Nature Reviews Cancer | Published online 23 Sep 2016

IN BRIEF

TUMOUR METABOLISM

Metabolic flexibility

Glutamine supports cancer cell growth, yet cancer cells can survive glutamine depletion. Reid *et al.* reveal a novel pathway exploited by tumours to adapt to glutamine starvation through the activation of inhibitor of nuclear factor-κB (NF-κB) kinase subunit-β (IKKβ). Independently of inducing NF-κB transcriptional activity, IKKβ directly phosphorylates and inhibits the glycolytic enzyme 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3 (PFKFB3), decreasing aerobic glycolysis under low glutamine conditions. The combined inhibition of glutamine metabolism and IKKβ synergistically reduced tumour growth *in vivo*, suggesting that to target this metabolic adaptation may be beneficial to cancer patients.

ORIGINAL ARTICLE Reid, M. A. *et al.* IKKβ promotes metabolic adaptation to glutamine deprivation via phosphorylation and inhibition of PFKFB3. *Genes Dev.* **30**, 1837–1851 (2016)

TUMOUR METABOLISM

Functions of fumarate

Sciacovelli *et al.* find that the higher levels of intracellular fumarate that result from loss of fumarate hydratase (*FH*), which causes hereditary leiomyomatosis and renal cell carcinoma (HLRCC), promotes epithelial-to-mesenchymal transition (EMT). Fumarate inhibits tet methylcytosine dioxygenase (TET) family enzymes, and the authors found that in *FH*-null cells and wild-type cells supplemented with fumarate, TET-mediated demethylation of the microRNA (miRNA) cluster *mir-200ba429* was inhibited, allowing expression of EMT transcription factors targeted by these miRNAs. Loss of *FH* was also associated with an EMT signature and poor outcomes in human HLRCC and papillary renal-cell carcinomas lacking *FH*.

ORIGINAL ARTICLE Sciacovelli, M. *et al.* Fumarate is an epigenetic modifier that elicits epithelial-to-mesenchymal transition. *Nature* http://dx.doi.org/10.1038/nature19353 (2016)

TUMOUR EVOLUTION

Evolving resistance in Tasmanian devils

Devil facial tumour disease (DFTD) is a transmissable cancer that affects Tasmanian devils and has substantially depleted their population, rasing concern that the species faces extinction. However, a new study offers some hope. Epstein *et al.* report that three populations of Tasmanian devil are exhibiting immune-modulated resistance to DFTD owing to modifications in certain genomic regions that may overcome immune suppression (which is how DFTD spreads between individuals). The selective pressure imposed by DFTD may therefore be encouraging its own undoing.

ORIGINAL ARTICLE Epstein, B. *et al.* Rapid evolutionary response to a transmissable cancer in Tasmanian devils. *Nat. Commun.* **7**, 12684 (2016)

GENETICS

Transcribing for the enemy

Clark *et al.* carried out genomic analyses of 775 meningiomas and found recurrent mutations in *POLR2A*, which encodes the catalytic subunit of RNA polymerase II, an essential enzyme that mediates the transcription of all protein-coding genes in eukaryotic cells. Mutant *POLR2A* allows tumours to hijack the transcriptional machinery and drive neoplasia. The authors found additional mutated genes that define distinctive meningioma subgroups with different clinical features.

ORIGINAL ARTICLE Clark V. E. *et al.* Recurrent somatic mutations in *POLR2A* define a distinct subset of meningiomas. *Nat. Genet.* http://dx.doi.org/10.1038/ng.3651 (2016)