

Poster presentation

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## Transcriptomic and immunohistologic analysis of pathogenetic and regeneration processes in pneumococcal meningitis

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from Infectious diseases of the nervous system: pathogenesis and worldwide impact  
Paris, France. 10–13 September 2008

Published: 23 September 2008

BMC Proceedings 2008, 2(Suppl 1):P23

This abstract is available from: <http://www.biomedcentral.com/1753-6561/2/S1/P23>

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### Background

Bacterial meningitis causes deficits in brain function as a consequence of neuronal apoptosis in the hippocampal dentate gyrus and ischemic necrosis in the cortex. The aim of our study was to define the cellular processes underlying brain injury and regeneration in the acute and late phase of the disease with a focus on neurogenetic pathways.

### Methods

An infant rat model of experimental pneumococcal meningitis was used. Cortex and hippocampus were dissected from animals in acute and late disease i.e. at 24 and 72 hours after infection. Gene expression profiles were assessed with Affymetrix GeneChip® Rat 230 2.0 arrays. Involved biological processes were identified by grouping gene with altered expression, using GO (Gene Ontology)-based statistics. Cell proliferation in the dentate gyrus was also investigated using BrdU incorporation. Infected animals and uninfected control littermates received BrdU for 3 consecutive days at different times after infection. Density of BrdU positive cells was determined by immunofluorescence.

### Results

In the acute phase (24 hours after infection) regulated genes predominantly fall in the category of the host immune response and inflammation followed by cellular turnover processes, and apoptosis. In contrast, during the late phase of the disease (72 hours after infection) the gen-

eral categories of transcriptomic changes diverge. While the predominant process in the cortex remained an immunogenic response, in the hippocampus, tissue remodelling, neuronal neogenesis and axonal guidance processes were initiated. This finding was confirmed by a significant increase in cell division in the neurogenic dentate gyrus region of the hippocampus assessed by immunohistologic detection of BrdU incorporation. This increased proliferation was documented directly after infection as well as 3 weeks after.

### Conclusion

Both the transcriptomic and immunohistologic data suggest that in pneumococcal meningitis, neuronal stem and/or progenitor cells in the hippocampus are activated in the sub-acute disease phase in order to repair inflammation-associated brain damage.