

P004 Structure and function of the archaeal DNA repair XPD helicase

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The XPD helicase (Rad3 in *Saccharomyces cerevisiae*) is a component of transcription factor IIH (TFIIH), which functions in transcription initiation and Nucleotide Excision Repair in eukaryotes, catalyzing DNA duplex opening localized to the transcription start site or site of DNA damage, respectively. XPD has a 5' to 3' polarity and the helicase activity is dependent on an iron-sulfur cluster binding domain, a feature that is conserved in related helicases such as FancJ. The *xpd* gene is the target of mutation in patients with xeroderma pigmentosum (XP), trichothiodystrophy (TTD) and combined XP with Cockayne's syndrome (XP/CS), characterized by a wide spectrum of symptoms ranging from cancer susceptibility to neurological and developmental defects. The 2.25 Å crystal structure of XPD from the crenarchaeon *Sulfolobus tokodaii*, recently obtained in our lab together with detailed biochemical analyses, allows a molecular understanding of the structural basis for helicase activity and explains the phenotypes of *xpd* mutations in humans. Furthermore, the interactions of archaeal XPD with labeled single-strand DNA has been studied by anisotropy and Fluorescence Resonance Energy Transfer (FRET). Preliminary data shown a strong significant fluorescence quenching with a 3'-labeled oligonucleotide supposing the 3'-end single-strand DNA sequestered by the iron-sulfur cluster.