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IN BRIEF

OCULAR DISORDERS

Vitamin B_3 blocks glaucoma

The mechanisms that mediate the degeneration of retinal ganglion cells (RGCs) during glaucoma development are unknown. Williams *et al.* report that decreased levels of NAD^+ and mitochondrial dysfunction are among the very first changes to occur in retinas of a mouse model of glaucoma. Orally administered vitamin B_3 (also known as nicotinamide, which is a precursor of NAD^+) and/or intravitreal injection of an adenovirus overexpressing NMNAT1 (a key NAD^+-producing enzyme) protected mice from glaucomatous RGC degeneration when given prophylactically or therapeutically.

ORIGINAL ARTICLE Williams, P. A. *et al.* Vitamin B3 modulates mitochondrial vulnerability and prevents glaucoma in aged mice. *Science* **355**, 756–760 (2017)

DRUG TOXICITY

Cardiac safety index for TKIs

Tyrosine kinase inhibitors (TKIs) represent efficacious anticancer agents, but their use has been linked with severe cardiotoxicity. Here, Sharma *et al.* generated human induced pluripotent stem cell (hiPSC)-derived cardiomyocytes, hiPSC-derived endothelial cells and hiPSC-derived cardiac fibroblasts to evaluate the cardiotoxicities of 21 US FDA-approved TKIs. The integration of cytotoxicity and contractility measurements enabled the development of a cardiac safety index for existing TKIs. VEGFR2- and PDGFR2-inhibiting TKIs exhibited low safety indices and high toxicity in the hiPSCs. These cardiotoxicities could be rescued by compensatory activation of pro-survival insulin and IGF1 signalling pathways.

ORIGINAL ARTICLE Sharma, A. *et al.* High-throughput screening of tyrosine kinase inhibitor cardiotoxicity with human induced pluripotent stem cells. *Sci. Transl Med.* **9**, eaaf2584 (2017)

CARDIOVASCULAR DISEASE

Thioredoxin lowers hypertension

The development of long-lasting antihypertensive therapies represents a crucial unmet need. Hilgers *et al.* now report that mice overexpressing the redox protein thioredoxin (TRX) are protected from age-related hypertension. Furthermore, injection of aged mice with recombinant human TRX (rhTRX) lowered blood pressure to levels seen in young mice, which were maintained for at least 20 days. RhTRX injection or TRX overexpression in mice also decreased arterial stiffness, attenuated endothelial dysfunction, increased nitric oxide production and reduced superoxide anion release.

ORIGINAL ARTICLE Hilgers, R. H. P. *et al.* Thioredoxin reverses age-related hypertension by chronically improving vascular redox and restoring eNOS function. *Sci. Transl Med.* **9**, eaaf6094 (2017)

CANCER

Bacterium-based immunotherapy

Anaerobic bacteria can accumulate and proliferate within hypoxic and necrotic regions of solid tumours, stimulating inflammation and triggering an antitumour immune response. Zheng *et al.* have engineered an attenuated strain of *Salmonella typhimurium* to overexpress and secrete a heterologous bacterial flagellin (FlaB), which is a ligand for Toll-like receptor 5 (TLR5). In tumour-bearing mice, the engineered FlaB-secreting bacteria effectively and safely suppressed tumour growth and metastasis, and prolonged survival through the activation of TLR4 and TLR5 signalling pathways in host immune cells.

ORIGINAL ARTICLE Zheng, J. H. *et al.* Two-step enhanced cancer immunotherapy with engineered *Salmonella typhimurium* secreting heterologous flagellin. *Sci. Transl Med.* **9**, eaak9537 (2017)