

## IN BRIEF

## NEUROBLASTOMA

### The right type of ALK

The anaplastic lymphoma kinase (ALK) was recently found to be mutated in neuroblastoma. Scott Bresler and colleagues used ALK-expressing neuroblastoma cell lines and xenografts to assess the efficacy of the ALK and MET tyrosine kinase inhibitor crizotinib. They found that neuroblastoma cell lines that had either amplified wild-type ALK or the ALK mutant R1275Q were sensitive to crizotinib. However, neuroblastoma cell lines with F1174L ALK mutations were relatively resistant to this drug, owing to the increased ATP-binding affinity of this mutant. The authors propose that patients with neuroblastomas that have the F1174L mutation might still respond to either high doses of crizotinib or to ALK inhibitors that have an increased binding affinity compared with crizotinib.

**ORIGINAL RESEARCH PAPER** Bresler, S. *et al.* Differential inhibitor sensitivity of anaplastic lymphoma kinase variants found in neuroblastoma. *Sci. Trans. Med.* **3**, 108ra114 (2011)

## NANOTECHNOLOGY

### Size matters

Although multiwalled carbon nanotubes show promise for delivering cancer therapy, there have been concerns raised over the potential of these nanotubes to cause cancer owing to their similarity in structure to asbestos. New research by Nagai *et al.* indicates that thin (approximately 50 nm in diameter) multiwalled carbon nanotubes with a crystalline-like structure can pierce the membrane of mesothelial cells and can lead to inflammation and the generation of mesotheliomas *in vivo*. Thick-walled (approximately 150 nm) or tangled (2–20 nm) multiwalled carbon nanotubes caused less damage and were less carcinogenic. Thus, controlling the diameter of multiwalled carbon nanotubes might reduce potential carcinogenic risk in humans.

**ORIGINAL RESEARCH PAPER** Nagai, H. *et al.* Diameter and rigidity of multiwalled carbon nanotubes are critical factors in mesothelial injury and carcinogenesis. *Proc. Natl Acad. Sci.* 14 Nov 2011 (doi:10.1073/pnas.1110013108)

## BREAST CANCER

### NOTCH and MAST are rearranged, but rarely

Dan Robinson and colleagues used pair-end transcriptome sequencing to examine gene fusions in breast cancer cell lines and tumours. Among the expressed gene fusions they found five microtubule-associated serine-threonine (MAST) kinase fusions and eight NOTCH fusions. Expression of the MAST gene fusions in benign breast epithelial cells increased proliferation, and small interfering RNAs targeted against MAST2 in cell lines expressing a *ARID1A*–*MAST2* fusion gene reduced growth and viability *in vitro*. Similar experiments overexpressing NOTCH1 and NOTCH2 fusion proteins in benign breast epithelial cells resulted in altered growth characteristics, such as anchorage independence. In addition, the inhibition of NOTCH signalling reduced the growth of NOTCH gene fusion-expressing breast cancer xenografts. These findings indicate that transcriptome analyses could identify patients with breast cancer who harbour rare gene fusions that are therapeutically relevant.

**ORIGINAL RESEARCH PAPER** Robinson, D. R. *et al.* Functionally recurrent rearrangements of the MAST kinase and Notch gene families in breast cancer. *Nature Med.* **17**, 1646–1651 (2011)