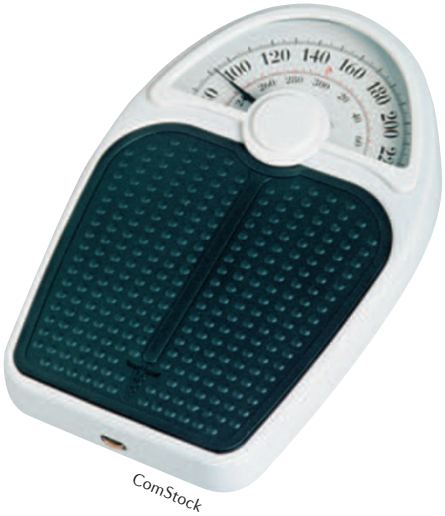
IN BRIEF



OBESITY AND DIABETES

The NLRP3 inflammasome instigates obesity-induced inflammation and insulin resistance

Vandanmagsar, B. *et al. Nature Med.* **17**, 179–188 (2011)

The link between obesity and the emergence of chronic inflammation — which can lead to obesity-associated pathologies such as type 2 diabetes — is not understood. This study showed that during obesity the NLRP inflammasome (which is a member of the NOD-like family of immune-sensing receptors) detects obesity-associated danger signals, such as ceramides. This leads to caspase 1 activation and interleukin production, which promote macrophage-mediated T cell activation in adipose tissue, resulting in inflammation and insulin resistance.

CANCER

Mouse and human iNKT cell agonist β-mannosylceramide reveals a distinct mechanism of tumor immunity

O'Konek, J. *et al. J. Clin. Invest.* **121**, 683–694 (2011)

Agonists of invariant natural killer T (iNKT) cells — such as the glycolipid α-galactosylceramide — can protect against cancer, largely through interferon-γ-dependent mechanisms. O'Konek and colleagues describe a new mechanism for inducing iNKT cell-dependent antitumour responses in mice that involves β-mannosylceramide. This mechanism was nitric oxide- and tumour necrosis factor-dependent and largely interferon-γ-independent. Moreover, subtherapeutic doses of β-mannosylceramide and α-galactosylceramide synergized to protect mice against tumour formation.

NEURODEGENERATIVE DISEASE

PKCε activation prevents synaptic loss, Aβ elevation and cognitive defects in Alzheimer's disease transgenic mice

Hongpaisan, J., Sun, M.-K. & Alkon, D. L. *J. Neurosci.* **31**, 630–643 (2011)

This study showed that decreases in levels of protein kinase Cε (PKCε) could provide a molecular basis for the correlation between synaptic loss and dementia that is seen in Alzheimer's disease (AD). In a transgenic mouse model of AD, a reduction in the levels of PKCε — an enzyme involved in synaptogenesis — occurs in association with the elevation of soluble amyloid-β protein, but before the appearance of amyloid plaques or neuronal loss. Treatment of mice with a PKCε activator prevented synaptic loss, amyloid plaque formation and cognitive deficits.

BIOTECHNOLOGY

Chemoproteomics profiling of HDAC inhibitors reveals selective targeting of HDAC complexes

Bantscheff, M. *et al. Nature Biotech.* 23 Jan 2011 (doi:10.1038/nbt.1759)

The identification of selective histone deacetylase (HDAC) inhibitors may be hampered owing to assay methods that use recombinant enzymes. Bantscheff and colleagues used chemoproteomics — namely, affinity capture methods combined with quantitative mass spectrometry — to probe the interaction of HDAC inhibitors with their megadalton protein complex targets. Data obtained on the selectivity of HDAC inhibitors using this approach differed from existing data obtained using isolated recombinant enzymes, thus indicating an unexpected degree of selectivity of certain HDAC inhibitors.