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1. 1.1 Executive Summary

Understanding the function of the nervous system constitutes a broad and central challenge of today's biology and medicine. Consequently, the discipline of Neuroscience has expanded worldwide and diversified dramatically in recent decades. Yet the integration of the structural and functional organization of the brain in physiology and disease continues to remain beyond our grasp. 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 the capacity to conduct clinical brain research sustained by cutting-edge basic Neuroscience is missing.

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 a suitable infrastructure to accomplish world-class scientific research and training. BNI provides a unified vision to explore the dynamic structural and functional organization of the brain under normal physiology and the mechanisms underlying disease from whole organisms to cells. Four particular qualities place BNI in a pivotal position to lead Neuroscience research in Chile and the region: (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 undergraduate plus Master, PhD in Biomedical Sciences, MD-PhD and MD Specialist programs, and (iv) a young body of researchers coexisting in a single campus capable of executing the long terms goals of the initiative.

During this period the three guiding principles of BNI have been embraced fully, explicitly and unanimously by BNI members. These principles are: (i) transdisciplinary research with members contributing with complementary expertise in cell and molecular neuroscience, neural development, morphogenesis, neuropathology, behavior, neural systems, clinical research, pharmacology, genetics, and a trademark of productive interactions between Neuroscience and applied mathematics, (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 the transfer of scientific and medical impact to the community. Research at BNI is organized around interconnected thematic platforms.

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 at the interface of basic neuroscience, neuropathology, and quantitative biology, (iii) produce high-standard clinical research and transfer the impact of its research to society by discovering novel diagnostic and therapeutic approaches to improve the life quality of patients with neurological and psychiatric disorders, and (iv) become a resource center for specialized clinical practitioners and the general public.

During this period we have work towards attaining each of these goals. Our research lines constitute long-term scientific programs and, therefore, have remained unchanged. We have published 32 ISI articles, including two reviews in leading journals with high impact factor and wide audiences (*Nature Reviews Neuroscience 2011 ISI Impact Factor 30.455 and Nature Reviews Molecular Cell Biology 2011 ISI Impact Factor 39.123*). We have carried out 9 encounters with clinical departments and institutions, generating interest in collaborative work and visualizing local biomedical problems and solutions. As a result, Hernán Silva is currently leading an initiative to bring together basic and clinical researchers and unify criteria for clinical research (informed

consents, ethical issues, sample management, etc), which will be essential to establish and strengthen our pioneering clinical research platform. Although the structure of the institute has remained unchanged the number a people associated to it has grown by 24%, with new students representing the majority of this increase. We have continued with our philosophy to invest more than 60% of the funds in common strategic aims. These collaborative efforts have been supported by an increased number of projects involving more than one BNI lab, in many instances including the co-mentoring of graduate students. We have funded three new pilot-projects led by young researchers in collaboration with BNI Associate and Adjunct Investigators (PM/José Ignacio Egaña, *Efecto de la analgesia en los indicadores electroencefalográficos de nocicepción en humanos*; CHz/José Manuel Matamala, *Perfil mutacional del gen PRNP en pacientes chilenos con la enfermedad de CREUTZFELDT - JAKOB: en búsqueda de nuevas variantes genética*s; CH/Andrea Paula - Lima, *Estudio de patrones oscilatorios anormales en sujetos con enfermedad de Alzheimer incipiente y en roedores inyectados con oligómeros del péptido beta-amiloide*), and 9 postdoc bridge fellowships. We have increased and diversified our activities by assigning specific common tasks to each BNI investigator. We have organized 3 major scientific events in Chile and 1 abroad, reaching top-quality scientific audiences, and also high-school students and the general public. Young BNI scientists and Associate Investigators have received national and international prizes. We highlight Steffen Härtel's Second Iberoamerican Prize for Innovation and Entrepreneurship (Spain) for his outstanding contributions to virtual microscopy and applications for pathology and diagnostics based on remote access that has allowed him to establish productive contacts with industry. Formal networks based on super-resolution microscopy (Göttingen) and improving interactions between Latin American Neuroscience centers (NeuroSur) have produced concrete advances in exchange of students, expertise, equipment and reagents. During this period International Advisor Dr. Charles Zuker (Columbia U) visited the institute and generated a written evaluation, which we are currently using to steer the institute's goals and strategies. A wide variety of high impact outreach activities were completed including lectures, visits to the institute, web, radio, printed press, and generation of physical and virtual material to reach the general public including a "brain hat" and *Dendros*, a web-based interactive comic. Importantly, during this period we became a non-profit organization and we have consolidated executive and grant management offices, which provide BNI investigators more quality time for research.

We are fully aware of the titanic task of understanding the function and dysfunction of the nervous system, and the current global interest and competition within the discipline. We also acknowledge the ambitiousness of our four specific aims. However, guided by a transdisciplinary program, a bottom-up multi-scale approach and an integrated biomedical strategy we firmly believe we have begun to consolidate a Neuroscience initiative in Chile that will improve the country's international visibility by generating recognizable high-quality results.

1.2 Resumen Ejecutivo

La comprensión de la función del sistema nervioso constituye un desafío amplio y central de la biología y la medicina actual. La disciplina de la Neurociencia se ha expandido en todo el mundo y se ha diversificado de manera espectacular en las últimas décadas. Sin embargo, la integración de la organización estructural y funcional del cerebro en la fisiología y la enfermedad sigue estando fuera de nuestro alcance. En Chile, miles de personas sufren de trastornos neurológicos y psiquiátricos sin tratamiento satisfactorio. Además, el país ha experimentado un crecimiento sostenido de la población de edad avanzada con aumentos concomitantes en las principales enfermedades neurodegenerativas y cognitivas, mientras que la capacidad para llevar a cabo investigación clínica del cerebro en asociación con Neurociencia básica de frontera es todavía incipiente.

La solución a esta problemática compleja requiere de un enfoque moderno basado en una estrategia interdisciplinaria integrada. El Instituto de Neurociencia Biomédica (BNI) constituye un amplio paraguas que reúne a una masa crítica de neurocientíficos básicos y clínicos junto a matemáticos aplicados y una infraestructura adecuada para llevar a cabo investigación científica y formación de capital humano de nivel internacional. BNI proporciona una visión unificada para explorar la organización estructural y funcional del cerebro en condiciones fisiológicas y los mecanismos que subyacen a enfermedades utilizando desde organismos completos a células. Cuatro cualidades del BNI lo posicionan en un lugar privilegiado para dirigir la investigación en Neurociencia en Chile y en la región: (i) un amplio historial de iniciativas de investigación individuales y de colaboración en Neurociencia, (ii) la asociación a los principales centros básico-clínicos de investigación nacionales e internacionales, (iii) un vasto potencial en la formación de pregrado en ciencias de la salud además de formación en grados de Magíster, Doctorado en Ciencias Biomédicas, programa MD-PhD y especialidad, y (iv) un cuerpo joven de investigadores que coexisten en el mismo campus capaces de ejecutar los objetivos de largo plazo de la iniciativa.

Durante este período, los tres principios rectores de BNI han sido abrazados plenamente, de forma explícita y por unanimidad por los miembros de BNI. Estos principios son: (i) la investigación transdisciplinaria con miembros que contribuyen con conocimientos complementarios en Neurociencia celular y molecular, desarrollo neural, morfogénesis, neuropatología, conducta, sistemas neurales, investigación clínica, farmacología, genética y un sello de interacciones productivas entre Neurociencia y matemáticas aplicadas, (ii) un enfoque multi-escala tipo *"bottom-up"* para estudiar la función desde los genes y las moléculas al comportamiento en modelos animales complementarios, y (iii) una estrategia integrada para promover la investigación biomédica de alto estándar, con contribuciones científicas que garanticen la transferencia de resultados científicos y médicos de impacto a la comunidad. La investigación en BNI se organiza en torno interconectados plataformas temáticas.

BNI tiene como objetivos: (i) establecer un centro de referencia internacional para la exploración de la "estructura y función del cerebro en condiciones fisiológicas y patológicas", (ii) constituirse en una sede de entrenamiento para una nueva generación de investigadores y clínicos en un ambiente transdisciplinario sólido, vibrante y único en la interfaz de la Neurociencia básica, la neuropatología y la biología cuantitativa, (iii) producir investigación clínica de alto nivel y transferir el impacto de su investigación a la sociedad mediante el descubrimiento de nuevos enfoques diagnósticos y terapéuticos para mejorar la calidad de vida de los pacientes con trastornos neurológicos y psiquiátricos, y (iv) convertirse en un centro de recursos para los profesionales clínicos especializados y para el público general.

Durante este período, hemos trabajado en cada uno de estos objetivos. Nuestras líneas de investigación constituyen los programas científicos centrales y de largo plazo del Instituto y, por lo

tanto, se han mantenido sin cambios. Hemos publicado 32 artículos ISI, incluyendo dos revisiones en revistas de alto factor de impacto y una amplia audiencia (*Nature Reviews Neuroscience 2011 Factor de Impacto ISI 30,455 y Nature Reviews Molecular Cell Biology 2011 Factor de Impacto ISI 39.123*). Hemos llevado a cabo nueve encuentros con departamentos e instituciones clínicas, generando interés en el trabajo colaborativo y en la visualización de problemas locales de biomedicina y sus potenciales soluciones. Como resultado, Hernán Silva lidera hoy una iniciativa para reunir a investigadores básicos y clínicos y unificar criterios para la investigación clínica (consentimientos informados, cuestiones éticas, manejo de muestras, etc), lo que será esencial para establecer y fortalecer nuestra plataforma pionera de investigación clínica en Neurociencia. Aunque la estructura del Instituto se ha mantenido sin cambios, el número de personas asociadas a él ha crecido en un 24%, con nuevos estudiantes representando la mayor parte de este incremento. Hemos continuado con nuestra filosofía de invertir más del 60% de los fondos en objetivos estratégicos comunes. Los esfuerzos de colaboración se demuestran con un mayor número de proyectos que involucran a más de un laboratorio de BNI, y que en muchos casos incluye la co-tutoría de estudiantes de posgrado. Hemos financiado tres nuevos proyectos piloto dirigidos por jóvenes investigadores en colaboración con Investigadores Asociados y Adjuntos BNI (*PM/José Ignacio Egaña, Efecto de la analgesia en los Indicadores electroencefalográficos de nocicepción en Humanos; CHz/José Manuel Matamala, mutacional del gen Perfil PRNP en Pacientes chilenos con la enfermedad de Creutzfeldt - Jakob: en Búsqueda de Nuevas Variantes genéticas; CH/Andrea Paula-Lima, Estudio de patrones oscilatorios Anormales en Sujetos con enfermedad de Alzheimer incipiente y en Roedores Inyectados con oligómeros del péptido beta-amiloide*) y 9 becas postdoctorales puente. Hemos incrementado y diversificado nuestras actividades mediante la asignación de tareas específicas comunes a cada investigador BNI. Hemos organizado tres eventos científicos importantes en Chile y 1 en el extranjero, alcanzando la más alta calidad de audiencias científicas, así como de estudiantes secundarios y público general. Jóvenes científicos e Investigadores Asociados al BNI han recibido premios nacionales e internacionales. Destacamos el Segundo Premio Iberoamericano para la Innovación y Emprendimiento (España) a Steffen Härtel por su destacada contribución a la microscopía virtual, aplicaciones en patología y el diagnóstico basado en el acceso remoto, lo que le ha permitido establecer contactos productivos con la industria. Las redes formales basadas en microscopía de súper-resolución (Göttingen) y el mejoramiento de las interacciones entre centros de Neurociencias de países latinoamericanos (NeuroSur) han producido avances concretos en el intercambio de estudiantes, conocimiento, equipos y reactivos. Durante este período nuestro asesor internacional Dr. Charles Zuker (Columbia U) visitó el instituto y generó una evaluación escrita que estamos utilizando para dirigir los objetivos y estrategias del Instituto. Una amplia variedad de actividades de difusión de alto impacto se completaron incluyendo conferencias, visitas al Instituto, web, radio, prensa impresa y la generación de material físico y virtual para llegar al público general, incluyendo un "gorro cerebro" y *Dendros*, una plataforma web basada en un *comic* interactivo. Es importante destacar que durante este período BNI se convirtió en una corporación sin fines de lucro y hemos consolidado oficinas ejecutivas y de administración contable, que proporcionan a los investigadores BNI más tiempo de calidad para su investigación.

Estamos plenamente conscientes de la tarea titánica que representa la comprensión de la función y disfunción del sistema nervioso, y del actual interés y competencia de la disciplina a nivel mundial. Reconocemos también que nuestros cuatro objetivos específicos son ambiciosos. Sin embargo, guiados por un programa transdisciplinario, un enfoque multi-escala y una estrategia biomédica integrada creemos firmemente que hemos comenzado a consolidar una iniciativa de Neurociencia en Chile que permitirá mejorar la visibilidad internacional del país mediante la generación de resultados reconocibles de alta 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.

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 glial cells. 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 used 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 evaluating the role of disease-related genes in common cellular processes leading to neuronal connectivity and synaptic function. The goal is to develop knowledge, expertise and technological approaches to understand the mechanisms by which disease-related genes affect common molecular/cellular/physiological processes involved in neuropathological conditions.
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, 23 Master, 20 undergraduate students, and 57 technicians. This represents a 22% increase relative to last year and highlights the appeal of the institute to younger scientists. 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 the 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 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 including association to other ICM centers such as MINREB and CNV. Dr. Charles Zuker (Columbia U), a member of BNI's International Advisory Board, completed a two-day visit to the institute and generated a written evaluation, which we are using to steer the institute's goals and strategies. The research team is supported by an executive office, which contributes to the organization of scientific activities, outreach 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 partially addressed all three specific aims of this line of research. Key findings obtained during this period are summarized below according to the original specific aims:

i) The morpho-functional organization of the endoplasmic reticulum (ER) and the consequences of altered organelle structure in protein trafficking and in human disease: Our published results now support the notion that non-canonical ER trafficking in the axon plays an important role in neuronal function (AC in collaboration with the Göttingen Network. See 5. Networking). Another manuscript will be submitted during 2013 describing new results in dendrites. Altered ER functions lead to "ER stress", which triggers adaptive cell responses mediated by proteins like XBP1. Unexpected findings indicate that XBP1 protein deficiency increases autophagy that protects against Huntington disease *in vitro* and *in vivo*. Thus, a gene therapy to target the XBP1 in Huntington *in vivo* has been developed (CHz). The mechanisms underlying the regulation of autophagy were further investigated. BAX inhibitor-1 was described as a new component that connects the response to stress with autophagy (CHz/JS). Moreover, a biological function for a newly discovered protein (GRINA/TMBIM3) in the nervous system as a key stress modulator has been reported (CHz/MC/JS). In addition, ER stress also induces apoptosis via a Perk-dependent repression of miR-106b-25 cluster, another ER stress-induced signaling pathway, highlighting the importance of an altered organelle structure in cell fate (CHz).

ii) Cytoskeletal associated proteins: Recently published studies show that Marlin-1 is required for the maintenance of an intact Golgi apparatus and its depletion produces the down-regulation a molecular motor with a central function in morphogenesis and migration (AC/MK). The study of recently identified proteins in the functional and structural organization of the cytoskeleton has been implemented using genome-wide illumina-microarrays and further qRT-PCR of intra and extra synaptic structural elements in brain samples from patients suffering from schizophrenia. Region specific down regulation of gene products associated to presynaptic vesicles, cytoskeletal proteins, and extracellular matrix proteins have been found (MH).

iii) The spatio-temporal activation of signaling molecules: Activation of small GTPases downstream of two cell adhesion receptors present in astrocytes, integrins and syndecan-4 has been observed. Short-term stimulation of astrocytes with the abundantly expressed neuronal protein Thy-1 increases RhoA-GTP and astrocyte adhesion; whereas, long-term stimulus results in RhoA inactivation and Rac1 activation, thereby leading to astrocyte migration (LL/SH). Time-lapse recording of migrating cells has been possible with a newly acquired Olympus FV10i confocal microscope purchased through an informal consortium established between BNI and other investigators at the FMed. The results obtained have revealed the remarkable morphological differences of astrocytes that migrate in response to Thy-1 versus those stimulated with serum, results that were previously overlooked with the methodology employed (LL/MH). In addition, integrin binding to Thy-1 in neurons was shown to stop axonal growth and induce retraction of existing processes by signaling mechanisms involving Thy-1 clustering and inhibition of Src (LL/CHz/SH). Complex formation of Thy-1 and Src are currently studied by molecular co-

localization experiments, which are possible thanks to the Olympus FV-1000 confocal microscope acquired by our Institute (LL/SH). Astrocyte-dependent changes in neuronal branching, neurite length and viability of hippocampal neurons induced by perinatal asphyxia have been studied in primary and organotypic cultures, also monitoring MAP-2 and DAPI at DIV 7 (MH/LL). Results obtained suggest that perinatal asphyxia induces impairment of synapses in hippocampus (MH).

The notion that non-canonical ER trafficking may play a role in axonal function has been published, *Valdés et al., 2012 PLoS One.* Autophagy increased by XBP1 deficiency, its control mechanisms as well as a gene therapy to target the XBP1 in Huntington disease were published in *Vidal et al., 2012 Human Mol Gen* and *Zuleta et al., 2012 BBRC.* The function of GRINA in the nervous system was reported in *Rojas et al., 2012 Cell Death Diff.* Perk-dependent repression of miR-106b-25 cluster as a requirement for ER stress-induced apoptosis was published in *Gupta et al., 2012 Cell Death Dis.* Marlin-1/Jakmip1 involvement in abnormal morphogenesis and migration of cortical neurons was published in *Vidal et al., 2012 Mol Cell Neurosci.* Region specific down regulation of different gene products of synaptic elements in schizophrenia brains was published in *Schmitt et al., 2012 Eur Arch Psych Clin Neurosc.* Signaling mechanisms in astrocyte adhesion/migration and neuronal processes growth/retraction were reported in *Herrera-Molina et al., 2012 PLoS ONE.* International recognition of the BNI-PIs expertise are underscored by invitations to write reviews for *Nature Rev Mol Cell Biol, Trends in Biochem Sci, Autophagy, BMC Biol, FEBS Letter, Cell Death and Differentiation, EMBO Reports and SCDB*. BNI investigators have been invited to participate in various meetings and symposia. Among them we highlight the *XXVI Annual Meeting of the Chilean Society for Cell Biology* and international presentations at the IX *Workshop on the Molecular Biology of Stress Responses* in Porto Alegre*, Congress 22nd IUBMB and 37th FEBS* in Sevilla*, Gordon Research Conference, Neurodegeneration: Opportunities for Collaboration Across Disease-Specific Research, McLean Neuroscience Seminar Series, Harvard Medical School McLean Hospital and Development Communities - A Workshop* in the US*,* as well as the *Conference and General TWAS meeting* in Tianjin.

RL2. Cellular identity and morphology: The central question of how gene expression determines morpho-functional features throughout the development and the lifespan of neurons is being pursued in *Drosophila*, zebrafish and mice. During the period we have made progress in:

i) The role of Marlin-1: Using *in utero* electroporation we have now demonstrated and published that Marlin-1 is a critical determinant of neuronal morphology and migration in the cerebral cortex. Specifically, Marlin-1 is required for the establishment of neuronal morphology and its depletion results in abnormal pyramidal cortical neuron migration in embryonic mice (AC/MK).

ii) CoREST and brain development: Using the same system we have now published the relevance of the chromatin remodeling protein CoREST in the behavior of progenitors and newly born 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 could explain part of the phenotype of the downregultaion of CoRest (MK).

iii) Neural morphogenesis and CTIP1: We have continued the study of this transcription factor that was originally identified in a *Drosophila* screen for genes involved in neuronal morphogenesis. 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).

iv) Synapse formation and Hindsight: In *Drosophila* we are currently investigating the target genes through which the transcription factor Hindsight affects axonal targeting and growth in the optic lobe. We have determined that one of the direct targets of Hindsight (HNT) is a *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.

The role of CoREST in neuronal migration has been published in *Cerebral Cortex,* one of the most important journals in the field, recognizing the quality of the work produced at BNI (*Fuentes et al., 2012 Cereb Cortex*). The study on Marlin-1, that involved two BNI labs, has been published in *Molecular and Cellular Neuroscience* (*Vidal et al., 2012 MCN*). Expertise in the field of the role of MAGUKs in synapse led to publish a review by invitation (*Oliva et al., 2012 Dev Neurobiol*). Additionally, the results on CTIP1 were presented as a short talk (*Cánovas et al., 2012, XXVI Chilean Society for Cell Biology Annual Meeting*) wining the best 2012 oral presentation. More recent results involving CoREST have been presented in a national meeting *(Saud et al, 2012; XXVI Chilean Society for Cell Biology Annual Meeting*). The results on MAGUK proteins have been presented in national and international meetings (*Moya and Sierralta, 2012; Ramírez et al. 2012 XXVI Annual Meeting of the Chilean Society for Cell Biology; Astorga et al., 2012 European-Neurobiology of Drosophila Meeting-Neurofly Padua 2012*). The latest results on the identification of targets of HNT have been presented in national and international meetings (López et al., 2012, *XXVI Chilean Society for Cell Biology Annual Meeting;* López et al., 2012 *European-Neurobiology of Drosophila Meeting-Neurofly Padua 2012).*

RL3. Supra-cellular development and circuits: This platform investigates the supra-cellular transformations of brain morphogenesis leading to the formation of multi-cellular aggregates such as nuclei and layers, and the migration of cells and axonal growth cones during the establishment of neuronal connectivity. During this period we generated considerable advances in the research of the main projects, and continued developing methodologies for 3D confocal visualization and analysis in collaboration with the BNI-BioMat platform (see RL7). The main results and stage of advance of the collaborative projects are:

(i) Asymmetric morphogenesis of the parapineal and habenulae in zebrafish (MC/SH): The F-actin modulator Daam1 is an effector of asymmetric morphogenesis downstream of the pathways that establish asymmetric subnuclear organization in the habenulae of zebrafish (manuscript under review in the journal *Development*). Nodal signaling modulates tensile properties of the parapineal to impose a left-sided bias in an Fgf-dependent evagination. A manuscript will be prepared after additional 4-8 months of experiments.

(ii) Chemokine and robo-slit signaling and habenular-IPN connectivity (MC/CH): Cxcl12-Cxcr4 interacts with Slit-Robo3 to modulate a Netrin-Dcc attractant responses of habenular axons, desensitizing habenular axons to repellent signals. We are currently performing the last set of experiments before writing a manuscript.

(iii) Role of tensile and migratory forces in shaping supra-cellular embryonic structures (MC/SH): This project, at an early stage of advance, explores adhesive interactions and the interplay of opposite mechanical and migratory forces aligned along the anterior-posterior axis are sufficient to shape the early primordium of the laterality organ in zebrafish.

(iv) Role of differential adhesion and contact inhibition in cell sorting during early morphogenesis (MC/SH): Spreading of cells during epiboly uses a piggy-back mechanism whereby cells are passively carried on the surface of the moving substrate due to E-cadherin cell-cell adhesive interactions. A manuscript with these results is currently under preparation.

(v) Comparative analysis of habenular asymmetry in vertebrates (MC): We have published a first systematic comparative analysis of structural and connectional asymmetries in a vertebrate, finding co-existence of striking inter-species variability in morphological asymmetry with an overall conserved laterotopic pattern of connectivity in the IPN. These results unveil a key conserved role of this connectivity trait in the function of the circuit (*Villalón et al., 2012 PLoS ONE*).

Based on our contributions a review was published on the topic of this research line in *Nat Rev Neurosci* a high-impact factor and leading journal in the field (2011 ISI Impact Factor 30.455). Additionally, results were presented at the national level in the *XXVI Annual Meeting of the Chilean Society for Cell Biology (Puerto Varas)*, and the *Developmental Biology Symposium (CIMARQ-Quintay)*. At the international level, presentations included the *EMBO Conference - Morphogenesis and dynamics of multicellular systems (Germany)*, the *EMBO | FEBS Lecture Course - Mesoscopic origins of cell behaviors during tissue morphogenesis (France)*; the *VI International Meeting of the Latin American Society for Developmental Biology (Uruguay)*, the *Second Meeting of the Latin American Zebrafish Network (LAZEN) (Argentina)*, the *Cell Symposia: Hallmarks of Cancer (USA)*, and the *Workshop on Generation, Degeneration and Regeneration of the Nervous System (Chile)*.

RL4. Plasticity and behavior: The central objective of this research line is to understand how genetic interactions and signaling pathways control synaptic plasticity and long-lasting memories. During this period we have carried out studies on the role of ryanodine-receptor (RyR) calcium release channels on hippocampal long-term potentiation (LTP) and behavior (contextual fear conditioning) (CH). Results obtained in this period confirm the complete inhibition of LTP induction (theta burst stimulation of Schaffer collateral fibers, fEPSP recorded in the CA1 region) in hippocampal slices pre-incubated with ryanodine at concentrations that suppress RyR activity. In parallel studies in hippocampal slices, we have shown that RyR2 and BDNF protein content, but not RyR3 or PKMz contents, increased significantly after 1 h of LTP induction by TBS. Of note, inhibitory ryanodine completely prevented the RyR2 protein increase observed after 1 h of LTP induction, suggesting that the activity-dependent RyR2 increase requires RyR-mediated calcium signals. We have also found that KCl-induced calcium signals in hippocampal slices decrease markedly after RyR inhibition, suggesting that neuronal depolarization by KCl elicits cytoplasmic calcium signals originating mostly via RyR-mediated calcium-induced calcium release. We are currently performing experiments with injection of RyR2 antisense oligonucleotides to test if decreasing RyR2 protein content intrahippocampus interferes with LTP induction and prevents spatial learning in rats. Additionally, we have continued to investigate how non-lethal concentrations of soluble amyloid β-peptide oligomers (AβOs) generate abnormal RyR-dependent calcium signals that induce mitochondrial fragmentation. We have recently published two articles on this subject (*San Martín et al., 2012 Neurodegener Dis; San Martín et al., 2012 Biometals*). During the reported period, we presented our work in several national and international meetings, including the *European Calcium Society Meeting,* held in Toulouse, France and the *FALAN meeting* held in Mexico. New projects, currently at an early stage of development, have emerged from collaborations between AC/SH/CH investigating the propagation of intracellular Ca^{2+} waves in dendrites of hippocampal neurons. Additional projects at an early stage include collaborations between CH, young investigator Andrea Paula-Lima and Adjunct investigator José Luis Valdés.

RL5. Systems Neuroscience: During this period we initiated a series of studies to determine the neuronal mechanisms related to visual perception and interoception. PhD student Christ Devia is completing her thesis examining electrophysiological aspects of visual perception in humans (PM). We presented several abstracts of these studies (***See Annex 2***) and submitted one paper to Frontiers in Neuroscience. We found that eye movements correspond to motor activities that are tightly correlated with changes in perception and we have investigated the neuronal mechanisms that explain some aspects of visual perception.

Another project currently explores the neuronal mechanisms involved in interoception, and is the continuation of a completed grant funded by Fondecyt (Anillo ACT 66). In a model of alcohol-addicted rats we are recording the activity of the insular cortex to explore its involvement in

monitoring the internal state. At the same time we have tested whether electrical microstimulation of the vagus nerve modulates the craving behavior in these animals (PM). These studies are the basis of two doctoral thesis (students Sergio Vicencio and Dr. Carlos Ibañez). In addition, a series of studies exploring the pupillary dynamics, as a marker for insular and autonomic activity, in relation to emotional responses has been conducted last year by postdoctoral fellow Enzo Brunneti. Masters' student Rocio Mayol is finishing her thesis and writing a manuscript relating pupil response and emotional response during decision making (PM). Masters' student Susana Brugues, who is co-tutored by two BNI investigators (PM/MH) has explored the pharmacological contribution of the autonomous nervous system in these responses.

During this period we have also initiated a large study that combines basic and clinical aspects in patients affected with schizophrenia. This study, which involves two BNI Associated Investigators (HS/PM), is aiming for biometrics in schizophrenic patients. In this project, we are studying a group of diagnosed patients in order to find behavioral, genetic, and electroencephalographic 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. During this period we also recruited the Centro Renoval. Dr. José Ignacio Egaña a BNI-funded postdoctoral fellow has been involved in this project. We have recorded electroencephalographic signals from more than 30 patients and 10 controls. Along with EEG recordings, we have recorded eye movements and pupil dynamics. We submitted one abstract reporting results on eye movements (***See Annex 2***, 86), and one manuscript. Finally, we did report the results of studies in monkeys and rats performed previously. One study demonstrate that microstimulation in the cerebral cortex of rats can mimic real stimuli by synchronized activity, while in monkeys we demonstrate that the visual path during free viewing of natural scenes follow distinct statistical features (***See Annex 2***).

RL6. Neural dysfunction and pharmacological targets: This transversal platform fosters an *in vivo* genetic/pharmacological/functional approach centered on evaluating the role of disease-related genes in common cellular processes leading to neuronal connectivity and synapse formation. During this past year, we have performed several studies to address novel disease mechanisms using animal models. In addition, we published our first clinical study with Chilean patients. Main results obtained in the collaborative projects during this period included:

(i) Disease models: We have finished several studies in mouse models of disease to investigate pathogenic mechanisms in several neurological diseases. We have been able to develop studies to perform genetic manipulation of the disease models and identify novel targets for therapeutic interventions. For example, CHz has targeted two main transcription factors involved in adaptation to cellular stress using knockout models (i.e. XBP1 and ATF4) and breed them to two Huntington´s disease transgenic mouse models. Using this approach we identified a key component of Huntington´s pathogenesis (*Vidal et al., 2012 Hum Mol Gen*). Using genetic tools we established the relative contribution of cellular stress to spinal cord injury, demonstrating a key role of both ATF4 and XBP1 in this pathological model (*Valenzuela et al., 2012 Cell Death Dis*). Similar studies have been finished in models of ALS, peripheral nerve degeneration, prion disease, and Parkinson´s disease. We have also reported the contribution of micro RNAs and ER stress to motoneuron degeneration in ALS (Gupta et al., 2012 *Cell Death Dis*). Additionally, we characterized new components of this stress response through collaborative efforts with research groups in the US, Spain, Chile and France (Rodriguez et al., 2012 *EMBO J*). Based on our contributions several reviews and editorial comments were published on the topic, highlighting one in *Nat Rev Mol Cell Biol* (2011 ISI Impact Factor 39.123).

We are also investigating the role of the polymerase PARP-1 on the long-term effects of perinatal asphyxia, proposing that PARP-1 overactivation is a target for neuroprotection. We published a new study in this area of research (*Allende Castro, 2012 Neurotox Res*). The issue was also investigated in primary cultures, focusing on astrocyte-neuron interactions, developing a model implying chemically-induced hypoxia, focusing on HIF-1alpha, a key transcription factor for cell response to hypoxia, interacting with the DNA-repairing enzymes, such as PARP-1. The studies were performed by Edgardo Rojas-Mancilla, who has been pivotal for the integration of research between MH and LL (*Rojas-Mancilla et al. 2012, in preparation*). CH has advanced the development of cellular models of Alzheimer´s disease and studies the effects of mitochondrial dynamics in the disease (*San Martin et al., 2012 Neurodeg Dis*). The effects of iron in models of the disease were also investigated (*San Martin et al., 2012 Biometals*).

(ii) Therapeutic strategies: As described last year in the annual report, BNI members established collaboration with the biotechnology company Genzyme Corporation. Together we are currently developing Adeno-Associated Viruses (AAVs) for future gene therapy. We have been able to test methods to deliver a transcription factor into the spinal cord in animal models of injury. This strategy enhanced motor recovery after trauma (*Valenzuela et al., 2012 Cell Death Dis.*) and decreased abnormal protein aggregation on a Huntington´s disease model *in vivo* (*Zuleta et al., 2012 Biophys Biochem Res Comm*). These two studies were published in collaboration with two Genzyme scientists.

(iii) Studies in Chilean patients: HS and PM continue developing a large study that combines basic and clinical aspects searching for biometrics in patients with schizophrenia. The specific aim is to contribute to improve diagnostics and therapeutics follow-up (See also RL5). These studies were highlighted in CNN and in newspaper reports. We have also developed a large analysis of most Chilean patients affected with Creutzfeldt-Jacob Disease. We have analyzed the CSF of 40 patients and performed the regular diagnostic test based on the detection of 14-3-3 protein. We have investigated the expression pattern of the prion protein and found interesting changes that will help for future diagnostic tests (*Torres et al., 2012 PLoS One*). These studies were also highlighted in CNN and printed press.

RL7. Applied mathematics and biomedical informatics: During this period the mathematics and biomedical informatics group has been consolidated (BNI-BioMat). Image processing and medical imaging specialists Dr. M Cerda (BNI-BioMat) and Dr. V Castañeda (SH) obtained BNI-postdoctoral fellowships for their projects *'Dynamics of morphology, topology, and transport processes in tubular cellular structures'* and *'Light sheet based microscopy and data processing for the analysis dynamics, multicellular events in large specimens'*. Dr. G Reig has been awarded with a 3-year CONICYT postdoctoral fellowship in collaboration with MC. S Vargas, MSc in Biophysics, entered BNI-BioMat. Electronics engineer F Santibáñez (BNI-BioMat) enrolled in a PhD program, and bioinformatics engineer Luis Briones (BNI-BioMat) together with J Jara (BNI PhD-student) and Dr. O Ramírez (currently a BNI postdoctoral fellow with SH) established a strong and collaborative team. During this period we have fostered:

(i) New imaging techniques: Components for Super-resolution Optical Fluctuation Imaging (SOFI) in combination with a new confocal microscope LEICA LSI have been installed combining makro-zoom LSI (mm range), confocal imaging (250 nm range), and SOFI (80 nm range) into a unique research equipment for Latin American researchers. Funding to install a NanoZoomer Whole-Slide Tissue Scanner (Hamamatsu) has been awarded to SH's 3-years R&D FONDEF project '*Microscopía Virtual - Centro de Patología Digital Asistida (CPD) por Internet*' to allow tissue imaging for the first time in Chile.

(ii) High-, mid-, and low level mathematical-computational methods for microscopic image analysis in combination with high performance computing (HPC): Computational backbone for cumulant calculations with SOFI were implemented with J Enderlein's Group for Biophysics / Complex Systems, U-Göttingen, Ger. SH's new 3-years FONDECYT project *'Fast Computational Schemes for the Analysis of Morpho-Topological Data from High Throughput Microscopy*' together with a novel 2-year U-Redes Project *'BioMed-HPC: Network for Biologic and Medical HPC'* (Director SH) will connect BNI to the National Laboratory for HPC (www.nlhpc.cl).

(iii) R&D of internet assisted services for diagnosis and clinical research: SH's *spin-off* for Internet Assisted Medical Services CEDAI SpA, www.cedai.cl, received awards from UNIVERSA and the General Iberoamerican Secretary 2012 on a national and international level. R&D services have been installed as pilot versions at national public hospitals and private clinics.

Together these tools, equipment and procedures provide a continuous and flexible support to the studies of dynamic and large-scale phenomena from sub- to supra-cellular levels with PIs of the BNI (see respective research lines).

Two publications in 2012 applied novel, quantitative approaches for true and random colocalización (*Astorga et al., 2012 PLoS ONE*, CDA imageJ plugin published by SCIAN-Lab) and live cell imaging and tracking (*Urra et al., 2012 PLoS ONE*, with LL). CDA plugin is constantly improved by ourselves and others (e.g U-Sussex). A special issue of '*Machine Vision and Applications*' summarized our advances for motion analysis based on optical flow techniques and documented source code has been submitted to the new online journal *IPOL-LA* (Latin American Section of *Image Processing On Line*). Finally, novel techniques to determine surface properties of 3D biophysical model systems have been published (Husen *et al.,* 2012). Besides numerous contributions for national and international meetings, summer schools in medical informatics and neuroscience imaging technologies, symposia, and workshops (in collaboration with MC/AC/LL/CH). The most relevant prize during this period was the Iberoamerican Award on Innovation and Entrepreneurship for CEDAI SpA. € 20.000 were awarded during the 2012 Ibero-American Summit of Heads of State and Governments in Jerez (Spain). We were invited to the VIII Ibero-American Business Conference, which contributes to the elaboration of Economic Perspectives for Latin-America 2013 (ISBN 9789264183742). Through this, BNI-BioMat contributed to develop imaging technologies from basic science to applied medicine and tele-medical services with a high degree of visibility within the Ibero-American context.

RL8. Clinical research and capacity building: During this period we have continued working in the comparison between bipolar II patients and borderline personality disordered patients (HS in collaboration with S. Jerez, P. Iturra and J. Villarroel). The long-term aim of this study is to define clinical and genetic differences between these entities to contribute to their differential diagnosis. We have investigated the relationship between neuroticism and clinical response to fluoxetine in impulsive aggression in borderline personality disorder, and the association between neuroticism and 5-HTTLPR polymorphisms and suicide response to SSRIs. Four posters were presented in the *20th European Congress of Psychiatry in Prague, Czech Republic*. Other results have been presented at the *LXVII Congreso Chileno de la Sociedad Chilena de Neurología, Psiquiatría y Neurocirugía (SONEPSYN)*.

We have continued a large study of schizophrenic patients in search of genetic, behavioral and electroencephalographic markers (PM/HS). This project includes patients from Clínica Psiquiátrica Universitaria (U Chile), Hospital del Salvador (U Chile) and Instituto Psiquiátrico Dr. José Horwitz in Santiago (see also RL 5).

Another project driven by Rodrigo Nieto MD, a young clinician currently enrolled in a PhD. program, currently evaluates the use of the levels of circulating brain-derived neurotrophic factor

(BDNF) as a biomarker for cognitive function and clinical response to atypical antipsychotics. Results have been presented at *American Psychiatric Association (APA) Annual Meeting* in Philadelphia U.S.A., and in the *Asociación Psiquiátrica de América Latina (APAL) Meeting* in Buenos Aires, Argentina. A review about BDNF and Schizophrenia was submitted to *Frontiers in Schizophrenia* (*Nieto, Silva, and Kukuljan 2012, submitted*).

As a result of multiple clinical encounters the concept of a clinical research platform has gathered momentum. A BNI clinical coordinator has been hired and multiple agreements between BNI and clinical services are currently under preparation. Agreement has been reached among BNI members to secure additional strategic funds to support the clinical research platform and to prepare the project for additional funding and collaborations. This project will focus initially in establishing unifying criteria for clinical research (informed consents, ethical issues, sample management, etc). These topics will be evaluated in depth during the first BNI clinical symposium in April 2013.

b) Publications:

During this funding period BNI members published 36 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	31	34
	Other Researchers		2
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		
	Other Researchers		
Total of Publications		32	36

c) Other achievements:

Patents:

No changes relative to the previous period are reported.

Intellectual property:

No changes relative to the previous period are reported.

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)	43	30
Invited presentations (not included in above row)		7
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)		1

- **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 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 of Adjunct Investigators José Luis Valdés, Adrián Ocampo and Nancy Hitschfield. In total we met on 34 formal occasions during 2012. Additionally, we have carried out a series of internal seminars open to the entire institute using a dynamic and highly formative formula. Briefly, projects of specific research lines were presented in short 5 min talks plus 3 min questions, in English, by their leading students or postdocs. Each session was dedicated to one particular research line, and they were perceived as useful to communicate advances and very effective as a training experience. We have also invited external speakers for regular seminars in the area of neuroscience.

We supported four larger scientific initiatives during this period. First we sponsored a symposium at the *14th International Neuroscience Winter Conference* held in Austria. BNI Investigator Mario Herrera-Marschitz was responsible for its organization. The symposium provided a great opportunity to promote the research and aims of BNI within an international audience. In addition, three scientific events took place in Chile. Lisette Leyton organized a BNI-sponsored symposium at the *Chilean Society for Cell Biology* in Puerto Varas. This meeting represents one of the largest scientific conferences in the country with more than 400 attendants, most of them graduate and undergraduate students. BNI also co-sponsored the "*Generation, Degeneration and Regeneration of the Nervous System*" workshop. BNI's investigator Manuel Kukuljan co-organized the activities that included scientific lectures by a leading group of neuroscientists from University of California, San Diego, and national researchers from BNI and MINREB, a Millenium Initiative Nucleus. The event that had more than 300 participants allowed local researchers and graduate students to engage in

top-quality scientific discussions. It also included the active role of high-school students and was particularly attractive to a group of approximately 19 students from the virtual community "Chile Va!" that traveled to Santiago from cities that are normally perceived to have lower education opportunities. The collaboration between BNI and MINREB was highly praised by all attendants, and the program and central venue (Centro Cultural Gabriela Mistral) contributed to its impact within and beyond academia. Finally, Jimena Sierralta co-organized the international course "*Small Brains, Big Ideas*" that centered on the value of animal research models to understand the brain and behavior. The use of multiple animal models is at the core of BNI's philosophy and this event was ideal to explore their advantages and applications in the context of lectures and practical work. Students from Chile and South America attended the workshop, and a team of national and international neuroscientists led the scientific and outreach activities, in total more than 50 people were involved. The workshop was a joint effort between BNI and CNV, another Millenium Initiative Institute, demonstrating the productive collaborative approach of BNI (***see Annex 4***).

- **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), *Current Opinion in Cell Biology* (CHz, Editor Special Edition 2011), *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 Neurobiology* (MK, Editor), *Frontiers in Integrative Neuroscience* (PM, Editor). Additionally BNI members are committed to raising the impact of *Biological Research*, an ISI indexed national journal (CH and LL, Editors).

- **Awards:**

During 2012 Claudio Hetz received an award from the Christopher Reeve Spinal Cord Injury and Paralysis Foundation (US) for his work on spinal cord injury and potential applications using gene therapy. He was also awarded the FEBS Anniversary Prize 2012 (Spain) for his outstanding contributions to molecular biology and biochemistry as a young investigator. Steffen Härtel received the Second Iberoamerican Prize for Innovation and Entrepreneurship (Spain) for his outstanding contributions to quantitative digital sperm analysis. Steffen has been actively promoting research and development in telemedicine, and this achievement sets the basis for future work on virtual microscopy and applications for pathology and diagnostics based on remote access. His award exemplifies the efforts of BNI to establish productive contacts with industry and applied science. *Photograph (right): Claudio Hetz and Steffen Härtel, awardees 2012.*

Young BNI investigators were also awarded during 2012. Andrea Paula-Lima was awarded the Third World Academy of Sciences (TWAS) Young Affiliate Award, allowing her to become a young member of this influential body of scientists for the Latin American community. Vicente Valenzuela, a BNI student working under the supervision of Claudio Hetz received the two important awards this year. From the Chilean Foundation of Cell Biology he received the Best Undergraduate Thesis Award 2012. The Foundation confers the award to the best undergraduate thesis in the country in the area of cell biology. Additionally, he was awarded best poster presentation at the Young Science Conference (U. de Chile). Both awards acknowledge his contribution to spinal cord injury and gene therapy in models of amyotrophic lateral sclerosis (ALS).

José Cánovas, a PhD student currently working under the supervision of Manuel Kukuljan received the best presentation award at the *Chilean Society for Cell Biology Meeting 2012* for his work on neuronal migration in the mouse brain. Fernanda Lisbona working with Claudio Hetz was awarded a traveling fellowship from the American Society for Biochemistry and Molecular Biology (ASBMB) to work at Dana-Faber Cancer Institute, Harvard Medical School. Together, these awards continue to demonstrate the quality of our young investigators and the dedication of the entire BNI team to creative thinking. We are particularly aware of the relevance of Dr. Paula-Lima's Fernanda's award, which confirm our commitment in creating equal opportunities for women. *Photograph (left): Young scientist awardees 2012 Vicente Valenzuela, Fernada Lisbona, Andrea Paula-Lima and José Cánovas.*

4. Education and Capacity Building

a) Education and Capacity Building:

As stated in the first report, the main 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 the realm of ongoing research of the highest level, i.e. 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.

A specific budget is allocated to each Investigator, who is expected to support students, through full or partial stipends, within the collaborative philosophy and guidelines of BNI. These may be used to complement existing fellowships from other sources (CONICYT, MECESUP). Additionally, BNI contributes with leverage and bridge funds to allow students to complete ongoing projects or resources to conduct their projects in competitive conditions. Overall, BNI directly supported the scientific training of 106 students. As in previous years, the quality of our students was guaranteed by the selection process at the FMed, which is highly competitive.

Postdoctoral candidates are invited to apply to bridge BNI funds twice a year. Eligibility includes commitment to apply to a Fondecyt postdoctoral fellowship during the corresponding period. Applications are managed and reviewed by MC/LL in collaboration with additional BNI members to avoid conflicts of interest. During 2012 BNI provided 9 full postdoctoral fellowships and contributed indirectly to support another 13.

Many students and young investigators currently interact with more than one Associate Investigator and as a result we have increased the number of co-mentoring (e.g. Gabriela Martínez AC/CHz, Cristián De Gregorio AC/JS, José Cánovas MK/JS, Susana Brugues PM/MH). 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 BNI's events such as the "Generation, Degeneration and Regeneration of the Nervous System" workshop or the "Small Brains, Big Ideas" course. Additionally, students, postdocs and young investigators from several BNI labs have been particularly active in the outreach activity *Dendros.* We highlight the roles of Jonathan Wimmer (PM), Cecilia López (MK), Felipe Santibañez (SH), Jorge Jara (SH) and Jorge Toledo (AC). Students we also co-interviewed alongside Associate Investigators in each of the 9 radio programs entitled "*Conciencia en la Salud Mental*", which took advantage of the fact that many of them come from cities than smaller than Santiago or from rural areas, and we considered this to be a highly motivational theme for the programs.

Besides training in direct experimental research activities, all BNI Associate Investigators hold full time faculty positions at the FMed and Clinical Hospital of the Universidad de Chile. From these positions they lead or participate in formal teaching activities in graduate and/or clinical training (medical residency) programs, as well as basic science for medical and allied health profession students. As examples of graduate courses we mention "Neuropharmacology" (MH), "Cellular and Molecular Neuroscience" (MK), "Medical Informatics" (SH), Psychiatiy Residency Program (HS), "Mechanisms of Adaptation to Cellular Stress and its Role in Disease" (CHz) and "Cellular Physiology" (AC). Additionally, BNI Investigators are actively involved in the scientific education of professional (medical) students in research rotations.

b) Achievements and Results:

The great majority of BNI publications are co-authored by students (32 out of 36). Importantly, student presentations in national and international meetings also represent the majority of authorships. Many of these reflect the convergence of disciplines (neurobiology/applied maths, neurobiology/clinic or applied math/clinic). 8 students and young investigators, Luis Briones, Milene Kong, Fernanda Lisbona, Gabriela Martínez, Valentina Muñoz, Rina Ortiz, Eduardo Pulgar and Felipe Salech did short-term traineeships abroad.

During this period BNI continued its program of postdoctoral position awards, aimed at recruiting young investigators able to apply to external funding. In 2012 version of this system 7 postdoctoral investigators were supported (Areli Cárdenas, Mauricio Cerda, Melissa Nassif, Patricio Ahumada, Víctor Castañeda, Danilo Bilches, Germán Reigg) with a total of 9 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 20 undergraduate, 23 Masters and 63 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 postoctoral 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 Faculty of Medicine. 17 students trained at BNI are currently active in research, 7 are pursuing advanced studies and 3 are conducting clinical work. One former postdoc (Viviana Valdés) is currently Graduate Director of the Biotechnology Institute at Universidad Mayor.

Together, our training capacity and achievements during this period indicate that our students actively participate in transdisciplinary research, networking and outreach activities contributing to attain our goal of hosting a new generation of leading researchers and clinicians in a vibrant environment.

Summary Table*:*

Obtained Degree	Academy	Industry and Services	Studies	Research	Other (Specify the other type of activity
Doctoral				2	
Master					
Undergraduate			3	5	1
TOTAL			3	7	1

5. Networking and other collaborative work

a) Networking:

1. SOFI implementation in the framework of BNI

A network including BNI-Chile and scientists, mostly from the Georg August University in Göttingen, Göttingen, Germany, was established during 2010, for fostering an integrated *in vivo* genetic-morphogenetic approach to reveal the microscopic mechanisms that generate form, structure, and functional organization in the central nervous system. The network was first financed by a *Deutsche Forschungsgemeinschaft* (DFG) grant (€ 20.000 for a bilateral meeting in Santiago and € 9.000 for the visit of three Chilean researchers to Germany). Thus, an international collaborative platform could be created, focusing on a wide range of expertise, covering cellular physics, cellular and developmental neurobiology, genetics and microscopic imaging. The goal was to study genetic and molecular networks, associated to cell/tissue behavior, encompassing the morphological and functional organization of the brain.

A first "Initiation Phase" took place during January-December 2010. A second "Cooperation Phase" took place during January-December 2011. A third phase has taken place during 2012, organizing a visit of 5 BNI scientists to Göttingen (AC/MC/SH/LL/JS) and a symposium and workshop in Santiago, strengthened by additional funds obtained by BNI from an ICM Network Funds competition (Chile). The initiative also implied the exchange of students and investigators. Göttingen researchers working in close collaboration with Prof. Jörg Enderlein, an expert in the development of new methods of single molecule fluorescence spectroscopy and super-resolution imaging and their application to complex biological systems, visited BNI labs in Chile, and two young investigators from BNI (Omar Ramírez, Felipe Santibáñez) visited Göttingen for training in Super-resolution Optical Fluctuation Imaging (SOFI), a super-resolution microscopy technique developed by Prof. Enderlein.

2. NeuroSur

In the framework of the BNI-Chile and the Pasteur Institute-Montevideo, Uruguay, a network of scientific excellence, *NeuroSur*, was proposed in 2011, involving leading research groups from Argentina, Brazil, Chile and Uruguay. The objective was to identify 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 framework of excellence for scientific development and exchange of expertise, involving established senior and young scientific leaders, postdocs and students. The goal was to create a first class and highly synergistic scientific hub addressing relevant biomedical problems in the region to achieve global impact. A challenge was to promote translational development addressing the major mental health problems affecting the population of the region and worldwide. *NeuroSur* would provide the possibility of sharing expensive technological platforms not always available for individual laboratories, profiting from established international expertise, partnership and collaboration by individual research groups. A first meeting took place in Montevideo, Uruguay, during August 1-3, 2012, jointly organized by Pasteur Institute-Montevideo and BNI. The program included presentation of the main platforms supporting the initiative, Institute Pasteur-Montevideo (Dr. Luis Barbeito) and BNI-Chile (Dr. Andres Couve), as well as the Biomedicine Institute of Buenos Aires (CONICET-Argentina-Max Planck Institute-Germany). Five symposia provided a framework for individual presentations by the labs associated to the initiative, as well as presentation of available technological platforms already established in the region. In a round table the idea of a *NeuroSur* initiative, as well as that of

scientific and granting policies, inserted into international macro initiatives, was discussed, aiming to increase competitiveness and impact. The aim is to establish a pole of scientific excellence in the region, able to compete for international funds supporting and promoting the region. Agreement was achieved on three lines of propositions:
(1) Promotion of bilateral and multilateral institutional agreements, within the framework of Pasteur Institute-Montevideo and BNI Institute-Chile, involving technological platforms, expertise and international networks. The challenge of finding common topics of research was discussed, as well as the idea of enlarging the network, identifying other institutions already established in the region.
(2) Promotion of scientific collaboration on a lab basis, looking for synergy and improvement of scientific impact. Identification and setting up of high throughput and state of the art technological platforms. Exploring common scientific interests, objectives, goals and complementary methodologies, eventually leading to sharing rationales and working hypotheses, resulting in the formulation of original projects and publications.

(3) Promotion of International Educational ventures taking place in the region such as international schools, graduate courses and workshops taking. Promotion and/or affiliation to international initiatives, such as Gordon Conferences and other highly promoted conferences. Promoting reciprocal visiting of senior and young researchers, and graduate and undergraduate students mobility. Promoting the idea of co-mentorship and participation in evaluation committees. An important immediate goal is to establish a network for regional and international recruiting of postdocs (***see Annex 6***).

b) Other collaborative activities:

Several collaborative initiatives are already established. Individual initiatives involve the exchange of personnel and expertise with laboratories of US, Europe and Latin America, funded by DAAD-CONICYT (C.P. Heisenberg), FONDAP-CEMC, PBCT-Research-Rings (A. Maas, C. Best, C.P. Heisenberg, G. Randall), NIH (S. Moss), European Union (S Wilson), the Harold Leila Mathers Foundation (L Glimcher), and FONDECYT (L. Bagatolli, R. Kaufman, T. Blanpied), among others. 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. Álvaro Álvarez (U Queensland, Australia); Gabriela Martínez (Harvard School of Public Health, USA); Jorge Jara (U Heidelberg, Germany); Pamela Valdés (Ecole Polytechnique Fédérale de Lausanne, Switzerland); Valentina Muñoz Vio (Instituto Clemente Estable, Montevideo, Uruguay); Mario Rivera Meza (Dept. of Psychopharmacology, Central Institute of Mental Health J5, Mannheim, Germany). Furthermore, BNI has been host for prominent scientists from Europe, America and Latin America, giving lectures, participating in workshops, and/or Diploma initiatives. In summary, networks are established looking for innovation, synergy, partnership, and impact, promoting BNI as an international centre of scientific excellence.

6. Outreach and connections with other sectors

a) Outreach:

During 2012 we generated a variety of activities to consolidate a wide outreach platform. Our target included high-school students, medical communities, and the general public. In order to increase visibility we continued to work on our corporate image. A constant release of updated information about investigators, students, research lines, scientific activities and news related to the institute is now available on our website (www.bni.cl). We also created material to be printed or distributed electronically (brochures and newsletters), to provide relevant information about BNI activities to other sectors. *Photograph (right): brochure cover.*

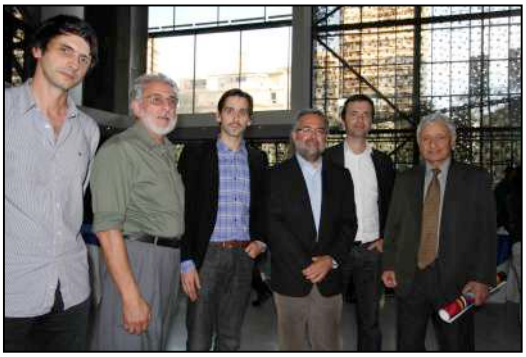
Regarding the general community, activities were designed to raise the interest in neuroscience. We provided tools to learn about the brain and its diseases, thus promoting awareness on mental health. We generated a set of 9 radio programs entitled "*Conciencia en la Salud Mental*", which was broadcasted on 125 stations, distributed in 15 regions, covering over 100 rural communities throughout the country. These programs were additionally compiled in a CD, which was distributed in 12 educational institutions nationwide. During this period BNI had strong media coverage. Scientists from the institute met with representatives of the Chilean Journalists Association (ACHIPEC), the Circle of Health Journalists and important printed media such as El Mercurio and La Tercera. We achieved 91 publications in print, digital and television (***See the list of BNI press in Annex 7.3***). *Photograph (left): La Tercera, Dr. Claudio Hetz and student Vicente Valenzuela*.


Tendencias

Científicos chilenos crean terapia con genes para reparar daño a médula espinal

Coordinating clinical meetings and seminars improved our connections with the medical community. We held 9 encounters with health professionals whose clinical practice is related to the research areas of BNI. The director and co-director of BNI attended all meetings, along with the authorities of each clinical service and researchers from all institutions numbering more than 250 in total. These activities allowed us to discuss up-to-date concepts, technology and approaches, and especially get a deeper understanding of relevant and local clinical problems. A number of partnerships and collaborative projects were generated as a result of these meetings. A particular event that generated considerable interest in the media and the general public was the release of the book *"La Esquizofrenia, de Kraepelin al DSM-V"* by Dr. Hernán Silva, a BNI Associate Investigator. This meeting gathered more than 200 health professionals, was co-sponsored by the pharmaceutical company Lundbeck and was featured in "La Cuarta" newspaper.

Three main activities were developed to reach the high-school student community: (i) Twelve scientific talks were carried out, most of them in collaboration with Explora-CONICYT, reaching over 1000 students from Santiago and other regions. *Photograph (right): Jimena Sierralta videoconference.* (ii) To promote direct interactions between high-school students and the active scientific community at BNI young students were invited to "BNI lab tours". In this context we created a strong partnership with the virtual student community "Chile-Va!" that allowed us to invite 19 young students from different cities to mingle with BNI scientists and visit their laboratories for three days. This activity was framed within the international workshop "Generation, Degeneration and Regeneration of the Nervous System" conducted on September 25-27, which brought together national and international researchers, graduate students and about 400 high-school students. The event attracted considerable media attention. *Photograph (left): Andrés Couve (UChile-BNI), Eduardo Macagno (UCSD), Felipe Court (PUC-MINREB), Manuel Kukuljan (UChile-BNI), Claudio Hetz (UChile-BNI) and Claudio Wernli (MSI) at the GAM workshop.*



We also sponsored an award for the Best Neuroscience Project at the 9th Science and Technology Regional School Congress, which was given to students Nicolás Kast-lend and Francisco Montero, from *Liceo Industrial Ingeniero Ricardo Fenner Ruedi de La Unión*, for their project "*The Postnatal Neurogenesis is Altered During Aging*". Both students along with their science teacher were invited to visit the BNI and share with researchers and students. (iii) Our third strategy was to develop scientific material to reach the general public. Whether physical or virtual, our aim was to catch people's attention, to raise interest in science and promote neuroscience as a fundamental aspect of everyday's life. In collaboration with Explora-CONICYT we produced a paper "brain hat", which is a do-it-yourself helmet that simulates a human brain indicating with a colorful display the location and function of different lobes within the cortex. This material was extensively used by Explora-CONICYT to promote last year's science theme: *Neurociencia: qué tienes en mente?* 30.000 "brain hats" were made and distributed throughout the country. The largest project we embraced last year was the creation of a web-comic called "*Dendros: a journey through the brain*" (*http://www.bni.cl/dendros/*). This material consists of a web platform that displays a fully interactive comic story, 3D animations, and neuroscience content. The comic is a science-fiction story about 2 young students that enter the brain using a machine called *Dendros*. They must travel within the brain in order to mechanistically fix a medical condition of amnesia. *Dendros* was specifically created to motivate high school students, using an entertaining story while providing accurate scientific information and up-to-date facts. Dendros was officially released in December with more than 200 students and authorities. The release included a scientific lecture on memory, presentation of the web platform, and a round of interactive comic through several touch screens. The event received considerable media attention.

In addition, during the National Week of the Science, our institute had a brain-shaped tent in the central and popular park, Quinta Normal, to welcome students from all over de country. During 4 days, 25,000 students enjoyed our stand, watched the trailer of Dendros, browsed through the interactive comic in specially installed touch screens and learned about the brain aided by BNI instructors and education material such as the "brain hat". *Photograph (right): A brief summary of the project "Dendros" appeared in El Mercurio.*

Científicos del Instituto Milenio de Neurociencia Biomédica:

A través de un web-cómic los alumnos pueden viajar al interior del cerebro

Programa Dendros es una herramienta interactiva que enseña acerca del funcionamiento del sistema nervioso.

Dr. Andrés Couve, director del proyecto.

El proyecto Dendros se expondrá durante 2013 en diversos establecimientos educacionales, donde se enseñarán sus distintas aplicaciones.

Together these outreach activities contribute to consolidate BNI as a resource center for specialized clinical practitioners and the general public (***see Annex 7***).

b) Connections with other sectors.

During this period we raised significant matching funds to support a number of activities. These included U$ 4,900 from Lundbeck for the release of the book "La Esquizofrenia, de Kraepelin al DSM-V" by Dr. Hernán Silva; advertising funds from Editorial Mediterráneo for the same event; U$7,500 from Explora RM for the National Week of the Science; and U$9,500 from Explora to print 30,000 "brain hats". Paola Cañón, Executive Director of BNI, played a major role in fund raising.

7. *Administration and Financial Status*

a) Organization and administration:

During 2012 BNI became a non-profit organization (RUT 65.059.721-4) and has completed all the legal requirements of the MSI. The temporary directory is currently constituted by Andrés Couve (President), Claudio Hetz (Vicepresident), Miguel Concha (Secretary), Manuel Kukuljan (Tresurer), Cecilia Hidalgo (Director), Cecilia Sepúlveda, Dean of the FMed (Director), Luis Michea, Director of Research and Development FMed (Director). Paola 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 more recently working towards creating a formal clinical research platform. The executive office is additionally constituted by recently hired reporter Antonella Sanguinetti, whose work focuses on web and press activities, and Johanna Jiménez, a law student who provides legal assistance. The grant management office is currently constituted by Ana Timmermann, who has extensive expertise in accounts managing and Millenium funds, Sandra Carrasco assistant accountant and Jorge Mansilla, informatics expert. Mrs. Timmerman monthly financial reports to the Ministerio de Economía have been spotless. A graphic design team led by Nicolás Vasquez and a team of journalists led by Inés Llambías contributed significantly to consolidate BNI's corporate image and promote its scientific and outreach activities. Rodrigo Tapia is BNI's artist in residence. He and his team have provided their unique talent to conceive and execute our main outreach products such as the "brain hat" and *Dendros*. *Photograph (right): Jorge Mansilla, Ana Timmermann, Sandra Carrasco, Johanna Jiménez and Paola Cañón.*

Category	*Female*	*Male*	*TOTAL*
Assistant & Technicians	33	24	57
Administrative Staff	4	1	5
TOTAL			

b) Financial Status:

See Annexes 9.1-9.3

8. Annexes

Annex 1.- Institute Researchers

1.1 Associate Researchers

Name	Research Line	Nationality	Gender	Date of birth	Profession	Academic Degree	Affiliation	Current Position	Relation with Center
Couve Correa, Andres Oscar	1, 2, 3, 4, 7, 8	Chilean	M	23-10-68	Biologist	D	University of Chile	Full 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 Muller, Mario	1, 3, 6, 8	Chilean	M	25-06-44	Medicine	D	University of Chile	Full Professor	2
Kukuljan Padilla, Mario	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 Esteban	5, 7	Chilean	M	30-04-60	Biologist	D	University of Chile	Associate Professor	2
Sierralta Jara, Jimena Alejandra	2, 3, 7	Chilean	F	12-09-62	Biochemist	D	University of Chile	Associate Professor	2
Silva Ibarra, Hernán	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	Affiliation	Current Position	Relation with Center
Hidalgo Tapia, Cecilia	4, 6	Chilean	F	10-06-41	Biochemist	D	University of Chile	Full Professor	2
Hitschfeld Kahler, Nancy	7	Chilean	F	20-11-60	Science Computer	D	University of Chile	Associate Professor	2
Ocampo Garcés, Adrián	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
Valdés Guerrero, José 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:

Valdés V, Valenzuela JI, Salas DA, Jaureguiberry-Bravo M, Otero C, Thiede C, Schmidt CF, **Couve A**. (2012). Endoplasmic Reticulum Sorting and Kinesin-1 Command the Targeting of Axonal GABA(B) Receptors. PLoS One 7(8):e44168.

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Rodriguez DA, Zamorano S, Lisbona F, Rojas-Rivera D, Urra H, Cubillos-Ruiz JR, Armisen R, Henriquez DR, H Cheng E, Letek M, Vaisar T, Irrazabal T, Gonzalez-Billault C, Letai A, Pimentel-Muiños FX, Kroemer G, **Hetz C**. (2012). BH3-only proteins are part of a regulatory network that control the sustained signalling of the unfolded protein response sensor IRE1α. EMBO J. 31(10):2322-35.

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Gupta S, Read DE, Deepti A, Cawley K, Gupta A, Oommen D, Verfaillie T, Matus S, Smith MA, Mott JL, Agostinis P, **Hetz C**, Samali A. (2012). Perk-dependent repression of miR-106b-25 cluster is required for ER stress-induced apoptosis. Cell Death Dis. 3:e333. doi: 10.1038/cddis.2012.74.

Martínez G, **Hetz C**. (2012). Cell-nonautonomous control of the UPR. EMBO Rep. 13(9):767-8. doi: 10.1038/embor.2012.117.

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Nassif M, **Hetz C**. (2012). Autophagy impairment: a crossroad between neurodegeneration and tauopathies. BMC Biol. 10:78.

Urra H, **Hetz C**. (2012). The ER in 4D: a novel stress pathway controlling endoplasmic reticulum membrane remodeling. Cell Death Differ. 19(12):1893-5. doi: 10.1038/cdd.2012.127.

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Oliva C, Escobedo P, Astorga C, Molina C, **Sierralta J**. (2012). Role of the MAGUK protein family in synapse formation and function. Dev Neurobiol. 72(1):57-72.

Copaja M, Venegas D, Aránguiz P, Canales J, Vivar R, Avalos Y, García L, Chiong M, Olmedo I, Catalán M, **Leyton L**, Lavandero S, Díaz-Araya G. (2012). Simvastatin disrupts cytoskeleton and decreases cardiac fibroblast adhesion, migration and viability. Toxicology 294(1):42-9.

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3.1.2.- Other researchers:

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3.2.- SCIELO Publications or Similar to SCIELO

3.3.- Scientific Books and Chapters

3.3.1 ***Associate Researchers***

Silva, H (2012) La Esquizofrenia De Kraepelin Al DSM-V. Ed Mediterráneo, Santiago, Chile, 163p

3.4.- Other Publications

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	32	89	3	8	1	3		
SCIELO Publications or Similar to SCIELO Standard								
Books and chapters	1							
Other Publications								
Total of publications	33	89	3	8	1	3		

Annex 4.- Organization of Scientific Events

Scope	Title	Type of Event	City	Country	Responsible Researcher
Internacional	14th International Neuroscience Winter Conference, BNI Symposium: Conditioned vulnerability elicited by metabolic insults ocurring at birth: New paradigms for understanding neurophysiatric disorders with delayed clinical onset	Symposium	Solden	Austria	M Herrera-Marschitz
	Genration, Degeneration and Regeneration of the Nervous System	Workshop	Santiago	Chile	M Kukuljan
	Chilean Society for Cell Biology XXVI Annual Meeting: Symposium The Biomedical Neuroscience Institute, a MillenniumScience Initiative Institute and The Fogarty International research Collaboration Award (FIRCA)-NIH: Cell-Cell interactions governing cell m	Symposium	Puerto Varas	Chile	L Leyton
	International Course: Small Brains, Big Ideas	Workshop	Santiago	Chile	J Sierralta
Nacional	BNI Seminar: Bioquímica en tiempo real con microscopía FRET	Seminar	Santiago	Chile	A Couve
	BNI Seminar: Sub-cellular functional dynamycs	Seminar	Santiago	Chile	A Couve
	BNI Seminar: Cellular identity and morphology: to understand how gene expression determines morpho-fuctional features throughout the development and lifespan of neurons	Seminar	Santiago	Chile	A Couve
	BNI Seminar: Visión iconoclasta sobre el EEG: de sincronías y envolventes	Seminar	Santiago	Chile	A Couve
	BNI Seminar: Complexina regula la velocidad de la transmisión sináptica	Seminar	Santiago	Chile	A Couve
	BNI Seminar: Dysfunction of proyein degradation pathways in Alzheimer´s desease: the case of Amyloid Precursor Protein	Seminar	Santiago	Chile	A Couve
	BNI Seminar: Supra-cellular development and circuits	Seminar	Santiago	Chile	A Couve
	BNI Seminar: Efecto de la experiencia en la función sináptica	Seminar	Santiago	Chile	A Couve

Annex 5.- Education and capacity building

5.1 Capacity Building inside MSI Centers

MSI RESEARCHER	NUMBER												TOTAL NUMBER PER MSI RESEARCHER		
	Undergraduate students			Graduate students						Postdoctoral researchers					
				Masters			Doctoral								
	F	M	T	F	M	T	F	M	T	F	M	T	F	M	T
A Couve	1	1	2	2		2	3	3	6	1		1	7	4	11
C Hetz	4	1	5	1	2	3	4	4	8	5	4	9	14	11	25
M Concha	2		2	1	1	2	3	6	9	1	2	3	7	9	16
S Härtel	1	2	3	2	1	3	2	2	4		2	2	5	7	12
M Herrera-Marschitz		1	1	1	2	3	2	2	4		1	1	3	6	9
C Hidalgo							2	1	3				2	1	3
M Kukuljan							2	2	4	1		1	3	2	5
L Leyton	1		1				2	1	3	1		1	4	1	5
P Maldonado				3	5	8	1	7	8		3	3	4	15	19
J Sierralta	1	4	5	2		2		3	3				3	7	10
H Silva											1	1		1	1
A Couve, J Sierralta								1	1					1	1
L Leyton, M Herrera-Marschitz								1	1					1	1
L Leyton, A Quest		1	1				3	5	8				3	6	9
M Kukuljian, H Silva								1	1					1	1
TOTAL	10	10	20	12	11	23	24	39	63	9	13	22	55	73	128

Annex 5.2.- Short-term Traineeships of MSI students

Student name	Institution	Country	Advisor	Project Description	Starting Date [dd/mm/yy]	Ending Date [dd/mm/yy]
Briones Montecinos, Luis	King's College London	United Kingdom	Claudia Linker	Analyze in detail the process of cell migration. Quantifying the behavior as a group, and their dynamics, and to analyze the morphological changes undergone by these cells during the migration process.	11-11-12	15-01-13
Kong, Milene	University of North Carolina, Chapel Hill	USA	Rafael Garcia-Matta	Evaluation of GTPase activation: kinetics and regulation	09-04-12	29-06-12
Lisbona, Fernanda	Dana-Farber Cancer Institute. Harvard Medical School	USA	Dr. Anthony Letai	Verification if the putative BH3 motifs present in RECS1 are functional.	17-11-12	17-02-13
Martinez, Gabriela	Harvard School Public Health - Harvard University	USA	Dr. Laurie Glimcher	In Dr. Laurie Glimcher's laboratory at Harvard School of Public Health,Boston USA, I was developing part of aim 1 of my doctoral thesis related to cloning of the kif17 promoter region, and I measured the activation of the transcription factor XBP1 in this region using the luciferase assay. Within this context, I am learning and developing the technique of chromatin immunoprecipitation to assess the direct binding of XBP1 in this region.	28-09-11	26-02-12
Munoz Vio, Valentina	Instituto Clemente Estable, Montevideo	Uruguay	Federico Dajas	Evaluation of toxicity of nanoparticles in PC12 cells	15-10-11	26-10-12
Ortiz, Rina	The University of Queensland	Australia	Justin Cooper-White	The group in Australia specialize in nanoengineer and prepare microchambers to study cell migration, which can be covered with different extracellular matrix proteins. These chambers were used to study the role of caveolin-1 on cell migration.	30-01-12	03-05-12
Pulgar, Eduardo	Janelia Farm, HMMI	USA	Phillip Keller	Perform imaging of developing kupffer vesicles in zebra fish using Light Sheet Microscopy	22-10-12	09-11-12
Salech Morales, Felipe	Stanford University	USA	Theo Palmer	To determine if klotho protein is an inhibitor of Adult Hippocampal Neurogenesis in mice	11-05-12	12-08-13

Annex 6.- Networking and other collaborative work

6.1 Networking

Network Name	Network Scope	Network Participants				Institutions
		From the Center		External		
		Researchers	Postdocs/ Students	Researchers	Postdocs/ Students	
NeuroSur	LatinoAmerican	Andrés Couve, Claudio Hetz, Miguel Concha, Steffen Hartel, Mario Herrera-Marschitz, Cecilia Hidalgo, Manuel Kukuljan, Lisette Leyton, Pedro Maldonado, Jimena Sierralta, Hernán Silva		Luis Barbeito, Eduardo Arzt, Alfredo Cáceres, Flavio Zolessi, José Luis Badano, Alejandro Schinder, Federico Dajas, Fernando Pitossi, Raul Russo, Marcelo Rubinstein, Sergio Ferreira		BNI; Instituto Pasteur Montevideo; Instituto de BioMedicina de Buenos Aires-CONICET-Partner Sociedad Max Planck, y UBA; Facultad de Ciencias, Universidad de la República. Pasteur-Montevideo, Uruguay;Fundación Instituto Leloir, BA, Argentina;Clemente Estable Institute, Montevideo, Uruguay; University of Rio de Janeiro, Rio de Janeiro, Brazil
Superresolution optical fluctuation imaging (SOFI) Network for Neuroscience	Internacional	Andrés Couve, Miguel Concha, Steffen Hartel, Lisette Leyton, Jimena Sierralta	O Ramirez, V Castañeda, M Cerda	Joerg Enderlein, U Kubischeck	Anja Huss	BNI, U-Goettingen, U-Bonn

Annex 6.2.- Other collaborative activities

Activity Name	Co-Participant Institution(s)	Participants [Number]				Products [Type & Number]
		MSI center		External		
		Researchers	Postdocs/ Students	Researchers	Postdocs/ Students	
Workshop ¨Generation, Degeneration and Regeneration of the Nervous System¨	University od San Diego (UCSD), Millenium Nucleous for Regenerative Biology (MINREB)	4	at least 10 postdoc/ at least 40 students	9	0	12 scientific conferences, 6 outreach talks, 4 meetings with postdocs and graduate students
International Course: Small Brains, Big Ideas	Centro Interdisciplinario de Neurociencia de Valparaíso (CINV), UMASS medical School, Pasteur Institure, Wellcome Trust	1	0/3	9	1 postdoc/30 students	15 lectures, 7 practical sessions, 12 scientific Conferences, 2 outreach conferences
Chilean Society for Cell Biology XXVI Annual Meeting: Cell-Cell interactions governing cell migration	The Fogarty International research Collaboration Award (FIRCA)-NIH	2	0	1	0	1 Special edition with reviews from each researcher

Annex 7.- Outreach

7.1.- Outreach activities throughout the period

a. International Events

b. National Events:

Title of the Event	Date	Place	Target Audience
Clinical Meeting	25-10-11	Hospital clínico psiquiátrico, Santiago	Medical public services, medical student, general community
Clinical Meeting	20-01-12	Hospital Clínico Universidad de Chile, Santiago	Medical public services, medical student, general community
Clinical Meeting	11-04-12	Clínica Alemana, Santiago	Medical public services, medical student, general community
Clinical Meeting	24-04-12	Clínica Las Condes, Santiago	Medical public services, medical student, general community
Clinical Meeting	05-06-12	Hospital San Borja, Santiago	Medical public services, medical student, general community
Clinical Meeting	18-07-12	Hotel Sheraton, Santiago	Medical public services, medical student, general community
Clinical Meeting	26-06-12	Instituto Neurocirugia Asenjo, Santiago	Medical public services, medical student, general community
Clinical Meeting	05-09-12	Teletón, Santiago	Medical public services, medical student, general community
Clinical Meeting	21-12-12	Hospital UC, Santiago	Medical public services, medical student, general community
Educational talk *¨Miércoles en la Academia¨: Los secretos detrás de la memoria*	14-09-12	Science Academy, Santiago	Student, general comunity
Educational talk *¨Miércoles en la Academia¨: Educación y Neurociencia, los desafíos de una convergencia necesaria¨*	13-06-12	Science Academy, Santiago	Student, general comunity
Video conference: *¨Las moscas y cómo funciona el cerebro¨*	24-05-12	Universidad Austral, Los Ríos	Secondary students
Video conference: *¨Mitos y realidades del cerebro¨*	09-05-12	Faculty of Medicine, University of Chile, Santiago	Secondary students
Scientific activity for college students *¨Fiesta de la Neurociencia¨*	03-10-12	Parque Quinta Normal, Santiago	Students in general, general comunity
Education activity *¨Lanzamiento web-comic Dendros¨*	11-12-12	Faculty of Medicine, University of Chile, Santiago	Students in general, general comunity
Educational talk The Magnificent Migration of the Monarch Butterfly	05-11-12	Faculty of Medicine, University of Chile, Santiago	Secondary and university students
Conference for undergrade student	25-09-12	Centro Cultural Gabriela Mistral, Santiago	Secondary and university students
Conference for undergrade student	26-09-12	Centro Cultural Gabriela Mistral, Santiago	Secondary and university students
Conference for undergrade student	27-09-12	Centro Cultural Gabriela Mistral, Santiago	Secondary and university students
College students activity *¨Dendros: un viaje por el cerebro¨*	01-10-12	San Sebastián University, Los Ríos	Secondary students

7.2.- Products of outreach

Type of product	Quantity	Target Audience	Scope
Reading text to stimulate interest in neuroscience : *Cómic Dendros*	1	University, Secondary and Primary students and Community in general	Local
Didactic material to introduce brain and neuroscience subjects *¨Gorro-cerebro¨*	1 (more than 30.000 print material)	University, Secondary and Primary students and Community in general	National
Radio program and CD with nine interviews with researchers	1 (more than 200 copies)	University, Secondary and Primary students and Community in general	National
Book with Institute news: written, internet and television news in the public media	1	University, Secondary and Primary students, Community in general, Companies, Industries, Services and Public Services	National
Newsletter with information of the activities of the Institute	2 (semester)	Community in general and Companies, Industries, Services and Public Services	Local
Institute brochure	1	Community in general and Companies, Industries, Services and Public Services	Local
Institutional website	1	University, Secondary and Primary students, Community in general, Companies, Industries, Services and Public Services	National, International
On line platform: web-comic Dendros	1	University, Secondary and Primary students and Community in general	National, International
Promotional material: Dendros Trailer	1	University, Secondary and Primary students and Community in general	National, International

7.3.- Articles and Interviews

Type of media and scope	Local/Regional		National		International		**TOTAL**
	N° Interviews	N° Articles	N° Interviews	N° Articles	N° Interviews	N° Articles	
Written		8		27			**35**
Internet		7	1	31		1	**40**
Audiovisual		1	9	3	3		**16**
TOTAL		**16**	**10**	**61**	**3**	**1**	**91**

Annex 8.- Connections with other sectors:

9.1 Total incomes:

Funds	Accumulated incomes to last year [$]	2012 Incomes		Total incomes to 2012 [$]
		Amount [$]	Percentage of resources used by the Center [%]	
MSI	524.726.500	1.057.441.500	100	1.582.168.000
FONDECYT (AC) 1100137	50.000.000	50.000.000	60	100.000.000
FONDECYT (CHz) 1100176	105.000.000	51.287.500	0	156.287.500
FONDECYT (MC, SH) 1090242	45.000.000	-	-	45.000.000
FONDECYT (SH) 1090246	18.607.500	-	-	18.607.500
FONDECYT (MHM) 1080447	50.000.000	75.000.000	20	125.000.000
FONDECYT (CH) 1100052	51.250.000	51.250.000	20	102.500.000
FONDECYT (LL) 1110149	50.000.000	50.000.000	0	100.000.000
FONDECYT (MK) 1090281	40.000.000	45.000.000	100	85.000.000
FONDECYT (PM) 1090101	21.600.000	3.000.000	100	24.600.000
FONDECYT (JS) 1090272	45.000.000	45.000.000	50	90.000.000
FONDECYT (YI/MH) 1095021	50.000.000	-	-	50.000.000
FONDECYT (Paola Morales & MHM) 11070192	50.000.000	75.000.000	20	125.000.000
FONDAP 1501006 (CH, LL, CHz)	700.000.000	-	-	700.000.000
ANILLO-CONICYT ACT 66 (PM)	175.000.000	15.100.000	50	190.100.000
HHMI (MC) 55005940	48.500.000	-	-	48.500.000
FIRCA NIH-USA (AC)	11.000.000	11.000.000	25	22.000.000
FIRCA NIH-USA (LL)	48.000.000	-	-	48.000.000
CONICYT/DAAD No 1378-09529	10.000.000	-	-	10.000.000
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	5.000.000	50.000.000	5	55.000.000
Micheal J Fox Foundation For Parkinson Research, USA (CHz)	62.500.000	42.791.500	1	105.291.500
ALS Association, USA (CHz)	37.500.000	32.157.500	0	69.657.500
Guillermo Puelma Foundation	2.500.000	2.500.000	100	5.000.000
Genzyme, USA (CHz)	29.000.000	-	-	29.000.000
FONDEF (SH) D07I1019	51.688.000	-	-	51.688.000
FONDEF (SH) D11I1096	-	344.822.000	0	344.822.000
FONDECYT (SH) 1120579	-	156.007.500	10	156.007.500
U-REDES (SH)	-	244.927.500	0	244.927.500
ICM (SH)	-	30.538.500	100	30.538.500
FONDECYT (MEQ/MHM) 1130012	-	75.000.000	20	75.000.000
FONDECYT (MC) 1120558	-	55.396.500	20	55.396.500
FONDEF (AC, PM)	-	125.000.000	30	125.000.000
TOTAL	2.324.372.000	2.688.220.000		5.012.592.000

Exchange rate: US$1 = $500

9.2 Outcome structure

ITEM	Accumulated expenses to last year [$]	2012 Expenses [$]				Total expenses to 2012 [$]	%
		Operative	Networking	Outreach	**Total**		
Honoraria Researchers	51.200.000	102.400.000					
Honoraria students and other personnel	101.673.000	204.023.999					
Tickets and travel expenses	12.864.267	28.143.491	10.000.000	1.438.922	39.582.413	52.446.680	9,74
Materials/supplies	45.011.446	77.486.439	823.192	1.036.692	79.346.323	124.357.769	23,09
Goods and equipment	66.269.020	83.978.862	21.773.808	1.125.041	106.877.711	173.146.731	32,15
Infrastructure	7.000.000	49.000.000			49.000.000	56.000.000	10,40
Administrative expenses	17.899.057	46.209.729			46.209.729	64.108.786	11,91
Publications and subscriptions	-			1.812.890	1.812.890	1.812.890	0,34
Consultancies	700.000	3.910.000		13.839.280	17.749.280	18.449.280	3,43
Overhead	10.629.668				-	10.629.668	1,97
Insurance costs	-	1.741.580			1.741.580	1.741.580	0,32
Legal personality expenses	-				-	-	-
Others	-			35.783.993	35.783.993	35.783.993	6,65
Total Expenses ($)	**313.246.458**	**596.894.100**	**32.597.000**	**55.036.818**	**378.103.919**	**538.477.377**	**100**

9.3 Financial accounting

ITEM	2012 [$]			
	Operative	**Networking**	**Outreach**	**Total [$]**
Income	918.765.000	34.997.000	55.037.000	1.008.799.000
Outcome	596.894.100	32.597.000	55.036.818	684.527.918
Annual balance	321.870.900	2.400.000	182	324.271.082