# IN BRIEF

## DRUG DELIVERY

### Improving drug potency and efficacy by nanocarrier-mediated subcellular targeting

Murakami, M. *et al. Sci. Transl. Med.* **3**, 64ra2 (2011)

Drugs linked to nanocarriers selectively accumulate in tumours. This paper investigated, in human cancer cells, the real-time subcellular fate of polymeric micelles that incorporated an analogue of the anticancer drug oxaliplatin. Compared with free oxaliplatin, the drug selectively dissociated within late endosomes, enhancing delivery to the nearby nucleus. Nanocarrier-associated drug exhibited higher antitumour activity in mice than oxaliplatin alone, even against oxaliplatin-resistant tumours, suggesting that nanocarriers that target subcellular compartments could have clinical benefit.

## NEURODEGENERATIVE DISEASE

### Caspase-3 triggers early synaptic dysfunction in a mouse model of Alzheimer's disease

D'Amelio, M. *et al. Nature Neurosci.* **14**, 69–76 (2011)

Although cognitive decline in Alzheimer's disease is correlated with synaptic loss, the molecular mechanisms underlying synaptic failure are unknown. This study identified a new caspase 3-dependent mechanism that drives synaptic failure and contributes to cognitive dysfunction in Alzheimer's disease. In mouse models of the disorder, hippocampal injection of a caspase 3 inhibitor restored postsynaptic density composition, glutamatergic synaptic transmission and size of dendritic spines, and partially rescued memory defects.

## BLOOD DISORDERS

### Detrimental effects of adenosine signaling in sickle cell disease

Zhang, Y. *et al. Nature Med.* **17**, 79–86 (2011)

This study showed that increased adenosine signalling through the adenosine 2B receptor (A2BR) has a pathological role in sickle cell disease (SCD). Using a transgenic mouse model of SCD and human erythrocytes, it was shown that increased activation of A2BR promotes sickling by inducing production of 2,3-diphosphoglycerate, which decreases the oxygen binding affinity of haemoglobin. Administration of an A2BR antagonist in mice reversed symptoms of SCD, suggesting that modulation of adenosine signalling could be beneficial in preventing sickling in individuals with SCD.

## MUSCULAR DISORDERS

### Biglycan recruits utrophin to the sarcolemma and counters dystrophic pathology in mdx mice

Amenta, A. R. *et al. Proc. Natl Acad. Sci. USA* **108**, 762–767 (2011)

The dystrophin homologue utrophin is a potential target for Duchenne muscular dystrophy (DMD) therapy. Amenta and colleagues showed that the extracellular matrix protein biglycan regulates utrophin expression in immature muscle. In a mouse model of DMD, systemically delivered recombinant human biglycan localized to muscle, where it upregulated utrophin at the sarcolemma, reduced muscle pathology, improved muscle function and was well tolerated in animals dosed for up to 3 months. These results suggest that recombinant human biglycan could be a therapy for DMD.