IN BRIEF

BONE DISORDERS

Clopidogrel prevents bone loss

This study investigated the role of P2Y purinergic receptor 12 (P2Y12) in osteoclast function. ADP-mediated stimulation of P2Y12 on osteoclasts enhanced adhesion and resorptive activity; these effects were not seen in *P2y12*$^{-/-}$ osteoclasts. *P2y12*$^{-/-}$ mice had decreased osteoclast resorptive activity and were partially protected from bone loss that occurred as a result of age, arthritis, osteoporosis or tumour growth. Moreover, wild-type mice treated with the clinical P2Y12 inhibitor clopidogrel were protected from bone loss, suggesting that P2Y12 inhibition is a potential target for this disorder.

ORIGINAL RESEARCH PAPER Su, X. *et al.* The ADP receptor P2RY12 regulates osteoclast function and pathologic bone remodeling. *J. Clin. Invest.* **122**, 3579–3592 (2012)

VIRAL INFECTION

Single antibody loop can neutralize influenza A

Immune recognition of antigens usually relies on the interaction of multiple antibody loops. Ekiert *et al.* identified an antibody (from a patient who survived H5N1 infection) that recognized a conserved region of the receptor binding site on the haemagglutinin (HA) protein through an interaction that was mediated by a single heavy-chain complementarity-determining region 3 loop. The antibody bound H1, H2, H3, H9 and H12 HA, and when given prophylactically or therapeutically to mice it protected against lethal challenge with H1N1 or H3N2 types of influenza A. Single-loop antibodies that target small conserved regions might be therapeutically exploited to achieve broad neutralization of influenza.

ORIGINAL RESEARCH PAPER Ekiert, D. C. *et al.* Cross-neutralization of influenza A viruses mediated by a single antibody loop. *Nature* **489**, 526–532 (2012)

IMMUNE REGULATION

Modulating monocytes could benefit ALS

Aberrant immune responses are probably involved in the pathogenesis of amyotrophic lateral sclerosis (ALS). This paper studied the role of innate immunity in a mouse model of ALS. During disease progression, inflammatory monocytes — the LY6C^{hi} subset — were recruited via chemokine receptor 2 to the spinal cord (but not the brain), and this correlated with neuronal loss. Treatment of mice with an LY6C-specific antibody reduced neuronal loss and increased survival. Moreover, analogous monocytes from patients with ALS had a similar inflammatory phenotype to monocytes from the mouse model.

ORIGINAL RESEARCH PAPER Butovsky, C. *et al.* Modulating inflammatory monocytes with a unique microRNA gene signature ameliorates murine ALS. *J. Clin. Invest.* **122**, 3063–3087 (2012)

ANTICANCER DRUGS

A new target for ovarian cancer

Xu *et al.* identified a class of propynoic acid carbamoyl methyl amides that were toxic to several human ovarian cancer cell lines. They showed that one of the most active compounds acted as an irreversible inhibitor of protein disulphide isomerase (PDI) — a chaperone protein found in the endoplasmic reticulum — by forming a covalent bond with the active site cysteines of PDI. The compound suppressed ovarian tumour growth in mice, suggesting that PDI is a novel cancer target and that these PDI inhibitors could serve as a starting point for the development of ovarian cancer therapies.

ORIGINAL RESEARCH PAPER Xu, S. *et al.* Discovery of an orally active small-molecule irreversible inhibitor of protein disulfide isomerase for ovarian cancer treatment. *Proc. Natl Acad. Sci. USA* **109**, 16348–16353 (2012)