IN BRIEF

BONE DISORDERS

A new promoter of bone regeneration

Cell-to-cell communication facilitates the healing of bone fractures. By screening molecules secreted from human mesenchymal stem cells during osteogenesis, this study identified DJ1 as a novel angiogenic factor that mediated crosstalk between osteoblasts and endothelial cells, and promoted osteogenesis through the activation of fibroblast growth factor receptor 1 signalling. In a rodent model of bone fracture repair, application of DJ1 to the injured site increased bone regeneration by stimulating the formation of blood vessels and new bone, suggesting that targeting DJ1 could have therapeutic potential in bone fracture healing.

ORIGINAL RESEARCH PAPER Kim, J-. M. *et al.* DJ-1 promotes angiogenesis and osteogenesis by activating FGF receptor-1 signaling. *Nature Comm.* **3**, 1296 (2012)

INFECTIOUS DISEASE

A broad protozoan drug target?

Misassembled proteins can be degraded by a process called endoplasmic reticulum-associated degradation (ERAD). Using a bioinformatics approach, this study showed that protozoan pathogens contain a simpler ERAD network than higher eukaryotic cells. Because of this, *Plasmodium falciparum* was very sensitive to the inhibition of ERAD components, in particular signal peptide peptidase (SPP) inhibitors, which disrupted the degradation of unstable proteins and inhibited proteolytic activity. SPP inhibitors were also active against liver-stage malaria parasites and several other pathogenic protozoan parasites, suggesting that SPP could be a potential pan-protozoan drug target.

ORIGINAL RESEARCH PAPER Harbut, M. B. *et al.* Targeting the ERAD pathway via inhibition of signal peptide peptidase for antiparasitic therapeutic design. *Proc. Natl Acad. Sci. USA* **109**, 21486–21491 (2012)

NEUROMUSCULAR DISORDERS

Reducing androgen receptor-mediated toxicity

Spinobulbar muscular atrophy (SBMA) is caused by an expansion of a CAG repeat in the androgen receptor (AR), resulting in a polyglutamine tract in the AR. Wang *et al.* showed that overexpression of heat shock protein 70 (HSP70)-interacting protein (HIP), a chaperone that promotes binding of HSP70 to its substrates, promoted the clearance of polyglutamine AR *in vitro*. They identified a compound that acted similarly to HIP (by allosterically promoting HSP70 binding to unfolded substrates) and reduced toxicity in a fruitfly model of SBMA.

ORIGINAL RESEARCH PAPER Wang, A. M. *et al.* Activation of Hsp70 reduces neurotoxicity by promoting polyglutamine protein degradation. *Nature Chem. Biol.* 9 Dec 2012 (doi:10.1038/nchembio.1140)

NEUROLOGICAL DISEASE

Inflammasome activation in Alzheimer's disease

Deposition of amyloid-β in Alzheimer's disease (AD) activates microglia, which drive cerebral neuroinflammation. This paper showed increased expression of caspase 1 (a component of the NLRP3 (NOD-, LRR- and pyrin domain-containing 3) inflammasome) in brain samples from patients with AD. Mice that lacked *Nlrp3* or *Casp1* and had mutations associated with familial AD were protected from loss of spatial memory and had enhanced amyloid-β clearance. In another mouse model of AD, *Nlrp3* deficiency resulted in decreased deposition of amyloid-β, suggesting that targeting the NLRP3 inflammasome could be beneficial in AD.

ORIGINAL RESEARCH PAPER Heneka, M. T. *et al.* NLRP3 is activated in Alzheimer's disease and contributes to pathology in APP/PS1 mice. *Nature* 19 Dec 2012 (doi:10.1038/nature11729)

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