1. Abstract

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Project Title : Investigation of changes in conformation and oligomeric state of the nucleotide excision repair proteins during repair reaction

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Abstract:

Nucleotide excision repair (NER) is distinguished from other DNA repair pathways by its ability to correct a wide range of structurally and chemically unrelated DNA lesions. UvrA is the key bacterial NER protein that recognizes DNA damage. Together with UvrB, it forms $UvrA_2B_2$ complex that searches for the lesion and triggers a downstream repair cascade that restores the DNA. Unlike other NER proteins, UvrA can bind to DNA without other NER components. Based on previous structural and biochemical data, models have been proposed for how UvrA discriminates damaged from undamaged DNA through interconversion between the 'open dimer' and 'closed dimer' conformations, and for how two UvrB molecules could function to select the appropriate DNA strand for incision.

We proposed to use a combination of biochemical and biophysical methods to test the described models. Although we were not able to dissect the roles of the transition between 'open dimer' and 'closed dimer' conformations of UvrA, our results showed, for the first time, that the conformational change of the β-hairpin of the third Zn module of UvrA (Zn3hp) is crucial for lesion recognition. The movement of Zn3hp is controlled by ATP hydrolysis at the distal nucleotide binding site, and is required for damage-sensing, ATP hydrolysis and UvrB loading.

Keywords : nucleotide excision repair, DNA repair, UvrA, disulfide crosslinking