

## **Crystal Structures of Mismatch Repair Protein MutS and its Complex with a Substrate DNA**

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**Introduction:** DNA mismatch repair is critical for increasing replication fidelity in organisms ranging from bacteria to humans. MutS protein, a member of the ABC ATPase superfamily, recognizes mispaired and unpaired bases in duplex DNA and initiates mismatch repair. Mutations in human MutS genes cause predisposition to hereditary nonpolyposis colorectal cancer (HNPCC) as well as sporadic tumors.

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

**Results:** Here we report the crystal structures of a MutS protein alone and in complex with a heteroduplex DNA containing an unpaired base.

**Conclusions:** The structures reveal the general architecture of members of the MutS family, an induced-fit mechanism of recognition between four domains of a MutS dimer and a heteroduplex kinked at the mismatch, a composite ATPase active site composed of residues from both MutS subunits, and a transmitter region connecting the mismatch-binding and ATPase domains. The crystal structures also provide a molecular framework for understanding HNPCC mutations and for postulating testable roles of MutS.

**Acknowledgments:** Z. Dauter, C. Ogata

**References:** Nature, 2000, Vol. 7, p703