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IN BRIEF

CARDIOVASCULAR DISEASE

CRHR2 blockade prevents heart failure

Despite improvements in the treatment of cardiovascular diseases, the prognosis of heart failure remains poor. To identify potential novel therapeutic targets, Tsuda *et al.* analyzed G-protein-coupled receptor (GPCR) expression in mouse cardiomyocytes 2 weeks following transverse aortic constriction (TAC) and identified markedly increased expression of corticotropin-releasing hormone receptor 2 (CRHR2). Mice with cardiomyocyte-specific deletion of *Crhr2* were protected from TAC-induced cardiac dysfunction, whereas mice treated with the CRHR2 antagonist antisauvagine-30, one week after TAC surgery, did not develop heart failure.

ORIGINAL ARTICLE Tsuda, T. *et al.* Corticotropin releasing hormone receptor 2 exacerbates chronic cardiac dysfunction. *J. Exp. Med.* **214**, 1877–1888 (2017)

TYPE 2 DIABETES

Broccoli extract lowers glucose levels

Targeting elevated hepatic glucose production in type 2 diabetes (T2D) represents an attractive therapeutic approach. To investigate this, Axelsson *et al.* first analyzed liver gene expression in a diabetic mouse model, in combination with other genetic data, to identify a 50-gene liver disease signature. Interrogation of a library of 3800 drug signatures indicated that sulforaphane (SFN) — an isothiocyanate found in broccoli — may reverse this disease signature. In rats fed a high-fat or high-fructose diet, SFN prevented or reversed glucose intolerance. In obese patients with dysregulated T2D, concentrated broccoli extract improved fasting glucose and glycated haemoglobin without adverse effects.

ORIGINAL ARTICLE Axelsson, A. *et al.* Sulforaphane reduces hepatic glucose production and improves glucose control in patients with type 2 diabetes. *Sci. Transl Med.* **9**, eaah4477 (2017)

NEURODEGENERATIVE DISORDERS

SRC-ABL inhibitors protect motor neurons

Currently approved therapies for amyotrophic lateral sclerosis (ALS) — a progressive neurodegenerative disease characterized by loss of motor neurons — exhibit limited effectiveness. By screening a panel of existing drugs in induced pluripotent stem cell (iPSC)-derived motor neurons from patients with familial ALS, Imamura *et al.* discovered that SRC-ABL inhibitors may protect against motor neuron degeneration. In ALS motor neurons, the SRC-ABL inhibitor bosutinib promoted autophagy, reduced the amount of misfolded superoxide dismutase 1 (SOD1) protein and restored energy homeostasis. In a mouse model of familial ALS, bosutinib delayed disease onset and extended survival.

ORIGINAL ARTICLE Imamura, K. *et al.* The Src/c-Abl pathway is a potential therapeutic target in amyotrophic lateral sclerosis. *Sci. Transl Med.* **9**, eaaf3962 (2017)

CANCER

mRNA-encoded bispecific antibodies eliminate tumours

The development of therapeutic bispecific T cell-engaging antibodies, which recruit cytotoxic T cells to tumour cells, has been hampered by manufacturing challenges as well as their short serum half-life. To circumvent these issues, Stadler *et al.* generated 1-methylpseudouridine-containing mRNAs encoding bispecific antibodies directed against the T cell receptor-associated molecule CD3 and a tumour-associated antigen. In mice, injected antibody-encoding mRNAs achieved sustained therapeutic antibody levels and safely eliminated tumours in human ovarian carcinoma xenograft models.

ORIGINAL ARTICLE Stadler, C. *et al.* Elimination of large tumors in mice by mRNA-encoded bispecific antibodies. *Nat. Med.* **23**, 815–817 (2017)

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