IN BRIEF

LYMPHOMA

A malaria mechanism

Endemic Burkitt lymphoma occurs at a high incidence in areas with high levels of infection with the parasite *Plasmodium falciparum*, which causes malaria. However, whether *Plasmodium* influences lymphomagenesis is not clear. Robbiani *et al.* used *Plasmodium chabaudi* infection to induce chronic malaria in mice and found that *P. chabaudi* induces expansion of germinal centres (GCs). GC B cells in *P. chabaudi*-infected mice expressed the mutator enzyme activation-induced cytidine deaminase (AID) and had increased DNA damage and chromosomal translocations. Mice lacking p53 in B cells develop lymphoma; *P. chabaudi* infection did not change the incidence of lymphoma in these mice but it favoured the development of AID-dependent mature B cell lymphomas that carried chromosomal translocations.

ORIGINAL RESEARCH PAPER Robbiani, D. F. *et al.* *Plasmodium* infection promotes genomic instability and AID-dependent B cell lymphoma. *Cell* **162**, 727–737 (2015)

ONCOGENES

Altered traffic flow

Using an RNA interference screen in HeLa cells, Wheeler *et al.* found that the small GTPase RAB35 is a regulator of PI3K signalling. Several RAB proteins, which are known to regulate endomembrane trafficking, were identified in the screen. Further study of RAB35 — which has been reported to be mutated in human cancers — confirmed that RAB35 loss in several cell lines suppressed phosphorylation of AKT, indicating that RAB35 is a positive regulator of PI3K signalling. Furthermore, activated RAB35 was sufficient to stimulate PI3K–AKT signalling and altered the localization of platelet-derived growth factor receptor-α (PDGFRα) to lysosomal-associated membrane protein 2 (LAMP2)-positive endomembranes. Analysis of two cancer-associated somatic mutations previously reported in RAB35 indicated that these constitutively activate PI3K–AKT signalling and transform cells. However, whether the tumour-associated RAB35 mutants also alter PDGFRα trafficking or have another mechanism of action is unknown.

ORIGINAL RESEARCH PAPER Wheeler, D. B. *et al.* Identification of an oncogenic RAB protein. *Science* http://dx.doi.org/10.1126/science.aaa4903 (2015)

CANCER STEM CELLS

Different in the details

Tumour-initiating cells (TICs) have been suggested to arise through the activation of normal stem cell programmes, including those driving epithelial-to-mesenchymal transition (EMT). Ye *et al.* report that although both mammary stem cells (MaSCs) and TICs undergo EMT, the underlying programmes induced in these cells are different. Previous studies have relied on xenograft models and ectopic expression of EMT transcription factors, such as the paralogues SNAIL and SLUG. In this study, the authors used genetically engineered mice expressing reporter constructs that mimic endogenous SNAIL or SLUG expression to show that while SLUG was highly expressed in MaSCs, SNAIL was induced in mammary tumour cells exhibiting mesenchymal traits. Several lines of evidence suggested that SNAIL expression was associated with a tumour-initiating phenotype, whereas SLUG expression was not. Furthermore, the transcription programmes controlled by SNAIL and SLUG in mammary tumour cells differed. This suggests that MaSCs and TICs might also use different signalling circuits to induce EMT.

ORIGINAL RESEARCH PAPER Ye, X. *et al.* Distinct EMT programs control normal mammary stem cells and tumour-initiating cells. *Nature* **525**, 256–260 (2015)