IN BRIEF

ANALGESIA

Targeting the EP_3 receptor to combat pain

Although the receptors of prostaglandin E2 (EP_1–EP_4) are considered mediators of pronociceptive signalling, this study showed that the EP_3 receptor can mediate antinociceptive effects. In rats, administration of an EP_3 receptor agonist induced analgesia and reduced responses of nociceptive neurons, but only when the joint was inflamed. Moreover, the EP_3 receptor was expressed in the peripheral nerves of afflicted joints in patients with painful osteoarthritis. The authors suggest that the EP_3 receptor provides endogenous pain control and that agonists of this receptor may be a novel approach to inhibit inflammatory pain.

ORIGINAL RESEARCH PAPER Natura, G. *et al.* Neuronal prostaglandin E_2 receptor subtype EP3 mediates antinociception during inflammation. *Proc. Natl. Acad. Sci. USA* 2013 (dx.doi:10.1073/pnas.1300820110)

GENE THERAPY

Decoy viral capsids boost vector delivery

Although adeno-associated virus (AAV) vector-mediated gene therapy has shown promise in animal models, humans can develop AAV-specific neutralizing antibodies that block gene transfer. Mingozzi *et al.* showed that the addition of an empty viral capsid to the vector formulation could adsorb these antibodies to increase the efficacy of transduction in mouse and primate models. Moreover, an immunologically inert capsid that did not bind to target cells could still adsorb antibodies. Doses of empty capsids — based on a patient's anti-AAV titres — might increase the efficacy of gene transfer in humans.

ORIGINAL RESEARCH PAPER Mingozzi, F. *et al.* Overcoming preexisting humoral immunity to AAV using capsid decoys. *Sci. Transl. Med.* **5**, 194ra92 (2013)

HEART DISEASE

Tacrolimus shows promise in PAH models

Dysfunctional bone morphogenetic protein receptor 2 (BMPR2) signalling is implicated in pulmonary arterial hypertension (PAH). This study identified tacrolimus as an inhibitor of BMPR2 signalling, which bound FK-binding protein 12 (a repressor of BMP signalling) and also inhibited calcineurin. In pulmonary arterial cells from patients with idiopathic PAH, low doses (non-immunosupressive) of tacrolimus reversed dysfunctional BMPR2 signalling. The drug also reversed disease in a mouse model of PAH and in a rat model of progressive severe disease, suggesting that low-dose tacrolimus — which is used to prevent transplant rejection — could be useful in the treatment of PAH.

ORIGINAL RESEARCH PAPER Spiekerkoetter, E. *et al.* FK506 activates BMPR2, rescues endothelial dysfunction, and reverses pulmonary hypertension. *J. Clin. Invest.* **123**, 3600–3613 (2013)

DRUG PROPERTIES

A method to measure target engagement in cells

This paper describes a method that allowed the measurement of target engagement by drugs in cells and tissue samples. The assay was based on the principle that ligands induce thermal stabilization of their target that confers a 'fingerprint' of drug–target engagement. In whole cells, this assay could measure levels of target engagement of several types of anticancer drugs (such as antifolates, cyclin-dependent kinase inhibitors and vemurafenib). This assay could also be used in *ex vivo* tissue, as demonstrated by its ability to monitor target engagement of an anti-angiogenic compound in mouse tissue.

ORIGINAL RESEARCH PAPER Molina D. M. *et al.* Monitoring drug target engagement in cells and tissues using the cellular engagement thermal shift assay. *Science* **341**, 84–87 (2013)