This Week in The Journal

- Cellular/Molecular
  **Histone Deacetylase Can Enhance Inhibitory Transmission**

  Jesse E. Hanson, Lunbin Deng, David H. Hackos, Shih-Ching Lo, Benjamin E. Lauffer, et al.
  (see pages 5924–5929)

  Transcription factors bind to regulatory elements in DNA and activate or suppress gene transcription. DNA is tightly wound around histone proteins, however, and before transcriptional regulators can bind, histones must loosen their grip. This is achieved by acetylation, which is mediated by histone acetyltransferases (HATs) and reversed by histone deacetylases (HDACs). Both HATs and HDACs have roles in neuronal plasticity; HDAC2, for example, appears to limit memory formation, because exogenous HDAC inhibitors enhance memory formation in mice. Furthermore, overexpression of HDAC2 reduces dendritic spine density, synapse number, and synaptic plasticity, whereas HDAC2 knock-out increases excitatory synapse number and facilitates long-term potentiation (LTP). Hanson et al. now show that HDAC2 regulates inhibitory, as well as excitatory synaptic transmission. Overexpressing HDAC2 in a subset of rat hippocampal neurons reduced the amplitude of miniature (m) EPSCs and increased the amplitude of mIPSCs. HDAC2 knockdown had the opposite effects. The reduction in mIPSC amplitude appeared to result in part from reduced synaptic targeting of GABA_A receptors.

- Systems/Circuits
  **Morphine Has Opposite Effects on Spinal Pain and Itch Neurons**

  Hannah R. Moser and Glenn J. Giesler, Jr.
  (see pages 6093–6101)

  Itch and pain pathways have much in common: both are unpleasant; both are sensed by TRPV1-expressing C-fibers; and itch-responsive spinal cord neurons also respond to stimuli that activate nociceptors. Interestingly, itch and pain seem antagonistic: scratching relieves itch, but activates pain pathways; and morphine suppresses pain, but can produce itch. To investigate how pain and itch are distinguished, Moser and Giesler first identified dorsal horn neurons that responded to noxious mechanical stimuli and then tested their responses to pruritic agents. Pruriceptive (itch-sensitive) neurons were indistinguishable from itch-insensitive nociceptive neurons in their somata position, terminal projection region in the thalamus, and responses to mechanical stimuli. But whereas intrathecal morphine application suppressed responses of itch-insensitive nociceptive neurons to skin pinches, it did not affect pruriceptive neurons’ responses to pinching, and it significantly increased pruriceptive neurons’ responses to intradermal application of pruritic agents and to innocuous brushing. Whether morphine increased firing of pruriceptive neurons by directly exciting the neurons or by suppressing inhibitory inputs remains unknown, however.

- Behavioral/Cognitive
  **CRF and NPY Have Opposing Roles in Pain-Induced Aversion**

  Soichiro Ide, Taiki Hara, Atsushi Ohno, Ryuta Tamano, Kana Koseki, et al.
  (see pages 5881–5894)

  Nociceptor activation produces not only pain sensation, but also unpleasant affective experiences that lead to subsequent avoidance of the pain-inducing stimulus. For example, injection of formalin into rodents’ paws induces nociceptive behaviors (e.g., licking) and subsequent avoidance of the chamber where the injection was received (i.e., conditioned place aversion; CPA). CPA requires the bed nucleus of the stria terminalis (BNST), a part of the extended amygdala in which the neuropeptide corticotropin-releasing factor (CRF) is involved in inducing, and neuropeptide Y (NPY) is involved in reducing negative affective states. Injection of CRF into the BNST induces CPA, and Ide et al. now show that intraplantar injection of formalin caused a transient increase in BNST CRF. Injection of CRF antagonists or NPY into BNST reduced formalin-induced CPA without affecting nociceptive behaviors. The effects of CRF and NPY on CPA appeared to result from opposing effects on the same BNST neurons: CRF depolarized and increased spiking of type II neurons, whereas NPY hyperpolarized the neurons and reduced spiking.

- Neurobiology of Disease
  **PERK Protects Oligodendrocytes from Autoimmune Attack**

  (see pages 5980–5991)

  Multiple sclerosis (MS) is an autoimmune disease in which immune cells attack oligodendrocytes, causing apoptosis, demyelination, and ultimately, axonal degeneration. Preventing oligodendrocyte apoptosis might slow or stop the progress of MS. In experimental autoimmune encephalomyelitis (EAE), a mouse model of MS, the inflammatory cytokine interferon-γ protected oligodendrocytes via activation of pancreatic endoplasmic reticulum kinase (PERK); but whether PERK was activated in oligodendrocytes or other cell types, e.g., microglia, was unresolved. Therefore, Lin et al. generated mice in which PERK could be activated selectively in mature oligodendrocytes (right) reduces spinal axon degeneration after EAE (left, control). See the article by Lin et al. for details.