This Week in The Journal

● Cellular/Molecular

Sorting Out the Bitters

Maik Behrens, Susann Foerster, Frauke Staehler, Jan-Dirk Raguse, and Wolfgang Meyerhof

(see pages 12630–12640)

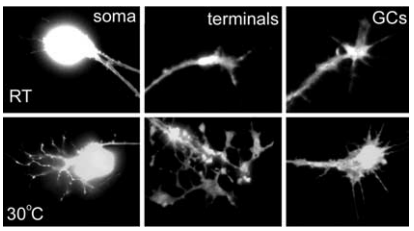
The story goes that bitter taste receptors are there to protect us from toxins, which, of course, have diverse chemical structures. It has been debated whether we can discriminate between bitter-tasting compounds and thus whether we need multiple bitter receptors. Bitter taste is encoded by a family of 25 TAS2 receptors (TAS2Rs) expressed on taste receptor cells in circumvallate (CV) taste buds. This week, Behrens et al. show that human taste receptor cells differ in the expression level of TAS2R genes and in the number of cells expressing a particular TAS2R. All 25 human receptors were expressed in CV taste buds, suggesting that they act as bitter sensors. However, the number and expression level of TAS2Rs differed between human taste receptor cells. The authors estimate that an individual cell may express no more than 4 to 11 TAS2Rs, and they suggest that no two CV taste buds have the same complement of TAS2Rs.

▲ Development/Plasticity/Repair

Warming Up to Plasticity in the Fly

I-Feng Peng, Brett A. Berke, Yue Zhu, Wei-Hua Lee, Wenjia Chen, and Chun-Fang Wu

(see pages 12611–12622)



Images of GFP-labeled *Drosophila* neurons show enhanced growth cones (GCs) and neurite terminal complexity at 30° C compared with room temperature (RT). See the article by Peng et al. for details.

In this issue, Peng et al. report a cell-autonomous enhancement of axonal arborization with increased environmental temperature. Using the GAL4-UAS system, the authors visualized green fluorescent protein-labeled mushroom body Kenyon cells in the *Drosophila* brain. Warming flies at 30°C for days 2 to 7 after eclosion increased axonal branching as well as the overgrowth of nerve terminals. Similar effects were seen for embryonic neurons *in vitro*. The temperature-sensitive morphological changes were accompanied by changes in cell excitability and ion channel expression. As a result, spontaneous calcium transients were more frequent, particularly in growth cones. The increase in intracellular calcium was blocked by tetrodotoxin and accompanied by upregulation of calcium currents and downregulation of potassium currents. Signaling through cAMP pathways downstream of calcium, including Ca^{2+}/calmodulin-dependent adenylate cyclase, appear to link the channel activity to more robust growth.

■ Behavioral/Systems/Cognitive

Cocaine, Serotonin, and Conditioned Place Preference

Thomas S. Hnasko, Bethany N. Sotak, and Richard D. Palmiter

(see pages 12484–12488)

The corner bar for the alcoholic or the candy shop for the chocoholic can be irresistible. In the laboratory, conditioned place preference (CPP) is a behavioral measure of the learned association between a rewarding drug and the place where it was received. CPP for cocaine is usually attributed to increases in extracellular dopamine, but cocaine also inhibits serotonin and norepinephrine transporters. This week, Hnasko et al. examined CPP in dopamine-depleted (DD) mice. These animals lacked the catecholamine-synthesizing enzyme tyrosine hydroxylase, but only in dopaminergic neurons. DD mice showed CPP for cocaine at higher doses than controls, but fluoxetine, a selective serotonin reuptake inhibitor, also produced CPP. CPP for either cocaine or fluoxetine required $5\text{-}HT_1$ receptors, suggesting that in the absence of dopamine, CPP arises from cocaine blockade of serotonin reuptake. The authors postulate that CPP in DD mice involves serotonin activation of dopamine neurons.

♦ Neurobiology of Disease

Targeted Immunotherapy of T-Cells in EAE

Sushmita Sinha, Sandhya Subramanian, Thomas M. Proctor, Laurie J. Kaler, Marjorie Grafe, Rony Dahan, Jianya Huan, Arthur A. Vandenbark, Gregory G. Burrows, and Halina Offner

(see pages 12531–12539)

Regulating T-cell responses is one therapeutic strategy for autoimmune diseases such as multiple sclerosis (MS). Specific recombinant T-cell receptor ligands (RTLs) can prevent or treat experimental autoimmune encephalomyelitis (EAE), a commonly used animal model of MS. These RTLs contain encephalitogenic peptides linked to the outer two domains of restricting MHC class II molecules. This week, Sinha et al. constructed a new one, RTL551, from the outer domains of the $I\text{-}A^b$ class II molecule and an encephalitogenic peptide derived from myelin oligodendrocyte protein (MOG-35-55). RTL551 reduced the severity of active and passive MOG-induced EAE in mice. For passively transferred EAE, the authors introduced green fluorescent protein-labeled, MOG-35-55-reactive T-cells. The transferred cells preferentially expressed the pathogenic cytokine IL-17 and tumor necrosis factor α (TNFα), which were downregulated by RTL551. RTL551 also reduced the infiltration of inflammatory cells into the spinal cord of mice with passive EAE.