S 16-2

LONG-RANGE Ca^{2+} SIGNALING FROM GROWTH CONE TO SOMA MEDIATES REVERSAL OF NEURONAL MIGRATION INDUCED BY SLIT-2

Xiao-bing Yuan

Institute of Neuroscience and Key Labortary of Neurobiology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China

Neuronal migration and growth cone extension are both guided by extracellular factors in the developing brain, but whether these two types of guidance events are mechanistically linked is unclear. We found that application of Slit-2 in front of the leading process of cultured cerebellar granule cells led to growth cone collapse as well as the reversal of soma migration, an event preceded by a propagating Ca^{2+} wave from the growth cone to soma. This Ca^{2+} wave was required for the Slit-2 effect and by itself sufficient for inducing the reversal of soma migration. The Slit-2-induced reversal required active RhoA but not Cdc42 or Rac1. RhoA was accumulated at the front of the migrating neuron, and the polarized soma distribution of RhoA was reversed during Slit-2 and Ca^{2+} wave-induced reversal of migration. Thus, long-range Ca^{2+} signaling mediates the coordinated motility of two distant parts of the migrating neuron in response to Slit-2 by regulating RhoA distribution.

S 16-3

SYNAPTIC MAINTENANCE BY ACTIVITY DEPENDENT IP_3-Ca^{2+} SIGNALING IN CEREBELLAR PURKINJE CELLS

Masamitsu Iino

Department of Pharmacology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

The maintenance of synaptic functions is essential for neuronal information processing, but cellular mechanisms that maintain synapses in the adult brain are not well understood. We imaged intracellular inositol 1,4,5-trisphosphate (IP_3) signalling in cerebellar Purkinje cells (PCs), and found that a burst of synaptic inputs from parallel fibers (PFs) generate IP_3 signaling in fine PC dendrites via the metabotropic glutamate receptor (mGluR). Here, we report an activity-dependent IP_3-mediated maintenance mechanism of PF-PC synapses. When postsynaptic mGluR or IP_3 signaling was chronically inhibited *in vivo*, PF-PC synaptic strength decreased due to a decreased transmitter release probability. The same effects were observed when PF activity was inhibited *in vivo* by the suppression of NMDA receptor-mediated inputs to granule cells. PF-PC synaptic strength similarly decreased after *in vivo* application of an anti-BDNF antibody. Furthermore, the weakening of synaptic connection caused by the blockade of mGluR-IP_3 signaling was reversed by *in vivo* application of BDNF. These results indicate that a signaling cascade comprising PF activity, postsynaptic mGluR-IP_3 signaling, and subsequent BDNF signaling maintains presynaptic functions in the mature cerebellum.