A structural mechanism of DNA polymerase lambda action that promotes error-free bypass of bulky modifications in DNA

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Different environmental factors such as ultraviolet, ionizing radiation and air pollutions are influence on the genomic DNA damage that negatively impact on the human cells. The products of incomplete combustion of hydrocarbon fuels and waste of various industries are main sources of polycyclic aromatic hydrocarbons. DNA can be damaged by several metabolites of these compounds through forming the bulky DNA adducts that can lead to cancer and mutagenesis. Benzo(a)pyrene is the most widely known polycyclic aromatic hydrocarbon. BaP after metabolic activation, to toxic and reactive intermediates, reacts with DNA to form bulky adducts with mutagenic, and carcinogenic properties. Such damages can be repaired.

DNA pol λ is an eukaryotic enzyme belonging to the pol X family. Pol λ consists of two domains: 31 kDa polymerization domain (bearing the three conserved subdomains: fingers, palm, thumb) and 8 kDa domain. Pol λ has a dRP lyase activity, and play an important role in base excision repair (BER). Also DNA pol λ has been suggested to play a role in meiotic recombination and DNA repair.

In order to find out what effect on the localization of the protein in the active center of the enzyme affects the presence of the total number of BPDE-N2-dG residues that are in different regions, we carried out molecular modeling using the molecular dynamics method of the complexes of the enzyme with DNA duplex containing BPDE-N2-dG in the central part of the duplex. The complex also contains dCTP, forming a complementary pair with BPDE-N2-dG; triphosphate coordinated by the Mg^{2+} ion and is in a position of readiness for the reactions of incorporation of the nucleotide into the DNA chain.

In summary, we have shown here how a family X polymerase utilizes subtle active site adaptations to carry out a critical repair reaction.

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