ATG5 did not bind to BAX; however, only truncated ATG5 binds to BCL-X_L in apoptotic, but not in non-apoptotic, cells. The authors speculated that truncated ATG5 promotes apoptosis by blocking the function of the anti-apoptotic 'survival' protein BCL-X_L, which leads to BAX and/or BAK activation. Although this hypothesis requires further testing, it is supported by the observation that ATG5-induced cell death was blocked by high levels of BCL2.

Although the details of this molecular link between autophagy and apoptosis need to be worked out further, this finding has clearly important implications for anti-cancer therapies.

Arianne Heinrichs

ORIGINAL RESEARCH PAPER Yousefi, S. *et al.* Calpain-mediated cleavage of Atg5 switches autophagy to apoptosis. *Nature Cell Biol.* **8**, 1124–1132 (2006)
FURTHER READING Codogno, P. & Meijer, A. J. Atg5: more than an autophagy factor. *Nature Cell Biol.* **8**, 1045–1047 (2006)

is necessary for the rapid induction of gene expression. By contrast, constitutively active genes are trimethylated at H3K36, and the amount of lysine methylation at these loci is unaffected by the deletion of *fpr4*.

The authors propose that the isomerization of H3P38 to its *cis* conformation by Fpr4 alters the secondary structure of the H3 tail so that H3K36 no longer fits into the active site of Set2. But, during active transcription, the passage of RNA polymerase through genes disrupts the nucleosome, exposing H3K36 to Set2 methylation. Trimethylated H3K36, in turn, inhibits Fpr4, overriding Fpr4 regulation and locking the chromatin in an active state.

There are several nuclear proline isomerases in higher eukaryotes, and deciphering how isomerization interacts with the complex patterns of modified histones in mammalian cells will be the next challenge.

Shannon Amoils

ORIGINAL RESEARCH PAPER Nelson, C. J. *et al.* Proline isomerization of histone H3 regulates lysine methylation and gene expression. *Cell* **126**, 905–916 (2006)

DNA REPAIR

Deinococcus does the two-step

In 1956, *Deinococcus radiodurans* was isolated from canned ground meat that had been irradiated at a dose 250-times higher than that used to kill *Escherichia coli*. Radiation, heat and dehydration normally kill cells by causing double-stranded breaks (DSBs) in their DNA — one of the most difficult kinds of DNA damage to repair — but *D. radiodurans* can withstand 1.5 million rad, a thousand times more than any other organism. The ability of this extremophile to survive the virtual disintegration of its chromosome has attracted widespread interest. Now, reporting in *Nature*, Zahradka and colleagues describe evidence for a two-step DNA-repair mechanism that allows *D. radiodurans* to completely reassemble its radiation-shattered chromosome from hundreds of short fragments in just a few hours.

There are at least six different mechanisms — non-homologous end-joining; homologous recombination at the fragment ends; intra- and interchromosomal single-strand annealing; synthesis-dependent strand annealing (SDSA); break-induced replication; and copy choice — that can stitch together the fragments of partially overlapping DNA that are produced by DSBs. Until now, none of these mechanisms had been excluded for DNA repair in *D. radiodurans*, but this latest study excludes all of them and invokes a completely novel repair mechanism.

Zahradka *et al.* showed that following exposure to extreme radiation, massive DNA synthesis and assembly of DNA fragments occurs, which is dependent on DNA polymerase I. The DNA synthesis that was observed was faster than normal DNA replication, which was puzzling. Researchers recapitulated the classic Meselson–Stahl experiment, in which newly synthesized DNA is distinguished by labelling it with a heavy thymidine analogue (5-bromodeoxyuridine). Their results showed that, unlike normal semi-conservative DNA replication in *D. radiodurans*, DNA-polymerase-I-mediated synthesis and repair produces a patchwork of new and old DNA fragments that are stuck together in a 'distributive' mechanism of DNA repair.

By using a modified immunofluorescence-microscopy method to scrutinize DNA synthesis directly, Zahradka *et al.* showed that most, if not all, of the DNA synthesized by DNA polymerase I was single-stranded DNA that rapidly converted to double-stranded DNA. It seems likely that DNA polymerase I achieves fragment reassembly by extended synthesis-dependent strand annealing (ESDSA). How does ESDSA differ from SDSA? Crucially, it requires at least two genome copies that are broken at different positions. Once overlapping fragments have aligned, a single-round multiplex PCR-like step — a variant of PCR that simultaneously amplifies different target sequences by using multiple primer pairs — occurs to produce long single-stranded overhangs that anneal accurately to produce reassembled chromosomal segments. Last, RecA-mediated homologous recombination using long intermediates synthesized by DNA-polymerase-I produces full-length chromosomes.

Details of the mechanism still need to be refined, including the priming step for DNA-polymerase-I-mediated DNA synthesis and the identification of mechanisms that ensure the fidelity of DNA replication.

Susan Jones, Senior Editor,
Nature Reviews Microbiology

ORIGINAL RESEARCH PAPER Zahradka, K. *et al.* Reassembly of shattered chromosomes in *Deinococcus radiodurans*. *Nature* **443**, 569–573 (2006)
FURTHER READING Cox, M. M. & Battista, J. R. *Deinococcus radiodurans* — the consummate survivor. *Nature Rev. Microbiol.* **3**, 882–892 (2005)

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