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ERA-NET NEURON II KICK-OFF MEETING

JANUARY 2012, PARIS

The Kick-off meeting of the ERA-NET NEURON II took place in Paris, January 2012.

NEURON II will build on the achievements of its predecessor NEURON. We will launch a series of transnational joint calls for proposals, continue with the tradition of scientific workshops with the participation of world renowned scientists and organize additional workshops dealing with issues that further relate to and promote neuroscience research.

In the first phase of the ERA-NET NEURON, the tasks related to supporting young scientists were allocated to several work packages, where they were regarded as modules within different coordination and funding activities. In NEURON II, these tasks are brought together to make their coordination more coherent and efficient.

We have introduced a monitoring process into our work plan in NEURON II. This process will allow our partners to continuously improve our work, both on strategic planning (monitoring the joint call outputs) and at the operational level (monitoring NEURON II activities). In addition, this process will further strengthen the cooperation and integration between partners and facilitate the development of a sustainable framework for cooperation.

The ERA–NET NEURON II will address new ambitious goals by developing strategies towards a self-sustainable network with a long term perspective for a transnational funding program with regularly repeated funding initiatives. The financial, administrative and legal conditions to develop such a funding framework concept in a coordinated network of ministries and funding agencies will be explored.

NEWS FROM ERA-NET NEURON

On January 20 2012, ERA-NET NEURON announced the publication of its fifth Joint Call for application: "Novel Methods and Approaches towards the Understanding of Brain Diseases". Due to the broad topic 198 applications involving 787 research groups from 13 participating countries submitted pre-proposals to the Joint Call secretariat. Decisions on pre-proposals were announced on May 2012: 34 consortia were asked to submit a full proposal in the second step of the 2012 NEURON call. The deadline for full proposals submission was June, 25th.

Final funding decisions will be made in October 2012, and funding of selected projects will start in early 2013.

ERA-Net NEURON members and the scientific advisory board. Maison de la Recherche, Paris, France

Funded by the European Commission

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

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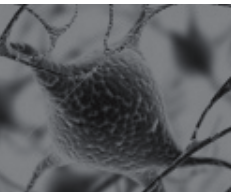

Scientific Workshop "Neuroinflammation"

Paris, January 2012

In conjunction with the Kick-off meeting, we organized a scientific workshop on "Neuroinflammation". In this workshop very important areas related to healthy brain functioning and brain diseases were tackled. The summary of the presentations and discussions is presented in the following pages.

The workshop was focused on neuroinflammation. The interest on this research area is indeed increasing due to relationship between neuroinflammation and Central Nervous System (CNS) diseases. The first presentation by Prof. P.O. Couraud described the structure and the biological function of the Blood Brain Barrier controlling the homeostasis of the brain and inducing a very specialized immunological landscape inside the brain. Pr. A. Vincent focused her talk on CNS diseases related to auto-antibodies and to the need to identify targets of these antibodies to define specific treatments. Pr. V.H. Perry addressed the question of the neuroprotective or neurotoxic role of the strong innate immune response observed in neurodegenerative disorders and on the role of infections in acceleration of neurodegenerative conditions. The two following presentations were devoted to Multiple Sclerosis (MS). Prof. M. Kerschensteiner presented the neurobiology of MS and highlighted the fact that axonal loss started before demyelination and therefore the necessity to define strategies to avoid it. Pr. A. Compston discussed genes and immunity in MS: among the 57 loci associated with MS, the most part were found on immune system related genes. The last presentation by Dr. M. Schwarz was dedicated to immunity and psychiatric disorders and more particularly on the molecular tryptophan-serotonin-kynurenine pathway (TSKP) for which an imbalance could be associated to schizophrenia.
Taking in account all the presentations, it is clear that a large volume of evidence points to the existence of a cross-talk between the immune system and CNS. Depicting the alphabet, the words and the language of this cross-talk is therefore a keystone to define new strategies and new therapeutics to treat the numerous CNS diseases in which the immune system is involved.

From right to left: NEURON coordinator PD Dr. Marlies Dorlöchter, speakers of the "Neuroinflammation" symposium: Prof. M. Kerschensteiner, Dr. M. Schwarz, Prof. A. Compston, Prof. V.H. Perry, Prof. A. Vincent, Prof. P-O Couraud, organizers of the symposium: Prof. Bernard Bioulac, Prof. Alexis Brice, Dr. Francois Bourre.

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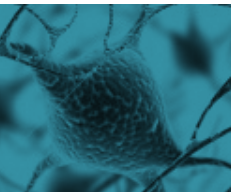

INTRODUCTION TO NEURO-IMMUNITY AND BRAIN INFLAMMATION

Prof. P-O Couraud

Institut Cochin, INSERM, CNRS, Paris Descartes University, Paris, France

The blood-brain barrier (BBB) is crucial to maintain brain homeostasis and avoid major inflammation and consequently neuronal death. However, very tuned immunological responses are able to fight local infections, the brain being a very specialized immunologic site. In particular, microglial cells, belonging to the innate immune system, can orchestrate local immune responses via cytokine secretion. Moreover, despite the lack of lymph vessels, antigens in the brain parenchyma can nevertheless gain access to peripheral lymph nodes where they can stimulate systemic immune responses, notably through perivascular spaces of brain penetrating blood vessels. Knowledge of mechanisms controlling BBB permeability, regulating leukocyte infiltration and cytokine production will be powerful to define new therapeutic pathways to fight CNS inflammatory diseases.

AUTO-IMMUNE DISEASES OF THE NERVOUS SYSTEM

Prof. A. Vincent

Oxford University, England

Traditionally, antibody-mediated diseases include 1) myasthenia gravis (MG) which is antibody-mediated and responds very well to immunotherapies and 2) paraneoplasic neurological syndromes with antibodies to intracellular onconeuronal proteins and a poor response to immunotherapies. In the last ten years, however, it has become clear that there are antibodies to neuronal cell surface proteins in central nervous system diseases associated with a very good response to immunosuppressive treatments. The targets are receptors, ion channels and related proteins on neurons and glia, and the patients can present with many debilitating features. This is an important and developing area of neurology. Identifying new targets and their association with different neurological syndromes will lead to more efficient diagnosis and treatments.

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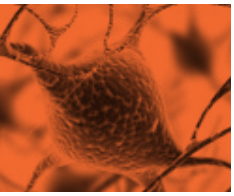

SYSTEMIC INFLAMMATORY INFLUENCES ON NEURODEGENERATION

Prof. V.H. Perry
Southampton University, England

A strong innate immune response is observed in neurodegenerative disorders. Is this neuroprotective or neurotoxic? How it contributes to the disease progression? In a mouse model of prion-disease, it has been shown that injection of LPS (lipopolysaccharides, simulating bacterial infections) induced production of inflammatory cytokines, microglial activation and increased sickness behavior and neural loss compared to the non-prion mice. This synergistic inflammatory exacerbation of a CNS neurodegenerative condition by a peripheral inflammation is also present in other models. Immunization strategies against Aß peptides were not able to change the cognitive decline although efficient to reduce the plaques. There is increasing evidences that systemic inflammation and/or infections lead to an acceleration of neurodegenerative conditions. It is therefore crucial to know which components of the immune system are involved to define new therapies.

NEUROBIOLOGY OF MULTIPLE SCLEROSIS

Prof. M. Kerschensteiner
Ludwig-Maximilians University, Munich, Germany

Multiple Sclerosis (MS), affecting 2.5 million persons worldwide, is classically described as an auto-immune disease leading to demyelination in the brain and spinal cord. Nevertheless, accumulating evidences showing that axonal loss starts early in the disease suggest that neuronal pathology is crucial for the MS. In particular using the classical EAE mouse model of MS, it has been shown that axonal loss begins before demyelination. Moreover, treatments with ROS scavengers (Reactive Oxigen Species) or with glutamate receptor antagonists were able to stop axonal degeneration. As many neuroprotective compounds are also immunologic modulators, one of the challenges is to develop new assays and compounds for selective neuroprotection.

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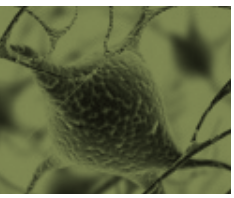

GENES AND IMMUNITY IN MULTIPLE SCLEROSIS

Prof. A. Compston

University of Cambridge, England

As the prevalence of MS varies with geographic region and ethnicity, genetic determinants have been suggested as one component of the complex aetiology. GWAS (Genome Wide Association Studies) allow identification of loci associated with MS. A strong association between a polymorphism in the major histocompatibility complex and MS was found in the 1970s. Now 57 new loci have been identified as associated to MS, most of them implicsating immune-system related genes and specifically those involved in T-cell differentiation or maturation. Very few appear related to primary neurodegeneration. In support of the primary immune basis for MS, treatment with the monoclonal antibody alemtuzumab targeting specifically mature T-cells iis significantly more efficient than the classical INFß treatment but at least 30% of treated MS patients develop a secondary thyroid autoimmune disease. Developing new antibodies, finding a better compromise between efficiency and safety are clearly the future of MS drugs.

IMMUNITY AND PSYCHIATRIC DISORDERS

Dr. M. Schwarz

Ludwig-Maximilians University, Munich, Germany

Although a longstanding history of potential association between immune system and psychiatric disorders, little is known about details of these connections. A strong association between MHC loci and increased risk of schizophrenia has been reported. Cytokines, like IFNα or IL-1ß, are known to be linked to the sickness behavior. For example, treatments with IFNα of patients suffering of rheumatoid arthritis who develop depression strongly reduce these psychiatric symptoms. Nevertheless biological and molecular ways by which immune system is associated to these disorders are largely unknown. One of these ways could be linked to the tryptophan metabolism giving rise to serotonin, in one hand, and to endogenous NMDA-receptor agonists and antagonists in another hand towards the tryptophan-serotonin-kynurenine pathway (TSKP), some immune actors being able to regulate this pathway. Clinical and biological studies suggest also that an imbalance in the kinurenine pathway could be associated with schizophrenia. Depicting the molecular ways by which psychiatric disorders and inflammation are linked is surely a great promise to develop new therapies.