



# The Brain as a Target for Inflammatory Processes

Berlin, September 7 – 9, 2006

## Executive Summary

The ESF EMRC Exploratory Workshop 'The Brain as a target for inflammatory processes' took place from 07-09 September 2006 at Inselhotel Potsdam-Hermannswerder, where the participants of the workshop also were accommodated.

16 Scientists from 6 different countries took part in presentations and discussions. Additional 6 scientists completed as chairs and discussion partners the workshop. Since the meeting site was on a peninsula with a very rural character the participants stayed together the entire time and had little opportunity to escape this community. This also included common meals, common meetings in the evening after the sessions and one common excursion. This structure led to intense discussions since the meeting had the typical retreat character.

The Workshop started Thursday afternoon at 15:00 and finished on Saturday at 12:00. The presentations were usually for 20 min. We sometimes had questions during the talk but commonly we had an intense discussion after each presentation. Since the program was not too tight we sometimes run a bit over time since many topics were heavily discussed. As we stated in the application and as it is also evident from the program the main topic was the brain as target for inflammatory processes. One focus certainly was multiple sclerosis and the cellular and molecular consequences.

The scientific part of the meeting was preceded by a presentation of the European Science Foundation given by Monika Bradl, Austria. She clearly explained the goals of the ESF, their possibilities for the European science community and potential ways

of funding. We also had changes in the program: We had one replacement, namely Adriano Fontana's co-worker Ursula Malipiero, Suisse, presented the work of this research group. Unfortunately, both Adriano Aguzzi, Suisse, and Roger Nitsch, Suisse, got both stuck in a plane from Zurich on Friday morning. Since there was a serious departure problem in Zurich they could not make it to the meeting but contacted us and apologized.

At the end of the meeting we had an intense round table discussion how we could foster our interactions and in particular about the options of creating a European network on the topic of inflammatory processes of the brain. We all agreed that it would be a timely effort and we decided to explore the possibilities as one of our future goals. Helmut Kettenmann, Germany, got the mandate of the group to explore possibilities in Bruxelles and inform the group.

### **Scientific content**

The main theme was to discuss molecular and cellular mechanisms of inflammatory processes in the central nervous system. We had been focusing both on basic cellular mechanisms and on disease-related questions. The meeting started with mechanisms triggered by bacterial meningitis presented by Ursula Malipiero, Suisse, and A. Marceline van Furth, Netherlands, chaired by Jörg Weber, Germany. The next section focused on mechanisms in multiple sclerosis. There Wolfgang Brück, Germany, was alluding on the interplay between inflammation and degeneration while Christine Dijkstra, Netherlands, was discussing the role of macrophages and axonal loss in this disease state. The session was chaired by Frauke Zipp, Germany. On Friday we started to discuss mechanisms of cross-talk between nerve and immune cells. Bente Finsen, Denmark, reported on fate of microglial cells in acute and chronic central nervous system pathology while Hugh Perry, UK, discussed the impact of a systemic inflammation. Robin Franklin, also from the UK, reported on his findings how precursor cells in the CNS are affected by inflammation. The chapter chaired by Harald Neumann, Germany, was focusing on specific molecules important in inflammation. Nancy Rothwell, UK, discussed the role of Interleukin-1 and also its potential as a therapeutic target while Krzysztof Selmaj, Poland, discussed the role of stress-induced proteins in the inflammatory process. In the last talk on Friday Ulrich Dirnagl, Germany, discussed inflammatory mechanisms which become evident in the late phase of stroke while Burkhard Becher, Suisse, discussed the role of T-cells and

the interactions with the intrinsic brain cells. On Saturday Gennadij Raivich, UK, discussed the neuroimmune surveillance while Jennifer Pocock, UK, was focusing on glutamate receptors in microglial cells which seem to play a very important role in neurodegeneration and in the interaction of microglia in particular with neurons. The last talks were given by Hartmut Wekerle, Germany, about the auto-immune milieu and finally by Frank Heppner, Suisse, reported on the development of a new animal model to paralyze microglia and, thus, determining the role of these cells in inflammatory and pathologic processes.

### **Outcome**

This meeting manifested existing interactions and collaborations. Moreover, new collaborations were discussed and organized. I can report for myself that I have newly launched two collaborations during this workshop.

As already alluded in the Executive Summary we had an intense discussion about plans for further research and common consortia. While there were mutual interactions between participants we also thought about a general strategy to implement this theme as a European network program. With this goal in mind we departed.

## Final Programme

Time for each speaker is 30 minutes (20 minutes presentation and afterwards 10 minutes discussion).

### Thursday 7 September 2006

Morning *Arrival*

15.00 **Introduction**

**Presentation of the European Science Foundation (ESF)**

**Monika Bradl** (Standing Committee for European Medical Research Councils)

**Acute neuroinflammation of the CNS**

Chair: **Jörg Weber**

15.30 - 16.30

**Adriano Fontana**, Switzerland substitute: **Ursula Malipiero**

On the role of transforming growth factor beta in bacterial meningitis

**A. Marceline van Furth**, The Netherlands

Pathophysiological aspects of bacterial meningitis

16.30 – 17.00

*Break*

**Chronic neuroinflammation of the CNS**

Chairs: **Frauke Zipp**

17.00 - 18.00

**Wolfgang Brück**, Germany

Inflammation and degeneration in multiple sclerosis

**Christine D. Dijkstra**, The Netherlands

Macrophages and axonal loss in multiple sclerosis

18.30

Shuttle to Park Sanssouci

19.00-20.00

Guided Tour Park Sanssouci

20.00 - 22.00

*Dinner (Krongut Bornstedt)*

### Friday 8 September 2006

**Crosstalk of the nervous and the immune system**

Chairs: **Christine Stadelmann/Robert Nitsch**

09.30 - 11.00

**Bente Finsen**, Denmark

Inflammation in acute and chronic CNS pathology

**Victor Hugh Perry**, United Kingdom

Impact of systemic inflammation on the brain in health and disease

**Robin Franklin**, United Kingdom

Inflammation of precursor activation - a critical step in remyelination

11.00 - 11.30

*Break*

## Molecular mechanisms in neuroinflammation and neurodegeneration

Chair: **Harald Neumann**

11.30 - 12.30

**Nancy Rothwell**, United Kingdom  
Interleukin-1 as a therapeutic target in CNS

**Krzysztof Selmaj**, Poland  
The role of stress-induced proteins (hsps) in regulation of autoimmunity within CNS

12.30 - 14.30

*Lunch*

### Secondary neuroinflammation

Chair: **Mathias Bähr**

14.30 - 16.00

**Adriano Aguzzi**, Switzerland  
Immunobiology of prion diseases

**Ulrich Dirnagl**, Germany  
Inflammatory and immune responses in stroke

**Roger Nitsch**, Switzerland  
Immunotherapy of Alzheimer's Disease

16.00 - 16.15

*Break*

16.15 - 17.45

**Discussion about plans for follow-up research activities and collaborative actions**

18.30 - 20.30

*Dinner*

## Saturday 9 September 2006

### Role and function of immune cells within the CNS

Chair: **Helmut Kettenmann/Ralf Gold**

09.00 - 10.30

**Burkhard Becher**, Switzerland  
Autoaggressive T Cells in the CNS: Pathogenicity genes and broken paradigms

**Gennadij Raivich**, United Kingdom  
Neuroimmune surveillance: chemical signals and their effects on the neurodegenerative process

**Jennifer Pocock**, United Kingdom  
Microglial glutamate receptors; switching off toxicity

10.30 - 11.00

*Break*

11.00 - 12.00

**Hartmut Wekerle**, Germany  
(Auto-)Immune milieus before and within the central nervous system

**Frank Heppner**, Switzerland  
Microglial paralysis in vivo

12.00 - 12.30

**Closing remarks**

Afternoon

*Departure*

## Final List of Participants

### Convenor:

1. **Helmut KETTENMANN**  
Max-Delbrück-Zentrum für Molekulare Medizin  
Zelluläre Neurowissenschaften Abteilung  
Germany

10. **Ulrich DIRNAGL**  
Neurologische Klinik  
Charité - Universitätsmedizin Berlin  
Germany

### Co-Convenors:

2. **Joerg WEBER**  
Neurologische Klinik  
Universitätsklinikum Charité  
Humboldt University Berlin  
Germany

11. **Bente FINSEN**  
Anatomy and Neurobiology  
Odense University  
Denmark

3. **Frauke ZIPP**  
Charité Campus Virchow  
Neuroscience Research Center  
Department of Neuroimmunology  
Humboldt University Berlin  
Germany

12. **Ursula Malipiero**  
Clinical Immunology  
Internal Medicine  
Unispital Zürich  
Switzerland

### Organiser:

4. **Stefanie KORTHALS**  
Max-Delbrück-Zentrum für Molekulare Medizin  
Office ESF Workshop  
Germany

13. **Robin FRANKLIN**  
Department of Clinical Veterinary Medicine  
University of Cambridge  
United Kingdom

### ESF Representative:

5. **Monika BRADL**  
Medical University Vienna  
Department of neuroimmunology  
Austria

14. **Frank HEPNER**  
Institute of Neuropathology  
University Hospital Zurich  
Switzerland

15. **Victor Hugh PERRY**  
School of Biological Science  
University of Southampton  
United Kingdom

### Participants:

6. **Mathias BÄHR**  
Universitätsklinik Göttingen  
Germany

16. **Jennifer POCOCK**  
Dept. of Neurochemistry  
Institute of Neurology  
Univ. College London  
United Kingdom

7. **Burkhard BECHER**  
Neurologische Klinik  
Universitätsspital Zürich  
Switzerland

17. **Gennadij RAIVICH**  
Dept. of Obstetrics and Gynaecology  
University College London  
United Kingdom

8. **Wolfgang BRUECK**  
Institut für Neuropathologie  
Georg-August-Universität Göttingen  
Switzerland

18. **Nancy ROTHWELL**  
School of Biological Sciences  
University of Manchester  
United Kingdom

9. **Christine DIJKSTRA**  
Molecular Cell Biology  
VU Medical Center  
Netherlands

19. **Krzysztof SELMAJ**  
Department of Neurology  
Medical University of Lodz  
Poland

20. **A. Marceline VAN FURTH**  
Department of Pediatrics  
VU Medical Center  
Netherlands

21. **Hartmut WEKERLE**  
MPI für Neurobiologie  
Germany

## Statistics on Participation

Total number of participants including convenors (3): 20

*Age distribution:*

The age bracket was between 30 and 55 years.

*Gender distribution:*

Female: 6      Male: 14

*Geographical distribution:*

Austria	1
Denmark	1
Germany	7
Netherlands	2
Poland	1
Switzerland	4
United Kingdom	5