IN BRIEF

SIGNALLING

Death-associated protein kinase 1 phosphorylates Pin1 and inhibits its prolyl isomerase activity and cellular function

Lee, T. H. *et al. Mol. Cell* **42**, 147–159 (2011)

Peptidyl-prolyl *cis-trans* isomerase NIMA-interacting 1 (PIN1) is frequently deregulated in cancer but how PIN1 is regulated is unclear. Lee and colleagues showed that the tumour suppressor death-associated protein kinase 1 (DAPK1) phosphorylates PIN1, which inactivates its catalytic activity. Moreover, they found that PIN1-mediated centrosome amplification and transformation was prevented when DAPK1 was expressed and that PIN1 phosphorylation correlated with DAPK1 expression and lack of centrosome amplification in human breast cancer.

ONCOGENES

c-Raf, but not B-Raf, is essential for development of K-Ras oncogene-driven non-small cell lung carcinoma

Blasco, R. B. *et al. Cancer Cell* **19**, 1–12 (2011)

Barbacid and colleagues used a mouse model of $KRAS^{G12D}$-driven non-small-cell lung carcinoma (NSCLC), combined with gene knockouts, to identify which of the downstream components of KRAS signalling is required for tumorigenesis. The authors found that CRAF, but not BRAF, was required for $KRAS^{G12D}$-driven NSCLC. In addition, loss of either ERK1 or ERK2 was insufficient to block tumorigenesis, in contrast to the loss of both ERK isoforms, and the same was true for MEK1 and MEK2. CRAF may therefore be a useful therapeutic target in KRAS-driven NSCLC.

THERAPY

The ABL switch control inhibitor DCC-2036 is active against the chronic myeloid leukemia mutant BCR-ABL^{T315I} and exhibits a narrow resistance profile

Eide, C. A. *et al. Cancer Res.* **71**, 3189–3195 (2011)

Mutations in breakpoint cluster region (BCR)–ABL1, particularly BCR–ABL1-T315I, often cause resistance to ABL1 inhibitors such as imatinib and dasatinib and relapse of chronic myeloid leukaemia. Eide and colleagues evaluated the activity of the multi-targeted tyrosine kinase inhibitor DCC-2036 and found that it inhibited most kinase domain mutants, as well as BCR–ABL1-T315I. In addition, cell-based mutagenesis screens identified mutations in the P-loop of ABL1 that could cause resistance to DCC-2036 and other ABL1 inhibitors.

HYPOXIA

Akt2 regulates all Akt isoforms and promotes resistance to hypoxia through induction of miR-21 upon oxygen deprivation

Polytarchou, C. *et al. Cancer Res.* 9 May 2011 (doi:10.1158/0008-5472.CAN-11-0365)

Tsichlis and colleagues expressed single AKT isoforms in AKT-triple-knockout lung fibroblasts and found that AKT2 was uniquely able to cause resistance to hypoxia. The microRNA miR-21, the transcription of which was facilitated by AKT2, was required for this resistance to hypoxia. Furthermore, miR-21 can downregulate PTEN expression, leading to activation of all three AKT isoforms, which hints at a master-regulator role for AKT2.