

IN BRIEF

ANTICANCER DRUGS

Androgen receptor promotes hepatitis B virus-induced hepatocarcinogenesis through modulation of hepatitis B virus RNA transcription

Wu, M.-H. *et al. Sci. Transl. Med.* **2**, 32ra35 (2010)

Hepatitis B virus (HBV)-mediated hepatocellular carcinoma (HCC) is associated with increased serum androgen levels. Wu and colleagues showed that the androgen receptor increases HBV viral titres by enhancing HBV RNA transcription by direct binding of the receptor to the androgen response element near the core promoter of the virus. A compound that degraded androgen receptors suppressed HCC tumour size in mouse models, demonstrating that targeting the androgen receptor — rather than the androgen — could be a new strategy in treating HBV-induced HCC.

HIV

Rational design of small-molecule inhibitors of the LEDGF/p75-integrase interaction and HIV replication

Christ, F. *et al. Nature Chem. Biol.* **6**, 442–448 (2010)

Christ and colleagues rationally designed a series of 2-(quinolin-3-yl)acetic acid derivatives that potently inhibited the interaction between HIV-1 integrase and lens epithelium-derived growth factor (LEDGF/p75). The compounds inhibited HIV-1 replication and showed no cross-resistance with two clinical integrase inhibitors. The discovery of these novel allosteric HIV-1 integrase inhibitors highlights the feasibility of inhibiting the protein–protein interaction between a viral protein and a cellular host factor.

CANCER

A genome-wide RNA interference screen reveals an essential CREB3L2–ATF5–MCL1 survival pathway in malignant glioma with therapeutic implications

Sheng, Z. *et al. Nature Med.* **16**, 671–677 (2010)

This study identified a new cell survival pathway in malignant glioma that could represent a new therapeutic target. Activation of a Ras–mitogen-activated protein kinase or phosphoinositide 3-kinase signalling cascade leads to induction of the transcription factor CREB3L2, which directly activates activating transcription factor 5 (ATF5) expression. ATF5 then promotes cell survival by stimulating transcription of myeloid cell leukaemia sequence 1. Expression of ATF5 inversely correlated with disease prognosis, and the RAF kinase inhibitor sorafenib inhibited glioma growth in mouse models.

ANTIVIRAL DRUGS

Rapid emergence of protease inhibitor resistance in hepatitis C virus

Rong, L. *et al. Sci. Transl. Med.* **2**, 30ra32 (2010)

Drug-resistant hepatitis C virus (HCV) variants were discovered to rapidly emerge in clinical trials of telaprevir, a HCV protease inhibitor. This study analysed published clinical data to calculate the generation rates of HCV variants and showed that all possible single-mutant and double-mutant viruses exist before treatment. Furthermore, one additional mutation is expected to arise during therapy. The authors also generated a model to predict the best use of combination therapies of direct antivirals to inform future treatment paradigms.

