IN BRIEF

OBESITY

Leptin responsiveness restored by amylin agonism in diet-induced obesity: evidence from nonclinical and clinical studies.

Roth, J. D. *et al. Proc. Natl Acad. Sci. USA* **105**, 7257–7262 (2008)

Leptin regulates energy homeostasis, but its development as a stand-alone anti-obesity drug has been unsuccessful. Roth and colleagues report a marked synergy for weight loss and decrease in adiposity in diet-induced obese rats when leptin was administered with the islet-derived peptide amylin. This was attributed to amylin modulation of leptin signalling within the hypothalamus and caudal hindbrain. In a 24-week clinical proof-of-concept study in overweight/obese subjects, co-administration of the approved amylin analogue pramlinitide with recombinant human leptin yielded greater weight loss than either agent alone.

VIRAL INFECTION

CLEC5A is critical for dengue-virus-induced lethal disease.

Chen, S. T. *et al. Nature* **453**, 672–676 (2008)

Dengue virus infection can progress to haemorrhagic fever and lethal hypovolaemic shock. Chen and colleagues investigated whether dengue virus binds and activates candidate pattern recognition factors on immune cells. They showed that CLEC5A (C-type lectin domain family 5, member A) directly interacts with the dengue virion to stimulate pro-inflammatory cytokine release. In mice, anti-CLEC5A monoclonal antibodies inhibited dengue-virus-induced plasma leakage, reduced subcutaneous and vital-organ haemorrhage, and reduced mortality by ~50%.

ANTICANCER DRUGS

Discovery, *in vivo* activity, and mechanism of action of a small-molecule p53 activator.

Lain, S. D. *et al. Cancer Cell* **13**, 454–463 (2008)

Lain and colleagues carried out a cell-based screen to identify small molecules that activate the tumour suppressor p53. Two hits — tenovin-1 and the more water-soluble analogue tenovin-6 — were shown to act through inhibition of the protein-deacetylating activities of sirtuin-1 and -2. Tenovin-6 decreased melanoma-cell-derived tumour growth *in vivo* as a single agent. This study highlights the utility of tenovins as biological tools for the study of sirtuin function and their potential therapeutic use.

VIRTUAL SCREENING

Discovery of novel human histamine H_4 receptor ligands by large-scale structure-based virtual screening.

Kiss, R. *et al. J. Med. Chem.* **51**, 3145–3153 (2008)

The histamine H_4 receptor is a promising target for the treatment of allergy and inflammation, but only a limited number of H_4-selective ligands have been discovered. Kiss and colleagues report a large scale, structure-based virtual screen on a homology model of the H_4 receptor. More than 8.7 million 3D structures derived from different vendor databases were investigated by docking to the H_4 receptor binding site. From a total of 255 selected compounds, 16 had *in vitro* affinity and several novel scaffolds were identified that could be used to develop selective H_4 ligands.