IN BRIEF

LUNG CANCER

Tumour-propagating cells evade the immune system

Xu, Fillmore and colleagues generated genetically engineered mice in which *Stk11* (which encodes LKB1) and *Pten* are inducibly ablated through nasal administration of Cre recombinase. Following ablation, these mice develop lung squamous cell carcinomas (SCCs) that resemble human SCCs. Lung SCC tumour-propagating cells (TPCs), as well as the proposed TPCs in human lung SCCs, expressed high levels of PD-L1, indicating that these cells evade the immune system through immune checkpoint signalling.

ORIGINAL RESEARCH PAPER Xu, C. *et al.* Loss of *Lkb1* and *Pten* leads to lung squamous cell carcinoma with elevated PD-L1 expression. *Cancer Cell* **25**, 590–604 (2014)

TRANSLATION

Regulating *TP53* mRNA structure

Malbert-Colas, Ponnuswamy and colleagues found that MDMX (also known as MDM4) binds to nascent *TP53* mRNA on phosphorylation of MDMX by the DNA damage response kinase ataxia-telangiectasia mutated (ATM). This binding allows the correct folding of the internal ribosome entry sequence (IRES) in *TP53* mRNA, which in turn allows MDM2 binding and promotes *TP53* translation. MDM2 can prevent MDMX binding to *TP53* mRNA, whereas ATM-phosphorylated MDM2 promoted MDMX binding to *TP53* mRNA. Therefore, MDM2 and MDMX have non-redundant but synergistic effects on *TP53* mRNA translation that may be important in cancer.

ORIGINAL RESEARCH PAPER Malbert-Colas, L. *et al.* HDMX folds the nascent *p53* mRNA following activation by the ATM kinase. *Mol. Cell* **54**, 500–511 (2014)

IMMUNOTHERAPY

Cancer mutation-specific immune responses

Tran and colleagues showed that $CD4^+$ T helper 1 (T_H1) cells that recognized mutant ERBB2-interacting protein (ERBB2IP) were present in tumour-infiltrating lymphocytes (TILs) that were isolated from a patient with metastatic cholangiocarcinoma. The patient achieved regression and prolonged stabilization of disease when treated with these TILs — 25% of which were T_H1 cells that recognized mutant ERBB2IP. On disease progression, the patient again received adoptive cell transfer, but this time the ERBB2-mutant-specific T_H1 cells comprised >95% of the therapy. The tumour again exhibited regression, demonstrating that a $CD4^+$ T cell-directed immune response towards a cancer-associated mutation can be used therapeutically.

ORIGINAL RESEARCH PAPER Tran, E. *et al.* Cancer immunotherapy based on mutation-specific CD4+ T cells in a patient with epithelial cancer. *Science* **344**, 641–645 (2014)

TUMORIGENESIS

Understanding how the field effect arises

The field effect describes a region of epithelium with preneoplastic changes from which a tumour might arise; but how is the field effect induced? Alcolea and colleagues used lineage tracing to track oesophageal epithelial progenitor cells in which Notch signalling is abrogated. They found that mutant clones do not undergo differentiation and so they are not naturally lost from the epithelium. Instead, the mutant clones promote the differentiation of neighbouring wild-type cells, leading to expansion of the mutant clones.

ORIGINAL RESEARCH PAPER Alcolea, M. P. *et al.* Differentiation imbalance in single oesophageal progenitor cells causes clonal immortalization and field change. *Nature Cell Biol.* http://dx.doi.org/10.1038/ncb2963 (2014)