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CONFÉRENCES
JACQUES-MONOD

Glial cells at the crossroads of innate immunity and brain functions

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Roscoff, France

Chairperson: **Etienne AUDINAT**

Vice-chairperson: **Melanie GRETER**

Résumé français du rapport sur la conférence

La conférence Jacques Monod sur «Les cellules gliales au carrefour de l'immunité innée et des fonctions cérébrales» s'est tenue à Roscoff (Bretagne) du 12 au 16 juin 2017. Elle a réuni 64 scientifiques de 12 pays différents, 24 conférenciers invités et 39 candidats sélectionnés, dont 23 jeunes scientifiques (12 post-doctorants et 11 doctorants).

La motivation générale pour organiser cette conférence était de promouvoir les interactions entre les chercheurs de deux domaines en pleine croissance, celui des interactions neurone-glie et celui de la neuroimmunologie. En effet, des avancées récentes ont clairement démontré que le système nerveux central (SNC), même protégé par la barrière hémato-encéphalique (BHE), n'est pas à l'abri de l'influence du système immunitaire et que les cellules gliales sont des acteurs clés dans les interactions entre les systèmes nerveux et immunitaire. Ainsi, une partie importante de la réunion a été consacrée aux nouvelles études sur les cellules microgliales, les cellules immunitaires résidentes du SNC : Deux conférences plénières (45 minutes) ont été données par deux leaders mondiaux, pionniers de l'étude des microglies, Helmut Kettenmann et Richard Ransohoff, une session importante était dédié aux interactions neurones-glie dans des conditions physiologiques et une autre à l'aspect phylogénique des interactions neurones-microglie. Une session a porté sur l'unité neurovasculaire, qui constitue l'interface principale entre les systèmes immunitaire et nerveux. Pendant les dernières sessions de la conférence consacrées au système neuro-immunitaire dans les troubles neurologiques et psychiatriques, la présentation de nouveaux résultats sur les propriétés et les rôles des cellules non-neuronales du SNC et des cellules immunitaires dans diverses neuropathologies telles que l'épilepsie, la maladie d'Alzheimer, les lésions et tumeurs périnatales et les troubles cognitifs, a mis en évidence de nouveaux concepts qui pourraient ouvrir la voie au développement de nouvelles thérapies plus efficaces.

En plus des deux conférences plénières (45 minutes) et des 22 présentations des conférenciers invités (30 minutes), sept présentations courtes (15 minutes) ont également été sélectionnées à partir des résumés soumis par les conférenciers inscrits et ont été incluses dans les différentes sessions. Les six post-doctorant(e)s et la doctorante sélectionnés sur la base de la qualité et du sujet de leur travail ont fait d'excellentes présentations. Tous les autres participants ont présenté leur travail au cours de deux sessions posters qui ont duré plus de deux heures chacune, ont attiré beaucoup de monde et ont donné lieu à des discussions animées.

Le financement de la réunion a été principalement assuré par le CNRS et l'INSERM, ce dont nous sommes très reconnaissants. Nous tenons également à remercier les généreux soutiens de la "Company of Biologists" et de l'Ecole des Neurosciences de Paris Île-de-France (ENP), qui nous ont permis de réduire les frais d'inscription et d'hébergement des jeunes scientifiques. L'entreprise "Luigs and Neumann" a également parrainé le voyage et l'hébergement d'un conférencier invité. La société "HelloBio" a également contribué à certaines dépenses de conférence. L'excursion traditionnelle à l'île de Batz a été particulièrement agréable, avec un beau temps, permettant des discussions informelles et informelles.

Lors de la réunion d'organisation le dernier jour de la conférence, Melanie Greter, Université de Zurich, Suisse, a été confirmée comme la présidente d'une possible nouvelle conférence (en 2020). Par ailleurs, François Rassendren (CNRS, Montpellier, France) a été élu à l'unanimité comme nouveau

vice-président. Ce choix de président et de vice-président augure bien de futures rencontres qui développeront de nouveaux thèmes en neurosciences et en neuro-immunité. Nous avons eu d'excellents retours sur le contenu scientifique de la conférence mais aussi sur son format. Tout le monde s'accordait sur le fait que le rassemblement de scientifiques d'horizons très différents, de l'électrophysiologie des synapses à l'immunologie, tous intéressés par les interactions neuronales et neuro-immunitaires, était extrêmement intéressant et générait de nouvelles idées et collaborations. L'atmosphère détendue de la conférence, la beauté du site et l'excellente organisation (y compris la qualité de la nourriture!) du CNRS ont également été très appréciées et ont contribué à la qualité des échanges scientifiques.

Report on the conference

1. Meeting overview

The Jacques Monod Conference on « Glial cells at the crossroads of innate immunity and Brain functions" was held in Roscoff (Brittany) from the 12th to the 16th of June 2017. It gathered together 64 scientists from 12 different countries, 24 invited speakers and 39 selected applicants, including 23 young scientists (12 postdocs and 11 PhD students).

The overall motivation for organizing this conference was to promote interactions between researchers of two growing fields of the neuroscience domain: neuron-glia interactions and neuroimmunology. Indeed, the concept of the CNS as an immune-privileged organ has led to the misleading idea that it is not an active immune organ, protected from its surroundings by an impermeable blood-brain barrier (BBB). Recent advances in the field, however, have clearly demonstrated that this was not the case and that glial cells are key players in the interactions between the nervous and immune systems. Accordingly, an important part of the meeting was devoted to new studies on microglial cells, the resident immune cells of the CNS, with the two keynote lectures (45 minutes) given by two world leaders who pioneered the study of microglia, Helmut Kettenmann and Richard Ransohoff, an important session on neuron-glia interactions in physiological conditions and another one on the phylogenic aspect of neuron-microglia interactions. A session focused on the neurovascular unit, which constitutes the main interface between the immune and nervous systems. During the last sessions of the conference on the neuroimmune system in neurological and psychiatric disorders, the presentation of new results on the properties and roles of non-neuronal CNS and immune cells in various neuropathologies, such as epilepsy, Alzheimer disease, brain tumors, perinatal lesion and cognitive disorders, highlighted novel concepts that could pave the road for the development of new and more efficient therapies.

Invited speakers gave most of the talks (30 minutes each) during these sessions but 7 short presentations (15 minutes) were also selected from the abstracts submitted by the applicants and were included in the different sessions. The six postdocs and the PhD student who were selected on the basis of the quality and the topic of their work gave excellent presentations. All other attendees presented their work during 2 poster sessions that lasted more than 2 hours each, were well-attended and led to vivid discussions.

The funding for the meeting was provided mainly by the CNRS and the INSERM, which we very gratefully acknowledge. We would also like to acknowledge the generous supports of the "Company of Biologists" and of the"Ecole des Neuroscience de Paris Île de France" (ENP), which allowed us to reduce the registration and accommodation of the young scientists. The company "Luigs and Neumann" also sponsored the travel and accommodation of an invited speaker. The company "HelloBio" also contributed to some conference expenses.

The traditional excursion to the island of Batz was particularly pleasant, with a beautiful weather, allowing unformal and friendly discussions.

At the business meeting on the last day of the conference Professor Melanie Greter, University of Zürich, Switzerland, was confirmed as the president of a possible the next meeting (in 2020). Furthermore, François Rassendren, Research Director at CNRS, Montpellier, France, was unanimously

elected as the new vice-president. This choice of president and vice-president bode well for future meetings, which will develop new themes in neuroscience and and neuroimmunity.

We had excellent feedback on the scientific content of the conference but also on its format. Everyone agreed on the fact that the gathering of scientists with very different backgrounds, from synapse electrophysiology to immunology, all interested in neuron-glia and neuro-immune interactions, was extremely interesting and generated new ideas and collaborations. The relaxed atmosphere of the conference, the beauty of the site and the excellent organization (including the quality of the food!) by the CNRS were also very much appreciated and contributed to the quality of the scientific exchanges.

2. Report on scientific aspects

Day 1

The meeting started on the first evening with a welcome reception and dinner followed by an introduction from Etienne Audinat. This was followed by an impressive keynote lecture from Helmut Kettenmann on the diverse microglial activation in different pathologies, highlighting the importance of microglia purinergic signaling in mouse models of schizophrenia, Alzheimer disease and glioma. The high quality of the talk by a pioneer of the study of microglia physiology was an excellent introduction to the conference and set the tone for the subsequent presentations during the meeting.

Day 2

The first session was devoted to neuron-microglia interactions in physiological conditions and to the role of microglia during development. Florent Ginhoux described an original new method to differentiate microglia from mouse and human induced pluripotent stem cells (iPSC) that will be a useful microglial source for biological, pathophysiological, and therapeutic studies. Michel Mallat described how microglia, through VEGFR1-Nox2 signaling pathway, controls cortical astrogliogenesis during development and may thereby impact the formation of neuronal networks. Sonia Garel showed that microglia dysfunction and immune risks during embryonic development impair the assembly of cortical circuits and lead to pathological brain wiring. Etienne Audinat presented data supporting the role of microglial brain-derived neurotrophic factor on the functional maturation of excitatory and inhibitory synapses during the postnatal development of thalamocortical networks. Alain Bessis shows that microglia regulates the activity-dependent plasticity of glycinergic synapses in the spinal cord by controlling the diffusion dynamics and synaptic trapping of glycine receptors. Wenbiao Gan presented new data on in vivo imaging of dendritic spines and of extracellular glutamate dynamics highlighting the role of microglia in controlling neuronal structure and functions in different physiological and pathological conditions. Three short talks presented by Celine Cansell (Nutritional lipids and glial remodeling), Stéphanie Giera (Microglia regulate myelination via GPCR signaling in oligodendrocytes) and Ivana D'Andrea (Microglia drives behavioral flexibility through serotonin 2B receptors: implications for stress vulnerability?) were also included in this session that nicely highlighted the new concepts that are emerging in the field of neuron-microglia interactions. Importantly, speakers presented largely unpublished, cutting edge results.

At lunch long tables ensured that speakers and participants mixed and discussed their work. After lunch there was the first of the 2 poster sessions, which were both very well attended with a lot of interactions.

The second session of the day was on phylogenic aspects of neuron-glia interactions. Hartenstein Volker provided a nice overview of the origin and development of the different classes of glia in Drosophila, with an interesting comparison with other animal species. Christophe Lefebvre then talked about interactions between microglia and neurons in the medicinal leech in the context of neuroprotection. The last presentation of the day was a short talk given by Fernandes M Vilaiwan on an unexpected role for wrapping glia in coordinating neuronal development across distinct brain regions of the Drosophila visual system to ensure proper timing and neuronal patterning. Throughout the first day and subsequent days of the conference the level of audience participation was extremely high with many questions and discussions after each talk.

Day 3

The third day started with the continuation of the session on the phylogeny of neuron-glia interactions. Alicia Hidalgo, nicely described a network of genes that drives glial regenerative response to injury to enable functional recovery in Drosophila. Finally, Angela Giangrande closed this session with an elegant study on the role of a single transcription factor that controls the development of macrophages within and outside the *Drosophila* nervous system. This session nicely revealed the power of invertebrate models in deciphering the different functions of glia and of their interactions with neurons.

The morning was ended by the session on the neurovascular unit. Pierre-Olivier Couraud presented an overview of the structural characteristics of the blood-brain barrier and its functional involvement in brain homeostasis and cross-talks between the nervous and immune systems. David Attwell showed his last results on the role of astrocytes and pericytes in the control of the brain blood flow and on how pericytes respond to neurodegenerative conditions. Thomas Blank finally showed that brain endothelial and epithelial cells play an active role in transmitting signals elicited by an immune response in the periphery to the brain. Unfortunately, Anne Joutel who was supposed to talk about small vessel diseases of the brain and the microvascular extracellular matrix was sick and could not attend the meeting. Melanie Greter who actively contributed to the preparation of the program and was supposed to present her last results on peri-vascular macrophages could not attend the conference for family reasons.

After the visit to Batz Island in the early afternoon, the late afternoon session opened the first part of the presentations on the neuroimmune system in neurological disorders. Annamaria Vezzani presented her last results on innate immunity and inflammation in epilepsy and the pathophysiological role of glial cells in this disorder. Christian Steinhauser talked about the uncoupling of hippocampal astrocytes as a cause of human temporal lobe epilepsy. Amanda Sierra showed data on the efficiency of microglial phagocytosis to determine the dynamics of neuronal apoptosis in neurodegenerative disorders.

The third day was closed by the stimulating keynote lecture of Richard Ransohoff entitled “Microglia: Unique myeloid brain cells“ and during which he proposed that microglia are bristling with drug targets that only await our deciphering.

Day 4

The session on the neuroimmune system in neurological disorders continued on this last day of the conference with Marie-Eve Tremblay presenting her new data on dark microglia that could represent a subset of cells that become stressed as a result of their hyperactive involvement with the remodeling of neuronal circuits. François Rassendren described RNAseq data that define the microglia reactivome, a core of microglial genes deregulated in all different pathological conditions. Melanie Morin-Bureau gave a short talk on the immune response of microglia in human temporal lobe epilepsy and, in a second short talk, Nadia Gasmi provided evidence suggesting that extravasating monocytes in adult rats can transdifferentiate into monocyte-macrophages. After the coffee break, Claudia Verderio presented new findings linking inflammation and synapse dysfunction that uncover a previously unrecognized role of vesicles-associated miRNAs in silencing key synaptic genes. Cristina Limatola described how enriched environment in mice reverts the immunosuppressive phenotype of invading myeloid cells in glioma by modulating inflammatory gene expression and promoting phagocytic activity. Emilie Faivre then gave a short talk on the dysregulation of astrocytic adenosine A2A receptors during the development of Alzheimer's disease.

After the second poster session in the early afternoon, Pierre Gressens described the last results of his lab suggesting that canonical Wnt pathway activation in microglia could thus be a novel neuroprotective strategy against brain damage in preterm infants and other neuroinflammatory disorders. Sophie Layé then talked about the role of dietary lipids and microglia in mood and cognitive disorders. Unfortunately, Roland Liblau who was supposed to close the conference with a presentation on adaptive immunity in inflammatory diseases of the CNS had to leave the conference early on for family reasons.

3. Conclusions and recommendations

The meeting combined outstanding scientific presentations of the very latest research on neuron-glia interactions. The audience engagement at the oral session but also during the poster presentations was impressive and the scientific discussion was animated. Due to the continued interest and the venue of the conference, the attendance remained close to its maximum from the beginning to the very last talk. Our informal feedback from the participants was extremely positive, both on the scientific content of the conference but also on its format. Everyone agreed on the fact that the gathering of scientists with very different backgrounds, from synapse electrophysiology to immunology, all interested in neuron-glia and neuro-immune interactions, was extremely interesting and generated new ideas and collaborations. The relaxed atmosphere of the conference, the beauty of the site and the excellent local CNRS organization (including the quality of the food!) run by Nathalie Babic were also very much appreciated and contributed to the quality of the scientific exchanges. During the business meeting, everyone agreed on the idea of organizing another conference on the same topic. It was suggested to invite more immunologists to really bridge the two fields of neuroscience and immunology. The year of the next conference should also be carefully chosen to avoid the main conferences on glia (Euroglia, GRC on glia…).