

**S005** Exploiting our shared ancestry with the Archaea: structure and mutation of the DNA repair helicase XPD

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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, catalysing DNA duplex opening localised 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, trichothiodystrophy and Cockayne's syndrome, characterised 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*, presented here 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.