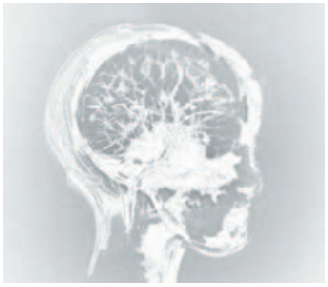
IN BRIEF



NEURODEGENERATIVE DISEASES

Sustained hippocampal IL-1β overexpression mediates chronic neuroinflammation and ameliorates Alzheimer plaque pathology.

Shaftel, S. S. *et al. J. Clin. Invest.* **117**, 1595–1604 (2007)

Neuroinflammation, driven by interleukin 1β (IL1β) activity, is thought to contribute to neurodegeneration in Alzheimer's disease (AD). Shaftel and colleagues describe a transgenic mouse model in which sustained IL1β overexpression was capable of driving robust neuroinflammation lasting months after transgene activation. Surprisingly, 4 weeks of IL1β overexpression led to a reduction in amyloid pathology. These results indicate a possible adaptive role for IL1β-driven neuroinflammation in AD, and so might explain recent failures of anti-inflammatory therapeutics for this disease.

DOI:
10.1038/nrd2391

ANTIVIRAL DRUGS

Small molecule activators of RNase L with broad spectrum activity.

Thakur, C. S. *et al. Proc. Natl Acad. Sci. USA* **104**, 9585–9590 (2007)

Antiviral drugs that stimulate host immunity have advantages over those that block viral proteins, such as a broad-spectrum of activity. Thakur and colleagues identified activators of RNase L — a mediator of innate immunity required for a complete interferon antiviral response against certain RNA viruses — with improved drug-like properties. The low-molecular-mass activators had broad-spectrum antiviral activity against diverse types of RNA viruses, including the human pathogen parainfluenza virus type 3. These activators could therefore be prototypes for a new class of antiviral agents.

ENDOCANNABINOIDS

Attenuation of allergic contact dermatitis through the endocannabinoid system.

Karsak, M. *et al. Science* **316**, 1494–1497 (2007)

Cannabinoids mediate analgesia largely via peripheral type cannabinoid receptors in nociceptors.

Agarwal, N. *et al. Nature Neurosci.* **10**, 870–879 (2007)

Two papers report advances in the understanding of the endocannabinoid system. In the first of these papers Karsak and colleagues used an animal model of allergic contact dermatitis — a leading cause of occupational disease — to show that mice lacking type 1 and type 2 cannabinoid (CB1 and CB2) receptors displayed exacerbated allergic inflammation. By contrast, mice deficient in fatty-acid amide hydrolase (FAAH), the enzyme responsible for endocannabinoid breakdown, displayed reduced allergic responses. In wild-type mice, CB1- and CB2-receptor agonists attenuated inflammation. Therefore, FAAH inhibitors or cannabinoid agonists might be beneficial in the treatment of this condition. However, the clinical use of cannabinoid-receptor agonists is severely hindered by side effects resulting from the central actions of cannabinoids. In the second paper, Agarwal and colleagues deleted the CB1 receptor specifically in nociceptive neurons in the peripheral nervous system of mice. The nociceptor-specific loss of CB1 reduced analgesia produced by local and systemic, but not intrathecal, delivery of cannabinoid agonists in models of inflammatory and neuropathic pain. Therefore, the contribution of peripheral CB1 receptors to analgesia is paramount, suggesting that peripherally acting CB1 agonists could provide pain relief without central side effects.