This Week in The Journal

Cellular/Molecular

Glia as Recruiters of the Injury Response
Chemokine Expression by Glial Cells Directs Leukocytes to Sites of Axonal Injury in the CNS
Alicia A. Babcock, William A. Kuziel, Serge Rivest, and Trevor Owens (see pages 7922–7930)

Most of us were taught that the brain is immunologically “privileged” (i.e., protected from circulating immune cells by the blood–brain barrier). However, this barrier can be breached during brain injury or autoimmune-mediated disorders such as multiple sclerosis. In this issue, Babcock et al. show that innate glial-derived factors can help direct an immune response within the CNS. They transplanted entorhinal dentate axons in mice, a lesion known to induce glial reactivity at the site as well as glial activation associated with retrograde degeneration. After the lesion, macrophages infiltrated within 12 hr followed by T cells at 24 hr. The axonal transaction induced a range of chemokines in the hippocampus, including early astrocyte production of the macrophage chemotactant MCP-1/CCL2. This chemokine was a critical component of the response, because macrophage and T cell infiltration did not occur in mice lacking its receptor, CCR2. Presumably macrophage and T cell infiltration are part of the normal response to neural injury. Thus the therapeutic challenge is to enhance the repair aspects of immune cell infiltration while avoiding negative consequences such as an autoimmune response.

Development/Plasticity/Repair

Regenerating Optic Nerves: Cells and Sugars
Transplanted Olfactory Ensheathing Cells Promote Regeneration of Cut Adult Rat Optic Nerve Axons
Ying Li, Yves Sauvé, Daqing Li, Raymond D. Lund, and Geoffrey Raisman (see pages 7783–7788)

Two papers in this week’s Journal examine mammalian retinal ganglion cell axon regeneration after nerve damage. First, Ying Li et al. use transplanted olfactory ensheathing cells (OECs), which have been shown previously to promote axonal growth and functional rescue in spinal cord. In the current work, OECs were transplanted into the rat optic nerve at the site of a transaction. The OECs displayed a familiar supportive role, wrapping themselves around the neurons in a Schwann cell-like manner and guiding new axonal growth 10 mm beyond the site of injury. Alas, the shepherding was incomplete: the axons terminated short of the optic chiasm in a tangled web of fine astrocytic processes. The authors hypothesize that the “failure” may reside in the lack of an aligned glial tract in the distal stump of the optic nerve. Although retinal ganglion axons cannot successfully regrow in mammals, they do so in goldfish. The second paper, by Yiming Li et al., examines what might allow fish to succeed where mammals fail. The group isolated and identified a goldfish growth factor, previously dubbed AF-1, as a carbohydrate. Although the goldfish neurons seemed to respond equally to mannose and the plentiful available glucose, rat ganglion cell regrowth was selective for o-mannose and required cAMP. These papers shed new light on the complex requirements for mammalian retinal ganglion cell repair.

Behavioral/Systems/Cognitive

Seizure Prediction In Vitro
Transition from Interictal to Ictal Activity in Limbic Networks In Vitro
Volodymyr I. Dzhala and Kevin J. Staley (see pages 7873–7880)

Probably the most disabling aspect of epilepsy is its unpredictability. If patients knew when a seizure was about to occur, therapy could be tailored accordingly. Unfortunately, we have limited understanding of the transition from normal brain activity to seizure (ictal) activity. Dzhala and Staley examine this problem using rat hippocampal/entorhinal slices bathed in increased potassium or the K channel blocker 4-aminopyridine. The hippocampus is involved in many cases of acquired (i.e., nongenetic) intractable epilepsy. In these experiments, synchronized bursts of activity (interictal spikes) originated in the CA3a-b subregion. The authors found several predictors of subsequent seizure-like activity: more rapid propagation of interictal spikes, reverberation discharges between CA3a and CA3c, and a shift in the initiation site from CA3a-b to CA3c. At least for these models, removal of the entorhinal cortex had no effect. Perhaps the most hopeful outcome is that additional studies of this kind may provide means to monitor interictal activity and predict seizures before they occur.

Before sustained ictal-like activity, the velocity of extracellular interictal spike discharges increased and the initiation site shifted. The relative time delays of the discharges are shown in pseudocolor, with the initiation site in red.