

Crystal Structure of the Xrcc4 DNA Repair Protein and Implications for End Joining

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Introduction: XRCC4 is essential for carrying out non-homologous DNA end joining (NHEJ) in all eukaryotes and in particular V(D)J recombination in vertebrates. Xrcc4 protein forms a complex with DNA ligase IV that rejoins two DNA ends in the last step of V(D)J recombination and NHEJ to repair double strand breaks. XRCC4-defective cells are extremely sensitive to ionizing radiation and disruption of the XRCC4 gene results in embryonic lethality in mice.

Methods and Materials: Macromolecular crystallography with SeMet substituted protein and MAD method.

Results: Here we report the crystal structure of a functional fragment of Xrcc4 at 2.7Å resolution.

Conclusions: Xrcc4 protein forms a strikingly elongated dumbbell-like tetramer. Each of the N-terminal globular head domain consists of a β -sandwich and a potentially DNA-binding helix-turn-helix motif. The C-terminal stalk comprising a single α -helix over 120Å in length is partly incorporated into a four-helix-bundle in the Xrcc4 tetramer and partly involved in interacting with ligase IV. The Xrcc4 structure suggests a possible mode of coupling ligase IV association with DNA binding for effective ligation of DNA ends.

Acknowledgments: Z. Dauter

References: EMBO J. (2000) Nov. 15 issue