This Week in The Journal

Cellular/Molecular

The Cytoskeleton and the Paranode
Yasuhiro Ogawa, Dorothy P. Schafer, Ido Horresh, Vered Bar, Kimberly Hales, Yang Yang, Keichiro Susuki, Eilior Peles, Michael C. Stankewich, and Matthew N. Rasband
(see pages 5230–5239)

Paranodal junctions that flank nodes of Ranvier contain a cytoskeleton specialized to prevent membrane protein diffusion in and out of the nodes. This week Ogawa et al. used three known paranodal cell adhesion molecules to fish out additional paranodal molecules. As starting material, the authors isolated optic nerve membranes enriched in glial protein NF155 and the axonal proteins Caspr and contactin. Of 51 molecules identified by liquid chromatography–tandem mass spectrometry, αII spectrin, βII spectrin, and ankyrinB cofractionated with Caspr as part of a paranodal complex. These proteins also associated with protein 4.1B. Immunostaining revealed these cytoskeletal proteins also associated with protein 4.1B. Caspr and contactin. Of 51 molecules identified by liquid chromatography–tandem mass spectrometry, αII spectrin, βII spectrin, and ankyrinB cofractionated with Caspr as part of a paranodal complex. These proteins also associated with protein 4.1B. Immunostaining revealed these cytoskeletal proteins at paranodes in the central and peripheral nervous system. An enzymatic treatment that caused myelin retraction from the axon left βII spectrin and ankyrinB staining intact, identifying them as axonal proteins. AnkyrinB localization required Caspr, but not the juxtaparanodal protein Caspr2, indicating that paranodal axon–glia interactions are required for formation of the paranodal cytoskeleton.

Development/Plasticity/Repair

Lining Up the Hair Cells
Mireille Montcouquiol, Nathalie Sans, David Huss, Jacob Kach, J. David Dickman, Andrew Forge, Rivka A. Rachel, Neal G. Copeland, Nancy A. Jenkins, Debora Bogani, Jennifer Murdoch, Mark E. Warhol, Robert J. Wenthold, and Matthew W. Kelley
(see pages 5265–5275)

How is it that cells in an epithelial sheet line up with the same orientation? In this week’s Journal, Montcouquiol et al. examine some of the proteins involved in this planar cell polarity (PCP) problem in the mammalian system that perhaps best illustrates the process: cochlear hair cells. Mutations in mice have led to the identification of Vang2, Scr1, and Celsr1 as genes integral to PCP. Here the authors raised an antibody to Vang2 and demonstrated its asymmetric expression at cell–cell boundaries between cochlear hair and support cells. In looptail mice that harbor a mutation in Vang2, polarization failed in the cochlea and in vestibular sensory epithelium. A yeast two-hybrid screen revealed an interaction between the postsynaptic density/Discs large/zonula occludens 1 (PDZ)-binding domain of Vang2 and PDZ domains in Scr1. Celsr1 was required for Vang2 asymmetry. The authors also identified Fz3 that was asymmetrically localized in cochlear cells and depended upon Vang2 expression.

Behavioral/Systems/Cognitive

Calming an “ADHD” Mouse
Kazuhiro Tanaka, Norihito Shintani, Hitoshi Hashimoto, Naofumi Kawagishi, Yukio Ato, Toshiro Matsuda, Ryota Hashimoto, Hiroshi Kunugi, Akiko Yamamoto, Chihiro Kawaguchi, Takeshi Shimada, and Akemichi Baba
(see pages 5091–5097)

The paradoxical therapeutic actions of psychostimulant drugs in people with attention deficit and hyperactivity disorder (ADHD) are still mysterious. This week, Tanaka et al. shed some light on this question in mice lacking Adcyap1, the gene that encodes PACAP (pituitary adenylate cyclase-activating polypeptide). These mice are hyperlocomotive and have deficits in prepulse inhibition (PPI), a measure of sensorimotor gating in which a weak acoustic stimulus reduces the subsequent reaction to a startling stimulus. In the Adcyap1+/- mouse,amphetamine normalized PPI responses and diminished hyperlocomotive behavior. Although the dopamine receptor antagonist haloperidol had no effect on PPI, a 5-HT1A receptor antagonist blocked the antihyperkinetic effect of amphetamine. There also was an amphetamine-induced increase in activity in prefrontal cortex as measured by c-Fos labeling. Although not quite an animal model of ADHD, the Adcyap1+/- mouse may help explain the antihyperkinetic effect of psychostimulants.

Neurobiology of Disease

Lighting up ApoE Expression Patterns
Qin Xu, Aubrey Bernardo, David Walker, Tiffany Kanegawa, Robert W. Mahley, and Yadong Huang
(see pages 4985–4994)

Amyloid plaques and neurofibrillary tangles of Alzheimer’s disease (AD) contain apolipoprotein E (apoE), the e4 allele of which considerably increases risk for late-onset AD. An individual with two e4 alleles has a 50–90% chance of developing AD by age 85. To track the expression pattern of apoE in brain, Xu et al. created EGFPapoE reporter mice by expressing enhanced green fluorescent protein (EGFP) on one apoE allele and leaving the other allele functionally intact. As expected, hepatocytes and macrophages expressed high levels of apoE. Approximately 75% of astrocytes expressed apoE under normal conditions, and even after kainic acid-induced injury, a subset did not express EGFP. In contrast, only a small minority of activated microglia expressed EGFP. Hippocampal neurons expressed EGFP only after injury with kainic acid. Smooth muscle cells of large blood vessels, cells surrounding small vessels, and cells of the choroid plexus also expressed apoE.