IN BRIEF

AGEING

Telomerase gene therapy increases longevity

Telomere shortening and the resulting cellular senescence promotes ageing in mammals. This study showed that administration (via an adeno-associated virus) of telomerase reverse transcriptase (TERT) — an enzyme that maintains the length of telomeres — to old mice decreased the incidence of age-related osteoporosis and glucose intolerance, improved neuromuscular function and partially improved memory without increasing the incidence of cancer. Furthermore, TERT therapy extended the lifespan of adult and aged mice by a median of 24% and 13%, respectively, showing the feasibility of gene therapy for ageing.

ORIGINAL RESEARCH PAPER Bernardes de Jesus, B. *et al.* Telomerase gene therapy in adult and old mice delays aging and increases longevity without increasing cancer. *EMBO Mol. Med.* 15 May 2012 (doi: 10.1002/emmm.201200245)

CARDIOVASCULAR DISORDERS

A new class of antithrombotic agents

This paper showed that an inhibitor of protein disulphide isomerase (PDI) can block thrombus formation. Quercetin-3-rutinoside — which was identified from a screen of ~5,000 compounds — inhibited both platelet aggregation and endothelial cell-mediated fibrin generation. In mice, intravenous infusion or oral administration of quercetin-3-rutinoside blocked thrombus formation (which could be reversed by infusion of recombinant PDI). The authors suggest that PDI inhibitors could be used as an adjunct in thrombotic disorders that are not controlled by current therapies.

ORIGINAL RESEARCH PAPER Jasuja, R. *et al.* Protein disulfide isomerase inhibitors constitute a new class of antithrombotic agents. *J. Clin. Invest.* **122**, 2104–2113 (2012)

NEURODEGENERATIVE DISORDERS

Alzheimer's toxic chain reaction

Pyroglutamylated forms of amyloid-β (pE-Aβ) have been proposed as initiators of Alzheimer's disease pathogenesis. Here, Nussbaum *et al.* used cultured neurons to elucidate mechanisms of how pE-Aβ could trigger Alzheimer's disease. They showed that $Aβ_{3(pE)–42}$ co-oligomerizes with $Aβ_{1–42}$ to form structurally distinct hypercytotoxic oligomers, and that this toxicity is tau-dependent. Furthermore, the co-oligomers of $Aβ_{1–42}$ and $Aβ_{3(pE)–42}$ can then use a template-based mechanism to trigger the formation of new toxic oligomers from excess $Aβ_{1–42}$ (without the addition of further $Aβ_{3(pE)–42}$). This process is similar to how prion proteins propagate.

ORIGINAL RESEARCH PAPER Nussbaum, J. M. *et al.* Prion-like behaviour and tau-dependent cytotoxicity of pyroglutamylated amyloid-β. *Nature* **486**, 651–655 (2012)

DIABETES

A mechanism of metabolically driven pain

There is a limited understanding of the mechanisms that cause diabetic neuropathy. This study showed that increased concentrations of methylglyoxal — production of which is enhanced by elevated glucose concentrations — may be involved in metabolic hyperalgesia. After demonstrating that individuals with diabetic neuropathy had high methylglyoxal concentrations, the authors showed that methylglyoxal caused post-translational modifications of the $Na_v1.8$ sodium channel that were associated with increased firing of nociceptive neurons. In mouse models of diabetes, a methylglyoxal scavenger reduced hyperalgesia.

ORIGINAL RESEARCH PAPER Bierhaus, A. *et al.* Methylglyoxal modification of $Na_v1.8$ facilitates nociceptive neuron firing and causes hyperalgesia in diabetic neuropathy. *Nature Med.* **18**, 926–933 (2012)