Abstract

DNA damage refers to any alteration or modification in the DNA structure that deviates from its natural state. Abasic site (Ap site) is one of the most common DNA lesions resulting from spontaneous depurination/depyrimidination or enzymatic base excision. When left unrepaired it can lead to a cascade of genetic mutations, potentially causing diseases like cancer. Understanding DNA repair mechanisms is vital for medical research and applications.

Bacterial MutM is a DNA repair glycosylase, removing DNA damage generated by oxidative stress and preventing mutations and genomic instability. MutM belongs to the Fpg/Nei family of procaryotic enzymes, sharing structural and functional similarities with their eukaryotic counterparts, such as NEIL1-NEIL3. Here, I present two crystal structures of MutM from pathogenic *Neisseria meningitidis*: MutM holoenzyme and MutM bound to DNA. The free enzyme exists in an open conformation, while upon binding to DNA, both the enzyme and DNA undergo substantial structural changes and domain rearrangement.

One of the DNA lesion repaired by MutM is the Ap site, which, if not repaired, may spontaneously lead to the formation of an abasic site interstrand crosslink (Ap-ICL) with an adjacent adenine in the opposite strand. NEIL3 glycosylase is known to remove Ap-ICL. With a panel of different oligonucleotides, we investigated the rates of formation, the yields, and the stability of Ap-ICL. Our findings demonstrate how different bases in the vicinity of the AP site change crosslink formation *in vitro*. Based on our experimental data on Ap-ICL formation and known biochemistry of the Ap site we have estimated the number of Ap-ICLs within the cell.