This Week in The Journal

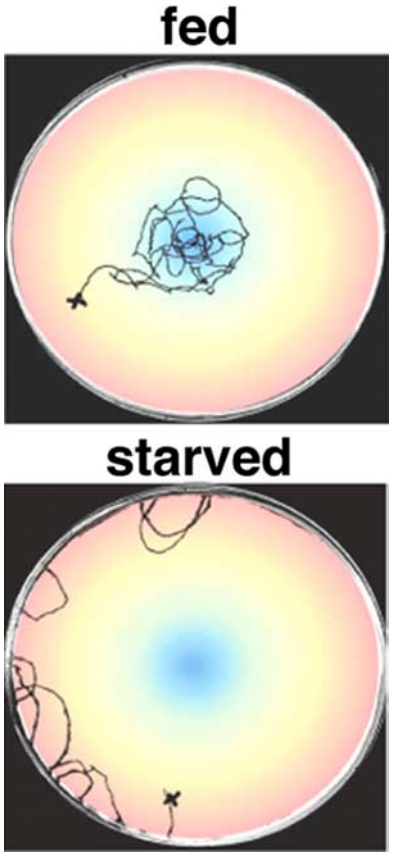
● Cellular/Molecular

Probing the Thermotaxis Circuit in C. elegans

Atsushi Kuhara and Ikue Mori

(see pages 9355–9364)

The relative simplicity of the nervous system in *Caenorhabditis elegans* provides some advantages in elucidating the molecular and cellular underpinnings of learning and memory. At least in captivity, worms memorize their cultivation temperature and move toward it when placed in a temperature gradient, but they learn to avoid that temperature if cultured without food. This week, Kuhara and Mori pick apart the underlying neuronal circuit. The authors show that calcineurin, a calcium-activated phosphatase implicated in many forms of synaptic plasticity, is essential to this behavior. The authors engineered a mutant lacking calcineurin expression in interneurons but not sensory neurons. Whereas the mutant sensed temperatures normally, it did not stay away from temperatures associated with a lack of food. By measuring *in vivo* calcium transients evoked by temperature changes, the authors demonstrate that calcineurin downregulated the thermal response in the pair of interneurons critical to the circuit.



Wild-type worms cultivated at 17°C with food were attracted to the cultivation temperature (blue), whereas animals starved at 17°C avoided it. See Kuhara et al. for details.

▲ Development/Plasticity/Repair

Marginalizing Cajal-Retzius Cells

Mercedes F. Paredes, Guangnan Li, Omri Berger, Scott C. Baraban, and Samuel J. Pleasure

(see pages 9404–9412)

Focal cortical dysplasias, local disruptions of the laminar cortical pattern, are a common cause of epilepsy in young adults. Paredes et al. have now uncovered a potential role for the chemokine SDF1 in cortical lamination. The authors previously showed that mouse embryos exposed to the teratogen methylazoxymetanol (MAM) show disorganization of the cortical marginal zone and displacement of Cajal-Retzius (C-R) cells. C-R cells secrete the glycoprotein reelin required for the normal migration of cortical neurons during early development. Using a cortical slice preparation, the authors rescued the defects in MAM-treated slices by coculture with normal slices, suggesting that a soluble factor was required for positioning of C-R cells. Inhibition of CXCR4, the receptor for SDF1 that is secreted by the leptomeninges, blocked the rescue. *In utero* CXCR4 inhibition also interfered with normal C-R positioning during development. Thus, SDF1 signaling is essential for initial positioning as well as maintenance of C-R cells in the marginal zone.

■ Behavioral/Systems/Cognitive

Motor Goals and the Monkey Parietal Reach Region

Alexander Gail and Richard A. Andersen

(see pages 9376–9384)

As you reach toward an object, sensory signals coding the shape and location of the object are integrated with more abstract rules of behavior to transform the information into a motor goal. This week, Gail and Andersen looked at neuronal activity in the parietal reach region (PRR), which is involved in the planning of reach movements during such a sensorimotor transformation. Monkeys were trained to reach either toward the memorized location of a previously flashed green light (pro-reach) or to a location diametrically opposite to the visual cue if the light was blue (anti-reach). This task allowed spatial dissociation of the cue from the motor goal. Only a small fraction of visually responsive cells in the PRR were tuned during the brief period of cue visibility; rather, PRR predominantly encoded the motor goal from the end of the cue period on. Thus, PRR rapidly transforms sensory information into motor plans rather than storing spatial sensory information.

♦ Neurobiology of Disease

Neutralizing TNF and 6-OHDA Neurotoxicity

Melissa K. McCoy, Terina N. Martinez, Kelly A. Ruhn, David E. Szymkowski, Christine G. Smith, Barry R. Botterman, Keith E. Tansey, and Malú G. Tansey

(see pages 9365–9375)

Proinflammatory molecules, such as tumor necrosis factor (TNF), are abundant in the CSF of patients with Parkinson's disease (PD). However, it's unclear what role inflammation plays in the pathogenesis of PD. TNF exists in two biological active forms: a soluble form that acts on the TNFR1 (TNF receptor 1) and transmembrane TNF that acts through TNF receptor 2. TNFR1 is highly expressed on nigrostriatal dopamine neurons. This week, McCoy et al. report that neutralization of soluble TNF by a dominant-negative inhibitor, a TNF variant engineered to disrupt receptor binding of soluble TNF, reduced degeneration of rat dopaminergic neurons after intrastriatal injection of 6-hydroxydopamine. Direct nigral delivery reduced dopamine neuron death by 50%. The soluble TNF inhibitor also protected neurons from inflammatory damage triggered by bacterial lipopolysaccharide. The data provide a compelling link between soluble TNF and degeneration of dopamine neurons.