IN BRIEF

THERAPY

Targeting nucleotide synthesis in MYC-driven lymphoma

Using a mouse model of *Myc*-driven lymphomagenesis, Cunningham *et al*. observed that nucleotide metabolism is coupled to protein biosynthesis. As MYC hyperactivation results in increased levels of nucleotides through modulation of various metabolic pathways, the authors reasoned that MYC may regulate the orchestration of these two processes. They found that levels of phosphoribosyl pyrophosphate synthetase 2 (PRPS2) are specifically increased in *Myc*-driven lymphomagenesis and that this upregulation correlates with eukaryotic translation initiation factor 4E (eIF4E) expression, which is induced by MYC. PRPS2 is a rate-limiting enzyme in purine synthesis and its increased expression is coupled to MYC-dependent increases in nucleotide levels. The authors also showed that *Prps2* loss is synthetically lethal in *Myc*-transformed human and mouse cell lines, but its loss does not affect wild-type cells or mice. PRPS2 knockdown in *Myc*-driven lymphomas improved survival and induced complete tumour regression in 30% of mice. PRPS2 may therefore be an effective anticancer target.

RESEARCH PAPER Cunningham, J. T. *et al.* Protein and nucleotide biosynthesis are coupled by a single rate-limiting enzyme, PRPS2, to drive cancer. *Cell* **157**, 1088–1103 (2014)

TUMORIGENESIS

Mutation versus deletion

Familial retinoblastoma is caused by monoallelic germline inactivating mutations of *RB1*, such that retinoblastomas arise when both copies of *RB1* are inactivated (loss of heterozygosity). However, monoallelic large deletions or complete loss of *RB1* rarely results in retinoblastoma. Dehainault *et al*. identified a minimal genomic region that was associated with this reduced risk of retinoblastoma and found that the *RB1*-adjacent gene, mediator complex subunit 4 (*MED4*), is required for $RB1^{-/-}$ cells to survive. This suggests that germline monoallelic deletions that encompass *RB1* and *MED4* cannot survive loss of heterozygosity, which thus prevents retinoblastomagenesis.

ORIGINAL RESEARCH PAPER Dehainault, C. *et al.* The survival gene *MED4* explains low penetrance retinoblastoma in patients with large *RB1* deletion. *Hum. Mol. Genet.* http://dx.doi.org/10.1093/hmg/ddu245 (2014)

CANCER RISK

Sexually transmitted cancer risk?

Sexually transmitted infections of the parasite *Trichomonas vaginalis* in men can lead to colonization of *T. vaginalis* in the prostate, which correlates with risk of developing aggressive prostate cancer. Twu *et al*. found that *T. vaginalis* macrophage migration inhibitory factor (Tv-MIF), which is secreted by the parasite, has pro-inflammatory activity, like the human homologue. Tv-MIF also binds to the human MIF receptor, which resulted in activation of downstream signalling, including ERK and AKT phosphorylation. Furthermore, they showed that Tv-MIF increases the growth and invasion of prostate cancer cells and of benign prostate cells *in vitro*. This indicates that Tv-MIF from chronic *T. vaginalis* infections may drive prostate inflammation, which could lead to tumorigenesis.

ORIGINAL RESEARCH PAPER Twu, O. *et al. Trichomonas vaginalis* homolog of macrophage migration inhibitory factor induces prostate cell growth, invasiveness, and inflammatory responses. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1321884111 (2014)