Centre for Molecular Medicine
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Seminar Announcement

- All Welcome -

Date – **2pm, Thursday 11th January 2007**

Speaker – **Prof Milos Pekny**
Dept. of Clinical Neuroscience and Rehabilitation, Gothenburg University, Sweden

Title – **The role of reactive astrocytes in neurotrauma and CNS regeneration**


Professor Milos Pekny

Venue – **Creation Theatrette**, L4 Matrix, Biopolis

Host – Prof Birgit Lane (tel: 6586 9847)

Abstract: In neurotrauma, brain ischemia or neurodegenerative diseases, astrocytes become reactive (which phenomenon is known as reactive gliosis) and this is accompanied by an altered expression of many genes. Two cellular hallmarks of reactive gliosis are hypertrophy of astrocyte processes and the upregulation of intermediate filaments, which in reactive astrocytes are composed of nestin, vimentin and GFAP. Our aim has been to better understand the function of reactive astrocytes in CNS diseases. Using mice deficient for astrocyte intermediate filaments (GFAP-/-, Vim-/-, or GFAP-/-Vim-/-), we were able to attenuate reactive gliosis and slow down the healing process after neurotrauma. We demonstrated the key role of reactive astrocytes in neurotrauma - at an early stage after neurotrauma, reactive astrocytes have a neuroprotective effect, at a later stage, they facilitate the formation of post-traumatic glial scars and inhibit CNS regeneration, specifically, they seem to compromise neural graft survival and integration, reduce the extent of synaptic regeneration, inhibit neurogenesis in the old age as well as prevent regeneration of severed CNS axons. We propose that reactive astrocytes are the future target for the therapeutic strategies promoting regeneration and plasticity in the brain and spinal cord in various disease conditions.

Biography: Milos Pekny graduated in medicine (MD, *cum eminentia*) from the Charles University, Prague in 1989 and spent a period as Chief Medical Officer with the Czech Armed Forces before his PhD studies in Sweden at Uppsala, under Bengt Westermark and Christer Betscholtz. He obtained his DrMedSc in Pathology from Uppsala University in 1994. He has worked as a visiting scientist in Oxford, Cold Spring Harbor USA and Institute of Molecular Pathology (Vienna) and at the NIH. In 1997 he established the Laboratory of Astrocyte Biology and CNS Regeneration in Gothenburg, and he is now Professor at the Institute of Clinical Neurosciences in the Sahlgrenska Academy of Gothenburg University. In 2005 he received the Eric Ferström Prize in Lund, Sweden. He is the author of many seminal research publications in top journals on the importance of intermediate filaments for astrocyte function, the key role of astrocytes in regulating brain development and regeneration and on tissue responses to stress and injury.

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Seminar Announcement

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Date – **3pm, Thursday 11th January 2007**

Speaker – **Dr Marcela Pekna**
Dept. of Medical Chemistry and Cell Biology, Gothenburg University, Sweden

Title – **Complement: a novel factor in adult mammalian neurogenesis**

Venue – **Creation Theatrette**, L4 Matrix

Host – Prof Birgit Lane (tel: 6586 9847)

Abstract: Complement, a component of the humoral immune system, is involved in inflammation, opsonization, and cytolysis. The primary site of complement protein synthesis is the liver, however local complement production in the CNS is now well established in microglia, astrocytes and neurons. Cerebral ischemia leads to an increased expression of receptors for the complement-derived anaphylatoxic peptides C3a and C5a (C3aR and C5aR) in the ischemic cortex in mice.

Although the role of complement in normal CNS is unknown, in injury such as ischemia, complement activation has been suggested to exacerbate the inflammatory response, therefore contributing to secondary tissue damage. We have recently identified an additional and novel role for complement in the CNS. We have shown that neural stem cells in vitro as well as on neuroblasts in vivo express both C3aR and C5aR. Basal neurogenesis was impaired in C3aR deficient, C3aR antagonist treated as well as C3 deficient mice implicating signalling through C3aR as a positive regulator of adult neurogenesis. In contrast, signalling through C5aR does not appear to be involved in this process as basal neurogensis was not affected in C5aR deficient mice. Interestingly, the C3 deficient mice showed impaired ischemia- induced neurogenesis despite the larger infarct volume. Furthermore, other studies have demonstrated that both C3a and C5a can be neuroprotective against NMDA toxicity and glutamate-induced apoptosis through inhibition of caspase 3.

Complement activation in the CNS may have a dual role. Although it has generally been considered detrimental, it may be a physiological protective mechanism as well as participate in maintenance and repair of the adult brain. A detailed understanding of the non-immune functions of the complement system and other components of the immune system in the normal as well as injured and diseased CNS will conceivably aid in the development of novel therapeutic strategies to promote tissue repair and to prevent or reverse neurological deficits following CNS injury or disease.