

# ERA-NET NEURON

Make ends meet: celebrating 10 years of funding organizations co-operation

In September 2013 the ERA-NET NEURON celebrated its 10th anniversary with a scientific symposium in Warsaw, Poland. In ERA-NETs - projects that are funded by the European Commission in various fields - new types of co-operation between ministries and funding agencies are established. By co-operation and co-ordination on a national or regional level between funding bodies, a European Research

Area (ERA) was created. Cross border research is funded, allowing research groups to jointly work on specific questions, exchange ideas, and benefit from interdisciplinary expertise. Twenty-one funding organizations from 16 EU Member States, Israel, and Canada participate in NEURON, an ERA-NET for disease-related neuroscience.



NEURON was launched in Luxembourg on October 9th, 2003, with a small meeting of the founders from Luxembourg, Israel, Poland and Germany. Ten years, six Joint Transnational Calls (JTCs), and 224 funded research groups later NEURON has proved itself to be an invaluable tool for making the ends of science and research funding meet.

The development of this network can be described best by its prosperity: while four funding organizations started in 2003, already four years later 18 funding organizations from 13 countries joined forces. Since 2012 the number of funding organizations increased to 21 from 16 countries rising to a global dimension by participation of Canada since 2009.

The development comprised several steps among which the spirit of common and mutual trust was not least. To this end, the 32 well-attended ERA-NET NEURON meetings since 2007 contributed a great deal to NEURON's success. The number of 100 regular NEURON participants in these meetings also reveals that many of those permanently represented their funding organization - in other words NEURON has a very high degree of staff consistency. The impact and success of the ERA-NET NEURON can certainly be accounted to this personal engage- and involvement.

Why do these usually in national research funding commissioned organizations? It is because of the key instrument of the ERA-NET NEURON, the



Figure legend: Researchers and ERA-NET NEURON members at the 10th anniversary symposium in Warsaw, Poland, September 2013. From left to right: Alexander Klein (ERA-NET NEURON), Bernhard Sabel, Juan Antonio Barcia-Albacar, Andreas Fischer, Tracy Farr, Ferdinand Christoph Binkofski, Barbara Lukomska, Tim Magnus, Marlies Dorlöchter (coordinator of the ERA-NET NEURON at the PT-DLR in Germany on behalf of the German Ministry of Education and Research, BMBF), Martin Dichgans, Jens Dreier, Mirosław Janowski, Denis Vivien

Joint Transnational Calls for proposals (JTCs). Under the umbrella of the ERA-NET NEURON the last six JTCs addressed hot and cutting-edge scientific topics from mental disorders to method development and disorders of blood-supply of the brain (cerebrovascular). And the more funding organizations from different countries participate in a call the bandwidth of researchers that can apply in these JTCs increases. For instance non-NEURON partners Turkey participated in the JTC 2011, and Slovakia and Latvia in the JTC 2013 underlining the attractiveness of this funding measure. What was set out in 2003 as a new manifestation of a cooperation spirit among funding bodies in the fields of disease-related neuroscience has been put forward as an almost fixed point in the European funding measure map. Fifty-four international research consortia were or currently are funded, comprising 224 different research groups.

How are the JTC topics selected? Key elements of the ERA-NET NEURON are the foresight activities and scientific workshops with renowned researchers from the scientific community to integrate existing knowledge with new developments and future. Eleven publications on such foresight activities have already been released (<http://www.neuron-eranet.eu/en/353.php>) covering broad areas from new technologies in neurosciences to neurodevelopment and related disorders. Newsletters made the outcome of these activities available to the broad public. Based on these workshops future scientific research areas of high impact were and currently are being identified as possible call topics among the funding organizations. Particularly the well-attended workshops make ends of science and funding policies meet to the greater benefit of research.

Early-career scientist support is another main key component of the ERA-NET NEURON. The Excellent Paper in Neuroscience Award (EPNA) is an annual early-career scientist award for the best paper in neuroscience. The call is launched every May, and the awardee(s) is/are invited to present their work during a special lecture at a conference in the following year. In 2012, the award ceremony was organized as a specific session during the 8th FORUM of the Federation of European Neuroscience Societies (FENS) in Barcelona, Spain, attracting over 200 attendees. For the early-career scientists this offers thus a great opportunity to address a large audience besides the honor of the actual award. Not surprisingly, the EPNA calls became a prestigious award.

To celebrate the ERA-NET NEURON success and mark the 10th anniversary of the network, the scientific symposium of the JTC 2011 'Cerebrovascular Disorders' was used as a platform to celebrate the success story of the ERA-NET NEURON in Warsaw in September 2013. Cerebrovascular disease comprises brain dysfunctions related to diseases of the blood vessels supplying the brain (e.g. often resulting in a severe stroke as one of the most common cerebrovascular dysfunctions). Eleven scientific talks were held by the coordinators of the individual consortia to provide overviews about their ongoing research. Cutting-edge science was presented, often with close applicability to the clinics, thus increasing the hope to significantly improve therapy in such pathologies in the near future.

### **Models and mechanisms**

Developing an appropriate model reflecting the pathological symptoms of cognitive impairment in

humans is the topic of **Tracy Farr** from the Charité Hospital in Berlin, Germany, and her international consortium. They address the validity of current models including the quest for clinical biomarkers by using modern magnetic resonance imaging technique. Such is a highly promising candidate for testing novel therapies meaningfully under laboratory conditions, as Farr pointed out.

**Martin Dichgans** from the Ludwig-Maximilians-University Munich, Germany, and his consortium investigate brain damage and cognitive impairment that are caused by small vessel disease. Understanding the mechanisms behind the disease is important for precise diagnosis and rational therapy planning. In a well-designed approach from bench to bedside, the consortium succeeded in identifying some of the disease mechanisms in pre-clinical studies. In a next step they will extend investigation to clinical.

A different approach to understand the underlying mechanisms of small vessel disease pathology reported **Jens Dreier** from the Charité Hospital in Berlin, Germany. His international consortium examines the impaired electrical signaling in diseased brains. Brain function relies on a strictly regulated high-speed communication between neurons. This signal exchange is disturbed in diseases. The team identified a specific state of neurons from which cells either recover or die; the latter leading to neurodegenerative processes. "Such results will provide insights that may translate into future therapy by recruiting neurons back onto the recovery path" anticipated Dreier.

**Andreas Fischer** from the German Cancer Center in Heidelberg, Germany and his colleagues focus on a certain type of blood vessel malformations in the brain and spinal cord. By collecting data from patients suffering from this type of malformation, and also investigating the underlying molecular mechanisms the researchers aim to identify future drug targets that could eventually lead into clinical trials.

### Novel therapeutic approaches

Impaired vision, a common symptom stroke, reduces dramatically the quality of life of patients, reported **Bernhard Sabel** from the Otto-von-Guericke University of Magdeburg, Germany. In a pioneering approach his international consortium developed a method that improves vision by means of electrical stimulation of the neuronal pathways that are damaged or dysfunctional. "We plan to transfer the promising results to further clinical testing to improve the recovery of patients

after stroke" explained Sabel.

"Cell death and the lack of significant self-repair in the adult brain are one of the major obstacles in stroke therapy" reported **Juán-Antonio Barcia-Albacar** from the Fundación para la investigación biomédica del Hospital Clínico San Carlos, Madrid, Spain. The team's collaborative effort aims to overcome this insufficient self-repair by implanting biocompatible material into the damaged brain area and stimulating the remaining neurons.

Stem cells in stroke therapy play the main role in **Barbara Lukomska's** (Mossakowski Medical Research Centre, Warsaw, Poland) project. The researchers' goal is to direct injected stem cells to damaged brain areas where they should serve as sources of growth factors and other molecules to support the recovery of brain tissue. "By genetic engineering of the stem cells and by discovering the best route of application of the cells we want to prove that this approach has high potentials for a future clinical trial" says Lukomska.

"Acute stroke causes an inflammatory response; blocking this response could have an immensely beneficial effect on the recovery of patients", said **Tim Magnus** from University Medical Center Hamburg-Eppendorf, Germany. His consortium wants to use so-called nanobodies, small antibody-derived proteins, to shut down the inflammation after stroke. Promising results have been collected so far, and among them new biomolecular targets have already been identified enabling a potential alternative route in acute stroke therapy.

**Denis Vivien** from INSERM, France, reported that one of the main issues in stroke therapy is that patients usually receive treatment too late. Therefore, extending the time window during which patients can be treated is one of the main goals of his collaborative research. "We focus on the influence of proteases, a certain group of proteins that are involved in the course of acute stroke because they play a crucial role in future therapeutic approaches", as he pointed out.

Chronic motor disability is one of the symptoms in stroke that reduces significantly the quality of life of stroke patients. The optimization of existing protocols for an improved treatment of motor disabilities is one of the goals of **Ferdinand Binkofski's** consortium (University Hospital Aachen, RWTH Aachen University, Germany). They found out that sleep can help to improve impaired motor skill learning. "Now we try to



understand the underlying mechanisms and then to include the findings into the standard stroke therapy” explained Binkofski.

## **Perspectives**

### ***Joint Transnational Call 2014 launched***

The ERA-NET NEURON published its latest Joint Transnational Call for proposals for ‘European Research Projects on Neuroinflammation’ on January 10th, 2014 (<http://www.neuron-eranet.eu/>). The deadline for proposal submission was on March 10th, 2014.

The aim of the call is to facilitate multi-national, collaborative research projects that will address important questions relating to neuro-inflammation. The call will accept proposals ranging from understanding basic mechanisms of disease through proof-of-concept clinical studies in humans. These may include research on the role of inflammation in neurological or psychiatric disorders, or associated with traumatic brain injury, pathogen infection or toxicity in the nervous system.

### ***Excellent Paper in Neuroscience Award (EPNA) ceremony at the FENS Forum 2014 in Milan***

On Wednesday, July 9th, 2014, Nadia Kaouane from Vienna, Austria will present her award winning paper in an ERA-NET NEURON special lecture during the 9th FENS Forum of Neuroscience in Milan, Italy. The paper was published in March 2012 in the renowned scientific journal SCIENCE and addresses a

disease called Posttraumatic Stress Disorder (PTSD). This disorder is known to occur after extreme stressful events like war, tsunamis, terrorist attacks, or car accidents. Affected patients often suffer from excessive fear reactions. Although PTSD receives increased attention, effective treatments are missing, which might be due to the lack of models of the disease. The paper reports on a newly established laboratory model that can open new avenues for the development of innovative and successful treatments for PTSD. The work suggests that one of the crucial strategies to eliminate PTSD-related memory abnormalities will be to reduce the overproduction of a certain stress hormone in people traumatized by a highly stressful event.

## **Research into mental disorders**

From the funding program of 2013 “European Research Projects on Mental Disorders” twelve project proposals were selected on the basis of their scientific excellence. In total, 48 research groups from eleven European countries, Canada and Israel collaborate in these projects. The consortia address different neuro-psychiatric disorders. They range from autism spectrum disorders and other neurodevelopmental disorders, over depression, obsessive-compulsive disorders, to addiction. State-of-the-art methodology such as magnetic resonance imaging is employed to answer important research questions and to find ways to translate

the results into clinical application, for the benefit of the patients and their families and friends.

**Julia Stingl** (Germany) and her research consortium focus on specific genetic variants of proteins in the brain that are involved in metabolizing central nervous system-active substances such as antidepressants, antiepileptics, cannabinoids, and tryptamine derivatives. The investigations may have direct practical consequences for the treatment of affective disorders. In another genetic approach **Hannes Lohi** (Finland) and his team address the question of how genetic variants lead to childhood psychiatric disorders and strive to identify new avenues for early identification and treatment of these devastating conditions. The identification of a new autism genetic pathway in the brain is the focus of **Froylan Calderon de Anda** (Germany) and his research team. Autism spectrum disorders (ASDs) are neurodevelopmental disorders in which individuals have disrupted social communication and repetitive stereotyped behaviors, which lead to life-long difficulties. A number of mental disorders involve intellectual disability (ID) that is characterized by significant limitations both in intellectual functioning and in adaptive behavior. Researchers around **Vera Kalscheuer** (Germany) investigate genetically caused ID. By focusing on the loss of function mutations of a specific protein involved in chemical signal transduction they strive to identify novel targets that can be used for the development of drug therapies. Vulnerability to addiction is addressed by the team around **Salah El Mestikawy** (Canada). To communicate with each other brain cells use a combination of electrical and chemical signals. Dysfunction of communication in a specific brain region underlies the development of drug dependence. Sequential stages of the addiction process are investigated by **Veronique Deroche-Gamonet** (France) and her international researchers by exploiting new brain imaging methods. The studies will help to identify neurobiological dynamics into addictive behavior and potential treatment targets. In a pharmacological approach **Kristina Leuner** (Germany) and her team focus on the synthesis and detailed pharmacological and behavioral characterization of new derivatives of the antidepressant hyperforin. **Claudia Buss** (Germany) together with her international colleagues investigates the biological mechanisms of trans-generational transmission of early life stress (ELS). Research suggests the negative consequences of ELS exposure may not be restricted to the exposed individual alone but also may be transmitted to

her children. **Christine Winter's** (Germany) team investigates the Tourette syndrome to better understand the neurobiological disruptions and to develop a system directly targeting the origins of the symptoms in specific brain regions by advancing an established technology with proven benefits in Parkinson's disease. Obsessive-Compulsive Disorder (OCD) is a mental disorder featuring obsessions (intrusive ideas) and compulsions (repetitive overt behaviors) associated with high levels of anxiety. **Luc Mallet** (France) coordinates a consortium that investigates specific cognitive processes that, when dysfunctional, could lead to compulsive behavior and assesses the mechanisms of deep brain stimulation that may revert the symptoms. **Iiris Hovatta's** (Finland) research team uses modern genomic and proteomic methods to reveal novel molecular pathways and biomarkers of anxiety disorders. This approach will hopefully lead to an establishment of biomarkers for better diagnostics of anxiety disorders and molecular targets for development of better treatments. The role of inflammation and related processes in the development, phenomenology and treatment of depression is addressed by the researchers around **Martin Schaefer** (Germany). Interactions between the immune system and the brain might be important for the pathophysiology of mood changes or mood disorders and may offer a new field of interest to develop alternative treatment strategies.

Given the cutting-edge science of highly qualified and outstanding scientists in Europe, Israel, and Canada, the ERA-NET NEURON can look back on ten very successful years. The spirit of collaboration and multinational consortia has been very often leading into long-lasting cooperative approaches eventually benefiting the patients who suffer from devastating brain diseases. Not only could NEURON facilitate new alliances, but also harmonize neuroscience research between neuroscience funding organizations and provide a platform and support for early-career scientists to follow their academic path. All NEURON partners want to keep this spirit and apply for a third funding period within the framework of the EU Horizon2020 funding scheme.

**By Hella Lichtenberg, Alexander Klein and Marlies Dorlöchter**