# *This Week in The Journal*

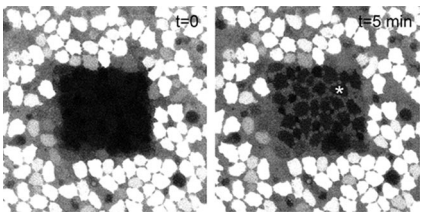
## ● Cellular/Molecular

### *An Earful of Connexins*

Regina Nickel, David Becker, and Andrew Forge

(see pages 6190 – 6199)

In the mammalian inner ear, connexin 26 (Cx26) and the inner-ear-specific Cx30 form heteromeric gap junctions. This unique distribution pattern likely underlies the nonsyndromic deafness (i.e., not associated with other nonauditory abnormalities) that accompanies mutations in these genes. In this week's *Journal*, Nickel et al. used degenerate reverse transcription-PCR to screen chicken auditory and vestibular end organs for connexins. The authors identified the avian orthologs cCx26 and cCx43 as the predominant connexins, along with the previously identified cCx30 (also called cCx31). The expression patterns of cCx26 and cCx30 were overlapping and encompassed gap junctions of sensory and ion-transporting epithelial cells. Fluorescent recovery after photobleaching of organotypic cultures of basilar papilla and utricle revealed dye transfer through gap junctions between supporting cells, consistent with a role in the unique potassium cycling in the inner ear.




Optical sections of the chick utricular macula taken immediately after photobleaching of calcein ($t = 0$) and after diffusion of unbleached calcein ($t = 5$ min). Fluorescence recovery occurred in supporting cells but not the hair cells (black silhouettes in the central bleached square).

## ▲ Development/Plasticity/Repair

### *Desert Hedgehog and the Schwann Cell*

Soheila Sharghi-Namini, Mark Turmaine, Carola Meier, Vishal Sahni, Fujio Umehara, Kristjan R. Jessen, and Rhona Mirsky

(see pages 6364 – 6376)

In the Hedgehog family, Sonic (Shh) has generated the most press, but this week one of Sonic's mammalian sibs, Desert, gets some attention for its role in glial–neuronal signaling. The third member (Indian) will have to wait for another day. These signaling proteins operate by binding to patched receptors and trigger intracellular signaling cascades that control such things as tissue patterning during development. Sharghi-Namini et al. examined mice deficient for *desert hedgehog* (*dhh*) that is selectively expressed and secreted from myelinating Schwann cells. Previous studies indicated that Dhh is important in peripheral nerve development and mutations cause a human peripheral neuropathy. The $dhh^{-/-}$ mice showed complex abnormalities including increased Schmidt–Lanterman incisures, fewer myelinated and unmyelinated axons, and a reduction in nonmyelinating Schwann cells. There was also a leaky blood–nerve barrier, degenerating neurons, and elevated levels of macrophages and neutrophils, consistent with a role for Dhh in formation of the perineural barrier.

## ■ Behavioral/Systems/Cognitive

### *The Organization of Motor Cortex*

Tyson N. Aflalo and Michael S. A. Graziano

(see pages 6288 – 6297)

The topographical mapping of motor cortex in monkey is complex, probably because it must conform to different elements such as the somatotopic body map, a map of the hand in space, and regional partitioning based on complex behaviors that involve multiple body parts, for example, hand-to-mouth movements. This week, Aflalo and Graziano created an artificial two-dimensional array that tried to optimize continuity between these elements. The strategy used a so-called Kohonen network based on the idea that cortical maps may self-organize to optimize nearest-neighbor relationships. The authors designed the map based on somatotopy, and then allowed the map to reconfigure according to the other two requirements. The map consisted of a grid of 36 × 20 nodes, each representing a movement. The resulting model reflected the real monkey motor cortical map in many aspects. Both included overlapping somatotopy, posterior and anterior strips, and three distinct hand representations.

## ♦ Neurobiology of Disease

### *γ-Secretase and p53-Mediated Cell Death*

Cristine Alves da Costa, Claire Sunyach, Raphaelle Pardossi-Piquard, Jean Sévalle, Bruno Vincent, Nicole Boyer, Toshitaka Kawarai, Nadège Girardot, Peter St. George-Hyslop, and Frédéric Checler

(see pages 6377– 6385)

The presenilins (PSs) are part of the γ-secretase complex that cleaves amyloid precursor protein (APP) into amyloid β (Aβ). The presenilin mutations that underlie familial Alzheimer's disease (FAD) increase Aβ production and also cause p53-dependent apoptotic cell death. This week, Alves da Costa et al. looked for the link between γ-secretase activity and cell death. Activation of p53 and transactivation of the p53 promoter were reduced in the absence of PS2 and were increased with PS2 overexpression. γ-Secretase inhibitors, as well as a mutant PS2 that blocks γ-secretase activity, decreased p53 activity in wild-type but not in PS2-deficient fibroblasts. Cleavage of APP results in the production of two C-terminal fragments, AICDC59 and AICDC50. Overexpression of these two peptides increased p53 expression and activity and p53-mediated cell death via caspase-3 activation. Thus, the AICD γ-secretase cleavage products appear to be the link to the increased p53-mediated cell death in FAD.