This Week in The Journal

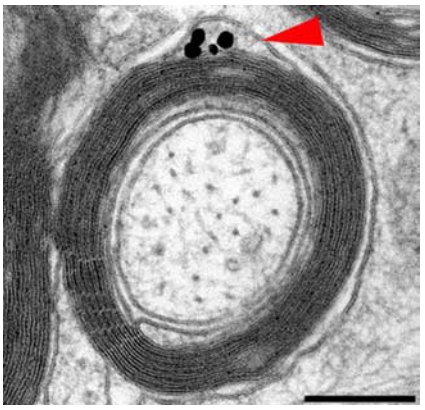
● Cellular/Molecular

A New Marker for CNS Myelin

Damian Brockschnieder, Helena Sabanay, Dieter Riethmacher, and Elior Peles

(see pages 757–762)

Although the textbook image of multiple layers of myelin wrapping around axons is well known to all neuroscientists, basic aspects of myelin formation remain poorly understood. To look for new molecules involved in myelination, Brockschnieder et al. used microarray expression profiling and compared normal mice with those in which oligodendrocytes were selectively ablated by diphtheria toxin. The authors identified a novel cytoskeleton protein that they called Ermin, based on its similarity to the ERM (ezrin, radixin, moesin) family of proteins. The protein organization was modular with a C-terminal actin-binding domain. Ermin was oligodendrocyte specific, expressed during the late stages of myelination, and located in the outer cytoplasmic lip of the myelin sheath (see figure). In cultured oligodendrocytes, Ermin was expressed at the tip of F-actin-rich spikes, and ectopic expression induced additional cell protrusions. Ermin marks a late stage in myelination and presumably has a role at the end of the wrapping and compaction phases.



Immunoelectron microscopy of the optic nerve reveals Ermin immunoreactivity (red arrowhead) at the cytoplasmic pocket between the compact myelin and the outer membrane of the myelin sheath. See the article by Brockschnieder et al. for details

▲ Development/Plasticity/Repair

Mice and Ferrets and Early Alcohol Exposure

Tatsuro Kumada, Madepalli K. Lakshmana, and Hitoshi Komuro

(see pages 742–756)

Alexandre E. Medina, Thomas E. Krahe, and Ary S. Ramoa

(see pages 1057–1060)

Several mechanisms may contribute to the abnormal brain development in fetal alcohol syndrome (FAS). This week, two groups look at impairments of neuronal migration and synaptic plasticity, respectively, in animal models of FAS. Both studies implicate cAMP signaling but in different ways. Kumada et al. examined granule cell migration in a brain slice preparation of neonatal mouse cerebellum. The early neonatal period in the mouse corresponds to the third trimester in the human, a time when alcohol exposure can cause abnormal cerebellar development. The authors report that acute alcohol exposure slowed the migration of granule cells. These effects appeared to be related to reductions in neuronal calcium transients and cGMP levels and increases in cAMP levels. Medina et al. used a ferret model of FAS in which alcohol was injected every other day between postnatal days 10 and 30. Subsequently, ocular dominance plasticity was impaired in FAS animals, an effect that was restored by a phosphodiesterase I inhibitor.

■ Behavioral/Systems/Cognitive

Nicotine and Its Sites of Reinforcement

Satoshi Ikemoto, Mei Qin, and Zhong-Hua Liu

(see pages 723–730)

Ikemoto et al. used an intracranial self-administration strategy to test for rat brain regions involved in the reinforcing effects of nicotine. Rats pressed levers to receive nicotine injections from chronically implanted cannulas in the posterior ventral tegmental area (VTA), the adjacent central linear nucleus, or the supramammillary nucleus of the posterior hypothalamus. However, administration into a number of surrounding areas was not self-reinforcing. Pretreatment with a D_2 dopamine receptor antagonist blocked self-administration of nicotine, consistent with the role of mesolimbic dopamine neurons in positive reinforcement. Of note, the posterior VTA and central linear nucleus contain dopamine neurons that project to the medial shell of the nucleus accumbens and the medial olfactory tubercle, areas in which dopaminergic drugs trigger reinforcing effects. However, the supramammillary nucleus projects to septum and hippocampus. Thus, these experiments suggest that multiple pathways can participate in the reinforcing effects of nicotine.

♦ Neurobiology of Disease

Brain Trauma and the T-Cell

Changying Ling, Matyas Sandor, M. Suresh, and Zsuzsa Fabry

(see pages 731–741)

The activation and infiltration of $CD4^+$ and $CD8^+$ T-cells contribute to inflammation and neurodegeneration in autoimmune CNS diseases such as multiple sclerosis. The distribution of these cells in the brain can be affected by local generation of cytokines, chemokines, and costimulatory molecules. This week, Ling et al. examined the effect of traumatic-injury-related focal inflammation on the localization of $CD8^+$ T-cells. Using intracerebral microinjection of ovalbumin as an antigen stimulus, the authors report that antigen-specific $CD8^+$ T-cells were recruited from peripheral lymphoid tissue and accumulated at intraparenchymal sites that contained antigen. These cells then proliferated locally. Infiltration of antigen-specific $CD8^+$ cells required the presence of antigen in the brain. However, traumatic injury attracted $CD8^+$ T-cells that were already resident in the brain to the trauma site. The latter mechanism was antigen independent and thus could serve to exacerbate inflammatory injury in the CNS.