IN BRIEF

COMPUTATIONAL CHEMISTRY

Designing optimal ligand-binding proteins

This study describes a new *in silico* method for designing ligand-binding proteins. The technique involved computationally generating potential binding proteins from protein scaffolds, followed by iterative *in vitro* screening to optimize binding affinity. Using this method, the authors generated proteins that bound to the steroid digoxigenin with picomolar affinity and high selectivity over related steroids. The authors note that this method could be useful for creating therapeutic scavengers and binding domains for diagnostics.

ORIGINAL RESEARCH PAPER Tinberg, C. E. *et al.* Computational design of ligand-binding proteins with high affinity and selectivity. *Nature* **501**, 212–216 (2013)

INFECTIOUS DISEASES

A new lead against drug-resistant tuberculosis

To discover new compounds for combating drug-resistant tuberculosis, Pethe *et al.* conducted a high-content phenotypic screen against macrophages infected with *Mycobacterium tuberculosis*. This identified a class of imidazopyridine amide compounds that targeted the respiratory cytochrome bc_1 complex of *M. tuberculosis* to inhibit growth. Optimization of one compound resulted in Q203, which potently inhibited the growth of multi- and extensively-drug-resistant clinical isolates of *M. tuberculosis*; the compound also reduced bacterial load and improved lung pathology in a mouse model. The authors suggest that Q203 could be a new clinical candidate against tuberculosis.

ORIGINAL RESEARCH PAPER Pethe, K. *et al.* Discovery of Q203, a potent clinical candidate for the treatment of tuberculosis. *Nature Med.* **19**, 1157–1160 (2013)

VIRAL DISEASES

An antibody that hits four paramyxoviruses

Human respiratory syncytial virus (HRSV) and human metapneumovirus (HMPV) cause disease in premature newborns, hospitalized children and immune-compromised patients, and are also involved in asthma exacerbations. Corti *et al.* identified a human monoclonal antibody (named MPE8) that neutralized HRSV and HMPV as well as bovine RSV and pneumonia virus of mice (PVM). MPE8 reduced viral titres in mouse models of HRSV and HMPV infection, and had therapeutic efficacy against lethal PVM infection. The antibody was found to selectively recognize epitopes on the pre-fusion viral F protein. These results suggest that MPE8 could be used against HRSV and HMPV infections and that the pre-fusion F protein could be a target for vaccine development.

ORIGINAL RESEARCH PAPER Corti, D. *et al.* Cross-neutralization of four paramyxoviruses by a human monoclonal antibody. *Nature* http://dx.doi.org/10.1038/nature12442 (2013)

AFFECTIVE DISORDERS

Selectively targeting COX2 decreases anxiety

Inhibition of cyclooxygenase 2 (COX2) activity is thought to activate endocannabinoid signalling. This study identified a substrate-selective COX2 inhibitor that did not modulate non-endocannabinoid lipids or prostaglandin synthesis. In mice, the inhibitor reduced anxiety-like behaviours by increasing endocannabinoid signalling without inducing detrimental cannabimimetic effects. The results confirm that COX2 regulates endocannabinoid signalling and suggest that substrate-selective COX2 inhibitors have therapeutic potential, possibly without gastrointestinal or cardiac side effects.

ORIGINAL RESEARCH PAPER Hermanson, D. J. *et al.* Substrate selective COX-2 inhibition decreases anxiety via endocannabinoid activation. *Nature Neurosci.* **16**, 1291–1298 (2013)