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IN BRIEF

DRUG SCREENING

Inhibiting protein–protein interactions

Inhibitors of a number of protein–protein interactions (PPIs) have emerged as potential anticancer drug candidates. Now, Nim *et al.* describe a novel high-throughput method that uses a pooled lentiviral dropout approach to screen a library of human peptide motifs for PPI inhibitors that specifically decreased viability of a pancreatic cancer cell line (RWP1). Target interactions of hits were identified computationally and a subset validated *in vitro*. Further analysis of the inhibitors in RWP1 cells revealed their mechanisms of action, which included apoptosis and cell-cycle arrest.

ORIGINAL ARTICLE Nim, S. *et al.* Pooled screening for antiproliferative inhibitors of protein–protein interactions. *Nat. Chem. Bio.* http://dx.doi.org/10.1038/nchembio.2026 (2016)

PAIN

FKBP51 inhibition reduces chronic pain

Polymorphisms in the gene encoding FK506 binding protein 51 (FKBP51) — a regulator of steroid hormone signalling — influence the severity of musculoskeletal pain symptoms after trauma. Here, using *Fkbp51*-knockout mice and siRNA-induced silencing of *Fkbp51* in the mouse spinal cord, Maiarù *et al.* demonstrate that FKBP51 regulates chronic but not acute pain states by modulating glucocorticoid signalling. Intrathecal administration of the FKBP51-specific inhibitor SAFit2 improved the mechanical hypersensitivity induced by ankle joint inflammation in mice.

ORIGINAL ARTICLE Maiarù M. *et al.* The stress regulator FKBP51 drives chronic pain by modulating spinal glucocorticoid signaling. *Sci. Trans. Med.* **8**, 325ra19 (2016)

CARDIOMYOPATHY

Inhibiting sarcomere contraction

Hypertrophic cardiomyopathy (HCM) is the most common inherited disease of the heart muscle and is characterized by hyperdynamic contraction and impaired relaxation. HCM can be caused by mutations in genes encoding sarcomere proteins, and such mutations may be responsible for increased power output. Green *et al.* identify the small molecule MYK-461, which reduces sarcomere power output by inhibiting cardiac myosin ATPase. In genetic mouse HCM models, oral administration of MYK-461 reduced cardiac contractility, prevented or ameliorated ventricular hypertrophy and attenuated myocardial disarray and fibrosis.

ORIGINAL ARTICLE Green, E. M. *et al.* A small-molecule inhibitor of sarcomere contractility suppresses hypertrophic cardiomyopathy in mice. *Science* **351**, 617–621 (2016)

INFECTIOUS DISEASE

TLR7 activation fights resistance

Vancomycin-resistant *Enterococcus faecium* (VRE) is a major cause of antibiotic-resistant infections and thrives in the intestine when colonization resistance is disrupted. Abt *et al.* report that norovirus infection partially reduces intestinal VRE colonization in mice with antibiotic-induced loss of colonization resistance. Oral resiquimod (R848) — a synthetic molecule that stimulates innate immune antiviral defences — similarly reduced mouse intestinal VRE colonization. R848 activates Toll-like receptor 7 (TLR7) on $CD11c^+$ dendritic cells, to induce interleukin-22 (IL-22) production by innate lymphoid cells and restore ileum expression of the antimicrobial regenerating islet-derived protein 3γ (REG3γ).

ORIGINAL ARTICLE Abt, M. C. *et al.* TLR-7 activation enhances IL-22-mediated colonization resistance against vancomycin-resistant enterococcus. *Sci. Transl Med.* **8**, 327ra25 (2016)