

IN BRIEF

ANTIBACTERIAL DRUGS

Type II fatty acid synthesis is not a suitable antibiotic target for Gram-positive pathogens

Brinster, S. *et al. Nature* **458**, 83–86 (2009)

This paper showed that the strategy for antibiotic development based on reportedly essential type II fatty acid synthesis (FASII) pathway targets is flawed. The authors found that Gram-positive pathogens — such as streptococci, pneumococci, enterococci and staphylococci — overcame drug-induced FASII pathway inhibition when supplied with exogenous fatty acids. Moreover, the FASII target enzymes were not required during *Streptococcus agalactiae* septicaemic infection *in vivo*. These findings question the use of FASII-based antimicrobials for treating sepsis caused by Gram-positive pathogens.

OBESITY AND DIABETES

Molecular therapy of obesity and diabetes by a physiological autoregulatory approach

Cao, L. *et al. Nature Med.* **15**, 447–454 (2009)

The authors of this study investigated the therapeutic efficacy of brain-derived neurotrophic factor (BDNF) — a key regulator of energy balance — delivered by gene transfer in mouse models of obesity and diabetes. They developed a molecular autoregulatory system that was responsive to BDNF-induced physiological changes so that, as body weight decreased and agouti-related protein expression was induced, BDNF microRNA expression was activated, inhibiting transgene expression. In contrast to the progressive weight loss that is associated with a non-regulated gene transfer approach, this method led to a sustainable plateau of body weight following weight loss.

VACCINE DESIGN

Instant immunity through chemically programmable vaccination and covalent self-assembly

Popkov, M. T. *et al. Proc. Natl Acad. Sci. USA* **106**, 4378–4383 (2009)

Popkov and colleagues used reactive immunization to create a reservoir of covalent polyclonal antibodies in mice. Following administration of designed integrin $\alpha\beta3$ and $\alpha\beta5$ adapter ligands, polyclonal antibodies self-assembled with these ligands and the animals mounted an instant, chemically programmed, polyclonal response against syngeneic tumours. There was a decrease in tumour growth, showing that elements of active and passive immunization can be combined to create an effective chemistry-driven approach to vaccine design.

STEM CELLS

A small molecule that directs differentiation of human ESCs into the pancreatic lineage

Chen, S. *et al. Nature Chem. Biol.* **5**, 258–265 (2009)

Differentiation of human embryonic stem cells (hESCs) is currently achieved by co-culturing the cells with other cell types and/or growth factors. As an alternative approach, Chen and colleagues developed a high-content screen to identify small molecules that increased the number of pancreatic progenitor cells derived from hESCs. One compound, (–)-indolactam V, worked by inducing pancreatic progenitors from definitive endoderm and activating protein kinase C. Moreover, indolactam-treated cells were able to form mature pancreatic cells.

