

Disrupting your Hollidays? Studies on Archaeal recombinational DNA repair enzymes.

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The Archaea provide an appealing target for structural studies of enzymes which interact with DNA, due to both their practical tractability and the genetic similarity in this functional area to eukaryotic systems rather than their eubacterial counterparts. The Holliday junction resolving enzymes of the Archaea - the Hjc family - belong to the nuclease superfamily, which also includes restriction enzymes and eukaryotic DNA recombination/repair enzymes (Mus81/Xpf). Furthermore, the archaeal recombinase RadA, which catalyses strand exchange, is extremely similar to its eukaryotic counterpart Rad51 (46% identity) rather than the well-characterised bacterial RecA molecule (16%). We have solved crystal structures of the resolving enzymes Hjc and Hje from the Crenarcheote *Sulfolobus solfataricus*, providing new insights into catalysis in the nuclease superfamily (a novel catalytic residue), and the determinants of Holliday-junction cleavage specificity (well-constrained models of Hjc/Hje-Holliday junction complexes). Our structure of the intact RadA polypeptide is in neither of the previously observed ring or filament forms, but approximates a filament in the crystal with conservation of critical interactions between subunits, providing a platform for detailed comparison to RecA and Rad51 and offering some insight into the interaction specificity of the eukaryotic Rad51 paralogs.