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# 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)