B·DEBATE International Center for Scientific Debate BARCELONA

INSTITUT GUTTMANN
HOSPITAL DE NEUROREHABILITACIÓ
Institut Universitari adscrit a la UAB

NEURO REGENERATION

IS IT THE COMMON FRONTIER FOR BIOENGINEERING, NEUROSCIENCE, ROBOTICS AND NEUROREHABILITATION?

October, 23rd and 24th, 2013

CosmoCaixa. C/ Isaac Newton, 26. Barcelona

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B·Debate International Center for Scientific Debate

BARCELONA

"B·Debate strives to help position Barcelona as a benchmark in generating knowledge and Catalonia as a country of scientific excellence"

B·Debate is an initiative of Biocat with support from "la Caixa" Foundation which aims to drive top-notch international scientific events to foster debate, collaboration and open exchange of knowledge among experts of renowned national and international prestige. The debates are focused on the integration of diverse disciplines of science in order to tackle major scientific and societal challenges.

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WELCOME

Dear colleagues and friends,

On behalf of the Institut Guttmann and B·Debate, it is our great pleasure to welcome speakers and attendees to the B-Debate workshop on Neuroregeneration. This scientific debate has been aimed to promote cooperative thinking about the barriers to restorative or curative therapies in central nervous system lesions, and how interdisciplinary approaches can overcome them.

Neuroregeneration is one of the most challenging endeavours in our time. Personal, familiar, social and economic burden of neurological diseases are extensively recognized. But while we are full of evidence of the potential capacity of neurons to regenerate in certain conditions and the plastic nature of the nervous system, we are still not able to provide curative or restorative treatments.

We are extremely thankful to the Scientific Committee to have assembled such a selected group of speakers from all different disciplines sharing the common endeavour of promoting recovery of neurological lesions. We hope that their contribution together with the debate of the attendees will enrich our thinking and provide an stimulating unique atmosphere to each one of us, promoting new thinking as the germen for innovative and, probably, interdisciplinary approaches.

We would also like to thank, Fundació Abertis, and TERCEL (Spanish Cooperative Network for Research in Cell Therapy, from the Instituto de Salud Carlos III), for allowing us to welcome you to Barcelona and giving us the opportunity of joining efforts in pushing frontiers away and building up a better world.

Yours sincerely,

Josep M. Ramírez (General Manager of Institut Guttmann) and **B·Debate** (Biocat and “la Caixa” Foundation)

PROGRAM

Wednesday, October, 23rd, 2013

9:00	**Registration**
9:30	**Welcome** **Ignasi López,** Deputy Director of Science, Research and Environment Area , "la Caixa" Foundation **Montserrat Vendrell**, CEO, Biocat **Josep Maria Tormos**, Research Director at the Institut Guttmann
9:50	**SESSION 1: NEUROREGENERATION, IS THERE ALREADY A TRANSLATIONAL EXPERIENCE IN CLINICAL PRACTICE?** Chair: **Joan Vidal**, Institut Guttmann, Barcelona, Spain
10:00	**Learning from Nerve Repair. Schwann Cell Transplantation into the Injured Spinal Cord** **James D. Guest**, University of Miami, Miami, USA
10:45	**Coffee break**
11:15	**Daniel P. Lammertse**, University of Colorado, USA
12:00	**John Steeves**, University of British Columbia, Vancouver, Canada
12:45	**Clinical Translation of Human Neural Stem Cells for Neurodegenerative Disorders** **Ann Tsukamoto**, StemCells INC, Newark, Canada
13:00	**Lunch**
15:00	**SESSION 2: WHICH ARE THE KEYSTONES IN NEUROREGENERATION TO BUILD UP A PATHWAY TO THE CLINICS?** Chair: **Anna Veiga**, Centre de Medicina Regenerativa de Barcelona, Barcelona, Spain
15:10	**Reprogramming and Regeneration Strategies for Healing and Improving Human Health** **Juan Carlos Izpisúa**, Salk Institute for Biological Studies, San Diego, USA and Center for Regenerative Medicine, Barcelona, Spain
15:50	**Preclinical Studies of Rho Inhibition to Enhance Axonal Regeneration After SCI** **Marina Mata**, University of Michigan, USA
16:30	**Coffee break**
16:40	**Preclinical Studies of Rho Inhibition to Enhance Axonal Regeneration After SCI** **David Fink**, University of Michigan, USA
17:20	**Challenges for Clinical Translation of Stem Cells in Amyotrophic Lateral Sclerosis** **Letizia Mazzini**, Eastern Piedmont University, Novara, Italy
18:00	**Visit to Cosmocaixa**
19:00	**Cocktail at Cosmocaixa**

PROGRAM

Thursday, October, 24th, 2013

9:30	**SESSION 3: IS NEUROREGENERATION THE "NEXT STOP" IN SPINAL CORD INJURY MEDICAL CARE?** Chair: **Xavier Navarro**, Institut de Neurociències, UAB Barcelona, Spain
9:40	**Future Regenerative Therapies** **James Fawcett**, University of Cambridge, United Kingdom
10:25	**Coffee break**
10:45	**Towards the Combination of Cell Therapy and Neurosteroid Treatment to Repair the Injured Spinal Cord** **François Féron**, Centre National de la Recherche Scientifique, Marseille, France
11:30	**Armin Blesch**, Universitätsklinikum Heidelberg, Germany
12:15	**Critical Issues in Stem Cell Therapy in Experimental SCI** **Alessandro Vercelli**, Neuroscience Institute of the Cavalieri Ottolenghi Foundation, Faculty of Medicine and Surgery, and Neuroscience Institute of Turin, Italy
13:00	**Lunch**
14:30	**SESSION 4: IS NEUROREGENERATION FEASIBLE WITHOUT A MULTIDISCIPLINARY APPROACH?** Chair: **Joan Comella**, Vall d'Hebron Institut de Recerca, Barcelona, Spain
14:40	**Conceptual and Actual Evidence That the Regenerative Potential Can only be Realized with a Multidimentional Approach** **V. Reggie Edgerton**, UCLA University, Los Angeles, USA
15:20	**Neuroregeneration and Neuroengineering – Competition or Convergence?** **Rüdiger Rupp**, Universitätsklinikum Heidelberg, Germany
16:00	**Coffee break**
16:10	**Neural Interfaces for Restoring Communication and Mobility** **Leigh R. Hochberg**, Brigham and Women's Hospital, Boston, USA
16:50	**Putting the Word "Cure" in Neurological Rehabilitation: a Field Comes of Age** **Rajiv Ratan,** Weill Cornell Medical College, New York, USA
17:30	**Characterization and Modulation of Brain Plasticity: Challenges and Opportunities** **Alvaro Pascual-Leone,** Harvard University, Boston, USA
18:10	**Conclusion and closing remarks**

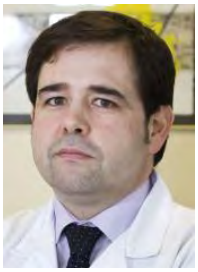
SCIENTIFIC COMMITTEE

Joan Vidal, Head of the Spinal Cord Injury Unit at **Institut Guttmann**, Barcelona, Spain

Specialist Physician in Physical Medicine and Rehabilitation. PhD University of Barcelona. Vice-president of the Spanish Society of Paraplegia since 2004, and Spanish representative at the International Society of Paraplegia - ISCOS- since 2006. And in 2008, he was member of SERMEF Board (Spanish Society of Physical Medicine of Rehabilitation). In 1992, he was the Medical healthcare coordinator of Institut Guttmann during the Paralympics Games in Barcelona. He is author and coauthor of more than a hundred scientific papers dealing with different aspects of spinal cord injury treatment and rehabilitation. As a researcher he has taken part of more than a forty national and international projects dealing with new technologies in rehabilitation. Coordinator of Regenerative Medicine Program in Institut Guttmann. He is also a professor and a researcher associated to UAB, and a prestigious international expert in the application of Neurotecnologies and innovative therapeutically Strategies for optimizing the regenerative capacity of the SNC and improve the prognosis of spinal cord injuries.

Montserrat Bernabeu, Head of Acquired Brain Damage Unit at **Institut Guttmann**, Barcelona, Spain

Montserrat Bernabeu is a specialist in Physical and Rehabilitation Medicine at the Institut Guttmann Neurorehabilitation Hospital in Badalona (Barcelona), Spain, since 1993. She started and, currently, leads the Brain Injury Unit which main goal is to provide rehabilitation treatment to people suffering sequel from any moderate/severe Acquired Brain Injury within an interdisciplinary framework and under high quality standards (JCI). She was born in Barcelona, Spain. She received her bachelor of Medicine and Surgery in 1988 from the “Universidad de Barcelona” University in Barcelona, Spain, and performed her Physical and Rehabilitation training at the “Universidad Autónoma de Barcelona” University in the same city, obtaining the specialist degree in 1992. She has been board member of the Catalan P&RM Society, she is a founder member of Spanish Society of Neurorehabilitation and she has been the President from 2004 to 2012. As a researcher she has taken part in several European projects dealing with new technologies in rehabilitation and was the Project Director of the ICF TBI-Core Sets which has been carried out in cooperation with the ICF Research Branch (DIMDI) at the Ludwing-Maximillian University in Munich, Germany. She is co-author of more than forty scientific papers dealing with different aspects of brain injury and is also a Board Member of International Journal of Rehabilitation Research Review.



Josep M. Tormos, Research Director at the **Institut Guttmann**, Barcelona, Spain

Jose M. Tormos Muñoz, MD PhD, Doctor in Medicine and Surgery for the University of Valencia, PhD special prize. Associated member of the Laboratory for Non Invasive Brain Stimulation of Harvard University, he is the Research Coordinator of the Institut Universitari de Neurorehabilitació Guttmann, and his areas of expertise include non-invasive Brain Stimulation, neurorehabilitation or brain plasticity, among others. He is the main investigator of the research projects "Non-invasive Brain Stimulation and robot-assisted rehabilitation to improve recovery in brain injury - FIS ECNI" and "eCENIT REHABILITA, Tecnologías Disruptivas para la Rehabilitación del Futuro"; and co-investigator on projects like "NeuroRehab 3e + D, modeling of electromechanical systems for automation, sensoring and monitoring in functional rehabilitation”, "BRAINABLE, Autonomy and social inclusion through mixed reality Brain-Computer Interfaces: Connecting the disabled people to their physical and social world " or "RETICS, Redes Temáticas de Investigación Cooperativa en Salud ", financed by different national and European institutions.

Xavier Navarro, Director of the group of Neuroplasticity and Regeneration at **Institut de Neurociències**, UAB, Barcelona, Spain

Xavier Navarro received the MD degree in 1978 and the PhD degree in 1985 from the Universitat Autònoma de Barcelona (UAB). He completed his specialty training in Neurology at the University of Barcelona, and in Neurophysiology at the University of Minnesota. He was Assistant Professor of the Department of Neurology of the University of Minnesota (1986-1988). He returned in 1988 to the UAB as Associate Professor in the Department of Cell Biology and Physiology, where he is currently full Professor of Physiology. He was founder of the Institute of Neurosciences of the UAB. Since 1989 he is heading the research Group on Neuroplasticity and Regeneration. His research interests are focused on axonal regeneration, functional restitution after nerve injuries, cell and molecular therapies for spinal cord injuries and motoneuron diseases, neuroprostheses, peripheral neuropathies and neuropathic pain. He has published more than 270 papers in refereed journals and books in these areas of the neurosciences, and directed 20 PhD theses. He also serves as scientific advisor of the Institut Guttmann. He has been member of the editorial boards of the journals: Restorative Neurology and Neuroscience, Journal of the Peripheral Nervous System, Muscle and Nerve, Frontiers in Neuroengineering. He was received "Ciutat de Barcelona" award in 1995, "Josep Trueta" award in 2000, ASPAYM award in 2009 for his scientific research.

Alvaro Pascual-Leone, Professor of Neurology at **Harvard Medical School**; Director of the **Berenson-Allen Center for Noninvasive Brain Stimulation**; Program Director of the **Harvard-Thorndike Clinical Research Unit**; and an Attending Neurologist at **Beth Israel Deaconess Medical Center**, Boston

Alvaro Pascual-Leone, MD, PhD, is Professor of Neurology at Harvard Medical School; Associate Dean of Clinical and Translational Research, Director of the Berenson-Allen Center for Noninvasive Brain Stimulation; Program Director of the Harvard-Thorndike Clinical Research Unit; and an Attending Neurologist at Beth Israel Deaconess Medical Center - all in Boston. He is a practicing behavioral neurologist and movement disorders specialist. Pascual-Leone is a world leader in research and development, clinical application, and teaching of noninvasive brain stimulation. His work has been fundamental in establishing noninvasive brain stimulation, particularly transcranial magnetic stimulation (TMS), as a valuable tool in cognitive neurology, increasing knowledge about its mechanisms of action, critically improving the technology and its integration with several brain-imaging methodologies, and helping to create the field of therapeutic noninvasive brain stimulation. In clinical trials, he has provided proof-of-principle evidence for the efficacy of noninvasive brain stimulation in treating various neurologic and psychiatric conditions, including epilepsy, stroke, Parkinson disease, chronic pain, autism, and drug-resistant depression. Pascual-Leone has authored more than 450 scientific papers as well as several books, and is listed inventor in several patents. Pascual-Leone's current research aims at understanding the mechanisms that control brain plasticity across the life span to be able to modify them for the patient's optimal behavioral outcome, prevent age-related cognitive decline, reduce the risk for dementia, and minimize the impact of developmental disorders such as autism. Presently he is also the principal investigator of two multicenter studies assessing the therapeutic utility of noninvasive brain stimulation in Parkinson disease.

Salvador Martínez, Head of Experimental Embriology Group at **Consejo Superior Investigaciones Científicas (CSIC)**, Universidad Miguel Hernández, Alicante, Spain

Salvador Martínez's laboratory consists of interdisciplinary research groups seeking basic understanding of the mechanisms that control the first steps in the proper development of the brain. The study focuses on those regions along the embryonic brain (secondary organizers) that secrete morphogenetic molecules (FGFs, SHH, WNTs) for further development of its various subdivisions. His research extends the understanding the fundamental alteration of these mechanisms (genetic and molecular) that are small or drastic events in the external and internal morphology of the different structures of the brain that are associated with clinically neurological disorders in humans such as autism, schizophrenia and mental retardation. Some of the tools used in this research are stem cells and the biotechnology related to this branch of biology for the development of palliative therapies applied in medicine (clinical trials). The long-term goal of this research is find and try procedures for diagnostics, prevention and treatment of congenital disorders of brain, both mental illness and in neurodegenerative diseases.

José Maria Moraleda, **Hospital Universitario Virgen de la Arrixaca**, Universidad de Murcia, Spain

José Maria Moraleda is director of the combined Adult and Pediatric Bone Marrow Transplant Program and director of the Cellular Therapy Unit at the University Hospital Virgen de la Arrixaca in Murcia, and is a Professor of Hematology at the University of Murcia Medical School. Since 2010 is the Coordinator of the Spanish Research Net of Cellular Therapy created by the Institute Carlos III. Moraleda earned his medical degree with honors at the University of Navarra Medical School in 1976. He completed an internal medicine program at the University Clinic of Navarra. He subsequently completed the residency in Hematology and earned a Ph.D. at the University of Salamanca in 1986. Moraleda performed a post-doctoral fellowship at the Hammersmith Hospital in London in 1987 and a research fellowship at the University of Washington and Fred Hutchinson Cancer Research Center during 1993-94. Since 1990 he has remained at the University of Murcia where he founded and directed the BMT program. His faculty appointments have been at the University of Salamanca Medical School and the University of Murcia Medical School where he served as vice-dean. He is member of various Spanish and International scientific societies such as EBMT, ASBMT, EHA, and AEHH. He has served as scientific assessor of the EMEA and the Spanish National Transplant Organization as well as Inspector of the JACIE program. Moraleda´s main research interest includes Hematopoietic Stem Cell Transplantation, Immunomodulation and translational research of Cellular Therapy and Regenerative Medicine. He has authored or co-authored ten book chapters, more than 90 research articles and 150 scientific abstracts.

Anna Veiga, Director of the Cell Bank at **Centre de Medicina Regenerativa de Barcelona (CMRB)** and Associate Professor at Universitat Pompeu Fabra, Barcelona, Spain

Anna Veiga Lluch (Barcelona 1956) received her Ph.D. in Biological Sciences from the Universitat Autònoma de Barcelona (UAB). She is currently director of the *Banc de línies cel·lulars* at the Centre de Medicina Regenerativa, Scientific Director of Service Reproductive Medicine at University Hospital Quirón-Dexeus, Associate Professor at Department of Experimental Sciences and Health, University Pompeu Fabra, and President of the European Society for Human Reproduction and Embryology until July 2013. Veiga was a pioneer in the study of reproduction and stem cell in Spain. Veiga is the recipient of several honors and awards, including Creu de Sant Jordi by the Generalitat of Catalonia (2004), Medalla Narcís Monturiol of Merit Science and Technology (2005), National Award for Scientific Culture of the Generalitat of Catalonia (2006), Medalla Josep Trueta for the Health Merit (2012), Honorary Member of the Institut Medicofarmacèutic of Catalonia (2013), and Honorary Medal of Parliament (Gold category, 2013) for her contribution on the promotion and consolidation of the science advances, especially in the field of biomedicine.

ORGANIZING COMMITTEE

Josep M. Ramírez, Managing Director at **Institut Guttmann**, Barcelona, Spain

Joan Vidal, Head of the Unit of the Spinal Cord Injury Unit at **Institut Guttmann**, Barcelona, Spain

Montserrat Bernabeu, Head of Acquired Brain Damage Unit at **Institut Guttmann**, Barcelona, Spain

Josep M. Tormos, Research Director at the **Institut Guttmann**, Barcelona, Spain

Montserrat Vendrell, CEO, **Biocat**, Barcelona, Spain

Laia Arnal, Head of Research and Scientific Debate, **Biocat**, Barcelona, Spain

INVITED SPEAKERS

Wednesday, October, 23rd, 2013

Joan Vidal, Head of the Spinal Cord Injury Unit at **Institut Guttmann**, Barcelona, Spain

Chair of the SESSION 1: NEUROREGENERATION, IS THERE ALREADY A TRANSLATIONAL EXPERIENCE IN CLINICAL PRACTICE?

(See his CV at the Scientific Committee Section)

James D. Guest, Associate Professor at Clinical Neurological Surgery, **University of Miami**, USA

James Guest has pursued treatment of spinal cord injury and disease for more than 15 years. He is extensively involved in national and international spinal cord injury research communities, employing his clinical and basic science knowledge in several arenas. He serves on the scientific committees of highly respected organizations such as the International Spinal Research Trust, the International Campaign for Cures of Spinal Cord Injury Paralysis, and the American Spinal Injury Association, and he recently completed a five year term as co-chair of the AANS/CNS Joint Section Spine and Peripheral Nerves Research Committee. In December, 2005, he was invited to speak and to chair a discussion group at the First International Spinal Cord Injury Treatments and Trials Symposium in Hong Kong. Currently, he is acquiring expertise in the area of spinal cord injury clinical trials. Cervical spinal cord injury and pathology, and the management of spinal pain are his main clinical interests. Although he has several years of surgical experience, he seeks to move toward less invasive procedures, whenever possible, in his practice. This interest has allowed Guest to work in partnership with medical professionals in the development of new experimental techniques and technology, and he currently holds a patent for percutaneous endoscope transplantation into the spinal cord. Guest truly esteems the stimulating scientific atmosphere at the Miami Project to Cure Paralysis. He is a faculty member of the Neuroscience Graduate Program. He finds teaching and scientific collaboration very rewarding. At the Miami Project, he seeks to integrate his clinical interests with his research. Over the last three to four years his lab group has worked on a cervical spinal cord injury model, in which hand dexterity is permanently impaired. This model may now serve as a platform to test regeneration and plasticity promoting therapies to determine if the next step, to clinical application, is warranted.

Learning from Nerve Repair. Schwann Cell Transplantation into the Injured Spinal Cord

Perhaps the most optimistic aspect of biology that has supported enthusiasm and hope for the possibility of structural repair of the damaged spinal cord is the regeneration that occurs after human peripheral nerve injury. Following nerve laceration, standardized techniques are in clinical practice to use autologous nerve graft segments as a bridge for axonal growth from the axotomized nerve terminals into the distal nerve segment that is undergoing Wallerian degeneration. These techniques have been applied for most major nerves of the body including the sciatic, tibial and brachial plexus nerves. Axonal regeneration usually occurs with measurable improvements in clinical outcome that are limited by factors such as changes in muscle or sensory receptors due to protracted denervation. Interest in applying peripheral nerve grafts to the central nervous system has a long history beginning with Ramon y Cajal and important contributions by Albert Aguayo and colleagues. The component of nerve grafts essential to axonal regeneration and myelination is the Schwann cell. The development of techniques to purify and expand Schwann cells from small segments of autologous donor nerve permitted testing of the impact of transplanted Schwann cells in the injured spinal cord. Schwann cells support the regeneration of several types of CNS neurons. Their limitations include restricted cell migration and incomplete CNS integration. Never-the-less, an abundance of pre-clinical data supports that autologous Schwann cell transplants to the spinal cord have reparative effects. Thus, translation to early phase clinical testing is justified. The FDA has approved a dose escalation study of autologous Schwann cell transplantation in subjects with severe thoracic spinal cord injury including long-term safety follow-up. Similar to the experience in other trials of spinal cord injury therapeutics, enrollment is complicated by logistics and exclusion criteria. Combinatorial therapies of cells and other biologics aimed at increasing the magnitude of axonal growth while reducing inhibition of regeneration, together with rehabilitation and neuromodulation may eventually lead to more robust clinical effects.

Daniel P. Lammertse, Medical Director of Research at Craig Hospital, and Clinical Professor at **University of Colorado Denver**, Colorado USA

Daniel Lammertse is the Co-Project Director of the Rocky Mountain Regional Spinal Injury System at Craig Hospital and past-chair of the National Institute on Disability and Rehabilitation Research SCI Model Systems Project Directors. Lammertse came to Craig Hospital in 1981 and served as Medical Director for 24 years from 1984 until 2008. He has served on the Board of Directors of the American Paraplegia Society (APS) and ASIA, and as President of ASIA from 2001-2003. He is currently serving on the Craig H. Neilsen Foundation Board of Directors and a member of the Editorial Board of the Journal of Spinal Cord Medicine. He is the recipient of the 2008 American Paraplegia Society Excellence Award and the 2012 American Spinal Injury Association Lifetime Achievement Award. Lammertse has an appointment as Clinical Professor of Physical Medicine & Rehabilitation at the University of Colorado Denver (UCD). He is internationally recognized as an expert in spinal cord injury treatment and has authored numerous chapters and scientific articles. He has been Principle Investigator on many clinical trials in SCI and served on the primary author committee that created the International Campaign for Cures for spinal cord Paralysis (ICCP) Guidelines for the Conduct of Clinical Trials in Spinal Cord Injury. He has provided consultation on protocol development and research design to private industry sponsors of SCI clinical trials and serves on the Roundtable leadership group of the Spinal Cord Outcomes Partnership Endeavor (SCOPE) which is comprised of representatives from academia, private industry and government agencies dedicated to furthering the rigor and success of SCI clinical research.

Abstract of Prof. Daniel P. Lammertse's presentation

Neuroregeneration: Is there already a translational experience in clinical practice? "No": I will take the position on that the translational effort to find effective treatments for paralysis and sensory loss for persons with SCI has *not* yielded a change in current *evidence-based* clinical practice. After three decades of clinical research on interventions to improve neurological outcomes in persons with SCI, the promise of preclinical discovery has yet to be translated into a consensus standard of care treatment. Nonetheless, SCI researchers remain hopeful that advances in preclinical discovery coupled with improved clinical trial performance will yield effective restorative treatment. The number of registered restorative intervention trials in SCI has been steadily increasing over the past decade which offers encouragement that the preclinical effort is now resulting in translation to human research. My presentation to the B Debate will review the history of key trials up to the present, and note that progress has been achieved in establishing a high standard in the conduct of clinical research while providing important lessons for improving trial design, conduct and reporting. Through application of these lessons, the performance of SCI trials can be improved, thereby shortening the pathway to successful translation and the development of effective therapies. I will also comment on the "clinical practice" available in some countries of "treatment" that has not been validated in scientific clinical trials. In bypassing the scientific process, provision of unvalidated therapies may hinder the path to successful translation.

John Steeves, Principal Investigator at I**nternational Collaboration On Repair Discoveries** (ICORD) and Professor in the Department of Neuroscience at the **University of British Columbia**, Canada,

John Steeves completed his PhD in neuroscience at the University of Manitoba (Department of Physiology, Faculty of Medicine) in 1978. After a fellowship at the University of Alberta Faculty of Medicine, he was first appointed to UBC in 1979 and has been affiliated with several departments in the Faculties of Science and Medicine at UBC. In 2002, he was the first appointment to the BC Leadership Endowed Chair program. He has also been a Wall Distinguished Scholar in Residence at UBC, recipient of the Champion of Change Award by the Toronto Rehabilitation Institute, a Killam Research award and involved in collaborations with NASA, Russian and Canadian Space agencies. More significantly, he is the founder of ICORD and was Director for the first fifteen years (1995-2010). ICORD currently has over 200 researchers led by over 30 faculty members investigating various aspects of spinal cord injury (SCI) from preclinical discovery, through acute clinical trials and best rehabilitation practices, to community integration and ongoing care of medical and social challenges. Steeves brings over 35 years experience in SCI and neuroscience. He is or has been an executive member or chair of many national and international committees and organizations concerned with SCI (e.g. ASIA & ISCoS). He currently chairs SCOPE (Spinal Cord Outcomes Partnership Endeavor), which is the international industry-academic-community roundtable for improving SCI clinical trial protocols. He has an extensive list of publications and patents. He has started biotechnology companies, and serves on scientific and clinical advisory boards to several pharmaceutical and biotechnology companies. Over the years, his basic science research characterized the neural pathways from the brainstem to the spinal cord and their roles in the initiation and modulation of locomotion in all vertebrates, including humans. He has made significant contributions to the identification of CNS myelin as inhibitory to functional CNS repair. More recently, he has focused his activities on translational research and human studies, including the development of: valid clinical trial protocols, neurological and electrophysiological outcome measures after human SCI, and activity-dependent rehabilitation of arm and hand function.

Abstract of Prof. John Steeves' presentation

Neuroregeneration: Is there already a translational experience in clinical practice? "YES" for early surgical decompression after SCI and "YES" for subsequent active rehabilitation therapy, but currently "NO" for drug and cell transplant interventions. I will take a cautious position for the affirmative, but with the usual caveats and qualifications. Recent observational studies have suggested early (<24 hour) decompression surgery after SCI yields improved outcomes for most patients. Admittedly, these studies were not randomized controlled trials, but many within the surgical community have adopted new treatment protocols. Likewise, active (patient-initiated) rehabilitation training has a large amount of data supporting the adoption of intensive rehabilitation training regimens for in-patients, followed by sustained physical participation activities within the community. Admittedly, much of the rehabilitation data is from small underpowered studies, but the benefits appear to outweigh the risks and comparable data is available for stroke and TBI. The development of more refined and specific strategies for each type of SCI is still required and will be reviewed. However, we have no validated clinical trial data confirming an experimental treatment providing neuroprotection or stimulating subsequent neural repair. Nevertheless, there are more ongoing clinical trials at this time than ever before, as well as an increased awareness of how to better design trial protocols to adequately detect subtle therapeutic benefits from the most appropriate target populations. I will review the challenges associated with subject selection, and outcome measurements, as well as the recent progress in resolving some of these issues.

Ann Tsukamoto, Executive Vice President, Scientific & Strategic Alliances of **StemCells, Inc.**, Newark, Canada

Ann Tsukamoto joined StemCells, Inc. in 1998 as Senior Director, Scientific Operations, to help start the Company's California operations, and has since held several leadership roles at the Company. In June 2013, Tsukamoto was appointed Executive Vice President, Scientific and Strategic Alliances and is responsible for developing the Company's alliances with research institutions, corporations, government agencies, and disease foundations. From September 2008 to June 2013, she served as the Company's Executive Vice President of Research and Development. Under her direction, the Company identified and purified the human neural stem cell and populations of human liver and pancreatic cells with stem cell-like properties, successfully transitioned into clinical translation, and initiated and completed its first human clinical trials. Before joining the Company, Tsukamoto was a co-discoverer of the human hematopoietic stem cell while at SyStemix, Inc., a stem cell and gene therapy company. Tsukamoto received her PhD from the University of California, Los Angeles and did postdoctoral research with Dr. Harold Varmus at the University of California, San Francisco where she worked on the wnt-1 gene, which is a key player in the stem cell self-renewal pathway. Tsukamoto is an inventor on seven issued US patents related to the human hematopoietic stem cell and gene transfer methods.

Clinical Translation of Human Neural Stem Cells for Neurodegenerative Disorders

Currently, there are few effective therapies for the treatment of neurodegenerative diseases or injuries to the brain, spinal cord and eye. Human neural stem cell transplants offer the prospect to treat such conditions and represent a potential exciting new medical therapy. A highly purified composition of human neural stem cells has been isolated, expanded and stored as banks of cells, HuCNS-SC. When transplanted into the brain of immunodeficient rodents, human neural stem cells reside and proliferate in host neurogenic sites, such as the subventricular zone and dentate gyrus of the hippocampus. Their progeny migrate globally throughout the brain and differentiate in a site appropriate manner into neurons, astrocytes and oligodendrocytes. When transplanted into the spinal cord above and below the injury site, these cells also migrate extensively and differentiate, remyelinate and make synaptic connections with host neurons. HuCNS-SC have also been shown to produce neurotrophic factors implicated in neuroprotection of host cells and also become mature oligodendrocytes which myelinate dys- or demyelinated host axons. Moreover, these human cells survive long-term in the host brain with no signs of tumor formation or adverse effects. Therefore, a single transplant of human neural stem cells offers the prospect of a durable clinical benefit.Studies transplanting HuCNS-SC cells into animal models of human diseases or injury have been performed to assess the cells' biological properties including their impact on these specific targets. Preclinical efficacy studies have demonstrated protection of host cells and/or improvements in specific functional deficits and provided the foundation for the neuroprotection and neural replacement strategies to support initiation of our clinical studies. Four clinical studies have been initiated to date. Two clinical studies have been completed; one in Batten disease, a fatal lysosomal storage disease, and the second in PMD, a fatal myelination disorder. Surviving NCL patients are now ~5 years post-transplant with no product safety concerns. In PMD patients, MRI imaging shows evidence of progressive and durable donor derived myelin. Modest gains in neurological function were noted in 3 of 4 patients, a departure from the natural history of this disease. A trial in chronic spinal cord injury has completed dosing of the most severely injured patients and continues to transplant incomplete thoracic injured patients. The Company has also initiated and dosed patients with dry AMD. Preclinical studies in a rat model of retinal degeneration, the RCS rat, have shown cone photoreceptor protection and maintenance of visual acuity following subretinal transplants of HuCNS-SC cells. The clinical data showing safety to these human cells should facilitate future clinical testing for demonstrating effectiveness of human neural stem cells transplants.

Anna Veiga, Director of the Cell Bank at **Centre Medicina Regenerativa de Barcelona** (CMRB), and Associate Professor at Universitat Pompeu Fabra, Barcelona, Spain

Chair of the SESSION 2: WHICH ARE THE KEYSTONES IN NEUROREGENERATION TO BUILD UP A PATHWAY TO THE CLINICS?

(See her CV at the Scientific Committee Section)

Juan Carlos Izpisua, Professor in the Gene Expression Laboratory, **Salk Institutefor Biological Studies**, San Diego, USA, and director of **Center for Regenerative Medicine** (CMRB), Barcelona, Spain

Juan Carlos Izpisua Belmonte graduated from the University of Valencia, Spain with a Bachelor's degree in Pharmacy and Science and a Master's degree in Pharmacology and received his Ph.D. from the University of Bologna, Italy and the University of Valencia, Spain in 1987. After postdoctoral stages at the EMBL in Heidelberg, Germany, and UCLA, Los Angeles, USA, in 1993 he moved to the Salk Institute for Biological Studies in La Jolla, California where he is currently a professor in the Gene Expression Laboratories. Since 2005 he is also the Director of the Center for Regenerative Medicine in Barcelona.
Izpisua Belmonte's research interests are focused on the understanding of stem cell biology, organ and tissue development and regeneration. He has helped to uncover the role of some homeobox genes in limb patterning and specification, as well as the identification of the molecular mechanisms that determine how the different cell type precursors of internal organs are organized spatially along the embryonic left right axis. During the last few years, he has concentrated on studying the molecular basis implicated during organ regeneration in higher vertebrates, the differentiation of human stem cells into various tissues, and the molecular basis underlying aging and somatic cell reprogramming. He has published over 300 articles in internationally peer reviewed journals and book chapters in these areas. The ultimate goal of his research is to apply this knowledge towards the development of cell and gene based therapies as well as new molecules for the treatment of diseases.

Reprogramming and Regeneration Strategies for Healing and Improving Human Health

Reprogramming technologies offer new opportunities for basic research into diseases and the development of therapeutic compounds. iPSCs can self-renew and can be differentiated to many cell types, offering a potentially unlimited source of material for study. I will discuss the conceptual and practical issues to consider when attempting to model central nervous system injuries using iPSCs.

Marina Mata, Co-director of Mata-Fink Laboratory and Professor of Neurology at **University of Michigan**, USA

David Fink, Co-director of Mata-Fink Laboratory and Robert Brear Professor and chair of the Department of Neurology at **University of Michigan**, USA

Marina Mata and David Fink co-direct the Mata-Fink laboratory at the University of Michigan in Ann Arbor, MI, where Mata is Professor of Neurology and Fink is Robert Brear Professor and chair of the Department of Neurology. Mata received her medical degree from the University of Barcelona and after post-doctoral training at the NIH completed clinical training in Neurology at the University of Michigan. Fink received his medical degree from Harvard Medical School, clinical training in Neurology at UCSF, and did post-doctoral research at the NIH. A major focus of their laboratory is the development of herpes simplex virus-based vectors for treatment of conditions affecting the nervous system including chronic pain, eripheral neuropathy, and neural regeneration. Their research is supported by grants from the NIH and the US Department of Veterans Affairs.

Preclinical studies of Rho inhibition to enhance axonal regeneration after SCI

If the ultimate goal of SCI treatment is to re-establish functional connectivity across the lesion, a key intermediate goal is to promote axonal elongation in the impermissive environment of the CNS, where components of the glial scar (CSPGs) and central myelin (MAG, OMgp and Nogo) serve to block axonal extension. Because the inhibitory effects of CSPG, MAG, OMgp and Nogo all converge on activation of RhoA in the axon, we have constructed a non-replicating herpes simplex virus (HSV)-based vector to express the RhoA inhibitor C3 transferase. Transduction of sensory neurons in the dorsal root ganglion by subcutaneous inoculation of the vector one hour after dorsal root crush resulted in expression of C3t within the injured neurons and promoted regeneration of primary sensory afferents through the myelinated dorsal root entry zone into the dorsal horn, and ascending into the dorsal column ipsilateral to the lesion. Transduction of cortical motor neurons by stereotactic intracranial inoculation of the vector one hour after dorsal over-hemisection of the cervical cord at C6 promoted substantial extension of descending motor axons in the corticospinal tract contralateral to the cortical injection. The HSV vector backbone employed has already been tested in clinical trials in patients; the next steps will be to determine the time window for treatment, and evaluate the establishment of functional synaptic connections.

Letizia Mazzini, Neurologist, Department of Neurology and Director of the National Expert Motor Neuron Diseases Center, University of Novara, Italy

Letizia Mazzini obtained her MD degree in 1981 from the Medical School, University of Pavia (Italy) and four years later a specialization in clinical Neurology at the University of Milano (Italy). Between 1985 and 2000 Mazzini worked as a neurologist at the Institute of Care and Research of Fondazione "S Maugeri", Veruno. Then, she moved to the Hospital Torino, where she practiced as a neurologist too until 2003. During this period she also was the Director of the National Expert Motor Neuron Diseases Center, at University of Novara. She has been member of the Italian Ministerial Committee regarding the diagnosis and care of ALS (2003-2004) and regarding the research of ALS (since 2004). She is also currently member of the European ALS Group, of the Italian neurological society subgroup on MND and of the scientific advisory board for the Italian ALS Association. The main interests of her investigations are in the field of basic and clinical research on motor neuron diseases. She has authored or co-authored 87 papers on peer-reviewed international journals, as well as books, edited books, e-books. She received more than 2151 citations, with h-index = 28. (Sources: ISI Web of Knowledge and Scopus). She cooperated as investigator in many multicenter therapeutic trials in ALS. Mazzini was the head of the phase 1 study authorized by the Italian Institute of Health on clinical application of mesenchymal autologous stem cells in ALS. She is currently coordinator of the phase 1 clinical study on neural fetal stem cell transplantation in ALS

Challenges for Clinical Translation of Stem Cells in Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis (ALS) is a devastating incurable neurodegenerative disease that targets motor neurons (MNs) in the primary motor cortex, brainstem, and spinal cord leading to muscle atrophy, paralysis and death due to respiratory failure within 2-5 years. Currently, there is no cure for ALS. Cell therapy offers much promise , but caution that the problems are complex and the solutions are likely to be slow and costly to achieve in order to overcome significant ethical and regulatory as well as scientific challenges. We review the first generations of clinical trials of novel cell therapies applied to ALS. and we then consider the scientific, technical, ethical, regulatory and logistic issues to be resolved in translating effective laboratory cell-based protocols to patients in clinical trials. We report on an ongoing Phase I trial, aimed at testing safety and feasibility of intraspinal injection of "clinical grade" (produced following the Good Manufacturing Guidelines in a pharmaceutical grade authorized facility) neural stem cells from natural miscarriages into a cohort of 18 ALS patients using a validated surgical apparatus and injection procedures. The clinical GMP-status of the NSCs used in this study was granted by the Italian Medicines Agency (AIFA) and the clinical study was approved by the Italian Institute of Health (ISS) as well as by all of the competent ethical committees. An independent Safety Monitoring Board of multidisciplinary experts was also nominated and periodically reviewed and evaluated the accumulated study data. Until now, six non-ambulatory patients have been recruited whom, following a three months observation period, received either unilateral (n = 3) or bilateral NSCs microinjections.(n = 3) into the lumbar spinal cord. No patients manifested severe treatment related adverse events. . We are now broadening the import of this trial, by testing intraspinal injections into the cervical spinal cord (C3-C4 level), of 12 ambulatory patients

INVITED SPEAKERS

Thursday, October, 24th, 2013

Xavier Navarro, Director of de group Neuroplasticity and Regeneration at **Institut de Neurociències,** Universitat Autònoma de Barcelona, Spain

Chair of the SESSION 3: IS NEUROREGENERATION THE "NEXT STOP" IN SPINAL CORD INJURY MEDICAL CARE?

(See his CV at the Scientific Committee Section)

James Fawcett, Chairman of the John van Geest Centre for Brain Repair at **Cambridge University**, United Kingdom

James Fawcett trained in medicine at Oxford University and St. Thomas' Hospital London. After practicing in hospital medicine for a few years he studied for a PhD under Michael Gaze at the National Institute for Medical Research in London. He moved to the Salk Institute in the laboratory of Max Cowan as junior faculty, then he set up his own laboratory in the Physiology Department in Cambridge. Since 2001 he has been Chairman of the John van Geest Centre for Brain Repair at Cambridge University. His early research work was on the formation of connections during brain development and he then became interested in using developmental biology principles to promote repair in the adult nervous system. His main interest has been the part played by molecules of the extracellular matrix in the inhibition of nerve fibre regeneration and in the restriction of plasticity in the adult nervous system. He showed that chondroitin sulphate proteoglycans in scar tissue block axon regeneration after spinal cord injury, and that digesting these molecules could promote repair. Recent work has shown that plasticity is restricted after childhood critical periods by the formation of matrix structures known as perineuronal nets and that plasticity can be reactivated in the adult CNS by digestion of proteoglycans in these nets with chondroitinase. For this digestion to improve function after spinal cord injury it is necessary to combine the treatment with rehabilitation. A recent focus has been working to increase the intrinsic ability of axons to regenerate. This work has concentrated on the role of integrins, integrin transport and integrin activation. He has also been involved in the design of microchannel interfaces for electrical recording from regenerated axons. He has worked with Spinal Research, the Christopher Reeve Foundation and with the international organization of spinal injury charities, the ICCP, to develop guidelines for the conduct of clinical trials in spinal cord injury.

Future Regenerative Therapies

Regenerative therapies have three main aims; to promote axon regeneration, to promote plasticity and to replace lost cells. Regeneration of cut axons in the spinal cord has been the subject of a large amount of research over the years, but the problem remains mostly unsolved. Treatments that neutralize inhibitory molecules can promote partial regeneration, but full regeneration is still elusive. Approaches based on the enhanced regeneration of sensory axons after damage, and on developmental changes in axonal transport show promise for the future. Several treatments that are in clinical trials or preclinical development have powerful effects on sprouting and synaptic plasticity, and can promote recovery of function after injury. Of these anti NogoA and chondroitinase are the furthest developed. These treatments can open a window during which rehabilitation has greater efficacy, but there can also be problematic interactions between plasticity and rehabilitation. Cell replacement in the damaged CNS can improve outcomes through neuroprotection, remyelination, glial replacement, secretion of trophic factors, and growth of new axons. Embryo-derived cells that differentiate mainly into oligodendrocytes are currently in clinical trials. Transplants of neuronal precursors able to differentiate and grow many axons show promise for the future. Regenerative therapies will need to be co-ordinated with a matched rehabilitation programme, and will also be combined with approaches using electrical stimulation and prostheses.

François Feron, Neurogenesis and Neuronal Repair, **Institut Fédératif de Recherche Jean Roche**, Marseille, France

Neurogenesis is the main and central research topic of François Feron's team. Which epigenetic modification can explain the altered neurogenesis shown in adult animals exposed pre/postnatally to olfactory cue or nutritional deficiency? What are the molecular mechanisms underlying the abnormal neurogenesis observed in neurodevelopmental disorders such as autism? What role do immune molecules play in the permanent neurogenesis observed in the olfactory system? How can olfactory stem and ensheathing cells increase neurogenesis in patients suffering from neurodegenerative diseases or affected by a spinal cord trauma? These are some of the questions we are aiming to answer to. The studies performed currently by the team can be classified into two subcategories: A) Imprinting and brain development; B) Olfactory neurogenesis and brain repair.

Armin Blesch, Associate Professor at the **University of California**, San Diego and Director of the Laboratory for Neuroregeneration at the Spinal Cord Injury Center, **University Hospital Heidelberg**, Germany

Armin Blesch has a long-standing interest in neuroregeneration particularly in animal models of spinal cord injury. His work is focused on cell and gene therapy, neurotrophic factors and neural stem cells for axonal regeneration. Dr. Blesch is an Assoc. Professor at the University of California, San Diego and Director of the Laboratory for Neuroregeneration at the Spinal Cord Injury Center, University Hospital Heidelberg, Germany.

Abstract of Prof. Armin Blesch's presentation

Regenerative approaches after spinal cord injury can be based on several different strategies including remyelination of axons spared after an injury, collateral sprouting of intact and regeneration of injured axons, and the generation of new neuronal circuits from neural stem cell transplants. Cellular regenerative therapies in initial clinical studies have primarily focused on the first approach. Regeneration of injured axons over sufficient long distances to become clinically meaningful remains mostly elusive. This might be at least partially due to a need to activate cell-intrinsic programs of axon regeneration and a need to address cell-extrinsic factors limiting robust axon growth. Finally, while the idea of generating neuronal relays at sites of spinal cord injury is not novel, recent evidence suggests that reciprocal host-graft connections can indeed improve motor and autonomic recovery in rodent models of spinal cord injury. I will discuss some recent work in neuroregenerative approaches in spinal cord injury and the steps necessary for future clinical translation.

Alessandro Vercelli, Vice-Director of the **Neuroscience Institute of the Cavalieri Ottolenghi Foundation**, Associate Professor at Dept Neuroscience Corso M., **Faculty of Medicine and Surgery**, and Head of **Neuroscience Institute of Turin**, Italy

Alessandro Vercelli obtained his MD at University of Turin in 1986. He received his PhD in Ophthalmologic Sciences at University of Turin in 1990 and other PhD in Anatomy at University of Lausanne in 1994. He spent several research periods at the Institute of Anatomy of Lausanne, at the Dept of Brain and Cognitive Neuroscience of Cambridge (MA, USA) and at the University Laboratory of Physiology (Oxford, UK). Vercelli is Professor in Human Anatomy at the Turin Medical School since 1996. From 2012 he is vice-Director of the Neuroscience Institute Cavalieri Ottolenghi. He also heads the Neuroscience Institute of Turin since July 2013. Vercelli is member of the Neuroscience Institute of Turin and of the Italian National Consortium of Neuroscience. Between 2006 and 2007 he became secretary of Italian Society for Neuroscience. He was Treasurer of IBRO world meeting in 2011. In 2014 he was member of the local committee of FENS. He had received several grants from National and International agencies, and from the EEC. He is referee for several international journals and grant agencies. Vercelli main research interests are focused on neuronal cell death and neuroprotection; stem cell transplantation in experimental models of spinal cord injury and motoneuron diseases (ALS and SMA). Vercelli utilizes different techniques in his laboratory: histochemistry (AChE, NADPH-d, CO); immunohistochemistry; anterograde and retrograde neuronal tract tracing; ionophoretic intracellular injections; morphometry; 3D-reconstruction of dendrites and axons at the PC; slice cultures; electron microscopy, CLSM, TUNEL; biochemical assays. Experimental models of glaucoma, retinal excitotoxicity, permanent and transient cerebral ischemia, spinal cord injury, SOD1 and SMAII mice.

Critical issues in stem cell therapy in experimental SCI

Spinal cord injury represents a great health and economic burden for patients and society, and a major challenge for both the physician and the researcher. Following a lesion, a series of anatomopathological changes (glial scar formation, neuroinflammatory reactions and cell death) occur, associated with the poor capability of the adult central nervous system to restore its connectivity due to growth inhibitory environment and the inactivation of the growth program. Some reorganization of local neural circuits and sprouting of axons can occur, and different therapeutic approaches are being tested in the early and delayed phases of disease by preventing glial scar formation, removing inhibitory molecules or stimulating axonal growth by trophic factors, inducing physical exercise. In addition, cell therapy has been envisaged to

replace and to restore lost neural circuits or, more simply, to modulate the environment, as well as different types of scaffolds. Finally, gene therapy could enhance axonal growth. In our studies, we have administrated neural stem cells or mesenchymal stem cells (or both) intraparenchymally in the acute or in the chronic phases of SCI, in association with enriched environment or exercise. We have obtained encouraging results in terms of reduction of glial scar/astrogliosis/microglial activation, axonal sprouting and, for NSCs, integration in local circuits.

Joan Comella, General director of the Research Institute of **Hospital de la Vall d'Hebron**

Chair of the SESSION 4: IS NEUROREGENERATION FEASIBLE WITHOUT A MULTIDISCIPLINARY APPROACH?

Joan Comella is Graduate and Doctor in Medicine and Surgery from the University of Barcelona and Professor of Cell Biology at the Universitat Autònoma de Barcelona (UAB). His training also includes visits to various research laboratories (France and England) and management training (IESE). Since 2009 Comella is the director of the Vall d'Hebron Hospital Foundation - Research Institute (VHIR). Comella began as director of the research group Molecular Neurobiology (1991) and Professor of Cell Biology - Histology (2002) in the Department of Basic Sciences, University of Lleida. In 2004 he moved with his group to the University Hospital Arnau de Vilanova in Lleida. He was the director of the research laboratory in this hospital, which became the nucleus of the Future Biomedical Research Institute of Lleida. In 2007 he was appointed Director of the Institute of Neuroscience at the UAB. Then, in 2009 he became the General Director of the Research Institute of the Hospital Vall d'Hebron (VHIR) position held until today. As a researcher, Comella has a long history with over 90 scientific articles in international journals and more than 100 lectures and seminars at national and international academic institutions. His research has been linked to understanding the mechanisms regulating neuronal survival and its relationship to the development of neurodegeneratives diseases such as Alzheimer. He has undertaken various management tasks in science policy at different levels, such as Vice President of research and postgraduate studies at the University of Lleida. director and head of the National Agency for Evaluation and Prospective (ANEP), general director of the Spanish Foundation for Science and Technology and general manager of the Catalan Foundation for Research and Innovation (FCRI). In 2011 he was elected secretary general of the Confederation of Scientific Societies of Spain (COSCE). In March 2012 he was appointed member of the Advisory Council of the National Agency for Research (AEI Minc). Since 2012 he is Chair of the national scientific representatives EATRIS (European Infrastructure for Translational Medicine) of the EU. In 2001 he received the distinction for Young Scientists Research, awarded by the Government of Catalonia in recognition of his scientific career. He received the National Award for Basic Research Foundation Pfizer in 2005. In 2008 he received the Dr. Santiago Ramon y Cajal award in basic research of the Spanish Society of Neurology.

V. Reggie Edgerton, Professor and Vice Chair of Integrative Biology and Physiology, and professor of Neurobiology at **UCLA University**, Los Angeles, USA

V. Reggie Edgerton received his Ph.D. in Exercise Physiology from Michigan State University, Masters from University of Iowa and BS from East Carolina University. He has been Professor at the University of California, Los Angeles, since 1968. V. Reggie Edgerton has led a research team over the past 10 years initiating the development of electrode array technology and the physiological assessment of the chronic implants in mice, rats and humans to improve lower limb function, primarily standing and stepping. They have published a number of papers demonstrating the feasibility of facilitating stepping after a complete spinal cord transection in rats, particularly when combined with pharmacological facilitation and step training over a period of weeks. Most recently, they have demonstrated that the intervention of epidural stimulation enabled a completely paralyzed subject to stand independently and to voluntarily control movement of all joints of the lower limb.

Conceptual and Actual Evidence That the Regenerative Potential Can only be Realized with a Multidimentional Approach

It is more than clear at this point that a single intervention to recover all of the desired functions following a spinal cord injury is without scientific logic. Indications that this point is being more widely recognized, is reflected in the increasingly higher incidence of referral in the spinal cord injury literature to "combination" approaches. Spinal cord injury results in the loss of many functions all of which are highly integrated physiologically. These losses need to be treated accordingly in understanding the basic science underlying spinal cord injury as well as in clinical practice. Assuming these conclusions are accepted by scientists and clinicians and society, our challenge is to begin to address effective ways to study the biology of recovery of function, within the concept of a highly integrated system. Further, there is need for a similarly integrative clinical perspective which requires the unique challenges of understanding the interactions of multiple physiological systems that impact quality of life. Finally, recognition of the economical requirements to carry out a "combination" strategy needs to be addressed.

Rüdiger Rupp, Head of a research group of the Spinal Cord Injury Center**, University Hospital in Heidelberg**, Germany, United States

Rüdiger Rupp received the Dipl.-Ing. (M.Sc.) degree in electrical engineering with focus on biomedical engineering and his Dr.-Ing. (Ph.D.) degree from the Technical University of Karlsruhe, Germany, in 1994 and 2008, respectively. After working at the Institute for Biomedical Engineering and Biocybernetics (Prof. G. Vossius) until 1996, he is currently with the Spinal Cord Injury Center (Head: Prof. N. Weidner) of the University Hospital in Heidelberg, Germany, where he holds the position as the head of the research group "Experimental Neurorehabilitation". His main research interests are in the field of rehabilitation engineering especially for spinal cord injured patients. This includes neuroprosthetics mainly of the upper extremity, application of functional electrical stimulation for therapeutic purposes, development and clinical validation of novel methods and devices for locomotion therapy, gait analysis in incomplete spinal cord injured and realization of software projects for standardized documentation of rehabilitation outcome. He is author of more than 170 journal articles, book chapters and conference abstracts and holds two patents. He has been awarded several times for his work and is a member of IEEE, IFESS, VDE, DMGP, DGOOC and ISCoS.

Neuroregeneration and Neuroengineering – Competition or Convergence ?

Due to the tremendous progress of technology neuroengineering approaches evolved as effective tools for rehabilitation of patients with stroke or spinal cord injury (SCI). Assistive devices are long-established components in compensatory rehabilitative approaches, while locomotion and upper extremity robotics have largely gained acceptance in a restorative therapy setting. In contrast to this neuroregenerative therapies are still in its clinical infancy. However, with in increasing number of phase I and II clinical trials important questions arise from a neuroengineering point of view: If neuroregeneration will be successful, will neuroengineering be redundant ? In the light of the recent achievements in neuroengineering, which subgroup of patients is presumably in need of neuroregeneration? Focusing on SCI we know that initially motor incomplete individuals show a substantial recovery. Clinical evidence arises that robotic therapies are not superior to manual ones applied with the same intensity. Is this an indicator that we already make full use of the patients' intrinsic rehabilitation capabilities ? The implementation of novel robotic control algorithms based on principles of motor learning shows that further enhancement of therapy outcome is possible. Do we need a neuroregenerative approach with all its associated risks as an add-on to plasticity enhancing neuroengineering methods in this patient population? Of course, the situation is completely different in individuals with complete SCI, in which neuroregeneration is highly needed, but most challenging. Is it likely that future neuroregenerative interventions will cure a paralysis ? Based on the preclinical work this seems not to be a realistic goal. But it can be assumed that minor muscular activities functions will recover, which may be used as a control modality for patient-cooperative neuroprostheses or exoskeletons. Are neuroengineers prepared for this situation ? Probably not, since it is much easier to build an exoskeleton with the assumption of a user being completely passive and rating any voluntary motor function as disturbance. In conclusion, neuroregeneration needs neuroengineering and vice versa. Synergistic, combinatorial approaches will contribute most to a better functional rehabilitation and an intense interdisciplinary discussion is necessary for alignment of realities and promises.

Leigh R. Hochberg, Director of **Neurotechnology Trials Unit**; Neurologist at **Massachusetts General Hospital**, **Brigham & Women's Hospital**, and **Spaulding Rehabilitation Hospital**; Senior Lecturer at **Harvard Medical School**; Associate Professor at **Brown University**; Associate Director at **Center for Neurorestoration and Neurotechnology**

Leigh Hochberg received his Bachelors in Science with Honors in Neural Science at Brown University. During his M.D. and Ph.D. research at Emory University he studied motor cortical plasticity, and with Donald Humphrey was the first to use cortical recordings from chronically implanted electrodes to drive a robot wrist. After residency and chief residency in Neurology at Massachusetts General Hospital/Brigham and Women's Hospital/Harvard Medical School, Hochberg stayed on as a fellow in Stroke and Neurocritical Care. Currently Dr. Hochberg is Associate Professor, School of Engineering and Institute for Brain Science, Brown University; Associate Director, Center for Neurorestoration and Neurotechnology, Providence VA Medical Center; and Senior Lecturer in Neurology at Harvard Medical School. Leigh also directs the Neurotechnology Trials Unit for MGH Neurology. Leigh's research focuses on the development and testing of neural interfaces to help people with paralysis and other neurologic disorders. His research is supported by the Department of Veterans Affairs, the National Institute for Deafness and Communication Disorders (NIDCD), and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NCMRR/ NICHD). He is the IDE Sponsor-Investigator and principal clinical investigator of the pilot clinical trials of the BrainGate2 Neural Interface System (www.braingate2.org). Leigh is also appointed as Neurologist and maintains clinical duties on the Neurocritical Care and Acute Stroke Services at Massachusetts General Hospital, and is on the neurology staff at Brigham & Women's Hospital and Spaulding Rehabilitation Hospital.

Neural Interfaces for Restoring Communication and Mobility

For people with cervical spinal cord injury, pontine stroke, neuromuscular disease including amyotrophic lateral sclerosis, and other neurologic illnesses, currently available assistive and rehabilitation technologies are inadequate. In severe brainstem stroke and advanced ALS, patients may suddenly or progressively enter a locked-in state of being awake and alert but unable to move or

communicate. Through clinical translation based on decades of fundamental neuroscience research, intracortically-based "brain-computer interfaces" are poised to revolutionize our ability to restore lost communication and mobility. Over the past decade, neurotechnologies to record the individual and simultaneous activities (action potentials, multi-unit activity, and local field potentials) of dozens to hundreds of cortical neurons have yielded new understandings of cortical function in movement, vision, cognition, and memory. This preclinical research, generally performed with healthy, neurologically intact non-human primates, has demonstrated that direct neural control of virtual and physical devices can be achieved. Recently, this exciting research has been translated into initial pilot clinical trials (IDE) of an intracortically-based neural interface system (BrainGate), seeking to determine the feasibility of persons with tetraplegia controlling a computer cursor or other devices simply by imagining movement of their own hand. A variety of methods for decoding brain signals are now being tested with the hope of not only restoring communication, but also providing a control signal for the reanimation of paralyzed limbs. In related research, intracortical recording technologies are providing early glimpses into the activities of dozens of individual cortical neurons during intracranial seizure monitoring, with the potential to provide new diagnostic and therapeutic modalities for people with epilepsy.

Rajiv Ratan, Executive Director, **Burke Medical Research Institute**, and Burke Professor of Neurology and Neuroscience, Associate Dean, Weill Medical College of **Cornell University**, New York, USA

Rajiv R. Ratan. is currently Director of the Burke Medical Research Institute and a member of the Board of Trustees of the Burke Rehabilitation Hospital in White Plains, New York. He is the Burke Professor of Neurology and Neuroscience and an Associate Dean at Cornell Medical School. He trained in Neurology and Neurorehabiltiation at Johns Hopkins, and spent 8 years at Harvard Medical School before assuming his current position in 2003. His laboratory has been interested in transcriptional and epigenetic mechanisms involved in adaptive responses to brain injury. He has codeveloped several novel small molecule drugs that activate these adaptive programs and which can protect and repair the brain following stroke or spinal cord injury. He has also assembled one of the leading brain and spinal cord injury repair groups in the world at the Burke Medical Research Institute, with efforts spanning structural biology to epigenetics of stem cells, to non invasive stimulation after stroke.

Putting the Word "Cure" in Neurological Rehabilitation: a Field Comes of Age

Classical approaches to rehabilitation after brain or spinal cord injury have sought to reduce disability via compensatory mechanisms (e.g. using an assistive device or teaching the use of a good arm). While these techniques have been enormously successful in reducing handicap, there is no question that optimal treatment of patients with disabilities will come from strategies that achieve partial to complete impairment reduction. Over the past several decades, studies at a molecular and cellular cellular level have identified targets that when manipulated enhance the propensity of the system to undergo adaptive change. These targets, which can be manipulated by cells, drugs, biologics, or non-invasive stimulation, alter the propensity of the injured nervous system towards plasticity. Harnessing this plasticity in adaptive ways toward functional improvement will also require proper shaping via experience, and novel modalities including robotics and virtuality reality with feedback are changing the way we standardize experience and measure outcome. It is clear that timing, spatial control, and dose will be important variables in optimizing interventions to reduce impairment post-injury. I will discuss the promises and challenges associated with implementing strategies to address each of these variables, in an attempt to stimulate a systems biology view of regeneration after nervous system injury.

Alvaro Pascual-Leone, Professor of Neurology at **Harvard Medical School**; Director of the **Berenson-Allen Center for Noninvasive Brain Stimulation**; Program Director of the **Harvard-Thorndike Clinical Research Unit**; and an Attending Neurologist at **Beth Israel Deaconess Medical Center**, Boston, USA

(See his CV at the Scientific Committee Section)

Characterization and Modulation of Brain Plasticity: Challenges and Opportunities

OPEN MEETING

Institut Guttmann XXV Scientific Debate

NEUROREGENERATION: WHERE ARE WE? AND WHAT SHOULD WE EXPECT?

Open introductory session to the B·DEBATE meeting, on the afternoon of October 22nd. Addressed to clinicians and also to the community of people suffering from spinal cord injury, brain injury or other neurological conditions, and focused on the topic: "Neuroregeneration: Where are we? And what should we expect?"

This Scientific Debate will be conducted by Jorge Wagensberg, scientist, writer and natural architecture professor at the School of Architecture La Salle, who was the creator and first director of the Science Museum in Barcelona. We would like to formulate turns of questions to you and the other scientists participating, centered on the question "Where we are in Neuroregeneration and Neurorestoration?", based on your clinical and scientific experience, and "What should we expect in the following years?" and "Which are the most relevant experiences in clinical trials, currently, related to advanced therapies in Spinal Cord Injury?"

Invited speakers participants: Prof. Daniel P. Lammertse, Prof. John Steeves, Prof. Rajiv Ratan and Prof. Joan Vidal

Following the discussion, will present the book "Children with head injury. A guide for parents" by the American speech therapist Lisa Schoenbrodt and edited into Spanish by Institut Guttmann. Brain injury traumatic origin and its aftermath are responsible of 40% of the major disabilities and the leading cause of death in children and young adults. These lesions affect the development of children altering their school environment, personal and family. This guide is intended to be a valuable tool for education and support directed to parents.

- Date: October 22nd
- Time: 16:00h-19:00h
- Venue: Auditori ONCE. Gran Vía, 400. Barcelona

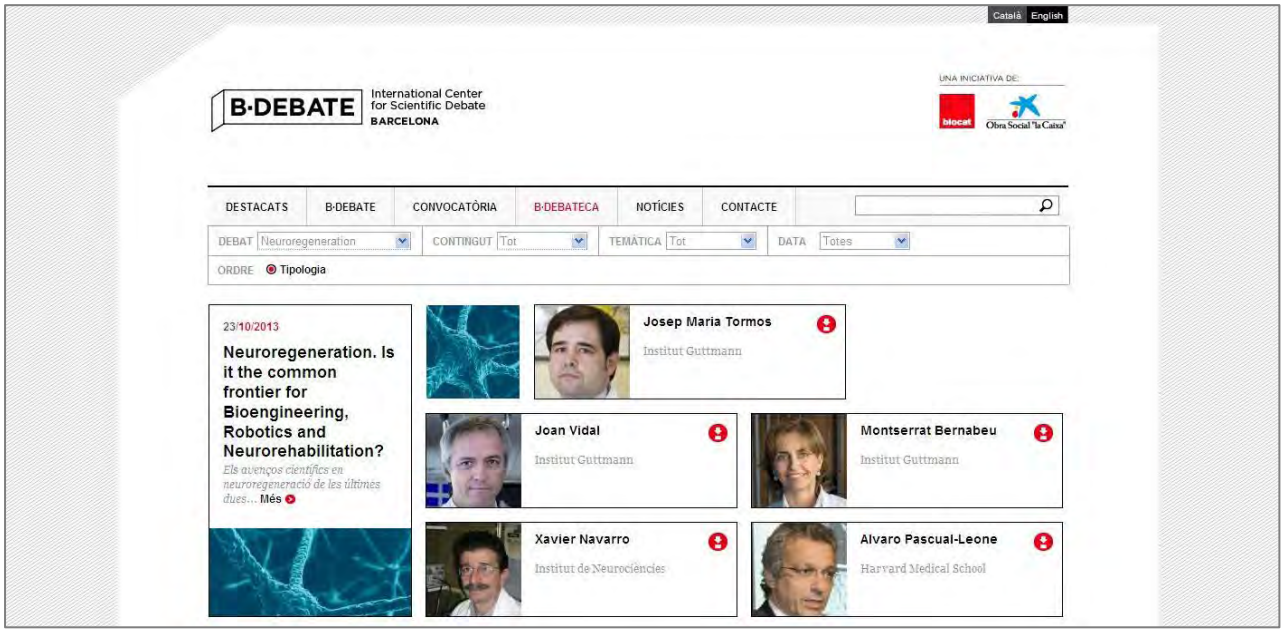
More information: www.guttmann.com/en

OUTCOMES

B·Debateca

On the website of **B·Debate**, you will find all the information related with the celebration of the meeting that includes reports, conclusions, scientific documents, interviews with the experts, speaker's CVs, presentations, videos, images, press documentation and other related materials. We invite you to visit the section **B·Debateca** on www.bdebate.org !

Contents of the meeting "NEUROREGENERATION: IS IT THE COMMON FRONTIER FOR BIOENGINEERING, NEUROSCIENCE, ROBOTS AND NEUROREHABILITATION?"



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PRACTICAL INFORMATION

Debates venue and Cocktail (October 23rd)

CosmoCaixa Barcelona
C/ Isaac Newton, 26 08022 Barcelona, Spain
http://obrasocial.lacaixa.es/laCaixaFoundation/home_en.html

Speakers' hotel

Hotel The Mirror
Carrer Còrsega, 255
08036 Barcelona, Spain
Phone: +34 93 2028685

http://www.themirrorbarcelona.com/

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ORGANIZERS

B·Debate International Center for Scientific Debate Barcelona is a **Biocat** initiative with support from **"la Caixa" Foundation**. It drives first-rate international scientific debates, to foster dialogue, collaboration and open exchange of knowledge with prestigious national and international experts, to approach complex challenges of high social interest in life sciences. B·Debate sees debate as a powerful, effective way to generate knowledge and strives to help position Barcelona as a benchmark in generating knowledge a nd Catalonia as a country of scientific excellence.

B·Debate sees debate as a powerful, effective way to generate new knowledge. The debates are top-notch international scientific meetings featuring a selection of experts of renowned international prestige and scientists that work in Barcelona and Catalonia, moderated by scientific leaders. Since 2009 B·Debate has invited about 800 recognized speakers and over 4.000 attendees. B·Debate seeks out answers to the challenges and needs of society in the field of life sciences, taking into account the complex, ever-changing conditions of this global world.

The debates foster the integration of different disciplines of science and deal with such diverse topics as ageing, new therapeutic approaches to various diseases, innovative technology to improve knowledge of the human genome, food resources, new tools to integrate knowledge management, clinical genomics, neurosciences, climate change, and new energy sources, among others. The knowledge and results obtained through these events is spread throughout both the scientific community and general society through the various B·Debate channels and instruments.

More info: www.bdebate.org

Institut Guttmann–NEUROREHABILITATION HOSPITAL, is the hospital of reference for medical-surgical treatment and for the comprehensive rehabilitation of people (adults and children) with spinal cord injury, acquired brain damage (head injuries, strokes) or other disabilities of a neurological origin. Institut Guttmann is accrediated as a Governmental Centre of Reference (CSUR) in the Comprehensive Care for complex spine cord injuries.

It has been located in Badalona since 2002, in a modern building covering over 17,000m2. The building is especially designed and equipped for its purpose. The modern and comfortable facilities, the 18,000+ patients seen and a team of over 400 professionals, as well as its scientific rigour and technical and human resources today make Institut Guttmann an internationally renowned centre of excellence in neurorehabilitation.

Institut Guttmann, as a highly-specialized hospital, has the mission of providing the best surgical, medical and rehabilitation treatment at all times. Treatment must be comprehensive, continuous, customized and at the highest possible level of human, scientific and technical excellence. Multidisciplinary team work, its own healthcare plans, expert and quality staff and scientific accuracy applied to all its procedures make Institut Guttmann a centre of excellence characterised by its ability to generate new knowledge and innovative techniques and its own therapeutic procedures for neurorehabilitation. These factors make it one of the leading hospitals in its field in the world. The Joint Commission International certify that the centre complies with all international standards of quality health care and organisational management since 2006.

Its teaching and research activities, through the University Institute for Neurorehabilitation, attached to the Autonomous University of Barcelona (UAB), make it a centre of knowledge committed to the field of neuroscience in general and neurorehabilitation and technologies applicable to personal autonomy in particular. As a research institute, it has the mission of developing the academic, scientific and research aspects of neuroscience in general and neurorehabilitation and technologies applicable to personal autonomy in particular. For better development of translational research, the Institut Guttmann has established cooperation agreements with more than 70 institutions around the world (institutions, universities, hospitals, research institutes and companies) using a model of open collaboration network, enhancing private public cooperation, with the aim to contribute to making a knowledge economy.

More info: www.guttmann.com / www.guttmanninnova.com

COLLABORATORS

CosmoCaixa offers interactive, enjoyable science and an open door for anyone who is eager to learn and understand and who never stops wondering why things are the way they are. **CosmoCaixa Barcelona** boasts the Geological Wall and the Amazon Flooded Forest, wich features more than 100 plant and animal species that convince visitors they have been transported from the Mediterranean to the very heart of the tropical jungle. In addition to its permanent facilities –Bubble Planetarium, digital Planetarium, Click and Flash, Touch, touch! and Explore your five senses– and its open areas, CosmoCaixa offers a scientific and educational programme that includes exhibitions, workshops, conferences, courses and debates involving experts from all over the world.

More info: http://obrasocial.lacaixa.es/laCaixaFoundation

Since 2009, the **abertis foundation** has been collaborating with the Guttmann Institute, a benchmark hospital for the medical-surgical treatment and comprehensive rehabilitation of individuals suffering from spinal injuries, acquired brain damage or other significant neurological disabilities. The collaboration has always focused on Corporate Social Responsibility projects and especially on the foundation's Road Safety Programme, given that a number of the Guttman Institute's patients are victims of road accidents. Both organisations have worked together in projects such as the "You've got one life left" campaign, implemented in Catalonia in 2009, and the charity "batukada" percussion session to raise funds for the TV3 programme, *La Marató*. In 2012, the collaborative work focused on the Auriga Project. A volunteer from the Guttmann Institute gave conferences in different Secondary Schools in the city of the Barcelona province to recount his experience – a motorbike accident at the age of 18 which left him paraplegic. The aim was to raise awareness among adolescents enjoying their first driving experiences of the need for safe, responsible mobility.

More info: www.fundacioabertis.org

The Spanish cell therapy network (TerCel) is a collaborative research project organized by the Spanish National Institute of Health Carlos III that started in 2003, to promote research in cell therapy and translate the scientific advances in this field to the clinic.
Based on a multidisciplinary approach and the interaction and cooperation between 33 groups of basic and clinical scientists across Spain, the main objective of TerCel is to develop new medical therapies based on the use of stem cells for cardiovascular diseases, neurodegenerative diseases and osteo-articular, immune-hematologic
and metabolic diseases.

More info: www.red-tercel.com

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