IN BRIEF

ASTHMA

β_2-Adrenoceptor signaling is required for the development of an asthma phenotype in a murine model

Nguyen, L. P. *et al. Proc. Natl Acad. Sci. USA* 26 Jan 2009 (doi:10.1073/pnas.0810902106)

β2-Adrenergic receptor (β2AR) agonists are used in the management of asthma, but their chronic use is associated with loss of disease control. This paper demonstrated the paradoxical result that β2AR signalling — by constitutively active receptors — is required for the asthma phenotype in animal models. A β2AR inverse agonist attenuated asthmatic symptoms, highlighting the potential of inverse agonists in this condition.

IMMUNE DISORDERS

Antibody to the dendritic cell surface activation antigen CD83 prevents acute graft-versus-host disease

Wilson, J. *et al. J. Exp. Med.* 26 Jan 2009 (doi:10.1084/jem.20070723)

Allogeneic haematopoietic stem cell transplantation is limited by acute graft-versus-host disease (GVHD). Using a mouse model of GVHD, Wilson and colleagues showed that CD83 antibody treatment prevented GVHD but, unlike conventional immunosuppressants, did not prevent engraftment of human T cells. Moreover, this treatment did not impair the induction of anti-leukaemic cytosolic T cell effectors. So, antibodies that target activated dendritic cells, which express CD83, could be a new therapeutic approach to the control of GVHD.

ANTICANCER DRUGS

PIM-1-specific mAb suppresses human and mouse tumor growth by decreasing PIM-1 levels, reducing Akt phosphorylation, and activating apoptosis

Hu, X. F. *et al. J. Clin. Invest.* 19 Jan 2009 (doi: 10.1172/JCI33216)

Overexpression of the *PIM1* proto-oncogene is crucial in the progression of prostatic malignancies. This paper describes the generation of a monoclonal antibody (mAb) specific for PIM1. The mAb induced cancer cell apoptosis and synergistically enhanced anti-tumour activity when used in combination with cisplatin. In two tumour models of prostate cancer, the mAb substantially inhibited growth, showing that treatment of prostate cancer may be possible by targeting PIM1 using an antibody-based therapy.

CARDIOVASCULAR DISEASE

Small-molecule inhibitors of integrin $\alpha_2\beta_1$ that prevent pathological thrombus formation via an allosteric mechanism

Miller, M. W. *et al. Proc. Natl Acad. Sci. USA* **106,** 719–724 (2009)

Collagen is crucial in the interaction between platelets and atherosclerotic blood vessels. Miller and colleagues used structure–activity studies to identify highly potent and selective small-molecule inhibitors of the integrin α2β1 collagen receptor. One compound was efficacious in an animal model of arterial thrombosis, demonstrating *in vivo* efficacy for inhibition of this platelet receptor. Moreover, computational studies revealed new insights into the activation mechanism of such I-domain-containing integrins.