IN BRIEF

DIABETES

Osteoporosis drug promotes β-cell proliferation

A primary treatment goal in type 1 and type 2 diabetes is normalization of pancreatic β-cell homeostasis. Kondegowda *et al.* report that the TNF receptor superfamily member osteoprotegerin — which is involved in bone formation — stimulates β-cell proliferation and enhances glucose homeostasis in young, aged and diabetic mice. These effects were mediated through binding receptor activator of NF-κB ligand (RANKL) and modulation of the CREB and GSK3 pathways. Treatment of humanized diabetic mice with the RANKL-specific antibody denosumab (an osteoporosis drug that is approved in the US) induced β-cell proliferation.

ORIGINAL RESEARCH PAPER Kondegowda, N. *et al.* Osteoprotegerin and Denosumab stimulate human beta cell proliferation through inhibition of the receptor activator of NF-κB ligand pathway. *Cell Metab.* **22**, 77–85 (2015)

INFECTIOUS DISEASE

Fusion toxin protein inhibits CMV infection

Current therapies for human cytomegalovirus (HCMV) are associated with serious side effects and drug resistance. Now, Spiess *et al.* describe a novel fusion toxin protein (FTP)-based strategy to target HCMV on the basis of the viral expression of the internalizing G protein-coupled receptor, US28, which binds chemokines (particularly CX3CL1) as part of the immune-evasive function of the virus. They engineered a synthetic CX3CL1 variant displaying high affinity for US28 and greater specificity for US28 than does the natural CX3CL1 receptor, CX3CR1, and fused this with the cytotoxic domain of *Pseudomonas* exotoxin A. The resulting FTP prevented HCMV replication in cells and mice with greater potency than ganciclovir.

ORIGINAL RESEARCH PAPER Spiess, K. *et al.* Rationally designed chemokine-based toxin targeting the viral G protein-coupled receptor US28 potently inhibits cytomegalovirus infection *in vivo*. *Proc. Natl Acad. Sci. USA* **112**, 8427–8432 (2015)

HYPERTENSION

BMP9 reverses PAH

Reduced endothelial bone morphogenetic protein type 2 receptor (BMPR2) signalling has been implicated in the pathobiology of pulmonary arterial hypertension (PAH). However, precisely how BMP signalling is involved in endothelial dysfunction and whether it can be exploited therapeutically remains uncertain. Here, Long *et al.* show that the BMPR2 ligand BMP9 prevents apoptosis, decreases angiogenesis and promotes monolayer integrity in human pulmonary arterial endothelial cells. Moreover, BMP9 effectively prevented and reversed disease in three different rodent models of PAH.

ORIGINAL RESEARCH PAPER Long, L. *et al.* Selective enhancement of endothelial BMPR-II with BMP9 reverses pulmonary arterial hypertension. *Nat. Med.* **21**, 777–785 (2015)

TYPE 2 DIABETES

ER stress modulator reverses diabetes

Chronic endoplasmic reticulum (ER) stress results in a defective unfolded protein response and is associated with a variety of pathologies, including metabolic syndrome. Using two novel high-throughput screening systems that measure ER chaperone availability and activity, Fu *et al.* identify the small molecule azoramide as a modulator of ER function. *In vitro*, azoramide protected against chemically induced ER stress, and in mouse obesity models the compound improved liver ER function, insulin sensitivity and glucose tolerance, preserving pancreatic β-cell function and survival.

ORIGINAL RESEARCH PAPER Fu, S. *et al.* Phenotypic assays identify azoramide as a small-molecule modulator of the unfolded protein response with antidiabetic activity. *Sci. Transl Med.* **7**, 292ra98 (2015)