

## IN BRIEF

**ANTICANCER DRUGS**

Inhibition of lung tumor growth by complex pulmonary delivery of drugs with oligonucleotides as suppressors of cellular resistance

Garbuzenko, O. B. *et al. Proc. Natl Acad. Sci. USA* **107**, 10737–10742 (2010)

Development of resistance, low drug accumulation and severe side effects are obstacles in the chemotherapy of lung cancer. To overcome these difficulties, Garbuzenko and colleagues used an inhaled nanoscale local delivery system containing the anticancer drug doxorubicin and antisense oligonucleotides targeted to *MRP1* mRNA and *BCL2* mRNA as suppressors of pump and non-pump cellular resistance, respectively. In an orthotopic murine model of human lung carcinoma this showed high antitumour activity and low adverse effects.

**ANTIVIRAL DRUGS**

Identification of influenza A nucleoprotein as an antiviral target

Kao, R. Y. *et al. Nature Biotech.* **28**, 600–605 (2010)

Kao and colleagues used forward chemical genetics to identify nucleoprotein as a novel druggable target in the influenza A virus. Furthermore, they found a small-molecule compound — termed nucleozin — that triggered the aggregation of nucleoprotein and inhibited its nuclear accumulation. Nucleozin impeded influenza A virus replication *in vitro* and protected mice that were challenged with lethal doses of the H5N1 strain of avian influenza A, suggesting that viral nucleoprotein is a target for the development of small-molecule therapies.

**CARDIOVASCULAR BIOLOGY**

GSK-3 $\alpha$  directly regulates  $\beta$ -adrenergic signaling and the response of the heart to hemodynamic stress in mice

Zhou, J. *et al. J. Clin. Invest.* 1 Jun 2010 (doi:10.1172/JCI41407)

This paper describes glycogen synthase kinase 3 $\alpha$  (GSK3 $\alpha$ ) as a key regulator of cardiac function. Mice lacking GSK3 $\alpha$  developed cardiac hypertrophy and contractile dysfunction, and surprisingly, displayed impaired responses to  $\beta$ -adrenergic stimulation. This phenotype was reproduced by acute treatment of wild-type cardiomyocytes with a small-molecule GSK3 inhibitor. As  $\beta$ -adrenergic responsiveness is essential in the hearts adaption to stress, these findings raise concerns over the development of compounds that target GSK3.

