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# A conserved mechanism of damage recognition by apurinic/apyrimidinic endonucleases from different structural families

Kuznetsov N.A.

*Institute of Chemical Biology and Fundamental Medicine, SB RAS, Novosibirsk, Russia*
*Department of Natural Sciences, Novosibirsk State University, Novosibirsk, Russia*
*Nikita.Kuznetsov@niboch.nsc.ru*

Apurinic/apyrimidinic (AP) endonucleases process intermediate DNA products generated by DNA glycosylases in the course of base excision repair (BER) and cleave an AP site. Data obtained over last two decades clearly indicate that members of the different structural families of AP endonucleases can recognise as a substrate not only an AP site but also various damaged nucleotides. Molecular origin of the wide substrate specificity of AP endonucleases, which can cleave damaged and undamaged DNA in endo- and exonuclease types of interaction, is not clear at present. Significant differences in the structure of target nucleotides support the idea that the recognition of a specific site by the enzyme is determined by some conformational properties of DNA at the lesion site.

Here, the mechanism of target nucleotide recognition by Nfo enzyme from *Escherichia coli* was analysed by pulsed electron–electron double resonance spectroscopy and pre–steady-state kinetic analysis with Förster resonance energy transfer detection of DNA conformational changes during DNA binding. To elucidate the stages of catalytic-complex formation and to reveal key factors responsible for inner-strand damage recognition, for discrimination of structurally different damaged nucleotides and for cleavage efficacy, a set of model DNA substrates was tested. Obtained results strongly support the notion that the recognition of diverse lesions by AP endonuclease Nfo depends on the ability of a damaged nucleotide to change the enzyme's DNA-bending and DNA-unwinding ability. Comparison of the present data and data obtained previously for human APE1 indicates that this strategy of damage recognition is suitable for AP endonucleases from both structural families.

The results for the first time show that AP endonucleases from different structural families utilise a common strategy of damage recognition, which globally may be integrated with the mechanism of searching for specific sites in DNA by other enzymes.

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