

## IN BRIEF

**COMPUTATIONAL CHEMISTRY****Targeting microRNA with small molecules**

Oligonucleotides have traditionally been used to target RNA, but they are hampered by poor cellular delivery. This paper reported a computational strategy, based on the structure of microRNA, for rationally identifying small molecules that target specific microRNA sequences. One compound that was identified using the technique inhibited microRNA-96 production (with selectivity that was comparable to an oligonucleotide), upregulated levels of the target protein (forkhead box protein O1) and induced apoptosis in cancer cells. The authors note this shows that small molecules targeting RNA can be designed solely from sequence information.

**ORIGINAL RESEARCH PAPER** Velagapudi, S. P. *et al.* Sequence-based design of bioactive small molecules that target precursor microRNAs. *Nature Chem. Biol.* <http://dx.doi.org/10.1038/nchembio.1452> (2014)

**IMMUNE REGULATION****IL-35: a new player in B cell activity**

B cells have a key role in the regulation of immunity. Using gene expression studies of activated B cells, Shen *et al.* identified interleukin 35 (IL-35) as a new mediator of B cell-mediated immune regulation. Mice with B cells that did not express IL-35 were unable to recover from experimental autoimmune encephalomyelitis, and had improved resistance to infection with *Salmonella enterica*, which was mediated in part by an increased function of B cells as antigen-presenting cells. So IL-35 could be a putative new target for modulating immune function.

**ORIGINAL RESEARCH PAPER** Shen, P. *et al.* IL-35-producing B cells are critical regulators of immunity during autoimmune and infectious diseases. *Nature* <http://dx.doi.org/10.1038/nature12979> (2014)

**OBESITY AND DIABETES****Diabetic interactions broken up**

Inflammation that is mediated by immune cells can contribute to the pathogenesis of obesity and diabetes. This study showed that blocking the interaction between CD40, a receptor found on immune cells, and the signalling mediator TRAF6 (TNF receptor-associated factor 6) could be a new way to target insulin resistance. Treatment of diet-induced obese mice with a small-molecule inhibitor of the CD40–TRAF6 interaction improved insulin sensitivity, reduced inflammation in adipose tissue and decreased hepatosteatosis.

**ORIGINAL RESEARCH PAPER** Chatzigeorgiou A. *et al.* Blocking CD40–TRAF6 signaling is a therapeutic target in obesity-associated insulin resistance. *Proc. Natl Acad. Sci. USA* **111**, 2686–2691 (2014)

**NANOMEDICINE****Unsticking neutrophils**

Excess accumulation of neutrophils on vascular endothelial cells leads to inflammation. This study showed that drug-loaded albumin nanoparticles could reduce neutrophil accumulation in mice. Nanoparticles loaded with the spleen tyrosine kinase (SYK) inhibitor piceatannol, which blocks the  $\beta 2$  integrin signalling that maintains neutrophil adhesion, were internalized by neutrophils, causing their detachment from lung epithelium and release into the circulation. This could be a broad new approach for treating disorders that result from inappropriate neutrophil activity.

**ORIGINAL RESEARCH PAPER** Wang, Z. *et al.* Prevention of vascular inflammation by nanoparticle targeting of adherent neutrophils. *Nature Nanotech.* **9**, 204–210 (2014)