Structure of XPF Endonuclease from *A. pernix*

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The XPF structure-specific endonucleases form part of the nucleotide excision repair machinery which is required to detect and remove bulky DNA lesions caused e.g. by UV light. XPF acts on splayed DNA substrates by cutting one strand of the duplex upstream of a 3' flap. XPF family members have a catalytic nuclease domain connected by a linker sequence to tandem DNA-binding HhH domains. Eukaryotic XPFs also have a N-terminal SF2-like helicase domain and form heterodimers with smaller partners such as ERCC1. Archaea have either a short form of XPF regulated by PCNA or a long form that has an active helicase domain.

We have solved the structure of the XPF homodimer from *A. pernix* both alone and bound to a DNA duplex. The flexibility of the linker allows the nuclease and $(HhH)_2$ domains to dimerise independently. On binding DNA a large interdomain rearrangement takes place, resulting in an asymmetric complex. This is the first structure of an essentially intact XPF, and provides insight into how XPF can recognise branched DNA substrates.

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