IN BRIEF

ANTIVIRAL DRUGS

Therapeutic silencing of microRNA-122 in primates with chronic hepatitis C virus infection

Lanford, E. R. *et al. Science* **327**, 198–201 (2010)

This study investigated the potential of microRNA-122 (miR-122), a microRNA that is expressed in the liver and binds the hepatitis C virus (HCV) genome, as an antiviral target. Treatment of chimpanzees that were chronically infected with HCV with a locked nucleic acid–modified oligonucleotide complementary to miR-122 led to long-lasting suppression of HCV viraemia without the development of viral resistance to the therapy. Livers from treated chimpanzees showed normalization of the interferon pathway and improvement of HCV-induced pathology. So, targeting miR-122 could offer advantages over current HCV therapy.

ANTICANCER DRUGS

Tissue-penetrating delivery of compounds and nanoparticles into tumors

Sugahara, K. N. *et al. Cancer Cell* **16**, 510–520, (2009)

The poor penetration of drugs into tumours is an obstacle in cancer treatment. Sugahara and colleagues describe a method that enables compounds to be delivered into the tumour parenchyma. Conjugation of compounds to a peptide (termed iRGD) that contained the RGD integrin recognition motif and a consensus motif that mediates tissue penetration enabled injected compounds to spread into the extravascular tumour parenchyma. Furthermore, conjugating the peptide to albumin-embedded paclitaxel nanoparticles resulted in enhanced antitumour activity.

PROTEIN–PROTEIN INTERACTIONS

Identification of a small-molecule inhibitor of the PICK1 PDZ domain that inhibits hippocampal LTP and LTD

Thorsen, T. S. *et al. Proc. Natl Acad. Sci. USA* 14 Dec 2009 (doi: 10.1073/pnas.0902225107)

This paper describes a small-molecule inhibitor (known as FSC231) of the PDZ domain in protein interacting with C kinase 1 (PICK1). In cell-cultured hippocampal neurons, FSC231 inhibited the interaction between the AMPA receptor GluR2 subunit and PICK1; accelerated GluR2 recycling following *N*-methyl-D-aspartate receptor-induced internalization; and blocked long-term depression and long-term potentiation. So, FSC231 might serve as a lead compound for therapeutics targeting the PDZ domain in PICK1.

ANTICANCER DRUGS

Novel mutant-selective EGFR kinase inhibitors against EGFR T790M

Zhou, W. *et al. Nature* **462**, 1070–1074 (2009)

The efficacy of current epidermal growth factor receptor (EGFR) kinase inhibitors — all of which contain a quinazoline-based core scaffold — is limited by the development of drug resistance. By screening a kinase inhibitor library against EGFRs that expressed T790M, a mutation that is present in 50% of patients demonstrating drug resistance, Zhou and colleagues identified a new class of pyrimidine EGFR inhibitors. *In vitro*, these compounds were more potent against EGFR T790M than quinazoline-based EGFR inhibitors, and, *in vivo*, a compound caused tumour regression in a model of lung cancer.