IN BRIEF

THERAPY

Small but loaded

Inhibition of epidermal growth factor receptor (EGFR) with erlotinib results in alterations to apoptotic signalling pathways that create a therapeutic window of sensitivity to doxorubicin. However, it is difficult to deliver these drugs sequentially and achieve therapeutic efficacy; so, Morton, Lee *et al*. developed a nanoparticle that was able to release both drugs sequentially. They incorporated erlotinib in the hydrophobic compartments of liposomes and doxorubicin in the hydrophilic compartments, which allowed erlotinib release followed by doxorubicin release. They also coated the liposome in folate to help to target it to cancer cells. These particles improved the induction of tumour cell killing and tumour shrinkage compared with sequential administration of the two drugs.

ORIGINAL RESEARCH PAPER Morton, S. W. *et al*. A nanoparticle-based combination chemotherapy delivery system for enhanced tumor killing by dynamic rewiring of signaling pathways. *Sci. Signal.* **7**, ra44 (2014)

SIGNALLING

Isoform-specific survival

PTEN loss, which frequently occurs in cancer, leads to PI3K–AKT activation. Chin *et al*. show that AKT2, and not AKT1, is the main driver of improved cell survival that is associated with PTEN loss. AKT2 knockdown caused the regression of prostate cancer xenograft tumours, whereas AKT1 knockdown did not. AKT2 was also required for cell survival in other solid tumours with PTEN loss, indicating that targeting AKT2 may be a promising anticancer strategy.

ORIGINAL RESEARCH PAPER Chin, Y. M. R. *et al*. Pten-deficient tumors depend on akt2 for maintenance and survival. *Cancer Discov.* http://dx.doi.org/10.1158/2159-8290.CD-13-0873 (2014)

REGENERATIVE MEDICINE

Cause for concern?

Regenerative medicine is fraught with safety concerns about whether using, for example, induced pluripotent stem cell (iPSC)-derived material poses a risk of developing cancer from that material. To investigate these safety concerns, Hong, Winkler *et al*. developed a non-human primate model. They used autologous iPSCs and showed that undifferentiated iPSCs formed teratomas *in vivo*, which activated an inflammatory immune response. However, when the iPSCs were first differentiated into mesodermal stromal-like cells, they formed new bone *in vivo*, without any evidence of teratoma formation, suggesting that differentiated iPSCs may be safe to use *in vivo*.

ORIGINAL RESEARCH PAPER Hong, S. G. *et al*. Path to the clinic: assessment of iPSC-based cell therapies in vivo in a nonhuman primate model. *Cell Rep.* **7**, 1298–1309 (2014)

TUMORIGENESIS

Splitting the jaw

Sweeney, McClary, Myers, Biscocho *et al*. undertook genomic analyses of samples of locally destructive odontogenic tumours of the jaw. Curiously, they found that smoothened (*SMO*) was frequently mutated in tumours of the upper jaw (maxilla), whereas tumours of the lower jaw (mandible) frequently had mutations in *BRAF*. The SMO-L412F mutation is activating and was sensitive to arsenic trioxide (which inhibits the hedgehog pathway), and the BRAF-V600E mutation in mandible tumours was sensitive to vemurafenib.

ORIGINAL RESEARCH PAPER Sweeney, R. T. *et al*. Identification of recurrent *SMO* and *BRAF* mutations in ameloblastomas. *Nature Genet.* http://dx.doi.org/10.1038/ng.2986 (2014)