IN BRIEF

OBESITY

Neuronal PTP1B regulates body weight, adiposity and leptin action.

Bence, K. K. *et al. Nature Med.* 16 July 2006 (doi:10.1038/mm1435)

Protein tyrosine phosphatase (PTP) 1B is a potential therapeutic target for obesity and type 2 diabetes. To investigate how PTP1B affects adiposity, Bence and colleagues generated mice with tissue-specific deletions of *Ptp1b* in brain, muscle, liver or fat. Only mice lacking neuronal PTP1B were resistant to high-fat diet-induced obesity and were protected from developing leptin resistance. Neuronal PTP1B also regulated adipocyte leptin production and insulin sensitivity independent of changes in body weight. So, it seems for effective obesity and type 2 diabetes therapy, PTP1B inhibitors should be directed to the brain.

ANTI-INFECTIVES

The protozoan inositol phosphorylceramide synthase; a novel drug target which defines a new class of sphingolipid synthase.

Denny, P. W. *et al. J. Biol. Chem.* 22 July 2006 (doi:10.1047/jbc.M600796200)

Infections caused by kinetoplastid protazoan parasites are prevalent in developing countries, but treatments are often toxic. Denny and colleagues identified and characterized a protozoan inositol phosphorylceramide (IPC) synthase, an enzyme essential for the synthesis of cell-membrane sphingolipids. Because this enzyme has no mammalian equivalent, it raises the possibility of developing antiprotozoal drugs with reduced side effects.

BIOTECHNOLOGY

Stem cell-derived erythroid cells mediate long-term systemic protein delivery.

Chang, A. H. *et al. Nature Biotechnol.* 16 July 2006 (doi:10.1038/nbt1227)

Chang and colleagues have developed a novel method of long-term, systemic therapeutic protein delivery by exploiting the globin-synthesis system in erythroid cells. By targeting human clotting factor IX expression to late-stage erythropoiesis, high-level secretion of clotting factor IX was achieved in a murine model of haemophilia B, resulting in phenotypic correction of the coagulation disorder. Advantages of this method include resistance to transcriptional silencing, induction of immune tolerance and a reduction of the risk of insertional oncogenesis.

TARGET VALIDATION

Expression of mammalian GPCRs in *C. elegans* generates novel responses to human ligands.

Teng, M. S. *et al. BMC Biol.* 20 July 2006 (doi:10.1186/1741-7007-4-22)

Current *in vitro* methods used to study mammalian G-protein-coupled receptor (GPCR)–ligand interactions might not accurately reflect *in vivo* interactions. Teng and colleagues have developed a simple *in vivo* method to study and screen GPCR ligands using the nematode *Caenorhabditis elegans*. In an avoidance assay, *C. elegans* expressing either mammalian somatostatin-2 receptor (Sstr2) or chemokine-5 receptor in gustatory neurons were able to detect and respond to appropiate agonists. Pre-exposure to ligand led to receptor desensitization and behavioural adaptation, and structure–function relationships could be established for Sstr2 ligands.