IN BRIEF

CELL MIGRATION

How neutrophils set their compass

Sustained directionality is an essential component of successful chemotaxis. Here, the authors show that the G protein Gαi and the mammalian homologue of the *Drosophila melanogaster* polarity protein Inscuteable (known as MINSC) are important for the maintenance of polarity and directionality during neutrophil chemotaxis. They observed that Gαi (which is released from Gβγ following ligand binding) accumulates at the leading edge of the cell. Gαi interacts directly with AGS3 or LGN, which themselves are bound to MINSC, recruiting it to this part of the cell. Moreover, MINSC is bound to the polarity complex PAR3–PAR6–aPKC, and this interaction targets the complex to the leading edge, thus establishing polarity. Notably, MINSC-deficient neutrophils, or neutrophils in which aPKC was blocked, showed normal motility but lacked directionality in their chemotaxis.

ORIGINAL RESEARCH PAPER Kamakura, S. *et al.* The cell polarity protein mInsc regulates neutrophil chemotaxis via a noncanonical G protein signaling pathway. *Dev. Cell* http://dx.doi.org/10.1016/j.devcel.2013.06.008 (2013)

DNA DAMAGE

Facilitating repair

The repair of DNA double-strand breaks (DSBs) can be hindered by the inability of repair factors to access damage sites in the tightly packaged chromatin. This study identifies a key role for the deacetylase sirtuin 6 (SIRT6) in facilitating chromatin relaxation and promoting repair. Toiber *et al.* observed that SIRT6 is rapidly recruited to DSBs, with much faster kinetics than previously reported. SIRT6 was shown to target the chromatin remodelling factor SNF2H to these sites and accelerate its association with them, as well as to deacetylate histone 3 at Lys56 (H3K56), which was required for SNF2H-mediated chromatin relaxation. Importantly, depletion of SIRT6 blocked downstream damage signalling, and loss of SIRT6, SNF2H or both proteins abolished repair by homologous recombination or resulted in defective repair by non-homologous end-joining.

ORIGINAL RESEARCH PAPER Toiber, D. *et al.* SIRT6 recruits SNF2H to DNA break sites, preventing genomic instability through chromatin remodeling. *Mol. Cell* http://dx.doi.org/10.1016/j.molcel.2013.06.018 (2013)

TECHNOLOGIES

Reducing the load of mtDNA mutations

The accumulation of mutant mitochondrial DNA (mtDNA) often leads to disease. Here, Bacman *et al.* engineered TALENs (transcription activator-like effector nucleases) so that they localize to mitochondria and cleave known pathogenic mtDNA mutations. The efficacy of mitochondrion-targeted TALENs (mitoTALENs) was tested by designing them to cleave mutant mtDNA carrying a large common deletion that is found in ageing tissues and in 30% of patients with mtDNA deletions. As TALENs function as dimers to bind and cleave specific DNA target sequences, each mitoTALEN monomer was designed to bind to a wild-type sequence flanking this deletion. As such, the monomers were only close enough to dimerize on and cleave mtDNA carrying this deletion. mitoTALEN expression in patient-derived cells was shown to permanently reduce the levels of pathogenic mtDNAs. Although the safety of mitoTALENs remains to be tested, this technique could potentially be used to treat mitochondrial diseases.

ORIGINAL RESEARCH PAPER Bacman, S. R. *et al.* Specific elimination of mutant mitochondrial genomes in patient-derived cells by mitoTALENs. *Nature Med.* http://dx.doi.org/10.1038/nm.3261 (2013)