ERA-Net Neuron

NEWSLETTER 5

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News from ERA-Net NEURON

In December 2008, ERA-Net NEURON announced the publication of its second Joint Call for application which was focused on **'Development and advancement in methods and technologies towards the understanding of brain diseases'**. Eleven partner organizations from 10 countries committed the total budget of 12-14 million Euros for funding of the best applications to be chosen. In response to the Call, 79 pre-proposals were received, out of which 29 research consortia were asked to apply with full proposals. The final results of the review and funding decisions are expected in October 2009 and funding of the selected projects is expected on February 2010.

A new initiative taken by ERA-Net NEURON is on a €5000 award for an excellent paper in neuroscience published in 2008. This award will recognize the most remarkable and outstanding scientific publications by **young researchers** in the field of disease-related neurosciences. The announcement was made in May 2009 and the deadline for submission is August 15th, 2009. Further information can be found in HYPERLINK "http://www.neuron-eranet.org/en/237.php"

Scientific Workshop : "New technologies in Neurosciences"

Warsaw, September 2008

Foreword – Alexis Brice, France

This workshop is the second of a series devoted to new technologies in Neurosciences. The goal was to identify new technologies and frontiers which will allow breakthroughs in this field. The challenges for understanding how our brain develops and functions at multiple levels of integration as well as those related to elucidating the mechanisms and treating disorders of the nervous system, particularly neurodegenerative disorders, remain numerous. After a series of technological advances illustrated in July 2008 in Geneva, six new areas were explored at the Warsaw workshop which should help understanding the normal functioning of the brain and better treat its disorders.

This workshop, combined with the previous one in Geneva, gave a large overview of the major frontiers and technological progresses in the field of neurosciences and provided solid scientific ground for the call for proposals coordinated by countries members of the ERA Net-Neuron.

German Aerospace Centre, Project Management Agency

Federal Ministry of Education & Research (BMBF), Germany

Austrian Scuence Fund (FWF), Austria

National Authority for Scientific - Ministry of Education, Researc and Youth (ANCS - MECT), Romania

Ministry of Science and Innovation (MEC), Spain

Ministry of Health (MOH), Italy

Academy of Finland (AKA), Finland

National Research Agency (ANR), France

National Center for Scientific Research (CNRS), France

National Institute for Medical Research (INSERM), France

Chief Scientist Office, Ministry of Health(CSO-MOH), Israel

National Research Fund (FNR), Luxemburg

The National Centre for Research and Development (NCBIR), Poland

Institute of Health Carlos III (ISCII), Spain

Swedish Research Council (SRC), Sweden

Medical Research Council (MRC), UK

National Centre For Programmes Management, Romania

Funded by the European Commission

More information can be found in our web page
http://www.neuron-eranet.eu/index.php

Scientific Workshop

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Current approaches to visualize neuronal circuits: Engineering tools for "connectomics"

Jean Livet, Institut de la Vision, Paris, France

To better understand neural circuits, a detailed knowledge of their structure is needed. "Connectomic" approaches for obtaining a complete rendering of this structure are currently emerging using serial EM or fluorescence imaging. For instance, the full motor neuron circuitry in muscles of transgenic Thy1-YFP mice has recently been reconstructed. J. Livet introduces a new transgenic strategy for circuit imaging called Brainbow. Neurons in Brainbow mice express a large number of color labels resulting from combinations of 3-4 fluorescent proteins. Those colors provide a way to identify and distinguish neurons. For instance, ~300 mossy fibre axons were traced in a confocal image stack of the cerebellum. Synaptic contacts between granule cells and mossy fiber axons could be visualized. In some mouse lines, glial cells were labelled and their limits visible, demonstrating Brainbow's general potential to visualize cellular anatomy and contacts.

Advances in Transcranial Brain Stimulation

John Rothwell, Institute of Neurology, London, United Kingdom

Transcranial Magnetic Stimulation (TMS) enables activation of the brain through the skull. It is non-invasive, painless, mimics peripheral nerve stimulation and can activate axons. Research on TMS focuses on developing new stimulation protocols to recruit mechanisms of synaptic plasticity, technological improvements to increase the accuracy and depth of stimulation and the combination between TMS and imaging techniques to study the functional connectivity of networks in health and disease.

Particular attention is focused on repetitive TMS (rTMS) in which repeated stimulation of the same site leads to after effects on function that outlast the period of stimulation. rTMS seems to initiate long term changes in synaptic plasticity, and some of its effects are abolished by drugs that interfere with NMDA receptor function. Treatment using rTMS has proven beneficial in small scale clinical studies of depression, stroke and tinnitus. Other types of non-invasive transcranial stimulation like the Transcranial Direct Current Stimulation (TDCS) were also discussed.

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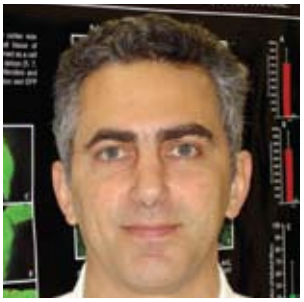
Current aims and hopes in cell based therapies of neurodegenerative diseases

Mohamed Jaber, Institute of Physiology and Cellular Biology, Poitiers, France



M. Jaber discussed cell therapy for treating degenerative diseases of the brain, such as Parkinson's disease (PD). Embryonic neuron grafts can overcome the limited regenerative capacity of the mature CNS, but such studies were hampered by lack of markers that distinguish graft from host. Using GFP-mice can overcome this hurdle. Recent results show that two months after transplantation, graft neurons maintain connections with most of the cortical and subcortical targets normally contacted by motor cortex neurons, including distant targets such as the spinal cord. Correct axon guidance is partly due to the fact that transplants-derived axons preferentially follow the demyelinated pathways of lesioned brain areas. Such grafts successfully treated PD in murine models, both structurally and behaviorally. The use of neural stem cells instead of embryo-derived graft tissue was also discussed.

High-resolution optical imaging in the living brain

Arthur Konnerth, Institute of Neuroscience, Munich, Germany

Dr. Konnerth introduced the approach of two-photon fluorescence imaging for the analysis of neural circuits at the level of individual neurons and even dendrites in the living brain. He presented recent work that showed that two-photon calcium imaging can be easily combined with other optical tools or with electrophysiological patch clamp recordings. Since two-photon imaging can only operate at depths of less than one millimeter, other methods, like optical fibre-based microendoscopy are needed for the detection of neuronal activity in deeper brain regions. Importantly, two-photon calcium imaging has revealed interesting insights in a mouse model of Alzheimer's disease. Thus, neurons in the vicinity of plaques were found to fire more frequently and in a correlated manner, thereby increasing the risk for seizure-like activity.

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Gene Therapy for Diseases of the Nervous System

Jacques Mallet, Pitié-Salpêtrière, Paris, France

The choice and design of vectors (vectorology) is the heart of gene therapy. Four types of vectors are currently used: "gutless"adenovirus, adeno-associated virus, oncoretrovirus and lentivirus. Gene transfer enables the prolonged and localized production of the therapeutic factor, avoiding both degradation and severe side effects. It is therefore particularly beneficial for improving regeneration and neuroprotection in various degenerative or traumatic CNS pathologies. GDNF vectors prevent neuron degeneration and behavioral impairment in a rat model of Parkinson's disease. RNAi gene therapy can induce regeneration in the injured spinal cord by suppressing formation of the glial scar. Finally, gene therapy could be used to fight obesity, by silencing OB-RGRP. Alongside the impressive technical advances in vectorology, there are still challenges in production, integration, immunogeneity and regulation of transgene expression. One project tackling these issues is INTEGRA, a consortium of 7 European laboratories.

Convergent-omics approaches as a major tool in neuropsychiatric research

Bertram Müller-Myhsok, Max-Planck-Institute of Psychiatry, Munich, Germany

Convergent genomic approaches help to identify candidate genes by combining serial analysis of gene expression with genetic linkage, as exemplified by the Genome-Wide case-control Association Study (GWAS) of Major Depression Disease (MDD). In this study, SNP genotyping identified 6 SNPs associated with MDD, leading to the identification of SLC6A15 as a novel candidate for MDD. This conclusion was strengthened by converging evidence, such as lower expression levels of the risk allele, a correlation between the risk-allele and various MDD related biological parameters and a trend for stress-induced anxiety in SLC6A15 knock-out mice. One problem with the convergent approach is that currently it lacks a clear mathematical or statistical basis. Compilation of various types of data may lead to non-linear relationships necessitating the use of new analysis methods, such as the Kernel methods.