

S004 Polymerase-mediated orchestration of DNA double-strand break repair processes

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Non homologous end-joining (NHEJ) is an essential DNA double-strand break (DSB) repair pathway required to maintain genome stability. Many prokaryotes possess a minimalist NHEJ apparatus required to repair DSBs formed in stationary phase, composed of two conserved core proteins, Ku and DNA ligase D (LigD). The simplicity of this DSB repair complex makes it an ideal model system for studying the molecular mechanisms that co-ordinate the processing and joining of DSBs by the bacteria NHEJ pathway and provides a conceptual framework for delineating related end-processing reactions in eukaryotes. The crystal structure of a mycobacterial NHEJ polymerase domain (*Mt*-PolDom) of LigD mediating the synapsis of two non-complementary DNA ends has recently been elucidated. Biochemical and biophysical studies confirmed that polymerase-induced end-synapsis also occurs in solution and the residues that facilitate this process have been identified. This DNA synaptic structure probably reflects an intermediate bridging stage of the NHEJ process, prior to end-processing and ligation. These recent findings illuminate the molecular basis for the unusual NHEJ activities associated with these repair polymerases and suggests how these enzymes can influence the sequential ordering of synapsis and remodelling of DNA breaks prior to end-joining.