This Week in The Journal

● Cellular/Molecular

PSD-95 and Dendritic Branching In Vitro

Erik I. Charych, Barbara F. Akum, Joshua S. Goldberg, Rebecka J. Jörnsten, Christopher Rongo, James Q. Zheng, and Bonnie L. Firestein

(see pages 10164–10176)

Many proteins are known to multitask, and postsynaptic density protein-95 (PSD-95) is no exception. As its name implies, this scaffolding protein came to attention for its role in the clustering of synaptic signaling molecules. However, PSD-95 can also be expressed outside synapses. This week, Charych et al. demonstrate an effect of PSD in regulating dendrite branching. When the authors overexpressed PSD-95 in cultured hippocampal neurons, there was a decrease in the proportion of primary dendrites that undergo additional branching as well as a decrease in the total dendritic length. Overexpression of other family members, SAP-97 or SAP-102, had no apparent effect on dendritic branching. Antisense knockdown of PSD-95 by 65% had the opposite effect, causing an increase in secondary dendrites. Thus, it appears that PSD-95 can act as a stop signal for dendrite outgrowth and branching by a process that is activity independent.

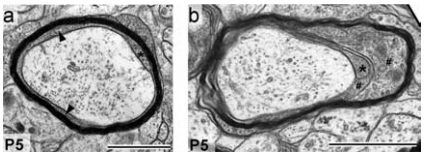
▲ Development/Plasticity/Repair

Rho GTPases and Myelin Formation

Tina Thurnherr, Yves Benninger, Xunwei Wu, Anna Chrostek, Sven M. Krause, Klaus-Armin Nave, Robin J. M. Franklin, Cord Brakebusch, Ueli Suter, and João B. Relvas

(see pages 10110–10119)

The formation of myelin sheaths is a carefully orchestrated process. In the CNS, oligodendrocyte progenitor cells respond to signals in their environment to proliferate and migrate, eventually differentiating into mature cells capable of wrapping CNS axons in sheet-like membranous extensions. The membrane layers are then compacted by the exclusion of cytoplasm to form myelin sheaths. Previous studies suggest that the Rho GTPases Cdc42 and rac1 regulate oligodendrocyte development. Thurnherr et al. sought to more precisely define their roles using Cre-recombinase technology to knock out Cdc42 or rac1 in the oligodendrocyte lineage. The authors demonstrate that the two proteins are required in a synergistic and dose-dependent manner for proper myelination but not oligodendrocyte maturation or migration. The absence of either protein led to an unusual myelin phenotype with abnormal accumulation of cytoplasm in the inner tongue of compact myelin sheaths and a reduction in myelin thickness.



Cross section of axon profiles in spinal cord cdc42 mutant mice (***b***) shows excess cytoplasm in the innermost loops of myelin (pound signs in mutant, black arrowheads in control) and inner tongue (asterisk) compared with control mice (***a***). See Thurnherr et al. for details.

■ Behavioral/Systems/Cognitive

Waking up to Histamine Neurons

Kazumi Takahashi, Jian-Sheng Lin, and Kazuya Sakai

(see pages 10292–10298)

Like a shot of espresso, neurons in the hypothalamus keep you awake and alert throughout the day, according to work by Takahashi et al. But the chemical is histamine, not caffeine, in this case. The authors monitored the activity of histaminergic neurons in the tuberomammillary nucleus (TMN) of mice during sleep and wake cycles. These neurons had previously been implicated in regulating wakefulness. Takahashi et al. used extracellular single-unit recordings combined with neurobiotin juxtacellular labeling and histamine immunochemistry to identify TMN histaminergic neurons. Their results demonstrate that these neurons are not active during sleep but exhibit slow (<10 Hz) irregular firing during waking hours. What's more, the neurons have higher activity during attentive waking than quiet waking. Because the neurons exhibit a pronounced delay in firing during the transition from sleep to alertness, they probably do not induce wakefulness, but rather act to maintain it.

♦ Neurobiology of Disease

Phox2b, Central Chemoreceptors, and Hypoventilation

Ruth L. Stornetta, Thiago S. Moreira, Ana C. Takakura, Bong Jin Kang, Darryl A. Chang, Gavin H. West, Jean-François Brunet, Daniel K. Mulkey, Douglas A. Bayliss, and Patrice G. Guyenet

(see pages 10305–10316)

After finding her husband in the arms of another woman, the mythological figure Ondine placed a curse on the adulterous spouse that he would stop breathing and die if he ever fell asleep. The story has lent its name, "Ondine's curse," to congenital central hypoventilation syndrome (CCHS), a condition in which individuals sometimes stop breathing in their sleep. Because mutations in the transcription factor Phox2b are associated with the syndrome, Stornetta et al. examined the anatomical and functional characteristics of Phox2b-expressing neurons in adult rat. CCHS is thought to arise from a block in the chemical drive to breathe. Consistent with this interpretation, the authors found that Phox2b-expressing neurons are not associated with respiratory rhythm and pattern generation. Instead, Phox2b expression is restricted to a group of central chemoreceptor neurons in the retrotrapezoid nucleus and a connected chain of neurons that relay information from peripheral chemoreceptors to the central respiratory column.