colleagues, who also generated mice that possess the *Trp53*^{R172H} structural mutation. The results from the two laboratories show that the same *Trp53* mutation causes different tumour spectra in different mouse strains; whereas Olive and co-workers found that *Trp53*$^{R172H/+}$ mice developed more carcinomas than *Trp53*$^{+/-}$ mice, the *Trp53*$^{R172H/+}$ mice generated by Lang *et al.* developed metastatic tumours.

Lang and colleagues also found that *Trp53*$^{R172H/R172H}$ and *Trp53*$^{R172H/+}$ mouse embryonic fibroblasts grow faster, have more DNA synthesis and have greater transformation potential than *Trp53*$^{+/+}$, *Trp53*$^{+/-}$ or *Trp53*$^{-/-}$ cells, again supporting the idea that mutant p53 proteins function differently to wild-type p53. So, how do missense mutant p53 proteins exert their oncogenic effects?

p53 interacts with its family members p63 and p73, which themselves activate several p53 target genes in response to DNA damage. Both groups found evidence that p53^{R172H} interacts with and inhibits endogenous p63 and p73 in cell lines that are derived from mouse tumours expressing this protein. Lang and colleagues also found that the disruption of p63 and p73 causes increased transformation of *Trp53*$^{-/-}$ cells and augments DNA synthesis to levels seen in *Trp53*$^{R172H/R172H}$ cells. The researchers conclude that the ability of mutant p53 to bind and inhibit p63 and p73 could explain why mutant p53 is more detrimental than the lack of p53, and why *TP53* missense mutations — rather than deletions of *TP53* — are so commonly found in human tumours.

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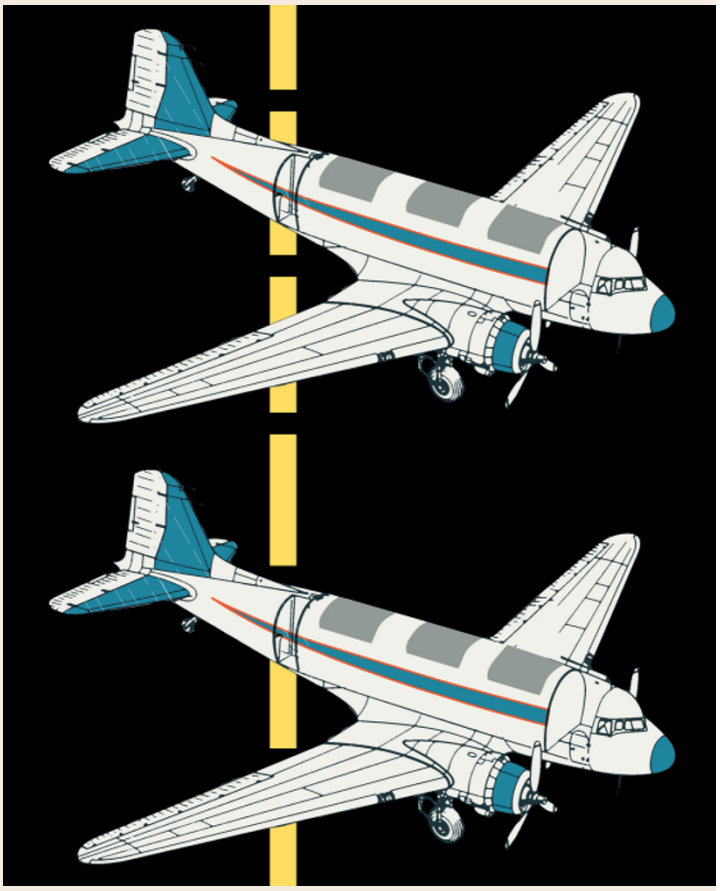
References and links

ORIGINAL RESEARCH PAPERS Lang, G. A. *et al.* Gain of function of a p53 hot spot mutation in a mouse model of Li–Fraumeni syndrome. *Cell* **119**, 861–872 (2004) | Olive, K. P. *et al.* Mutant *p53* gain of function in two mouse models of Li–Fraumeni syndrome. *Cell* **119**, 847–860 (2004)



IN BRIEF

EARLY DETECTION

Sensitive, non-invasive detection of lymph node metastases.

Harisinghani, M. G. & Weissleder, R. *PLoS Med.* **1**, 202–209 (2005)

Using a nanoparticle-enhanced lymphotropic magnetic resonance imaging (LMRI) technique, the authors compared the magnetic tissue parameters of normal lymph nodes with those of patients with metastases from a range of primary tumour types. They identified unique magnetic tissue parameters that could accurately distinguish metastasis-containing nodes from negative nodes, with a sensitivity of 98% and a specificity of 92%.

PROGNOSIS

Transcriptional activation of integrin β6 during the epithelial–mesenchymal transition defines a novel prognostic indicator of aggressive colon carcinoma.

Bates, R. C. *et al. J. Clin. Invest.* 20 Jan 2005 (doi:10.1172/JCI200523183)

Using a spheroid model of colon carcinoma to identify factors that mediate tumour progression, Bates *et al.* found that upregulation of the integrin-αvβ6 mediates epithelial–mesenchymal transition and tumour invasiveness. An analysis of almost 500 human colorectal carcinoma samples revealed that high expression levels of this receptor were associated with reduced patient survival, making it a useful marker for early-stage disease.

CANCER STEM CELLS

Sustained hedgehog signalling is required for basal cell carcinoma proliferation and survival: conditioned skin tumorigenesis recapitulates the hair growth cycle.

Hutchin, M. E. *et al. Genes Dev.* 29 Dec 2004 (doi:10.1101/gad.1258705)

Sustained Hedgehog (HH) signalling leads to the development and maintenance of basal-cell carcinoma (BCC) in the skin. These authors found that a small subset of tumour cells failed to die when HH signalling was inhibited. There cells remained as a non-proliferative population with the capacity to give rise to many epidermal cell lineages and to reform BCCs after reactivation of the HH pathway, indicating that they might be cancer stem cells.

EARLY DIAGNOSIS

Molecular and genetic analysis of disseminated neoplastic cells in lymphangioleiomyomatosis.

Crooks, D. M. *et al. Proc. Natl Acad. Sci. USA* **101**, 17462–17467 (2005)

Lymphangioleiomyomatosis (LAM) causes lung degeneration, renal angiomyolipomas and lymphatic abnormalities. LAM lesions involve the proliferation of smooth-muscle-like LAM cells, which vary in their appearance and are difficult to detect. These authors have developed a cheap and non-invasive way of detecting LAM cells. They show that loss of heterozygosity of the gene tuberous sclerosis complex 2 allows disseminated, potentially metastatic LAM cells to be identified in the body fluids of LAM patients.