DNA REPAIR

Persistent breaks

The events that accompany homologous recombination (HR)-mediated DNA double-strand break (DSB) repair are catalogued in detail. By contrast, little is known about what happens when no homology is found and DSBs persist.

By generating a single, irreparable DSB in budding yeast, Kalocsay *et al.* showed that the histone variant H2A.Z is deposited close to the break early but transiently, and that H2A.Z is required for DNA resection and DNA-damage checkpoint activation.

The recombinase Rad51, which functions in homology searching, spreads bidirectionally but selectively only across the broken chromosome for several hours. But what happens to the DSB itself if the search fails to find homologous sequences?

Live imaging studies revealed that, 5 hours after DSB induction, the DSB relocates to the nuclear periphery, where it associates with components of the nuclear envelope. Intriguingly, DSB relocalization independently requires DNA resection and DNA-damage checkpoint activation, and H2A.Z that is modified by the ubiquitin-related protein SUMO. The latter observation suggests that sumoylated H2A.Z functions as a specific chromatin mark for chromosome relocation, although its mechanistic role in DSB tethering to the nuclear periphery remains unclear.

So, the DNA damage response to persistent DSBs is multifaceted. The authors speculate that DSB relocalization and Rad51 spreading might be directly linked; DSB tethering might occur when Rad51-coated chromosome ends reach telomeric regions, which are known to localize to the periphery during interphase.

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ORIGINAL RESEARCH PAPER Kalocsay, M. *et al.* Chromosome-wide Rad51 spreading and SUMO–H2A.Z-dependent chromosome fixation response to a persistent DNA double-strand break. *Mol. Cell* **33**, 335–343 (2009)