IN BRIEF

G PROTEIN-COUPLED RECEPTORS

An endogenous allosteric cannabinoid modulator

This study showed that lipoxin A4 is an endogenous allosteric enhancer of cannabioid receptor 1 (CB1). Lipoxin A4 increased the affinity of the endogenous cannabinoid anandamide for CB1, and reduction of lipoxin A4 levels in mice reduced the cataleptic effect of anandamide, showing that lipoxin A4 modulates endocannabinoid signalling. Moreover, lipoxin A4 had CB1-mediated neuroprotective effects against amyloid-β ($A\beta_{1-40}$)-induced memory defects, suggesting that this allosteric modulator could be therapeutically exploited.

ORIGINAL RESEARCH PAPER Pamplona, F. A. *et al.* Anti-inflammatory lipoxin A_4 is an endogenous allosteric enhancer of CB_1 cannabinoid receptor. *Proc. Natl Acad. Sci. USA* 12 Nov 2012 (doi:10.1073/pnas.1202906109)

RNA INTERFERENCE

Reducing off-target effects of shRNA

The endoribonuclease Dicer heterogeneously cleaves short hairpin RNAs (shRNAs) into biologically active small interfering RNAs that have differing efficacies and off-target effects. This study found that promiscuous non-canonical cleavages by Dicer were prevented when the cleavage site was two nucleotides away from a bulge or loop structure. Hepatitis C virus-targeted shRNAs designed to include an internal loop two nucleotides away from the expected site of Dicer cleavage had reduced off-target effects. This finding could aid the design of shRNAs for inducing therapeutic RNA interference.

ORIGINAL RESEARCH PAPER Gu, S. *et al.* The loop position of shRNAs and pre-miRNAs is critical for the accuracy of Dicer processing *in vivo*. *Cell* **151**, 900–911 (2012)

OBESITY AND DIABETES

Tissue targeting of oestrogen

The therapeutic potential of oestrogens in obesity and type 2 diabetes is limited by their gynaecological and tumour-promoting actions. To overcome this, Finan *et al.* designed a conjugate of oestrogen and the antidiabetic hormone glucagon-like peptide 1 (GLP1) to selectively deliver oestrogen to specific tissues. The synergistic action of the conjugate on metabolic parameters and body weight reduction in mice depended on its activity at both GLP1 and oestrogen receptors. Moreover, the conjugate did not have the adverse effects associated with systemic oestrogen actions. The authors suggest that such combinations of peptides and small molecules could offer promise for other diseases.

ORIGINAL RESEARCH PAPER Finan, B. *et al.* Targeted estrogen delivery reverses the metabolic syndrome. *Nature Med.* **18**, 1847–1856 (2012)

DRUG DELIVERY

Injectable biomaterials

Injectable biomaterials such as cryogels that allow controlled delivery of therapeutic agents or cell therapies could minimize complications associated with surgical implantation. Bencherif *et al.* describe a strategy that enabled the delivery of loaded cryogels using conventional needle and syringe injection. Injection of cryogels to mice enabled sustained release of granulocyte–macrophage colony-stimulating factor, and cryogels loaded with cells and a cell adhesion peptide (as a model for cell transplantation) promoted cell survival, local retention and engraftment of transplanted cells.

ORIGINAL RESEARCH PAPER Bencherif, S. A. *et al.* Injectable preformed scaffolds with shape-memory properties. *Proc. Natl Acad. Sci. USA* **109**, 19590–19595 (2012)