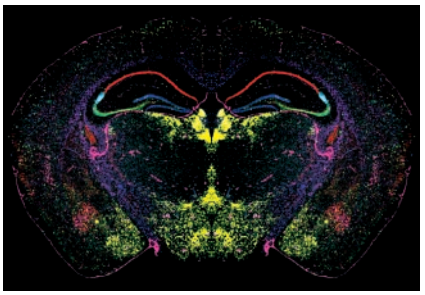
This Week in The Journal

● Cellular/Molecular

Gene Expression Patterns in the Hippocampus

Ed S. Lein, Xinyu Zhao, and Fred H. Gage
(see pages 3879–3889)

The subregions of the hippocampus are among the most intensively studied areas in the brain. The distinctive morphological differences between CA1–CA3 and the dentate gyrus, as recognized by Ramon y Cajal and Lorente de Nó, also translate into the functional differences well known to neuroscientists. Yet understanding how gene expression patterns orchestrate the complexity that is the hippocampus, or any brain region for that matter, remains a daunting task. As a starting point, Lein et al. use DNA microarrays to assess gene expression patterns in the CA1, CA3, and dentate gyrus. They verified the profiles by using *in situ* hybridization that was in agreement for 100 of 104 genes in which the arrays indicated high or low expression in hippocampal subregions. They found a number of genes that were expressed in a region-specific manner. The authors rightfully refer to the data as an atlas: it doesn't tell us a lot by itself, but it may guide us in some interesting directions.



Pseudocolored montage of highly specific gene expression created by overlay of *in situ* hybridization signals for α-mannosidase 1 (red), FGF-2, (light blue), Socs2 (green), EST AA087715 (dark blue), calretinin (yellow), claudin 11 (purple), and decorin (pink). See the article by Lein et al. for details.

▲ Development/Plasticity/Repair

Demyelination and the Neuromuscular Junction

Xinghua Yin, Grahame J. Kidd, Erik P. Pioro, Jennifer McDonough, Ranjan Dutta, M. Laura Feltri, Lawrence Wrabetz, Albee Messing, Ryan M. Wyatt, Rita J. Balice-Gordon, and Bruce D. Trapp
(see pages 3890–3898)

Some inherited diseases of myelin cause functional deficits because of dysmyelination, but permanent damage reflects subsequent axonal deterioration through mechanisms yet unknown. In this issue, Yin et al. use a transgenic mouse that overexpresses a Schwann cell structural protein, P_0, to examine the early stages of such a process. Axons of dysmyelinated lower motor neurons retracted and then regenerated synapses with altered properties. Although the axons were never myelinated, neuromuscular pathology and axonal degeneration developed slowly. The mice displayed behavioral and electrophysiological signs of muscle denervation. Indeed, axon retraction left only ~3% of the neuromuscular junctions (NMJs) intact after 90 d. When the overexpressing mutants were crossed with P_0 null mice, the wild-type NMJ phenotype was rescued. The authors conclude that normal synaptic function is an early casualty of dysmyelination.

■ Behavioral/Systems/Cognitive

Place Cells in the Young and Old

Iain A. Wilson, Sami Ikonen, Irina Gureviciene, Robert W. McMahan, Michela Gallagher, Howard Eichenbaum, and Heikki Tanila
(see pages 3870–3878)

Place cells are hippocampal pyramidal neurons that fire when an animal occupies a particular space. Hippocampal connectivity and plasticity deteriorates with age, including the spatial memory presumably mediated by these cells. Several groups have characterized place cells in young and aged rats, only to reach the seemingly disparate conclusions that aged place neurons become either rigid, unstable, or delayed in stabilizing to cues. Which way is it? In this week's *Journal*, Wilson et al. try to reconcile this question by recording from place cells of young and aged rats during repeated exposures to familiar or novel environments over several days. They assessed the performance of rats in a water maze and their ability to orient themselves in a rotated hexagonal arena. The authors conclude that all three views of place cell activity in the aged rat are apt, but that each applies to different environmental conditions, reflecting specific age-related changes in circuitry.

◆ Neurobiology of Disease

Myelin-Reactive T-Cells: Good or Bad?

T. Bucky Jones, Daniel P. Ankeny, Zhen Guan, Violeta McGaughy, Lesley C. Fisher, D. Michele Basso, and Phillip G. Popovich
(see pages 3752–3761)

T-lymphocytes activated by myelin basic protein (MBP) are generally considered to be indicative of neuropathology by mediating brain inflammation and injury. For example, these cells have long been used to induce experimental autoimmune encephalomyelitis (EAE), a disease model of multiple sclerosis. However, recent reports questioned this view by suggesting that T-cell activation could be a physiological response required for neuroprotection and repair. In an attempt to independently confirm this hypothesis, Jones et al. examined the functional and morphological status of neurons after exposure to myelin-reactive T-cells. They conclude that the historical view of these immune cells is correct. In rats with spinal contusion injury, both passive (MBP-activated T-cells) and active (MBP) autoimmunization resulted in worsening neuropathology. The different conclusions highlight the complexity of spinal injury, autoimmunity, and neuroprotection, as well as the experimental conditions used to assess them. At least for now, it appears that strategies to enhance or introduce myelin-reactive T-cells for the purpose of "protective autoimmunity" may not be worthwhile.