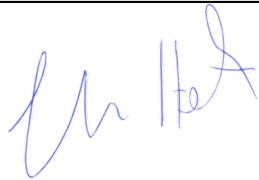
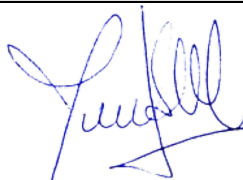




Name of the Center: BIOMEDICAL NEUROSCIENCE INSTITUTE	
Type (Institute or Nucleus)	INSTITUTE
Acronym	BNI
Reported period	January 1 to December 31, 2019
Starting date of the Center	June 28, 2011
Web Page	www.bni.cl / www.loligo.cl
Host Institution(s)	Universidad de Chile
Address	Avda. Independencia 1027, Independencia
Stage	Continuity
End date of the Center	June 2021
Total amount	USD \$10.000.000 for 10 years
Total amount for the reported period	USD \$1.000.000

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<i>Institute Director Name</i>	<i>Institute Alternate Director Name</i>
Claudio Hetz Ph.D.	Jimena Sierralta Ph.D.
<i>Director's Signature</i>	<i>Alternate Director's Signature</i>
	

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1. 1.1 Executive Summary

The Biomedical Neuroscience Institute (BNI) has reached a solid scientific reputation in Latin America, supporting, and bridging the research of leading neuroscientists, clinicians, mathematicians, physicists, engineers, entrepreneurs education health professionals with the aim of analyzing the structure function of the brain under normal physiology and disease, from cells to whole organisms to engage in transferring the knowledge and capacities to the society. 2019 is the fourth year of our second 5-year period.

We have continued to consolidate the strategies proposed in the mid-term review, and redefine the main components, and research scope of the “New Institute” for the competitive renewal process. The key objectives that currently drive BNI’s activities are: (i) to further enhance the quality of BNI trademark inter-disciplinary, collaborative research; (ii) to promote translational research, interactions with the private sector; (iii) to expand the impact of training, capacity building; (iv) to strengthen education and outreach. In this period, **CHz** and **JS** are leading the institute due to the assignment of **AC** as Minister of Science and Technology (December 2018). ‘Scientific research’, ‘innovation’, ‘outreach’ and ‘education’ areas within BNI have gained new administrative support to improve their institutional achievements. Furthermore, we started an auto-evaluation process to help us define better BNI signatures and areas of international scientific impact for the competitive renewal process.

According to our structure, six lines conduct our research based on the relationship between structure and function of the brain, following a bottom up, multi-scale approach complemented by the use of model organisms (flies, multiple fish models, mice, rats humans), and including clinical research. To promote our highly collaborative strategy two transversal research lines, conduct investigation and development in biomathematics (RL7) and neuropathology (RL8).

Nine new research agreements were signed in 2019 through the *Applied Neuromedicine & Technology Platform (NeuroTech)*, which aims to establish an effective link with Chilean companies, and the emerging national biomedical industry. In late 2019, three technologies in the field of gene therapy against neurodegenerative diseases were transferred into a biotechnology company through a patent license. The specific information of the company, and patents involved will be made public in mid-2020. The signing of this license is one of the greatest achievements in technology transfer since the creation of BNI.

BNI outreach program continued to grow in education, and out-of-school science activities. In recent years, our institute has established several initiatives as out-of-school activities, including a web comic, games, and “Domo cerebro” - a traveling exhibition. We have generated our own education program called “Mentes transformadoras”, comprised of workshops for biology teachers, open labs for school students, a national education conference for teachers, and a science book. All our digital resources are available in the new version of the web platform www.loligo.cl.

The productivity of BNI includes the achievements of now five Associated Investigators, one Senior Investigator, ten Adjunct Investigators, and six Staff Scientists. The core of the institute includes around 200 people. During 2019 the Adjunct investigators through their academic positions, and independent and funded research lines have continued successfully to fulfill their role to bridge, strengthen, and expand research areas, and to build their sustainability. Additionally, Adjunct Investigators, who have MD-Ph.D. degrees have continued to 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. Moreover, young Staff Scientists have been able to develop their independent research lines and to secure national and international highly competitive funding where BNI is currently sponsoring several projects such like *FONDECYT*, *MDA*, *ALSA*, *M J Fox Foundation for Parkinson Research* (US), and the *Alzheimer Association* (US).

Eight young investigators, 33 postdocs, 46 Ph.D., 35 Magister, and 13 undergraduate students, plus a team of 46 technical and professional staff complete BNI's multidisciplinary research team. During 2019, 8 theses were co-directed by BNI Investigators, and 6 students visited foreign laboratories to conduct collaborative research. BNI hosted 10 international students and postdocs from countries in North, and South America, Europa, and Asia, including the USA, Mexico, Germany, France, Ireland, Brazil, Argentina, Venezuela, and Japan. As part of their comprehensive scientific training, 40 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. 12 postdocs continued their scientific careers elsewhere.

During 2019 BNI investigators published 48 articles with an average ISI journal impact of 5.8, which compares favorably to similar centers in the developed world, maintaining our excellent trend. High impact factor articles were published in journals such as *Nature Cell Biology*, and reviews in prestigious journals such as *Cell*, *Nature Chemical Biology*, and *Trends in Cell Biology*, in addition to the participation of BNI's associated and adjunct investigators in the editorial board of prestigious scientific journals, demonstrate the international impact of research at BNI. A best Ph.D. thesis Award was granted to a BNI researcher by the *Cell Biology Society of Chile*. Despite the social outbreak in mid-October, BNI researchers continued their strong presence in national and international meetings, with 124 posters or oral presentations during 2019.

During 2019, several national, and international meetings gathering investigators, postdocs, students, and professionals took place at BNI. These instances have been critical to exchange information of research lines, and to drive BNI cross-disciplinary atmosphere into concrete collaborative projects to improve BNI commitment with the country's scientific goals. We organized 11 regular seminars, *Conversations in Neuromedicine*, in topics connecting neuroscience and medicine, which included local and international speakers. After one year of organization, between March 24, and April 5, 2019, we carried out the *Workshop EMBO Bridging cell, and tissue mechanics to fate specification in development*, which took place simultaneously with the *ICGEB Course Optics, forces & Development*, activities that brought together more than 100 people from different countries. The ICGEB course lasted 2 weeks and included students from different Latin American countries. Both activities were joined with two outreach activities: *How to Win a Nobel Prize: stumbling on the secrets of cell division (Tim Hunt)* for university students, and *Open Lecture: Manipulando el origen de la vida humana ¿En qué estamos?* for high school students, and general public. In parallel we carried out the *1st Cyted Innovation Day*, which gathered researchers from Colombia, Argentina, Chile, and Uruguay to share their technological transfer expertise with Chilean researchers, and with *ICGEB Course* students.

Press coverage of the institute's activities has firmly established BNI as a reference centre in Chile, and Latin America. BNI press appearances were valued in an outstanding amount of USD one Million, with 69 appearances in newspapers, 52 online news websites, 10 on radio 17 on television. Press coverage has contributed to position BNI as a resource centre for neuroscientists, clinical practitioners, high-school students, entrepreneurs, and the general public. G Martínez, B Cadiz S Reyes, who lead the Education, and Outreach, Communications, and Technology Transfer, and Innovation platforms, respectively, are based in the new building. This site is now consolidated as a centralized hub, and ideal setting to engage with the community. An Executive Office connects with other sectors, manages grants and coordinates with the Board of Directors.

1.2 Resumen Ejecutivo

El Instituto de Neurociencia Biomédica (BNI) ha alcanzado una sólida reputación científica en América Latina, apoyando y conectando la investigación de neurocientíficos, clínicos, matemáticos, físicos, ingenieros, emprendedores y profesionales de la salud. Nuestro objetivo es analizar la función de la estructura del cerebro bajo fisiología normal y enfermedad, desde las células a los organismos enteros, para participar en la transferencia del conocimiento y de capacidades a la sociedad. 2019 es el cuarto año de nuestro segundo período de 5 años.

Hemos seguido consolidando las estrategias propuestas en la revisión intermedia y redefiniendo los componentes principales de nuestra investigación para así proyectar el "Nuevo Instituto" con el proceso lograr una renovación competitiva. Los objetivos clave que actualmente impulsan las actividades de BNI son: (i) mejorar aún más la calidad de la investigación interdisciplinaria y colaborativa como sello distintivo de BNI; (ii) promover la investigación traslacional y las interacciones con el sector privado; (iii) ampliar el impacto de la capacitación, el desarrollo de capacidades científicas; (iv) fortalecer la educación y la divulgación. En este período, **CHz** y **JS** lideran el instituto debido al nombramiento de **AC** como Ministro de Ciencia y Tecnología (dic. 2018). Las áreas de "investigación científica", "innovación", "extensión & educación" dentro del BNI han sido reforzadas en su gestión para mejorar nuestros logros institucionales. Además, comenzamos un proceso de autoevaluación para ayudarnos a definir el sello distintivo de BNI como centro competitivo internacionalmente y las áreas de impacto para el proceso de renovación competitiva.

De acuerdo con nuestra estructura, seis líneas conducen nuestra investigación en función de la relación entre la estructura y la función del cerebro, siguiendo un enfoque ascendente y de múltiples escalas complementado por el uso de organismos modelo (moscas, múltiples modelos de peces, ratones, ratas y humanos) e incluyendo la investigación clínica. Dos de las líneas de investigación, biomatemáticas (RL7) y neuropatología (RL8), promueven una estrategia altamente colaborativa.

Nueve nuevos acuerdos de investigación con empresas se firmaron en 2019 a través de la *Plataforma de Neuromedicina Aplicada & Tecnología (NeuroTech)*, cuyo objetivo es establecer un vínculo efectivo con las empresas chilenas e internacionales y la emergente industria biomédica nacional. A fines de 2019, tres tecnologías en el campo de la terapia génica contra enfermedades neurodegenerativas se transfirieron a una empresa de biotecnología a través de una licencia de patente. La información específica de la compañía y las patentes involucradas se harán públicas a mediados de 2020. La firma de esta licencia es uno de los mayores logros en transferencia de tecnología desde la creación de BNI.

El programa de educación y extensión de BNI continuó creciendo en actividades educativas y científicas. En los últimos años, nuestro instituto ha establecido varias iniciativas como actividades de educación incluyendo un cómic web, juegos y nuestra exposición itinerante "Domo cerebro". Hemos generado nuestro propio programa educativo llamado "Mentes transformadoras", compuesto por talleres para maestros de biología, laboratorios abiertos para estudiantes, un congreso nacional de educación para maestros y un libro de ciencias. Todos nuestros recursos digitales están disponibles en la nueva versión de la plataforma web www.loligo.cl.

La productividad de BNI incluye los logros de los actuales cinco investigadores asociados, un investigador senior, diez investigadores adjuntos y seis Staff Scientist. El instituto está compuesto de alrededor de 200 personas. Durante 2019, los investigadores adjuntos, a través de sus puestos académicos y líneas de investigación independientes y con financiamiento propio, han seguido cumpliendo con éxito su función de liderar, fortalecer y expandir áreas de investigación, y construir su sostenibilidad. Además, los investigadores adjuntos con grado académico MD. Ph.D, han continuado realizando estudios en modelos animales y humanos en las áreas de trastornos neurológicos y psiquiátricos, proporcionando una estrategia práctica para lograr uno de nuestros principales objetivos relacionados con la investigación traslacional. Además, los *Staff Scientist* han podido desarrollar líneas de investigación independientes y asegurar una financiación altamente competitivo nacional e internacional, donde BNI actualmente

patrocina varios proyectos de *FONDECYT*, *MDA*, *ALSA*, la *Fundación MJ Fox para la Investigación de Parkinson* (EE.UU.) y la *Asociación de Alzheimer* (EE.UU.).

Ocho investigadores jóvenes, 33 posdoctorados, 46 estudiantes de doctorado, 35 estudiantes de Magister y 13 estudiantes de pregrado, más un equipo de 46 técnicos y personal profesional completan el equipo de investigación multidisciplinario de BNI. Durante 2019, 8 tesis fueron codirigidas por investigadores de BNI, y 6 estudiantes visitaron laboratorios extranjeros para realizar investigaciones en colaboración. BNI recibió a 10 estudiantes internacionales y postdocs de países de Norte y Sudamérica, Europa y Asia, incluidos EE. UU., México, Alemania, Francia, Irlanda, Brasil, Argentina, Venezuela y Japón. Como parte de su formación científica integral, 40 estudiantes de BNI participaron en actividades de divulgación. Varios investigadores formados en BNI continuaron sus carreras profesionales en otras instituciones nacionales o en el extranjero, mientras que otros se quedaron para obtener un título superior o un puesto postdoctoral. 12 postdocs continuaron sus carreras científicas en otros lugares.

Durante 2019, los investigadores del BNI publicaron 48 artículos con un impacto promedio en revistas ISI de 5.8, que se compara favorablemente con centros similares en el mundo desarrollado, manteniendo nuestra excelente tendencia. Artículos de alto impacto fueron publicados en revistas como *Nature Cell Biology*, y reseñas en revistas prestigiosas como *Cell*, *Nature Chemical Biology* y *Trends in Cell Biology*, además de la participación de investigadores asociados e investigadores adjuntos de BNI en el consejo editorial de prestigiosas revistas científicas, demuestran el impacto internacional de la investigación en BNI. El premio a la mejor tesis de Doctorado fue otorgado a una investigadora BNI por la *Sociedad de Biología Celular de Chile*. A pesar del estallido social a mediados de octubre, los investigadores de BNI continuaron su fuerte presencia en congresos nacionales e internacionales, con 124 posters o presentaciones orales durante 2019.

Durante 2019, se llevaron a cabo varios seminarios nacionales e internacionales que reunieron a investigadores, posdoctorados, estudiantes y profesionales en BNI. Estas instancias han sido críticas para intercambiar información de líneas de investigación y para impulsar la atmósfera interdisciplinaria de BNI en proyectos de colaboración concretos para mejorar el compromiso de BNI con los objetivos científicos del país. Organizamos 11 seminarios regulares, *Conversaciones en Neuromedicina*, en temas que conectan la neurociencia y la medicina, que incluyeron oradores locales e internacionales. Después de un año de organización, entre el 24 de marzo y el 5 de abril de 2019, llevamos a cabo el *Workshop EMBO Bridging cell, and tissue mechanics to fate specification in development*, que tuvo lugar simultáneamente con el *ICGEB Course Optics, forces & Development*, actividades que reunieron a más de 100 personas de diferentes países. El curso ICGEB duró 2 semanas e incluyó estudiantes de diferentes países latinoamericanos. Ambas actividades se unieron con dos actividades de divulgación: *How to Win a Nobel Prize: stumbling on the secrets of cell division (Tim Hunt)* para estudiantes universitarios, y la Conferencia abierta: *Manipulando el origen de la vida humana ¿En qué estamos?* para estudiantes de secundaria y público en general. Paralelamente, llevamos a cabo el *1er Día de Innovación Cyted*, que reunió a investigadores de Colombia, Argentina, Chile y Uruguay para compartir su experiencia en transferencia tecnológica con investigadores chilenos y con estudiantes del *Curso ICGEB*.

La cobertura de prensa de las actividades del instituto ha establecido firmemente a BNI como un centro de referencia en Chile y América Latina. Las apariciones de BNI en la prensa se valoraron en una cantidad sobresaliente de un millón de dólares, con 69 apariciones en periódicos, 52 sitios web de noticias online, 10 apariciones en radio 17 apariciones en televisión. La cobertura de prensa ha contribuido a posicionar a BNI como un centro de recursos para neurocientíficos, profesionales clínicos, estudiantes de secundaria, empresarios y público en general. G Martínez, B Cádiz S Reyes, quienes lideran las plataformas de Educación y Extensión, Cultura y Comunicaciones y Transferencia Tecnológica e Innovación, respectivamente, trabajan en el nuevo edificio. Este sitio ahora está consolidado como un espacio de encuentro en un entorno ideal para interactuar con la comunidad. Una Oficina Ejecutiva se conecta con otros sectores, administra las subvenciones y se coordina con la Junta Directiva.

1.3. Outstanding Achievements

Since its foundation BNI has fostered a cutting-edge culture of scientific research, becoming a regional reference center in biomedicine, neuroscience, life sciences, and biotechnology. The productivity and impact of our research are recognized internationally. We focus on technological transfer and education promoting a critical thinking environment. BNI scientific research continues to be published in journals with high impact factor, including *Nature Cell Biology* and *Trends in Cell Biology*, both articles highlighted with the cover image. During 2019 we have published in 48 journals with an average impact of 5.8. We are proud of this high productivity considering that we work in a developing country. A best Ph.D. thesis award was granted to a BNI investigator. In a context of scarce resources -and even considering the Chilean social outbreak since October 2019 - we have continued to perform scientific research, training, outreach and education activities. This continuity shows that BNI is a highly productive platform in terms of collaborative networks, in raising complementary funding from national and international agencies to perform “blue sky science” in innovation and clinical research. BNI adjunct researchers have led an important number of publications (23/48), which shows the increasing quality and development of the science made by BNI younger researchers. BNI was able to consolidate formal funded research networks with Brazil, Switzerland, France, Ireland, and Germany, in addition to a Latino-American network, in addition to hosting several grants from private US Foundations, and service contracts with the private sector in Chile. In terms of impact to the society, BNI in joint work with the U de Chile has licensed four technologies to an international institution, which represent new ways of funding the science made at BNI.

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 education experts who explore the structure, function of the brain under normal physiology, disease conditions, from cells to whole organisms, generating active, and effective strategies to interact with the scientific community, and the society. 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, and biotechnological research, and transfer its impact to society; and (iv) to become a resource center for specialized clinical practitioners, investors/private sector, 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, and quantitative biology strategies to uncover hidden biological phenomena, coupled to advanced microscopy, and genetic manipulations to perform research at multiples scales from genes to behavior. A special focus was placed on areas to develop *in vivo* approaches with different technological advances, to connect phenomenological scales to promote clinical research in neurology, and psychiatry. We have also promoted a strong sense of belonging 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 of our strategy in consolidating our research vision with solid outputs. We published a new study in *Nature Cell Biology* and obtained the cover image with an editorial comment. This article involved collaboration with 10 labs around the globe. Furthermore, we obtained a cover image in *Trends in Cell Biology*, and published review articles, and commentaries in *Cell*, *Nature Chemical Biology*, *Trends in Pharmacological Sciences* among others.

(ii) ***To promote translational research, and interactions with the private sector. A Neuromedicine, Gene Therapy, and Technology Platform***, which promotes an innovation culture, was established in 2016 to develop internationally competitive, and innovative solutions in biotechnology, neuro-systems data science that impact health, and other areas. Technology transfer, and interaction with industry grew rapidly at BNI. A full-time 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 strengthened our relations with the Technological Transfer Office at the Universidad de Chile, new patents were filled we moved into international PCT phases. One technology to treat ALS was licensed to Bravo Biotech in Australia where **CHz** is part of the Scientific Advisory Board. Then, this initiative translated in the **licensing of a package of 3 patents to a European Company in the area of gene therapy aiming to develop Phase I clinical trials** in Europe (**CONFIDENTIAL**). Significant funding was put in place to generate a new company in Belgium to develop the technologies generated at BNI, and to move BNI's technologies into the clinic aiming to reach commercialization if successful. The licensing agreement resulted in a two-years subcontract with BNI to further develop the technology at the preclinical level "in house" as partnership. New alliances with international biotech companies such as *Mounttam Biotechnology* in the US have been developed further to test the potential of rapalogues to treat Parkinson's disease, in addition to other interactions with Proteostasis therapeutics in the USA generating a new subcontract to test the efficacy of new compounds in cellular models of neurodegeneration. A new international grant was awarded by the **Michael J Fox Foundation Research in Parkinson** to improve gene therapy strategies to target neuronal proteostasis in Parkinson's disease. In addition, two FONDEF R&D grants in gene therapy in the area of Alzheimer's, and Parkinson's disease were developed in partnership with *Genzyme-Sanofy* in Boston. Remarkably, two Staff Scientists at BNI also raised important funding as PIs from national, and international agencies highlighting FONDECYT, and the **Muscular Dystrophy Association**, the **Alzheimers Association**, and the **ALS Association** to develop research, and therapeutics for neurodegenerative diseases.

(iii) ***To expand the impact of training, and capacity building***. Training efforts continue to focus on attracting young talent through formal university graduate programs to bridge initiatives for recruiting postdocs. We promote the incorporation of young international investigators as 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 fostered for a 3rd year collaborations, and interchange of students between labs in France, Ireland, Germany, and Greece. This involvement generated a joint thesis between Chile, and France, we received a Ph.D. student from France, and Ireland, and one of our postdocs spent a year in Ireland. We also established new networks to collaborate with France, and Switzerland by raising funding for bidirectional interactions from ECOS-Conicyt, and a seeding grant from the Swiss government. In addition, the CYTED grant led now by **RF** replacing **AC**, was consolidated to generate a network based on innovation in South America. The excellence in research, and training resulted in an award to Denisse Sepulveda as **Best Ph.D. thesis of Chile** from the Cell Biology Society of Chile.

(iv) ***To strengthen the impact of outreach activities***. Interactions with school students, and teachers are 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, complementing model organisms including clinical studies 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 shared facilities. Approximately 30% of funds are allocated directly to individual researchers for operational expenses whereas the remaining 70% are invested in common undertakings. Millennium funding constitutes approximately 30% 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 Grant management. Finally, we were able to close an agreement with the Fac. of Medicine, and obtained a full floor (250 m²) to consolidate the laboratory of J Sierralta, and an “**Advance Microscopy Unit**” coupled to shared space for image analysis that is connected with the current infrastructure built previously with BNI funding to strength scientific interactions between laboratories.

b) Research Lines:

During 2019 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: C Hetz (**CHz**), M Concha (**MC**), S Härtel (**SH**), C Hidalgo (**CH**), P Maldonado (**PM**), J Sierralta (**JS**) and Andrés Couve (**AC**). The last one mentioned researcher, AC, is now Minister of Science and Technology of Chile, but some of his main scientific projects and lab are still linked to BNI. *Annex 1*.

We are currently executing 8 research lines: **RL1**. Sub-cellular functional dynamics (**AC/SH/CHz/CH/JS/P Olgúin/ CGonzález**). **RL2**. Cellular identity, and morphology (**CHz/JS/P Olgúin**). **RL3**. Supra-cellular development, and circuits: (**MC/SH/CHz/M Cerda/P Olgúin**). **RL4**. Plasticity, and behavior (**CHz/CH/A Paula-Lima/JL Valdés/P Délano**). **RL5**. Systems Neuroscience (**PM/R Fuentes/JL Valdés/P Délano**). **RL6**. Clinical, and disease 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**). *Annex 2*.

c) Organization of researcher's team:

In December 2018, **AC** was appointed by the Chilean President to lead the newly created Ministry of Science-technology-innovation, and knowledge; because of this appointment AC resigned his participation in BN. Thus, BNI now consists of 5 Associated Investigators who conduct research at different biological scales or with different disciplinary approaches (**MC/SH/CHz/PM/JS**). Additionally, one Senior Investigator (**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 Olgúin, A Paula-Lima, JL Valdés, R Vidal, and the recently incorporated P Délano**). The average age of the team of 16 leading investigators is 45.8 years. 8 young investigators including 6 Staff Scientists, 33 national, and international postdocs, 46 Ph.D., 35 Master, and 13 undergraduate students, plus a group of 46 technicians, and professionals complete the multidisciplinary research team. Strategies to foster interactions include (i) leaders that coordinate platforms for collaborative research lines, share technology, and complementary animal models (flies, fish, and mice); (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 an annual retreat; (v) special funds to incite new ideas, and collaborative research (seed grants), and postdoctoral fellowships encouraging co-mentoring that includes 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 other scientific events.

3. Scientific, and technological research:

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

Each research line (RL1-8), although they were initially proposed to be mainly carried out by one or two Associate researchers, they evolved into 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-cellularfunctional dynamics. Despite AC's departure to assume duties as Science Minister, his former lab continued the research lines now led by Dr Carolina González (**CGonzález**); thus, we have continued studying endoplasmic reticulum function, and dynamics. The most recent paper was accepted, and published (2020) on the topic of unconventional channel traffic in axons of the sensory system (*Non-conventional Axonal Organelles Control TRPM8 Ion Channel Trafficking, and Peripheral Cold Sensing*. Cornejo et al., 2020 *Cell Reports* (AC, and **CGonzález**). A beautiful study demonstrated a non-canonical function of the ER stress sensor IRE1 α in the regulation of energy production by the mitochondria, via the control of calcium transfer, and bioenergetics (**CHz**) (*Carreras-Sureda et al., Nature Cell Biol.*), where the Staff Scientist Hery Urrea contributed to this work. This study was highlighted with the Cover Image, and an editorial comment in *Nature Cell Biology*, and another commentary in *Cell Calcium*, and involved collaboration with 10 different laboratories around the globe including a bilateral grant to collaborate with Guido Kroemer in France through the Ecos-Conicyt program. **CHz** has collaborated also to demonstrate the role of p75NTR neurotrophin receptor in the development of the neuromuscular synapse (*Perez et al., Acta Neuropathol Comm*), in addition to identifying a new regulator of autophagy in the CNS known as PACER (*Beltran et al., Mol. Neurodeg.*). A new channel controlling calcium homeostasis in lysosomes, and its implications to stress resistance was characterized (submitted to *Molecular Cell*; **CHz, MC**), and involved collaboration with the Millennium Institute for Neuroscience in Valparaiso. **CH** lab has published a study describing NMDA receptor modulation by NOX2 in animals exposed to ethanol pre, and postnatally (*Plaza et al., Antiox., and Redox signal*) (**CH**). Finally, our studies on the lactate metabolism, and glia-neuron relationship have moved forward describing for the first time the transfer of lactate during neuronal activity using an ex-vivo system, and metabolic sensors genetically encoded (*Gonzalez-Gutierrez et al., Glia*) (**JS**). Important review articles were also published in the area of subcellular function, linking proteostasis control with neuronal function, highlighting a review in *Trends in Cell Biology* that also



obtained the cover image led by a French postdoc (Gerakys et al 2019). Finally, **CHz** in collaboration with Staff Scientist Danilo Medina, and **MC** investigated the role of ER chaperones in the synthesis of synaptic proteins, and their implications to the sustain neuromuscular junction function in ALS (paper submitted to *PNAS*), in addition to identifying genetic mutations linked to intellectual disability (under revision in *EMBO J*).

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 Ph.D. Student A Kohler, and D Villegas, an undergraduate student, are working in this project). Additionally, a strong collaboration with the Leibniz Institute for Neurobiology at Magdeburg has allowed us to conduct STED microscopy in the system. We also continued the study of the regulation of *Drosophila* brain wiring in collaboration with Dr. Carlos Oliva with whom a paper was published on the regulation of the wiring in the optic lobe by the secreted factor Slit (Caipo et al., *Dev.Biol.*, **JS**) together with a review on the topic (Contreras et al., 2019, *Front.Mol.Neurosc.*, **JS**). We have continued the study of atlastin in a hereditary spastic paraplegias model in *Drosophila*. A Ph.D. student (MF Bertin, recently graduated) is writing (**AC/JS/POLguín**) now two papers on this topic.

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. Some results include:

A. Brain morphogenesis, and connectivity: we continued dissecting the role of Nodal-signaling in asymmetric brain morphogenesis finding a novel adhesion molecule downstream of the Nodal pathway that controls the establishment of left-right asymmetry in the zebrafish brain (**MC/SH**). We ended a comparative analysis of habenular connectivity in the Bichir (Polypteridae) demonstrating an ancestral trait in Actynopterigians of the laterotopicdorso-ventral segregation of left-right habenular connectivity in interpeduncular nucleus (Ahumada-Galleguillos et al. **MC/SH**; ready for submission). We found a previously undescribed orexinergic pathway contacting a subset of olfactory sensory neurons to the glomerular layer of the olfactory bulb a nucleus of the basal telencephalon in zebrafish (**MC**). We also characterized the function of ligands of the Robo family of receptors, finding that in zebrafish a novel ligand controls the exit of habenular axons during development (**MC/SH/CHz**) while in *Drosophila* the ligand Slit is secreted by medulla neurons to control boundary formation, and optic lobe morphogenesis (Caipo et al, *Developmental Biology*; **JS**). Finally, we identified novel genetic mutations underlying inherited intellectual disability that were mapped to the ER chaperone ERp57/PDIA3 (**CHz/MC/RVidal**). Using zebrafish models, we discovered that the expression of these genetic variants results in abnormal brain morphogenesis, altering neuronal connectivity. Using viral mediated delivery in the adult hippocampus of mice we observed that the expression of these mutations impaired cognitive function. Unbiased proteomic analysis uncovered a crucial role of adhesion molecules, and cytoskeleton components in the pathological phenotypes (*Medinas et al.*, under review *EMBO J*).

Tissue morphogenesis: we continued studying epithelial, and mesenchymal morphogenesis using *in vivo* imaging, biomechanical manipulation, and mathematical modeling. We explored the role of actomyosin-dependent mechanical forces during epithelial cell delamination using laser-based methods, and mathematical analysis of myosin flows in zebrafish (**MC/SH/M Cerda**). Using physical modelling, we showed that cell migration can be driven by spatial gradients of substrate deformation in a mechanical process of straintaxis (*Marquez et al*, *Physical Biology*; **MC**). In collaboration with groups outside BNI, we showed that (i) N-cadherin (cadherin 2) coordinates the internalization of cells during zebrafish neurulation by a Myosin-II dependent mechanism (*Araya et al*, *Scientific Reports*; **M Cerda**) that (ii) reprimin family member genes are required for blood tissue development during zebrafish development (*Stanic et al*. *Scientific Reports*; **MC**). Finally, we extended our mechanobiology approaches to humans,

assessing the tensile mechanical properties of the Achilles tendon in adult patients with haemophilic arthropathy (*Cruz-Montecinos et al, Haemophilia, M Cerda*).

Disease Models: in collaboration with the neuropathology platform we continued developing pre-clinical models of neurodegenerative diseases associated with aging such as Parkinson's Disease (PD). We finalized the characterization of the catecholaminergic (CA) system in the killifish *Nothobranchiusfurzeri*, finding a shared general organization of CA neurons as in other vertebrates (*Borgonovo et al. MC*; ready for submission). Importantly, we found a decrease of CA neurons in the homologous to the *substantia nigra* of mammals, and the aggregation of alpha-synuclein protein in the brain, and gut during physiological aging of killifish, highlighting the relationship of aging with the disease in this animal model. These features, in combination with the short lifespan make *N. furzeri* a useful vertebrate model to study Parkinson Disease (**MC/CHz**). Current efforts aim to reduce CA impairment, and alpha-synuclein aggregation by aging modifiers in the context of pre-existing predisposing factors induced by genetic, and non-genetic approaches.

RL4. Plasticity, and behavior: The central purpose of this research line is to explore in rodent models cellular mechanisms that bring about or modulate hippocampal synaptic plasticity (LTP, LTD, and structural plasticity), and hippocampal-dependent learning, and memory processes. In the reported period, **CHz** together with three staff scientists Gabriela Martinez, Claudia Duran Danilo Medinas investigated the significance of the unfolded protein response (UPR), a major signaling pathway to cope with ER stress, to normal brain aging. Genetic disruption of ER stress sensor IRE1 accelerated cognitive, and motor dysfunction during aging in multiple assays. Remarkably, artificial enforcement of the UPR by overexpressing an active form of transcription factor XBP1 using transgenic mice, and gene therapy restored synaptic function (LTP, dendritic spine content), and cognitive, and motor performance. Remarkably, proteomic profiling of hippocampal tissue indicated that XBP1s expression corrected age-related alterations in synaptic function. This study was reviewed in *Science*, and is available at *BioXriv* (Cabral-Miranda et al., 2020 doi: <https://doi.org/10.1101/2020.04.13.039172>). This project resulted on a **patent application** in the US (#62800229, inventors **CHz**, and postdoctoral fellow F Cabral) involved an international bidirectional cooperation grant from CONICYT funded by the governments of Chile, and Brazil with Sergio Ferreira, member of the *NeuroSur* network, in addition to collaboration with Adrian Palacios at the Millennium Institute of Neuroscience in Valparaiso, Genzyme, and other centers in Chile, and the world. *The Airforce at the Department of Defense* of the US pre-approved funding for this idea in 2020.

CH, and **SH** have initiated a three-year international collaborative project funded jointly by the Chilean, and German governments. The German team, led by Dr. Hilmar Bading, includes members of the Interdisciplinary Center for Neurosciences (IZN) at the University of Heidelberg. The Chilean team engaged in this project is composed by **CH**, and **SH** (Director, and Deputy Director of the project, respectively), BNI Adjunct Investigator **A. Paula-Lima**, together with BNI research associates T. Adasme, and G. Sánchez, and other collaborators from Universidad de Chile, and Universidad de Valparaiso. Two graduate students, P. Lobos, and S. Gleize, who are doing their Ph.D. thesis work under the joint direction of **CH**, and **A. Paula-Lima**, also form part of the Chilean team. This project - titled "*Unveiling how neuronal calcium signals reach the nucleus following synapse activation*" - is at the interface of neuroscience, calcium signaling advanced microscopy, and imaging techniques. A central topic in this project is to investigate how activity-generated neuronal calcium signals reach the nucleus, where they induce gene expression changes required for synaptic plasticity, and hippocampal-dependent learning, and spatial memory formation/consolidation. We are testing currently if calcium release channels present in the endoplasmic reticulum contribute to generate the nuclear calcium signals required for synaptic plasticity, and the formation-consolidation of hippocampal spatial memory. We have found that RyR-mediated calcium signals contribute to the generation of nuclear calcium signals that control gene expression. A manuscript is in preparation describing these results. In addition, together with BNI

Adjunct Investigators **JL Valdés**, and **A Paula-Lima**, BNI postdoctoral fellow A. Arias-Cavieres, and graduate students J. More, and P. Lobos, we have found that fat mice (generated by feeding them a high-fat diet), have significant defects in hippocampal LTP, and LTD, and display defective hippocampal learning, and memory processes. We are currently writing a manuscript describing these results. To conclude, **CH** published a review article addressing the noxious iron-calcium connections in neurodegenerative processes (*Nunez, and Hidalgo, Frontiers in Neuroscience*).

The role of brain proteostasis in adjusting global organismal physiology is investigated at the level of the brain-gut axis. Staff Scientist Gabriela Martinez in collaboration with **CHz** is currently investigating the consequence of manipulating the UPR transcription factor XBP1 in neurons to then address the consequences on gut physiology, and microbiota. Our results indicate that activation of the UPR in the brain improves gut physiology, providing resistance to experimental colitis. Finally, the interphase between the chronic exposure to environmental stress, and neuronal proteostasis is currently investigated by **CHz, and** Staff Scientist Gabriela Martinez through collaboration with Dr Carmen Sandi, director of the Brain, and Mind Institute in at EPFL, Switzerland, a project funded by the Swiss government. A Postdoc from Cuba already performed a research visit to the center at EPFL. We are investigating the significance of the UPR in environmental stress-induced behavioral alterations aiming to identify novel fundamental mechanisms underlying the resistance, and vulnerability to adverse stress conditions, and how they relate to proteostasis alterations.

RL5. Systems Neuroscience: During this year, we have continued work on this research line with the contributions of several laboratories, including those led by **PM, CH, A Paula-Lima, JL Valdés, P Gaspar,** and **R Fuentes**. This year we report the research activity of our new Adjunct Researcher **P Délano**, recently incorporated into BNI. Many projects include collaborations between two or more of BNI scientists. The research line included the work of 6 young scientists, 6 postdocs, 15 Ph.D. students, 10 Master's students 2 engineer students.

JL Valdés, and **PM** have continued their research work on the mechanisms of perception. This year they finished a behavioral study on active sensing, showing that the mechanisms that underlie sensory improvement during active behaviors have a constrained time dynamic, where the peak performances occur during the motor act, decreasing in proportion to the lag between the motor act, and the stimulus presentation. (*Concha-Miranda et al., F, Front. Behav. Neurosci.*). Also, **JL Valdés** explores the mechanisms that modulate neural plasticity related to exercise. This year his group showed that the increase in the Tuberomammillary nucleus activity induced by exercise might be the foremost contributor of the ascending arousal system to memory enhancement observed in exercised animals. (*Fuentealba et al., Brain Res.*) **JL Valdés** also published a study on motivated behavior, showing that the infralimbic cortex induces an increase in arousal during the appetitive phase of motivated behavior, and that this increase in arousal is, in turn, mediated by the activation of the brain histaminergic system, resulting in higher motivation for getting food rewards. (*Riveros et al., Frontiers in Neuroscience*).

This year, several basic studies in systems neuroscience were carried out. **PM's** group showed that finger's temperature can be used to predict attentional performance. In predicting attentional performance, finger temperature resulted to be a complement of the EEG spectral measurements, predicting aspects of attentional performance that had not been foreseen by spectral analysis of EEG activity or through the improvement of the model's fit. (*Vergara et al., Frontiers in Human Neuroscience*). In another Ph.D. thesis project conducted in **PM's** lab, Juan Mariman sought to explore the mechanisms of motor learning; his main findings were published showing that, when the environment demands great visual attention, error-based, and reinforced motor learning processes are implemented simultaneously, thus enabling efficient predictive behavior. A third paper resulted from a special collaboration between **PM, AC** (now the country's Minister of Science), and **R Fuentes** in a theoretical paper. The paper was significant since it is the first truly theoretical report in BNI, there we propose a new bottom-up conceptual paradigm: The Energy Homeostasis Principle, where the balance between

energy income, expenditure availability are key parameters that determine the dynamics of neuronal activity from molecular to behavioral levels. The high energy consumption that neurons display (20% of the whole-body oxygen uptake, representing only 2% of the bodyweight) requires important local energy management mechanisms, which constrain its possible outputs, and thus, may be enough to explain the emergence of behavior, based on the assessment of which properties could arise in neural circuits, and how. (*Vergara et al., Frontiers in Computational Neuroscience*). **P Délano**'s group, published Constantino Dragicevich Ph.D. thesis about selective attention during a visual-auditory task. He found the presence of low frequency (<10 Hz) brain, and cochlear amplifier oscillations during selective attention to visual, and auditory stimuli. Notably, switching between auditory, and visual attention modulates the amplitude, and the temporal order of brain, and inner ear oscillations. These results extend the role of the oscillatory activity network during cognition in neural systems to the receptor level. (*Dragicevich et al., Plos One*)

A significant number of studies in this research line explore the clinical consequences of brain circuitry. A subline of research in Line 5 is carried out by **R Fuentes**, who is interested in the regulation of motor circuits, and Parkinson's disease. Synchronized oscillations have been a frequent finding suggesting that excessive synchronization of neuronal activity may be a pathophysiological mechanism involved in a wide range of neurologic, and psychiatric conditions. This year they reviewed the experimental support for this hypothesis primarily in relation to Parkinson's disease but also in relation to dystonia, essential tremor, epilepsy psychosis/Schizophrenia. (*Halje et al. Journal of Neurophysiology*). **P Délano** explored the neuronal mechanism related to hearing loss. In this period, he showed that the neural abnormalities observed in presbycusis subjects with cochlear amplifier dysfunction extend beyond the core auditory network, and are associated with cognitive decline in multiple domains. (*Belkhiria et al., Front Aging Neurosci.*). Staff scientist Chris Devia, and **PM** published an article showing that EEG signals from a free-viewing paradigm discriminate patients from healthy controls, and have the potential to become a tool for the psychiatrist to support the positive diagnosis of Schizophrenia. (*Devia et al., IEEE Trans Neural Syst Rehabil Eng.*).

RL6. Clinical studies and RL8. Neuropathology.

Neurodegenerative diseases –A central goal of BNI is to conduct clinical brain research sustained by cutting-edge basic neuroscience. One of the major areas of biomedical development at BNI is focus on neurodegenerative diseases involving abnormal protein aggregation including ALS, Huntington's disease, Parkinson's disease, Fronto-Temporal dementia, and Alzheimer's disease. This research line involved the active participation of more than 10 postdocs, 12 research assistants 6 Ph.D. students, in addition to 4 Staff Scientists. This research is supported by a transversal, and open animal facility administrated by BNI that also contains the capacity to perform a battery of motor, and cognitive tests brain stereotaxis. We have moved forward in our studies in ALS to define the impact of the proteostasis network in neuronal degeneration and investigated the functional consequences of targeting the UPR with genetic, and pharmacological approaches (**CHz** Staff Scientist Danilo Medinas). In addition, the role of protein translation, and the integrated stress response is investigated in ALS but also frontotemporal dementia supported by two FONDECYT grants, involving one joint Ph.D. students (Luis Osorio; **CHz**, and **S Matus**). The role of ER chaperones in the synthesis of synaptic proteins, and the connection to neuromuscular function integrity in ALS is also investigated by **CHz**, and Staff Scientist Danilo Medinas, who also raised funding as PI from FONDECYT, the **Muscular Dystrophy Association, and the ALS Association** in the US to develop gene therapy strategies, and define the role of ER chaperones in ALS. **S Matus** is also investigated how sensors of the nutritional status (i.e. GCN2) regulates inflammation, and protein synthesis in ALS but also aging. Finally, in the last years we developed a gene therapy to develop the UPR transcription factor XBP1 into the CNS of ALS mouse models, that resulted on a previous **patent application**. This technology was licensed to a European community together with other 2 related patents by a new company aiming to develop clinical trials to

treat ALS patients. The licensing process together with the tech transfer office at U Chile resulted on a research contract of more than 700.000 USD to further develop the gene therapy approach in preclinical models of ALS.

CHz and R Vidal developed a FONDEF grant as director, and deputy director together with **S Matus**, to further develop a gene therapy approach with recombinant viral vector (AAVs) with artificial chimeric UPR transcription factors (a technology termed UPRplus) to reprogram gene expression toward adaptation to stress, and treat Parkinson's disease patients. A **patent was filed** previously as co-inventors between **CHz and R Vidal**, and the technology was recently licensed as part of the pack to a European Company (CONFIDENTIAL) to develop clinical trials together other two more patents. The data of the full study is under consideration in *Molecular Therapy*, and was submitted as co-correspondence between **CHz and R Vidal**. In addition, an extension grant was awarded from the *M J Fox Foundation for Parkinson Research* to further develop a gene therapy to improve ER proteostasis in models of idiopathic PD based on the misfolding, and spreading of alpha Synuclein aggregates. In addition, **CHz** uncovered the necroptosis machinery as a new pathway mediating axonal degeneration in Parkinson's disease (Oñate et al., *Cell Death Diff*; available at BioRxiv also). One postdoc, and a Ph.D. student are also studying the role of the UPR in Parkinson at the level of oligodendrocytes, and astrocyte-mediated inflammation as novel research angles. In addition, two international postdocs are investigating the possible impact of the UPR to cognitive deterioration in Alzheimer's disease, and its relation to the aging process. This research line was supported by an international grant funded by the *Alzheimer's Association* to Staff Scientist Claudia Duran, and a second R&D FONDEF grant led by **CHz**, and Adrian Palacios (Deputy Director, U Valparaiso, and member of the Millennium Institute of Neuroscience Valparaiso). This grant aims to develop a gene therapy to deliver the active form of the UPR transcription factor XBP1 into the hippocampus of Alzheimer's mice, and is based on a previous BNI patent application to use AAV-XBP1 to improve the basal learning, and memory capacity led by **CHz, and Staff Scientist Gabriela Martinez** (co-inventors).

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 Dr. Pedro 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, to accelerate discovery, and therapeutic approaches. We are seeking molecular blood markers in Huntington's patients to better understand the underlying molecular mechanisms of this disease. The level of IGF2 in the serum, and blood cells from 40 Chilean Huntington's patients was measured, observing a positive correlation with disease progression. This study involved one joint Postdoctoral fellow from Spain (Paula Garcia-Huerta), and one joint Ph.D. student (Paulina Troncoso) between **CHz, and R Vidal**. This study discovered a new neuroprotective activity of IGF2 on Huntington's disease, where its administration to neuronal cultures revealed that IGF2 treatment decreases the load of intracellular aggregates of mutant huntingtin, and a polyglutamine peptide. These results were validated using induced pluripotent stem cells (iPSC)-derived medium spiny neurons from HD patients. The decrease in the levels of abnormal protein aggregation triggered by IGF2 were linked to enhanced secretion, and degradation of mutant huntingtin species through exosomes, and microvesicles, involving changes in actin dynamics. Administration of IGF2 into the brain of HD mice using gene therapy led to a significant decrease in the levels of mutant huntingtin in three different animal models. This study is under consideration in *Acta Neuropathologica* as co-correspondance between **CHz and R Vidal** and is now available at *BioRxiv* (doi: <https://doi.org/10.1101/2020.05.28.119164>), and involved collaboration with labs in The Netherland, the US (Scripp Research Institute, Bandervit U. the Buck Institute), Israel, in addition to two US biotech companies (*Genzyme-Sanofi*, and *Proteostasis Therapeutics*). This study resulted previously in a **patent application** where **R Vidal, CHz**, and a Postdoctoral fellow (Paula Garcia-Huerta) are co-inventors. In addition, **R Vidal** is currently studying the significance of IGF2 to Parkinson's disease, and aging through funding by FONDECYT. Furthermore, a second joint Ph.D. thesis between **R Vidal, and CHz** (Maria Jose Hormazabal) is

exploring the neuroprotective properties of rapalogues in models of Parkinson's disease, and its relation to the diet in collaboration with the US company *Mounttam Biotech*.

In the same line of studies, in 2019, we have awarded a FONDECYT grant to investigate cortical neuroplasticity reserve in patients with ALS, in order to explore novel biomarkers of cortical dysfunction (**JM Matamala**). This grant will allow us to set up cortical excitability techniques using transcranial magnetic stimulation (TMS) in Chile, which will be a unique opportunity to explore brain mechanisms of cortical degeneration in Chilean patients with ALS, dementia, and movement disorders. We also participated in the Gold Coast ALS Consensus Meeting in Australia to establish new clinical diagnostic criteria for ALS patients (**JM Matamala**), which we hope would accelerate the diagnostic process in the fatal neurodegenerative disorder. Finally, the same group published the first complete clinical, imaging histological characterization of a Chilean family with Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts, and Leukoencephalopathy (CADASIL).

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 electrical neuromodulation of the spinal cord (**R Fuentes**). Additionally, we continued to study the effects of chronic spinal cord neuromodulation on gene expression using differential expression analysis of mRNA. We have identified 12 signaling pathways that are potentially involved in the long-term effects of spinal cord stimulation for Parkinson's disease (**R Fuentes/R Vidal**). We are also exploring the discovering of a specific biomarker such as gene, protein or metabolites in Chilean Parkinson Disease patient to determine the stage of patients (**R Vidal**).

A Paula-Lima research findings show that treatment with serotype b-LPS triggers the secretion of proinflammatory cytokines by microglia, induces neurite shrinking increases the extracellular A β 1-42 levels, all features strongly associated with the etiology of Alzheimer disease (*Díaz-Zúñiga et al. Journal of Oral Microbiology*). **CH** continues to work on calcium, and plasticity. Her work showed that prenatal alcohol exposure associates with NOX2 overexpression and increased NMDAR-mediated transmission, which might lead to impaired synaptic plasticity, and memory formation in a region-specific manner (*Plaza-Briceño et al., Antioxidants & Redox Signaling*). In addition, **CH** reported in a review article the multiple cell-damaging responses generated by the unregulated iron/calcium self-feeding cycle (*Nuñez & Hidalgo, Frontiers in Neuroscience*). Danilo Medinas, Staff Scientist, is currently developing new research line on intellectual disability funded by FONDECYT in collaboration with **CHz**. As mentioned, we identified a homozygous mutation in *protein disulfide isomerase A3 (PDIA3)* causing syndromic intellectual disability. PDIA3 catalyzes the formation of disulfide bonds in the ER. Overexpression experiments in zebrafish embryos with **MC** showed that PDIA3 mutant is pathogenic, causing developmental problems such as axonal disorganization, and bone abnormalities. In mammalian models, expression of mutant PDIA3 inhibited axonal growth, and impaired synaptic plasticity, and memory consolidation. Proteomic, and functional analysis revealed that mutant PDIA3 leads to dysregulation of cell adhesion, and actin cytoskeleton dynamics. This study is under revision in *EMBO J*. Finally, we collaborated (**CHz**) with other Universities to uncover novel genes involved in autophagy in ALS (*Beltran et al. Mol Neurodegen.*) signaling pathways mediating motoneurons dysfunction the disease (*Pinto et al., Neurobiol Dis.*).

Finally, a new research area of brain diseases is under develop at BNI led by the Staff Scientist HeryUrria as a natural result of his high impact paper published in *Nature Cell Biology* in 2018. Dr Urria is leading a FONDECYT project as PI, and is currently co-mentoring two students with **CHz** to develop models of brain cancer, more specifically glioblastoma investigate factors involved in brain tissue invasion, in addition to the role of the microenvironment, and stress responses in tumor growth. An MD-Ph.D. student (Rodrigo Fernandez, expert in brain surgery) is developing a clinical study in this new area to define the correlation between genetic factors driving brain cancer in Chilean patients, and the levels of ER stress. This Ph.D. project resulted in the isolation of 40 tumors, and the development of primary cultures, and neurospheres for further analysis. We already developed a pipeline in collaboration with U.

Mayor to sequence a large panel of genes to identify known mutations, and epigenetic changes associated with brain cancer. Finally, **CHz** published several review articles to highlight the significance of targeting ER proteostasis for the treatment of neurodegenerative diseases, brain cancer drug discovery, placing BNI as a relevant international center leading the area of neuronal proteostasis, and disease (*Hetz et al., 2019, Nature Chemical Biology*; *Gionzalez-Teuber et al, Trends Pharmacol Sci*; *Martinez et al., Biol Cell*; *Limia et al., Cancers*).

Psychiatric studies, and electrical recording in patients -We searched for neurophysiological markers of Schizophrenia, and in the early detection in ultra-high Psychosis risk (UHR) populations, and the 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 (**P Gaspar**). In 2019, we have awarded two FONDECYT grants to continue, and expand this line of research in the area of how motor disturbances could be associated to the cognitive deficits, and how motion alterations affect the social cognition in those populations. 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). The results found allowed us to discover that in patients with initial EA there are detectable electrophysiological alterations through surface EEG recording, and changes in eye-tracking during virtual space navigation. This line of research may 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. (**A Paula-Lima/PM**). We also have been developing a new software for virtual spatial navigation testing, specially adapted for our elderly population, and to be implemented in our public health system, as an early diagnostic tool for aMCA (**JL Valdés**).

In a separate study, **PM** aimed to find biomarkers in cardiology. **PM** demonstrates that pupillary response is different according to cardiovascular risk. Finally, **P Gaspar** wrote an important conceptual paper in psychosis research. Early detection, and intervention (EDI) are the main challenge in psychosis research. The Chilean Schizophrenia (SZ) national program has universal support, and treatment by law for all SZ patients, but this does not yet extend to earlier stages of illness. They have piloted an ultra-high risk (UHR) program to demonstrate the utility, and feasibility of this public health approach in Chile. (*Gaspar et al., Early Interventions in Psychiatry*)

Finally, another innovative line of research that we have implemented is the use of automatic language processing, and EEG resting state as reliable tools to characterize psychiatric interviews (**P Gaspar/M Cerda**). In 2019, we have awarded a FONDECYT grant to expand this line of research on how automatic language alterations in psychosis risk subjects could predict the appearance of the full-blown psychosis episode.

RL7. Biomathematics. The Biomedical Mathematics, and Informatics Group (BioMat, bni.cl/biomat.php) guided by BNI investigator **SH**, and adjunct investigator **M Cerda**: In 2019, we pushed collaboration with BNI labs by weekly sessions in microscopy, equipment, image/data processing. We highlight projects with **P Olgún** 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 morphotopological analysis of asymmetrical brain morphogenesis in zebrafish (J Jara); P Lobos/**MC** & I Vega/**A Paula-Lima** image segmentation (J Jara), and expansion microscopy (J Toledo); P Scavone (IIBCE Uy, article submitted), N Canales & K Chandía/**SH** deconvolution, segmentation, and tracking of bacteria, and biofilms (J Jara);, and A Figueroa (**P Gaspar**) lab with automatic analysis of psychiatric interview transcriptions, and audio signals. C Bolatto (IIBCE Uy) Quantification of apoptotic/mitotic hemocytes in null mutant Patched-related *Drosophila* embryos P Scavone (IIBCE Uy) Biofilm Formation, and 4-

lens Light Sheet Microscopy (two MS ¿submitted?). Three MS published in *Frontiers in Pharmacology*; *Scientific Reports*; *Journal of Biomechanics*.

BioMat, and the Center of Medical Informatics, and Telemedicine CIMT (www.cimt.cl) advanced in the following: B Rafael (supervisor **M Cerda**) finished her Master thesis, working on *Data sharing protocol to facilitate interinstitutional research in the field of psychology*; M Aguirre (supervisor **SH**), finished her Master thesis *Using Machine Learning to Study Obesity in Chile*; P Llanos continued her Ph.D. in Biophysical Simulations of Cytoskeleton (supervisor **SH/M Cerda**); C Cruz (**M Cerda**) continued his Ph.D. in biomechanics, publishing two papers (both Cruz-Montecinos C et al *Haemophilia* 2019). R Kindelan (**M Cerda**) officially started as Computer Science Ph.D. student in 2019. Six students (F Miranda, K Chandía, J Carrasco, M Lanás R Sagues) got the approval of their Master Thesis in Medical Informatics (supervisor **SH** or **M Cerda**). Ph.D. student J Jara finished his work on *Optimizing Adjacent Membrane Segmentation* (**SH**, article in press, thesis in submission).

BioMat, and associate members also advanced in: (i) Improvements of imaging techniques for 4-lens light-sheet with optical tweezers (L Alé, K Chandía), oil droplets for force measurements (P Maillard, N Canales), segmentation, and registration techniques (J Jara, A Lavado), 3D design & printing of optogenetics devices (P Maillard, K Palma/MC), confocal microscopy equipment diagnostics/maintenance (L Alé, P Maillard), expansion microscopy (J Toledo, D Castagnini/SH); (ii) facility design, and construction (P Maillard, L Alé). Data Center SASIBA, connected with 10 GBps connectivity, and 300 Terabytes for data storage, sharing server hosting is working on a regular base, and received major upgrades (**SH/M Cerda**); (iii) course/symposium organization/teaching/ presentation of the ICGEB Course “Optics, Forces, and Development” & EMBO Workshop “Bridging cell, and tissue mechanics to fate specification in development” (J Jara, L Alé, P Maillard);, and imaging courses in Medellín (Co), and Montevideo (Uy) (iv) publication, and outreach: BioMat member J Jara had one original research article in press co-authored two submitted MS. P Maillard, and K Palma/MC appeared in TV, and newspaper articles with LED Array optogenetics for *in vivo* imaging with confocal microscopy; (v) guided visits of school students (J Jara, L Alé) were offered at SCIAN-Lab during the entire year.

In 2019, three new projects were awarded, all at an international level. First **CH/SH/A Paula-Lima**: Unveiling how Neuronal Ca-signals reach the nucleus following synapse activation CONICYT-CI/BMBF-Ger (2019-2022). Second **SH**: Capacitaciones en Biofilm: “una respuesta para superar las bacterias multi-resistentes”, Agencia de Cooperación Chilena para el Desarrollo, Ministerio de Relaciones Exteriores, Cooperación Sur-Sur entre Chile y Uruguay. Asociadas: (BNI/IIBCE). (2019-2020). Third **SH**: Deep-Pathology: Plataforma de TelePatología Distribuida Basada en Blockchain y Diagnóstico Colaborativo Apoyado por Deep Learning, FONDEF (2019-2021), F-Med y HCUCH U-Chile. ITMS-Chile, Tiga-Center Steinbeiss-Ger.

b) Outstanding publications: *Annex 3*.

- Carreras-Sureda A., Jaña F., Urra H., Durand S., Mortenson D., Sagredo A., Bustos G., Hazari Y., Ramos-Fernández E., Sassano ML., Pihan P., van Vliet A., Gonzalez-Quiroz M., Tores A., Tapia-Rojas C., Kerkhofs M., Vicente R., Kaufman R., Inestrosa N., Gonzalez C., Wiseman R., Agostinis P., Bultynck G., Court F., Kroemer G., Cárdenes JC., and **Hetz C.** (2019). Non-canonical role of IRE1 as a functional determinant of mitochondria-associated endoplasmic reticulum composition to control calcium transfer, and bioenergetics. *Nature Cell Biology*. 21(6):755-767(**Cover illustration**). Commented in *Nature Cell Biology* (2019) 21, 667–668. *CellCalcium* (2019) 8, 83. At BNI we study the role of the ER stress sensor IRE1 in neurodegeneration and neuronal physiology. In this study we discovered that a subpopulation of IRE1 is located at the ER-mitochondrial contact sites, regulating calcium transfer and bioenergetics.

- Oñate M., Catenaccio A., Salvadores N., Saquel C., Martinez A., Moreno-Gonzalez I., Gamez N., Soto P., Soto C., **Hetz C****. (2019). The necroptosis machinery mediates axonal degeneration in a model of Parkinson disease. *Cell Death Diff*. doi: 10.1038/s41418-019-0408-4. Here we uncovered that

axonal degenerations is controlling by a signaling pathway that controls regulated cell death by necroptosis but at the level of the axonal compartments. We performed cell culture and in vivo studies using genetic and pharmacological manipulation of the pathway to demonstrate a role in axonal degeneration in models of parkinson's disease.**co-correspondence.

- **Hetz C**, Axten JM, Patterson JB. (2019). Pharmacological **Hetz C**, Axten J. Patterson J. (2019). Pharmacological targeting of the unfolded protein response for disease intervention. *Nature Chem Biol.* 15(8):764-775. This review article summarizes available drugs to target the UPR and treat diseases associated with protein misfolding including neurodegenerative disease.
- González-Gutierrez, A., Ibacache, A., Esparza, A, Barros, LF, **Sierralta, J** Neuronal lactate levels depend on glia-derived lactate during high brain activity in Drosophila. *Glia.* 1213-1227. ISSN: 1098-1136. Doi: 10.1002/glia.23772. In this paper we were able for the first time to measure lactate fluxes in glia and neurons in the same ex-vivo preparation and determine the changes occurring during conditions of high neuronal activity, additionally by the use of mutant animals for glial lactate transporters we were able to demonstrate the crucial role of the lactate shuttle from glia to neurons in this ex-vivo larval brain Drosophila preparation.
- Rodrigo C. Vergara, Sebastián Jaramillo-Riveri, Alejandro Luarte, Cristóbal Moëne-Loccoz, Rómulo Fuentesrés Couve, and **Pedro E. Maldonado** The Energy Homeostasis Principle: Neuronal Energy Regulation Drives Local Network Dynamics Generating Behavior *Frontiers in Computational Neuroscience.* (enblanco). ISSN: (enblanco). Doi: 10.3389/fncom.2019.00049. This is the first theoretical paper in BNI. Additionally is involves two BNI PIs and one adjunct researcher plus several postdocs. been a product of a true novel collaboration as a product of been in BNI. This paper proposes a new bottom-up conceptual paradigm: The Energy Homeostasis Principle, where the balance between energy income, expenditure availability are key parameters that determine the dynamics of neuronal activity from molecular to behavioral levels.

Publications: Summary table

Category of Publication¹	MSI Center Members	Number of Publications coauthored by students	Total Number of Publications
ISI/WOS Publications or Similar to ISI/WOS Standard	Associate Researchers	18	47
	Others Researchers	0	0
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	1
	Others Researchers	0	0
Books & Chapters of Books	Associate Researchers	0	0
	Others Researchers	0	0
Other Scientific Publications	Associate Researchers	0	0
	Others Researchers	0	0

¹<https://www.ncbi.nlm.nih.gov/pubmed/>; <https://scielo.conicyt.cl/>

c) Congress Presentations:

“Improving ER proteostasis delays brain aging”, presented at the EMBO Workshop Proteostasis: From organelles to organisms, in Lisboa, Portugal. **CHz** was invited as speaker to this important meeting in the field of proteostasis, physiology and disease where most relevant PIs attended. We presented for the first time our data on brain aging and the unfolded protein response. The RL1, RL4 and RL6 are impacted by this type of activities since we are one of the main centers studying the role of ER stress in brain diseases leading centers developing therapeutics.

JS presented “Characterization of the Lactate/Pyruvate transport in Drosophila larval central nervous system” at the Neurobiology of Drosophila conference, CSHL, New York, USA. The presentation was

during the period that the paper was sent but not yet accepted, so it was a perfect opportunity to discuss with colleagues the next experiments. This is the most important meeting for *Drosophila* neurobiology, and for that it represents a great platform to show the work and also to observe the work of others. This is related to RL1 and RL2.

PM & A Paula-Lima presented “Modification of functional connectivity as an early mechanism of impairment in spatial memory in patients with cognitive impairment” at the 48th Annual Meeting of the Society for Neuroscience., Chicago, USA. This poster presentation is relevant to the research line 5, because it combines the activity of **CH**, **A Paula-Lima** and **PM** laboratories, and because it shows the characterization of early electrophysiological marker for mild cognitive impairment.

SH & M Cerda organized the ICGEB course “Optics, Forces & Development”, CYTED-BNI Innovation Day & EMBO Workshop, held in Santiago de Chile. Combined international postgraduate school with theoretical and hands on practices with innovation event for microscopy and imaging facilities and scientific workshops. Many speakers gave lectures within the course, all students attended the EMBO Workshop. The subject of “Optics, Forces & Development” lies within the heart of the working philosophy of SCIAN-Lab, and the strong collaboration with LEO-Lab (Miguel Concha)-BioMat members and researchers using the fish facility contribute to common research and training in new techniques of in vivo imaging and image processing pipelines for high through put and data intensive light sheet microscopy.

MC participated as organizer of the EMBO Workshop -Bridging cell and tissue mechanics to fate specification in development, held in Santiago de Chile, where he presented his work "Selective physical interactions drive the collective motion and spatial segregation of organ progenitors". **MC** also presented "Guidance of collective mesenchymal locomotion by epithelial sheet traction" at LASDB Meeting, Buenos Aires, Argentina. Both presentations were held at high-level international conferences, where the most outstanding scientists from the field attended to. The presentations are framed within the "Cellular identity, and morphology" and “Supra-cellular development and circuits” Research Lines of BNI, particularly addressing studies the cell-tissue mechanics and the events shaping the vertebrate embryo.

Summary Table

Type of Researcher	Type of presentation	National Events	International Events
Associate Researchers	Conferences, oral communications, poster communications, others (Specify)	38	23
	Invited presentations (not included in above row)	4	10
Other researchers	Conferences, oral communications, poster communications, others (Specify)	20	16
	Invited presentations (not included in above row)	4	9
Students	Conferences, oral communications, poster communications, others (Specify)	0	0
	Invited presentations (not included in above row)	0	0

Other achievements:

S Reyes is head of Technology Transfer, and Innovation since 2015 leads our *Neuromedicine, and Technology Platform (NeuroTech)*. We have continued to promote intellectual property protection, technology transfer, applied research, private fundraising 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 provisional patent was filed during 2019: Claudio Hetz, Felipe Cabral. *Treatment of aging or age-related disorders using XBP1*. Provisional application for patent at USPTO, application number 62800229. Submitted 01/02/2019. Status: patent pending. Additionally, in late 2019, three technologies in the field of gene therapy against neurodegenerative diseases were transferred to a biotechnology company through a patent license. **The aim of this licence is to further develop the gene therapy technologies to undergo Phase I clinical trial.** The recombinant viral vectors (AAVs) will be optimized for clinical use, and tested in preclinical models of Parkinson, and ALS in mice, and also non-human primates. The licensing process also resulted in a research contract with BNI of more than 700.000 USD to validate the new technology in preclinical models of ALS as partnership with the European Company. The specific information of the company, and patents involved cannot be revealed yet due to the confidentiality clause contained in the license, it will be made public in mid-2020. The signing of this license is the institute's greatest achievement in technology transfer since its creation.

Organization of Scientific Events:



During 2019, meetings gathering all BNI investigators, and professionals took place weekly or monthly. These instances have been critical to exchange information of research lines, and drive BNI cross-disciplinary atmosphere into concrete collaborative projects, and to improve BNI commitment with the country's scientific development. We organized regular seminars, called *Conversations in Neuromedicine*, to discuss around topics that connect neuroscience, and medicine, that were animated usually by local, and international speakers. A representative poster of one *Conversation* done in 2019 is

presented in the figure A. We also promoted a second kind of gathering, called “Pizza talks”, were young scientists talk about their central scientific research questions and over the impact of their scientific endeavor in Chile. “Pizza talks “has contributed to create an intimate discussing environment that stimulates the scientific critical thinking of our researchers (figure B). A representative poster of “Pizza Talk” 2019 is presented in figure B. Finally, we are doing a set of practical sessions aimed to improve complementary capacities, and abilities necessary for scientific career development that are not usually trained at labs. These sessions are organized in a program called “BNI Transforma”. A representative poster of one done at 2019 is presented in the figure C. *Regular scientific events produced by BNI. Figure A: Sample of a topic discussed at Neuromedicine Conversations series; Figure B: Sample of a topic discussed at Pizza talks events; Figure C: Sample of a practical session at BNI Transforma.* During 2019 we carried out an EMBO workshop called *Bridging cell, and tissue mechanics to fate specification in development* (April 2-5th, 2019). In this context, we organized two outreach activities, an opening lecture done by the Nobel Prize Tim Hunt (April 2th, 2019; figure A) intended for undergraduate students an event called *Manipulando el origen de la vida ¿en qué estamos?* made up by two talks, and a panel discussion (figure B). This last one, took place at the ex-congress, and school students were the audience.





Figure 2. Outreach activities related with the EMBO workshop *Bridging cell, and tissue mechanics to fate specification in development*. A- Open lecture *How to win a nobel prize: stumbling on the secrets of cell division* by Tim Hunt. B- Ex-congress event *Manipulando el origen de la vida ¿en qué estamos?*.

In order to reinforce the identity of the Institute, and to promote the interaction between teams from different laboratories we organized a BNI retreat (Termas del corazón, San Esteban, Región de Valparaíso). Activities included an introduction of how BNI could help their members in diverse aspects related to their endeavor (science, operation, culture, communication, outreach, education, and innovation). We also performed a scientific elevator pitch exercise, a methodology called *Participatory Innovation* to improve our culture organization, and games. More than 140 people participated in this 2-day retreat (figure 3).

Figure 3. BNI Retreat at Termas del Corazón.



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 2019 most of the BNI researchers took part in the editorial boards of high impact ISI standard journals. BNI researchers are editors of *Frontiers in Behavioral Neuroscience* (**JS**, Guest Associate 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), *Biological Research* (**CH**, Editorial Board), *Frontiers in Physiology* (**CH**, Review Editor), *Journal of General Physiology* (**CH**, Editorial Advisory Board).

BNI Adjunct Investigators are currently part of the following editorial boards: *Frontiers in Psychiatry* (**P Gaspar**, Guest associate editor), *Journal of Neurology, Neurosurgery, and Psychiatry* (**JM Matamala**), *PloS One* (**P Délano**, Editorial Board), *Journal of Association for Research in Otolaryngology* (**P Délano**, Editorial Board), *Frontiers in Systems Neuroscience* (**P Délano**, Guest associate editor), *Frontiers in Neurology* (**P Délano**, Guest associate editor), *Frontiers in Integrative Neuroscience* (**P Délano**, Review Editor), and *Scientific Reports* (**S Matus**, Editorial board). Additionally, **P Delano** is Chief Editor in the journal *Revista Otorrinolaringología y Cirugía de Cabeza y Cuello* (SCIELO standard), and **P Gaspar** is Editorial Board in the *Contacto Científico* journal.

Awards:

During 2019 three young researchers were awarded. Denisse Sepúlveda, one of our current postdoctoral researchers was awarded with the **Best Ph.D. thesis of Chile**. This recognition is given for the Chilean Cell Biology Society, and her research was not only the best thesis of Chile but also was published as cover page in the prestigious journal *Molecular Cell* (Sepulveda, et al. 2018), in addition to an editorial comment, and the publication of her biography, and scientific motivations in the journal in the section “Meet the authors” (<https://www.cell.com/molecular-cell/meet-the-author/sepulveda-rojas-rivera-rodriguez>). Besides, this achievement resulted in important press release to the society to show the value of science since her research was published in numerous newspapers, and magazines in Chile.

María de los Ángeles Juricic, a postdoc researcher won the First Prize in the category of Ophthalmopediatrics, strabismus, and neuro-ophthalmology in the Second Meeting for Research carried out for the Department of ophthalmologist of the Faculty of Medicine, Universidad de Chile.

Finally, Alfredo Sagredo received award for the *Best Poster Presentation* in the EMBO meeting of Proteostasis in Portugal. This study was recently published in *Nature Communications* (Dufey et al., 2020).



Dr Alfredo Sagredo receiving an EMBO Award as “Best Poster Presentation” in Portugal with UCFS/HHMI Investigator Dr Peter Walter.

4. Education, and Capacity Building

a) **Education, Training and Capacity Building:**

BNI is a community formed by more than 200 persons, 5 of whom are associate investigators, and 10 are adjunct investigators. As a whole, BNI is the training, and career development site of a large number of scientists, and Staff, contributing significantly to the formation of human capital for our country, still unfulfilled needs. During the last nine years of operation, BNI has work in the context of the Universidad de Chile, the leading public educational institution in Chile, providing the largest, and most diverse network of undergraduate, and graduate programs in biomedical sciences, including Neuroscience. Because BNI is an Institute that operates in the Faculty of Medicine, we benefit from many graduate programs, including 6 Ph.D., and 17 Master programs. Besides, BNI has intense research, and teaching ties with other Faculties of the University, such as the Faculties of Sciences, Engineering, Chemistry 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 some academic committees at the Medical, Chemical & Pharmaceutical Sciences Science Faculties, U Chile. BNI Investigators also are lead teachers, and organize advanced graduate courses in Neuroscience, and related disciplines, including Introduction to Neuroscience, Cognitive, and Systems Neuroscience, Cell Physiology, Molecular Mechanisms of Neurodegenerative Disease, Molecular & Clinical Pharmacology, Topics in Biomedicine, and Neuropsychopharmacology. Importantly, **CHz** served the whole year as a member of the executive committee for the Ph.D. Program in Biomedical Sciences, the largest in the country. **PM** has served the last years as a member of the Graduate School Council, and headed the committee on a graduate program (CCPGA). Also, **JS** (director), and **JL Valdés** and **P Délano** (members) have served in the committee of the Masters in Neuroscience **SH** (director) and **M Cerda** (member) have served in the committee of the Master Program

in Medical Informatics. BNI scientists also participate in graduate programs in other Faculties at U Chile (Engineering & Mathematics, Chemistry & Pharmaceutical Sciences, Sciences Dentistry, Veterinary), and other universities in the metropolitan, and regional areas. **A Paula-Lima** was instrumental in the creation, and management of the Ph.D. Program in Odontology. Noteworthy, BNI was instrumental in establishing the new Department of Neuroscience at the Faculty of Medicine, which now holds 33 Faculty members. Nine faculty members of this department are currently associated with BNI. Principal investigator **PM** is serving as chairman of the Department of Neuroscience and JS is its Deputy Director.

BNI is part of a **European Training Network** funded by the RISE program from the European Community. This training grant known as INSPIRED connects labs between Chile (**CHz**), Ireland, France, Germany, and Greece, and funded during 2019 two joint Ph.D. thesis between Chile, and France (1 year visit), a Postdoctoral research stay to Galway, and the visit of students to BNI from France, and Ireland. Our Institute 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. Our focus is on education, and capacity building 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 other clinical specialties. Initiatives involve American Universities, such as Columbia, Harvard, USA McGill Canada, University of Osaka, Japan as well leading Universities, and Institutes in the European Union: Gottingen, Heidelberg, Magdeburg, Mannheim Institute of Mental Health, Germany; Jülich Forschungs zentrum, Germany; Cagliari University, Italy; Jaume I University, Castellon, Spain. International collaborations have provided a framework for research stays of graduate, and associated scientists. Several 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 makes possible to incorporate not only Chilean scientists but more than five international young researchers.

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 the impact on BNI's collaborative efforts.

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 2019, more than eight theses were co-directed by BNI Investigators. Students are encouraged to share BNI facilities, educational technology transfer opportunities. Postdocs, graduate undergraduate students take the initiative, and organize regular seminars, and symposiums in the framework of BNI, inviting foreign established scientists, or national postdocs carrying out research periods abroad.



Investigators, trainees Staff attended our annual retreat to share the research culture, which fosters a sense of belonging to a school of thought.

b) Achievements, and results: Annexes 5.1 y 5.2

During 2019 worked in BNI, the five principal investigators, plus 10 adjunct investigators. We also define a new category of Staff Scientists (6), young independent investigators who work in BNI labs. Staff Scientist have been extremely successful, and were able to raise 4 FONDECYT projects in addition to three international grants as PIs (ALSA, MDA, and AD Association), developing new ideas to expand the research capacity at BNI. We also include one senior investigator (CH) who is now President of the National Academic of Science. In our institute also worked 94 students (13 undergraduates, 35 at master's Programs, and 46 Ph.D. Students), and 33 postdoctoral fellows. Eight of these students are jointly tutored by two or more BNI investigators. BNI's staff members include 12 persons that help in administration, and financial offices. Our student body includes nine international students from countries in South America, and Europe, including Germany, Venezuela, Japan Uruguay. This period, 12 students completed their dissertation work. Some of these trainees have 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. Many BNI papers are published with students as co-authors. BNI students also participate regularly in national, and international meetings, in poster, and oral sessions (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, France, Switzerland, Canada, New Zealand Australia. Additionally, we received eight international students from Colombia, France, Ireland, Brazil, and Germany, who performed research at BNI labs. We have also run 21 national, and three international seminars, and courses that include several international students from the region.

As part of their comprehensive scientific training, more than 60 BNI students have also participated in outreach activities organized by BNI, such as visits to schools, in-lab training in our facilities, high student guidance our Loligo, and Dendros initiatives.

c) Destination of students:

BNI undergraduate, and master students usually follow advanced studies (Ph.D., MD-Ph.D.) or are directly involved in clinical research. Most BNI graduate students are recruited for scientific, and academic careers, pursuing postdoctoral fellows or faculty members in Chile or abroad. Twelve students graduated during 2019 five postdocs continued their scientific careers elsewhere, including academic positions in Chile, and the USA. Five graduates have remained in science, and academia. Some national institutions that have incorporated former BNI young investigators include U Chile, Pontificia U. Católica de Chile, Universidad, Andres Bello, Universidad Metropolitana de Ciencias de la Educación, and U. Austral de Valdivia, among others.

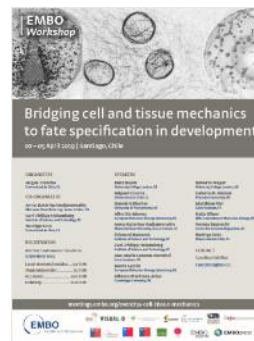
5. Networking, and other collaborative work. Annex 6

a) Networking:

BNI's working philosophy is shaped by three strategic lines: Scientific interactions within BNI, collaborative network formation, and consolidation on a regional, and international scale. In 2019, our philosophy deepened, and advanced within three strategic lines:

(i) Promote national, and international scientific networks. Individual, and collaborative multidisciplinary networks of BNI members have consolidated over the years. BNI investigators have

established active funded initiative to interact with several laboratories around the world. **CHz** established a network with Sergio Ferreira in Rio de Janeiro through a bilateral grant funded by the Chilean, and Brazilian government (CONICYT) allowing the interchange of postdocs, and students in the area of neurodegeneration, and aging. In addition, a bi-national research project was awarded by CONICYT-CHILE / BMBF-ALEMANIA 180051 (2019 - 2022), **CH, SH, A Paula-Lima** with investigators, Hilma Bading, and Peter Bengtson from (U-Heidelberg). **CHz** is further developing a collaboration with Guido Kroemer in Paris through an ECOS CONICYT grant, who collaborated in our study in Nature Cell Biology. **CHz** also established a formal network of collaboration with Carmen Sandi, the Director of the Brain, and Mind Institute at EPFL funded by seed grant from the Swiss government to study the adverse effects of stress to the function of the CNS. A formal scientific interaction with the **Buck Institute for Research in Aging** has been strengthened by **CHz** as Adjunct professor, a process that will lead to the establishment of a second laboratory in 2020.



In 2019, BNI members organized, and supported international events, such as “Microscopía Confocal, Superresolución y Procesamiento de Imágenes” Medellín (Co, 11-14 March) **SH/MC Cerda. SH**

participated as invited speaker in “Biofilms Microbianos: Rápido y Furioso” Montevideo (Uy, 14-28 October). **MC/SH/MC Cerda** organized the international hands-on ICGEB course on “Optics, Forces. Development”, Santiago (Cl), aimed primarily to Latin American students. All students, and most teachers attended the CYTED-BNI Innovation Day, and Evening Conference Reception with the Chilean Minister of Science, previous Director of BNIrés Couve (Cl, 1 April, see image below) (**SH**) attended the EMBO Workshop “Bridging cell, and tissue mechanics to fate specification in development” Santiago (Cl, 2-5 April) (**MC**). In addition, an outreach activity was carried out at the former National Congress building. Speakers of the Workshop celebrated a scientific agreement with the Chilean Government, gave lectures, and participated at round table to discuss the topic “Manipulating the origin of human life. What are we up to?” (400 participants, **MC**). In a tight collaboration with The Valparaíso Millennium Institute **CINV, JS** organized for 5th time the successful international course Small Brains Big Ideas, that counted with EMBO support. Teachers from UK, France, Canada, Uruguay, Argentina, and USA, came to give a 12 days hands-course directed to Latin-American students from Mexico, Colombia, Argentina, Uruguay, Perú, and Chile.

Young master students from Medical Informatics (BNI), and *Clemente Estable Institute* (IIBCE) have been awarded an international project to share capacities in microscopic image processing, and structure formation of bacterial microorganisms -biofilms-. The alliance strengthens research on multi-resistance to antibiotics in Latin America, specifically on urinary infections that mainly affect women, through training of young female researchers from both countries. The Chilean Agency for International Development Cooperation, under the Chilean Ministry of Foreign Affairs, and the Uruguayan Agency for International Cooperation (AUCI) finance 18 months, starting August 2018, contributing to workshops (20 participants), technical training extension (see image below). Press, and TV-interviews have been released, and two MS are under revision.

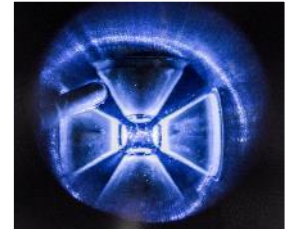
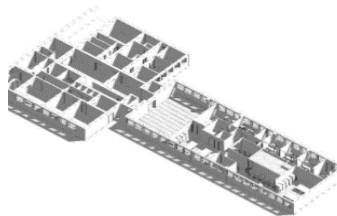
CURSO PEDECIBA-BIOLOGIA



The Neurosur Network
Un Cerebro para América Latina, of the Programa Iberoamericano de Ciencia y Tecnología para el Desarrollo

(CYTED) financed the following activities in 2019. (i) Innovation Day, and Workshop "Competencies, and Methodologies for Technology Transfer in Latin America" with 60 participants from the academic sector, mentioned above (SH), (ii) Course "New Signaling Pathways in Neurodegenerative Diseases", 17-18.12 2019, held at the Institute of Scientific Research, and High Technology Services - INDICASAT, Panama, with 57 participants from the academic sector. (iii) Course "Plasticity, autophagy, cell senescence, and apoptosis in the Central Nervous System: (iv) Event: "Nucleation Meeting of the Latin American Brain Initiative (LATBrain, 31.08-1.09.2019)", held at Clemente Estable Biological Research Institute, Montevideo, Uruguay (RF). The main objective of this initiative is to promote cooperation among neuroscientists in the region around a common project in the area of neuroscience. Researchers leading the Brain Initiatives in the USA, Australia, and Cuba, as well as organizations, societies, networks, and research institutes in the Latin American region, representatives of public, and private entities government authorities in the region are participating in these meetings. All of the abovementioned actions, and events evolve within the spirit of The NeuroSur Network that BNI researchers pushed from the beginning of the institute in order to promote scientific collaboration, and exchange between countries in the region.

(ii) Enhance the dynamics, and quality of collaborative projects within BNI. We continue to support series of collaborative initiatives such as Seed Grants (4), Bridge Fellowships (2) co-mentorship of students (6-10 per year). BNI continuously supports co-application to external funding (e.g. Fondecyt grants, and international grants such as CYTED, DAAD or AUCI/ACCI), young investigator grants (Fondecyt initiation, and insertion into the academia), equipment (e.g. Fondecyt) networking for science, and innovation (e.g. PCI



ANID, CORFO). In 2019, BNI investigators started executing the construction of a modern laboratories for investigators a microscopic imaging facility to amplify the shared space for interdisciplinary work of BNI scientists, and staff significantly (aprox 300 m2).

(iii) Create interactions with the industry. BNI has established sponsored research agreement, and formal collaboration with companies in the US, and Europe. A recent licensing agreement for 3 technologies in the area of gene therapy resulted on a formal contract to further develop preclinical studies at BNI. During 2019, BNI developed 9 innovation projects with companies from different sectors of the economy, as detailed in section 6B of this report. Also, contact was made with companies from different sectors, including the biotechnology (Cellus, Handle Biotechnologies, Proteostasis Therapeutics, Genzyme), health (Hospital del Trabajador, Clínica Los Coigües, Vidavisión), pharmaceutical (Knopp, Pfizer), industrial (CAP, Arauco), and mining (Antofagasta Minerals, Codelco, Angloamerican). Finally, BNI developed an important event together with SOFOFA (Chilean industrial association) to promote the integration with the productive area.

(iv) Foster scientific interactions within a multidisciplinary environment. BNI continuously fosters a multidisciplinary research 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 symposia (2-4 per year) BNI retreats (1 per year). The BNI building close to the new metro station *Hospitales*, and laboratories provides: (A) Open work, and coffee lounge for vibrant discussions of science & innovation. Regular, and informal meetings take place in an open, friendly lively atmosphere; (B) Seminar room (60 participants) equipped with modern infrastructure, and connectivity. It provides an essential complementary working space, especially due to its flexible management by BNI for events after working hours, and weekends. This is essential, e.g. for the International Master for Medical Informatics Program (academic director **SH/M Cerda**), diploma, summer schools; (C) Board meeting room (14 participants) used for group, and lab meetings, and strategic meetings with partners from associated scientific centers, projects, or industry. Seminar, and board rooms are equipped with modern infrastructure, 10Gbps network connectivity that facilitates meetings, and streaming via the Chilean University Network REUNA (www.reuna.cl), or the Latin American Network, CLARA.

The new imaging facility under construction by BNI provides optimal workspace for advanced microscopic equipment, image & data analysis through REDECA (<http://redeca.med.uchile.cl>). REDECA was organized by **SH** with equipment financed from additional competitive funding sources awarded to BNI members **CHz/MC/CH/AC/SH**, and collaborating researchers of the Institute of Biomedical Science (ICBM). REDECA is a pioneer facility for national, and regional researchers.

b) Other collaborative activities

Deeper integration of *e-health* related data science by BNI BioMat was pursued through the participation in the *La Serena School for Data Science: Applied Tools for Data-Driven Sciences*, at the interphase of health science, biomedicine astronomy. In 2019, (**SH/M Cerda**) planned, and performed the third 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 USA. During 2019, the international Master Program in Medical Informatics has become financially independent from DAAD-funding. However, it maintains a close partnership with U-Heidelberg within the Excellence Initiative fostered by the German Foreign Ministry (4 centers worldwide). With 38 applications, and 22 selected students by the end of 2019, the program has become one of the largest (and the only international) graduate program at the Medical Faculty of the Universidad de Chile.

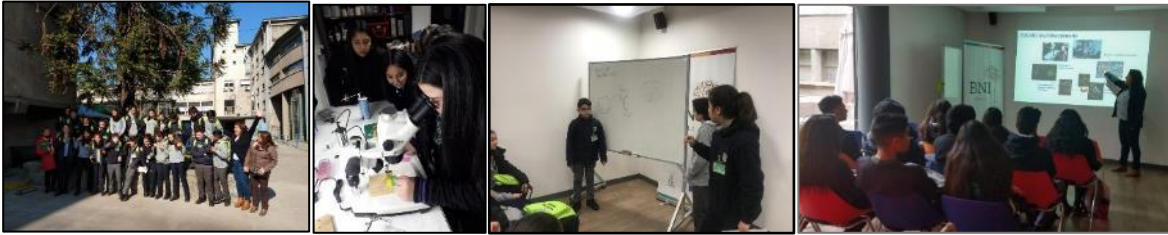
6. Outreach, and connections with other sectors Annexes 7.1 to 7.3.

Outreach: In 2019, BNI outreach program continued to grow in education, and out-of-school science activities. In recent years, our institute has established several initiatives including a web comic, games, “Domo cerebro” - a traveling exhibition - as out-of-school activities our education program called “Mente transformadoras”, that includes workshops for biology teachers, open labs for school students, a national education conference for teachers, and a science book. All the digital resources are available in our new web platform www.loligo.cl.

“Mentes transformadoras”: education program

1. **Open labs:** In 2019 we invited 9 schools to visit our laboratories. Students from primary to high school, and undergraduate came to our institute to see, and carry out experiments in different labs to discover the scientific questions that are researched in our institute. BNI Master, and PhD students are

involved in this activity preparing, and conducting the monthly activities. Students, and scientists get closer, and enjoy this experience.



2. **Workshops for biology teachers:** During 2019 we have continued with the development of our education program, we did 6 workshops using digital resources, and material produced by Biointeractive-HHMI. Workshops are linked to the national curriculum, and allow the teachers to learn, and practice inquiry-based activities. We maintained, and strengthened the relationship with HHMI this allowed us to develop new tools for the workshops. These resources are available in our platform www.loligo.cl/educacion. We have impacted on more than 700 teachers of different school levels coming from almost 90% of our country. We have received feedback from them describing that through these workshops they have developed teaching skills that now allow them to generate more significant learning for their students.

3.

4. **Ministry of Education – CPEIP:**

Considering the success of our program, we were able to sign an agreement with the Center for Improvement, Experimentation, and Pedagogical Research (CPEIP) of the Ministry of Education. We started a pilot project with three locations: Talagante, Santiago Sur, and Limarí. In these workshops, we follow the same methodology implemented in our workshops more than 100 teachers attended.



Dendros world: out-of-school science

1. **Domo Cerebro:** Our traveling exhibition received around 50,000 visitors during 2019. This activity through games, and applications motivates visitors to get closer to neuroscience. Besides the exhibitions, the Domo includes two experimental activities: an electroencephalography (EEG) station, which allows to detect the visitor’s brain electrical activity patterns, and a microscopy station where visitors can visualize samples of healthy brains, and brains obtained from models of neurodegenerative diseases. “Domo Cerebro” participated in several scientific events like: Festival Puerto de Ideas - Antofagasta, Planetario de Santiago, Fiesta de la Ciencia Explora.



2. 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 area of BNI is led by innovation specialist S Reyes.

Results of 2019 include signing nine new research contracts in the following fields: a) Occupational diseases: Three projects in collaboration with Asociación Chilena de Seguridad (ACHS); b) Laboral fatigue: Desert Point; c) Data science: Socialab; d) Vehicular behavior: In collaboration with ISCI, and Autopista Central; e) Biotechnology: PTI, and Regenero and f) Electronic sports: Solunova

Private initiatives are ongoing or were completed during this period. Strong links of collaboration, and trust were established with the companies, and the overall perception of the interaction with BNI has been positive. 2019 has been the year with the highest research contract activity with companies, the number of projects was significantly higher, tripling the contracts compared to the average carried out since 2016 (from 3 per year to 9 per year).

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.

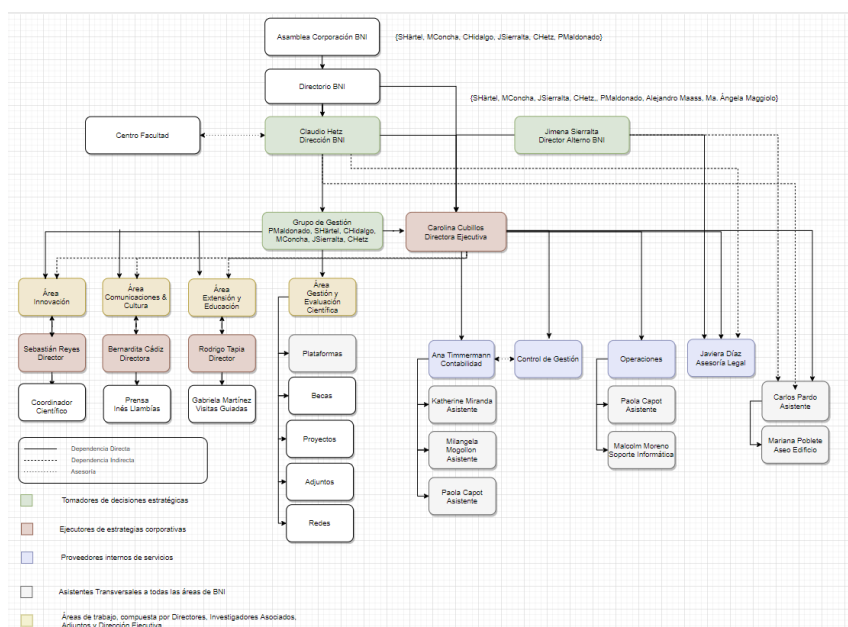
7. **Administration, and Financial Status**

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 2019 we continued with the same Directory board elected in 2018. **CHz** has continued as President, and **JS** as Vice-president, Likewise, **PM** (Dir), **SH** (Dir) , and **MC** (Sec) has continued in their positions. AMAass (F Mathematical, and Physical Sciences, and Center for Mathematical Modelling, U Chile) M Maggiolo (Vice-Dean, F Med U Chile) have continue supporting BNI Directory board as representants of U de Chile.

2019 was a year of changes in BNI. We hired Dr. G Martinez to lead the area of outreach, and education program (www.loligo.cl), after RTapia (previous director) was incorporated to form part of the Ministry of Technology, Innovation Knowledge of the Chilean Government. G Martinez has accomplished with success this work, and from her expertise she has led all projects of the area even generating more networks with teachers, and the Ministry of education of the Chilean Government. Since 2015 SReyes has work on BNI promoting applied projects, innovation, fundraising technology transfer. SReyes efforts also promotes the connection between scientist, and entrepreneurs evidencing the value of BNI scientific support to give significance to their products, and services. After AC departure the Executive Office, led by C Cubillos, an economy finance professional, has taken a pivotal role in the organization of BNI administration, helping additionally on the production of scientific events. This new role has given great support to all BNI areas, and has impulse a better order, and record of all meetings and tasks involving decisions from the PIs. Even more a new management software, and new financial process inside BNI team was acquired thanks to her impulse. BCadiz continues to lead our Culture, and Communications area. She focuses on web, social networks, internal cohesion, and has strengthened the cultural field inside BNI trough the promotion of internal programs to develop communicational abilities among our young scientist, and students to foster the building of integral scientist with more capabilities beyond the laboratory. J Díaz, an experienced lawyer since 2016 provides legal assistance. Since the beginning of BNI the Grant Management Office has been led by A Timmermann. Nowadays the office is constituted by three assistant accountants, K Miranda, M Mogollón, and PCapot, and a deputy chief accountant RLillo, who is leading the implementation of the new management software 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 I Llambías, journalist work under BCadiz direction, and contribute to consolidate BNI's corporate image, and promote its activities. BNI staff work closely with administrative, and technical personnel of all research groups.

To see more about our BNI team, please visit: <http://www.bni.cl/equipo.php?i=I>



Category	Female	Male	TOTAL
Assistant & Technicians	19	15	34
Administrative Staff	8	4	12
TOTAL	27	19	46

Financial Status: Annex 9

Item	2019 Expenses[CLP]			
	Operative	Networks	Outreach	Total
Honoraria researchers, and research personnel	229.272.366	0	0	229.272.366
Tickets, and travel expenses	41.407.402	0	0	41.407.402
Materials, and supplies	78.480.737	0	0	78.480.737
Goods, and equipment	33.433.285	0	0	33.433.285
Infrastructure	2.488.189	0	0	2.488.189
Administrative expenses	71.401.045	0	0	71.401.045
Publications, and subscriptions	13.996.490	0	0	13.996.490
Consultancies	12.037.968	0	0	12.037.968
Overhead	0	0	0	0
Others	272.486.254	0	9.563.787	282.050.041
Total	755.003.736	0	9.563.787	764.567.523

8. Annexes

Annex 1.- Institute / Nucleus Researchers

1.1 Associate Researchers

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Jimena Sierralta Jara	RL1 Sub-cellular functional dynamics . RL2 Cellular identity and morphology. RL8 Neuropathology.	Chilean	F	12-09-62	Biochemist	D	U 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.	German	M	24-11-68	Physicist	D	U de Chile	Full Professor	Part Time
Pedro Esteban Maldonado Arbogast	RL5 Systems Neuroscience. RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	30-04-60	Biologist	D	U 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	24-03-76	Biotechnologist	D	U 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	06-03-66	Physician	D	U de Chile	Full Professor	Part Time

1.2 Staff Scientist and Young Researchers

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Tatiana Adasme Rocha	RL4 Plasticity and behavior. RL5 Systems Neuroscience.	Chilean	F	21-02-77	Biochemist	D	U Bdo O'Higgins	Associate Professor and Researcher at CIBQA.	Part Time
José Ignacio Egaña Tomic	RL5 Systems Neuroscience. RL6 Clinical studies.	Chilean	M	09-10-73	Physician	D	U de Chile	Assistant Professor	Part Time
Danilo Bilches Medinas	RL8 Neuropathology.	Brazilian	M	23-11-81	Chemist	D	BNI / U de Chile	Staff Scientist BNI	Part Time
Claudia Durán Aniotz	RL4 Plasticity and behavior. RL8 Neuropathology.	Chilean	F	01-04-82	Biologist	D	BNI / U de Chile	Staff Scientist BNI	Full Time
Gabriela Martínez	RL4 Plasticity and behavior.	Chilean	F	01-04-83	Biologist	D	U de Chile	Staff Scientist BNI	Full Time
German Flavio Reig Cardarella	RL3 Supra-cellular development and circuits.	Argentinean	M	23-08-76	Agronomist	D	U de Chile	Young Investigator Leo Lab	Full Time
Christ Devia Manríquez	RL5 Systems Neuroscience.	Chilean	F	03-10-82	Psychologist	D	BNI / U de Chile	Staff Scientist BNI	Full Time
Carolina González	RL1 Sub-cellular functional dynamics .	Chilean	F	01-11-82	Biotechnologist	D	U de Chile	Staff scientist BNI	Full Time
Hery Urra	RL8 Neuropathology.	Chilean	M	13-02-84	Biochemist	D	U de Chile	Staff scientist BNI	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	RL1 Sub-cellular functional dynamics . RL4 Plasticity and behavior. RL5 Systems Neuroscience. RL6 Clinical studies. RL7 Applied mathematics and biomedical informatics. RL8 Neuropathology.	Chilean	F	10-06-41	Biochemist	D	U de Chile	Full Professor	Part Time

1.4 Postdoctoral Researchers

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Rodrigo Clemente Vergara Ortúzar	RL5 Systems Neuroscience.	Chilean	M	23-11-86	Biologist	D	U de Chile	Postdoc Neurosystem's Lab.	Full Time
María de los Ángeles Juricic	RL5 Systems Neuroscience.	Chilean	F	02-10-83	Biochemist	D	U de Chile	Postdoc Neurosystem's Lab.	Full Time
Eduardo Pulgar	RL2 Cellular identity and morphology. RL7 Applied mathematics and biomedical informatics.	Chilean	M	23-10-81	Biochemist	D	U de Chile	Postdoc Scian Lab.	Full Time
Alejandro Ernesto Luarte Navarro	RL1 Sub-cellular functional dynamics .	Chilean	M	22-01-84	Biochemist	D	U de Chile	Postdoc Carolina Gonzalez Lab (AC)	Full Time
Andrés Enrique González Gutiérrez	RL2 Cellular identity and morphology.	Chilean	M	07-07-79	Biochemist	D	U de Chile	Postdoc Sierralta Lab.	Full Time
Esteban Contreras Sepúlveda	RL1 Sub-cellular functional dynamics .	Chilean	M	10-05-84	Biochemist	D	U de Chile	Postdoc Sierralta Lab.	Full Time
Patricio Ahumada Galleguillos	RL3 Supra-cellular development and circuits.	Chilean	M	06-05-79	Biologist	D	U de Chile	Postdoc Leo Lab.	Full Time
Karina Palma	RL2 Cellular identity and morphology.	Chilean	F	10-08-79	Veterinarian	D	U de Chile	Postdoc Leo Lab.	Full Time
Carmen Gloria Lemus Cortes	RL3 Supra-cellular development and circuits.	Chilean	F	25-02-80	Biologist	D	U de Chile	Postdoc Scian Lab.	Full Time
Gonzalo Olivares Herane	RL2 Cellular identity and morphology.	Chilean	M	11-02-78	Biochemist	D	U de Chile	Postdoc Lab. Patricio Olguín	Full Time
Alexis Rivas Ahumada	RL8 Neuropathology.	Chilean	M	30-03-81	Biochemist	D	U de Chile	Postdoc Hetz Lab	Full Time
Felipe Cabral Miranda	RL4 Plasticity and behavior. RL5 Systems Neuroscience.	Brazilian	M	14-09-87	Biotechnologist	D	U de Chile	Postdoc Hetz Lab	Full Time

Full Name	Research Line	Nacionality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Vicente Spiro Valenzuela Paterakis	RL8 Neuropathology.	Chilean	M	08-07-83	Biotechnologist	D	U de Chile	Postdoc Hetz Lab	Full Time
Janina Edith Borgonovo Grosso	RL8 Neuropathology.	Argentinean	F	14-02-78	Biochemist	D	U de Chile	Postdoc Leo Lab.	Full Time
Paulina Falcón Urrutia	RL8 Neuropathology.	Chilean	F	05-10-87	Biotechnologist	D	Fundación Ciencia & Vida	Postdoc Soledad Matus Lab.	Full Time
Philippe Pihán	RL8 Neuropathology.	Chilean	M	04-06-86	Bioengineering	D	U de Chile	Postdoc Hetz Lab.	Full Time
Yannis Gerakis	RL8 Neuropathology.	French	M	22-03-89	Library science	D	U de Chile	Postdoc Hetz Lab.	Full Time
Jorge Alejandro Toledo Hernandez	RL7 Applied mathematics and biomedical informatics.	Chilean	M	31-07-84	Biochemist	D	BNI	Postdoc Scian Lab.	Full Time
Younis Mohammad Hazari	RL8 Neuropathology.	Indian	M	22-05-84	Biochemist	D	U de Chile	Postdoc Hetz Lab.	Full Time
Alexis Martínez Saavedra	RL8 Neuropathology.	Chilean	M	20-06-84	Biochemist	D	BNI	Postdoc Hetz Lab.	Full Time
Alicia Ivonne Figueroa Barra	RL6 Clinical studies.	Chilean	F	27-02-71	Pedagogy	D	BNI	Postdoc Psiquis Lab.	Full Time
Alfredo Sagredo Campos	RL1 Sub-cellular functional dynamics .	Chilean	M	02-07-86	Medical Technologist	PostD	U de Chile	Postdoc Hetz Lab.	Full Time
Karla Margarita Padilla Olvera	RL1 Sub-cellular functional dynamics .	Mexican	F	25-06-88	Food Chemical Engineer	D	BNI	Postdoc Maldonado Lab	Full Time
Pablo Felipe Báez Benavides	RL7 Applied mathematics and biomedical informatics.	Colombian	M	08-06-85	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	03-01-85	Informatics engineering	D	BNI / U de Chile	Postdoc Controlmotor & Neuromodulation lab	Full Time
Nicolás Leonardo Fuenzalida	RL4 Plasticity and behavior.	Chilean	M	01-04-86	Biochemist	D	BNI / U de Chile	Postdoc LEO Lab.	Full Time

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Emilio Ernesto Méndez Olivós	RL3 Supra-cellular development and circuits.	Chilean	M	24-09-87	Biochemist	D	BNI / U de Chile	Postdoc LEO Lab.	Full Time
Chama Belkhiria Belkhiria	RL5 Systems Neuroscience.	Tunisian	F	05-08-87	Neuroscience Researcher	PostD	U de Chile	Postdoc Délano Lab	Full Time
Mei-Li Diaz Hung	RL4 Plasticity and behavior.	Cuban	F	13-09-89	Biochemist	D	U de Chile	Postdoc Hetz Lab (U de Chile)	Full Time
Constantino Dragicevic Rebolledo	RL5 Systems Neuroscience.	Chilean	M	10-01-86	Biologist	D	U de Chile	Postdoc Neurosystem Lab	Part Time
Denisse Sepulveda Alvarado	RL8 Neuropathology.	Chilean	F	20-02-89	Biotechnologist	D	U Mayor	Postdoc Lab. René Vidal	Full Time

1.5 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	16-12-75	Biologist	D	U de Chile	Assistant Professor	Part Time
Andrea Paula-Lima	RL4 Plasticity and behavior. RL8 Neuropathology. RL6 Clinical studies.	Brazilian	F	20-11-77	Chemist y Farmacia	D	U de Chile	Assistant Professor	Part Time
Patricio Alejandro Olguin Aguilera	RL1 Sub-cellular functional dynamics. RL2 Cellular identity and morphology. RL3 Supra-cellular development and circuits. RL8 Neuropathology.	Chilean	M	23-10-75	Biochemist	D	U de Chile	Assistant Professor	Part Time
Pablo Gaspar	RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	20-08-75	Physician	D	U de Chile	Assistant Professor	Part Time
René Vidal	RL8 Neuropathology. RL6 Clinical studies.	Chilean	M	03-05-79	Biochemist	D	U Mayor	Assistant Professor	Part Time
Soledad Matus	RL6 Clinical studies. RL8 Neuropathology.	Chilean	F	23-06-74	Biochemist	D	Fundación Ciencia & Vida	PI of the laboratory of Biology of Neurodegeneration	Part Time

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Mauricio Cerda Villablanca	RL3 Supra-cellular development and circuits. RL7 Applied mathematics and biomedical informatics. RL8 Neuropathology.	Chilean	M	23-11-82	Informatics engineering	D	U de Chile	Assistant Professor	Part Time
Rómulo Antonio Fuentes Flores	RL5 Systems Neuroscience. RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	28-10-74	Biochemist	D	U de Chile	Assistant Professor	Part Time
Jose Manuel Matamala Capponi	RL6 Clinical studies. RL8 Neuropathology.	Chilean	M	13-11-83	Physician	D	U de Chile	Assistant Professor	Part Time
Paul Délano	RL5 Systems Neuroscience.	Chilean	M	06-02-76	Physician	D	U de Chile	Associate Professor	Part Time

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

N°	Research Line	Research Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date	Status
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/CGonzalez).	Alejandro Ernesto Duarte Navarro. Carolina González Claudio Hetz Steffen Härtel. M. Cecilia Hidalgo. Jimena Sierralta. Patricio Olguín. Karla Padilla. Esteban Contreras. Alfredo Sagredo.	Biofísica. Biología celular. Bioquímica. Fisiología biofísica. Biotecnología. Genética y evolución.	01-07-16		Active
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. Claudio Hetz Steffen Härtel Jimena Sierralta Eduardo Pulgar Karina Palma Miguel Concha Patricio Olguín	Biología celular. Bioquímica. Biotecnología. Biofísica. Fisiología biofísica.	01-07-16		Active

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date	Status
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 Olgún); 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 Steffen Härtel Mauricio Cerda Carmen Lemus. Patricio Ahumada. Miguel Concha. Patricio Olgún. 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.	01-07-16		Active
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).	M. Cecilia Hidalgo. Felipe Cabral. Claudia Durán. Gabriela Martínez. Claudio Hetz. Tatiana Adasme. JLuis Valdés. Andrea Paula-Lima. Mei.Li Diaz Hung	Fisiología biofísica. Biología del desarrollo. Histología. Morfología.	01-07-16		Active

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date	Status
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 Siegmond. Rómulo Antonio Fuentes Flores. Tatiana Adasme Rocha. María de los Ángeles Juricic. Rodrigo Clemente Vergara Ortúzar.	Bioquímica. Biotecnología. Biofísica. Oftalmología. Métodos numéricos y computación. Probabilidades, matemáticas aplicadas y estadísticas. Fisiología biofísica.	01-07-16		Active
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).	Paulina Falcón. Yannis Gerakis. Amado Carreras. Janina Borgonovo. Miguel Concha. Andrea Paula-Lima Danilo Bilches. Denisse Sepulveda JManuel Matamala JIgnacio Egaña	Otras especialidades de la biología. Biología del desarrollo. Biología celular. Medicina psicosomática (incluyendo psiquiatría).	01-07-16		Active

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date	Status
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.	Claudio Hetz. Pablo Gaspar. MCecilia Hidalgo. Pedro. Maldonado Rómulo Fuentes René Vidal Soledad Matus Andrea Paula-Lima JLuis Valdés Alicia Figueroa Mauricio Cerda Jorge Toledo Steffen Härtel Eudardo Pulgar Miguel Concha Pablo Baez Cristóbal Moenne	Biología molecular. Bioquímica farmacología. Farmacología. Otra especialidades de la medicina. Métodos numéricos y computación. Biofísica. Biología celular. Fisiología biofísica. Ingeniería en computación.	01-07-16		Active

N°	Research Line	Research Line Objectives	Description of Research Line	Researcher	Research Discipline	Starting Date	Ending Date	Status
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).	Christ Devia. Pedro Maldonado. JIgnacio Egaña. MCecilia Hidalgo. Chama Belkhiria. Paúl Délano. JLuis Valdés Claudio Hetz Constantino Dragicevic. Claudia Durán. Alexis Rivas. Hery Urria. Philippe Pihán . Younis Hazari . Alexis Martínez. Claudio Hetz. Steffen Härtel. Rómulo Fuentes. René Vidal. JManuel Matamala Jimena Sierralta Mauricio Cerda Pablo Gaspar Patricio Olguín Soledad Matus Vicente Valenzuela	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.	01-07-16		Active

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

Nro	Category Researcher	Category of Publication	Quartil	Authors	Associated Researcher	N° of Associated Researchers	N° of Others researchers	N° of Students	Date
1	Associated	ISI	Q1	Carreras-Sureda A, Jaña F, Urrea H, Durand S, Mortenson D, Sagredo A, Bustos G, Hazari Y, Ramos-Fernández E, Sassano M, Pihán P, van Vliet A, González-Quiroz M, Torres A, Tapia-Rojas C, Kerkhofs M, Vicente R, Kaufman R, Inestrosa N, Gonzalez-Billault C, Wiseman R, Agostinis P, Bultynck G, Court F, Kroemer G, Cárdenas J, Hetz C. Non-canonical function of IRE1 α determines mitochondria-associated endoplasmic reticulum composition to control calcium transfer and bioenergetics. Nature Cell Biology. 913. ISSN: 1476-4679. Doi: 10.1038/s41556-019-0355-9	C Hetz	1	5	0	may-2019
2	Associated	ISI	Q1	Claudio Hetz, Jeffrey M. Axten & John B. Patterson Pharmacological targeting of the unfolded protein response for disease intervention. Nature Chemical Biology. 764-775. ISSN: 1552-4450. Doi: 10.1038/s41589-019-0363-x	C Hetz	1	0	0	aug-2019
3	Associated	ISI	Q1	Danilo B. Medinas , Felipe Cabral-Miranda , Claudio Hetz ER stress links aging to sporadic ALS. Aging US. 05 y 06 . ISSN: 1945-4589. Doi: 10.18632/aging.101705	C Hetz	1	2	0	jan-2019
4	Associated	ISI	Q1	Devia C, <u>Mayol-Troncoso R</u> , Parrini J, Orellana G, Ruiz A, Maldonado P, Egana J. EEG Classification During Scene Free-Viewing for Schizophrenia Detection. IEEE Transactions on Neural Systems and Rehabilitation Engineering. . ISSN: . Doi: 10.1109/TNSRE.2019.2913799	P Maldonado	1	2	1	apr-2019
5	Associated	ISI	Q1	Estibaliz Ampuero, Mauricio Cerda, Steffen Härtel, Francisco Javier Rubio, Solange Massa, Paula Cubillos, Lorena Abarzúa-Catalán, Rodrigo Sandoval, Albert M. Galaburda and Ursula Wyneken. Chronic Fluoxetine Treatment Induces Maturation-Compatible Changes in the Dendritic Arbor and in Synaptic Responses in the Auditory Cortex. Frontiers in Pharmacology. 804. ISSN: . Doi: 10.3389/fphar.2019.00804	S Hartel	1	1	0	jul-2019
6	Associated	ISI	Q1	Gerakis Y, Quintero M, Li H, Hetz C. The UFMylation System in Proteostasis and Beyond. Trends in Cell Biology . 974-986. ISSN: 0962-8924. Doi: 10.1016/j.tcb.2019.09.005	C Hetz	1	2	0	dec-2019

Nro	Category Researcher	Category of Publication	Quartil	Authors	Associated Researcher	N° of Associated Researchers	N° of Others researchers	N° of Students	Date
7	Associated	ISI	Q1	González-Gutierrez, A., Ibacache, A., Esparza, A, Barros, LF, Sierralta, J Neuronal lactate levels depend on glia-derived lactate during high brain activity in Drosophila. <i>Glia</i> . 1213-1227. ISSN: 1098-1136. Doi: 10.1002/glia.23772	Jsierralta	1	1	1	dec-2019
8	Associated	ISI	Q1	Gonzalez-Teuber V, Albert-Gasco H, Auyeung VC, Papa FR, Mallucci GR, Hetz C. Small Molecules to Improve ER Proteostasis in Disease. <i>Trends in Pharmacological Sciences</i> . 684-695. ISSN: 0165-6147. Doi: 10.1016/j.tips.2019.07.003	C Hetz	1	0	1	jul-2019
9	Associated	ISI	Q1	Karen Stanic, German Reig, Ignacio A. Wichmann, Juan C. Opazo, Gareth I. Owen, Alejandro H. Corvalán, Miguel L. Concha & Julio D. Amigo The Reprimo gene family member, reprimo-like (rprml), is required for blood development in embryonic zebrafish <i>Scientific Reports</i> . 7131. ISSN: 2045-2322. Doi: 10.1038/s41598-019-43436-8	M Concha	1	1	0	may-2019
10	Associated	ISI	Q1	Koopman M, Hetz C, Nollen EAA Preview: Saved by the Matrix: UPR Independent Survival under ER Stress <i>Cell</i> . 1246-1248. ISSN: 1097-4172. Doi: 10.1016/j.cell.2019.11.012	C Hetz	1	0	0	nov-2019
11	Associated	ISI	Q1	Limia C, Sauzay C, Urra H, Hetz C, Chevet E, Avril T. Emerging Roles of the Endoplasmic Reticulum Associated Unfolded Protein Response in Cancer Cell Migration and Invasion. <i>Cancers</i> . 5. ISSN: 2072-6694. Doi: 10.3390/cancers11050631.	C Hetz	1	1	0	may-2019
12	Associated	ISI	Q1	Oñate M, Catenaccio A, Salvadores N, Saquel C, Martinez A, Moreno-Gonzalez I, Gamez N, Soto P, Soto C, Hetz C, Court FA. The necroptosis machinery mediates axonal degeneration in a model of Parkinson disease. <i>Cell Death and Differentiation</i> . 1169-1185. ISSN: 1476-5403. Doi: 10.1038/s41418-019-0408-4	C Hetz	1	0	0	oct-2019
13	Associated	ISI	Q1	Pérez V, Bermedo-García F, Zelada D, Court FA, Pérez MÁ, Fuenzalida M, Ábrigo J, Cabello-Verrugio C, Moya-Alvarado G, Tapia JC, Valenzuela V, Hetz C, Bronfman FC, Henríquez JP. The p75NTR neurotrophin receptor is required to organize the mature neuromuscular synapse by regulating synaptic vesicle availability. <i>Acta Neuropathologica Communications</i> . . ISSN: 2051-5960. Doi: 10.1186/s40478-019-0802-7	C Hetz	1	1	0	sept-2019

Nro	Category Researcher	Category of Publication	Quartil	Authors	Associated Researcher	N° of Associated Researchers	N° of Others researchers	N° of Students	Date
14	Associated	ISI	Q1	Pinto C, Medinas D, Fuentes-Villalobos F, Maripillán J, Castro A, Martínez A, Osses N, Hetz C, Henríquez J. β -catenin aggregation in models of ALS motor neurons: GSK3 β inhibition effect and neuronal differentiation. <i>Neurobiology of Disease</i> . . ISSN: . Doi: 10.1016/j.nbd.2019.104497	C Hetz	1	1	0	jun-2019
15	Associated	ISI	Q1	Rodrigo C. Vergara, Sebastián Jaramillo-Riveri, Alejandro Luarte, Cristóbal Moëñne-Loccoz, Rómulo Fuentes, Andrés Couve and Pedro E. Maldonado The Energy Homeostasis Principle: Neuronal Energy Regulation Drives Local Network Dynamics Generating Behavior <i>Frontiers in Computational Neuroscience</i> . . ISSN: . Doi: 10.3389/fncom.2019.00049	P Maldonado	1	4	0	sept-2019
16	Associated	ISI	Q1	S. Beltran, M. Nassif, E. Vicencio, J. Arcos, L. Labrador, B. I. Cortes, C. Cortez, C. A. Bergmann, S. Espinoza, M. F. Hernandez, J. M. Matamala, L. Bargsted, S. Matus, D. Rojas-Rivera, M. J. M. Bertrand, . B. Medinas, C. Hetz, P. A. Manque & U. Woehlbier Network approach identifies Pacer as an autophagy protein involved in ALS pathogenesis. <i>Molecular Neurodegeneration</i> . 1750-1326. ISSN: . Doi: 10.1186/s13024-019-0313-9	C Hetz	1	3	0	mar-2019
17	Associated	ISI	Q1	Yannis Gerakis & Claudio Hetz. Brain organoids: a next step for humanized Alzheimer's disease models? <i>Molecular Psychiatry</i> . 474-478. ISSN: 1476-5578. Doi: 10.1038/s41380-018-0343-7	C Hetz	1	1	0	jan-2019
18	Associated	ISI	Q3	Juan J. Mariman, Pablo Burgos, Pedro E. Maldonado. Parallel learning processes of a visuomotor adaptation task in a changing environment. <i>European Journal of Neuroscience</i> . 106-119. ISSN: . Doi: 10.1111/ejn.14258	P Maldonado	1	0	1	jan-2019
19	Associated	ISI	Q3	Susana Márquez, German Reig, Miguel Concha and Rodrigo Soto Cell migration driven by substrate deformation gradients <i>Physical Biology</i> . 66001. ISSN: . Doi: 10.1088/1478-3975/ab39c7	M Concha	1	1	0	sept-2019
20	Associated	ISI	Q4	Gajardo A, Madariaga S, Maldonado P Autonomic nervous system assessment by pupillary response as a potential biomarker for cardiovascular risk: A pilot study <i>Journal of Clinical Neuroscience</i> . 41-46. ISSN: . Doi: 10.1016/j.jocn.2018.11.015	P Maldonado	1	0	1	jan-2019

Nro	Category Researcher	Category of Publication	Quartil	Authors	Associated Researcher	N° of Associated Researchers	N° of Others researchers	N° of Students	Date
21	Associated	ISI	Q2	<u>Caipo L</u> , González-Ramírez MC, Guzmán-Palma P, Contreras EG, Palominos T, Fuenzalida-Uribe N, Hassan BA, Campusano JM, Sierralta J, Oliva C Slit neuronal secretion coordinates optic lobe morphogenesis in <i>Drosophila</i> . <i>Developmental Biology</i> . 32-42. ISSN: 0012-1606 . Doi: 10.1016/j.ydbio.2019.10.004	Jsierralta	1	1	1	oct-2019
22	Associated	ISI	Q2	Contreras EG, Sierralta J, Oliva, C Novel Strategies for the Generation of Neuronal Diversity: Lessons From the Fly Visual System. <i>Frontiers in molecular Neuroscience</i> . . ISSN: 1662-5099. Doi: 10.3389/fnmol.2019.00140	Jsierralta	1	0	0	aug-2019
23	Associated	ISI	Q2	Martinez A, Lopez N, Gonzalez C, Hetz C Targeting of the unfolded protein response (UPR) as therapy for Parkinson's disease. <i>Biology of the Cell</i> . 161-168. ISSN: . Doi: 10.1111/boc.201800068	C Hetz	1	0	1	mar-2019
24	Associated	ISI	Q2	Rodrigo C. Vergara, Cristóbal Moënné-Loccoz, Camila Ávalos, José Egaña, and Pedro E. Maldonado. Finger Temperature: A Psychophysiological Assessment of the Attentional State. <i>Frontiers in human neuroscience</i> . . ISSN: . Doi: 10.3389/fnhum.2019.00066	P Maldonado	1	3	0	mar-2019
25	Associated	Other Publications	N/A	Evelyn Cueva, Matias Courdurier, Axel Osses, Victor Castañeda, Benjamin Palacios, Steffen Härtel. Mathematical Modeling for 2D Light-Sheet Fluorescence Microscopy image reconstruction. <i>Mathematics</i> . . ISSN: . Doi:	S Hartel	1	0	0	sept-2020
26	Others	ISI	Q2	<u>Miguel Concha-Miranda</u> , <u>Javier Ríos</u> , <u>Joaquín Bou</u> , Jose Luis Valdes, and Pedro E. Maldonado Timing Is of the Essence: Improvement in Perception During Active Sensing <i>Frontiers in Behavioral Neuroscience</i> . . ISSN: . Doi: 10.3389/fnbeh.2019.00096	P Maldonado	1	1	3	may-2019

Nro	Category Researcher	Category of Publication	Quartil	Authors	Associated Researcher	N° of Associated Researchers	N° of Others researchers	N° of Students	Date
1	Others	ISI	Q1	Claudio Araya, Hanna-Maria Häkkinen, Luis Carcamo, Mauricio Cerda, Thierry Savy, Christopher Rookyard, Nadine Peyriéras & Jonathan D. W. Clarke. Cdh2 coordinates Myosin-II dependent internalisation of the zebrafish neural plate of the zebrafish neural plate Scientific Reports. 7699. ISSN: 2045-2322 . Doi: 10.1038/s41598-019-43789-0		0	1	0	feb-2019
2	Others	ISI	Q1	Dharmadasa T, Matamala JM, Howells J, Vucic S, Kiernan MC Early focalicity and spread of cortical dysfunction in amyotrophic lateral sclerosis: A regional study across the motor cortices Clinical Neurophysiology. 958-966. ISSN: . Doi: 10.1016/j.clinph.2019.11.057		0	1	0	dic-2019
3	Others	ISI	Q1	Gaspar PA, <u>Castillo RI</u> , Maturana A, Villar MJ, Ulloa K, González G, Ibaceta O, Ortiz A, Corral S, <u>Mayol R</u> , De Angel V, <u>Aburto MB</u> , Martínez A, Corcoran CM, Silva H. Early psychosis detection program in Chile: A first step for the South American challenge in psychosis research. Early Intervention in Psychiatry. . ISSN: . Doi: 10.1111/eip.12766		0	1	3	abr-2019
4	Others	ISI	Q1	Montoya A, Elgueta D, Campos J, Chovar O, Falcón P, Matus S, Alfaro I, Bono MR, Pacheco R. Dopamine receptor D3 signalling in astrocytes promotes neuroinflammation. Journal of Neuroinflammation. . ISSN: . Doi: 10.1186/s12974-019-1652-8		0	2	0	dic-2019
5	Others	ISI	Q1	Nimeshan Geevasinga, James Howells, Parvathi Menon, View ORCID Profile Mehdi van den Bos, Kazumoto Shibuya, José Manuel Matamala, Susanna B. Park, Karen Byth, Matthew C. Kiernan, Steve Vucic Amyotrophic lateral sclerosis diagnostic index Toward a personalized diagnosis of ALS Neurology . e536-e547. ISSN: . Doi: 10.1212/WNL.0000000000006876		0	1	0	feb-2019

Nro	Category Researcher	Category of Publication	Quartil	Authors	Associated Researcher	N° of Associated Researchers	N° of Others researchers	N° of Students	Date
6	Others	ISI	Q1	Olivares GH, Olguín P, Klein AD. Modeling Parkinson's Disease Heterogeneity to Accelerate Precision Medicine. Trends in Molecular Medicine. . ISSN: . Doi: 10.1016/j.molmed.2019.09.004		0	2	0	dic-2019
7	Others	ISI	Q1	Plaza W, Estay Vizcarra SF, de la Fuente-Ortega E, Gutierrez C, Sanchez G, Hidalgo C, Chávez AE, Haeger P NMDA receptor modulation by NOX2 drives synaptic plasticity and spatial memory impairments in rats exposed pre and postnatally to ethanol Antioxidants & Redox Signaling. . ISSN: . Doi: 10.1089/ars.2019.7787	C Hidalgo	0	1	0	dic-2019
8	Others	ISI	Q3	<u>Díaz-Zúñiga J</u> , Muñoz Y, Melgar-Rodríguez S, More J, Bruna B, <u>Lobos P</u> , Monasterio G, Vernal R, Paula-Lima A. Serotype b of Aggregatibacter actinomycetemcomitans triggers pro-inflammatory responses and amyloid beta secretion in hippocampal cells: a novel link between periodontitis and Alzheimer's disease? Journal of Oral Microbiology. . ISSN: . Doi: 10.1080/20002297.2019.1586423		0	1	4	apr-2019
9	Others	ISI	Q3	Thanuja Dharmadasa, José M.Matamala, James Howells, Neil G.Simon, Steve Vucic, Matthew C.Kiernan. The effect of coil type and limb dominance in the assessment of lower-limb motor cortex excitability using TMS Neuroscience Letters. 84-90. ISSN: . Doi: 10.1016/j.neulet.2019.01.050		0	1	0	apr-2019
10	Others	ISI	Q4	Gallardo A, Latapiat V, Rivera A, Fonseca B, Roldan A, Sandoval P, Sánchez C, Matamala JM. NOTCH3 Gene Mutation in a Chilean Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy Family. Journal of Stroke and Cerebrovascular Diseases. . ISSN: . Doi: 10.1016/j.jstrokecerebrovasdis		0	1	0	dec-2019
11	Others	ISI	Q2	Carlos Cruz-Montecinos , Sofía Pérez-Alenda, Mauricio Cerda, Huub Maas Neuromuscular control during gait in people with haemophilic arthropathy Haemophilia. e69-e77. ISSN: . Doi: 10.1111/hae.13697		0	1	1	feb-2019

Nro	Category Researcher	Category of Publication	Quartil	Authors	Associated Researcher	N° of Associated Researchers	N° of Others researchers	N° of Students	Date
12	Others	ISI	Q2	Chama Belkhiria ¹ , Rodrigo C. Vergara, <u>Simón San Martín</u> , Alexis Leiva, Bruno Marcenaro, Melissa Martinez, Carolina Delgado, and Paul H. Delano. Cingulate Cortex Atrophy Is Associated With Hearing Loss in Presbycusis With Cochlear Amplifier Dysfunction Frontiers in Aging Neuroscience. 97. ISSN: . Doi: 10.3389/fnagi.2019.00097		0	3	1	abr-2019
13	Others	ISI	Q2	<u>Constantino D. Dragicevic</u> , Bruno Marcenaro, Marcela Navarrete, Luis Robles, Paul H. Delano Oscillatory infrasonic modulation of the cochlear amplifier by selective attention PLOS ONE. . ISSN: . Doi: 10.1371/journal.pone.0208939		0	1	1	ene-2019
14	Others	ISI	Q2	Cruz-Montecinos C, Pérez-Alenda S, Contreras-Sepúlveda F, Querol F, Cerda M, Maas H. Assessment of tensile mechanical properties of the Achilles tendon in adult patients with haemophilic arthropathy. Reproducibility study. Haemophilia. . ISSN: . Doi: 10.1111/hae.13622		0	1	1	ene-2019
15	Others	ISI	Q2	<u>Grinspun N</u> , <u>Fuentealba Y</u> , Falcon R, Valdés JL. c-Fos expression in the ascending arousal system induced by physical exercise in rats: Implication for memory performance. Brain Research. . ISSN: 0006-8993 . Doi: 10.1016/j.brainres.2019.146376		0	1	2	aug-2019
16	Others	ISI	Q2	Halje P, Brys I, Mariman JJ, da Cunha C, Fuentes R, Petersson P. Oscillations in cortico-basal ganglia circuits: implications for Parkinson's disease and other neurologic and psychiatric conditions. Journal of Neurophysiology. . ISSN: . Doi: 10.1152/jn.00590.2018		0	1	1	jul-2019
17	Others	ISI	Q2	José Manuel Matamala, Renato J. Verdugo Single fiber EMG guidelines: Moving towards a "single" methodological consensus Clinical Neurophysiology. 1399-1400. ISSN: . Doi: 10.1016/j.clinph.2019.04.610		0	1	0	may-2019

Nro	Category Researcher	Category of Publication	Quartil	Authors	Associated Researcher	N° of Associated Researchers	N° of Others researchers	N° of Students	Date
19	Others	ISI	Q2	Nuñez M.T., Hidalgo C. Noxious Iron–Calcium Connections in Neurodegeneration <i>Frontiers in neuroscience</i> . . ISSN: . Doi: 10.3389/fnins.2019.00048	C Hidalgo	0	1	0	feb-2019
20	Others	ISI	Q2	Paulina Falcón, <u>Marcela Escandón</u> , <u>Álvaro Brito</u> , and Soledad Matus Nutrient Sensing and Redox Balance: GCN2 as a New Integrator in Aging <i>Oxidative Medicine and Cellular Longevity</i> . . ISSN: . Doi: 10.1155/2019/5730532		0	1	3	may-2019
21	Others	ISI	Q2	Riveros ME, Forray MI, Torrealba F, Valdés JL. Effort Displayed During Appetitive Phase of Feeding Behavior Requires Infralimbic Cortex Activity and Histamine H1 Receptor Signaling. <i>Frontiers in neuroscience</i> . . ISSN: 1662453X. Doi: 10.3389/fnins.2019.00577		0	1	0	jan-2019
22	Others	ISI	Q2	Sandro R. Freitas, André Antunes, Pierre Salmon, Bruno Mendes, Telmo Firmino, <u>Carlos Cruz-Montecinos</u> , Mauricio Cerda, João R.Vaz. Does epimuscular myofascial force transmission occur between the human quadriceps muscles in vivo during passive stretching? <i>Journal of Biomechanics</i> . 91-96. ISSN: . Doi: 10.1016/j.jbiomech.2018.11.026		0	1	1	jan-2019
23	Others	ISI	Q2	Rodrigo Fernández-Gajardo, José Manuel Matamala, Rodrigo Gutiérrez, Prudencio Lozano, Ignacio A. Cortés-Fuentes, Camilo G. Sotomayor, Gonzalo Bustamante, Juan A. Pasten, Gabriel Vargas, Rodrigo Guerrero, Pablo Reyes, Gabriel Cavada, Walter Feuerhak , Ramón Rodrigo Relationship between infarct size and serum uric acid levels during the acute phase of stroke <i>PLOS ONE</i> . e0219402. ISSN: . Doi: 10.1371/journal.pone.0219402		0	1	0	jul-2019
24	Others	Scielo	Q4	Ignacio Acosta, José Manuel Matamala, Paula Jara, Francisca Pino, Alejandra Gallardo, Renato Verdugo Miopatías inflamatorias idiopáticas: una mirada actualizada al diagnóstico y el manejo <i>Revista Médica de Chile</i> . . ISSN: . Doi: 10.4067/S0034-98872019000300342		0	1	0	mar-2019

3.5.- Collaborative publications:

Category of Publication	1 researcher		2 researchers		3 researchers		4 or more	
	N°	%	N°	%	N°	%	N°	%
ISI/WOS Publications or Similar to ISI/WOS Standard	40	83,33%	5	10,42%	0	0,00%	2	4,17%
SCOPUS Publications or Similar to SCOPUS Standard	0	0,00%	0	0,00%	0	0,00%	0	0,00%
SCIELO Publications or Similar to SCIELO Standard	1	2,08%	0	0,00%	0	0,00%	0	0,00%
Books and chapters	0	0,00%	0	0,00%	0	0,00%	0	0,00%
Other Publications	0	0,00%	0	0,00%	0	0,00%	0	0,00%
Total of publications	41	85,42%	5	10,42%	0	0	2	4,17%

Annex 4.- Organization of Scientific Events

Scope	Title	Type of Event	City	Country	Responsible Researcher	URL
Internacional	ICGEB Course Optics, forces & Development	Workshop	Santiago	Chile	Miguel Concha	http://www.cellmorphodynamics.cl/course2019/
Internacional	Workshop EMBO Bridging cell and tissue mechanics to fate specification in development;	Workshop	Santiago	Chile	Miguel Concha	https://meetings.embo.org/event/19-cell-tissue-mechanics
Internacional	How to Win a Nobel Prize: stumbling on the secrets of cell division (Tim Hunt)	Conferencia	Santiago	Chile	Miguel Concha	https://www.dropbox.com/s/Oak1wxfkdwjzox0/Poster%20Charla%20Tim%20Hunt%202019.pdf?dl=0
International	Small Brains, Big Ideas. EMBO Global Exchange Lecture Course	Conference and short practical course	Las Cruces	Chile	Jimena Sierralta	https://smallbrains.org/previous-workshops/2019-2/
International	Small Brains Big Ideas Open Lecture The I of the Fly	Conference	Valparaíso	Chile	Jimena Sierralta	https://smallbrains.org/previous-workshops/2019-2/
Nacional	Conversaciones sobre Neuromedicina: "Signal transduction by caveolae mechanics" (Christophe Lamaze Ph.D. Institut Curie); Getting out the Golgi complex thanks to the RAB6 GTPase (Stéphanie Miserey-Lenkei Ph.D., Institut Curie)	Seminario	Santiago	Chile	Carolina González	

Scope	Title	Type of Event	City	Country	Responsible Researcher	URL
Nacional	Conversaciones sobre Neuromedicina: Cambios Dinamicos en la conectividad Cerebral ¿cuál es la melodía de la Musica Cerebral? (Dr. Nicolas Crossley)	Seminario	Santiago	Chile	Gonzalo Olivares	
Nacional	Conversaciones sobre Neuromedicina: Modificaciones en la dinámica dopaminérgica del circuito nigro-estriatal asociadas a la exposición repetida a drogas (Dr. José Fuentealba)	Seminario	Santiago	Chile	Gonzalo Olivares	https://www.facebook.com/photo?fbid=1821584624609672&set=a.348884848546331
Nacional	Treasure your exemptions: Exploiting natural variations for uncovering modifier genes of lysosomal biology in health and disease (Andrés D. Klein, U del Desarrollo)	Seminario	Santiago	Chile	Gonzalo Olivares	https://www.facebook.com/photo?fbid=1974176162683850&set=a.516307841804030
Nacional	Conversaciones sobre Neuromedicina; Mechanisms of Hypothalamic Autophagy in Obesity (Eugenia Morselli)	Seminario	Santiago	Chile	Claudio Hetz	
Nacional	Conversaciones sobre Neuromedicina: New strategies and approaches to tackle neurological disorders (Mauro Costa-Mattiolo)	Seminario	Santiago	Chile	Gonzalo Olivares	
Nacional	Conversaciones sobre Neuromedicina: El nuevo paradigma de investigación en psiquiatría en el ejemplo del estudio de la depresión (Juan Pablo Jimenez)	Seminario	Santiago	Chile	Jimena Sierralta	
Nacional	Conversaciones sobre Neuromedicina: Neurodegeneration: From Molecules to Medicine (Dra.Giovanna Mallucci)	Seminario	Santiago	Chile	Claudio Hetz	https://www.facebook.com/photo?fbid=1687178634716939&set=a.348884848546331
Nacional	Conversaciones sobre Neuromedicina: CRACKing de CRAC: Exploring novel mechanism for Orai1-STIM1 function (Oscar Cerda)	Seminario	Santiago	Chile	Gonzalo Olivares	https://www.facebook.com/photo?fbid=2060387370729395&set=a.348884848546331
Nacional	1st Chilean Drosophila meeting 2019	Conferencia	Santiago	Chile	Jimena Sierralta	
Nacional	Conversaciones sobre Neuromedicina: Cerebro, lenguaje y conciencia: ¿ Cómo es que un papagayo repite lo que oye? (Jorge Mpodozis Ph.D, U de Chile)	Seminario	Santiago	Chile	Pedro Esteban Maldonado Arbogast	https://www.facebook.com/photo?fbid=1858609750907159&set=a.348884848546331

Scope	Title	Type of Event	City	Country	Responsible Researcher	URL
Nacional	Conversaciones sobre Neuromedicina: Investigating the effects of spinal cord stimulation for treating gait dysfunction in parkinsonian patients (Dra. Olivia Samotus)	Seminario	Santiago	Chile	Gonzalo Olivares Herane	https://www.facebook.com/photo?fbid=1765027083598760&set=a.516307841804030
Nacional	Conversación de Neurociencia e Inteligencia Artificial: los desafíos que se vienen (Dr. Rafael Yuste)	Seminario	Santiago	Chile	Pedro Esteban Maldonado Arbogast	https://www.facebook.com/photo?fbid=1881847288583405&set=a.348884848546331

Annex 5.- Education, and capacity building

5.1 Capacity Building inside MSI Centers

Tutor	Undergraduated Student		Graduated Students				Total
	F	M	Master		Doctoral		
			F	M	F	M	
Pedro Esteban Maldonado Arbogast	1	0	1	10	3	5	20
Steffen Härtel Gründler	0	1	3	0	0	1	5
Claudio Andrés Hetz Flores Soledad Matus	0	0	0	0	0	1	1
Pedro Esteban Maldonado Arbogast José Luis Valdés Guerrero	0	0	0	0	0	2	2
Jimena Sierralta Jara	0	1	0	0	0	1	2
Jimena Sierralta Jara Andrés Oscar Couve Correa	0	0	0	0	1	0	1
Rómulo Antonio Fuentes Flores René Vidal Claudio Andrés Hetz Flores	0	0	0	0	1	0	1
Rómulo Antonio Fuentes Flores	0	0	2	1	1	1	5
Rómulo Antonio Fuentes Flores Pedro Esteban Maldonado Arbogast	0	0	0	0	1	0	1
Andrea Paula-Lima	0	1	1	0	0	3	5
José Luis Valdés Guerrero	0	1	3	3	1	0	8
René Vidal	0	0	0	0	2	1	3
Pablo Gaspar	0	0	1	0	1	2	4
Claudio Andrés Hetz Flores	0	1	1	1	3	4	10
Andrés Oscar Couve Correa	0	0	0	0	1	0	1
Claudio Andrés Hetz Flores René Vidal	0	0	0	0	1	0	1
Mauricio Cerda Villablanca	1	2	0	5	0	2	10
Steffen Härtel Gründler Mauricio Cerda Villablanca	0	0	0	0	1	0	1
Miguel Concha Nordemann	1	0	0	0	1	2	4
Patricio Alejandro Olguín Aguilera	0	2	0	0	1	0	3
Paul Délano	0	0	0	3	0	1	4
María Cecilia Hidalgo Tapia	0	0	0	0	1	0	1
Soledad Matus	1	0	0	0	0	0	1
Total	4	9	12	23	20	26	94

Annex 5.2. - Short-term Traineeships of MSI students

Internships

Student Name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Matías Eduardo González Quiroz	Université Rennes	France	Eric Chevet	My research project seeks to identify the molecular link between DDR and IRE1 α , and thus explain the mechanisms of action by which IRE1 α is activated by genotoxic stress.	03/03/2019	30/04/2019
Rocio Loyola	Universitat Pompeu Fabra	Spain	Rubén Moreno Bote	The internship goal is to analyze behavioural and electrophysiological data	03/12/2018	03/05/2019
Miguel Alejandro Concha Miranda	Humboldt University zu Berlin	Germany	Dr. Professor Michael Brecht	Study of the neural correlates of playful interaction of rats on prefrontal cortex, using tetrode recording on behaving animals.	27/11/2018	04/03/2019
Francisca Cecilia Bertin Johnson	Leibniz Institute for Neurobiology	Germany	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 AtI expression (AtI-KD and AtI null mutant), BMP signaling (Tkv-CA overexpression and Tkv-KD) and with double knock-down: AtI-KD/Tkv-KD (establishing a rescue in the BMP upregulated signaling in an AtI-KD background).	27/11/2018	27/03/2019

Student Name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Alejandra Verónica Parra Peña	University of Otago, Dunedin - New Zealand	New Zealand	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."	01/11/2018	29/03/2019
Celia María Limia León	Université Rennes	France	Eric Chevet	Experiments for doctoral thesis	01/08/2019	12/08/2020
Andrés Ignacio Köhler Solís	Leibniz Institute for Neurobiology	Germany	Ulrich Thomas	During this stay my goal was to obtain images in a COncocal microscopy with STED in order to demonstrate a toight relationship between PMCA and DLG	10/04/2019	01/09/2019

Internship at BNI

Intern Type	Intern Name	Academic Degree	Home Institution	Destination Institution	Country	Project Description	Starting Date	Ending Date
Student	Josselyn Barahona	Undergraduate Student	Williams College	Universidad de Chile- Instituto de Neurociencia Biomédica	Estados Unidos de America	Fulbright Research Scholar at Fulbright Association	01/03/2019	31/12/2019
Student	Diana Mitzi Aguilar Quiroz	Undergraduate Student	Universidad Nacional Autónoma de México	Universidad de Chile- Instituto de Neurociencia Biomédica	México	Academic stay for research methods knowledge	22/07/2019	22/09/2019
Researcher	Sergio Bazaes Latrille	Doctoral Student	Universidad de Chile	Universidad de Chile- Instituto de Neurociencia Biomédica	Chile	Clinical rotation in the psychosis program. Deepen knowledge in first psychotic episode and overview of last findings in the neurobiology of schizophrenia and first psychotic episode.	02/01/2019	31/03/2019
Student	Roman Delucenay Clarke	Magister Student	Sorbonne- Université	Universidad de Chile- Instituto de Neurociencia Biomédica	Francia	The Integrative Biology and Physiology (BIP) master program at Sorbonne University encourages	20/04/2019	02/08/2019
Student	Taiki Harada	Undergraduate Student	Tokyo Medical and Dental University	Universidad de Chile- Instituto de Neurociencia Biomédica	Japón	Theoretical Neuroscience, simulating neural or neural network model on computer	03/06/2019	08/11/2019
Student	Gamze Guney	Magister Student	Charite Medical University Berlin	Universidad de Chile- Instituto de Neurociencia Biomédica	Alemania	Learning registrations in Eye-tracker and EEG, and how to analyse the obtained data with MATLAB	15/07/2019	20/09/2019

Intern Type	Intern Name	Academic Degree	Home Institution	Destination Institution	Country	Project Description	Starting Date	Ending Date
Student	Sara Chernicky	Undergraduate Student	Robert Morris University	Universidad de Chile- Instituto de Neurociencia Biomédica	Estados Unidos de America	In my 8 weeks in the laboratory, I was able to complete a literature review of the published laboratory works. In addition, I observed human trials with eye tracker	19/06/2019	08/08/2019
Student	Agustin Rolando	Doctoral Student	Universidad Nacional del Cuyo	Universidad de Chile- Instituto de Neurociencia Biomédica	Argentina	Pendiente	01/06/2019	03/12/2019
Student	Gisela Redondo	Undergraduate Student	Massachusetts Institute of Technology	Universidad de Chile- Instituto de Neurociencia Biomédica	Estados Unidos de America	Cómo establecer latencias entre el pulso de estimulación y la respuesta supra-espinal	17/06/2019	23/08/2019

Annex 6.- Networking, and other collaborative work

6.1 Formal Collaboration networks

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.

Annex 6.2.- Collaboration Networks

Activity Name	Objective	Description	Co-Participants Institutions	Number of Research from the Center	Number of Postdocs / Students from the Center	Number of External Research	Number of External Postdocs/Student	Product	Name of the Center Associate Researchers Participating in the activity
Visits	Collaboration in projects associated to Drosophila larval NMJ	Use of STED microscopy	Leibniz Institute for Neurobiology	2	2	3	2	Thesis and three papers in the writing process	Dr- Eckart Gundelfinger, Dr. Ulrich Thomas (MConcha)
Visits	Collaboration in projects associated to zebrafish and killifish tissue morphogenesis	Use of physical modelling to investigate cellular morphogenesis	Faculty of Mathematical and Physical Sciences, University of Chile	3	2	1	2	One paper published (Márquez et al 2019) and a manuscript under revision	Dr. Rodrigo Soto (MConcha)
	Collaboration in projects associated to zebrafish development	Use of CRISPR-Cas9 to study gene function in development	Faculty of Biological Sciences, Pontifical Catholic University of Chile	3	2	1	1	One paper published (Stanic et al 2019)	Dr. Julio Amigo (MConcha)
La Serena School for Data Science	30 students from different disciplines including astronomy, computer science, statistics, mathematics, life science, biomedicine, or medicine, from Chile, and USA	<i>Applied Tools for Data-Driven Sciences</i> , at the interphase of health science, biomedicine astronomy	NSF founded collaborative initiative	2	5		30	Annual Course	SH, MCerda

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
Open lab for students	Open Lab.	National	Secondary Students	26/04/2019	Chile	Metropolitana de Santiago	5	30	1	Jimena Sierralta. Pedro Maldonado. Claudio Hetz. Rómulo Fuentes. Steffen Härtel. Miguel Concha.	Gabriela Martinez
Open lab for students	Open Lab.	National	Secondary Students	17/05/2019	Chile	Metropolitana de Santiago	5	25	1	José Luis Valdés. Steffen Härtel. Claudio Hetz. Pedro Maldonado. Miguel Concha.	Gabriela Martinez
Open lab for students	Open Lab.	National	Primary Students	04/07/2019	Chile	Metropolitana de Santiago	4	20	1	Steffen Härtel. Cecilia Hidalgo. Rómulo Fuentes. Miguel Concha.	Gabriela Martinez
Open lab for students	Open Lab.	National	University Students	09/07/2019	Chile	Metropolitana de Santiago	2	10	1	Patricio Olguín. Claudio Hetz.	Gabriela Martinez
Open lab for students	Open Lab.	National	Primary Students	09/08/2019	Chile	Metropolitana de Santiago	4	20	1	Carolina González. Steffen Härtel. Pedro Maldonado. Jimena Sierralta.	Gabriela Martinez
Open lab for students	Open Lab.	National	Secondary Students	11/10/2019	Chile	Metropolitana de Santiago	3	15	1	Miguel Concha. Rómulo Fuentes. Claudio Hetz.	Gabriela Martinez
Workshops for teachers	Workshop	National	Secondary Students	01/06/2019	Chile	Metropolitana de Santiago	1	40	1		Gabriela Martinez

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
BNI Transforma "Habilidades Comunicacionales"	Seminar	National	Secondary Students	23/01/2019	Chile	Metropolitana de Santiago	12	28	1	Gonzalo Olivares.	Bernardita Cadiz
Fiesta de la Neurociencia	Conference	National	Secondary Students	05/04/2019	Chile	Metropolitana de Santiago	10	140	1	Jimena Sierralta. Rómulo Fuentes.	Rodrigo Tapia
Workshops for teachers	Workshop	National	Teachers	15/01/2019	Chile	Metropolitana de Santiago	2	40	1		Gabriela Martinez
Enfoques de política CTCI: fundamentos y relevancia en el marco de una nueva institucionalidad	Workshop	National	Secondary Students	12/04/2019	Chile	Metropolitana de Santiago	15	18	1	Pedro Maldonado.	Bernardita Cadiz
Open Lecture: Manipulando el origen de la vida humana ¿En qué estamos?	Conference	National	Secondary Students	03/04/2019	Chile	Metropolitana de Santiago	10	400	1	Claudio Hetz. Miguel Concha. Cecilia Hidalgo.	Bernardita Cadiz - Miguel Concha
Open lab for students	Open Lab.	National		14/06/2019	Chile	Metropolitana de Santiago	5	25	1	Miguel Concha. Steffen Härtel. Pedro Maldonado. Cecilia Hidalgo. Carolina González.	Gabriela Martinez
Domo Cerebro en Planetario	Exhibition	National	General Public	13/07/2019	Chile	Metropolitana de Santiago	0	30.000	16		Gabriela Martinez
Domo Cerebro en Semana de la ciencia Explora Gam	Exhibition	National	General Public	06/10/2019	Chile	Metropolitana de Santiago		3.000	1		Gabriela Martinez
Open lab for students	Open Lab.	National	General Public	06/09/2019	Chile	Metropolitana de Santiago		15	1	Carolina González. Steffen Härtel. Miguel Concha.	Gabriela Martinez

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
Workshops for teachers	Workshop	National	General Public	04/05/2019	Chile	Metropolitana de Santiago		45	1		Gabriela Martinez
Workshops for teachers	Workshop	National	General Public	05/05/2019	Chile	Metropolitana de Santiago		35	1		Gabriela Martinez
Workshops for teachers	Workshop	National	General Public	24/08/2019	Chile	Metropolitana de Santiago		2	1		Gabriela Martinez
Domo Cerebro en Puerto de Ideas	Exhibition	National	General Public	14/04/2019	Chile	Metropolitana de Santiago		6.000	2		Gabriela Martinez
Domo Cerebro en Semana de la ciencia Explora Cerro San Cristobal	Exhibition	National	General Public	13/10/2019	Chile	Metropolitana de Santiago		3.000	1		Gabriela Martinez

7.2.- Articles, and Interviews

Type of Media and Scoupe	Local / Regional		National		International		Total
	N° Interviews	N° Articles	N° Interviews	N° Articles	N° Interviews	N° Articles	
Written	1	9	11	31	0	0	52
Internet	0	3	26	34	0	4	67
Audiovisual	0	0	19	5	2	0	26
Total	1	12	56	70	2	4	145

Annex 8. - Connections with other sectors:

Activity	Type of Connection	Type of Activity	Institution Country	Agent Type	Economic Sector
Regenero	Technological Agreement	Project Development	Chile	Industry	
Desert Point	Technological Agreement	Project Development	Chile	Industry	
Research within BNI on the production of Knowledge in contemporary Chile	Collaboration	Project Development	Chile	Public or Private Institutions	
ACHS 246	Technological Agreement	Project Development	Chile		
Solunova e-sports	Technological Agreement	Project Development	Chile	Industry	
ACHS 245	Technological Agreement	Project Development	Chile		
ISCI-Autopista Central	Technological Agreement	Project Development	Chile	Research	
CCHV-BNI Scientific Artistic Residence	Collaboration	Project Development	Chile		
ACHS 243	Technological Agreement	Project Development	Chile		
Proteostasis Therapeutics Inc. (PTI)	Service Agreement	Project Development	USA	Industry	Biotechnology
Socialab	Technological Agreement	Project Development	Chile	Social Innovation	
Handl	Service Agreement	Project Development	Belgium	Industry	Biotechnology

NOMENCLATURE:

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

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

[Agent Type] [1] Industry, and Services [2] Organizations, and Public Services [3] Educational Sector

Annex 9.- Total incomes:

Funds	Amount [\$]	Percentage of total income [%]
MSI Funds	1.026.265	28,4%
Fondecyt	1.383.993	38,3%
Other Public Funds	42.953	1,2%
Other Funds	6.040	0,2%
Anillo Funds	289.933	8,0%
Other Conicyt	95.973	2,7%
Other International Funds	468.456	13,0%
Fondef	74.631	2,1%
Fondap	70.872	2,0%
Other Private Funds	128.859	3,6%
Conicyt Basal	13.423	0,4%
Internship Funds	9.664	0,3%
Total	3.611.064	100%

Annex 10.- Outstanding Activities

Name of the activity relevant in your discipline	Type of activity relevant in your discipline carried out	Description of the relevant activity in your discipline	Importance in your discipline of the activity	Possibility to maintain or replicate this activity
<i>International collaboration with Dr. Mauro Costa-Mattioli Laboratory from Baylor College, USA (RVidal)</i>	<i>International collaboration</i>	<i>We generated a collaboration with Dr. Mauro Costa-Mattioli expert in regulation of protein synthesis and its impact in learning.</i>	<i>This collaboration supports the investigation related to the neuroprotective effect of Rapalogs in Parkinson Disease models</i>	<i>This activity can be maintained on the time</i>
<i>National collaboration with Dr. Carlos Aguilera from FACH Hospital (RVidal)</i>	<i>National collaboration</i>	<i>We generated a collaboration with Dr. Carlos Aguilera neurologist expert in Parkinson Disease</i>	<i>This collaboration supports the currently research related to the load of a-synuclein protein from neuronal exosomes in Parkinson Disease patients</i>	<i>This activity can be maintained on the time</i>
<i>Member of FONDEF Adulto Mayor committee (RVidal)</i>	<i>Member of committee</i>	<i>I belong to FONDEF Adulto Mayor Committee to evaluate the national project of ANID</i>	<i>This activity contributes to know the state of art in translational medical project in special Parkinson Disease</i>	<i>This activity can be maintained on the time</i>
<i>Opening of an international laboratory at the Buck Institute, California. (CHz)</i>	<i>New Institutional collaborations</i>	<i>The Director of the Institute Dr Claudio Hetz if in the final stage of opening a satellite lab at the Buck Institute, involving 15% of dedication. Staff Scientist of BNI Dr hery Urra will get a full time position there to manage the laboratory.</i>	<i>New collaborations and access to technological platforms (proteomics, use of C elegans, mouse genetics etc) with be available to BNI investigators in the area of of brain heath.</i>	<i>This will be prolonged for 3 years and will allow raising funding from the US to complement BNI's activities</i>
<i>Searching for new investors in gene therapy (CHz)</i>	<i>BNI is part of the Know Hub funded by CORFO.</i>	<i>We aim to search for licensing partners for the AAV-IGF2 gene therapy. Patent from R Vida and CHz.</i>	<i>This will continue helping BNI to place our biomedical research on an international level</i>	<i>2020-2021 will be invested in searching for biotech partners</i>
<i>Filling new patents (CHz)</i>	<i>New technologies to improve neuromuscular junctions</i>	<i>ALSA funded Staff Scientist Danilo MEDina to develop a gene therapy to improve neuromuscular junctions in ALS</i>	<i>New data will be protected aiming to generate international patents</i>	<i>2020-2021</i>