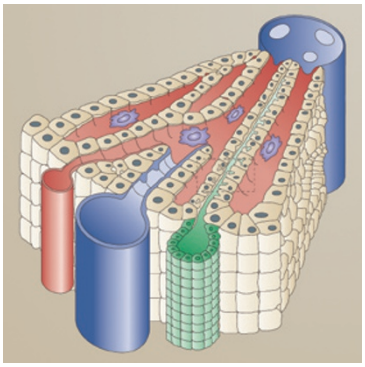
IN BRIEF

LIVER DISORDERS

Resolution of liver cirrhosis using vitamin A-coupled liposomes to deliver siRNA against a collagen-specific chaperone.

Sato, Y. *et al. Nature Biotech.* **26**, 431–442 (2008)

There are currently no approved antifibrotic therapies for liver cirrhosis. Using three animal models of liver cirrhosis, Sato and colleagues showed that injection of vitamin A-coupled liposomes carrying small interfering RNA against mRNA encoding rat gp46 — a homologue of the collagen-specific chaperone HSP47 — rapidly resolved liver fibrosis and prolonged survival in rats. The efficacy and specificity of this approach in acute and chronic models of liver fibrosis suggest its therapeutic potential for reversing human liver cirrhosis.



PULMONARY DISORDERS

Ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis.

Teichgräber V. *et al. Nature Med.* **14**, 382–391 (2008)

Microbial lung infections are a major cause of morbidity in patients with cystic fibrosis. Teichgräber and colleagues showed that deficiency of *Cftr* in mice resulted in the accumulation of cellular ceramide in the respiratory tract, caused by the alkalinization of *Cftr*-deficient vesicles in respiratory cells. Accumulation of ceramide was also detected in respiratory epithelial cells and airways of subjects with cystic fibrosis. Normalization of pulmonary ceramide — such as with amitriptyline — prevented chronic pulmonary inflammation, impairment of mucociliary clearance and high susceptibility to severe infections.

VACCINES

Single-round infectious particles enhance immunogenicity of a DNA vaccine against West Nile virus.

Chang, D. *et al. Nature Biotech.* 20 April 2008 (doi:10.1038/nbt1400)

There are currently no commercial human vaccines for medically important flaviviruses such as West Nile and dengue viruses. Chang and colleagues illustrated proof of concept in a flavivirus DNA vaccine design that combined the advantage of replicon-based DNA technology, the ability to generate pseudoinfectious virus particles and the immunogenicity of capsid-deleted flavivirus RNAs. The vaccine protected mice after West Nile virus infection, and elicited virus-neutralizing antibodies in horses.

ANTICANCER DRUGS

SGX393 inhibits the CML mutant Bcr–Abl^{T315I} and preempts *in vitro* resistance when combined with nilotinib or dasatinib.

O'Hare, T. *et al. Proc. Natl Acad. Sci. USA* **105**, 5507–5512 (2008)

T315I mutations in the oncogenic tyrosine kinase Bcr–Abl leads to chronic myeloid leukaemia (CML) that is resistant to all ABL kinase inhibitors — imatinib, nilotinib and dasatinib — that are in clinical use. O'Hare and colleagues identified an inhibitor, SGX393, that blocked the growth of leukaemia cell lines, primary haematopoietic cells and *in vivo* xenografts that expressed Bcr–Abl^{T315I}. Combining SGX393 with nilotinib or dasatinib pre-empted the emergence of resistant subclones, including Bcr–Abl^{T315I}, suggesting that this strategy may be useful for reduction of Bcr–Abl mutants in CML.