hp0421 mutants rapidly cleared the bacteria from the stomach, providing conclusive evidence that glucosylation of cholesterol promotes bacterial immune evasion.

Although the mechanisms by which cholesteryl α-glucoside inhibits phagocytosis remain to be elucidated, these studies highlight a new potential metabolic target for the immune-mediated eradication of *H. pylori* infection. These data also raise interesting questions about how dietary changes affect the gut microflora, with a spin-off effect on host tissue immune regulation.

Shannon Amoils

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BACTERIAL GENETICS

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 rads, 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.

Researchers have identified 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. By recapitulating the classic Meselson-Stahl experiment, in which newly synthesized DNA is distinguished by labelling with a heavy thymidine analogue (5-bromodeoxyuridine), these researchers revealed 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. Finally RecA-mediated homologous recombination using DNA-polymerase-I-synthesized long intermediates produces full-length chromosomes. Details of the mechanism still need to be refined, including the priming step for DNA polymerase I DNA synthesis and identification of mechanisms to ensure the fidelity of DNA replication.

The authors speculate that understanding how fragmented chromosomes are reassembled could eventually lead to methods for generating shuffled sequences from DNA fragments found in environmental samples. This might be important in drug discovery, where new combinations of shuffled sequences can generate novel enzymatic activities.

Susan Jones

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