IN BRIEF

BIOTECHNOLOGY

Design of therapeutic proteins with enhanced stability

Chennamsetty, N. *et al. Proc. Natl Acad. Sci. USA* **106**, 11937–11942 (2009)

Therapeutic proteins such as antibodies tend to aggregate when stored under the concentrated conditions required for their usage, which leads to a decrease in activity. Using a technology known as spatial-aggregation propensity, this study identified antibody regions that were prone to aggregation and performed target mutations of the regions to engineer stable variants of two therapeutic antibodies. The authors concluded that such technology could be incorporated during the screening of antibodies in the discovery phase.

OBESITY AND DIABETES

Pigment epithelium-derived factor contributes to insulin resistance in obesity

Crowe, S. *et al. Cell Metab.* **10**, 40–47 (2009)

Although several possible mediators of the insulin resistance that is associated with obesity have been identified, the mechanistic link between insulin resistance and obesity is not well defined. Using mouse models of obesity and isolated-tissue studies, Crowe and colleagues showed that pigment epithelium-derived factor (PEDF) — a non-inhibitory member of the serine protease inhibitor family — has a causal role in insulin resistance. Given that PEDF serum levels are increased in individuals with type 2 diabetes, PEDF might be a target in the treatment of obesity-induced insulin resistance.

ANTICANCER DRUGS

Inhibition of prostate cancer cell growth by second-site androgen receptor antagonists

Joseph, J. D. *et al. Proc. Natl Acad. Sci. USA* **106**, 12178–12183 (2009)

To identify androgen receptor antagonists that retain activity in castration-resistant prostate cancer, Joseph and colleagues developed a conformation-based screen to identify androgen receptor antagonists with novel mechanisms of action. Two allosteric inhibitors were identified that blocked androgen action in cellular models of prostate cancer. The compounds were mechanistically different to classical androgen receptor antagonists: they did not promote androgen receptor nuclear translocation, but did inhibit the association of the androgen receptor with DNA, even under conditions of overexpression.

AUTOIMMUNE DISEASE

Targeted depletion of lymphotoxin-α-expressing T_H1 and T_H17 cells inhibits autoimmune disease

Chiang, E. Y. *et al. Nature Med.* **15**, 766–773 (2009)

Proinflammatory T helper type 1 (T_H1) and T_H17 cells are associated with autoimmune responses. This paper identified surface lymphotoxin-α — a member of the tumour necrosis factor superfamily — as a product common to T_H0, T_H1 and T_H17 cells. Treatment of mice with a lymphotoxin-α-specific monoclonal antibody ameliorated disease in models dependent on T_H1 and T_H17 cells, including delayed-type hypersensitivity, experimental autoimmune encephalomyelitis and collagen-induced arthritis. These data suggest a new strategy for depleting T_H1 and T_H17 cells, which may be beneficial in the treatment of autoimmune disease.