

IN BRIEF

▶ METABOLIC DISEASE**Cough suppressant reverses diabetes**

The role of *N*-methyl-D-aspartate receptors (NMDARs) in pancreatic islet β -cells remains poorly understood. Here, Marquard *et al.* report that the NMDAR antagonist MK-801 increases glucose-stimulated insulin secretion and improves glucose tolerance in mouse and human islet cells, by extending the depolarization phase in β -cells. Similar effects occurred in isolated islet cells and in mice administered another NMDAR antagonist (the cough suppressant dextromethorphan (DXM)). In diabetic *db/db* mice, oral DXM administration increased islet insulin content, cell mass and survival, and improved blood glucose control. In a Phase IIa trial in patients with type 2 diabetes, a single oral dose of DXM increased serum insulin concentrations and glucose tolerance.

ORIGINAL RESEARCH PAPER Marquard, J. *et al.* Characterization of pancreatic NMDA receptors as possible drug targets for diabetes treatment *Nature Med.* **21**, 363–372 (2015)

▶ KIDNEY INJURY**TRIM family protein protects the kidney**

Insufficient repair of proximal tubular epithelium (PTE) cells following acute kidney injury (AKI) can result in inflammatory and fibrotic responses, which may progress to chronic renal failure. Now, Duann *et al.* show that MG53 — a TRIM family protein involved in the cell-membrane-repair machinery — mediates membrane repair in PTE cells and protects against AKI-induced damage. MG53-deficient mice exhibited exacerbated kidney damage following ischaemia–reperfusion (I–R) AKI, whereas recombinant MG53 protected rats against I–R-induced damage. Intravenous delivery of recombinant MG53 also ameliorated the effects of cisplatin-induced AKI without affecting antitumour activity.

ORIGINAL RESEARCH PAPER Duann, P. *et al.* MG53-mediated cell membrane repair protects against acute kidney injury *Sci. Transl. Med.* **7**, 279ra36 (2015)

▶ INFECTIOUS DISEASE**Disrupting two-pore channels blocks Ebola virus infection**

Calcium signalling is important for entry of ebola virus (EBOV) into the host. Here, Sakurai *et al.* report that EBOV infection can be blocked *in vitro* by various calcium-channel antagonists — in particular, the small molecule tetrandrine. *In vitro* knockout, short interfering RNA (siRNA) and overexpression experiments revealed that two-pore channels were the specific calcium channels required for EBOV infection, and that these were inhibited by tetrandrine. Tetrandrine potently blocked EBOV infection of human monocyte-derived macrophages — an initial target of virus infection — and, when given every 2 days for a week to EBOV-challenged mice, eliminated virus and significantly enhanced survival.

ORIGINAL RESEARCH PAPER Sakurai, Y. *et al.* Two-pore channels control Ebola virus host cell entry and are drug targets for disease treatment. *Science* **347**, 995–998 (2015)

▶ EPILEPSY**LDH inhibition suppresses seizures**

Neuronal excitation is regulated by energy metabolism, and specific diets have been shown to suppress seizures in some patients with epilepsy. Targeting brain metabolism may therefore represent a new antiepileptic strategy. Here, Sada *et al.* report that blocking a key metabolic pathway in the brain — the astrocyte–neuron lactate shuttle — by inhibiting or knocking down lactate dehydrogenase (LDH) hyperpolarizes neurons and suppresses seizures in mouse seizure models. The authors optimized the structure of the antiepileptic agent stiripentol — which they found to inhibit LDH — to produce isosafrole, which potently suppressed seizures in the mouse kainate epilepsy model.

ORIGINAL RESEARCH PAPER Sada, N. *et al.* Targeting LDH enzymes with a stiripentol analog to treat epilepsy. *Science* **347**, 1362–1367 (2015)