IN BRIEF

VIRAL DISEASES

Discovery of a hepatitis C target and its pharmacological inhibitors by microfluidic affinity analysis.

Einav, S. *et al. Nature Biotech.* **26**, 1019–1027 (2008)

More effective therapies are urgently needed against hepatitis C virus (HCV). This paper showed that HCV binds RNA of NS4B — a transmembrane protein that has an essential role in HCV RNA replication — and this binding is specific for the 3′ terminus of the negative strand of the viral genome. A high-throughput microfluidic screen identified 18 compounds that inhibited binding of RNA by NS4B. One compound, clemizole hydrochloride, inhibited HCV RNA replication in cell culture with little toxicity for the host cell, and represents a candidate for further optimization.

CANCER

Glycogen synthase kinase 3 in *MLL* leukaemia maintenance and targeted therapy.

Wang, Z. *et al. Nature* 17 Sep 2008 (doi:10.1038/nature07284)

Glycogen synthase kinase 3 (GSK3) inhibition has attracted interest as a therapeutic strategy but there has been some concern that GSK3 inhibitors might be oncogenic. This paper demonstrates an unexpected oncogenic requirement for GSK3 in the maintenance of a human leukaemia that has poor prognosis (defined by mutations in *MLL*). GSK3 paradoxically supported *MLL* leukaemia cell proliferation and transformation by a mechanism involving destabilization of the cyclin-dependent kinase inhibitor $p27^{Kip1}$. In a mouse model of *MLL* leukaemia, inhibition of GSK3 prolonged survival, highlighting the potential of GSK3 as a cancer drug target.

DIABETES

Selective death of autoreactive T cells in human diabetes by TNF or TNF receptor 2 agonism.

Ban, L. *et al. Proc. Natl Acad. Sci. USA* **105**, 13644–13649 (2008)

Destroying the rare autoreactive T lymphocytes that cause autoimmune diseases could offer benefits over current non-specific treatments. Using blood from patients with type 1 diabetes, Ban and colleagues showed that a subpopulation of CD8 T cells were susceptible to tumour-necrosis factor (TNF) or TNF agonist-induced death. This subpopulation was traced specifically to autoreactive T cells to insulin — a known autoantigen. This study shows that autoreactive T cells can be selectively destroyed and suggests that TNF or a TNF receptor 2 agonist may offer targeted therapies for diabetes.

ANTICANCER DRUGS

Therapeutic effect against human xenograft tumors in nude mice by the third generation microtubule stabilizing epothilones.

Chou, T.- C. *et al. Proc. Natl Acad. Sci. USA* **105**, 13157–13162 (2008)

Epothilones — natural products isolated from a myxobacterium — are a promising class of antitumour compounds. Chou and colleagues describe biological studies using iso-fludelone, an epothilone with drug-like properties produced through total synthesis. In mice, iso-fludelone achieved therapeutic cures against mammarian, ovarian and neuroblastoma xenografts. A strong therapeutic effect was observed against drug-resistant lung and mammary xenografts, and in an intracranially implanted brain tumour model.