Plenary Speakers

Philip G. Haydon, Ph.D.

Glia: Listening and Talking to the Synapse

The University of Pennsylvania, Philadelphia, Pennsylvania

In many regions of the central nervous system it is apparent that synapses are tripartite structures in which in addition to the pre and postsynaptic terminal, the astrocyte acts as a third element that wraps around the synaptic structure. Recent studies are changing the view of the role of astrocytes in synaptic transmission: astrocytes detect synaptic activity and are able to release chemical transmitters that in turn regulate neurons. This lecture will highlight the dynamic roles of astrocytes in regulating synaptic transmission, neuronal network function, and as a consequence their role in the control of certain behaviors.

Jeffrey D. Macklis, M.D., D.HST

Molecular Development and Cellular Repair of Corticospinal Motor Neuron (and Other Forebrain Projection Neuron) Circuitry

Harvard University, Massachusetts General Hospital, Boston, Massachusetts

Given the heterogeneity of CNS neuronal subtypes, and the complexity of their connections, detailed understanding of molecular controls over differentiation, connectivity, and survival of specific neuronal lineages will contribute not only to 1) understanding of the development, evolution, organization, and function of CNS circuitry, but also to 2) support or regeneration of vulnerable populations in neurodegenerative disease, to 3) enabling accurate models of neuron type-specific disease, to 4) identification of disease genes, and to 5) attempts to functionally repair CNS circuitry. For example, data from our lab demonstrate that new neurons can be added to adult neocortical circuitry via manipulation of transplanted or endogenous precursors in situ (including induction of limited neurogenesis of clinically important corticospinal motor neurons– CSMN– in adult mice), indicating that cellular repair of cortical and cortical output circuitry is possible, if controls over specific lineage differentiation are understood. Using FACS-purified CSMN and other projection neuron populations at critical stages of development in vivo, we have identified both developmentally regulated transcriptional programs of novel and largely uncharacterized gees, and cell-extrinsic controls, that are instructive for development of specific neuron lineages as they develop in vivo (in particular, for CSMN and other projection neuron populations); these control key developmental processes from arealization to subtype-specific differentiation and xonal outgrowth. Loss-of-function and gain-of-function analyses for multiple identified genes and molecules reveal combinatorial molecular-genetic controls over the precise development of key forebrain projection neuron populations that may allow directed control of neural precursors / "stem cells" (or ES cells) toward accurate disease models, neuronal support or regeneration, or functional CNS repair.

Marie T. Filbin, Ph.D.

Signaling Axonal Regeneration in the Injured Spinal Cord

Hunter College, New York, New York

The mammalian adult CNS does not regenerate after injury. Major obstacles to regeneration are inhibitors of regeneration that are present in myelin. Therefore to encourage axonal regeneration, these inhibitors must be identified and neutralized. We identified one of these inhibitors of regeneration as myelin-associated glycoprotein (MAG). We have characterized the signal transduction cascade that is initiated when MAG interacts with a growth cone. In addition, we have shown that MAG is a sialic acid binding protein and have mapped the sialic acid binding site to Arg118 in the extracellular domain of MAG. However, sialic acid binding alone is insufficient to inhibit axonal growth. Consequently we are now mapping the site on MAG responsible for inhibition. Coupled to this line of study we also have identified the functional MAG receptor on neurons. Finally, rather than identify and neutralize inhibitors of axonal regeneration in myelin individually we have found that if the neuron's endogenous levels of cAMP are raised, its intrinsic growth state changes such that inhibitors are all overcome simultaneously. This cAMP effect is transcription-dependent and we have identified a number of genes that are up-regulated and play a role in allowing axons to grow in an inhibitory environment. We are now characterizing the effect of these agents on regeneration in vivo. In this lecture we will highlight how the results of these investigations may contribute to the treatment of spinal cord injury.

Jeffrey D. Rothstein, M.D., Ph.D.

Astroglial Dysfunction and Degenerative Peri-synaptic events: A basis for therapeutics development

Johns Hopkins University, Baltimore Maryland

This lecture will focus on our studies into neuromuscular diseases, with a particular focus on Amyotrophic lateral sclerosis. Our investigations have included 1) Identification of various molecular mechanisms of selective neurodegeneration in motor neuron diseases; 2) Identification of novel drug or peptide therapeutics to delay or prevent motor neuron degeneration in ALS thru the use of cell culture and transgenic models of ALS; 3) Use of neuronal and non-neuronal stem cell therapies to treat motor neurons diseases including ALS and Spinal Muscular Atrophy; 4) Models of motor axon regeneration regrowth; 5) Clinical trials of novel therapeutics in ALS; 6) Basic biology of glutamate transporters and their role in acute and chronic neuronal degeneration (e.g. ALS, epilepsy, stroke, spinocerebellar ataxia); 7) Cloning and characterization of novel proteins which may be responsible for the cellular regulation of glutamate transporters