IN BRIEF

DOI:
10.1038/nrn2165

ION CHANNELS

TRPM8 is required for cold sensation in mice.

Dhaka, A. *et al. Neuron* **54**, 371–378 (2007)

Attenuated cold sensitivity in TRPM8 null mice.

Colburn, R. W. *et al. Neuron* **54**, 379–386 (2007)

The transient receptor potential melastatin 8 cation channel (TRPM8) is thought to be involved in thermosensation. Two studies used TRPM8-deficient mice to examine the role of TRPM8 in cold sensation *in vivo*. TRPM8-deficient mice had greatly reduced sensitivity to innocuous cooling and to noxious cooling chemicals. However, they did not display reduced sensitivity to noxious cold, suggesting that other cold receptors are also involved in the sensation of painful cold.

ADDICTION

A molecular basis of analgesic tolerance to cannabinoids.

Tappe-Theodor, A. *et al. J. Neurosci.* **27**, 4165–4177 (2007)

Cannabinoids have analgesic properties, but repeated use leads to analgesic tolerance, possibly caused by downregulation of the type 1 cannabinoid receptor (CB1). Prolonged exposure to a CB1-agonist downregulated CB1 *in vitro* and *in vivo*, and this effect required expression of G-protein-associated sorting protein 1 (GASP1). Moreover, repeated agonist administration produced analgesic tolerance in mice, which was reduced in animals expressing a dominant-negative form of GASP1. This indicates that GASP1 is crucial in regulating CB1 trafficking, providing a potential target for strategies to reduce the development of analgesic tolerance to cannabinoids.

EPIGENETICS

The histone H3K4 demethylase SMXC links REST target genes to X-linked mental retardation.

Tahiliani, M. *et al. Nature* 29 April 2007 (doi:10.1038/nature05823)

Mutations in the *SMCX* (also known as *JARID1C*) gene are common in X-linked mental retardation. Fisher *et al.* show that SMCX is a demethylating enzyme that acts at lysine residue 4 of histone H3 and interacts with the transcriptional repressor REST. SMCX and REST were found at promoter regions of REST target genes, and depleting SMCX caused de-repression of some of these genes, including several neurotransmitter transporters. This study sheds light on a mechanism by which mutations in the X-linked gene *SMCX* might cause mental retardation.

NEURODEGENERATIVE DISORDERS

Ccr2 deficiency impairs microglial accumulation and accelerates progression of Alzheimer-like disease.

El Khoury, J. *et al. Nature Med.* **13**, 432–438 (2007)

Microglia accumulate in plaques in the brains of patients with Alzhemer's disease, but whether their presence is beneficial or harmful is unclear. CC-chemokine receptor 2 (CCR2) is expressed by microglia and may facilitate their recruitment to the brain. The authors showed that knocking out *Ccr2* in a transgenic mouse model of Alzhemer's disease reduced microglial accumulation, increased the accumulation of amyloid-β protein and accelerated disease progression in these animals. This provides support for a neuroprotective role of microglia, which are likely to be involved in amyloid-β clearance.