

PLENARY SPEAKERS



JENNY P.Y. TING, PH.D.

Unexpected Roles of Inflammatory Cytokines in Neuropathology

University of North Carolina, Chapel Hill, North Carolina

During the course of multiple sclerosis (MS) and many other neurologic pathologies such as Alzheimer's, Parkinson's, ALS etc., elevated levels of immune and inflammatory cytokines are frequently detected. To test the importance of inflammatory molecules in a demyelinating model, we and our collaborators chose the toxin-induced cuprizone model where predictable demyelination and remyelination can be induced, and both phases are accompanied by inflammation. Characterization of this model has revealed many signs of MS including neuroinflammation accompanied by enhanced cytokines and chemokines, microglial and astroglial activation, followed by oligodendrocyte cell death and reduction in myelin. Thus the cuprizone model represents an ideal model to study the role of microglial and astroglial activation in demyelination and remyelination. To directly assess the role of immune/inflammatory molecules, we utilized transgenic mice lacking these molecules. The analysis of mice lacking IL-1 or TNF α mice revealed that both IL-1 and TNF α are necessary for optimal remyelination during the reparative phase of this model. The reparative effect of TNF α is mediated by TNFR2, but not TNFR1, and is correlated with increased proliferation and numbers of oligodendrocyte precursors. This may provide insights regarding a crucial clinical trial which concluded that the inhibition of TNF α is not beneficial to these patients, and may even be detrimental. More recently we extended this study to another TNF family member, lymphotoxin alpha (LT α) and its receptor, LT β R. In contrast to TNF α , we showed that LT α and LT β R exacerbate demyelination to a much greater extent than TNF α , yet has no detectable role in remyelination. An ongoing study is focusing on the testing of molecules that target LT α or LT β R as a therapeutic strategy.



RICHARD TSIEN, PH.D.

Insights into the Secret Life of Small Nerve Terminals

Stanford University, Palo Alto, California

Neurochemists and synaptic physiologists share an intense interest in the workings of the small nerve terminals that process and store information in the mammalian brain. The lecture will highlight our recent studies on presynaptic function which dissect multiple modes of vesicle fusion and retrieval, including kiss-and-run, and which suggest that transcripts are localized and translated in CNS nerve terminals.



HELMUT KETTENMANN, PH.D.

Mechanisms of Neuron Glia Interactions

Max-Delbrück Center for Molecular Medicine, Berlin, Germany

Glial cells have previously been considered as supporting elements for neurons. In the last decade, they have been recognized as elements involved in information processing in the central nervous system. A number of studies indicate that astrocytes can sense neuronal activity and respond with changes in intracellular calcium concentration. In the cerebellum, for instance, stimulation of parallel fibres triggers a local calcium response in Bergmann glia, a subtype of astrocytes. Responses are not only locally confined but can propagate within the astrocyte network in the form of calcium waves. We have recently demonstrated that these waves can also propagate in situ using acute slices from corpus callosum and cortex. The wave is accompanied by release of ATP. The mechanism of propagation is, however, different depending on the brain region. Microglial cells are commonly considered as the pathologic sensors in the brain and they respond with a defined pattern of activities to a pathologic event including release of cytokines and chemokines. They are able to sense the astrocyte activity via purinergic receptors. While microglial cells share many features with monocytes and thus express receptors relevant for immunological functions recent evidence also indicates that they express the classical transmitter receptors essential for neuronal signal transduction. With these receptors they are capable of detecting neuronal and astrocyte activity. Transmitter receptor activation in microglia modulates their cytokine release and is thus a potential route for the cross talk of immune and brain cells.



FREDA MILLER, PH.D.

Neural Precursor Cells: Novel Signals and Sources

The Hospital for Sick Children Research Institute, University of Toronto, Toronto, Canada

This lecture will describe our recent work examining two different populations of neural precursors, embryonic cortical precursors and SKPs, a dermally-derived adult neural crest population. With regard to cortical precursors, the lecture will focus on the mechanisms whereby growth factors regulate cell fate decisions in the embryonic CNS. With regard to SKPs, the lecture will focus on the endogenous role of adult neural crest precursors, and on our attempts to move this accessible neural precursor source towards therapeutic utility.