboration between several BNI laboratories (**AC, MC and CHz, including a PhD student from M Kukuljan former lab**), was published in *Nature Cell Biology* (Urra et al, 2018). The second interactor of the UPR stress sensor, Hsp47, (**CHz)** was validated in cell culture *in vitro*, in the fly and in a novel cKO mouse model *in vivo* (**CHz**/**JS**) (*Sepulveda et al., 2018 Moll Cell*). This study received the cover image, and editorial comments and a highlight with the profile of the students involved. **CH** lab has also published a study describing how the Ryanodine receptor (an endoplasmic reticulum calcium release channel) generates calcium signals essential for Long Term (*Arias-Cavieres et al.,2018, Front in Cellular Neurosci.)(***CH***).* Our studies on the lactate metabolism and glia-neuron relationship resulted in the publication of the work characterizing the first lactate transporter in *Drosophila* brain with a role in glial cells to protect from starvation and effects in synaptic function and locomotor behavior (*Delgado et al., Sci.Rep 2018*) (**JS**). This work allows us now to start the study of brain metabolism using *Drosophila* as a model system and a new paper with the characterization of the lactate/pyruvate transport ex vivo has been sent for review.

RL2. Cellular identity and morphology. We have continued the study of the presynaptic functions of DLG proteins (**JS**/**POlguín**) in the context of a FONDECYT grant, (a PhD. Student A Kohler and D Villegas, an undergraduate student, are working in this project). **JS** and **POlguín** labs are advancing in the study of the consequences of prenatal malnutrition in adult behavior and in the development of the nervous system, using *Drosophila* as animal model, we publish a work on the role of P53 in nutrient restriction in neurogenesis (*Contreras et al., PlosOne* , **JS**). In addition, we continued the study of the regulation of *Drosophila* brain wiring in collaboration with Dr. Carlos Oliva and a manuscript was published exposing the regulation of the wiring in the optic lobe by the transcription factor SoxD (Contreras et al., Sci. Rep., **JS**). We have continued the study of atlastin in a hereditary spastic paraplegias model in *Drosophila* a Ph.D. student (MF Bertin) and an Ms student (A. Ibacache) are working in this line of research (**AC**/**JS**/**POlguín**); two papers are in

preparation on this topic. Moreover, a work on the function of the Filamin-Jitterbug to maintain the polarity of the tendon cells during development of the muscular system in *Drosophila* was published by **POlguín** lab., this work advances in the coupling between force and dynamical changes in transcription that this lab has been investigating.

RL3. Supra-cellular development and circuits. We used live imaging, cellular approaches, genetics and mechanical manipulation in model organisms (zebrafish, killifish, Drosophila) to study the mechanisms that direct supra-cellular organization and circuit formation during ontogeny. In collaboration with the BioMat platform, we also implement/develop new imaging approaches (e.g. expansion microscopy, automated cell tracking; *Cerda et al 2018 Computer Physics Communications*) and techniques for the *in vivo* assessment of cell and tissue mechanics (e.g. laser ablation). In brain morphogenesis and connectivity, the discovery of the Interaction between IRE1- α and filamin commented in RL1, implies a novel function of the UPR in neuronal migration during brain development (Urra et al., 2018 *Nature cell Biology*). Additionally, we continued dissecting the role of genetic signals in asymmetric brain morphogenesis. We continued our comparative study of brain asymmetry in vertebrates assessing habenular connectivity in the Bichir (Polypteridae). We found that the laterotopic segregation pattern of left-right habenular efferents in the dorso-ventral axis of the interpeduncular nucleus, which was initially described in the teleost zebrafish, is present in the Bichir and thus represents an ancestral trait of Actynopterigians (**MC/SH**). Finally, we continued to study the molecular control of axonal guidance in the context of the habenulo-interpeduncular circuit, studying the function of Robo3 (**MC/SH/CHz**) and in the visual system of Drosophila, studying the role of SoxD (*Contreras et al 2018 Scientific Reports;* **JS**). In tissue morphogenesis we continued studying epithelial and mesenchymal morphogenesis using *vivo* imaging, biomechanical manipulation and mathematical modeling, beginning to dissect the role of cell-autonomous and non-cell-autonomous force-dependent mechanisms that cell delamination of progenitor cells (**MC/SH/M Cerda**). We developed new tools for imaging whole killifish embryos through light-sheet microscopy and for subsequent tracking and assessment of cell morphology in a semi-automated manner (**MC/SH/M Cerda**). Additionally, we continued work in the pre-clinical models of neurodegenerative diseases for Parkinson and aging using killifish model *Nothobranchious furzeri* (**MC/CHz**).

RL4. Plasticity and behavior. The central aim of this research line is to explore cellular mechanism that modulate long-term potentiation (LTP) and long-term depression (LTD), structural plasticity and hippocampal-dependent learning and memory processes. In the reported period **CH,** Adjunct Investigators **JL Valdés** and **A Paula-Lima**, together with BNI research associates T. Adasme and G. Sánchez, other collaborators from the Universidad de Chile and the Universidad de Valparaiso, postdoc A. Arias-Cavieres and graduate students J. More, R. Torres and P. Lobos have reported that calcium release mediated by the redox-sensitive RyR2 channel isoform has a key role in in hippocampal structural plasticity and spatial memory in male rats, since RyR2 downregulation prevents all these responses (*More et al 2018 Antioxid Redox Signal;***CH/JLValdés/APaula-Lima**). We reported also that induction of hippocampal long-term depression (LTD) requires RyR-mediated calcium release from the ER (*Arias-Cavieres et al 2018 Frontiers in Cellular Neuroscience;* **CH/JLValdés***)*, and we are currently investigating the role of presynaptic RyR-mediated calcium release on LTD induction. In an additional report we described how contextual fear memory formation/destabilization induces hippocampal RyR2 calcium channel up-regulation (*Haeger et al 2018 Neural Plasticity;* **CH***).* These results add to our previous findings reporting RyR2 up-regulation in rodents which have performed several different hippocampal-dependent spatial memory tasks. Additionally, we reported that the widely used antimicrobial agent Triclosan decreases RyR2 protein content, impairs hippocampal LTP and structural plasticity and causes

severe defects in a previously learned spatial memory task (*Arias-Cavieres et al 2018 Front Mol Neurosci;* **CH/ JL Valdés***).* Moreover, we reported that the signaling pathways underlying BDNF-induced Nrf2 hippocampal nuclear translocation involve ROS, RyR-Mediated Ca^{2+} signals, ERK and PI3K (*Bruna et al 2018 Biochem Biophys Res Commun.;* **CH/ APaula-Lima***).* N-Acetylcysteine prevents the spatial memory deficits and the redox-dependent RyR2 decrease displayed by an Alzheimer's disease rat model. (*More et al 2018 Front Aging Neurosci.;* **CH, JL Valdés, APaula-Lima**). These results highlight the specific participation of redox-dependent RyR2-mediated calcium release on AβOs-induced spatial memory defects.

RL5. Systems Neuroscience. As previous year, this line of research has included studies performed in the laboratories of **PM**, **CH**, **APaula-Lima, JLValdes, PGaspar and RFuentes.** Many projects include collaborations between two or more of BNI scientists. This line of research included the work of five of our young scientists, five post-docs, twelve Ph.D. students, 15 Master's students, and two engineers' students. **CH, APaula-Lima**, and **JLValdes** continued to collaborate in order to explore the relationship between synaptotoxic amyloid beta oligomers (AβOs) and Alzheimer's disease. This year they found that AβOs injections directly into the hippocampus, by engaging oxidation-mediated reversible pathways significantly decreased RyR2 protein content but increased single RyR2 channel activation by Ca2+ and caused considerable spatial memory deficits. They proposed that redox-sensitive neuronal RyR2 channels partake in the mechanism underlying AβOs-induced memory disruption in rodents (*More et al., Frontiers in Aging Neuroscience,* **CH/JLValdés/APaula-Lima**). **RFuentes** has keep working in Neuromodulation by spinal cord stimulation as a symptomatic treatment for Parkinson's disease. He and colleagues at the Clinica Las Condes adopted a method of spinal stimulation that was used for one patient with Parkinson's disease. The patient showed great improvement in his motor disabilities, proving that the method has significant clinical potential. **PGaspar** and **PM** have finalized a study in early psychosis, eye movements and EEG, which was the basis of the Ph.D. thesis of Rocio Mayol, who graduated this year. We found that people affected with schizophrenia present alterations in the bottom-up mechanisms to observe salient elements of an image. We demonstrated that the decrease in the visual attentional response evoked by the saliency of visual stimuli in patients affected with schizophrenia contributes to the reduction of visual exploration in these patients. This study has a manuscript in preparation. **JLValdés** and **PM** have completed a study on the Neosaxitoxin (NeoSTX) toxin. This substance has been successfully used as local anesthetic and muscle relaxants due to its ability to block voltage-gated sodium channels However, most of these non-classical sodium channel blockers act with a reduced time effect and neurotoxicity. This work showed that the use of local NeoSTX injections inactivates the hippocampal neuronal activity reversibly with a by long-term dynamics, without neuronal damage. (*Galindo et al., Journal of Neuroscience Methods* **PM/JL Valdés**). In other cognitive studies, Rodrigo Montefusco et al., (*Vision Research* **PM**) demonstrated that that unsupervised discrimination learning occurs through changes in the stimulus processing that increase the sensory evidence and/or the precision of the working memory. The acquired discrimination ability was fully transferred to novel exemplars of the practiced stimuli category, in agreement with the acquisition of a category specific perceptual expertise. In a separate cognitive study of patients with minimal consciousness, they showed that reduced modulation of spectral activity in the delta band in response to stimuli indicates a dissociation in the activity of the neural networks that oscillate in delta and theta ranges and contribute to the generation of the P300 (*Rivera et al, Clinical Neurophysiology,* **PM**). In another study of the **PM** lab, we reported the cortical dynamics of visuomotor learning (*Burgos et al, Human Brain Mapping; Mariman et al, European Journal of Neuroscience,* **PM**). Two other studies focused on attentional visual orientation during free viewing of natural images (*Astudillo et al., Frontiers in Human Neuroscience,* **PM**), and on local cortical activity of distant brain areas, that can phase-lock to the

olfactory bulb's respiratory rhythm in freely behaving rats (*Rojas-Libano et al., Journal of Neurophysiology,* **PM***).* Finally, we are developing a new project linking brain proteostasis and gut biology, describing cell-nonautonomous signals that are controlled by the UPR (**CHz** and staff scientist G Martinez).

RL6. Clinical studies. A central goal of BNI is to conduct clinical brain research sustained by cutting-edge basic Neuroscience. We searched for neurophysiological markers of Schizophrenia and we are promoting the use of eye movements and EEG signals in the early detection in ultra-high Psychosis risk (UHR) populations and First episode of Psychosis (**PM/HS/P Gaspar**). We have found that a potential delta/theta EEG biomarker that predicts the transition from a UHR to first episode psychosis patients We have published this innovative work in the leading top journal in this field, *the American Journal of Psychiatry* **(P Gaspar).** We have extended this approach to identify EEG and behavioral markers for Alzheimer's disease (**PM/A Paula-Lima/JL Valdés**). To do this, we combined electroencephalography (EEG) and eye movement recordings during the performance of a virtual navigation task, where subjects had to find a submerged platform in a computerized (virtual) version of the Morris Water Maze (MWM). Several parameters were evaluated while performing the navigation task, including pathway traveling and ocular behaviors, brain activity during perception and cognitive integration of visuospatial information. The results obtained until now indicate that, unlike control subjects, subjects with aMCI: 1) did not exhibit spatial learning along the task, as indicated by the observation of sustained increased latency, increased error rate, decreased mean velocity and longer pathways to find the platform in the virtual MWM memory task; 2) displayed altered patterns of visual exploration, and 3) exhibited significantly lower electrical activity associated with visual information extraction. The visual information in aMCI subjects did not spread from occipital regions to association cortices; in each subject, the level of activity correlated with the score on the MoCA test. These combined results represent a significant advance in the understanding of the mechanisms involved in the loss of spatial encoding in AD and could be used either as an early diagnostic test or in the search for new drugs to treat AD. (**APL/PM**). We also have been working on determining whether the dysfunctions caused by AβOs produce abnormal oscillatory patterns in rat hippocampus that resemble the oscillatory alterations found in AD patients **(APL/JLV).**

Clinical approaches will expand to innovative new therapeutic tools in the area of neurology, focusing on the development of therapies for Parkinson's disease based on two different methods of electrical neuromodulation of the spinal cord. Single electrical pulses delivered epidurally to the spinal cord are able to uncouple pathological long-range synchronization of the sensory-motor circuit by differential phase-shift of ongoing oscillatory activity in the different areas, providing, for the first time, a mechanism that explain the observation that electrical neuromodulation methods interrupt pathological synchronization in Parkinson's disease. **(R. Fuentes).** Additionally, the effects of regular spinal cord neuromodulation on gene expression are studied by differential expression analysis of mRNA (**R Fuentes/R Vidal**). We are also interested in describing new and specific biomarker such as gene, protein or metabolites in Chilean Parkinson Disease patient in prodromal stage (**R Vidal**). The therapeutic potential of unfolded protein response components to treat neurodegenerative diseases are also being explored. We are focusing on the role of the ATF6-XBP1 heterodimer in Parkinson's and Huntington's diseases using *in vivo* models through a gene therapy approach. In addition, we are evaluating the impact of IGF2 growth factor in Parkinson's and Huntington's animal models of disease (**CHz/R Vidal**). Using pharmacological and genetic approaches, we are exploring the role of the integrated stress response, an adaptive pathway aimed at restoring cellular homeostasis in neurodegeneration. We are studying the consequences of targeting integrated stress response (ISR) kinases in different cellular populations in the neurodegenerative process in ALS, Parkinson Disease and aging (**CHz/S Matus/R Vidal/P**

Olguín). We are focused in the ISR nutrient sensor kinase, GCN2, as an integrator of metabolic signals and proteostatic pathways, analyzing the consequences of genetic, nutritional and pharmacological modulation of GCN2 in synaptic maintenance, re-myelination, neurodegeneration and aging in mouse and fly models.

We also developed new animal models that resembles sporadic ALS features to study sporadic ALS, which included the analysis of human tissue derived from patients to confirm our hypothesis about the link between aging, ER stress and ALS (Medinas et al., 2018 *PNAS*) (**CHz**). We also developed a clinical project to identify new biomarkers of ALS and discovered the presence of circulating microRNAs using mRNA sequencing to screen for possible candidates by combining the use of multiple ALS transgenic mice and human blood derived from Chilean ALS patients. All subjects were recluted at Hospital El Salvador by our new adjunct investigator JM Matamala (Matamala et al., 2018 *Neurobiol Aging*) (**CHz/S Matus/JM Matamala**). Matamala also developed secveral clinical studies to define biomarkers of brain cancer and also degeneration published in national medical journals. We are developing a basic-clinical study in Chilean patients affected by Huntington's disease in collaboration with the *Center for Movement Disorders* (CETRAM) led by P Chana (**CHz/R Vidal**). This center is associated with the international EnRoll program that is dedicated to connecting research centers in the study of Huntington's disease, in order to accelerate discovery and therapeutic approaches. We are seeking molecular blood markers (levels of IGF2) in Huntington's patients to better understand the underlying molecular mechanisms of this disease.

We have made progress in the *Neuro-Psychiatric Diseases Biobank*, which aims to become an important resource for the characterization and investigation of major psychiatric and neurological illnesses in Chile. By collecting DNA and plasma/serum samples from groups of patients of interest in an orderly, safe and traceable manner, the *Biobank* will constitute an essential tool for clinical, genetic, and molecular studies and personalized medicine (**HS**). Finally, new lines of biomedical research have been established to study human brain cancer where a strong component of unam biopsy analysis was incorporated using bioinformatics (Lhomond et al 2018 *EMBO Mol Med).* This brain cancer project is supported by the INSPIRED international training network funded by the European Community.

Finally, another innovative line of research we have implemented is the use of automatic language processing and machine learning as reliable tools to characterize psychiatric interviews. We have analyzed until now, 30 language features: 4 verbal fluency measurements, 6 semantic lexicons based on sentences coherence, and 20 verbal productivity features. We used those features to identify 123 Spanish-speaking patients from 3 groups: 49 controls, 35 with a first episode of psychosis and 39 with chronic Schizophrenia. Using this data, we assessed if the proposed features were language specific or universal. To illustrate clinical applications as a biomarker, we proposed a binary classifier to discriminate between control versus other conditions. We have found that most features are language independent when comparing English and Spanish speaking patients, with the exception of syntactic features such as determinants and pronouns production. The proposed classifications based on language and clinical information are comparable with the state of the art using techniques such as EEG or MRI, but applicable in a clinical context **(P Gaspar/M. Cerda).**

RL7. Biomathematics. As in previous years, the biomedical mathematics and informatics group (BioMat) is guided by BNI investigator **SH** and adjunct investigator **M Cerda**: In 2018, we pushed collaboration with BNI labs by weekly sessions in microscopy, equipment, image/data processing, and collaboration in articles. We highlight projects with **POlguín** to quantify cell morphology in Drosophila epithelia (L Alé), F Bertín/**JS** segmentation and quantification of synaptic vesicles/buttons in Drosophila (J Jara), P Liddle (IIBCE Uy) clustering of gamma-H2AX foci (J Jara, I Castro), C Lemus/**MC** 3D morpho-topological analysis of assymmetrical brain

morphogenesis in zebrafish (J Jara), M Juricic/**AC** measuring ERGIC dynamics, and A Figueroa (**P Gaspar**) lab with automatic analysis of psychiatric interview transcriptions and audio signals.

BioMat and the Center of Medical Informatics and Telemedicine CIMT (www.cimt.cl) advanced in co-directed on Biophysical Simulations of Cytoskeleton (**SH/M Cerda**), on Systems to Support the Detection of Critical Results in Imaging Reports through Automatic Learning (supervisor **M Cerda**), on Optimizing Adjacent Membrane Segmentation in Multi-Cellular Aggregates by Piecewise Active Contours (**SH**) and Nanoscale Characterization of E- & N-Cadherin Clusters, and N Navarro in ZnO:MgO nanoparticles as potential anthracycline nanocarriers sensitive to tumor pH (**SH**). Electrical engineer L Ale and Computer engineer A Lavado finished fast light-sheet microscope calibration and improved multi-view scripting. Digital pathology for research and education were fully integrated into the University Hospital (HCUCH), and new telemedicine projects matured at HCUCH (**SH**/P Gomez, academic directors). BioMat and associative members also advanced in: (i) continuous improvements of imaging techniques: acquisition speed and processing software to calibrate lasers, cameras and views for 4-lens light-sheet (L Ale), tracking and segmentation techniques (J Jara, I Castro, S Vargas, A Lavado), laser ablation was incorporated for in vivo spinning disk microscopy and is fully functional (collaboration with IST Vienna, L Ale). Results were obtained with STORM/PALM (C Reyes & P Aceiton **J Toledo/SH/AC**). Data Center SASIBA with 10 GBps connectivity and 300 Terabytes for data storage, sharing, and server hosting is working on a regular base (BioMed-HPC, REUNA, STI, and NLHPC **SH/M Cerda**), and incorporated into the platform for advanced scientific equipment and services REDECA (http://redeca.med.uchile.cl). In 2018, the concept of a new location and infrastructure of an imaging facility was elaborated and will be executed in 2019 (ii) high-, mid-, and low-level mathematical-computational methods for microscopic image analysis in combination with high performance computing: developed algorithms contributed to publications (*González et al., Imbio 2018; Cerda et al., Comp Phys Comm 2018*), and Chang et al. 2017, was honored paper in *Ciaccio: Comput Biol Med 2018*). (iii) Research and Development of internet assisted services for diagnosis and clinical research are handled on a regular base within the spin-off for *Internet Assisted Medical Services CEDAI SpA* (**SH**). E Pulgar (former Postdoc **SH**) was incorporated into CEDAI with the advanced human capital proyect of the productive sector CONICYT 2018. Expansion of the service on an international level is successful with the U Nacional de Cuyo, Mendoza, Arg (G de Blas, Collaboration Agreement signed 2018).

RL8. Neuropathology and applied biomedicine.

A central goal of BNI is to conduct biomedical research and biotechnology to transfer the impact of science to the clinic and industry. The therapeutic potential of unfolded protein response (UPR) components to treat neurodegenerative diseases is continuously being explored. We are focusing on the role of the transcription actor XBP1 heterodimer in Parkinson's, Alzheimer and ALS using *in vivo* models through a gene therapy approach in close collaboration with **Genzyme-Sanofy** at the US. We have risen funding from two FONDEF grants to further develop two technologies generated at BNI, *Proteostaser-1®* and *UPRplus®*, which were patented nationally and are currently under international phases (**CHz**). In addition, a new patent to delay brain aging was submitted in the US. We are evaluating the impact of the IGF2 growth factor in Parkinson's and Huntington's animal models of disease (**CHz/R Vidal**). We have licensed one patent to **Bravo Biotech** in Australia to move forward *Proteostaser-1®* into the clinic to treat ALS patients. We are currently negotiating the licencing of three patents to the UK company **Handl Bio**, who is seeking partnership with **Novartis Benchor Funds** in Switzerland to clinicaly develop our technologies.

Using pharmacological and genetic approaches we are studying the consequences of targeting integrated stress response (ISR) kinases of this signaling pathway in different cellular populations in the neurodegenerative process in ALS and aging (**CHz/S Matus/R Vidal**). We have published in

collaboration with Glaxo Smith Kline **GSK** and **Genzyme** in the US the use of a small molecule to inhibit one UPR signaling branch in Parkinson´s disease models (Mercado et al., 2018 *Neurobiol Dis*) (**CHz/S Matus/R Vidal**). We also developed new animal models to study sporadic ALS, wich included the analysis of human tissue with our advisory board member Dr R Brown at UMASS (Medinas et al., 2018 *PNAS*) (**CHz**), and also the spreading of alpha Synuclein in the brain (Mercado et al., 2018 *BBRC*). We are focusing in testing the potential of the integrated stress response nutrient sensor kinase, GCN2, as an integrator of metabolic signals and proteostatic pathways, in neurodegeneration and aging (**S Matus**). We have established a collaboration with Gionanna Malluci (U Cambridge, UK) and Peter Walter (UCSF, USA) to test the efficacy of two drugs to target the pathway in models of ALS and FTD (**CHz** and **S Matus**). We are also studying derivatives of the small molecule rapamycin to treat Parkinson´s disease in collaboration with Mounttam Biotechnology in the US (**CHz** and **R Vidal**). The staff scientist C Duran raised funding from the **Alzheimer Association** USA to study a new drug to target ER proteostasis in Alzheimer Disease, complementing another study funded by the department of defense and the **Muscular Dystrophy Association** to test the same drug in ALS in collaboration with **Fosun Orinove Pharma Tech** in China (**CHz**). We developed a new gene therapy to deliver the growth factor IGF2 into the brain that was patented (**CHz/R Vidal**). Our staff scientist D Medinas is currently investigating the role of ER chaperones in intellectual disability funded by FONDECT (**CHz**, **MC**), in addition to their role in ALS funding by **ALS Association** and **Muscular Dystrophy Association** as PI.

Finally, new lines of biomedical research have been stablished to study brain cancer, leading to the first collaborative study with Eric Chevet in France (Lhomond et al 2018 *EMBO Mol Med*. This line is now consolidated by the staff scientist H Urra who received FONDECYT funding and by a neurosurgeon who is performing his MD/PhD training at BNI (**CHz**). This brain cancer project is supported by the **INSPIRED** international training network funded by the European Community. We are also setting models of environmental stress to study its connection with cellular stress in close collaboration with Carmen Sandi, Director of the Brain and Mind Institute at EPFL Switzerland, which lead to a seeding money award to stablish a bidirectional program from Leading House for Latin American Region from the U of San Gallen.

b) **Outstanding publications:**

- Urra H., Henriquez D., Cánovas J., Villarroel-Campos D., Carreras-Sureda A., Pulgar E., Molina E., Hazari Y., Limia C., Alvarez-Rojas S., Figueroa R., Vidal R., Rodriguez D., Rivera C., Court F., Couve A., Qi L., Chevet E., Akai R., Iwawaki T., Concha M., Glavic A., Gonzalez-Billault C., Hetz. (**RVidal/AC/MC/CHz**) *IRE1α governs cytoskeleton remodeling and cell migration through a direct interaction with Filamin A.* ***Nature Cell Biology.*** Commented in ***Science Signaling*** (2018). This article describes for the first time that the Endoplasmic Reticulum Stress Sensor IRE1 can regulates the actin cytoskeleton dynamics and the cell movement. The molecular mechanism implies the specific regulation over Filamin A trough an interaction with IRE1 that regulates the phoshorylation status of Filamin A. The model was validated in Zebrafish and Drosophila models. Moreover, this article describes that IRE1 is a crucial protein involved in the development of mammalian brain cortex. This paper was the result of the collaboration between the three BNI labs as well as the expertise of Dr. José Canovas in "in utero electroporation"in mice, expertise obtained during his PhD. Thesis with Dr. Manuel Kukuljan (currently the Faculty of Medicine Dean and former member of the BNI). It also involved several researchers from different part of the world. This paper described an unsuspected role of the UPR receptor IRE1α in the regulation of the cytoskeleton that has a direct impact in the cell migration, particularly during the development of the brain cortex

- More JY, Bruna BA, Lobos PE, Galaz JL, Figueroa PL, Namias S, Sánchez GL, Barrientos GC, Valdés JL, Paula-Lima AC, Hidalgo C, Adasme T. (**JLValdés/ APaula-Lima, CH)** *Calcium Release Mediated by Redox-Sensitive RyR2 Channels Has a Central Role in Hippocampal Structural Plasticity and Spatial Memory*. ***Antioxidants & Redox Signaling***.
- Sepulveda D., Rojas-Rivera D., Rodriguez D., Groenendyk J., Köhler A., Lebeaupin C., Ito S., Urra H., Carreras-Sureda A., Vasseur-Cognet M., Chevet E., Campos G., Godoy P., Vaisar T., Bailly-Maitre B., Nagata K., Michalak M., Sierralta J., and Hetz C. **(JS/CHz)** *Interactome screening identifies a novel function of the collagen chaperon Hsp47 as an adjustor of the unfolded protein response (UPR) transducer IRE1α.* ***Mol Cell.*** 69:238-252. *# (**Cover illustration**). Using proteomic screening and a functional validation in different models (in vitro and in vivo), we discovered that Hsp47 is part of a chaperone network that adjusts IRE1α signaling by fine-tuning the threshold to engage an adaptive or prosurvival unfolded protein response. This research opens the field connecting two pathways: Collagen biosynthesis and the UPR, giving some clues to the develop specific and new therapeutic interventions involving the UPR for the treatment of human diseases.
- González C, Cornejo VH**,** Couve A (2018). *Golgi bypass for local delivery of axonal proteins, fact or fiction?* ***Current Opinion in Cell Biology*** **(AC).** In this review we discuss about the presence of exocytic elements and examples of autonomous axonal trafficking that impact development and maintenance of peripheral and central axons. We also examine whether unconventional post-endoplasmic reticulum pathways may replace the canonical Golgi apparatus and their role in local trafficking of membrane proteins.
- Delgado MG, Oliva C, López E, Ibacache A, Galaz A, Delgado R, Barros LF, Sierralta J, *Chaski, a novel Drosophila lactate/pyruvate transporter required in glia cells for survival under nutritional stress*. ***Scientific Reports*** (Sci Rep). This article describes for the first time a lactate/pyruvate transporter in the Drosophila brain that is essential for locomotion and survival during starvation. This work will allow us to use Drosophila as a model to study brain metabolism since we were able to show similarities in the way Drosophila brain and mammalian brain metabolism works. *Annex 3.*

Publications: Summary Table

Category of Publication[1]	MSI Center Members	Number of Publications coauthored by students	Total Number of Publications
ISI/WOS Publications or Similar to ISI/WOS Standard	Associate Researchers	10	34
	Others Researchers	11	16
SCOPUS Publications or Similar to SCOPUS Standard	Associate Researchers	0	0
	Others Researchers	0	0
SCIELO Publications or Similar to SCIELO Standard	Associate Researchers	0	0
	Others Researchers	0	1
Scientific Books & Chapters	Associate Researchers	0	1
	Others Researchers	0	1
Other Scientific Publications	Associate Researchers	0	0
	Others Researchers	0	0
Total		21	53

Publications not informed in previous annual report.

Category of Publication[2]	MSI Center Members	Number of Publications coauthored by students	Total Number of Publications
ISI/WOS Publications or Similar to ISI/WOS Standard	Associate Researchers	1	4

[1] https://www.ncbi.nlm.nih.gov/pubmed/; https://scielo.conicyt.cl/
[2] https://www.ncbi.nlm.nih.gov/pubmed/; https://scielo.conicyt.cl/

Other achievements:

Like the previous years (2015-today) S Reyes has continued to lead our Neuromedicine and Technology Platform (NeuroTech). He as the head of Technology Transfer and Innovation continues to promote intellectual property protection, technology transfer, applied research, private fundraisings and collaboration with the central R&D office at U Chile.

Patents

As a result of the ongoing collaboration between our technology transfer specialist S Reyes and the central R&D office at U Chile one disclosure was filed during 2018: *Gene therapy that overexpresses the transcription factor of XBP1 reduces the alterations produced in Alzheimer's Disease*. Finally, the strategy was not to file a patent application as it interfered with claims of a prior technology.

Additionally, the first license option was signed with the Australian BravoBiotech company for the technology *Method for genetic treatment using the AAV-XBP1s/GFP virus and use thereof in the prevention and treatment of amyotrophic lateral sclerosis*.

Intellectual property

During 2018 we continued to protect the corporate image of BNI and a number of brands associated to the Institute. Our legal advisor J Díaz has efficiently led this process: BNI: after a legal dispute with an international private company that uses the same acronym of our institute's corporate name and logo, we have obtained the ownership for BNI brand in trademark category 41. Our argument was based on the different kinds of services that both institutions provide.

Congress presentations

During this fund period BNI investigator and their teams attended and presented their works in 99 national and international events. Their relevance and impact have been describedin the preceding *3a Current status of research lines*. See summary table below.

Presentations Summary Table

Type of Researcher	Type of presentation	National Events	International Events
Associate Researchers	Conferences, oral communications, poster communications, others (Specify)	26	14
	Invited presentations (not included in above row)	12	23
Other researchers	Conferences, oral communications, poster communications, others (Specify)	0	12
	Invited presentations (not included in above row)	7	0
Students	Conferences, oral communications, poster communications, others (Specify)	2	1
	Invited presentations (not included in above row)	1	1

Organization of Scientific Events

Meetings gathering Associated or all BNI investigators took place weekly or monthly respectively. These instances have been critical to exchange information of research lines and drive BNI's cross-disciplinary atmosphere into concrete collaborative projects. We organized regular seminars calls, *Conversations in Neuromedicine*, in topics that connect Neuroscience and medicine, and which include local and international speakers. A representative list of the topics done in 2018 is presented in the figure 1A. We also do a second kind of gathering call “Pizza talks” in were young scientist present their researches, creating an intimated environment in were we discuss their

results stimulating their scientific critical thinking and promoting their communication abilities (figure 1B). A representative poster of Pizza Talk 2018 is presented in figure 1B. Finally, this year we did a pilot of an aimed future program call *"BNI Transforma",* in which we develop a series of activities oriented to improve the capacities and abilities necessary for career development but that are not usually worked in labs o scientific meeting. The list of the four topics done in 2018 is presented in figure 1C.

Figure 1. Regular activities done by BNI. A-Sample of topics discussed at Neuromedicne Conversations series, B-Sample of topics discussed at Pizza talks events, C-Sample of topics discussed at BNI Transforma series.

As indicated in Networks, during 2018 we carried out another *NeuroSur* meeting, *Frontiers in Neurotechnology: A Latin American perspective* (dec 5th, 2018). In this symposium attended 12 international and 5 national speakers, a long with 64 participants. *NeuroSur* represents a collaborative network strategy between BNI and centers of excellence in Neuroscience in Latin America (Brazil, Argentina, Uruguay and Chile).

Figure 2. NeuroSur meeting, Frontiers in Neurotechnology: A latin American perspective. A-Poster of 2018 NeuroSur meeting, B-Organizers and speakers of to the event.

In order to reinforce the identity of the Institute and to promote the interaction between teams from different laboratories we organized a BNI retreat (Mantagua, Concon, Región de Valparaíso). Activities included the introduction *Science at BNI* by BNI Director **AC**, an *Interdisciplinary Science challenge* by **CHz**, short talks by students/postdocs to evaluate *Seed Grants*, a science-social activity *Table-Topics* to discuss relevant topics in science and social activities. More than 150 people participated in this 2-day retreat.

To browse through our extensive photographic record showing the exciting BNI atmosphere during scientific, innovation, education and outreach activities please visit:

https://www.facebook.com/pg/InstitutoBNI/photos/

Scientific Editorial Boards

During 2018 most of the BNI researchers took part in the editorial boards of high impact ISI standard journals. BNI researchers are editors of Frontiers in Synaptic Neuroscience (**AC**, Review Editor), Cell Death and Disease (**CHz**, Associate Editor), Cell Stress (**CHz**, Editor), Current Molecular Medicine (**CHz**, Associate Editor), Mechanisms of Development (**MC**, Editor), Open Behavioral Sciences Journal (**MC**, Editor), Frontiers in Integrative Neuroscience (**PM**, Review Editor), Asia-Pacific Psychiatry (**HS**, Editor), Biological Research (**SH, CH**, Editorial Board), Frontiers in Physiology (**CH,** Review Editor), Journal of General Physiology (**CH**, Editorial Advisory Board).

BNI Adjunct Investigators are currently part of editorial boards, as well: Frontiers in Psychiatry (PGaspar, Guest associate editor), Journal of Neurology, Neurosurgery and Psychiatry (JM Matamala), Frontiers in Systems Neuroscience (PDélano, Guest associate editor), Frontiers in Neurology (PDélano, Guest associate editor), Journal of Association for Research in Otolaryngology (Associate editor) and Scientific Reports (SMatus, Editorial board).

Additionally, PDelano is editor in the journal Revista Otorrinolaringología y Cirugía de Cabeza y Cuello, SCIELO standard.

Awards

During the ceremony of the 176th anniversary of U Chile 2018 BNI researchers received many awards because their contribution to research and high impact publication in journals that ranks in the top 6% of their discipline in 2017. "Extra-embryonic tissue spreading directs early embryo morphogenesis in killifish", in Nature Communications (**MC/SH**), "Directional asymmetry in the volume of the human habenula", disclosed in Brain Structure & Function Magazine (**MC/SH**), "Epigenetic editing of the Dlg4/PSD95 gene improves cognition in aged, Alzheimer's disease mice", disclosed in BRAIN Magazine (**SH**), "Drug repurposing to target proteostasis and prevent neurodegeneration: Accelerating translational efforts" disclosed in BRAIN Magazine (**CHz**) and "IRE1 signaling exacerbates Alzheimer's disease pathogenesis" disclosed in Acta Neuropathologica Magazine.

Additionally, **SH** was awarded in the same ceremony because his contribution to the value that university internationalization must play in the development of the University of Chile and the country and SH received a recognition for his FONDECYT fund for stand in the evaluation in 10% superior of the engineering study group 2 stands out "5D Image Processing and Physical Models for the Quantification of Cell Migration and Multicellular Architecture with 4-Lens Light Sheet Fluorescence Microscopy". Meanwhile, **CHz** received a recognition for his FONDECYT fund for stand in the evaluation in 8% superior or the biology study group 2 stands out "'Defining the role of ER stress signaling in C9orf72-mediated ALS", as well. Finally, Universidad de Chile recognized **CHz** for his contribution to protect his technology named "Uso de extractos de hojas Ugni Molinae silvestres en el tratamiento de las enfermedades asociadas a mal plegamiento proteico"

APaula-Lima received the award Adelina Gutiérrez. This award is given from the Chilean Science Academy to young women researchers up to 40 years old, Chilean or foreign with residence in Chile and with excellent academic research performance. This award was announced in June 2018.

We would like to mention that during 2018 the government of Chile called for a contest named "Ideas con Ciencia" which consisted in proposing ideas that will solve an actual problem for the Chilean society with innovative solution from the science (https://www.ideasconciencia.cl/) In spite of the fact that finally our proposal did not win, we are proud that our proposal "Registro único de pacientes afectados por enfermedades Neurodegenerativas" presented by VValenzuela (BNI postdoc) was within the finalists and it stood between the two better proposals in the Region Metropolitana.

4. Education and Capacity Building

a) Education and capacity building

During all years of operation, BNI has worked in the context of the U Chile, the main public educational institution in Chile, providing the largest and most diverse network of undergraduate and graduate programs in biomedical sciences, including Neuroscience. Currently, the Faculty of Medicine hosts 6 Ph.D. and 17 Master programs. In addition, BNI has strong research and teaching ties with other Faculties of the University such as the Faculties of Sciences, Engineering, Chemistry, and Pharmacology. BNI provides advanced training, supporting institutional efforts, in close interaction with central administration and the Faculty's authorities. BNI Investigators play a leading role in doctoral and master programs, chairing academic committees at the Medical, Chemical & Pharmaceutical Sciences, and Science Faculties, U Chile. BNI Investigators also organize Advanced Graduate Courses in Neuroscience and related disciplines, including Cognitive Neuroscience, Cell Physiology, Molecular Mechanisms of Neurodegenerative Disease, Molecular & Clinical Pharmacology, Topics in Biomedicine and Neuropsychopharmacology. Importantly, during 2018, our director has served as a member of the executive committee for the Ph.D. Program in Biomedical Sciences, the largest in the country. Also, **JS** (director) and PDélano and **JLValdés** (member) have served as members of the Masters in Neuroscience (**JS** Director); **SH** has served as director of the program in Medical Informatics. BNI scientists also participate in graduate programs in other Faculties at U Chile (Engineering & Mathematics, Chemistry & Pharmaceutical Sciences, Sciences Dentistry, and Veterinary) and programs in other universities in the metropolitan and regional areas. APaula-Lima was instrumental in the creation and management of the Ph.D.: Program in Odontology. Noteworthy, BNI was instrumental in the establishment of the new Department of Neuroscience at the Faculty of Medicine. Currently, 10 faculty members of this department are currently associated to BNI, furthermore principal investigator **PM** is serving as chair while deputy director **JS** is serving as co-chair.

Our Institute also provides a framework for several undergraduate and graduate students, carrying out their investigation units and thesis in one or several BNI labs. Furthermore, BNI facilities and equipment are available for faculty members and students of the Institute of Biomedical Sciences (ICBM) at large and associated clinical campuses. The focus is on education and capacity building, and in training neuroscientists involved in basic and clinical research. One main contribution is on medical specialties, contributing to the education of psychiatrists, neurologists, neuro-pediatricians, pharmacologists and other clinical specialties. Initiatives involve American Universities, such as Columbia, Harvard, USA and McGill Canada, University of Osaka, Japan as well as leading Universities and Institutes in the European Union: Gottingen, Heidelberg, Magdeburg, Mannheim Institute of Mental Health, Germany; Jülich Forschungszentrum, Germany; Cagliari University, Italy; Jaume I University, Castellon, Spain. International collaborations have provided a framework for research stays of graduate and associated scientists. A number of graduate students (>40students) are receiving full or partial stipends, easing their progress and completion of their doctoral programs. Furthermore, associated BNI scientists participate in multiple evaluation committees, warranting the excellence required by the graduate programs. Young scientists, especially from other institutions in Chile or abroad, holding a Ph.D. degree are invited to apply to BNI Bridge Fellowships twice a year (once last year). Eligibility includes a commitment to apply for a Fondecyt postdoctoral fellowship during the corresponding academic period. Applications are managed and reviewed by BNI scientists according to a protocol that emphasizes competitiveness and minimizes conflicts of interest. BNI provides both full postdoctoral fellowships through Bridge Fellowships and contributes indirectly to support other postdoctoral initiatives. The results of this program are summarized in the attached tables. This year

we granted three bridge-fellowships. This program has the ability to incorporate not only Chilean nationals but more than 5 international young scientists.

Also, we continue to run a funding program for students and postdocs named “Semilla” (seed), where they compete for BNI's funding of small projects to establish preliminary data or “proof of concept” of scientific ideas which may turn in full-fledged research projects and can be submitted to external granting agencies. The criteria to obtain such a grant include critically, a novelty aspect and the impact on collaborative efforts within BNI.

We also encourage the interaction of students with more than one laboratory and mentor, as a manner to enrich the opportunities and cross-fertilizing fields. During 2018, more than 10 theses were co-directed by BNI Investigators. Students are encouraged to share BNI facilities, educational and technology transfer opportunities. Postdocs, graduate, and undergraduate students take the initiative and organize regular seminars and symposium in the framework of BNI, inviting foreign established scientists, or national postdocs carrying out research periods abroad. Investigators, trainees, and staff attended our annual retreat as a means to share the research culture, which fosters a sense of belonging to a school of thought.

Photograph (above): The BNI team at the annual retreat in Mantagua.

b) Achievements and results

During 2018 almost 150 researchers worked in BNI, 10 adjunct investigators, 13 young investigators, 2 senior investigators, 16 undergraduate students, 24 master's students, 44 Ph.D. students, and 40 postdoctoral fellows. 12 of these students are jointly tutored by two or more BNI researchers. This body includes 6 international students from countries in South America and Europe, including Ireland, Germany, Venezuela, Netherlands, and Uruguay. This period, 11 students completed their dissertation work. Some these trainees have left BNI, continuing their careers paths in other national institutions or abroad, while others have stayed to pursue a higher

degree or a postdoctoral position. Many BNI papers are published with students as coauthors (21/53). BNI students also participate regularly in national and international meetings, in poster and oral sessions (99 this year: see *Congress Presentations summary table*).

BNI's support of students has allowed the completion of projects, smoothing transitions, supporting further students without additional fellowship support. As part of our aim to internationalize BNI, we also promoted international experience for our students. During this period 8 BNI students carried short term research and trainee periods abroad, which included research activities in Spain, Germany, Canada, New Zeland, and Australia. Additionally, we received five international students from Colombia and Germany who performed research at BNI labs. Also, we have run 21 national and 3 international seminars and courses that include several international students from the region.

As part of their comprehensive scientific training, more than 50 BNI students have also participated in outreach activities organized by BNI, such as visits to schools, in-lab training in our facilities, high students' guidance and our Loligo and Dendros initiatives.

c) **Destination of students**

BNI undergraduate and master students normally follow advanced studies (Ph.D., MD-PhD) or are directly involved in clinical research. Most BNI graduate students are recruited for scientific and academic careers, conducting research as postdoctoral fellows or faculty members in Chile or abroad. 5 students graduated during 2018, and five postdocs continued their scientific careers elsewhere, including academic positions in Chile and USA. Graduates have remained in science and academia. Also noteworthy is that many young investigators that were recruited as adjunct researchers (which include: JL Valdes, RFuentes, P Gaspar, S Matus, POlguin, and RVidal) continue to work in BNI. Last year we added one more adjunct researcher, Dr. P Délano.

5. Networking and other collaborative work

a) Networking

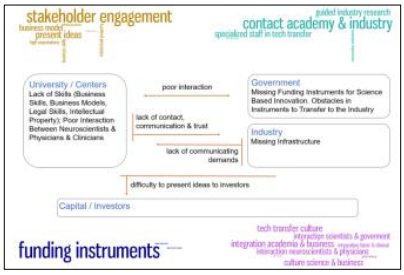
Scientific interactions within BNI, collaborative network formation and consolidation on a regional and international scale continuously mark BNI's working philosophy. In 2018, we pursue and deepen three strategic lines that operate successfully:

(i) Enhance the dynamics and quality of collaborative projects within BNI. We continue to support series of collaborative initiatives such as *Seed Grants* (4 in 2018), *Bridge Fellowships* (6 during 2018), and co-mentorship of students (6 during 2018). Internal seminars also are held every month where the different lines of research are presented to all members of BNI. BNI continuously supports co-application to external funding (e.g. Fondecyt grants and international grants, # national, # international grants and 2 Fondecyt initiation grants were awarded, sponsored by BNI during 2018)) by young investigator, and networking for science and innovation (e.g. PCI Conicyt and CORFO). Moreover, even outside a grant framework two high impact papers were published thanks to the collaboration between groups in BNI (Urra et al., 2018 and Sepulveda et al., 2018)

(ii) Foster scientific interactions within a multidisciplinary environment. BNI fosters a multidisciplinary environment by promoting regular scientific activities such as internal seminars with young speakers (1 per month), seminars with invited speakers (1 per month), international courses, workshops, and symposia (2-4 per year), as well as an annual BNI retreat. The BNI building connects BNI laboratories and becomes an important component of the F-Med and the Northern Campus of the University and is now fully accessible through the new metro station *Hospitales*. Together with the F Med Library and the *Public Library Pablo Neruda* of Independencia, the BNI building with its front garden has become an architectonical hallmark of the *Plaza Blest*, which

is presently under construction and will be open to the academic and student community during 2019. The 3rd floor of the BNI building is constantly used for vibrant science & coffee meetings and discussions. Regular and informal meetings take place in an open, friendly, and lively atmosphere: (i) the seminar room (max capacity 60 participants) is equipped with modern infrastructure and connectivity, and it is used on a daily basis. It provides an essential complementary working space, especially due to its flexible management by BNI for events after working hours and weekends, a service harder to obtain from the F Med due to regulations. The building continuously hosts students of the international Master for Medical Informatics (academic director **SH**), diploma, summer schools, participants of courses or events for continuous education, or outreach, etc; (ii) the Board meeting room (with video conference equipment and capacity for 12-14 participants) is used for group and lab meetings and strategic meetings with partners from associated scientific centers, projects, or industry. 19. In 2018, BNI investigators elaborated a concept for a new, common infrastructure of microscopic equipment within a new imaging facility which will be implemented in 2019 and amplifies the shared space for BNI scientists and groups.

(iii) Promote national and international scientific networks. Individual and collaborative multidisciplinary networks of BNI members consolidate over the years. Interest of Argentinan, Uruguayan, Brazilian, and Colombian facility leaders is expressed in invited talks (e.g. the 2018 Humboldt Kolleg ´Impact of Structural Biology and Bioimaging in Life Science´. Rio de Janeiro, 8–10.11.2018 with the exposition "From Scientific Imaging, Biomedical Imaging, to Medical Informatics, and Health Information Systems in Chile and the Region (**SH, MC, M Cerda**). The organization of advanced microscopy courses on a regional level (to be perfomed in March 2019 in Medellin, Co), or the organization of international facility meetings to foster innovation (to be performed 01.04.2019 in Santiago de Chile) within the context of the NeuroSur Network: Un cerebro para América Latina, an initiative created by BNI under the leadership of **AC** in 2018, and transferred to **R Fuentes** in 2019. In 2018, the general objective of the network was to improve the quality and impact of neuroscience research from 13 different Latin American centers and to maximize the use of their technological capacities through a network of integration and thematic cooperation. The NeuroSur network promotes scientific collaboration and exchange between countries in the region. In terms of transfer, the network's research results should also be focused on impact on the public and the private health systems. The program is focused to quantify the relevance and solve factors like (i) the lack of interaction with industry, (ii) funding shortfalls, (iii) lack of skills, knowledge and experience, (iv) interdisciplinary shortfalls, and (v) cultural barriers. Between 5-6.12.2018 the Symposium "*Frontiers in Neurotechnology - A Latin American Perspective*" and the coordination meeting of the NeuroSur network focused on "Technology Transfer Challenges in Latin America". 13 Scientists from 7 countries (AR, BR, ES, BO, PT, CL, VE) identified limiting factors for technology transfer and innovation. Factors could be sorted into four categories: skills, institutionality, culture and financing. In addition, limiting factors were related to different entities and the deficient relations between them (see figure).



To understand what competencies, have to be developed to close the gaps, a second innovation day is organized for 01.04.2019. The members of the network grew from 6 to 13 in 2018. According to our information, this meeting is the first to evaluate the importance of limiting factors in the region, and of relevant competencies that are needed for the creation of training programs. Results of the Neurosur Meetings and Workshops will be published in form of guidlines in 2019. In 2018, the *NeuroSur* initiative continued to promote state-of-the-art imaging technology and neuroscience

The network activities of CENS and the Center of Medical Informatics and Telemedicine (CIMT) are closely related to the BNI biomedical mathematics and informatics group (BioMat). The BNI network strategy is complemented by the internationalization activities performed with researchers from Latin America, EEUU, and Europe in the field of biomedical/medical informatics and telemedicine. In 2018, an academic internationalization symposium was organized by **SH**, in Santiago, and Concepción (November 2018). The meetings focus on novel scientific interactions and advanced human capital building towards an international PhD in Medical Informatics on the basis of the already established international Master in Medical Informatics within the BNI-BioMat group.

*Photographs: International Network for Biomedical / Medical Informatics Competencies organized by BNI-BioMat (**SH**) (left): participants of the Santiago Meeting at Heidelberg Center (12.12.2018) from Europe, Colombia, Honduras, Bolivia, Ecuador and the Head of DAAD-Chile (right): visits (14.12.2018, U-Concepción).*

In 2018, BNI researchers continued interactions with scientific, clinical and governmental institutions such as CINV, ISCI, CMM, FONDAP-GERO, NLHPC, REUNA, MINSAL, INC, HCUCH, Clínica Alemana, CLC, and Neurounion. Interactions with clinicians continue through our Basic-Clinical network *Encounters*, although no formal meetings were held during 2018. New impact on clinical data science and management in terms of interoperability within the national health system is fostered by CIMT and CENS (**SH**, see above). CIMT/CENS associate private and public institutions (MINSAL, FONASA, Rayen, Intersystems, Christus Health, and ITMS), and support the public and the private health sector in Chile with topics on international interoperability standards, observatory on *e*-health, consulting, and formation of advanced human capital. Both centers have improved infrastructure within the perimeter of the BNI building.

Two of our formal networks, *Network for Advanced Microscopy and Quantitative Developmental Biology* as well as the International Course *Small Brains Big Ideas* are been organized to be held on the end of March-April 2019, both of them will be financed partially by EMBO. Small Brains is an international course co-organized with the CINV in which 27 students from Colombia, Perú, Ecuador, Brazil, Uruguay and Argentina as well as Chile have been accepted. Support from IBRO and Company of Biology is also secured. Promoted by **JS** the first Chilean *Drosophila* meeting took place at the BNI building. The objective is to form a network of Chilean Drosophila researchers that would promote sharing reagents and expertise with the goal of support young investigators and promote the use of the Drosophila model in Chile. ***Annex 6.1.***

b) Other collaborative activities.

Deeper integration of *e*-health related data science by BNI BioMat, also participated in new summer/winter school *La Serena School for Data Science: Applied Tools for Data-Driven Sciences*, at the interphase of health science, biomedicine, and astronomy. In 2018, (**SH/M Cerda**) performed the second out of five common winter schools within this NSF founded collaborative initiative. La Serena Schools take place annually in August on the AURA Observatory campus in La Serena, Chile, with approximately 30 students from different disciplines including astronomy, computer science, statistics, mathematics, life science, biomedicine, or medicine, from Chile and the USA. In 2018, we further promoted the development of academic careers within the BioMat-disciplines within German-Chilean Center of Excellence for Innovative Research and Education in Medical

Informatics (DAAD 57220037) with U Heidelberg, and the Chilean Interoperability and Process Challenge CHIP (DAAD 57168868) with U Heilbronn/U de la República (Uruguay), with workshops and scientific symposia. BNI participated in the 2018 version of the Antofagasta Science Festival Puerto de Ideas which seeks to contribute to the consolidation of Antofagasta as the city of scientific dissemination par excellence in Chile and to promote the idea that science is everywhere, and that It is not the privilege of scientists or scholars. A. Couve and S. Matus of BNI were part of the Foundation Puerto de Ideas, who runs the Festival. They were instrumental in organizing and suggesting participants for the program. In addition, BNI area of Education participated in presenting our Dendros Platforms. This year we presented Dendros: a journey through the brain. In this platform, we display video games that teach while we entertain. We also display a stand with "Play-Doh and the mystery of a neuron: Create your own version of a neuron with the fun Play-Doh cakes" and Displayed tissues and nerve cells in this fantastic installation of virtual microscopy.

Also, last year we established a joint program with the The Chilean Corporation of Video and Electronic Arts CChV which aim to work for a professional context for training, research, production, dissemination, and exchange of video art and media arts, creating under this eaves the Video and Media Arts Biennial , today Biennial of Medial Arts of Chile BAM. This year we created a Residence program which started with the Infraleve residence. This residence was proposed as a hybrid meeting place between artists and scientists, where experimentation and research between both disciplines seek to generate new relationships, exchanges, and spaces of knowledge in order to generate new knowledge and/or sensitive experiences. The artist Uwe Smith is the first resident of this instance. Through first approaches and conversations with BNI scientists, a consensus was reached that their research will be focused on infrasound. The purpose of this research is to re-value the old vision of seeing music as a scientific-artistic relationship. For this and as a result of the residency, the creation of interdisciplinary work in sound installation format is proposed. This work will be shown at the 14th Medial Arts Biennial of Santiago and it is expected to become a new milestone in the relationship between the arts and sciences.

Among the multiple spheres of the society with which BNI interacts, since 2016 we have received the support from Ministry of Foreign Affairs of Chile, especially throught the Dirección de Energía, Ciencia y Tecnología e Innovación (DECYTI) in each Neurosur meeting we have organized. They have supported us with a Camaraderie Reception in its roof terrace in the historical building next to Palacio de la Moneda, our president's house. There scientists, national and from Latin-American countries, attendees to our Neurosur meeting, have found a place where to discuss in an informal environment about science, society, culture and how to improve their research and connect it with high impact in public policies. ***Annex 6.2***.

5. Outreach and connections with other sectors

a) Outreach

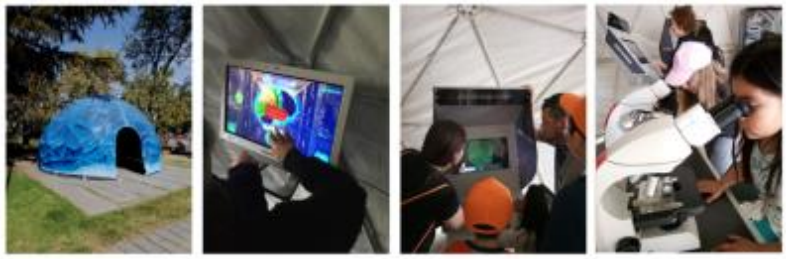
Our institute continues to develop its outreach program through two areas, education and out-of-school science activities. The education program called "Mentes Transformadoras" includes workshops for biology teachers, open labs for school students, a science book and an education conference for teachers. The out-of-school initiatives include a neuroscience web comic, games and a traveling exhibit with games and experimental hands-on activities. All the digital resources are available in our new web platform www.loligo.cl.

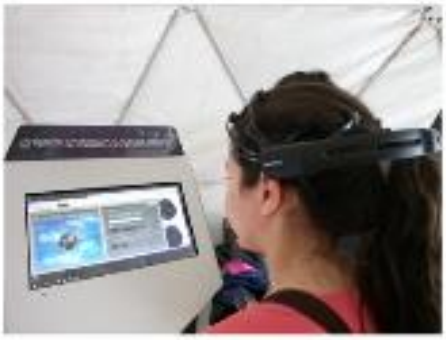
Mentes Transformadoras: Education program: During 2018 we did 8 workshops to trained high school teachers to use our digital material along with inquiry-based activities to teach biology. The digital resources were produced by Biointeractive – Howard Hughes Medical Institute, an institution that collaborates with us since 2016. These resources are available in our platform www.loligo.cl/educacion. We have worked with 500 teachers so far, reaching more than 5.000 students. To deepen our contribution to science education we organized the first Metting for High School Science Teachers, which during a 3-day conference, we offered workshops, seminars and discussion panels about educational policies. 160 teachers from all the country participated.

During 2018 we invited 6 schools to visits our labs. Students from primary, middle and high school had a chance to see and do experiments in several labs, getting them closer to what neuroscientists do. This activity involves many PhD students from our institute, who enjoy doing this "open lab" activity once a month.

Mundo dendros: out-of-school science: We created a new chapter for our web comic dendros, available in our platform www.loligo.cl/dendros. Including new topics on neuroscience like "brain-machine interfaces". The neuropacman game was also updated, including additional brain areas like the hippocampus and new challenging questions.

Our brain dome traveling exhibits received around 40,000 visitors during 2018. We included a new activity, a wireless EEG brain monitoring. Visitors interact with a computer simulation to command actions through their "minds". The brain dome participated in several scientific events like: Festival Puerto de Ideas - Antofagasta, Planetario de Santiago, Fiesta de la Ciencia Explora and Festival de Ciencias de Ingeniería.





b) Connections with other sectors.

According to our proposal for the second five-year period (2016-2021), during 2016 we launched the new *Applied Neuromedicine & Technology Platform*, which aims at establishing an effective connection with Chilean companies and the emerging biomedical industry in the country. This new area of BNI is led by innovation specialist S Reyes. Results of 2018 include signing two new research contracts in the field of occupational diseases (Asociación Chilena de Seguridad, ACHS) and labor fatigue prevention (Neurotechnia).

During 2018, we consolidated collaboration with specialized research centers in other sectors of the economy through a memorandum of understanding (MOU) to execute projects together with the industry. Two MOU were signed with ISCI (retail and transport sector) and SMI-ICE-Chile (mining sector).

Private initiatives are ongoing or were completed during this period. Research contracts with industry (ACHS and Cellus) provide scientific support for telemedicine and stem cell research. Strong links of collaboration and trust were established with the companies and the overall perception of the interaction with BNI has been positive.

BNI is member of the Know-Hub Chile project, a group of Chilean universities and research centers. This off-campus platform focuses on international transfer of national technologies.

Press coverage of the institute's activities has firmly established BNI as a reference center in Chile and Latin America. BNI press appearances were valued in an outstanding $1.037.613 USD, with 91 appearances in newspapers, 3 in weekly magazines, 57 online, 9 on radio, and 7 on television which sum 44 minutes valorized in $ 321.303.556 US$.

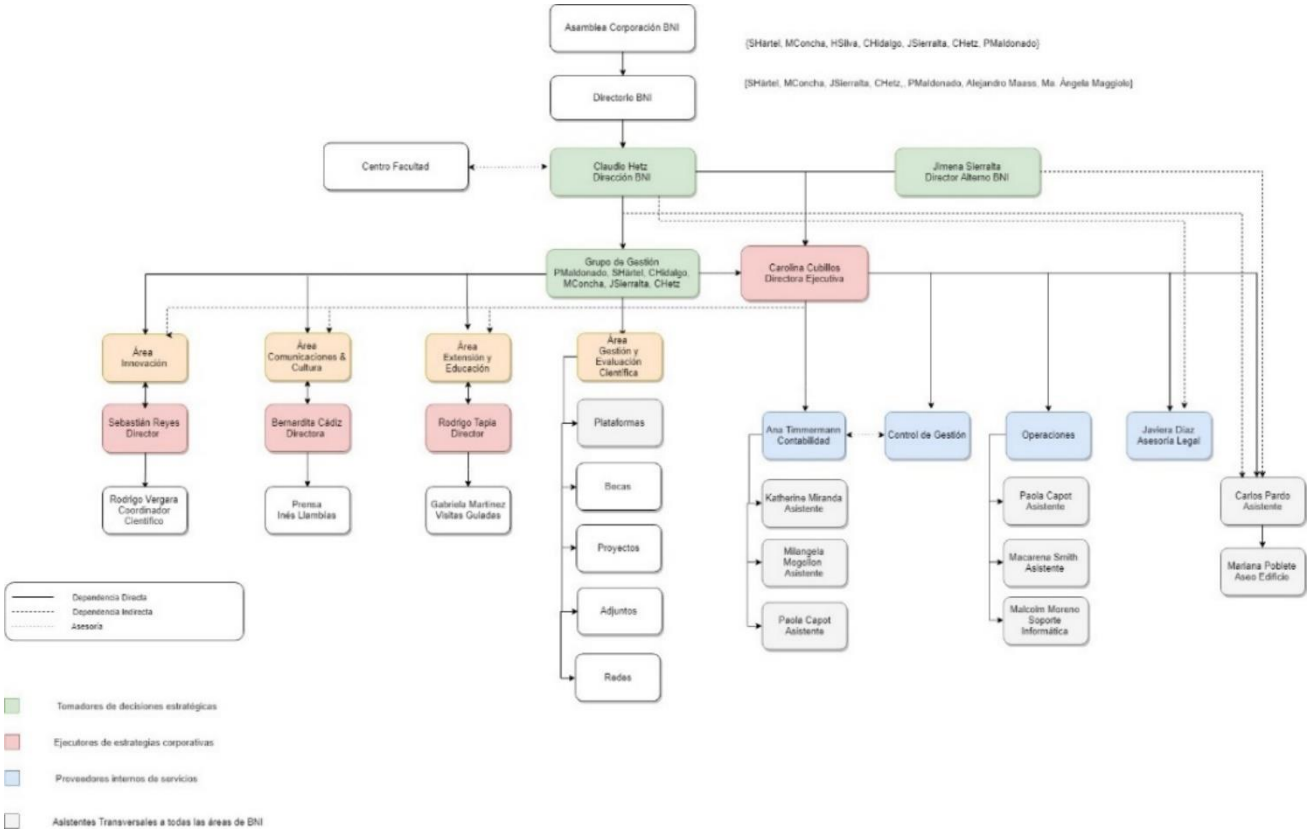
6. Administration and Financial Status

a) Organization and administration.

BNI is a non-profit organization (RUT 65.059.721-4) and fulfills all legal requirements of the Ministry of Justice and the Municipalidad de Independencia. During December 2018 **AC** (Pres) was named Minister of Science, Technology, Innovation, and Knowledge of the Chilean Government. Because of that, he must quit in December 2018. On an extraordinary Directory board meeting in December 2018, **CHz** was elected as President and **JS** elected as Vice-president of the BNI Corporation. **SH** was also incorporated as Director of the Current Board which also includes between its members: **MC** (Sec), **PM** (Dir), A Maass (F Mathematical and Physical Sciences and Center for Mathematical Modelling, U Chile), and M Maggiolo (Vice-Dean, F Med U Chile).

Different areas continue to cover by professional staff with specialized responsibilities that provide continuity to our initiative. R Tapia, biochemist and BNI's artist in residence leads an established outreach and education program, Loligo (www.loligo.cl). S Reyes focuses on applied projects, innovation, fundraising, and technology transfer. This year we have hired a young scientist R Vergara for the Innovation area who supports S Reyes in many scientific aspects of applied technologies. The Executive Office continues to lead by C Cubillos, an economy, and finance professional who focuses on BNI administration, production of scientific events and group managing. Since June B Cadiz, a young scientist trained in neurosciences, has been working with us focuses on web, social networks, internal cohesion, connections with high-school students combining scientific and media expertise and started to focus on Cultural field and connections between science, art, and society. J Díaz, an experienced lawyer provides legal assistance. The Grant Management Office is constituted by A Timmermann, two assistant accountants, K Miranda and M Mogollón, and informatics expert M Moreno. Our monthly financial reports to the Ministerio de Economía continue to be of the highest quality. C Pardo is Assistant to the Director and manages the BNI building. N Vásquez, graphic designer, and I Llambías, journalist, contribute to consolidate BNI's corporate image and promote its activities. BNI staff work closely with administrative and technical personnel of all research groups.

Category	Female	Male	TOTAL
Assistant & Technicians	35	23	58
Administrative Staff	13	9	22
TOTAL	**48**	**32**	**80**



b) Financial Status.

Item	2018 Expenses [$]			
	Operative	**Networks**	**Outreach**	**Total**
Honoraria researchers and research personnel	501.481.831	0	0	501.481.831
Tickets and travel expenses	49.223.572	0	0	49.223.572
Materials and supplies	171.966.585	0	0	171.966.585
Goods and equipment	54.455.754	0	0	54.455.754
Infrastructure	6.140.875	0	0	6.140.875
Administrative expenses	63.718.202	0	0	63.718.202
Publications and subscriptions	9.572.614	0	0	9.572.614
Consultancies	37.836.591	0	4.594.387	42.430.978
Overhead	26.700.000	0	0	26.700.000
Others	7.210.041	0	9.879.187	17.089.228
Total	**928.306.065**	**0**	**14.473.574**	**942.779.639**

Annexes

Annex 1.- Institute Researchers

1.1 Associate Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Andrés Oscar Couve Correa	RL1 Sub-cellular functional dynamics. RL4 Plasticity and behavior. RL7 Applied mathematics and biomedical informatics. RL8 Neuropathology.	Chilean	M	23/10/1968	Biologist	D	Universidad de Chile	Full Professor	Full Time
Jimena Sierralta Jara	RL1 Sub-cellular functional dynamics. RL2 Cellular identity and morphology. RL8 Neuropathology.	Chilean	F	12/09/1962	Biochemist	D	Universidad de Chile	Full Professor	Part Time
Steffen Härtel Gründler	RL1 Sub-cellular functional dynamics. RL2 Cellular identity and morphology. RL3 Supra-cellular development and circuits. RL7 Applied mathematics and biomedical informatics. RL8 Neuropathology.	Alemán	M	24/11/1968	Physicist	D	Universidad de Chile	Full Professor	Part Time
Pedro Esteban Maldonado Arbogast	RL5 Systems Neuroscience. RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	30/04/1960	Biologist	D	Universidad de Chile	Full Professor	Part Time
Claudio Andrés Hetz Flores	RL1 Sub-cellular functional dynamics . RL2 Cellular identity and morphology. RL4 Plasticity and behavior. RL5 Systems Neuroscience. RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	24/03/1976	Biotechnologist	D	Universidad de Chile	Full Professor	Part Time
Miguel Concha Nordemann	RL2 Cellular identity and morphology. RL3 Supra-cellular development and circuits. RL7 Applied mathematics and biomedical informatics. RL8 Neuropathology.	Chilean	M	06/03/1966	Physician	D	Universidad de Chile	Full Professor	Part Time

1.2 Young Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Tatiana Adasme Rocha	RL5 Systems Neuroscience. RL4 Plasticity and behavior.	Chilean	F	21/02/1977	Biochemist	D	Universidad Bernando O'Higgins	Researcher at CIBQA.	Part Time
José Ignacio Egaña Tomic	RL6 Clinical studies. RL5 Systems Neuroscience.	Chilean	M	09/10/1973	Physician	D	Universidad de Chile	Assistant Professor	Part Time
Danilo Bilches Medinas	RL8 Neuropathology.	Brazilian	M	23/11/1981	Chemist	D	BNI / U de Chile	Staff Scientist BNI	Part Time
Víctor Antonio Castañeda Zeman	RL7 Applied mathematics and biomedical informatics. RL2 Cellular identity and morphology.	Chilean	M	29/08/1980	Engineering	D	Hospital Clínico Universidad de Chile	Young Reseacher	Part Time
Rodrigo Montefusco Siegmund	RL5 Systems Neuroscience. RL4 Plasticity and behavior.	Chilean	M	01/02/1980	Biochemist	D	Universidad de Chile	Young Researcher Neurosystem Lab	Full Time
Claudia Durán Aniotz	RL4 Plasticity and behavior. RL8 Neuropathology.	Chilean	F	01/04/1982	Biologist	D	BNI / U de Chile	Staff Scientist BNI	Full Time
Gabriela Martinez	RL4 Plasticity and behavior.	Chilean	F	01/04/1983	Biologist	D	Universidad de Chile	Postdoc Hetz Lab	Full Time
German Flavio Reig Cardarella	RL3 Supra-cellular development and circuits.	Argentinean	M	23/08/1976	Agronomist	D	Universidad de Chile	Young Researcher Leo Lab	Full Time
Felipe Salech	RL6 Clinical studies.	Chilean	M	22/05/1981	Physician	D	Facultad de Medicina Universidad de Chile	Young Researcher Couve Lab	Part Time
María Gabriela Mercado Guerra	RL8 Neuropathology.	Chilean	F	29/03/1981	Molecular biotechnology engineering	D	Universidad de Chile	Young Researcher Hetz Lab	Full Time
Enzo Brunetti	RL5 Systems Neuroscience.	Chilean	M	07/01/1975	Physician	D	Hospital Clínico Universidad de Chile	Resident in Neurology	Part Time
Christ Devia Manriquez	RL5 Systems Neuroscience.	Chilean	F	03/10/1982	Engineering	D	BNI / U de Chile	Staff Scientist BNI	Full Time
German Flavio Reig Cardarella	RL3 Supra-cellular development and circuits.	Argentinean	M	23/08/1976	Agronomist	D	Universidad de Chile	Young Researcher Leo Lab	Full Time

1.3 Senior Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
María Cecilia Hidalgo Tapia	RL4 Plasticity and behavior. RL1 Sub-cellular functional dynamics. RL5 Systems Neuroscience. RL6 Clinical studies. RL7 Applied mathematics and biomedical informatics. RL8 Neuropathology.	Chilean	F	10/06/1941	Biochemist	D	University of Chile	Full Professor	Part Time
Hernán Silva Ibarra	RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	01/07/1949	Psychiatrist	D	Psychiatry and Mental Health, Faculty of Medicine, Universidad de Chile	Full Professor	Part Time

1.4 Others

1.4.1 Adjunct Researchers

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
José Luis Valdés Guerrero	RL4 Plasticity and behavior. RL5 Systems Neuroscience. RL6 Clinical studies.	Chilean	M	16/12/1975	Biologist	D	Universidad de Chile	Assistant Professor	Part Time
Andrea Paula-Lima	RL4 Plasticity and behavior. RL8 Neuropathology. RL6 Clinical studies.	Brazilian	F	20/11/1977	Chemist Pharmaceutical	D	Universidad de Chile	Assistant Professor	Part Time
Patricio Alejandro Olguín Aguilera	RL1 Sub-cellular functional dynamics . RL8 Neuropathology. RL2 Cellular identity and morphology. RL3 Supra-cellular development and circuits.	Chilean	M	23/10/1975	Biochemist	D	Universidad de Chile	Assistant Professor	Part Time
Pablo Gaspar	RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	20/08/1975	Physician	D	Universidad de Chile	Assistant Professor	Part Time

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
René Vidal	RL8 Neuropathology. RL6 Clinical studies.	Chilean	M	03/05/1979	Biochemist	D	Universidad Mayor	Biochemical PhD in Sciences	Part Time
Soledad Matus	RL6 Clinical studies. RL8 Neuropathology.	Chilean	F	23/06/1974	Biochemist	D	Fundación Ciencia & Vida	Principal investigator of the laboratory of Biology of Neurodegeneration	Part Time
Mauricio Cerda Villablanca	RL7 Applied mathematics and biomedical informatics. RL3 Supra-cellular development and circuits. RL8 Neuropathology.	Chilean	M	23/11/1982	Computer Sciences	D	Universidad de Chile	Assistant Professor	Part Time
Rómulo Antonio Fuentes Flores	RL5 Systems Neuroscience. RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	28/10/1974	Biochemist	D	Universidad de Chile	Assistant Professor	Part Time
José Manuel Matamala Capponi	RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	13/11/1983	Physician	D	Neurology Sciences Department, Faculty of Medicine, University of Chile	Neurology Assistant Professor	Part Time
Paul Délano	RL5 Systems Neuroscience.	Chilean	M	06/02/1976	Physician	D	Universidad de Chile	Associate Professor	Part Time

1.4.2 Postdocs

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Carolina Blanca González Silva	RL1 Sub-cellular functional dynamics .	Chilean	F	01/11/1982	Biotechnologist	D	Universidad de Chile	Postdoc Couve Lab	Full Time
Rodrigo Clemente Vergara Ortúzar	RL5 Systems Neuroscience.	Chilean	M	23/11/1986	Biologist	D	Universidad de Chile	Postdoc Neurosystem's Lab.	Full Time
María de los Ángeles Juricic	RL5 Systems Neuroscience.	Chilean	F	02/10/1983	Biochemist	D	Universidad de Chile	Postdoc Neurosystem's Lab.	Full Time
Eduardo Pulgar	RL2 Cellular identity and morphology. RL7 Applied mathematics and biomedical informatics.	Chilean	M	23/10/1981	Biochemist	D	Universidad de Chile	Postdoc Scian Lab.	Full Time

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Violeta Chang Camacho	RL7 Applied mathematics and biomedical informatics.	Peruano	F	20/11/1977	Computer Sciences	D	Universidad de Chile	Postdoc Scian Lab.	Part Time
Amado Carreras Sureda	RL8 Neuropathology.	Spanish	M	25/06/1986	Biologist	D	Universidad de Chile	Postdoc Hetz Lab	Full Time
Víctor Hugo Cornejo Corona	RL1 Sub-cellular functional dynamics .	Chilean	M	31/03/1989	Science Degree	D	Universidad de Chile	Postdoc Couve Lab	Full Time
Alejandro Ernesto Luarte Navarro	RL1 Sub-cellular functional dynamics .	Chilean	M	22/01/1984	Biochemist	D	Universidad de Chile	Postdoc Couve Lab	Full Time
Andrés Enrique González Gutiérrez	RL2 Cellular identity and morphology.	Chilean	M	07/07/1979	Biochemist	D	Universidad de Chile	Postdoc Sierralta Lab.	Full Time
Esteban Contreras Sepúlveda	RL1 Sub-cellular functional dynamics .	Chilean	M	10/05/1984	Biochemist	D	Universidad de Chile	Postdoc Sierralta Lab.	Full Time
Patricio Ahumada Galleguillos	RL3 Supra-cellular development and circuits.	Chilean	M	06/05/1979	Biologist	D	Universidad de Chile	Postdoc Leo Lab.	Full Time
Almudena Laliena Izquierdo	RL8 Neuropathology.	Spanish	F	19/02/1985	Biologist	D	Universidad de Chile	Postdoc Leo Lab.	Full Time
Karina Palma	RL2 Cellular identity and morphology.	Chilean	F	10/08/1979	Veterinarian	D	Universidad de Chile	Postdoc Leo Lab.	Full Time
Carmen Gloria Lemus Cortes	RL3 Supra-cellular development and circuits.	Chilean	F	25/02/1980	Biologist	D	Universidad de Chile	Postdoc Scian Lab.	Full Time
Gonzalo Olivares Herane	RL2 Cellular identity and morphology.	Chilean	M	11/02/1978	Biochemist	D	Universidad de Chile	Postdoc Lab. Patricio Olguín	Full Time
Paula García	RL8 Neuropathology.	Spanish	F	18/12/1981	Biochemist	D	Universidad de Chile	Postdoc Hetz Lab	Full Time
Alexis Alfonso Rivas Ahumada	RL8 Neuropathology.	Chilean	M	30/03/1981	Biochemist	D	Universidad de Chile	Postdoc Hetz Lab	Full Time
Hery Urra	RL8 Neuropathology.	Chilean	M	13/02/1984	Biochemist	D	Universidad de Chile	Postdoc Hetz Lab	Full Time
Felipe Cabral Miranda	RL4 Plasticity and behavior. RL5 Systems Neuroscience.	Brazilian	M	14/09/1987	Biotechnologist	D	Universidad de Chile	Postdoc Hetz Lab	Full Time
Vicente Spiro Valenzuela Paterakis	RL8 Neuropathology.	Chilean	M	08/07/1983	Biotechnologist	D	Universidad de Chile	Postdoc Hetz Lab	Full Time
Janina Edith Borgonovo Grosso	RL8 Neuropathology.	Argentinean	F	14/02/1978	Biochemist	D	Universidad de Chile	Postdoc Leo Lab.	Full Time
Paulina Falcón Urrutia	RL8 Neuropathology.	Chilean	F	05/10/1987	Biotechnologist	D	Fundación Ciencia & Vida	Postdoc Soleda Matus Lab.	Full Time

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Yannis Gerakis	RL8 Neuropathology.	Francés	M	22/03/1989	Biotechnologist	D	Universidad de Chile	Postdoc Hetz Lab.	Full Time
Philippe Pihán	RL8 Neuropathology.	Chilean	M	04/06/1986	BioEngineering	D	Universidad de Chile	Postdoc Hetz Lab.	Full Time
Jorge Alejandro Toledo Hernandez	RL7 Applied mathematics and biomedical informatics.	Chilean	M	31/07/1984	Biochemist	D	BNI	Postdoc Scian Lab.	Full Time
Margarita Bórquez Quintas	RL5 Systems Neuroscience.	Chilean	F	28/02/1979	Psichology	D	BNI	Postdoc JLValdés Lab.	Full Time
Andrea González Zúñiga	RL3 Supra-cellular development and circuits.	Chilean	F	14/09/1983	Biochemist	D	BNI	Postdoc LEO Lab.	Full Time
Younis Mohammad Hazari	RL8 Neuropathology.	Indian	M	22/05/1984	Biochemist	D	Universidad de Chile	Postdoc Hetz Lab.	Full Time
Nancy María Farfán Troncoso	RL3 Supra-cellular development and circuits.	Chilean	F	12/09/1984	Biochemist	D	BNI	Postdoc LEO Lab.	Full Time
Alexis Martínez Saavedra	RL8 Neuropathology.	Chilean	M	20/06/1984	Biochemist	D	BNI	Postdoc Hetz Lab.	Full Time
Alicia Ivonne Figueroa Barra	RL6 Clinical studies.	Chilean	F	27/02/1971	Education degree	D	BNI	Postdoc Psiquis Lab.	Full Time
Alfredo Sagredo Campos	RL1 Sub-cellular functional dynamics .	Chilean	M	02/07/1986	Medical Technologist	D	Universidad de Chile	Postdoc Hetz Lab.	Full Time
Karla Margarita Padilla Olvera	RL1 Sub-cellular functional dynamics .	Mexican	F	25/06/1988	Food Chemical Engineer	D	BNI	Postdoc Couve Lab	Full Time
Pablo Felipe Báez Benavides	RL7 Applied mathematics and biomedical informatics.	Colombian	M	08/06/1985	Microbiologist and Bioanalyst	D	BNI / U de Chile	Postdoc Scian Lab	Full Time
Cristóbal Matías Moenne Vargas	RL7 Applied mathematics and biomedical informatics.	Chilean	M	03/01/1985	Computer Sciences	D	BNI / U de Chile	Postdoc Controlmotor & Neuromodulation lab	Full Time
Nicolás Leonardo Fuenzalida	RL4 Plasticity and behavior.	Chilean	M	01/04/1986	Biochemist	D	BNI / U de Chile	Postdoc LEO Lab.	Full Time
Emilio Ernesto Méndez Olivos	RL3 Supra-cellular development and circuits.	Chilean	M	24/09/1987	Biochemist	D	BNI / U de Chile	Postdoc LEO Lab.	Full Time
David Hernán Aguirre Padilla	RL8 Neuropathology.	Chilean	M	05/10/1983	Physician	D	U de Chile	Postdoc	Part Time
Chama Belkhiria Belkhiria	RL5 Systems Neuroscience.	Tunisian	F	05/08/1987	Physiologist	D	U de Chile	Postdoc Délano Lab	Full Time
Rosana del Valle Muñoz Videla	RL2 Cellular identity and morphology.	Argentinean	F	07/02/1974	Biologist	D	U de Chile	Postdoc LEO Lab.	Full Time

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

Annex 2.- Research Lines

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date
1	RL1 Sub-cellular functional dynamics	To understand how the dynamic structures of the secretory pathway and the cytoskeleton are organized, and how this organization affects neuronal function	Differentiation and maintenance of neural structure and function throughout the life of the organism requires an asymmetrical organization of intracellular components within neurons and glia Thus, it is fundamental to understand how the dynamic structures of the secretory pathway and the cytoskeleton are organized, and how this organization affects neuronal function We analyze subcellular components in vivo and in cultured neurons using transgenic mice, rat peripheral nerve, and Drosophila motoneurons We combine genetic screens, genetic manipulation and high spatio-temporal resolution fluorescent microscopy to investigate the role of the endoplasmic reticulum and other organelles in local trafficking in long axons, and the consequences of altered organelle structure or loss of function of specific genes in neuronal protein trafficking, protein folding and calcium dynamics in normal animals and in models of human disease (AC/CH/CHz/JS/SH/P Olguín)	Alejandro Luarte, Carolina González, Claudio Hetz, Andrés Couve, Steffen Härtel, Cecilia Hidalgo, Jimena Sierralta, Patricio Olguín, Karla Padilla, Víctor Cornejo, Esteban Contreras, Alfredo Sagredo	Biofísica, Biología celular, Bioquímica, Fisiología biofísica, , Biotecnología, Genética y evolución	01/07/2016	
2	RL2 Cellular identity and morphology	To understand how gene expression determines morphofunctional features during development and the lifespan of neurons	Morpho-functional features of differentiated neurons define a structural backbone upon which connectivity is established, determining how electrical signals are shaped to integrate them into sophisticated computational-like devices and produce cell-to-cell communication Neuronal morphogenesis is intimately linked to the control of cell specification and differentiation A central question is how gene expression determines morphofunctional features during development and the lifespan of neurons We use fluorescent microscopy, mathematical analysis of neurons and circuits, morphological-features and genetic/genomic approaches in Drosophila (genetic alteration of specific group of neurons), mice (in utero electroporation of siRNA) and zebrafish (focal electroporation of morpholino antisense oligonucleotides in the embryonic brain) to investigate genetic and epigenetic (chromatin remodeling) mechanisms involved in this process (JS/CHz/MC/SH/MK/P Olguín)	Andrés González, Gonzalo Olivares, Víctor Castañeda, Claudio Hetz, Steffen Härtel, Jimena Sierralta, Rosana Muñoz, Eduardo Pulgar , Karina Palma , Miguel Concha, Patricio Olguín,	Biología celular, Bioquímica, Biotecnología, Física, Biofísica, Fisiología biofísica	01/07/2016	

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date
3	RL3 Supra-cellular development and circuits	To understand how gene activity and mechanical forces control the process of brain morphogenesis that involves the formation of multi-cellular neuronal aggregates and the establishment of neuronal connectivity, among other cellular processes and how interaction among cells and their connectivity patterns modulate the shaping of developing circuits	Brain morphogenesis involves the formation of multi-cellular neuronal aggregates and the establishment of neuronal connectivity, among other cellular processes How this is achieved in vivo is still poorly understood Central questions are how gene activity and mechanical forces control these processes, and how interaction among cells and their connectivity patterns modulate the shaping of developing circuits We use recent advancements in genetics, laser microscopy, image analysis and modeling in zebrafish and Drosophila, to study: (i) the interplay of genetic and physical determinants that control processes of collective cell migration and epithelial morphogenesis underlying the formation and shaping of multi-cellular aggregates (MC/SH/M Cerda/P Olguín); and (ii) the genetic/cellular mechanisms that break the initial morphological symmetry of the brain and then propagate asymmetric patterns of cell identity and connectivity within developing circuits (MC/SH/M Cerda)	German Reig, Andrea González, Nancy Farfán, Steffen Härtel, Mauricio Cerda, Carmen Lemus, Patricio Ahumada, Miguel Concha, Patricio Olguín, Emilio Méndez, ,	Álgebra, Biología celular, Análisis de Señales, , Biofísica, Bioquímica, Métodos numéricos y computación, Ingeniería electrónica, Física, Otras especialidades de la física, Biología del desarrollo, Biología molecular	01/07/2016	
4	RL4 Plasticity and behavior	To analyze the role of activity-induced calcium release on mitochondrial function and calcium signal propagation to the nucleus to control gene expression To study spatial memory in aged rats and in rodent models of Alzheimer's disease To analyze whether stress responses (ROS and protein misfolding) alter cell physiology leading to defective neuronal function , and the role of transcription factors involved in protein folding stress responses in learning and memory processes	Hippocampal synaptic plasticity is an activity-dependent neuronal response associated with learning and memory that entails significant modifications in the efficacy of synaptic transmission We recently found that endoplasmic reticulum-mediated calcium release is essential for hippocampal synaptic plasticity and spatial learning We analyze the role of activity-induced calcium release on mitochondrial function and calcium signal propagation to the nucleus to control gene expression, using primary hippocampal neurons and slices from young and old animals We also study spatial memory in aged rats and in rodent models of Alzheimer's disease, both of which display increased reactive oxygen species (ROS) generation and anomalous calcium release (CH/AC/JL Valdés/A Paula-Lima) We also analyze whether stress responses (ROS and protein misfolding) alter cell physiology leading to defective neuronal function (CH/CHz), and the role of transcription factors involved in protein folding stress responses in learning and memory processes (CHz)	Cecilia Hidalgo, Felipe Cabral, Claudia Durán Aniotz, Rodrigo Montefusco, Gabriela Martinez, Claudio Hetz, Andrés Couve, Tatiana Adasme, José Luis Valdés, Andrea Paula-Lima , Nicolás Fuenzalida	Biología celular, Biología molecular, Fisiología biofísica, Biología del desarrollo, Histología, Morfología	01/07/2016	

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date
5	RL5 Systems Neuroscience	To incorporate behavioral testing and benchmarks of neurodegenerative disease (CHz/PM/R Fuentes) and measure behavioral consequences of modifying cellular calcium signaling on learning and memory tasks	To understand the neuronal mechanisms involved in cognitive function it is fundamental to examine, compare and model neuronal activity when animals and humans engage in ecological experimental paradigms We have studied neuronal activity in animals and patients to elucidate aspects of memory consolidation, active sensing and psychiatric conditions (PM/CH/JL Valdés) We now consolidate these research lines, but also add behavioral paradigms to test for additional mechanisms that have been approached from cellular or molecular levels We incorporate behavioral testing and benchmarks of neurodegenerative disease (CHz/PM/R Fuentes) and measure behavioral consequences of modifying cellular calcium signaling on learning and memory tasks (CH/PM/JL Valdés)	Rodrigo Montefusco, Rómulo Fuentes, Felipe Cabral, Tatiana Adasme, Ma Ángeles Juricic, Rodrigo Clemente, Enzo Brunetti , Christ Devia, Pedro Maldonado, José Ignacio Egaña, Cecilia Hidalgo, Chama Belkhiria, Margarita Bórquez, Paul Délano , José Luis Valdés, Claudio Hetz	Bioquímica, Biotecnología, Biofísica, Oftalmología, Métodos numéricos y computación, Probabilidades, matemáticas aplicadas y estadísticas, Fisiología biofísica	01/07/2016	
6	RL6 Clinical studies	To conduct clinical brain research sustained by cutting-edge basic Neuroscience To extend neurophysiological markers of Schizophrenia to identify EEG and behavioral markers To expand to the general area of neurology, focusing on neurodegenerative diseases and the search for biomarkers for ALS and Alzheimer's disease To explore the underlying molecular mechanisms of ALS, Alzheimer’s and Parkinson’s diseases and to search for novel therapeutic strategies using gene therapy and pharmacological approaches	One central goal of BNI is to conduct clinical brain research sustained by cutting-edge basic Neuroscience We recently searched for neurophysiological markers of Schizophrenia (HS/PM) and we now extend this approach to identify EEG and behavioral markers (PM/JL Valdés), and to promote the use of genetic markers, eye movements and EEG signals in Psychosis (PM/HS/P Gaspar) Clinical approaches expand to the general area of neurology, focusing on neurodegenerative diseases and the search for biomarkers for ALS and Alzheimer's disease (CH/JM Matamala/A Paula-Lima), as well as therapeutic approaches to treat Parkinson's patients through electrical micro-stimulation of the spinal cord (CHz/PM/R Fuentes) Recently recruited basic and clinical Adjunct Investigators work together in preclinical models to explore the underlying molecular mechanisms of ALS, Alzheimer’s and Parkinson’s diseases and to search for novel therapeutic strategies using gene therapy and pharmacological approaches (CHz/S Matus/R Vidal)	J Manuel Matamala, J Ignacio Egaña, Felipe Salech, Hernán Silva, Claudio Hetz, Pablo Gaspar , Cecilia Hidalgo, Pedro Maldonado, Rómulo Fuentes, René Vidal , Soledad Matus , Andrea Paula-Lima , José Luis Valdés, Alicia Figueroa,	Otras especialidades de la biología, , Biología del desarrollo, Biología celular, Medicina psicosomática (incluyendo psiquiatría), , , Biología molecular, Bioquímica farmacología, , Farmacología, Otras especialidades de la medicina	01/07/2016	

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date
7	RL7 Applied mathematics and biomedical informatics	To decode physiological and behavioral patterns, and developing capacities in clinical research To generate faster image processing routines to manage data from advanced microscopy within the new network for advanced scientific equipment To integrate image processing with new physical and hybrid model approaches for interpretation of organelle dynamics	The BNI-BioMat platform aims to unravel the architectonic and functional principles of neuronal processes on sub-cellular to supracellular levels, decoding physiological and behavioral patterns, and developing capacities in clinical research We generate faster image processing routines (GPU and parallel) to manage data from advanced microscopy within the new network for advanced scientific equipment (REDECA) 10 GBps access from BNI-labs (SH) to HPC (via NLHPC) guarantees new design of fast data analysis tools (BioMed-HPC) within BNI and network for Reproducible Research in Image and Signal Processing (ReRISiP-IPOL, STIC-AmSud) We also integrate image processing with new physical and hybrid model approaches for interpretation of organelle dynamics (SH/AC) and cell migration with 4-lens LSFM (SH/MC) Data analysis and storage for clinical data is addressed on the basis of a new data center (SH/MC/CH/M Cerda) and the new Center for Medical Informatics and Telemedicine (CIMT) in areas of clinical data, bioinformatics, and telemedicine directed by SH	Víctor Castañeda, Violeta Chang, Mauricio Cerda, Jorge Toledo, Steffen Härtel, Cecilia Hidalgo, Andrés Couve, Eduardo Pulgar , Miguel Concha, Pablo Báez, Cristóbal Moenne,	Métodos numéricos y computación, Biofísica, Biología celular, Fisiología biofísica, Ingeniería en computación	01/07/2016	
8	RL8 Neuropathology	To develop an integrative approach centered on studying novel mechanisms underlying a group of neurodegenerative and psychiatric disorders	This transversal platform aims to develop an integrative approach centered on studying novel mechanisms underlying a group of neurodegenerative and psychiatric disorders We continue focusing on prevalent diseases involving protein misfolding and aggregation, including Alzheimer's (CH/CHz/A Paula-Lima), Parkinson's (MC/CHz/R Vidal/R Fuentes) and ALS (CHz/S Matus/ JM Matamala) We emphasize the use of in vivo approaches in complementary model systems through shared animal facilities to accelerate the use of Drosophila (JS), zebrafish (MC) and mouse models (CHz) This platform interacts with multiple research lines to uncover how disease-related genes alter common cellular processes leading to impaired neuronal connectivity and synaptic dysfunction BNI provides a rich array of clinical research opportunities in Neuroscience, based on the access to patients and samples, reliable records, and motivated clinicians To take full advantage of these resources we have recently incorporated Adjunct Investigators with MD degrees to bridge studies in animal models and humans in the areas of neurological (JM Matamala) and psychiatric disorders (P Gaspar)	Claudia Durán Aniotz, Alexis Rivas , Almudena Laliena, Gabriela Mercado, Hery Urra , Philippe Pihán , Younis Hazari , Alexis Martínez, Claudio Hetz, Steffen Härtel, Cecilia Hidalgo, Pedro Maldonado, Rómulo Fuentes, René Vidal , Paula García , J Manuel Matamala, Jimena Sierralta, Mauricio Cerda, Pablo Gaspar , Patricio Olguín, Soledad Matus , David Aguirre, Vicente Valenzuela, Andrés Couve, Paulina Falcón, Yannis Gerakis , Amado Carreras, Janina Borgonovo, Miguel Concha, Andrea Paula-Lima , Hernán Silva, Danilo Bilches	Biofísica, Biología celular, Biología del desarrollo, Biología molecular, Bioquímica, Biotecnología, Farmacia, farmacología clínica, laboratorio, Fisiología biofísica, Medicina psicosomática (incluyendo psiquiatría),Otras especialidades de la biología,	01/07/2016	

Annex 3.- Publications (Total or partially financed by MSI)

Category of Publication	MSI Center Members	Reference
ISI Publications or Similar to ISI Standard	Associate Researchers	Valenzuela V, Nassif M, **Hetz C**., (2018). Unraveling the role of motoneuron autophagy in ALS, Autophagy. Doi: 10.1080/15548627.2018.1432327
		Matamala JM, Arias-Carrasco R, Sanchez C, Uhrig M, Bargsted L, Matus S, Maracaja-Coutinho V, Abarzua S, van Zundert B, Verdugo R, Manque P, **Hetz C.** (2018). Genome-wide circulating microRNA expression profiling reveals potential biomarkers for amyotrophic lateral sclerosis. Neurobioly of aging (Neurobiol of aging) . Doi: 10.1016/j.neurobiolaging.2017.12.0201
		Contreras EG, **Sierralta J**, Glavic A., (2018),p53 is required for brain growth but is dispensable for resistance to nutrient restriction during Drosophila larval development., PLoS One. Doi: 10.1371/journal.pone.0194344
		Sepulveda D, Rojas-Rivera D, Rodríguez DA, Groenendyk J, Köhler A, Lebeaupin C, Ito S, Urra H, Carreras-Sureda A, Hazari Y, Vasseur-Cognet M, Ali MMU, Chevet E, Campos G, Godoy P, Vaisar T, Bailly-Maitre B, Nagata K, Michalak M, **Sierralta J**, **Hetz C**., (2018). Interactome Screening Identifies the ER Luminal Chaperone Hsp47 as a Regulator of the Unfolded Protein Response Transducer IRE1α., Molecular Cel (Mol Cell). Doi: 10.1016/j.molcel.2017.12.028
		Delgado MG, Oliva C, López E, Ibacache A, Galaz A, Delgado R, Barros LF, **Sierralta J**, (2018). Chaski, a novel Drosophila lactate/pyruvate transporter required in glia cells for survival under nutritional stress. Scientific Reports (Sci Rep). Doi: 10.1038/s41598-018-19595-5
		Contreras EG, Palominos T, Glavic Á, Brand AH, **Sierralta J**, Oliva C. (2018). The transcription factor SoxD controls neuronal guidance in the Drosophila visual system. Scientific Reports (Sci Rep). Doi: 10.1038/s41598-018-31654-5
		González A, **Härtel S**, Mansilla J, Sanchez-Valdéz F and A Ferreira, (2018). Variable Numbers of Calreticulin Genes in Trypanosoma cruzi Correlate with Atypical Morphology and Protein Expression. Immunobiology. Doi: 10.1016/j.imbio.2018.08.005
		Hetz C., Papa F. (2018). The unfolded protein response and cell fate control, Molecular Cell. Doi: 10.1016/j.molcel.2017.06.017
		Carreras-Sureda A., Pihan P. , **Hetz C.** (2018). Calcium signaling at the endoplasmic reticulum: fine-tuning stress responses.Cell Calcium. Doi: 10.1016/j.ceca.2017.08.004
		Rojas-Rivera D, Rodriguez DA, Sepulveda D, **Hetz C**., (2018). ER stress sensing mechanism: Putting off the brake on UPR transducers. Oncotarget. Doi: 10.18632/oncotarget.25114
		Mercado G., Lopez N., Martínez A., Sardi P., **Hetz C**. (2018). A new model to study cell-to-cell transfer of alpha Synuclein in vivo. Biochemical and Biophysical Research Communications (Biochem Biophys Res Commun.). Doi: 10.1016/j.bbrc.2018.07.053
		Lhomond S., Avril T., Dejeans N., Voutetakis K., Doultsinos D., McMahon M., Pineau R., Obacz J., PapadodimaO., Jouan F., Bourien H., Logotheti M., Jégou G., Pallares-Lupon N., Schmit K., Le Reste P., Etcheverry A., Mosser J., Barroso K., Vauléon E., Maurel M.,Samali A., Patterson J., Pluquet O., **Hetz C**., QuillienV., Chatziioannou A. , Chevet E., (2018). Dual IRE1 RNase functions dictate glioblastoma development. EMBO Molecular Medicine (EMBO Mol Med). Doi: 10.15252/emmm.201707929
		García-González P., Cabral-Miranda F., **Hetz C**., Osorio F. (2018). Interplay Between the Unfolded Protein Response and Immune Function in the Development of Neurodegenerative Diseases. Frontiers in Inmunology (Frontiers Immunol.). Doi: 10.3389/fimmu.2018.02541
		Lebeaupin C., Vallée D., Hazari Y., **Hetz C**., Chevet E., Bailly-Maitre B. (2018). Endoplasmic Reticulum stress signaling and the pathogenesis of Non-Alcoholic Fatty Liver Disease. Journal of Hepatology (J Hepatol.) Doi: 10.1016/j.jhep.2018.06.008
		Gonzalez M., Urra H., Lima C., **Hetz C.** (2018). Homeostatic interplay between FoxO protein and ER proteostasis in cancer and other diseases. Seminars in Cancer Biology (Seminars Cancer Biol.). Doi: 10.1016/j.semcancer.2018.01.011

Category of Publication	MSI Center Members	Reference
ISI Publications or Similar to ISI Standard	Associate Researchers	Galluzzi L et all, (2018). Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. Cell Death & Differentiation (Cell Death Differ.) Doi: 10.1038/s41418-017-0012-4
		Aboitiz F, **Concha ML** , Gonzalez-Billault C , Mpodozis J (2018). From Ecology to Brain Development: Bridging Separate Evolutionary Paradigms. Frontiers in Neuroscience. Doi: 10.3389/fnins.2018.00447
		Urra H., Henriquez D., Cánovas J., Villarroel-Campos D., Carreras-Sureda A., Pulgar E., Molina E., Hazari Y., Limia C., Alvarez-Rojas S., Figueroa R., Vidal R., Rodriguez D., Rivera C., Court F., **Couve A**., Qi L., Chevet E., Akai R., Iwawaki T., **Concha M**., Glavic A., Gonzalez-Billault C., **Hetz C**. (2018). IRE1α governs cytoskeleton remodeling and cell migration through a direct interaction with Filamin A. Nature Cell Biology. Doi: 10.1038/s41556-018-0141-0
		Valenzuela V, Jackon K, Sardi P, **Hetz C**, (2018). Gene therapy strategies to restore ER proteostasis in disease. Molecular Therapy (Mol. Ther.) Doi: 10.1016/j.ymthe.2018.04.004
		Gerakis Y., **Hetz C.**, (2018). Emerging roles of ER stress in the aetiology and pathogenesis of Alzheimer's disease. The FEBS Journal (FEBS J). Doi: 10.1111/febs.14332
		Medinas D., Rozas P., Martinez F., Woehlbier U., Brown RH., Bosco D., **Hetz C**. (2018). Endoplasmic reticulum stress leads to accumulation of wild-type SOD1 aggregates associated with sporadic amyotrophic lateral sclerosis, Proceedings of the National Academy of Sciences of the United States of America (Proc Natl. Acad. Asci USA). Doi: 10.1113/JP276624
		Mercado G., Castillo V., Soto P., López N., Axten J., Sardi P., Hoozemans J., **Hetz C**. (2018). Targeting PERK signaling with the small molecule GSK2606414 prevents neurodegeneration in a model of Parkinson's disease. Neurobiology of Disease (Neurobiol. Dis.). Doi: 10.1016/j.nbd.2018.01.004
		Martínez G., KhatiwadaS., Costa-Mattioli M., **Hetz C.** (2018). ER proteostasis control of neuronal physiology and synaptic dysfunction.Trends in Neurosciences (Trends Neurosci.). Doi: 0.1016/j.tins.2018.05.009
		Groenendyk J, Paskevicius T, Urra H, Viricel C, Wang K, Barakat K, **Hetz C**, Kurgan L, Agellon LB, Michalak M.(2018). Cyclosporine A binding to COX-2 reveals a novel signaling pathway that activates the IRE1α unfolded protein response sensor. Scientific Reports (Sci Rep.) Doi: 10.1038/s41598-018-34891-w
		Pérez-Arancibia R, Rivas A, **Hetz C.** (2018). (off)Targeting UPR signaling: the race toward intervening ER proteostasis, Expert Opinion on Therapeutic Targets (Expert Opin Ther Targets). Doi: 10.1080/14728222.2018.1420169
		Montefusco-Siegmund R, Toro M, **Maldonado P**E, Aylwin ML. (2018). Unsupervised visual discrimination learning of complex stimuli: Accuracy, bias and generalization.,Vision Research (Vision Res.). Doi: 10.1016/j.visres.2018.05.002.
		Rivera-Lillo G, Rojas D, Burgos P, Egaña JI, Chennu S, **Maldonado PE**. (2018). Reduced delta-band modulation underlies the loss of P300 responses in disorders of consciousness. Clinical Neurophysiology (Clin Neurophysiol.). Doi: 10.1016/j.clinph.2018.09.104
		Rojas-Líbano D, Wimmer Del Solar J, Aguilar-Rivera M, Montefusco-Siegmund R, **Maldonado PE**. (2018). Local cortical activity of distant brain areas can phase-lock to the olfactory bulb's respiratory rhythm in the freely behaving rat. Journal of Neurophysiology (J Neurophysiol.) Doi: 10.1152/jn.00088.2018
		Burgos PI, Mariman JJ, Makeig S, Rivera-Lillo G, **Maldonado PE**. (2018). Visuomotor coordination and cortical connectivity of modular motor learning. Human Brain Mapping (Hum Brain Mapp.) Doi: 10.1002/hbm.24215
		Galindo J, Contreras M, **Maldonado P**, Torrealba F, Lagos N, **Valdés JL**. (2018). Long-lasting, reversible and non-neurotoxic inactivation of hippocampus activity induced by neosaxitoxin. Journal of Neuroscience Methods (J Neurosci Methods.) Doi: 10.1016/j.jneumeth.2018.08.013
		Mariman JJ, Burgos P, **Maldonado PE**. (2018). Parallel learning processes of a visuomotor adaptation task in a changing environment. ,European Journal of Neuroscience (Eur J Neurosci.) Doi: 10.1111/ejn.14258
		Astudillo C, Muñoz K, **Maldonado PE**. (2018). Emotional Content Modulates Attentional Visual Orientation During Free Viewing of Natural Images. Frontiers in Human Neuroscience (Front Hum Neurosci.) Doi: 10.3389/fnhum.2018.00459

Category of Publication	MSI Center Members	Reference
ISI Publications or Similar to ISI Standard	Associate Researchers	González C, Cornejo VH**, Couve A** (2018). Golgi bypass for local delivery of axonal proteins, fact or fiction? Current Opinion in Cell Biology (Curr Opin Cell Biol.) Doi: 10.1016/j.ceb.2018.03.010
		Stanic K, Quiroz A, Lemus CG, Wichmann IA, Corvalán AH, Owen GI, Opazo JC, **Concha ML**, Amigo JD. Expression of RPRM/rprm in the Olfactory System of Embryonic Zebrafish (Danio rerio). Frontiers in Neuroanatomy (Front Neuroanat.) Doi: 10.3389/fnana.2018.00023
	Others	Jimenez D, **Matamala JM**, Chiti A, Vergara C, Tissera C, Melo R, Cartier L. (2018) . Cerebral ring enhancing lesion with diffusion restriction in a South American patient. Neurologia i Neurochirurgia Polska (Neurol Neurochir Pol.) Doi: 10.1016/j.pjnns.2017.11.008
		Cerda M, Navaro CA, Silva J, Waitukaitis SR, Mujica N, Hitschfeld N. (2018). A high-speed tracking algorithm for dense granular media. Computer Physics Communications. Doi: 10.1016/j.cpc.2018.02.010
		Jimenez D, **Matamala JM**, Chiti A, Vergara C, Tissera C, Melo R, Cartier L. (2018). O6-methylguanine-DNA-methyltransferase immunostaining intensity in glioblastoma. Neurologia i Neurochirurgia Polska (Neurol Neurochir Pol.) Doi: 10.1016/j.pjnns.2017.10.014
		Cruz-Montecinos C, Pérez-Alenda S, Contreras-Sepúlveda F, Querol F, **Cerda M**, Maas H, (2018). Assessment of tensile mechanical properties of the Achilles tendon in adult patients with haemophilic arthropathy. Reproducibility study. Haemophilia. Doi: 10.1111/hae.13622
		More J, Casas MM, Sánchez G, **Hidalgo C**, Haeger P. (2018). Contextual Fear Memory Formation and Destabilization Induce Hippocampal RyR2 Calcium Channel Upregulation. Neural Pasticity (Neural Plast.) Doi: 10.1155/2018/5056181
		More JY, Bruna BA, Lobos PE, Galaz JL, Figueroa PL, Namias S, Sánchez GL, Barrientos GC, **Valdés JL**, **Paula-Lima AC, Hidalgo C**, Adasme T. (2018). Calcium Release Mediated by Redox-Sensitive RyR2 Channels Has a Central Role in Hippocampal Structural Plasticity and Spatial Memory. Antioxidants & Redox Signaling (Antioxid Redox Signal.) Doi: 10.1089/ars.2017.7277
		Arias-Cavieres A, Barrientos GC, Sánchez G, Elgueta C, Muñoz P, **Hidalgo C**. (2018). Ryanodine Receptor-Mediated Calcium Release Has a Key Role in Hippocampal LTD Induction. Frontiers in Cellular Neuroscience (Front Cell Neurosci.) Doi: 10.3389/fncel.2018.00403
		Bruna B, Lobos P, Herrera-Molina R, **Hidalgo C**, **Paula-Lima A,** Adasme T. (2018). The signaling pathways underlying BDNF-induced Nrf2 hippocampal nuclear translocation involve ROS, RyR-Mediated Ca2+ signals, ERK and PI3K. Biochemical and Biophysical Research Communications (Biochem Biophys Res Commun.) Doi: 10.1016/j.bbrc.2018.09.080
		Díaz-Vegas AR, Cordova A, Valladares D, Llanos P, **Hidalgo** C, Gherardi G, De Stefani D, Mammucari C, Rizzuto R, Contreras-Ferrat A, Jaimovich E. (2018). Mitochondrial Calcium Increase Induced by RyR1 and IP3R Channel Activation After Membrane Depolarization Regulates Skeletal Muscle Metabolism. Frontiers in Physiology (Front Physiol.) Doi: 10.3389/fphys.2018.00791
		Arias-Cavieres A, More J, Vicente JM, Adasme T, Hidalgo J, **Valdés JL**, Humeres A, Valdés-Undurraga I, Sánchez G, **Hidalgo C**, Barrientos G. (2018). Triclosan Impairs Hippocampal Synaptic Plasticity and Spatial Memory in Male Rats. Frontiers in Molecular Neuroscience (Front Mol Neurosci.) Doi: 10.3389/fnmol.2018.00429
		Manieu C, Olivares GH, Vega-Macaya F, Valdivia M, **Olguín P**. (2018). Jitterbug/Filamin and Myosin-II form a complex in tendon cells required to maintain epithelial shape and polarity during musculoskeletal system development. Mechanisms of Development (Mech Dev.) Doi: 10.1016/j.mod.2018.09.002
		Troncoso-Escudero P, Parra A, Nassif M, **Vidal RL**. (2018). Outside in: Unraveling the Role of Neuroinflammation in the Progression of Parkinson's Disease. Frontiers in Neurology (Front Neurol.) Doi: 10.3389/fneur.2018.00860
		Muñoz Y, **Paula-Lima AC**, Núñez MT., (2018). Reactive oxygen species released from astrocytes treated with amyloid beta oligomers elicit neuronal calcium signals that decrease phospho-Ser727-STAT3 nuclear content. Free Radical Biology and Medicine (Free Radic Biol Med.) Doi: 10.1016/j.freeradbiomed.2018.01.006
		Martínez A, **Gaspar PA**, Hillyard SA, Andersen SK, Lopez-Calderon J, Corcoran CM, Javitt DC. (2018). Impaired Motion Processing in Schizophrenia and the Attenuated Psychosis Syndrome: Etiological and Clinical Implications. The American Journal of Psychiatry (Am J Psychiatry.) Doi: 10.1176/appi.ajp.2018.18010072
		More J, Galusso N, Veloso Matta P, Montecinos L, Finkelstein JP, Sanchez G, Bull R, **Valdes JL, Hidalgo C , Paula-Lima AC.** (2018). N-Acetylcysteine prevents the spatial memory deficits and the redox-dependent RyR2 decrease displayed by an Alzheimer's disease rat model. Frontiers in Aging Neuroscience (Front. Aging Neurosci) Doi: 10.3389/fnagi.2018.00399

Category of Publication	MSI Center Members	Reference
SCIELO Publications or Similar to SCIELO Standard	Associate Researchers	
	Others	Jimenez D, **Matamala JM**, Chiti A, Vergara C, Tissera C, Melo R, Cartier L. (2018). O6-methylguanine-DNA-methyltransferase (MGMT) expression in Chilean patients with Glioblastoma multiforme. Rev Med Chile 2018; 146: 7-14. Doi: 10.4067/s0034-98872018000100007
		Jara P, Matamala JM, Verdugo RJ, (2018), Neuropathy and Fabry's disease. Report of five cases, Revista Médica de Chile (Rev Med Chile 2018) Doi: 10.4067/s0034-98872018000901079
Books & Chapters of Books	Associate Researchers	**Maldonado PE**. (2018). Anatomia-Funcional de la percepción Visual. Editores: Andrea Slachevsky, Facundo Manes, Edith Labos, Patricio Fuentes. Editorial Akadia, BS, Argentina. Tratado de Neuropsicología Clínica.
	Others	**Matamala JM,** Butler R, Simon MV. (2018). Monitoring and Mapping in Pediatric Surgery., Intraoperative Neurophysiology: A Comprehensive Guide to Monitoring and Mapping. Second Edition. Springer Publishing Company. Doi: ISBN 13 9781620701171
Other Publications	Associate Researchers	
	Others	

Annex 3.1: Publication 2017 not informed previously

Category of Publication	MSI Center Members	Reference
ISI Publications or Similar to ISI Standard	Associate Researchers	Izquierdo AL, Castañeda V, **Härtel S, Concha M**, (2017). Sleep/wake disorders and the hypocretin/orexin system in a zebrafish model of Parkinson's Disease. Mechanisms of Development. Doi: 10.1016/j.mod.2017.04.352
		Lemus C, Palma K, Jara J, Härtel S, Concha M, (2017). Asymmetric morphogenesis of the parapineal organ in the embryonic zebrafish brain. Mechanisms of Development. Doi: 10.1016/j.mod.2017.04.112
		Rojas-Moraleda R, Valous NA ,Gowen A, Esquerre C, **Härtel S** , Salinas L , O'Donnell C. (2017). A frame-based ANN for classification of hyperspectral images: assessment of mechanical damage in mushrooms. Neural Computing and Applications. Doi: 10.1007/s00521-016-2376-7
		Palma K, Meynard M, Cornejo V, Cerda M, Jara J, **Härtel S, Concha M**, (2017). Light/dark cycles modulate asymmetic parapineal connectivity to the left habenula in zebrafish larvae. Mechanisms of Development. Doi: 10.1016/j.mod.2017.04.334

3.2.- Collaborative publications:

Category of Publication	1 researcher		2 researchers		3 researchers		4 or more	
	N°	%	N°	%	N°	%	N°	%
ISI Publications or Similar to ISI Standard	48	84.21%	6	10.53%	2	3.51%	0	0,00%
SCIELO Publications or Similar to SCIELO Standard	0	0,00%	0	0,00%	0	0,00%	0	0,00%
Books and chapters	1	1,75%	0	0,00%	0	0,00%	0	0,00%
Other Publications	0	0,00%	0	0,00%	0	0,00%	0	0,00%
Total of publications	49	85.96%	6	10.53%	2	3.51%	0	0,00%

Annex 4.- Organization of Scientific Events

Scope	Title	Type of Event	City	Country	Responsible Researcher
Nacional	BNI TRANSFORMA: Hetz tips proyectos	Seminar	Santiago	Chile	Claudio Andrés Hetz Flores
Nacional	BNI TRANSFORMA: Más allá del Laboratorio	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Fondos Area Innovación Meeting	Seminar	Santiago	Chile	Claudio Andrés Hetz Flores
Nacional	Course; Introducción to Freesurfer	Course	Santiago	Chile	Chama Belkhiria Belkhiria
Nacional	Neurosur: Frontiers in Neurotechnology a Latin American Perspective	Seminar	Santiago	Chile	Rómulo Antonio Fuentes Flores
Nacional	Retreat BNI	Workshop	Mantagua	Chile	Andrés Oscar Couve Correa
Nacional	Division Orientation in epithelial Tissue	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Descubriendo los Mecanismos de Procesamientos de las Histrias Sintetizadasde Novo	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Long-Term Memory Gating and Energy Metabolism in Drosophilla	Seminar	Santiago	Chile	Jimena Alejandra Sierralta Jara
Nacional	The Architecture of Memory retrieval neuronal circuits in Drosophilla	Seminar	Santiago	Chile	Jimena Alejandra Sierralta Jara
Nacional	TRP Channels and Calcium influx. The love Story starts at fertilization	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Charting Cell-specific epigenomic features in the adaptive immune system	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Watching eyes take Shape: A genetic dissection of retinal growth in zebrafish	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Señalización celular en la Generación de nuevas Neuronas en cerebro adulto	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Beyond Oxygen and Nutrients Supply: The Role of the Vascular Niche in CNS Remyelination Cisne UACH	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Neuroplastin ablation causes retrograde amnesia of associative memories and identifies a novel fuction in calcium homeostasis	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Neuroplastin interacts whit TRAF6 and PMCA to regulate signaling transduction synapse formation, calcium clearance, and plasticity in neurons	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	ER proteostasis in cancer Biology: From Novel insights to Therapeutic Interventions	Workshop	Santiago	Chile	Claudio Andrés Hetz Flores
Nacional	BNI TRANSFORMA: Capitalización de las Habilidades Científicas	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	Relojes Biológicos y Horarios	Seminar	Santiago	Chile	Andrés Oscar Couve Correa
Nacional	4to Encuentro de Investigadores en Biología del Desarrollo	Meeting and Symposium	Santiago	Chile	Esteban Contreras Sepúlveda

Annex 5.- Education and capacity building

5.1 Capacity Building inside MSI Centers

Tutor	Undergraduated Student		Graduated Students				Total
			Master		Doctoral		
	F	M	F	M	F	M	
Miguel Concha Nordemann	2	1	0	0	1	2	6
Pedro Esteban Maldonado Arbogast	0	0	1	5	2	6	14
Steffen Härtel Gründler	0	1	1	1	0	1	4
Claudio Andrés Hetz Flores / Soledad Matus	0	0	0	0	0	1	1
Claudio Andrés Hetz Flores	0	1	1	1	2	3	8
Andrea Paula-Lima	0	1	0	0	0	3	4
Pedro Esteban Maldonado Arbogast Pablo Gaspar	0	0	0	0	1	0	1
Rómulo Antonio Fuentes Flores Pedro Esteban Maldonado Arbogast	0	0	0	0	1	0	1
Pedro Esteban Maldonado Arbogast José Luis Valdés Guerrero	0	0	0	0	0	2	2
Andrea Paula-Lima José Luis Valdés Guerrero María Cecilia Hidalgo Tapia	0	0	0	0	1	0	1
Rómulo Antonio Fuentes Flores	0	1	1	1	1	1	5
Steffen Härtel Gründler/Mauricio Cerda	0	0	0	0	1	0	1
Patricio Alejandro Olguín Aguilera	0	2	0	0	0	0	2
Jimena Sierralta Jara	0	0	0	1	0	1	2
Rómulo Antonio Fuentes Flores René Vidal Claudio Andrés Hetz Flores	0	0	0	0	1	0	1
Andrés Oscar Couve Correa	0	0	1	0	1	0	2
Jimena Sierralta Jara / Andrés Couve	0	0	0	0	1	0	1
José Luis Valdés Guerrero	0	1	0	0	1	1	3
René Vidal	1	0	0	0	1	0	2
Mauricio Cerda Villablanca	0	1	0	3	0	0	4
Claudio Andrés Hetz Flores René Vidal	0	0	0	0	1	0	1
Pablo Gaspar	0	0	1	0	1	2	4
Soledad Matus	1	0	0	0	0	0	1
Paul Délano	0	0	0	2	0	0	2
Total	**4**	**9**	**6**	**14**	**17**	**23**	**73**

Annex 5.2. - Short-term Traineeships of MSI students

Student Name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Daniel del Aguila Herrera	IMBI - Universidad de Heidelberg	Alemania	Matthias Gietzielt	Master thesis project to prove that it is possible to generate a computer algorithm, based on machine learning (ML), capable of suggesting which treatment scheme could lead to a better prognosis for a patient, according to their initial clinical and biochemical data. This will be done in the context of multiple myeloma (MM), a cancer disease.	01-09-17	28-02-18
María Florencia Álamos Grau	London Movement Disorders Centre	Chile	Dr Mandar Jog	During my four-month stay here (August 1st 2018 – January 1st 2018) I learned about spinal cord stimulation programming, new movement analysis technologies, human and animal electrophysiology and other neuromodulation approaches (including; deep brain stimulation and transcranial magnetic stimulation). I participated in laboratory meeting discussions and Parkinson neuromodulation clinic, which will provide her a new insight about the challenges and open question that are unresolved in the field.	01-08-18	31-12-18
Rocio Loyola	Universitat Pompeu Fabra	España	Rubén Moreno Bote	The internship goal is to analyze behavioural and electrophisiological data	03-12-18	03-05-19
Miguel Alejandro Concha Miranda	Humboldt University zu Berlin	Alemania	Dr. Professor Michael Brecht	Study of the neural correlates of playful interaction of rats on prefrontal cortex, using tetrode recording on behaving animals.	27-11-18	04-03-19
Miguel Alejandro Concha Miranda	Institute of Neuroscience and Medicine	Alemania	Prof. Dr. Sonja Grün	Analysis of neural data obtained using an Utha array (100 channels recording system), with focus on population coding and synchrony .	05-03-18	23-03-18
Francisca Cecilia Bertin Johnson	Leibniz Institute for Neurobiology	Alemania	Ulrich Thomas	Using STED microscopy, I will characterize and correlate SV marker distribution (using CSP and VGUT antibodies) and FM 1-43 dye signal in unstimulated and stimulated (using KCl) third instar larvae motor neurons with modifications in Atl expression (Atl-KD and Atl null mutant), BMP signaling (Tkv-CA overexpression and Tkv-KD) and with double knock-down: Atl-KD/Tkv-KD (establishing a rescue in the BMP upregulated signaling in an Atl-KD background).	27-11-18	27-03-19
Giuliana Bucci Mansilla	Garvan Institute	Australia	David Ryugo	Learning of auditory neuroanatomy in mouse model. and presentation of thesis project.	11-07-18	06-08-18

Student Name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Alejandra Verónica Parra Peña	University of Otago, Dunedin - New Zealand	Nueva Zelandia	Dra. Dorothy Oorschot, Associated professor Anatomy department, University of Otago.	"Parkinson's disease (PD) is a neurodegenerative pathology characterized by the formation of α-synuclein protein aggregates known as Lewis Bodies and the death of dopaminergic neurons in the substance nigra pars compacta, which causes the appearance of a series motor symptoms characteristic of this disease. In the search for new alternatives, the therapeutic strategy known as Spinal cord Stimulation (SCS) has shown a positive effect in the relief of motor symptoms, both in the short and long term, in animal models and patients in advanced stages of the disease PD. Preliminary studies suggest that the EME would be able to counteract neuronal death processes and / or induce neuroplasticity processes, capable of preventing the progression of the disease by increasing neurotrophic factors such as VEGF, in neurotoxic models of the disease. Something unprecedented in the treatment of PD. However, it is unknown if these same mechanisms could be observed in overexpression models of α-synuclein, which recapitulate in part the progression and death mechanisms observed in the disease. The purpose of the work to be carried out in conjunction with Dr. Oorschot is to determine the potential effect of SCS on the nigrostriatal dopaminergic system, comparing the effect of SCS on Parkinsonian groups subjected or not to treatment. Particularly during the internship, I focused on the neuroanatomical characterization of the striatal axonal projections, evaluating aspects such as the number of axonal projections, axonal volume and counting of varicosities. Given the relevance of these structures for the synthesis and release of dopamine in the basal ganglia."	01-11-18	29-03-19

Annex 6.- Networking and other collaborative work

6.1 Networking

Network Name	Network Scope	Researchers				Institutions
		From the Center		External		
		Researchers	Postdocs / Students	Researchers	Postdocs / Students	
Neurosur	Internacional	11	0	25	0	Instituto Leloir (Buenos Aires) , Instituto de BioMedicina de Buenos Aires-CONICET-Parter Sociedad Max Planck , INGEBI-CONICET Buenos Aires, Universidad de Buenos Aires, Instituto de Investigación Medica Mercedes y Martín Ferreyra, Universidad Católica de Argentina, Buenos Aires-CONICET, Federal University of Rio de Janeiro, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Instituto Pasteur Montevideo, Instituto Clemente Estable, Universidad de la República, Montevideo,
Network for Advanced Microscopy and Quantitative Developmental Biology	Internacional	11	20	8	6	BNI, U. Göttingen, Germany / IST, Vienna, Austria/ U.Bonn, Germany
Small Brains Big Ideas	Internacional	1	1	36	0	Universidad Mayor, Santiago, CHILE; Arizona State University, USA; University of Oxford, Centre for Neural Circuits and Behaviour Oxford, UK; University of Massachusetts, USA; INIBIBB, ARGENTINA; Fundación Instituto Leloir, ARGENTINA; Universidad de Chile, CHILE; Universidad de Valparaiso, CHILE; Pontificia Universidad Católica de Chile, CHILE; University of Massachusetts Medical School, USA; University of Massachusetts Medical School, USA; Universidad Santo Tomás, Santiago CHILE; University of Oxford, Centre for Neural Circuits and Behavior Oxford, UK.

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

Annex 6.2.- Other collaborative activities

Activity Name	Objective	Description	Co-Participants Institutions	From de Center		External		Product	Name of the Center Associate Researchers Participating in the activity
				Nro. of Reseachers	Nro. of Postdocs / Students	Nro. of Reseachers	Nro. of Postdocs / Students		
Puerto Ideas 2018	Sociabilización Científica	Vinculación Ciencia - Sociedad	Fundación Puerto Ideas	1				Exposiciones, charlas abiertas a la comunidad	A Couve
Memorando de Entendimiento BNI - Facultad de Ciencias Puras y Naturales, Universidad Mayor de San Andrés (UMSA)	Crear un marco general para las futuras colaboraciones en el campo de la investigación y cooperación científicas	Memorando de Entendimiento	Facultad de Ciencias Puras y Naturales, Universidad Mayor de San Andrés (UMSA)	1				1, Memorando de Entendimiento	A Couve / C Hetz / M Concha / P Maldonado / J Sierralta / S Härtel / R Fuentes
Convenio de Cooperación BNI - Corporación Chilena de Video y las Artes Electrónicas (CChV)	Crear un marco de colaboración con el fin de realizar actividades de interés común científicas, culturales y de desarrollo institucional.	Crear un marco de colaboración con el fin de realizar actividades de interés común científicas, culturales y de desarrollo institucional.	Corporación Chilena de Video y las Artes Electrónicas (CChV)	1				1, Participación en la Bienal de Artes Visuales	A Couve
Congreso de Educación Científica de Ciencias de la Vida	Promover el uso de herramientas innovadoras entre educadores y acercar nuevas técnicas de enseñanza, para ser aplicadas dentro del aula y mejorar la calidad del aprendizaje en escolares.	Congreso de Educación Científica de Ciencias de la Vida	Centro de Perfeccionamiento, Experimentación e Investigaciones Pedagógicas, CPEIP, del Ministerio de Educación.	1				1, Congreso de Educación Científica de Ciencias de la Vida	A Couve
Memorando de Entendimiento BNI - SMI ICE Chile /Universidad de Queensland	Promover investigación colaborativa, proyectos conjuntos, intercambios de capacitación y académicos.	Promover investigación colaborativa, proyectos conjuntos, intercambios de capacitación y académicos.	SMI ICE Chile /Universidad de Queensland	1				1, Memorando de Entendimiento	A Couve
Memorando de Entendimiento BNI - Instituto de Investigaciones Científicas y Servicios de Alta Tecnología (INDICASAT AIP)	Proveer un contexto general a las actividades conjuntas que acuerden realizar las partes en el futuro en la campo de la investigación y cooperación científica, enmarcado en la red Cyted Neurosur.	Establece bases de colaboración entre las partes.	Instituto de Investigaciones Científicas y Servicios de Alta Tecnología (INDICASAT AIP)	3		1		1, Symposium	A Couve / R Fuentes / A Paula-Lima

Activity Name	Objective	Description	Co-Participants Institutions	From de Center		External		Product	Name of the Center Associate Researchers Participating in the activity
				Nro. of Reseachers	Nro. of Postdocs / Students	Nro. of Reseachers	Nro. of Postdocs / Students		
Memorando de Entendimiento BNI - Instituto de Sistemas Complejos de Ingeniería	Enmarcar y proveer un contexto general a las actividades conjuntas que acuerden realizar las partes en el futuro en el campo Consumer Analytics, Transporte y Data Science.	Bases de colaboración entre las partes	Instituto de Sistemas Complejos de Ingeniería	1				1, Memorando de Entendimiento	A Couve
Camaraderie Reception at Ministry of Foreign Affairs	To Link scientist with public authorities	Informal space to interact between scientist and public representatives.	DECYTI - Dirección de Energía, Ciencia, Tecnología e Innovación del Ministerio de Relaciones Exteriores.	2				1, Camaraderie Reception	A Couve / R Fuentes

Annex 7. - Outreach

7.1. - Outreach activities throughout the period

Event Title	Type of Event	Scope	Target Audience	Date	Country	Region	N° of Student from the Center	N° of Attendees	Duration in days	Participating Researchers	Responsible for the activity
II Workshop de Estadística Aplicada	Workshop	Nacional	Comunidad en General; Industrias / Servicios	23/01/2018	Chile	Metropolitana de Santiago		25	4		Rodrigo Vergara Ph.D.
Celebración Científica BNI	Conferencia	Nacional	Comunidad en General	16/04/2018	Chile	Metropolitana de Santiago	20	85	1	A Couve, A Paula-Lima, Alexis Martínez, Alejandro Luarte, S Matus, P Maldonado, José Ignacio Egaña, Esteban Contreras, Claudia Durán, Víctor Hugo Cornejo, Carmen Gloria Lemus, Patricio Ahumada, Gonzalo Olivares, R Fuentes, JL Valdés, Hery Urra, Víctor Castañeda, Carolina González, Paulina Falcón, M Cerda, Younis Hazari , P Olguín	Andrés Couve
Foro de Difusión Científica	Foro	Nacional	Estudiantes Universitarios	15/03/2018	Chile	Metropolitana de Santiago		100	1		
Programa de Perfeccionamiento Docente Mentes Transformadoras	Workshop	Nacional	Profesores Educación Básica y/o Media	11/01/2018	Chile	Metropolitana de Santiago	6	200	8		Rodrigo Tapia
Itinerancias Domo Cerebro / Dendros	Exhibición	Nacional	Comunidad en General	13/04/2018	Chile	Antofagasta	4	40.000	24		Rodrigo Tapia
Visitas Experimentales	Visitas a los laboratorios del Instituto	Nacional	Estudiantes Secundarios	24/08/2018	Chile	Metropolitana de Santiago	30	100	6		Carolina Astudillo
Congreso de Educación Científica Mentes Transformadoras	Conferencia	Nacional	Profesores Educación Básica y/o Media	05/10/2018	Chile	Metropolitana de Santiago	6	160	3	A Couve	Rodrigo Tapia

7.3.- Articles and Interviews

Type of Media and Scoupe	Local / Regional		National		International		
	N° Interviews	N° Articles	N° Interviews	N° Articles	N° Interviews	N° Articles	Total
Written	2	49	1	50	0	0	102
Internet	0	16	5	62	1	8	92
Audiovisual	0	0	16	0	0	0	16
Total	2	65	22	112	1	8	210

Annex 8. - Connections with other sectors:

Activity	Type of Connection	Type of Activity	Institution Country	Agent Type	Economic Sector
Meeting with high executives from PFizer	Networking	Meeting	Estados Unidos de America	Industria	Farmacológica
Uso de sensores inerciales en Estudios de Puesto de Trabajo	Proyecto de innovación con empresa	Desarrollo de Proyecto	Chile	Instituciones Públicas o Privadas	
Evaluación de cabina SonicDrops	Proyecto de innovación con empresa	Desarrollo de Proyecto	Chile	Spin Off	Medicina y salud humana

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

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

Annex 9.- Total incomes:

Item	Accumulated expenses to last year [$]	2018 Expenses [$]				Total expenses to 2018 [$]	%
		Operative	Networks	Outreach	Total		
		844.208.000	0	9.563.796	853.771.796		
Honoraria researchers and research personnel	2.434.752.062	501.481.831	0	0	501.481.831	2.936.233.893	48,4
Tickets and travel expenses	340.011.890	49.223.572	0	0	49.223.572	389.235.462	6,4
Materials and supplies	693.952.332	171.966.585	0	0	171.966.585	865.918.917	14,3
Goods and equipment	434.477.029	54.455.754	0	0	54.455.754	488.932.783	8,1
Infrastructure	448.591.860	6.140.875	0	0	6.140.875	454.732.735	7,5
Administrative expenses	325.174.120	63.718.202	0	0	63.718.202	388.892.322	6,4
Publications and subscriptions	29.540.483	9.572.614	0	0	9.572.614	39.113.097	0,6
Consultancies	126.848.758	37.836.591	0	4.594.387	42.430.978	169.279.736	2,8
Overhead	118.649.552	26.700.000	0	0	26.700.000	145.349.552	2,4
Others	170.524.885	7.210.041	0	9.879.187	17.089.228	187.614.113	3,1
Total	**5.122.522.971**	**928.306.065**	**0**	**14.473.574**	**942.779.639**	**6.065.302.610**	**100,0**

ITEM	2018 [$]				TOTAL TO 2017
	Operative	Networking	Outreach	Total	
Income	844.208.000	0	9.563.796	853.771.796	5.796.784.481
Outcome	928.306.065	0	14.473.574	942.779.639	5.122.522.971
Annual balance	**-84.098.065**	**0**	**-4.909.778**	**-89.007.843**	**674.261.510**

Annex 10.- Exchange:

a) BNI's Reserachers traveling abroad

Name of the Researcher	Reason for the trip	Stay [Days]	Destiny Country	Funding [MSI, Mixed, External]
Pedro Maldonado	LASCON (Escuele de verano computational)	7	Brazil	External
Pedro Maldonado	Congreso Conciencia Barcelona	7	Spain	MSI
Pedro Maldonado	Colaboracion proyecto Sonja Grun (Jülich)	7	Germany	Mixed
Jimena Sierralta	Establecer colaboraciones con Dr. Thomas Preas	2	France	Mixed
Jimena Sierralta	Renovar colaboraciones con Dr. U. Thomas	3	Germany	Mixed
Miguel Concha	Congreso	5	Switzerland	External
Carmen Lemus	Congreso	5	Switzerland	External
Miguel Concha	Curso	14	USA	Mixed
Miguel Concha	Simposio	5	Germany	Mixed
Miguel Concha	Taller	4	Argentina	External
Miguel Concha	Conferencia Internacional	5	USA	Mixed
Miguel Concha	Simposio	5	Germany	Mixed
Romulo Fuentes	Presentacion en Congreso, Neuroscience 2018	7	USA	External
Romulo Fuentes	Presentacion en congreso, Primer Congreso de Innovación Internacional de Estudiantes de Medicina	3	Bolivia	External
Soledad Matus	FASEB Conference: Nutrient Sensing and Metabolic Signaling	5	USA	External
Andrea Paula Lima	Invitada por la Universidad de Salamanca como evaluadora de Comisión de Tesis Doctoral	5	Spain	External
Steffen Härtel	conhIT Berlin: Connecting Healthcare IT (17-19 Abril). También visitará Universidades de Groningen en Holanda y Heidelberg y Heilbronn en Alemania	15	Germany and the Nederlands	External
Steffen Härtel	Amia 2018 Informatics Educators Forum	8	USA	External
Steffen Härtel	Humboldt Kolleg: The Impact of Bioimaging and Structural Biology in the Field of Life Science	4	Brazil	External
Steffen Härtel	Match Making Workshop	4	Germany	External
Steffen Härtel	Workshop 3: Biological Sciences & Biomedical ICT Applications durante el III Foro Académico Chile-Japón	4	Japan	MSI
Steffen Härtel	Colaboración entre U. Harvard y U. Chile	8	USA	External
Claudio Hetz	Formal research Seminar series Buck Institute for Research in Aging /	2	USA	External
Claudio Hetz	Seminar at the University of San Francisco	2	USA	External
Claudio Hetz	FASEB meeting: Functional disulfides bonds in health and disease	2	USA	External
Claudio Hetz	ER Stress in Cancer and Neurodegeneration	2	USA	External
Andres Couve	Congreso, "Society Neuroscience 2018"	7	USA	Mixed
Andres Couve	Cyted	3	Bolivia	External
Andres Couve	Reunion iniciativa NeuroSur (Cyted)	3	Panama	External
Andres Couve	Reunión de coordinación proyectos CYTED	2	Brazil	External
Dr. JM Matamala	Congreso Mundial de Neurofisiologia Clinica	5	USA	External
Soledad Matus	Seminar at Baylor College of Medicine	5	USA	External

b) Visiting Researchers to BNI's members

Name of the visitor	Nationality	Reason of the visit	Stay [Days]	Origin Country	Funding
Olivia Samotus	Canadiense	Fortalecer redes y futuras cooperaciones, ver el estado de avacences de los proyectos del laboratorio de Neuromodulacion y control motor	7	Canadá	External
Per Petersson	Sueco	Cooperacion internacional, analisis y discusion de resultados obtenidos en registos electrofiologicos, preparacion de manuscritos	17	Suecia	External
Antígona Martínez	Panameña	a dar dos charlas magistrales y participóde reuniones de trabajo con investigadores y estudiantes del laboratorio Psiquiatría Traslacional	10	Estados Unidos	External
Daniel Javitt	EstadoUnidense	A dar Charla Magistral en X CONFERENCIA INTERNACIONAL DE LA CLÍNICA PSIQUIÁTRICA UNIVERSITARIA y I CONFERENCIA INTERNACIONAL DEL INSTITUTO PSIQUIÁTRICO J. HORWITZ B., además participó de mesas de trabajo con estudiantes de doctorado y magíster del Laboratorio Psiquiatría Traslacional	7	Estados Unidos	External
Michael Green	American	Dio charla magistral en X CONFERENCIA INTERNACIONAL DE LA CLÍNICA PSIQUIÁTRICA UNIVERSITARIA y I CONFERENCIA INTERNACIONAL DEL INSTITUTO PSIQUIÁTRICO J. HORWITZ B. y participó en mesas de trabajo con estudiantes de magíster y doctorado del laboratorio Psiquiatría Traslacional	7	Estados Unidos	External
Stephanie Miserey Lenkei	Francesa	Cooperación Internacional, colaboración en síntesis local de proteínas en axón	9	Francia	External
Di Genova Bravo Alex Humberto	Chileno	Bioinformatics Workshop	15	Francia	ICBM
García Calavaro Christian	Chileno	Charla "Procesamiento de Señales en Salud: Aplicación de Wavelets para Determiner la Dinámica de Influenza en Chile"		USA	CIMT-CMM-CENS
Grieve Graham	Australiano	CENS Tech Talks Workshop - FHIR implementation around the world - transforming expectations of healthcare IT	5	Australia	CENS
Kaminker Diego	Argentino	CENS Tech Talks Workshop - FHIR en América Latina - ¡es ahora!	5	Argentina	CENS
Agnew James	Canadiense	CENS Tech Talks Workshop - Dos and Don'ts in the implementation for a FHIR project	5	Canadá	CENS
Heckmann Simone	Alemana	CENS Tech Talks Workshop - FHIR didn't reinvent the wheel	5	Alemania	CENS
Gruber Christian	Austriaco	CENS Tech Talks Workshop - Experiences from the development and operation of ELGA	5	Austria	CENS

Name of the visitor	Nationality	Reason of the visit	Stay [Days]	Origin Country	Funding
Christian Fegeler	Aleman	Workshop HPI: International Experience	4	Alemania	HPI
Patrick Werner	Aleman	Workshop HPI: International Experience	4	Alemania	HPI
Pablo Orefice	Uruguayo	Workshop HPI: International Experience	4	Uruguay	HPI
Christian Haux	Aleman	Diploma Internacional Informatica Medica	14	Alemania	Universidad de Heidelberg
Blanca Flores	Mexicana	Diploma Internacional Informatica Medica	14	Alemania	Universidad de Heidelberg
Christian Fegeler	Aleman	HPI – TFC – CMI CHIP CENS Workshop: Hands On for Demonstrators: Health Provider Index, Terminología Farmaceutica Chilena, Cuenta Médica Interoperable 2018	4	Alemania	HPI
Patrick Werner	Aleman	HPI – TFC – CMI CHIP CENS Workshop: Hands On for Demonstrators: Health Provider Index, Terminología Farmaceutica Chilena, Cuenta Médica Interoperable 2018	4	Alemania	HPI
Daniel Zsebedits	Aleman	HPI – TFC – CMI CHIP CENS Workshop: Hands On for Demonstrators: Health Provider Index, Terminología Farmaceutica Chilena, Cuenta Médica Interoperable 2018	4	Alemania	HPI
Andreas Keil	Aleman	HPI – TFC – CMI CHIP CENS Workshop: Hands On for Demonstrators: Health Provider Index, Terminología Farmaceutica Chilena, Cuenta Médica Interoperable 2018	4	Alemania	HPI
Andres Navarro	Colombiano	International Academic Workshop in Medical Informatics: Trends, Perspectives. Health Information Systems, Telemedicine, Digital Pathology, Bioinformatics, Data Security/Security Access	4	Colombia	CIMT
Luis Acevedo Arroyave	Colombiano	International Academic Workshop in Medical Informatics: Trends, Perspectives. Health Information Systems, Telemedicine, Digital Pathology, Bioinformatics, Data Security/Security Access	4	Colombia	CIMT
Harmut Dickhause	Aleman	International Academic Workshop in Medical Informatics: Trends, Perspectives. Health Information Systems, Telemedicine, Digital Pathology, Bioinformatics, Data Security/Security Access	4	Alemania	Universidad de Heidelberg
Igor Nova	Aleman	International Academic Workshop in Medical Informatics: Trends, Perspectives. Health Information Systems, Telemedicine, Digital Pathology, Bioinformatics, Data Security/Security Access	4	Alemania	Universidad de Heidelberg
Matthias Ganzinger	Aleman	International Academic Workshop in Medical Informatics: Trends, Perspectives. Health Information Systems, Telemedicine, Digital Pathology, Bioinformatics, Data Security/Security Access	4	Alemania	Universidad de Heidelberg
Javier Robalino	Ecuatorian	First Chilean Congress for Science teachers organized joint to BNI	4	USA	HHMI
Name of the visitor	**Nationality**	**Reason of the visit**	**Stay [Days]**	**Origin**	**Funding**

				Country	
Jennifer Bricken	American	First Chilean Congress for Science teachers organized joint to BNI	4	USA	HHMI
Eric Chevet	French	Workshop	5	France	French National Institute for Health and Medical Research (Inserm).
Roberto Mayor	Chilean	RIBID Workshop and meeting	2	UK	UCL
María Carreira	Panamanian	First Chilean Congress for Science teachers organized joint to BNI	4	Panama	INDICASAT
Andre Perrota	Portuguese	Neurosur 2019.	6	Portugal	Cyted
Eduardo Rocon	Peruvian	Neurosur 2019.	6	Spain	Cyted
Daniela Andres	Argetinian	Neurosur 2019.	6	Argentina	Cyted
Verónica Piatti	Argetinian	Neurosur 2019.	6	Argentina	Cyted
Rolando Gittens	Panamamian	Neurosur 2019.	6	Panama	Cyted
Rosalinda Pieruzzini	Venezuelan	Neurosur 2019.	6	Venezuela	Cyted
Rosa Flores	Bolivian	Neurosur 2019.	6	Bolivia	Cyted
Solaiman Shokur	Brazilian	Neurosur 2019.	6	Brazil	Cyted
Nara Muraro	Argetinian	Neurosur 2019.	6	Argentina	Cyted
Teodiano Freire Bastos	Brazilian	Neurosur 2019.	6	Brazil	Cyted
Hugo Peluffo	Venezuelan	Neurosur 2019.	6	Venezuela	Cyted
Carlos Ayala	Panamamian	Neurosur 2019.	6	Panama	Cyted