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Index

Section	Page
1. 1.1 Executive Summary 1.2 Resumen Ejecutivo	3 5
2. Introduction	7
3. Scientific and Technological Research	9
4. Education and Capacity Building	20
5. Networking	22
6. Outreach and Connections with Public and Private Sectors	25
7. Administration and Financial Management	27
Annexes	28

1. Summary

1.1 Executive Summary

Understanding the function of the nervous system constitutes a broad and central challenge of today's biology and medicine. Consequently, Neuroscience has expanded and diversified dramatically in recent decades. Yet despite these efforts the current integration of the structural and functional organization of the brain in physiology and disease remains beyond our grasp. The scale of this challenge is exemplified by the recent decision of the U.S. government to allocate U$ 300 million/year for 10 years to the most ambitious associative scientific project since the Human Genome Project called Brain Initiative, that seeks to determine the activity of each neuron in the human brain and is expected to contribute substantially to health and technology. In Chile thousands of people suffer from neurological and psychiatric disorders with no satisfactory treatment. In addition, the country has experienced a sustained growth in the aged population with concomitant increases in major neurodegenerative and cognitive diseases, but our capacity to conduct clinical brain research sustained by cutting-edge basic Neuroscience is still missing.

As demonstrated by a number of successful international initiatives, tackling this complex issue requires a modern approach grounded on an integrated transdisciplinary strategy. The Biomedical Neuroscience Institute (BNI) constitutes a broad umbrella that brings together a critical mass of leading basic and clinical neuroscientists along with mathematicians under suitable infrastructure to accomplish world-class scientific research and training. BNI provides a unified vision to explore the structural and functional organization of the brain under normal physiology and the mechanisms underlying disease from whole organisms to cells. BNI may lead Neuroscience in Chile and the region due to: (i) an extensive track record of individual and collaborative research initiatives in Neuroscience, (ii) the association to major basic-clinical centers of national and international relevance, (iii) a vast training potential in health science, and (iv) a young body of researchers coexisting in a single campus capable of executing the long terms goals of the initiative.

Three principles guide the operation of BNI: (i) transdisciplinary research, (ii) a bottom-up multi-scale approach to study the function of genes from molecules to behavior in complementary animal models, and (iii) an integrated biomedical strategy to promote high-standard scientific contributions guaranteeing their transfer to the community. During 2013 these guiding principles were embraced fully and explicitly by BNI members, organized around interconnected thematic platforms. Through them BNI aims to: (i) establish an international reference centre for the exploration of the 'structure and function of the brain under physiological and pathological conditions', (ii) train and host a new generation of leading researchers and clinicians in a vibrant, solid and unique transdisciplinary environment, (iii) produce high-standard clinical research and transfer the impact of its research to society, and (iv) become a resource center for specialized clinicians and the general public.

During this period we have worked towards attaining each of these goals. Importantly, operating as a non-profit organization, we have continued with our philosophy to invest more than 60% of the funds in common strategic aims. This financial strategy has been complemented by a collaborative commitment to co-mentor students and postdocs, and to collaborate in basic and applied projects.

Although the structure of the institute has remained unchanged the number of people increased for the third consecutive year (7%), with new students and postdocs representing the majority of this expansion. The increment in the number of postdocs is a direct consequence of BNI's policy to allocate common funds to competitive "*Bridge Fellowships*", which have allowed us to incorporate approximately 7 postdocs/year, most of whom have made successful transitions to other funding sources (5 average). Importantly, BNI holds a favorable female:male ratio of 42:58 among its students and postdocs.

Research lines constitute long-term scientific programs and, therefore, have remained mostly unchanged. We have published 35 ISI articles, including two reviews in journals with high impact

factor and broad audiences (*Hetz et al., 2013, Nat Rev Drug Discov 12:703, Impact Factor 33; Hetz, 2013, Nat Rev Mol Cell Biol 14:404, Impact Factor 37*). Research from multiple BNI labs has been published in leading journals such as *Nat Commun, J Neurosci, J Cell Sci, Curr Mol Med, Semin Immunol, Development, Cell Res, Trends Mol Med, Autophagy* and *Biol Psychiat*.

Besides central funds from the Millenium Scientific Initiative BNI investigators continue to secure grants for basic research from national sources such as FONDECYT (all BNI investigators), CONICYT-USA (C. Hetz, J. Sierralta, A. Couve) and U-Redes (S. Härtel). Additionally, they have obtained national grants for medium-size equipment (FONDEQUIP) to expand BNI's capacity in automated fluorescence imaging for large-scale cellular studies, drug discovery and signaling (cellomics, C. Hetz), confocal and light-sheet microscopy (L. Leyton, M. Concha, S. Härtel), and ultracentrifugation (C. Hidalgo). Moreover, significant funds have been secured from international agencies such as the Micheal J Fox Foundation for Parkinson Research, the ALS Association, and Genzyme (C. Hetz). Furthermore, three FONDEF applied research grants continue to involve several BNI investigators (C. Hetz, S. Härtel, P. Maldonado and A. Couve). Finally, successful applications to outreach grants such as EXPLORA and INNOVA-CORFO (A. Couve) have generated an important new source of funding. BNI has funded four new pilot-projects mostly led by young researchers in collaboration with Associate Investigators (R. Vidal/C. Hetz; R. Nieto/H. Silva; A. Paula-Lima/C. Hidalgo; M. Concha/S. Härtel). These projects contribute to promote interactions and incorporate young investigators to the central activities of the institute.

We have continued with our weekly investigator meetings, regular seminar series with national and international guests, and our short internal seminars, which have significantly contributed to motivate young investigators and students. We have organized 7 major scientific events in Chile, which promoted the research and aims of BNI within international speakers and a national audience that reached more than 1000 people. Consolidating our 2012 experience with clinical departments we carried out 2 basic-clinical encounters at the FMed with international speakers and clinical departments, consolidating collaborations, visualizing local biomedical problems and evaluating progress in reaching concrete solutions. Accordingly, we have incorporated psychiatrist/geneticist L. Bustamante, MD-Ph.D., as clinical research platform coordinator to work in association with H. Silva in unifying criteria for clinical research (informed consents, ethical issues, bio-banking). A wide variety of high impact outreach activities were completed during 2013 including lectures, lab visits, web, radio, printed press, and generation of physical and virtual material to reach the general public to strengthen our interactive platform *Dendros*.

The Institute, young scientists and Associate Investigators have received national and international prizes. We highlight the *Prize in National Innovation in Scientific Education*, organized by Fundación Ciencia Joven and Fundación Telefónica to our interactive platform *Dendros*. This is the result of a fully committed and creative work of the institute, and the product of collaborations between our art directors, students and postdocs that continuously help with scientific content and support for the activities.

A formal network based on microscopy and image processing has promoted the participation of 26 students and postdocs, and produced concrete advances in exchange of expertise, equipment and reagents. In addition, the second meeting between BNI and a network of Latin American Neuroscience centers and laboratories was carried out in Buenos Aires (*NeuroSur-II*), consolidating the initiative as a viable and attractive concept to improve flexible and economic interactions.

Once again, guided by a transdisciplinary program, a bottom-up multi-scale approach and an integrated biomedical strategy we firmly believe we have continued to consolidate an initiative that will improve the country's international presence in the field of brain sciences by generating recognizable high-quality results.

1.2 Resumen Ejecutivo

La comprensión del sistema nervioso constituye un desafío amplio y central de la biología y medicina de hoy. Por ello la Neurociencia ha crecido y se ha diversificado de manera espectacular en las últimas décadas. Sin embargo, a pesar de estos esfuerzos, la comprensión de la organización estructural y funcional del cerebro en condiciones normales y patológicas sigue fuera de nuestro alcance. La magnitud del desafío es ejemplificada por la reciente decisión del gobierno de EE.UU. de asignar U$ 300 millones/año durante 10 años al proyecto asociativo más ambicioso desde el Proyecto Genoma Humano, llamado *Brain Initiative*, que tiene por objetivo determinar la conectividad funcional de cada neurona del cerebro humano, y que espera contribuir de manera sustancial a la medicina y la tecnología. En Chile miles de personas sufren de trastornos neurológicos y psiquiátricos sin tratamiento satisfactorio. Además, el país ha experimentado un crecimiento sostenido en la población envejecida con aumentos concomitantes en enfermedades neurodegenerativas y cognitivas, pero nuestra capacidad de llevar a cabo investigación clínica del cerebro sustentada por Neurociencia fundamental de vanguardia es todavía insuficiente.

Como lo han demostrado iniciativas internacionales, abordar esta compleja problemática requiere de un enfoque moderno basado en una estrategia transdisciplinaria integrada. El Instituto de Neurociencia Biomédica (BNI) constituye un amplio paraguas que reúne a una masa crítica de líderes neurocientíficos, matemáticos e infraestructura para llevar a cabo investigación científica de frontera y formación de personas. BNI proporciona una visión unificada para explorar la organización estructural y funcional del cerebro y los mecanismos que subyacen a enfermedades, desde los organismos a las células. BNI puede liderar la Neurociencia en Chile y en la región debido a: (i) una amplia trayectoria de iniciativas de investigación individuales y de colaboración en Neurociencia, (ii) su asociación a los principales centros básico-clínicos de relevancia nacional e internacional, (iii) un vasto potencial en la formación de personas en ciencias de la salud, y (iv) un cuerpo joven de investigadores capaz de ejecutar los objetivos a largo plazo de la iniciativa.

Tres principios guían el funcionamiento del BNI: (i) la investigación transdisciplinaria, (ii) un enfoque multi-escala para estudiar la función de genes desde las moléculas al comportamiento en modelos animales complementarios, y (iii) una estrategia biomédica integrada para generar contribuciones científicas de alto estándar y garantizar su transferencia a la comunidad. Durante 2013 estos principios rectores fueron abrazados plena y explícitamente por los miembros de BNI, organizados en torno a plataformas temáticas interconectadas. A través de ellos BNI tiene por objetivo: (i) establecer un centro de referencia internacional para la exploración de la estructura y función del cerebro en condiciones fisiológicas y patológicas, (ii) entrenar a una nueva generación de líderes investigadores y clínicos en un ambiente transdisciplinario único, sólido y vibrante, (iii) producir investigación clínica de alto nivel y transferir su impacto a la sociedad, y (iv) convertirse en un centro de recursos para médicos especializados y el público en general.

Durante este período se ha trabajado en la consecución de cada uno de estos objetivos. Operando como una organización sin fines de lucro hemos continuado invirtiendo más del 60% de los recursos en objetivos estratégicos comunes. Esta estrategia financiera se complementa con nuestro compromiso para co-tutorear estudiantes y postdocs, y colaborar en proyectos básicos y aplicados. Aunque la estructura del Instituto se ha mantenido sin cambios sustanciales, el número de personas aumentó por tercer año consecutivo (7%), con nuevos estudiantes y postdocs representando la mayor parte de esta expansión. El incremento en el número de investigadores posdoctorales es consecuencia directa de la política BNI de asignar fondos comunes al concurso "*Becas Puente*", que ha permitido incorporar aproximadamente 7 postdocs/año, la mayoría de los cuales han hecho una transición exitosa a otras fuentes de financiamiento (5 promedio). Además, BNI tiene una tasa favorable de investigadores femenino:masculino de 42:58 entre sus estudiantes y postdocs.

Las líneas de investigación constituyen programas científicos de largo plazo y, por lo tanto, se han mantenido sin cambios. Hemos publicado 35 artículos ISI, incluyendo dos revisiones en revistas de alto impacto (*Hetz et al., 2013, Nat Rev Drug Discov 12:703, Impact Factor 33; Hetz, 2013, Nat Rev Mol Cell Biol 14:404, Impact Factor 37*). Además, la investigación BNI ha sido publicada en revistas destacadas como *Nat Commun, J Neurosci, J Cell Sci, Curr Mol Med, Semin Immunol, Development, Cell Res, Trends Mol Med, Autophagy* y *Biol Psychiat*.

Aparte de los fondos centrales de la ICM los investigadores BNI han continuado asegurando fondos para la investigación básica a partir de fuentes nacionales como FONDECYT (todos los investigadores de BNI), CONICYT-USA (C. Hetz, J. Sierralta, A. Couve) y U-Redes (S. Härtel). Además, han obtenido fondos nacionales para equipos de mediano tamaño (FONDEQUIP) para ampliar la capacidad en microscopía automatizada para estudios celulares a gran escala, señalización intracelular y búsqueda de fármacos (Cellomics, C. Hetz), microscopía confocal y de tipo *light-sheet* (L. Leyton, M. Concha, S. Härtel) y ultracentrifugación (C. Hidalgo). Se han obtenido fondos de organismos internacionales como la Fundación Micheal J Fox para la Investigación de Parkinson, la Asociación ALS, y Genzyme (C. Hetz). Por otra parte, tres proyectos aplicados FONDEF continúan involucrando a investigadores BNI (C. Hetz, S. Härtel, P. Maldonado y A. Couve). Por último, postulaciones exitosas a fondos de divulgación como EXPLORA e INNOVA CORFO (A. Couve) han generado una nueva fuente de financiamiento. BNI ha financiado cuatro nuevos proyectos piloto, en su mayoría dirigidos por jóvenes investigadores en colaboración con Investigadores Asociados (R. Vidal/C. Hetz, R. Nieto/ H. Silva, A. Paula-Lima/C. Hidalgo, M. Concha/S. Härtel). Estos proyectos promueven las interacciones e incorporan investigadores jóvenes a las actividades centrales de la institución.

Hemos continuado con nuestras reuniones semanales de investigadores, seminarios periódicos con invitados nacionales e internacionales, y seminarios internos. Hemos organizado 7 eventos científicos de envergadura en Chile, que promovieron la investigación y los objetivos del BNI dentro de ponentes internacionales y el público nacional que alcanzó más de 1000 personas. Llevamos a cabo 2 encuentros básico-clínicos en la FMed con expositores internacionales y departamentos clínicos, consolidando colaboraciones, visualizando problemas biomédicos locales y evaluando el progreso de soluciones concretas. Hemos incorporado a L. Bustamante, MD-Ph.D, psiquiatra y genetista, como coordinadora de investigación clínica para trabajar en asociación con H. Silva en la unificación de criterios (consentimientos informados, ética, bio-bancos). Actividades de difusión de alto impacto se completaron durante el 2013 incluyendo conferencias, visitas, entrevistas en radio, web, prensa escrita, y la generación de material físico y virtual para llegar al público general y fortalecer nuestra plataforma interactiva *Dendros*.

Hemos recibido premios nacionales e internacionales. Destacamos el primer premio en el concurso Nacional de Innovación en Educación Científica otorgado por la Fundación Ciencia Joven y la Fundación Telefónica a *Dendros*. Este es el resultado de un trabajo comprometido y creativo del instituto, y el producto de la colaboración entre nuestros directores de arte, estudiantes de BNI y postdocs que ayudan continuamente con contenido científico y apoyo a las actividades.

Una red basada en microscopía y procesamiento de imágenes ha promovido la participación de 26 estudiantes y postdocs, y producido avances en el intercambio de conocimientos, equipos y reactivos. Además, la segunda reunión con una red de centros y laboratorios de Neurociencia de América Latina se llevó a cabo en Buenos Aires (*NeuroSur-II*), consolidando la iniciativa como un concepto viable y atractivo para mejorar interacciones de manera flexible y económica.

Una vez más, guiados por un programa transdisciplinario, un enfoque multi-escala y una estrategia biomédica integrada creemos firmemente que continuamos consolidando una iniciativa que mejorará la presencia internacional del país en el campo de las ciencias del cerebro, generando resultados reconocibles alta de calidad.

2. Introduction

a) Description of the Institute:

The Biomedical Neuroscience Institute (BNI) constitutes a broad umbrella that brings together a critical mass of leading basic neuroscientists, clinicians and mathematicians to explore the dynamic structural and functional organization of the brain under normal physiology and the mechanisms underlying disease from whole organisms to cells. BNI aims to: (i) accomplish world-class scientific research, (ii) train and host a new generation of leading researchers and clinicians in a vibrant, solid and unique transdisciplinary environment, (iii) produce high-standard clinical research and transfer the impact of its research to society, and (iv) become a resource center for specialized clinical practitioners and the general public. Research at BNI is built upon 8 interconnected thematic platforms. 5 platforms conduct research on the relationship between structure and function of the brain, following a bottom up, multi-scale approach in complementing model organisms (flies, zebrafish, mice, rats, and humans). Two transversal platforms foster the collaborative strategy conducting research and development in applied mathematics and biomedical informatics, and diseases affecting the nervous system and pharmacological target validation. A clinical research platform strengthens the bridge between basic and medical research, and promotes the translation of knowledge to and from the clinic. BNI's research is supported by students, postdocs, young investigators and young clinicians. An Executive Office contributes to connect with other sectors, a Grant Management Office is responsible for the financial administration, and a Board of Directors steers the Institute's strategy.

b) Research Lines:

Research lines embody the strategic aims and the core of the collaborative effort at BNI. They are envisioned as long-term research programs and therefore have remained unchanged.

RL1. Sub-cellular functional dynamics: Neuronal differentiation requires the secretory pathway and the cytoskeleton within neurons and glia. In this context, it is fundamental to understand how the dynamic structures of the secretory pathway and the cytoskeleton are organized in different cell types of the nervous system, and how this organization determines neuronal function or dysfunction.

RL2. Cellular identity and morphology: Morpho-functional features of differentiated neurons define a structural backbone upon which connectivity is established. These features determine how electrical signals are shaped to render simple elements of cell-to-cell communication and integrate them into sophisticated computational-like devices. A central question is how gene expression determines morpho-functional features throughout the development and the lifespan of neurons.

RL3. Supra-cellular development and circuits: The transformation of brain morphogenesis involves the re-organization of multi-cellular aggregates into nuclei and layers, and the migration of axonal growth cones to establish neuronal connectivity. Thus, it is fundamental to understand how gene activity is translated into brain morphogenesis, and how the acquisition of novel states of supra-cellular and connectional organization influences patterning and brain function.

RL4. Plasticity and behavior: Hippocampal synaptic plasticity is an activity-dependent neuronal response associated with learning and memory that entails significant modifications in the efficacy of synaptic transmission. Cytoplasmic and nuclear Ca^{2+}-dependent signaling cascades are required for sustained long-term potentiation (LTP) and alteration of neural assemblies. Thus, an essential question is how genetic interactions and signaling pathways control long-lasting memories.

RL5. Systems Neuroscience: While most paradigms used to examine the neuronal mechanisms of cognitive functions and to predict neuronal activity have employed simple and controlled stimuli, the responses of neurons to complex and more ecological situations differ substantially. Thus, it is

fundamental to examine, compare and model the neuronal activity when animals and humans engage in ecological behavioral paradigms and classical psychiatric conditions.

RL6. Neural dysfunction and pharmacological targets: This transversal platform fosters an *in vivo* approach centered on understanding the mechanisms by which disease-related genes affect common molecular/cellular/physiological processes leading to neuronal connectivity and synaptic function in neuropathological conditions, and developing technological approaches.

RL7. Applied mathematics and biomedical informatics: A deeper understanding of architectonic and functional principles of neuronal processes requires a transdisciplinary approach. Biophysics and applied mathematics combined with advanced imaging and computing clusters foster an integrative view to study the design of biological structures and their functional patterns. The central aim is to uncover novel neural processes based on mathematical models that reveal morpho-functional principles of organization at multiple scales.

RL8. Clinical research and capacity building: BNI provides a rich array of clinical research opportunities in Neuroscience, based on the access to patients and samples, reliable records, and motivated clinicians. Previously these opportunities have failed to produce the expected development in Chile due to dispersion of resources, lack of efficient channels of interaction of clinicians with scientific management structures and scarce access to state-of-the art technology. A central goal at BNI is the development and consolidation of clinical research and capacity building in the study of neurological and psychiatric pathologies.

c) Organization of researcher's team:

BNI consists of one Principal and ten Associate Investigators, all professors at the FMed, U of Chile, with complementing backgrounds and expertise. Additionally BNI is constituted by 4 Adjunct Investigators, 1 Senior Investigator, 6 Young Investigators, 22 postdocs, 63 PhD, 27 Master, 25 undergraduate students, 57 technicians and 9 administrative staff. This represents a 7% increase relative to last year and highlights the appeal of the institute to younger scientists. *Photograph: Part of the BNI team at our first social retreat.*

Specific strategies to foster interactions include: (i) definition of research line leaders that coordinate efforts and funds within and between thematic platforms, (ii) co-mentorship of students/postdocs/young investigators/clinicians in a cross-disciplinary, open-lab atmosphere to generate effective exchanges, (iii) shared facilities for microscopy, data analysis, genetic manipulation, and animal behavior, (iv) organization of internal seminars, and theoretical/practical courses to enhance a cross-disciplinary atmosphere, (v) weekly internal meetings to evaluate the progress of collaborative research, adjust strategies and maintain a strong sense of thematic direction and philosophy, and (vi) an outstanding advisory board. The majority of funds are allocated to common strategic aims such as animal facilities, a biomath team, postdoctoral fellowships, pilot projects to test and evaluate ideas of common interest, infrastructure, equipment, outreach and administration. Approximately 30% of the funds are allocated to operational expenses freely executed by each Associate Investigator within BNI's guiding principles. Each BNI investigator is responsible for specific tasks such as reviewing postdoctoral applications and pilot projects, coordinating collaborative networks, organizing databases, editing the scientific content of outreach activities, connecting with clinicians, and organizing scientific events. The research team is supported by an Executive Office, which contributes to the organization of scientific activities, outreach, press and connection with other sectors, and by a Grant Management Office, which provides accounting and legal support. ***See Annex 1.***

3. Scientific and Technological Research:

a) Current status of research lines:

Each research line involves the interaction of multiple laboratories. To facilitate the revision process in this and other sections we have used initials to refer to each BNI scientist involved in a particular project, publication or other activity: A. Couve (**AC**), C. Hetz (**CHz**), M. Concha (**MC**), S. Härtel (**SH**), M. Herrera-Marschitz (**MH**), C. Hidalgo (**CH**), M. Kukuljan (**MK**), L. Leyton (**LL**), P. Maldonado (**PM**), J. Sierralta (**JS**), H. Silva (**HS**). ***See Annex 2.***

RL1. Sub-cellular functional dynamics: We have continued addressing, in parallel, all three specific aims of this line of research. Key findings include: i) Endosome dynamics, regulated by small GTPases of the Rab family, controls dendritic branching (**AC**). Intracellular receptor trafficking has been revealed by SOFI, super resolution microscopy methodology (**AC/SH**). A failure in ascorbic acid flux from astrocytes to neuronal cells occurs preceding the onset of Huntington disease-like symptoms in mice (**CHz**). A functional role for a transcription factor (ATF4) has been described for amyotrophic lateral sclerosis (**CHz**). BI-1-dependent Ca^{2+} leak from the ER is reduced by acidic pH, indicating a pore mechanism that is regulated during cytosolic acidosis (**CHz**). ii) Using genome-wide illumina-microarrays and further qRT-PCR of brain samples from patients suffering from schizophrenia, region specific down regulation of gene products associated to presynaptic vesicles, cytoskeletal, and ECM proteins have been found (**MH**). iii) Activation of GTPases of the Rho family downstream of cell adhesion receptors present in astrocytes has been observed. Short-term contact of neurons and astrocytes increases RhoA-GTP and astrocyte adhesion; whereas, long-term stimulus results in RhoA inactivation and Rac1 activation, thereby leading to astrocyte migration, as observed by single cell recording (**LL/SH/MH**). Dynamics of cell adhesion and signaling involved in adhesion and migration have been studied using astrocytes, cells derived from the oral mucosa of patients suffering schizophrenia and cancer cells (**LL**).

Results from these studies have been published in leading journals. These include dendritic branching regulated by endosome dynamics (*Lazo et al., 2013 J Neurosci);* SOFI of neurotransmitter receptors in neurons, a pioneer study of chilean scientists in super-resolution microscopy (*Huss et al., 2013 Proc. SPIE);* failure in energy metabolism and antioxidant uptake in HD (*Acuña et al., 2013 Nat Commun);* the function of Trehalose in ALS (*Castillo et al., 2013 Autophagy*); the ER protein Herp operates by modulating autophagy levels (*Quiroga et al., 2013 Biochim Biophys Acta*); measurement of autophagy flux in the nervous system *in vivo* (*Castillo et al., 2013 Cell Death Dis*); a functional role of ATF4 in ALS, offering a novel target for disease intervention (*Matus et al., 2013 PloS One*); Bax Inhibitor-1-mediated Ca^{2+} leak is decreased by cytosolic acidosis (*Kiviluoto et al., 2013 Cell Calcium*); gene expression in superior temporal cortex of schizophrenia patients in (*Sellmann et al., 2013 Eur Arch Psychiatry Clin Neurosci*); neuron–astrocyte binding engages receptors and signaling molecules to promote cell motility (*Kong et al., 2013 BBA. Mol Cell Res*); altered focal adhesion dynamics are altered in Schizophrenia (*Fan et al., 2013 Biol Psychiat*); signaling in focal adhesion dynamics and cell migration was published (*Lobos-Gonzalez et al., 2013 Pigm Cell Melanoma Res* and *Mendoza et al., 2013 J. Cell Sci*).

International recognition of the expertise of PIs has continued to be demonstrated by invitation to write influential reviews (*Nature Rev Mol Cell Biol, Nature Rev Drug Discovery, Int. J Cell Biol, Biochim Biophys Acta, Trends Mol. Med, Semminars Immunol, Curr Mol Med, International Rev of Cell and Mol Biol),* editorial comments (*Cell Metabolism, Cell Res*) and a book chapter (*Cell Adhesion Molecules: Implications in Neurological Diseases. Springer).* BNI participated in various meetings and symposia including the *XXVII Annual Meeting of the Chilean Society for Cell Biology*

and international presentations at the *Japanese Neuroscience Society* in Kyoto, Japan*; Emerging concepts on neuronal cytoskeleton* in Marbella, Chile*; FASEB Science Research Conference: From Unfolded Proteins in the ER to Disease; Gordon Research Conference: Stress proteins in growth, development & disease; 10th Calreticulin Workshop,* Vermont USA*; VI Neurotoxicity Society Meeting,* Valdivia, Chile*; FENS Regional Meeting,* Prague, Czech Rep., *XXVIth International Symposium on Cerebral Blood Flow, Metabolism and Fucntion,* Shangai, China*; ASCB Annual Meeting,* New Orleans, USA*; Proceedings SPIE,* California, USA.

RL2. Cellular identity and morphology: During the period we have made progress in:

i) Neural morphogenesis and CTIP1: Using *in utero* electroporation in mice, we have continued the study of this transcription factor that was originally identified in a screen for genes involved in neuronal morphogenesis in *Drosophila*. Our results are compatible with a role of CTIP1 in the specification of subclasses of projection neurons in layer V of the cerebral cortex (**JS/MK**).

ii) CoREST and brain development: Using the same system we have now continued the study of the chromatin-remodeling protein CoREST. We have not focused in progenitors (published in 2012) but in the role of CoREST in the arborization of neurons. Our ongoing work is aimed at understanding the relationship between signal transduction pathways and epigenetic regulation in this system. We have obtained new targets that partially explain the phenotype of CoREST downregulation (**MK**).

iii) Synapse formation and Hindsight: We are currently investigating the target genes through which the transcription factor Hindsight affects axonal targeting and growth in the optic lobe in *Drosophila*. We have determined that one of the direct targets of Hindsight (HNT) is a homolog of *Drosophila* Filamin, Jitterburg, whose knockdown mimics the downregulation of HNT in axonal growth. In addition, we are studying the role of MAGUK proteins in the formation, function and plasticity of the synapses by electrophysiology and microscopy. We have demonstrated that DLG proteins are essential for the efficiency of presynaptic neurotransmitter release (**JS**).

iv) Lactate metabolism and glia-neuron relationship: We have initiated the study of a gene originally identified as important for neuronal morphogenesis in a loss of function *Drosophila* screen, similar to the one where CTIP and Hindsight were identified. This gene is a putative lactate transporter that may be essential for viability when expressed in *Drosophila* glial cells (**JS**).

v) Search for genes associated to motorneuron degeneration: We have also initiated a modification screen in *Drosophila* to seek for genes that affect the motor phenotype associated to the decrease in the expression of the gene atlastin, directly associated to Hereditary Spastic Paraplegias (HSP) in humans. This is a collaboration between two BNI labs that has also won support from an International Collaboration CONICYT-USA Grant associated to UMASS (**AC/JS**).

The role of CTIP1 has been recently sent for consideration to *J Neurosci*. Studies of the role CoREST in neuronal migration and morphogenesis, the study of Hindsight, as well as the new lines of research that are part of PhD and Ms theses have been presented as posters in a national meeting (*López et al.; Saud et al.; Maureira et al.; Delgado et al.; De Gregorio et al., XXVII Annual Meeting Chilean Society for Cell Biology*). Recent results on MAGUK proteins have been presented in a neuroscience national meeting (*Astorga et al., 2013, Annual Meeting Chilean Society for Neuroscience*).

RL3. Supra-cellular development and circuits: During this period we have made progress in the experimental approaches of all projects, and implemented new methodologies for 3D confocal visualization of living embryos and mathematical analysis in collaboration with the BNI-BioMat platform (see RL7 for more details). The main results and stage of advance of the collaborative projects are:

(i) Asymmetric morphogenesis of the parapineal and habenulae in zebrafish (**MC/SH**): We have finished a project that demonstrated that the F-actin modulator Daam1 works as an effector of asymmetric brain morphogenesis by differentially regulating axonal and dendritic extension of habenular neurons in left and right sides of the zebrafish brain. This study has been published in a leading journal in the field (*Colombo et al., 2013 Development*; 2012 ISI Impact Factor 6.208). We also implemented new mathematical analyses of time-lapse image data to gain novel insights into the role of Nodal signaling in the asymmetric control of parapineal cell behavior during morphogenesis.

(ii) Chemokine and Robo-Slit signaling and habenular-IPN connectivity (**MC/CH**): We have established a new collaboration with J. Campusano (PUC, Chile) to implement the technique of primary cultures of zebrafish habenular neurons, in order to complement the *in vivo* analysis of the role of Cxcl12-Cxcr4 in regulating Slit-Robo3 function in zebrafish. A manuscript is under preparation.

(iii) Role of tensile and migratory forces in shaping supra-cellular embryonic structures (**MC/SH**): We have advanced in this new project to link mechano-chemical embryonic processes that shape the early primordium of the zebrafish laterality organ to mechanisms that protect or ensure the normal acquisition cell fate during development. This project is multidisciplinary and combines techniques of cell biology, developmental biology, image analysis, and mathematical modeling.

(iv) Role of differential adhesion and contact inhibition in cell sorting during early morphogenesis (**MC/SH**): We have generated important data that demonstrates a mechanism of cell-mediated contact guidance as a driving force of tissue spreading during development. To deepen our analysis, we started to implement new methodological approaches of image analysis to resolve the movement of cell population *in vivo*, to analyze cell polarity *in vivo* (Rac detection via FRET), and to simulate contact guided behavior *in silico* through mathematical modeling.

(v) Comparative analysis of habenular asymmetry in vertebrates (**MC**): We extended our initial systematic comparison of asymmetric habenular morphology and connectivity among various teleost species (published in 2012), to found a conserved link between the strength of habenular asymmetry and the strength of lateralization in a visually-guided behavior ('detour test').

Results were presented at the international level in the *International Society of Developmental Biologists 17th International Congress of Developmental Biology*, the satellite symposium *Making and Breaking the left-right axis: laterality in development and disease*, and the *Society for Neuroscience Annual Meeting*. At the national level, presentations included the *XXVII Annual Meeting of the Chilean Society for Cell Biology*, *the XXIV Meeting of the Chilean Reproduction and Development Society*, and the *BNI Summer Symposia Advanced Microscopy and Image Processing*.

RL4. Plasticity and behavior: During this period, we have continued the studies on the role of ryanodine-receptor (RyR) Ca^{2+} release channels on hippocampal long-term potentiation (LTP) and hippocampal-dependent behavior (**CH**, in collaboration with BNI adjunct investigator J.L.Valdés). Results obtained to date indicate that selectively suppressing RyR activity by using inhibitory ryanodine eliminates LTP induction by the theta burst stimulation (TBS) protocol of Schaffer collateral fibers, fEPSP recorded in the CA1 region. This result was unexpected, since previous publications by other authors indicate that inhibiting RyR decreased but did not suppress LTP induction by TBS, or prevented LTP maintenance after high frequency stimulation without inhibiting its induction. The suppression of LTP induction after TBS by inhibitory ryanodine is due to postsynaptic inhibition of RyR-mediated Ca^{2+} release, since the paired-pulse response (reflecting pre-synaptic activity) remained unaffected in slices treated with inhibitory ryanodine. We also found that suppressing the induction of LTP by TBS with inhibitory ryanodine, prevents Ca^{2+} signal

generation in the soma of CA1 neurons in response to TBS. This is an important result, because it indicates that Ca^{2+} influx mediated by NMDA receptors, which is the first post-synaptic response to TBS, does not make a detectable contribution to the somatic Ca^{2+} increases induced by TBS in neuron of the CA1 hippocampal region. Inhibitory ryanodine, by preventing the increase of Ca^{2+} in the soma after TBS, probably prevents the nuclear Ca^{2+} increase required for the changes in gene expression that underlie synaptic plasticity. Indeed, we found that slices incubated with inhibitory ryanodine did not exhibit the increases in RyR1 and RyR2 mRNA, or the increased levels of RyR2, BDNF and Arc proteins displayed by control slices after inducing LTP for 1 h. In parallel studies, we found that inhibiting RyR2 isoform expression by an antisense oligonucleotide (anti-RyR2) prevents the formation of new dendritic spines after stimulating hippocampal neurons in primary culture with the neurotrophin BDNF. Furthermore, bi-lateral injection intra-hippocampus of anti-RyR2 interrupts learning and memory in rats in the Oasis maze, a hippocampal-dependent spatial task. These combined results indicate that Ca^{2+} release mediated by the RyR2 isoform is essential for the hippocampal synaptic plasticity that underlies spatial learning and memory. We have been invited to write a review on the role of Ca^{2+} release channels in hippocampal-dependent synaptic plasticity, learning and memory, which will be published during 2014 (**CH** in collaboration with young investigator A. Paula-Lima). Additionally, we have continued to investigate how non-lethal concentrations of soluble amyloid β-peptide oligomers (AβOs) generate abnormal RyR-dependent Ca^{2+} signals that perturb normal neuronal function, and provoke mitochondrial fragmentation. We have published an article on this subject (*Paula-Lima and Hidalgo 2013 Front Cell Neurosci*) and another will be published during 2014 (**CH** in collaboration with young investigator A. Paula-Lima). In a new project we have begun to investigate the role of RyR and other neuronal channels in the propagation of intracellular Ca^{2+} waves in dendrites of primary hippocampal neurons (**AC/SH/CH**). During the reported period we presented our work in several national and international meetings.

RL5. Systems Neuroscience: During 2013 we have completed a series of studies to determine the neuronal mechanisms related to visual perception. C. Devia, Ph.D. has completed her thesis examining electrophysiological aspects of visual perception in humans (**PM**). We have presented four abstracts of these studies and are currently preparing two manuscripts. We have also published a proceedings article on the analytical processing of this data (*Montefusco-Siegmund et al., 2013 6th Annual International IEEE EMBS Conference on Neural Engineering San Diego*). International collaborations based on data acquired in our labs resulted in an additional publication (*Ito et al., 2013 Front Syst Neurosci*).

We have continued to explore the neuronal mechanisms involved in interoception. Recording the activity of the insular cortex in a model of alcohol-addicted rats we have tested whether electrical microstimulation of the vagus nerve modulates craving behavior (**PM**), which is the basis of a doctoral thesis (C. Ibañez, MD). In addition, we have continued a series studies exploring the pupillary dynamics as a marker for insular and autonomic activity. This research has been supervised by a postdoctoral fellow (E. Brunneti, MD). R. Mayol finished her thesis relating pupil and emotional responses during decision making (**PM**). S. Brugues also finished her thesis, which was co-tutored by two BNI investigators (**PM/MH**). In this work, she explored the pharmacological contribution of the autonomous nervous system in the pupillary responses. An abstract was presented at the *Annual Meeting of the Society for Neuroscience*, and a manuscript is under preparation. Preliminary work from these studies contributed to secure a new applied research grant (FONDEF IDEA CA12I 10061) between BNI members (**PM**/**AC**) and J. Velásquez (Instituto Milenio Sistemas Complejos de Ingeniería, ISCI). The aim of the study is to examine eye movement and pupillary dynamics (emotional responses) during the free exploration of web pages. The project will enable us to predict user responses and preferences, which in turn can be used to improve web

page design. This project has served as substrate for one Masters thesis (C. Astudillo) and three Engineering internship-type projects (C. Aracena, G. Martínez and J. Jadue). Additionally, it has promoted a regular interaction between two Millenium Institutes from distinct but highly complementary disciplines, a priority strategy for the Millenium Science Initiative.

During this period, we have continued to combine basic and clinical efforts to study psychiatric patients. A central study involves two BNI Associated Investigators (**HS/PM**) and aims at establishing biometrics for schizophrenic patients. Specifically, we are studying a group of diagnosed patients in order to obtain behavioral, genetic, and electroencephalographic (EEG) markers for this pathological condition. The study involves the development of a multi-center collaborative network, including the Instituto Psiquiátrico Dr. José Horwitz, and two health centers associated to Universidad de Chile (Hospital del Salvador and Clínica Psiquiátrica). J. Ignacio Egaña MD, a BNI-funded postdoctoral fellow has been involved in this project. We have recorded EEG signals from more than 30 patients and 10 control subjects. Along with EEG recordings, we have recorded eye movements and pupil dynamics. We have published one manuscript on eye movements (*Egaña et al., 2013*). We have also obtained a BNI-funded pilot project aimed at identifying EEG markers for pain perception. The main goal is develop EEG analytical tools to evaluate and predict cortical response to pain, validating the hypothesis that EEG markers can be used to monitor pain and analgesia during surgery.

RL6. Neural dysfunction and pharmacological targets: During this past year, we have performed several studies to address novel disease mechanisms using animal models. We have developed several studies in mouse models of disease to investigate pathogenic mechanisms in several neurological diseases and also test new therapeutic strategies. We have been able to perform genetic manipulation of the disease models and identify novel targets for therapeutic interventions. For example, we have targeted a main transcription factor involved in adaptation to cellular stress using knockout models (i.e. ATF4) and evaluated its function in an ALS transgenic mouse model (**CHz**). Using this approach we have identified a key component of ALS pathogenesis that mediates motoneuron loss in the disease, possibly due to the control of apoptosis genes (*Matus et al., 2013 PLoS One*). Similar studies have been completed in models of peripheral nerve degeneration and Parkinson's disease that have been submitted for publication. These studies included collaboration with the biotech company Genzyme (USA) to generate gene therapy tools to treat these diseases.

We have also tested novel therapeutic approaches to induce the degradation of toxic aggregates in ALS (*Castillo et al., 2013 Autophagy*). We have identified the compound trehalose as a possible therapeutic agent to treat ALS. This compound is active orally and was able to attenuate disease signs and extend the life span of transgenic animals expressing the disease gene SOD1. This paper had high scientific impact (for example it was highlighted by the Muscular Dystrophy Association in the US) and was also strongly covered by the written press and TV in Chile. We also completed a collaboration with M. Castro (Universidad Austral, Chile) on the context of Huntington's disease and published an high impact factor paper (*Acuña et al., 2013 Nat Commun*). Finally, we have developed a new method to measure autophagy levels in the brain using adeno-associated viruses (AAVs) and fluorescent reporters, solving a central need in the field. We have used this method to demonstrate the activation of autophagy in models of axonal damage including spinal cord injury and peripheral nerve degeneration, and after treatments with drugs such as trehalose and rapamycin (*Castillo et al., 2013 Cell Death Dis*). Based on our contributions several reviews and editorial comments were published on the topic, highlighting one in *Nat Rev Drug Discov* (ISI Impact Factor 33). We published several review articles discussing novel aspects of the molecular pathogenesis of Parkinson's, Alzheimer's, ALS, and schizophrenia (**CHz, LL, MK, HS, and CH**), highlighting

publications in high impact journals such as *Cell Metab, Trends Mol Med, Nat Rev Mol Cell Biol,* and *Front Psychiatry*.

Finally, this platform is currently developing and establishing new models of neurodegeneration, including transgenic mice of Alzheimer's disease, new models of ALS, in addition to genetically modified animals for several stress genes. In collaboration with R. Brown (UMASS) we have identified new gene mutations that may contribute to ALS and have generated several transgenic lines in mouse, in addition to performing an initial analysis in zebrafish. These studies will be strengthened by a recent International Collaboration CONICYT-USA Grant secured for international collaborations (**CHz**).

RL7. Applied mathematics and biomedical informatics: During 2013, the mathematics and biomedical informatics group (BNI-BioMat) and associated members of SCIAN-Lab (**SH**) advanced in the following issues: S. Vargas (BNI-BioMat) contributed with a publication awarded with a cover figure (*Busso et al., 2013 Rep Fert Dev*), L. Briones (BNI-BioMat) participated in a publication with BNI investigators **MC/SH** (*Colombo et al., 2013 Development*) and, together with J. Mansilla (BNI-BioMat) enrolled in the first International Master Program for Medical Informatics in Latin America that was established December 2013 at the U Chile (academic director **SH**, www.postgradomedicina.uchile.cl). BNI postdocs M. Cerda and V. Castañeda obtained FONDECYT postdoctoral fellowships for three years and contributed with publications (*Cerda et al., 2013 Biol Cybern; Terissi et al., 2013 EURASIP JASMP; Castaneda et al., 2013 IEEE Trans Pattern Anal Mach Intell*). F. Santibáñez (BNI-BioMat) together with J. Jara (BNI PhD student) and O. Ramírez (BNI-BioMat) established a strong collaborative team to foster:

(i) *New imaging techniques:* Super-resolution Optical Fluctuation Imaging (SOFI) in combination with spectral confocal microscope LEICA LSI (mm range), confocal imaging (250 nm range), and SOFI (80 nm range) represent a unique combination of microscopy infrastructure for Latin American researchers. Two BNI investigators (**AC/SH**) participated in a first SOFI study published in a proceedings publication (*Huss et al., 2013 Proceedings of SPIE*). New NanoZoomer Whole-Slide Tissue Scanner (Hamamatsu) is presently installed within the FONDEF project *Microscopía Virtual - Centro de Patología Digital Asistida (CPD)* (**SH**) and a recently awarded FONDEQUIP project (**MC/SH**) will enable the installation of a light sheet microscope in collaboration with U. Kubischeck (U Bonn, Ger).

(ii) *High-, mid-, and low level mathematical-computational methods for microscopic image analysis in combination with high performance computing (HPC):* Besides the publications mentioned above we contributed to the Latin American Initiative for reproducible software and code in the field of image processing (IPOL-LA) with a contribution to the IPOL library (*Jara et al., 2013 Image Processing On Line*). The acceleration of existing and novel image processing algorithms (through HPC or GPU) was tackled in collaboration with FONDECYT project *Fast Computational Schemes for the Analysis of Morpho-Topological Data from High Throughput Microscopy* (**SH**). The application of HPC for high throughput microscopy data depends on a new 10Gbps connection to the National Laboratory for HPC (NLHPC, www.nlhpc.cl), which has been prepared in 2013 within the U-Redes Project *BioMed-HPC: Network for Biologic and Medical HPC* with a total budget of $240,000,000 CLP. During 2013 the framework has contributed to build the necessary conditions to connect the Campus Norte of U Chile (FMed, Faculty of Odontology, University Hospital, and Faculty of Chemistry and Pharmaceutics), the STI, REUNA, and the CMM via a 10Gbps connectivity. Final components will be installed during 2014, providing a unique infrastructure for big data science at the interface of basic and clinical research with computational science and engineering.

(iii) *R&D of internet assisted services for diagnosis and clinical research:* The *spin-off* for Internet Assisted Medical Services CEDAI SpA (**SH**), has improved pilot versions with national public hospitals and private clinics. Digital pathology is being integrated into remote services for image-based analytics for clinical practices on the basis of the new imaging techniques mentioned above. First results for tissue imaging, strategies to insert digital pathology into the work flow of Chilean hospitals, and the benefit for education have been presented at the international meeting *3rd European Conference on Whole Slide Imaging and Analysis, Hamamatsu TIGA Center, University of Heidelberg, Germany* (*García et al.; Rojas-Moraleda et al.; Díaz et al.*). Together with our joined contribution to host and enroll patient data within the U.S. Latin-American Cancer Research Network-Chile (USLACRN), we have started to work on the integration of distributed data sources (clinical, pathological, genomic data) to contribute towards personalized medicine in Chile within an international network. Our new *International Master Program for Medical Informatics* will help to bridge the gap between disciplines and improve capacity building within inspiring endeavor.

RL8. Clinical research and capacity building: During 2013 we addressed one of our central aims by identifying factors that pose an increased risk for psychosis in late life, or a deterioration in the outcome of a psychotic disorder in spite of adequate treatment. Our two main research projects were:

(i) Pharmacogenomics of antipsychotic responses in schizophrenia. During 2013 the project finished recruiting patients, and we are currently analyzing the clinical information as well as biomarkers (blood BDNF levels) and genetic information (BDNF Val66Met polymorphism). Future directions for this line of work include carrying out a more extensive genomic analysis. A recent development originating from our preliminary study is the collaboration between two BNI labs as a result of the approval of a Pilot Project 2014 (**HS/CHz**). Because we are interested in studying the nervous system by employing a multi-scale approach, from genes to behavior, we will measure and correlate clinical parameters with BDNF protein and RNA levels in blood, and study their modulation by a transcription factor currently under investigation at BNI and a likely candidate in the BDNF functional pathway (**CHz**).

(ii) Studies in 22qDS. This condition, caused by a known chromosomal deletion, determines an increased risk for schizophrenia, and therefore it is a relevant model for understanding the genetic risk of the pathology, as well as other genotype-phenotype relationships. Of special relevance for us, the majority of individuals affected by the deletion will not develop schizophrenia, but they will present significant neuropsychological disturbances. We have obtained funding through U-INICIA 2013, to carry out a study to measure and correlate the risk for psychosis in carriers of the 22q deletion as well as relatives with alterations in their social cognition.

Other projects advanced during 2013 include: Endophenotypes in Attenuated Psychosis Syndrome (APS). APS describes a condition characterized by recent onset of modest psychotic-like symptoms, clinically-relevant distress and significant disability. During 2013, we have proposed a family-based, dimensional and retrospective pilot project to search for genetic predictors in subjects that have exhibited symptoms compatible with APS, and who later on converted from APS to full psychotic disorder. We will develop this research project in collaboration with the New York Genomic Center.

As an effort associated to our scientific activities, BNI undertook the task of developing the resources to foster translational research (led by **HS**). The first solution to be implemented corresponds to a bio-banking facility available for all BNI researchers and other research institutions. A bio-bank is a repository of clinical and biological information, in this case of information related with neuropsychiatric disorders. The hallmark of a bio-bank is the systematical approach to the collection, storage and manipulation of samples and information for the purposes of

research. We have identified potential partners who share the vision. We are in the process of establishing an agreement with the Cancer Center of U Chile to optimize the use of common resources (infrastructure and human capital). In addition, the Department of Psychiatry, North Division of the FMed, has provided valuable support by agreeing to acquire a laboratory information management system, which will be implemented in April 2014. BNI has contributed by incorporating psychiatrist/geneticist L. Bustamante, MD-Ph.D. who is currently coordinating the activities. Therefore, our bio-bank will offer services of sample and data acquisition and storage in the short term. As we will be able to assure confidentiality and quality control of the information, we will expand the type of services to encompass different conditions. We will also establish new partnerships with qualified third-parties.

b) Publications:

During this funding period BNI members published 35 ISI articles. Their relevance and impact for each research line have been described above in section 3a. ***See also Annex 3***.

Summary table

Category of Publication	**MSI Center Members**	**Number of Publications coauthored by students**	**Total Number of Publications**
ISI Publications or Similar to ISI Standard	Associate Researchers	15	35
	Other Researchers	-	3
SCIELO Publications or Similar to SCIELO Standard	Associate Researchers	-	-
	Other Researchers	-	-
Scientific Books and chapters	Associate Researchers	-	1
	Other Researchers	-	-
Other Scientific Publications	Associate Researchers	2	2
	Other Researchers	-	-
Total of Publications		20	41

c) Other achievements:

- **Patents:**

No changes relative to the previous period are reported.

- **Intellectual property:**

We have begun to protect the corporate image of BNI and a number of brands associated to the Institute. This process has been efficiently led by Ms. J. Jiménez, our legal advisor. Brands that are currently in the process of protection include:

1. *Dendros*: a web-based interactive platform for education (brand and logo).
2. *BNI*: a Neuroscience research institute (brand and logo).
3. *El Escape de Kai*: an arcade-type video game with Neuroscience content (brand).
4. *Loligo*: an interactive space for audiovisual creativity to promote the value of scientific knowledge (brand and logo).
5. *Mentes Transformadoras:* a think-tank type platform to promote the value of scientific knowledge (brand and logo).

- **Congress Presentations:**

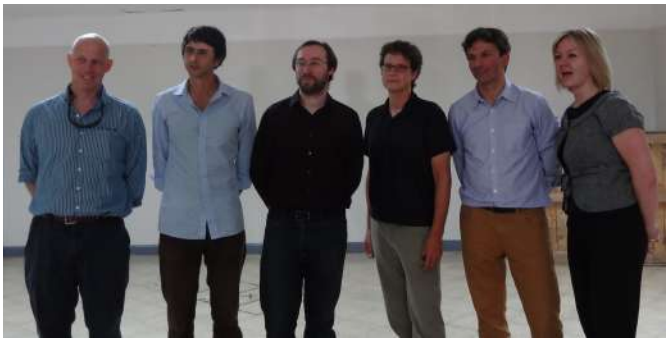
During this funding period BNI Associate Investigators and their teams attended, presented their work and organized numerous meetings and symposia. To evaluate them in the context of the corresponding research line they have been described in section 3a. ***See Summary Table.***

Summary Table

Type of presentation	National Events [Number]	International Events [Number]
A. Associate Researchers		
Conferences, oral communications, poster communications, others (specify)	58	50
Invited presentations (not included in above row)	-	2
B. Other researchers (Adjunct Researchers, Senior Researchers, Young Researchers, Postdoctoral Researchers and Students)		
Conferences, oral communications, poster communications, others (specify)	3	7
Invited presentations (not included in above row)	-	-

- **Organization of Scientific Events:**

We have continued our weekly Associate Investigator meetings to socialize research lines and translate BNI's cross-disciplinary atmosphere into concrete collaborative projects. We completed 26 formal meetings during the 2013 Academic Year. In these meetings we have provided the appropriate environment to sustain rich scientific discussions while allowing time to manage and steer the institute. These meetings have included scientific presentations by guest M. Hamuy, Director of the newly awarded Millenium Institute in Astrophysics, and Progress Report Presentations of BNI pilot projects by A. Couve, J. Egaña/P. Maldonado, L. Bustamante/H. Silva, A. Paula-Lima/E. Brunetti/C. Hidalgo, and J.M. Matamala/C. Hetz. Additionally, we have continued with our highly motivating and formative series of short 5 min internal seminars open to the entire institute dedicated to one particular research line. We have also invited a number of national and international speakers for regular seminars in the area of neuroscience including: System level reconstruction of brain development and function with light-sheet microscopy (P. Keller); KEOPS, el constructor originario (A. Glavic); Chile frente al desafío del envejecimiento (B. Kennedy); Señalización y plasticidad neuronal en condiciones normales y en ELA (B. van Zundert); Insight into chromatin remodeling machines: The mammalian ISWI homologue Snf2h mediates nucleosome dynamics and chromatin ultrastructure to govern gene expression, sensorimotor and cognitive control (M. Álvarez-Saavedra); Plasticidad homeostática mediada por óxido nítrico: relevancia en epileptogénesis (U. Wyneken); Extensión, educación y redes BNI (P. Cañón); El canal de protones: del sensor de potencial a la vía de conducción (C. González); Cellomics: Una plataforma de microscopía automatizada de alta de alta capacidad y complejidad (X. Chen); Balance excitatorio/inhibitorio y esquizofrenia: Desde las moléculas a las redes neuronales (E. Leiva); Ojo, cerebro y envejecimiento en Octodon degus (A. Palacios). We supported several larger scientific initiatives in Chile during this period. These activities provided a great opportunity to promote the research and aims of BNI within international speakers and a national audience. These included: the *BNI Summer Symposium* celebrating the book *Physical Biology of the Cell* (Jan 9, 2013, organized by A. Couve in collaboration with C. Torrealba, Fundación Ciencia & Vida, and including 3 authors of the book R. Phillips, H. García, J. Kondev) that gathered 100 attendants, mostly motivated students from BNI working in cross-disciplinary projects and the *BNI Summer Symposium Advanced Microscopy and Image Processing* (Jan 28, 2013, organized by M. Concha and S. Härtel) that provided continuity to a series of successful symposia and courses in the BNI strategic area of light microscopy.



Photograph: BNI Summer Symposium Physical Biology of the Cell.

In addition we organized the *BNI Symposium* at the Third CMM Pucón Symposium Advanced Tools Applied to Frontier Astronomy and other Massive Data-driven Sciences (Aug 20-23, organized by S. Härtel); the *BNI Symposium Calcium Signaling in Excitable Cells* at the XII Panamerican Association for Biochemistry and Molecular Biology Congress (Sept 9-14, 2013, organized by C. Hidalgo); the *BNI Symposium: Synaptic Plasticity* at the VIII Congreso Iberoamericano de Biofísica – IX Reunión Anual Sociedad Chilena de Neurociencia (Oct 1-4, 2013, organized by C. Hidalgo). The symposia organized by Dr. Hidalgo were presented at meetings that gathered a total of approximately 750 people. The *BNI Symposium: Papel de las Neurociencias en la Psiquiatría a del Siglo XXI* at the 2013 Sociedad de Neurología, Psiquiatría y Neurocirugía meeting (Oct 19, organized by H. Silva) that allowed BNI scientists to share their recent advances in

clinical research with a committed clinical audience. Clinical research is at the core of BNI's philosophy and this event was ideal to explore their advantages and applications in the context of the national community. The *BNI Workshop: Analysis of electrophysiological signals, Theoretical and practical approaches* (Oct 29-31, 2013, organized by P. Maldonado) with 50 participants.

- **Scientific Editorial Boards:**

BNI investigators continue to participate in editorial boards of general and specialized international journals covering Neuroscience and biomedical research. Currently BNI researchers are editors of *Frontiers in Synaptic Neuroscience* (**AC**, Review Editor), *Current Molecular Medicine* (**CHz**, Executive Editor), *Mechanisms of Development* (**MC**, Editor), *Open Behavioral Sciences Journal* (**MC**, Editor), *Neurotoxicity Research* (**MH**, Associated Editor), *Journal of Amino Acids* (**MH**, Associated Editor), J. *Pediatric and Neonatal Individualized Medicine* (**MH**, Editor), *Frontiers in Skeletal Muscle Physiology* (**CH**, Editor), *Biochemical and Biophysical Research Communications* (**CH**, Editor), *Developmental Neurobiology* (**MK**, Editor), *Frontiers in Integrative Neuroscience* (**PM**, Editor), *Frontiers in Neuroscience* (MH, Guest Editor), *The World Journal of Biological Psychiatry* (**HS**), *Official Journal of the World Federation of Societies of Biological Psychiatry* (**HS**), *Editorial Board of Asia-Pacific Psychiatry* (**HS**). BNI young investigator Pablo Gaspar is currently associated Editor in *Frontiers in Psychiatry*. Additionally BNI members are committed to raising the impact of *Biological Research*, an ISI indexed national journal (**CH** and **LL**, Editors).

- **Awards:**

BNI received multiple and exciting awards during 2013. The interactive platform *Dendros* received the first *Prize in National Innovation in Scientific Education* organized by Fundación Ciencia Joven and Fundación Telefónica. This recognition to the Institute's outreach effort immediately promoted a wide interest in our scientific communication activities and significantly motivated BNI students to increase their participation in the program.

Individual awards were also important during 2013. **LL** was promoted to Full Professor and received the FMed Medal of the U Chile. Likewise **SH** was awarded the Academic Excellency Award for highest impact publication at the FMed in his field during 2013. Of special importance, several BNI young investigators were awarded during 2013. A. Paula-Lima was invited by the Brazilian Academy of Sciences to participate in the 13th TWAS-ROLAC Young Scientists Conference. She also received the Junior Faculty Award at the 11th International Conference on Alzheimer's and Parkinson's Diseases (Florence, Italy), for her exceptional professional contribution to the study of Alzheimer's disease. P. Gaspar received the RedAmerica's Columbia University Career Development Award, as a Latin American leader in clinical research. Finally, T. Adasme received the Chilean Neuroscience Society Award and was invited to present her research at the Young Scientist Symposium at the Society's meeting and at the VIII Meeting of the Society of Latin American Biophysicists. *Photograph: BNI awardees P. Gaspar, A. Paula-Lima and T. Adasme.*

4. Education and Capacity Building

a) Education and capacity building:

BNI operates in the context of the institution (U Chile) that offers the largest and more diverse set of undergraduate and graduate programs in biomedical sciences, including Neuroscience in Chile. Therefore, its support of advanced training provides both leverage to larger institutional efforts as well as BNI-specific initiatives. The focus of education and capacity building at BNI is the training of competent and competitive scientists in the field of Neuroscience, a task only feasible within active laboratories. The facilities and support provided by BNI foster advanced scientific opportunities (research lines) for students (undergraduate, Ph.D., M.Sc. and professional/scientific careers) and postdoctoral researchers. Therefore, providing competitive laboratories and resources to carry out research in the forefront of their fields is a central manner of BNI to provide support for students.

Besides this general support, a specific budget is allocated to each Investigator ($5,450,000 each PI) to prioritize, among other items, support for students through full or partial stipends. A total of 52 students and postdocs received direct financial support from BNI, either as the sole source or as a complement existing fellowships from other sources. As in previous years, the quality of our students was guaranteed by the selection process at the FMed and other competitive programs offered by the U Chile.

A significant initiative started by BNI in 2011 and continued during this term is the postdoctoral program. Young scientists holding a Ph.D. degree are invited to apply to BNI *Bridge Fellowships* twice a year (fall and spring). Eligibility includes commitment to apply to a Fondecyt postdoctoral fellowship during the corresponding period. Applications are managed and reviewed by BNI scientists according to a protocol that emphasizes competitiveness and minimizes conflicts of interest. During 2013 BNI provided both full postdoctoral fellowships through *Bridge Fellowships* and contributed indirectly to support other postdoctoral researchers. The results of this program are summarized in a section below.

As an Institute, BNI encourages the interaction of students with more than one laboratory and mentor, as a manner to enrich the opportunities and cross-fertilize fields. Several Ph.D. thesis are being co-directed by BNI members, and many students share facilities, discussion opportunities, seminars and courses within BNI daily activities. These interactions are beginning to produce results in presentations or publications co-authored by 2 or 3 BNI investigators. Students, postdocs and young investigators participate as speakers in BNI's internal seminars on a regular basis and when they are not presenting they constitute an active audience. During this period they engaged in many scientific discussions in the 26 BNI-sponsored events or meetings carried out during 2013. These include events such as the Basic-Clinical Encounters and BNI Summer Symposia (celebration of the book Physical Biology of the Cell; BNI Summer Symposium Advanced Microscopy and Image Processing).

In addition to the scientific training in the lab and scientific discussions, all BNI Associate Investigators continue to hold full time faculty positions at the FMed and Clinical Hospital of the U Chile. From these positions they lead or participate in regular teaching activities in graduate and/or clinical training (medical residency) programs, as well as basic science for medical and allied health profession students. All courses mentioned as examples in the previous report are offered on a regular basis and therefore are reported now too. Additionally, BNI Investigators are actively involved in the scientific education of professional (medical) students in research rotations.

b) Achievements and results:

A grand total of 119 students (undergraduate though postdoctoral) were associated to BNI during 2013. Until now approximately 10 trainees have left the institute and continued careers paths in Chile or abroad. The great majority of BNI publications are co-authored by students. Student presentations in national and international meetings also represent the majority of authorships. 7 students or junior researchers associated to BNI conducted short-term traineeships abroad. As stated above, during this period BNI continued its program of postdoctoral position awards, aimed at recruiting young investigators able to apply to external funding. In the 2013 version of this system 7 postdoctoral investigators were supported (C. Duran, R. Lagos, P. Mardones, R. Rivera, I. Signore, P. Garcia, A. Izquierdo) with a total of 8 fellowships. BNI's support of students has allowed the completion of projects and smoothed transitions, besides supporting students in programs not receiving additional fellowship support. Direct support, as full stipends or complements, was awarded to 38 students. In total the activity of 15 undergraduate, 25 Masters and 57 Ph.D. students and 22 postdoctoral researchers is funded through different mechanisms at BNI.

For detailed numbers of graduate and undergraduate theses and statistics for students working within the institute ***see Annexes 5.1 y 5.2.*** For description of prizes see *page 18,* ***Awards***.

c) Destination of Students:

According to the scope of BNI, most of our students aim to pursue scientific and academic careers. Thus, most of our recent PhD graduates are conducting research as postdoctoral students in Chile or abroad. Master and undergraduate students are following advanced studies or directly involved in research. "Other" outcomes comprise clinical work, as expected from the initial training of part of our students and our context within the FMed. 7 students trained at BNI in the latest term are currently active in research, 3 are pursuing advanced studies and 3 are conducting clinical work.

Summary Table*:*

Obtained Degree	Academy	Industry and Services	Studies	Research	Other (Specify the other type of activity
Doctoral			1	6	
Master			1	1	2
Undergraduate			1		1
TOTAL			3	7	3

5. Networking and other Collaborative Work

a) Networking:

Network 1. *International Workshop: In-vivo 3D imaging approaches to study cell behaviour in developing embryos. International Symposium Advanced Microscopy and Image Processing in Neurobiology II, and Summer School Computational Biomedicine.*

During 2013, we enhanced our international association within leading experts in microscopic imaging, neuroscience, and developmental biology. In January 2013 BNI organized and supported three events:

(i) the *International Course Optics, Forces, and Development: In-vivo 3D Imaging Approaches to Study Cell Behavior in Developing Embryos*
(www.scian.cl/portal/globals.php?COD_SECCION=2960&OPCODE=00100&CS=3169) (organized by **SH/MC**), with 12 selected students from 6 Latin American countries and 16 lectures from Chile, Germany, and Austria. The 2-week practical/theoretical course combined optics and microscopic techniques for in vivo 3D visualization and analysis of cell and tissue dynamics.

(ii) The *International Symposium Advanced Microscopy and Image Processing*
(www.scian.cl/portal/globals.php?COD_SECCION=2960&OPCODE=00100&CS=3173) with topics from super-resolution fluorescense microscopy, strategies for the analysis of cell dynamics, carbon nanotubes and protein dynamics, structure of the stem cell cytoskeleton, *in vivo* collective cell migration, cell and tissue mechanics, and mechanosensing with primary cilia. The symposium was open to a broad audience of students and researchers.

(iii) The *Summer School Computational Bio-Medicine*
(www.scian.cl/portal/globals.php?COD_SECCION=2960&OPCODE=00100&CS=3170), which combined topics from mathematical modeling in biology, systems biology, computational medicine, and fundamentals and applications of signal processing in biomedicine with lecturers from Chile and Germany (Heidelberg).

The consolidated network catalyzed student exchanges between the participating laboratories during 2013, and follow up invitations to national and international courses and symposia on related topics such as *Microbial World Through Different Eyes,* ICGEB, Montevideo (UY) (www.icgeb.org/meetings-2013.html) and the *IBRO College 2013 Dynamic Imaging in Neuroscience* Valdivia (Chile) (www.cecs.cl/ibrocollege). The consolidated bonds not only enhanced visits of students and PIs among the institutions, but also contributed to securing new funds for the installation of novel microscopic techniques such as SOFI-imaging (consolidated 2013), whole slide tissue-imaging (www.microscopiavirtual.cl), and light-sheet imaging through a FONDEQUIP grant (**MC/SH** in collaboration with U. Kubitscheck, U-Bonn, Ger). In combination with a novel project U-Redes BioMed-HPC (www.scian.cl/portal/globals.php?COD_SECCION=2960&OPCODE=00100&CS=3204) for the installation of a 10 Gbps network between the FMed, REUNA, and the National Laboratory for High Performance Computing (www.nlhpc.cl), we have set an important milestone to propel BNI imaging and data analyses capacities towards new dimensions in size, speed, and connectivity to the scientific community. *Photograph: International Network on Advanced Microscopy and Image Processing in Neurobiology.*

Network 2. *NeuroSur: Neuroscience in the Southern Cone*

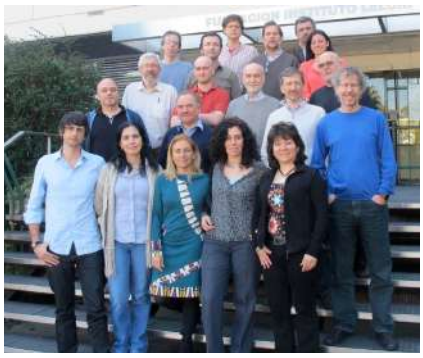
NeuroSur is a collaborative network between BNI and centers of excellence in biomedical neuroscience working in the American Southern Cone (Chile, Argentina, Uruguay, Brazil) involving established senior investigators, young scientific leaders, postdocs and students. The goal of *NeuroSur* is to create a first class and highly synergistic scientific hub addressing relevant biomedical problems in the region to achieve global impact. The strategies to achieve this goal include (i) identifying common research objectives, complementary methodological approaches, up to date techniques, protocols, molecular and biological tools, as well as state of the art equipment, to support a regional (South America) framework of excellence for scientific development and exchange of expertise, and (ii) contribute to improve success rates in competitions for international funds, which will in turn support and promote science in the region.

We have organized two *NeuroSur* meetings. A first meeting (*NeuroSur-I*) took place in Montevideo, Uruguay, between August 1-3, 2012, jointly organized by Pasteur Institute-Montevideo and BNI. A second meeting (*NeuroSur-II*) took place in Buenos Aires, Argentina, between August 28-30, 2013, jointly organized by investigators of Instituto Leloir and BNI. This version gave continuity to collaborations generated in *NeuroSur-I* and continued to promote the interaction between BNI and centers of excellence within South American countries. The 2013 program included scientific presentations of researchers from Chile (BNI), Argentina (Instituto Leloir, Pontificia Universidad Católica Argentina, INGEBI and Instituto de Investigación Médica Mercedes y Martín Ferreyra) and Uruguay (Institute Pasteur-Montevideo, Centro Universitario Paysandú and Instituto Clemente Estable). In addition, a number of topics were discussed in a round table, including (i) the future of *NeuroSur*, (ii) regional scientific and granting policies, and (iii) strategies to increase competitiveness and impact through international macro-initiatives. Finally, the meeting included a visit to the laboratories and facilities of the Instituto Leloir and the Biomedicine Institute of Buenos Aires (CONICET-Argentina-Max Planck Institute-Germany).

As a result of *NeuroSur-I and II*, a collaboration between the laboratories of **AC** (BNI) and A. Cáceres (Instituto de Investigación Médica, Córdoba, Argentina; participant of NeuroSur-I and II) has been established on non-conventional neuronal trafficking and a joint manuscript is currently under preparation. Additionally four BNI students participated in a microscopy course organized by A. Cáceres. **SH** (BNI) established a new collaboration with G. Folle (*NeuroSur-II* participant) and a manuscript has been recently submitted for publication (*Bleomycin-induced yH2AX foci map preferentially to replication domains in CHO9 interphase nuclei, P.Lidde, L Laffon-Hughes, MV Di Tomaso, AL Reyes-Abalos, J Jara, M Cerda, S Hartel and G. Folle*). Moreover, two young BNI investigators from S. Hartel's lab completed a research visit to Montevideo co-financed by the Pasteur Institute. Additionally, collaboration with the Pasteur Institute and Clemente Estable Institute included reciprocal visits of academics and students with the lab of **MH** (BNI). L. Barbeito (Pasteur Institute) visited the lab of **MH** on September 2013, discussing further collaborations, and giving a conference in the framework of the IV Diploma on Neuropsychopharmacology (MEDICHI, BNI, Programme of Molecular & Clinical Pharmacology, ICBM), entitled "*Neuron/glia interaction: pathophysiological and therapeutic implications*". Within the same framework, F. Dajas and C. Scorza (Clemente Estable Institute, Uruguay), visited BNI labs, giving two conferences ("*Neuroprotection against neurovascular, hypoxia and neurodegenerative insults*" and "*Reward systems and drug abuse*"), on November and December 2013. These visits were opportunities for tightening already established collaborations, and for organizing the "*Third Latin-American School of Neurochemistry*", supported by the International Society of Neurochemistry, to take place in Montevideo, November 24-December 4, 2014. Finally, together with investigators from the CONICET-Argentina-Max Planck Institute led by E. Arzt, a collaborative network has been

discussed for addressing the issue of monoaminergic modulation of hippocampal neurochemistry and cell proliferation.

NeuroSur has consolidated as a valuable association between BNI and centers of excellence of the region, including Argentina, Uruguay and Brazil. The success of the initiative is further demonstrated by the fact that we have secured a date and a place for *NeuroSur-III*, which will take place in Rio de Janeiro, Brazil, co-hosted by W. Savino (Fundación Oswaldo Cruz) and S. Ferreira (Instituto Nacional de Neurociencia Translacional, Rio de Janeiro). (***see Annex 6 for details***). *Photograph: NeuroSur-II, Buenos Aires*



b) Other collaborative activities:

Strong collaborative initiatives not included as formal BNI networks have continued to be promoted by BNI scientists. They have provided additional support for exchange of students, postdocs and expertise with laboratories of Chile, Latin America, the U.S. and Europe. Although they have not changed significantly from previous periods we highlight collaborations in the framework of the following funds: Other MSI Centers (F. Aboitiz), FONDAP-CEMC (A. Quest, S. Lavandero), PBCT-Research-Rings (F. Court, A. Maas, C. Best, C.P. Heisenberg, G. Randall), U-Redes (E. Vera, N. Hitschfeld-Kahler), NIH (S. Moss), European Union (S. Wilson), the Harold Leila Mathers Foundation (L Glimcher), FONDEF (J. Velásquez), FONDECYT (P. Morales, F. Bronfman, L. Bagatolli, R. Kaufman, T. Blanpied, A. Cáceres, C.P. Heisenberg), CONICYT-USA (V. Budnik, R. Brown), and others (M. Castro, J. Enderlein, V. Torres). Network initiatives have been set between BNI associated centers and research Institutions in Latin America and Europe. An agreement with the International Institute of Neuroscience of Natal (Brazil) exists since 2007, including a program of faculty/student exchange. Networks are also established with the Central Institute of Mental Health J5, Mannheim, Germany, and Karolinska Institutet, Stockholm, Sweden. BNI students have participated in short-term research and traineeship periods as indicated in the advances each of the RLs. Furthermore, BNI has received an increasing number of international students in internship and exchange programs, or through their enrollment in graduate programs at U Chile. Together these collaborations consolidate BNI as an international centre of scientific excellence by promoting synergy in partnership.

6. Outreach and Connections with other Sectors

a) Outreach:

During 2013 we have generated a variety of activities to consolidate the outreach platform of BNI, according to our main goals of (i) increasing the visibility of the institute and (ii) bringing science closer to the community. In order to increase the institute's visibility we have generated a corporate video explaining the structure, vision and strategy of BNI in 5 minutes. The video explains simply and accurately the internal organization of the institute, the principal research lines and other areas of development (training, outreach and networking). This video has been extremely useful when presenting BNI at scientific meetings, outreach activities and networks, and is exhibited permanently on our website. We have additionally upgraded our website in order to increase the scientific content and include new sections to improve the search for user information.

During 2013 we officially inaugurated the institute. We invited M. Nicolelis (Duke University, USA) as a keynote speaker, who gave the talk "*Science as an agent of Social Transformation*". M. Nicolelis is an established researcher in the field of Neuroscience and is playing an increasingly important role in promoting social and educational development in Brazil and the U.S. The event gathered 500 guests, including university professors, university officials, researchers, graduate, undergraduate and high-school students, journalists and members of the general public. We recorded this ceremony and used it to generate an additional video promoting the institute in the social networks (Facebook, Twitter). The event was highly covered by the written press (El Mercurio, La Cuarta, La Hora) and TV (Canal 13). *Photograph: Official inauguration of BNI*

Regarding our second aim of bringing science closer to the community, during 2013 we continued having strong media coverage with 96 publications in written press, digital media and TV (***See Annex 7.3***). We also produced the 5th chapter of the second season of the TV series "*Vida Conciencia*" called "*Neuronal Connectivity*". To make the chapter more accessible to the non-specialized viewer we invited V. Ruiz, a Mexican marathon runner diagnosed with Huntington's disease, who runs around world to promote the importance of investing in clinical research related to degenerative disease, who participated along BNI researchers. This series aired on CNN-Chile during December and our chapter had a rating of 1.40 points on average, which means an audience of about 90,000 viewers, constituting the second most viewed chapter of the series. *Photograph: C. Hetz, V. Ruiz, R. Vidal, and C. Molina the leading team in Huntington's disease research at BNI.*

Additionally, we built important alliances with public organizations (Ilustre Municipalidad de Recoleta, Centro Cultural Palacio La Moneda, Programa EXPLORA-CONICYT Coordinación Norte and Consejo del Futuro de Senado de Chile). Through them we have continued to promote and motivate the curiosity for knowledge, especially in young students in a series of high-impact activities.

We created an interactive installation that includes multiple devices that progressively lead users from gaming to learning. First we recycled a pinball machine with the graphics and characters of our comic *Dendros*, purely with motivational purposes. Second, we developed a videogame based on

the comic *Dendros*, *"El escape de Kai"*, in recycled arcade machines where users need to acquire knowledge of the function of different regions of the brain (movement, visual activity and coordination) to win. Third, we created a 3D multi-touch brain app to relate different areas of the brain with specific functions, with educational purposes. Finally, we created a dark room containing touch-screen computers with the *Dendros* comic, where users read a story with strong Neuroscience content and use their knowledge to solve brain riddles. The installation included the graphic design and illumination of different rooms in accordance with the esthetics of *Dendros*. We launched a preliminary version of the installation at the "Ilustre Municipalidad de Recoleta", where we placed the material inside a dome and exhibited it for approximately one week, receiving approximately 700 people, mostly families and children. The success of the activity resulted in an invitation to exhibit the installation at the "Art, Technology and Innovation Room" of the "Centro Cultural Palacio La Moneda", a high-quality and high-impact showroom. The installation was a total success, with more than 10,000 visitors in 3 months. It also allowed us to organize guided visits for high-school students, led by BNI students and PIs (**AC, PM**) who gave talks during their visits ("Biology, memory and oblivion" and "Myths and Facts about the Brain"). The initiative received strong media coverage. Importantly, the interactive platform was awarded the *Innovation Prize for Science Education*, award given by "Fundación Ciencia Joven" and "Fundación Telefónica". *Photograph: BNI team receiving the award at Telefónica.*

Additionally, multiple outreach lectures were given to different audiences, such as school students, undergraduate students and medical professionals. Some highlights included: "*Diálogos con la Ciencia*", "*2º Congreso del Futuro*" (ex National Congress building in Santiago), and "*2nd Simposium of Interactive Science Animation*" (Universidad Católica de La Santísima Concepción, Concepción). Finally, other activities were directed towards the medical community, a key target audience of our program. We organized two "*Clinical Encounters*" to discuss how neurological conditions may be approached through fundamental research, and how research can be improved by clinical results and evidence. International researchers C. Zuker (University of Columbia, USA), O. Boespflug (Robert Debré Hospital, France), and E. de Cristofaro (University College London, UK) participated in these events that gathered more than 200 guests. Together our outreach activities continue to consolidate BNI as a resource center for specialized clinical practitioners, educational science programs and the general public.

b) Connections with other sectors:

We have established relevant alliances with private and public institutions such as Ilustre Municipalidad de Recoleta, Centro Cultural Palacio La Moneda, Programa EXPLORA-CONICYT Coordinación Norte and Consejo del Futuro de Senado de Chile. We have obtained additional funds and support from these organizations to produce and implement the interactive installation *Dendros* with multiple gaming and learning devices. Their valuable contribution has been direct or indirect (Programa EXPLORA-CONICYT Coordinación Norte $2,500,000 CHP to build the installation at La Moneda. Ilustre Municipalidad de Recoleta $2,000,000 CHP non-pecuniary to host the exhibition. Centro Cultural Palacio La Moneda $6,000,000 CHP non-pecuniary to host the exhibition) and the results of the interactions has been positively evaluated in multiple press appearances.

7. Administration and Financial Status

a) Organization and administration:

During 2013 BNI operated as a non-profit organization (RUT 65.059.721-4) and has fulfilled all the legal requirements of the Ministry of Justice and the Municipalidad de Independencia. 4 meetings of the Directory Board were held during 2013. The Directory Board is currently constituted by A. Couve (President), C. Hetz (Vicepresident), M. Concha (Secretary), M. Kukuljan (Tresurer), C. Hidalgo (Director), C. Sepúlveda, Dean of the FMed (Director), L. Michea, Director of Research and Development FMed (Director). P. Cañón, Ph.D. has excelled in her role as Executive Director by managing the institute, coordinating numerous internal and external activities, leading the outreach program, linking the institute to the FMed, communicating with the clinical community and, importantly, establishing numerous contacts with the private sector. The Executive Office is additionally constituted by A. Sanguinetti, a reporter whose work focuses on web, social networks and press activities to connect with the public and high-school students in particular, J. Jiménez, a law student who provides legal assistance, and R. Tapia, BNI's artist in residence who has acquired increasing responsibilities and established our successful outreach program *Dendros* as a national reference in scientific communication and impact. The Grant Management Office is currently constituted by A. Timmermann, who has extensive expertise in accounts managing and Millenium funds, S. Carrasco and K. Miranda assistant accountants, and J. Mansilla, informatics expert. Mrs. Timmerman monthly financial reports to the Ministerio de Economía have been spotless. A graphic design team led by N. Vasquez and a team of journalists led by I. Llambías have continued contributing to consolidate BNI's corporate image and promote its scientific and outreach activities. *Photograph: Executive and Grant Management Offices of BNI.*

Category	Female	Male	TOTAL
Assistant & Technicians	34	24	58
Administrative Staff	6	2	8
TOTAL	40	26	66

b) *Financial Status:*

See Annexes 9.1-9.3

8. Annexes

Annex 1.- Institute Researchers

1.1 Associate Researchers

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliaton	Current Position	Relation With Center
Couve Correa, Andres	1, 2, 3, 4, 7, 8	Chilean	M	23-10-68	Biologist	D	University of Chile	Associate Professor	1
Hetz Flores, Claudio	1, 4, 6, 8	Chilean	M	24-03-76	Biotechnology Engineering	D	University of Chile	Full Professor	2
Concha Nordemann, Miguel	1, 2, 3, 7, 8	Chilean	M	06-03-66	Medicine	D	University of Chile	Full Professor	2
Härtel Gündel, Steffen	1, 3, 5, 6, 7	Germany	M	24-11-68	Physical	D	University of Chile	Assistant Professor	2
Herrera-Marschitz, Mario	1, 3, 6, 8	Chilean	M	25-06-44	Medicine	D	University of Chile	Full Professor	2
Hidalgo Tapia, Cecilia	4 ,6	Chilean	F	10-06-41	Biochemist	D	University of Chile	Full Professor	2
Kukuljan Padilla, Manuel	2, 3, 7, 8	Chilean	M	08-08-63	Medicine	D	University of Chile	Full Professor	2
Leyton Campos, Lisette	1, 3, 6	Chilean Swiss	F	22-07-59	Biochemist	D	University of Chile	Associate Professor	2
Maldonado Arbogast, Pedro	5, 7	Chilean	M	30-04-60	Biologist	D	University of Chile	Associate Professor	2
Sierralta Jara, Jimena	2, 3, 7	Chilean	F	12-09-62	Biochemist	D	University of Chile	Associate Professor	2
Silva Ibarra, Hernan	5, 7, 8	Chilean	M	01-07-49	Physician	D	University of Chile	Full Professor	2

1.2 Young Researchers

Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Bustamante Cadiz, Diego	6	Chilean	M	11-03-52	Biochemist	M	University of Chile	Associate Professor	2
Egaña Tomic, Jose Ignacio	5,7	Chilean	M	09-10-73	Medicine	D	University of Chile	Assistant Professor	2
Gebicke-Haerter, Peter	6	German	M	26-04-47	Biologist	D	Mannheim, DE	Professor	2
Morales Retamales, Paola	6	Chilean	F	18-11-66	Biologist	D	University of Chile	Associate Professor	2
Paula-Lima, Andrea	4, 6	Brazilian	F	20-11-77	Pharmaceutics	D	University of Chile	Assistant Professor	2
Sánchez, Gina	4, 6	Chilean	F	11-12-54	Biochemist	D	University of Chile	Assistant Professor	2

1.3 Senior Researchers

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Yedy Israel Jacard	6	Chilean	M	19-04-39	Biochemist	D	University of Chile	Full Professor	2

1.4 Others

Full Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliaton	Current Position	Relation With Center
Hitschfeld Kahler, Nancy	7	Chilean	F	24-03-76	Science Computer	D	University of Chile	Associate Professor	2
Ocampo Garces, Adrian	4, 5	Chilean	M	21-10-65	Medicine	D	University of Chile	Assistant Professor	2
Ortega Palma, Jaime	7	Chilean	M	16-10-67	Mathematic	D	University of Chile	Associate Professor	2
Valdes Guerrero, Jose Luis	4	Chilean	M	16-12-75	Biologist	D	University of Chile	Assistant Professor	2

NOMENCLATURE:
[Gender]
[M] Male [F] Female

[Academic Degree]
[U] Undergraduate [M] Master [D] Doctoral

[Relation with Center]
[1] Full time [2] Part time

Annex 2.- Research Lines

Nº	Line Research	Objective	Description	Researcher	Discipline	Starting Date	Ending Date
1	Sub-cellular functional dynamics	To understand how the dynamic structures of the secretory pathway and the cytoskeleton are organized in different cell types of the nervous system, and how this organization determines neuronal function or dysfunction.	We have developed methodologies to analyze subcellular components in cultured neurons and astrocytes at high spatio-temporal resolution using fluorescent microscopy and investigated neuropathological conditions where organelle and cytoskeletal functions are dramatically affected. Here we combine manipulation of gene expression in cultured brain cells with the use of genetically modified organisms to study: (i) the morpho-functional organization of the endoplasmic reticulum and the consequences of altered organelle structure in protein trafficking and in human disease (XBP-1/ATF4 deficiency); (ii) the role of recently identified proteins (Marlin1) in the functional and structural organization of the cytoskeleton; (iii) the spatio-temporal activation of signaling molecules downstream of cell adhesion receptors governing changes in astrocyte and neuron morphology during neurodegeneration and injury. This strategy provides a quantitative view of the dynamics of sub-cellular structures and their implications in normal and disease conditions.	Miguel Concha, Andrés Couve, Steffen Härtel, Mario Herrera-Marschitz, Claudio Hetz, Lisette Leyton	6, 25, 59, 61, 63, 65, 143	28-06-11	
2	Cellular identity and morphology	To understand how gene expression determines morpho-functional features throughout the development and the lifespan of neurons.	We have combined fluorescent microscopy and expression in Drosophila, mice, and zebrafish to address the genetic mechanisms involved in the control of neuronal morphology. Here we combine these experimental models with electrophysiology and tools to quantify morpho-topological features of cells and neuronal networks to study the role of: (i) transcriptional control by chromatin remodeling complexes in the acquisition and maintenance of neuronal morphology (REST/NRSF and CoREST) and (ii) novel genes identified by ongoing genetic screens in Drosophila and zebrafish and candidate molecules involved in cytoskeleton dynamics in neuronal morpho-functionality (Marlin1).	Miguel Concha, Andrés Couve, Manuel Kukuljan, Jimena Sierralta	61, 63, 65	28-06-11	
3	Supra-cellular development and circuits	To understand how gene activity is translated into brain morphogenesis, and how the acquisition of novel states of supra-cellular and connectional organization in turn influences patterning and brain function.	Here we combine the use of genetic approaches in GFP-transgenic zebrafish and in hippocampal organotypic cultures with in vivo 3D confocal visualization and analysis of neuronal structure and function to study: (i) the cellular mechanisms that control adhesive, tensile and polarity changes leading to cell migration, formation of cell sheets and brain nuclei, and wound healing, (ii) the genetic and morphogenetic mechanisms that guide axonal growth cones and establish neuronal connectivity in vivo, focused on Wnt/PCP, FGF, Chemokines and Robo/Slit, and neurogenesis in hippocampal circuits, and (iii) the dynamic configuration and functional correlate of neuronal circuits using optogenetic probes and in vivo electrophysiology. This strategy provides a contextual view of the mechanisms that drive form, supra-cellular structure and neuronal circuit development, revealing general principles of brain organogenesis and function.	Miguel Concha, Andrés Couve, Steffen Härtel, Mario Herrera-Marschitz, Manuel Kukuljan, Lisette Leyton, Jimena Sierralta	6, 25, 59, 61, 63, 65, 67, 72, 110, 143	28-06-11	
4	Plasticity and behavior	To understand how genetic interactions and signaling pathways control long-lasting memories.	We have established methodologies to study the role of ryanodine-receptor (RyR) dependent Ca2+ signals on hippocampal long-term potentiation (LTP) and behavior (mazes, object recognition and contextual fear conditioning). By combining these approaches with cell and molecular biology, live-cell imaging and electrophysiology (single channel studies in bilayers, high density electrophysiology in freely moving animals) here we investigate: (i) the effect of RyR activity on the expression of plasticity-related mRNA/proteins and the role of RyR-generated Ca2+ signals on LTP (via pharmacology, intra-hippocampal delivery of antisense nucleotides or shRNAs), (ii) the effect of experience, neuromodulators, and modulators of RyRs on the dynamics of hippocampal neural assembles, and (iii) their behavioral correlates.	Andrés Couve, Claudio Hetz, Cecilia Hidalgo	61, 65, 73	28-06-11	

Nº	Line Research	Objective	Description	Researcher	Discipline	Starting Date	Ending Date
5	Systems Neuroscience	To examine, compare and model the neuronal activity when animals and humans engage in more ecological behavioral experimental paradigms and classical psychiatric conditions.	While most paradigms to examine the neuronal mechanisms of cognitive functions have used simple and controlled stimuli, the responses of neurons to complex and more ecological situations differ substantially. Because current models of functional organization fail significantly to predict neuronal activity during more realistic experimental conditions here we implement methodologies to study neuronal activity using single and multiple unit recordings, local field potentials, and electroencephalographic recordings under: (i) goal directed or (ii) naturalistic behaviors. We develop new analytical/statistical tools in signal processing and propose new models to account for the inclusion of top-down mechanisms in cognitive function.	Steffen Härtel, Pedro Maldonado, Hernán Silva	6, 25, 59, 73, 120, 143	28-06-11	
6	Neural dysfunction and pharmacologic al targets	To develop knowledge, expertise and technological approaches to gain a better understanding of the mechanisms by which disease-related genes affect common molecular, cellular and physiological processes involved in neuropathological conditions.	We implement disease models to mimic conditions associated with human pathologies, including transgenic mice, gene therapy, and cell biology approaches, in addition to human studies, to uncover pathological aspects underlying (i) Parkinson's disease, (ii) Alzheimer's disease, (iii) nerve injury/regeneration and Amyotrophyc lateral sclerosis (ALS), (iv) Creutzfeldt-Jacob Disease (CJD), and (v) epigenetics by characterizing the short and long-term effects of metabolic insults occurring at birth. We define the consequences of genetic manipulation of the disease model and identify novel targets for pharmacological interventions. Scientific aims benefit from new analytical mathematical approaches to model complex features related to neural dysfunction.	Steffen Härtel, Mario Herrera-Marschitz, Claudio Hetz, Lisette Leyton, Cecilia Hidalgo	65, 6, 25, 59, 143, 67, 72, 110, 61, 73	28-06-11	
7	Applied mathematics and biomedical informatics	To uncover novel neural processes based on mathematical models that reveal morpho-functional principles of organization at multiple scales.	Biophysics and applied mathematics combined with advanced imaging and computing clusters foster an integrative view to study the dynamic design of biological structures and their functional patterns, which emerge from the building process per se and/or as a requirement of functions at higher levels. This transdisciplinary approach allows the study of pattern organization in neurons in 2/3D and colocalization in confined sub-cellular compartments and fosters new approaches to: (i) localize/track proteins within sub-cellular organelles, (ii) study dendrite branching and axonal wiring, (iii) model cellular and supra-cellular descriptors for multi-cellular rosette formation based on partial differential equations, (iv) develop statistics to study spike trains in multiunit recordings, (v) model neuronal assembles to account for activity during natural behavior, and (vi) implement mathematical tools for image based tele-analysis within clinical research and diagnostic medicine.	Miguel Concha, Andrés Couve, Steffen Härtel, Manuel Kukuljan, Pedro Maldonado, Jimena Sierralta, Hernán Silva	6, 25, 59, 61, 56, 67, 73, 143	28-06-11	
8	Clinical research	To build the capacity and consolidate clinical research in the fields of neurological and psychiatric pathologies.	Here we provide the means to solve the lack of efficient channels of interaction between clinicians and the scientific management structures and the scarce access to state-of-the art technologies by establishing a program focused on the training of clinical scientists and specialists with international standards of competence, and by defining specific projects that include: (i) development of diagnostics tools such as chaperones for molecular markers in Creutzfeldt-Jacob Disease (CJD) and genetic/molecular markers for early prediction of anti-depressive treatments, (ii) therapeutic approaches such as gene therapy and small molecule testing in Amyotrophyc lateral sclerosis (ALS) and Parkinson's, (iii) genetic comparison of patients with bipolar disorders, and (iv) autism spectrum disorders and alterations of neural development.	Miguel Concha, Andrés Couve, Mario Herrera-Marschitz, Claudio Hetz, Manuel Kukuljan, Hernán Silva	61, 63, 65, 67, 72, 110, 120	28-06-11	

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

3.1.- ISI Publications or Similar to ISI Standard

3.1.1 Associate Researchers:

Lazo OM, Gonzalez A, Ascaño M, Kuruvilla R, **Couve A**, Bronfman FC (2013). BDNF regulates Rab11-mediated recycling endosome dynamics to induce dendritic branching. J Neurosci. 33(14):6112-22.

Hetz, C. (2013) The biological meaning of the UPR. Nature Rev Mol Cell Biol. 14(7):404.

Hetz C, Chevet E, Harding H (2013). Targeting the unfolded protein response in disease. Nature Rev Drug Discovery 12:703-719.

Medinas DB, **Hetz C** (2013). Proteostasis impairment: A molecular intersection between Alzheimer´s disease and diabetes. Cell Metabolism. In press. Editorial comment. 3;18(6):771-2.

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3.1.2 Other researchers:

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Paula-Lima, AC, Brito-Moreira J, Ferreira ST (2013). Dysregulation of glutamatergic neurotransmission in Alzheimer's disease. Review. The Journal of Neurochemistry. 126:191–202.

3.2.- SCIELO Publications or Similar to SCIELO

3.3.- Scientific Books and Chapters

*3.3.1 **Associate Researchers**:*

Leyton L, J Hagood (2013). Thy-1 modulates neurological cell-cell and cell-matrix interactions through multiple molecular interactions in Cell Adhesion Molecules: Implications in Neurological Diseases. Springer, Germany.

*3.3.2 **Other researchers***

3.4.- Other Publications

*3.4.1 **Associate Researchers**:*

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3.5.- Collaborative publications:

Category of Publication	1 researcher		2 researchers		3 researchers		4 or more researchers	
	Nº	**%**	**Nº**	**%**	**Nº**	**%**	**Nº**	**%**
ISI Publications or Similar to ISI Standard	35	86	3	8				
SCIELO Publications or Similar to SCIELO Standard								
Books and chapters	1	2						
Other Publications	1	2	1	2				
Total of publications	37	90	4	10				

Annex 4.- Organization of Scientific Events

Scope	Title	Type of Event	City	Country	Responsible Researcher
National	BNI Internal Seminar: Plasticity and behavior	Seminar	Santiago	Chile	P Maldonado
	BNI Internal Seminar: Extensión, educación y redes	Seminar	Santiago	Chile	A Couve
	BNI Internal Seminar: Cellomics: Una plataforma de microscopía automatizada de alta de alta capacidad y complejidad	Seminar	Santiago	Chile	C Hetz
	BNI Internal Seminar: Systems neuroscience	Seminar	Santiago	Chile	H Silva, P Maldonado
	BNI Internal Seminar: Neuronal Plasticity	Seminar	Santiago	Chile	M Herrera-Marschitz, C Hidalgo, H Silva
	BNI Open Seminar: KEOPS, El constructor originario	Seminar	Santiago	Chile	A Couve
	BNI Open Seminar: Señalización y plasticidad neuronal en condiciones normales y en ELA	Seminar	Santiago	Chile	C Hetz
	BNI Open Seminar: Insight into chromatin remodeling machines: The mammalian ISWI homologue Snf2h mediates nucleosome dynamics and chromatin ultrastructure to govern gene expression, sensorimotor and cognitive control	Seminar	Santiago	Chile	A Couve
	BNI Open Seminar: Plasticidad homeostática mediada por óxido nítrico: relevancia en epileptogénesis	Seminar	Santiago	Chile	J Sierralta
	BNI Open Seminar: El canal de protones: del sensor de potencial a la vía de conducción	Seminar	Santiago	Chile	J Sierralta
	BNI Open Seminar: Ojo, cerebro y envejecimiento en Octodon degus	Seminar	Santiago	Chile	J Sierralta
	BNI Open Seminar: System level reconstruction of brain development and function with light-sheet microscopy	Conference	Santiago	Chile	M Concha
	BNI Open Seminar: Chile frente al desafío del envejecimiento	Conference	Santiago	Chile	A Couve
	BNI Open Seminar: Balance excitatorio/inhibitorio y esquizofrenia: Desde las moléculas a las redes neuronales	Seminar	Santiago	Chile	H Silva
International	BNI Summer Symposia: Advanced Microscopy and Image Processing	Seminar	Santiago	Chile	S Härtel, M Concha
	BNI Summer Symposia: Physical Biology of the Cell	Seminar	Santiago	Chile	S Härtel, A Couve
	BNI Workshop: Analysis of electrophysiological signals, Theoretical and practical approaches	Workshop	San Pedro de Atacama	Chile	P Maldonado
	BNI Symposium: SYNAPTIC PLASTICITY. VIII Congreso Iberoamericano de Biofisica – IX Reunión Anual Sociedad Chilena de Neurociencia	Symposium	Valparaíso	Chile	C Hidalgo
	BNI Symposium: XII PABMB Congress, Calcium Signaling in Excitable Cells	Symposium	Puerto Varas	Chile	C Hidalgo
	BNI Symposium: Third CMM Pucón Symposium 2013: Advanced Tools Applied to Frontier Astronomy and other Massive Data-driven Sciences	Workshop	Pucón	Chile	S Härtel
	BNI Symposium: LXVIII Congreso Anual de Sonepsyn	Symposium	Valparaíso	Chile	A Couve

Annex 5.- Education and capacity building

5.1 Capacity Building inside BNI

BNI RESEARCHER	NUMBER												TOTAL NUMBER PER BNI RESEARCHER		
	Undergraduate students			Graduate student						Post Doctoral					
				Master			Doctoral								
	F	M	**T**	F	M	**T**	F	M	**T**	F	M	**T**	F	M	**T**
M Concha	2	1	3	2	1	3	3	6	9	1	2	3	8	10	18
S Härtel		1	1	2	1	3	2	2	4		3	3	4	7	11
L Leyton, A Quest							2	3	5				2	3	5
C Hetz	3	2	5	1	2	3	3	3	6	5	4	9	12	11	23
A Couve				1		1	3	3	6				4	3	7
P Maldonado		1	1	4	6	10		7	7		2	2	4	16	20
J Sierralta	1	3	4	2		2		3	3				3	6	9
C Hidalgo							2	1	3				2	1	3
L Leyton							2	1	3	1	1	2	3	2	5
M Kukuljan							2	2	4	1		1	3	2	5
A Couve, J Sierralta								1	1					1	1
L Leyton, M Herrera-Marschitz								1	1					1	1
M Herrera-Marschitz		1	1	1	2	3	2	2	4		1	1	3	6	9
H Silva											1	1		1	1
M Kukuljian, H Silva								1	1					1	1
TOTAL	6	9	15	13	12	25	21	36	57	9	15	22	48	71	119

5.2.- Short-term Traineeships of MSI students

Student name	Institution	Country	Advisor	Project Description	Starting Date	Ending Date
Paola Morales	Karolinska Institutet	Sweden	Dr. Tomas Hokfelt/Ernest Arenas	To evaluate the dopaminergic modulation of neurogenesis occurring in DG and SVz	17-08-13	20-09-13
Edgardo Rojas Mancilla	Shangai Jiao Tong University	China	Dr. Jun Chen	To discuss on cellular and molecular mechanisms underlying neuronal damage, DNA repair and neuroprotection in models of cerebral ischemia	16-05-13	27-05-13
Edgardo Rojas Mancilla	Institute of Experimental Medicine	Czech Republic	Dr. Eva Sykova	Tissue and primary /stem cells cultures	02-09-13	19-09-13
Horacio Maldonado	Leibniz Institute for Neurobiology	Alemania	Dra. Constanze Seidenbecher	Visualization of the aggregation of proteins in cortical neurons after a stimulate	02-01-13	15-04-13
Mario Rivera Meza	Central Institute of Mental Health J5	Alemania	Dr. Rainer Spanagel	Development of genic transfection experiment related with BNI proyects	01-01-13	28-02-13
Gabriela Martinez	Weill Cornell Medical College, Cornell University	USA	Dr.Laurie Glimcher	Experiment related to cloning the *bdnf* promoter region, and measured the binding of the transcription factor XBP1 in the *bdnf* promoter region by chromatin immunoprecipitation. Also, developed lentivirus including shRNA to evaluated the *xbp1* splicing under the activation of BDNF pathway	01-04-13	01-07-13
Alejandra Arias Cavieres	The Zanvyl Krieger Mind/Brain Institute, Johns Hopkins University	USA	Dr. Alfredo Kirkwood	Obtention of slices and register of perirhinal cortex in aged animals	01-07-13	31-07-13

Annex 6.- Networking and other collaborative work

6.1 Networking

Network Name	Scope	Network Participants (Number)				Institutions
		From the Center		External		
		Researchers	Postdocs / Students	Researchers	Postdocs / Students	
NeuroSur II	LatinoAmerican	Andrés Couve, Claudio Hetz, Miguel Concha, Steffen Hartel, Mario Herrera-Marschitz, Cecilia Hidalgo, Manuel Kukuljan, Lisette Leyton, Pedro Maldonado, Jimena Sierralta, Hernán Silva		Alejandro Schinder, Fernanda Ceriani, Guillermo Lanuza, Francisco Barrantes, Gustavo, Murer, Arturo Romano, Belén Elgoyhen, Alfredo Cáceres, Eduardo Arzt, Luis Barbeito, Federico Lecumberry, Juan Cardelino, José Sotelo.		BNI, Instituto Leloir/Argentina, Pontificia Universidad Católica Argentina /Argentina, Universidad de Buenos Aires/Argentina, INGEBI/Aregntina, Instituto de Investigación Médica Mercedes y Martín Ferreyra/Argentina, Max Planck/Argentina, Instituto Pasteur/Uruguay, Centro Universitario Paysandú/Uruguay, Instituto Clemente Estable/Uruguay
Network for Advanced Microscopy and Image Processing in Neurobiology	Internacional	Andrés Couve, Claudio Hetz, Miguel Concha, Steffen Hartel, Mario Herrera-Marschitz, Cecilia Hidalgo, Manuel Kukuljan, Lisette Leyton, Pedro Maldonado, Jimena Sierralta, Hernán Silva	20	8	6	BNI, U. Göttingen, Germany; IST, Vienna, Austria; U. Bonn, Germany.

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

Annex 6.2.- Other collaborative activities

No activites reported

Annex 7.- Outreach

7.1.- Outreach activities throughout the period

a. International Events

b. *Nacional Events*

Title of event	Date	Place	Target audience
Seminar - II Congreso del Futuro	18-01-13	Sede Congreso Nacional, Región Metropolitana	General community
Open Lecture - Advanced Microscopy and image processing	28-01-13	Faculty of Medicine, University of Chile, Región Metropolitana	University students
Clinical Meeting - 1er Encuentro de Integración básico-clínica	12-04-13	Faculty of Medicine, University of Chile, Región Metropolitana	University students, secondary students, general community
BNI Open Event : Science as an agent of social transformation	27-05-13	Faculty of Medicine, University of Chile, Región Metropolitana	University students, secondary students, general community
Sala interactiva DENDROS: un viaje por el cerebro	05-07-13	Ilustre Municipalidad de Recoleta, Santiago	Secondary students, general community
Open Seminar - Mitos y realidades del cerebro	31-07-13	Faculty of medicine, University of Chile, Región Metropolitana	Secondary students, general community
Visit to Campamento Chile Va!	18-07-13	Hacienda Picarquín, Región O'Higgins	Secondary students
Ending Talk in DENDROS	11-07-13	Ilustre Municipalidad de Recoleta, Región Metropolitana	Secondary students, general community
Seminar - Diálogos con la ciencia	25-07-13	Sede Congreso Nacional en Santiago, Región Metropolitana	Secondary students, general community
Seminar - Feria del postulante de la Universidad de Chile	08-08-13	Facultad de economía y negocios Universidad de Chile, Región Metropolitana	Secondary students, general community
Sala interactiva: Dendros un viaje por el cerebro	22-08-13	Centro Cultural Palacio La Moneda, Región Metropolitana	University students, secondary students, general community
Meeting - Encuentro de salud global	04-09-13	Faculty of Medicine, University of Chile, Región Metropolitana	University students
Open Talk at Café Científico	10-09-13	Confitería Torres, Región Metropolitana	General community
Open event - Lanzamiento 3D Brain App, Seminar - Mitos y realidades del cerebro	09-10-13	Centro Cultural Palacio La Moneda, Región Metropolitana	Secondary students, general community
Round Table - 1era Conferencia Internacional de Cultura científica	11-10-13	Universidad Nacional Andrés Bello, Región Metropolitana	University students, general community
Clinical Meeting - 2do Encuentro de Integración básico-clínica	21-11-13	Faculty of medicine, University of Chile, Santiago	University students, general community
Seminar - Muestra de animación interactiva	12-12-13	Universidad Católica de Concepción, región del BioBio	University students
Round Table - Tertulias porteñas: Magia para ciegos	19-12-13	Parque Cultural de Valparaíso, región de Valparaíso	University students, secondary students, general community
Open Seminar - Dendros en Carnaval del postulante	27-12-13	Facultad de Arquitectura y diseño Universidad de Chile, Región Metropolitana	Secondary students, general community

7.2.- Products of outreach

Type of Product	Quantity	Target Audience	Scope
Study text to stimulate interest in neuroscience: Dendros II	1	University, Secondary and Primary students and Community in general	National
Website that arranges all audiovisual and didactic material for students: Loligo.cl	1	University, Secondary and Primary students and Community in general	National, Internacional
A film about neuroscience issues: VidaConCiencia	1	University, Secondary students and Community in general	National, Internacional
Institutional video about Biomedical Neuroscience Institute	1	University, Secondary students and Community in general	National
Videogame to motivate in neuroscience: El escape de Kai	1	University, Secondary students and Community in general	National
Pinball machine	1	University, Secondary students and Community in general	National
Arcade machines	4	University, Secondary and Primary students and Community in general	National
Digital game to learn about the brains areas: 3D Brain App	1	University, Secondary and Community in general	National
Facebook Page	1	Secondary students and Community in general	National, Internacional
Support material about DENDROS	5	University, Secondary and Primary students and Community in general	National
Youtube Channel: Dendros TV	1	University, Secondary and Community in general	National, Internacional
Clipping book with the press news related to the Institute	1	University, Secondary and Primary students and Community in general	National

7.3.- Articles and Interviews

Type of media and scope	Local/Regional		National		International		
	N° Interviews	N° Articles	N° Interviews	N° Articles	N° Interviews	N° Articles	**TOTAL**
Written				33			**33**
Internet		7		34		3	**44**
Audiovisual			7	6	2	4	**19**
TOTAL		**7**	**7**	**73**	**2**	**7**	**96**

Annex 8.- Connections with other sectors

No activites reported

9.1 Total incomes:

Funds	Accomulated incomes to last year ($)	2013 Incomes		Total incomes to 2013 ($)
		Amount ($)	Percentage of resources used by the Center (%)	
ICM	1.582.168.000	869.450.021	100	2.451.618.021
National Funds				
FONDECYT (AC) 1100137	100.000.000	50.000.000	60	150.000.000
FONDECYT (CHz) 1100176	156.287.500	51.287.500	0	207.575.000
FONDECYT (MC, SH) 1090242	45.000.000	-	-	45.000.000
FONDECYT (SH) 1090246	18.607.500	-	-	18.607.500
FONDECYT (MHM) 1080447	125.000.000	75.000.000	20	200.000.000
FONDECYT (CH) 1100052	102.500.000	51.250.000	20	153.750.000
FONDECYT (LL) 1110149	100.000.000	50.000.000	0	150.000.000
FONDECYT (MK) 1090281	85.000.000	45.000.000	100	130.000.000
FONDECYT (PM) 1090101	24.600.000	3.000.000	100	27.600.000
FONDECYT (JS) 1090272	90.000.000	45.000.000	50	135.000.000
FONDECYT (YI/MH) 1095021	50.000.000	-	-	50.000.000
FONDECYT (Paola Morales & MHM) 11070192	125.000.000	75.000.000	20	200.000.000
FONDECYT (MEQ/MHM) 1130012	75.000.000	75.000.000	20	150.000.000
FONDECYT (MC) 1120558	55.396.500	51.283.500	20	106.680.000
FONDECYT (SH) 1120579	156.007.500	156.007.500	10	312.015.000
FONDAP 1501006 (CH, LL, CHz)	700.000.000	-	-	700.000.000
ANILLO-CONICYT ACT 66 (PM)	190.100.000	15.100.000	50	205.200.000
U-REDES (SH)	244.927.500	244.927.500	0	489.855.000
FONDEF (SH) D07I1019	51.688.000	-	-	51.688.000
FONDEF (SH) D11I1096	344.822.000	344.822.000	0	689.644.000
FONDEF (AC, PM)	125.000.000	125.000.000	30	250.000.000
CONICYT/DAAD No 1378-09529	10.000.000	-	-	10.000.000
CONICYT/USA2013-0020	-	50.000.000	0	50.000.000
Guillermo Puelma Foundation	5.000.000	2.500.000	100	7.500.000
EXPLORA EPA10037	-	20.000.000	100	20.000.000
INNOVA CORFO 13PAE-21453	-	46.500.000	100	46.500.000
International Funds				
HHMI (MC) 55005940	48.500.000	-	-	48.500.000
FIRCA NIH-USA (AC)	22.000.000	11.000.000	25	33.000.000
FIRCA NIH-USA (LL)	48.000.000	-	-	48.000.000
ICGEB, Italy (CHz)	32.500.000	-	-	32.500.000
DFG (MC, AC, SH, CHz, JS, MK)	10.000.000	-	-	10.000.000
Mh-Marschitz Foundation, Stockholm, Sweden	55.000.000	50.000.000	5	105.000.000
Micheal J Fox Foundation For Parkinson Research, USA (CHz	105.291.500	42.791.500	1	148.083.000
ALS Association, USA (CHz)	69.657.500	32.157.500	0	101.815.000
Genzyme, USA (CHz)	29.000.000	-	-	29.000.000
TOTAL	**4.982.053.500**	**2.582.077.021**		**7.564.130.521**

Exchange rate US$ 1 = $ 500

9.2 Outcome structure

ITEM	Accumulated expenses to last year [$]	2013 Expenses [$]				Total expenses to 2013 [$]	%
		Operative	Networking	Outreach	Total		
Honoraria Researchers	153.600.000	107.400.000			107.400.000	261.000.000	14,9
Honoraria students and other personnel	305.696.999	245.895.766			245.895.766	551.592.765	31,6
Tickets and travel expenses	52.446.680	43.545.848	21.270.046	2.455.364	67.271.258	119.717.938	6,8
Materials/supplies	124.357.769	120.834.458	750.000	4.007.151	125.591.609	249.949.378	14,3
Goods and equipment	173.146.731	92.117.682		1.155.780	93.273.462	266.420.193	15,2
Infrastructure	56.000.000				-	56.000.000	3,2
Administrative expenses	63.619.286	42.780.211			42.780.211	106.399.497	6,1
Publications and subscriptions	1.812.890				-	1.812.890	0,1
Consultancies	18.449.280	6.558.000		9.787.834	16.345.834	34.795.114	2,0
Overhead	10.629.668	10.927.071			10.927.071	21.556.739	1,2
Insurance costs	1.741.580	1.665.982	379.954	1.050.326	3.096.262	4.837.842	0,3
Legal personality expenses					-	-	-
Others	36.273.493	12.961.080	2.500.000	22.491.346	37.952.426	74.225.919	4,2
Total Expenses ($)	**997.774.376**	**684.686.098**	**24.900.000**	**40.947.801**	**750.533.899**	**1.748.308.275**	**100,0**

9.3 Financial accounting

ITEM	2013 [$]				TOTAL TO 2013
	Operative	Networking	Outreach	Total [$]	
Income	802.620.000	22.500.000	44.330.021	869.450.021	2.451.618.021
Outcome	684.686.098	24.900.000	40.947.801	750.533.899	1.748.308.275
Annual balance	120.359.902	-2.400.000	3.382.220	118.916.122	703.309.746