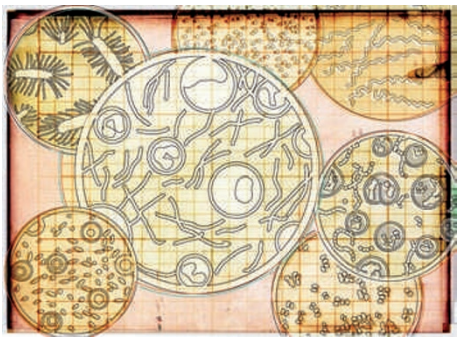
IN BRIEF



ANTIBACTERIAL DRUGS

Endogenous nitric oxide protects bacteria against a wide spectrum of antibiotics

Gusarov, I. *et al. Science* **325**, 1380–1384 (2009)

The physiological role of bacterial nitric oxide synthases (bNOS) is largely unknown. Gusarov and colleagues showed that nitric oxide generated by bNOS is used as a defence system against other antibiotic-producing microorganisms in the same habitat. bNOS expression increased the resistance of bacteria to a broad range of antibiotics, which was achieved by the chemical modification of toxic compounds and the alleviation of the oxidative stress imposed by antibiotics. So, bNOS inhibition might increase the effectiveness of antimicrobial therapy.

OBESITY AND DIABETES

The protein kinase IKKε regulates energy balance in obese mice

Chiang, S.-H. *et al. Cell* **138**, 961–975 (2009)

These studies showed that a high-fat diet increased nuclear factor κB activation in mice, which led to a sustained increase in the levels of IκB kinase ε (IKKε) in the liver, adipocytes and adipose tissue macrophages. IKKε-knockout mice were protected from obesity caused by a high-fat diet, chronic inflammation and insulin resistance, and showed increased energy expenditure and maintained insulin sensitivity in the liver and fat without activation of the proinflammatory Jun N-terminal kinase pathway. IKKε could therefore be a therapeutic target for obesity, insulin resistance and diabetes.

MEMORY

Selective activation of the M1 muscarinic acetylcholine receptor achieved by allosteric potentiation

Ma, L. *et al. Proc. Natl Acad. Sci. USA* **106**, 15950–15955 (2009)

Selective activation of muscarinic acetylcholine receptors (mAChRs) that are involved in memory — such as the M1 mAChR — could improve cognitive function in Alzheimer's disease. This paper describes benzyl quinolone carboxylic acid (BQCA), a selective allosteric potentiator of the M1 mAChR that reduced the concentration of acetylcholine required to activate the receptor by more than 100-fold. BQCA reversed memory deficits in a mouse model of contextual fear conditioning and increased wakefulness.

LYSOSOMAL STORAGE DISEASE

Molecular signatures of disease brain endothelia provide new sites for CNS-directed enzyme therapy

Chen, Y. H. *et al. Nature Med.* **15**, 1215–1218 (2009)

The vasculature of the CNS could provide a system to deliver secreted proteins, but inducing the secretion of a specific protein is problematic. Chen and colleagues screened a phage library to identify peptides that bound the vascular endothelia in diseased and normal mice. Different epitopes were identified in two models of lysosomal storage disease, suggesting there is a unique vascular signature in the disease state. Peripheral injection of epitope-modified adeno-associated viruses expressing the enzymes that were absent in mice with lysosomal storage disease reconstituted enzyme activity throughout the brain and improved disease phenotypes.