

IN BRIEF

 THERAPEUTICS
Mosaic glioblastoma

Snuderl *et al.* analysed receptor tyrosine kinase (RTK) mutations in glioblastoma and found that around 5% of samples had co-amplification of RTKs, including epidermal growth factor receptor (EGFR), MET and platelet-derived growth factor receptor- α . In several samples these amplifications were not evident in all the tumour cells. Instead, the amplification of specific RTKs identified subclones within the tumour. Further analyses indicated that the subclones have other genetic mutations in common and are, therefore, likely to have arisen from a common precursor. The clinical implications of these findings have not yet been determined.

ORIGINAL RESEARCH PAPER Snuderl, M. *et al.* Mosaic amplification of multiple receptor tyrosine kinase genes in glioblastoma. *Cancer Cell* **20**, 810–817 (2011)

 SIGNALLING
Wild type and mutant combine

This study by Walter Kolch and colleagues indicates that mutant KRAS leads to the stabilization of p53 through the MST2–LATS1 kinase pathway, which results in apoptosis. This is counteracted through mutant KRAS activation of the epidermal growth factor receptor and the remaining wild-type KRAS allele, which inhibits the MST2 pathway through the activation of AKT. Consistently, there is a negative correlation in mouse and human colorectal tumours between mutant KRAS expression and MST2 expression, and tumours that express both have increased levels of apoptosis.

ORIGINAL RESEARCH PAPER Matallanas, D. *et al.* Mutant KRAS activation of the proapoptotic MST2 pathway is antagonized by wild-type KRAS. *Mol. Cell* **44**, 893–906 (2011)

 METASTASIS
A new protector?

Pigment epithelium-derived factor (PEDF) is a cytokine that is expressed in human primary breast cancers but not in breast cancer brain metastases. Patricia Steeg and colleagues now show that human and mouse breast cancer cells expressing PEDF cannot establish large brain metastases. In addition, the neurons that surrounded the PEDF-expressing metastases that did form were less likely to die as a result of the damage induced by the growing metastases. Therefore, PEDF seems to both limit breast cancer cell growth and be neuroprotective.

ORIGINAL RESEARCH PAPER Fitzgerald, D. P. *et al.* Opposing effects of pigment epithelium-derived factor on breast cancer cell versus neuronal survival: implication for brain metastasis and metastasis-induced brain damage. *Cancer Res.* **72**, 144–153 (2012)

 METASTASIS
Building a niche

The colonization of new soil by metastatic seeds is a complex process, and a recent paper indicates that the education of stromal cells at a secondary site is important. Malanchi *et al.* show that the extracellular matrix component periostin (POSTN) is expressed by fibroblasts in the stroma of primary breast cancers. POSTN recruits WNT ligands and thereby increases WNT signalling in cancer stem cells. This expression of POSTN is required to allow cancer stem cell maintenance and to establish growth at a secondary site. Moreover, the development of metastases in the lung is reduced in *Postn*-null mice. Therefore, these authors conclude that cancer stem cells that successfully produce colonies at secondary sites do so by inducing stromal POSTN expression.

ORIGINAL RESEARCH PAPER Malanchi, I. *et al.* Interactions between cancer stem cells and their niche govern metastatic colonization. *Nature* **481**, 85–91 (2012)