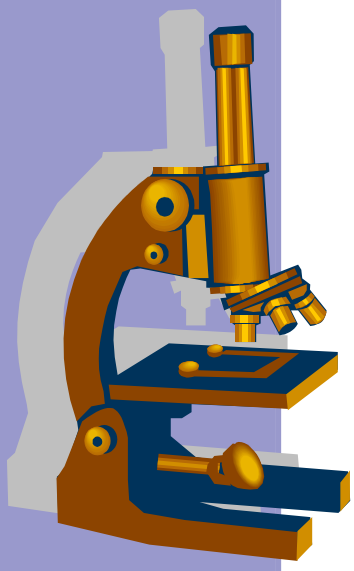
Featured Research Study



1: Bioorg Khim. 2007 Mar-Apr;33(2):195-228. Links

[NO-dependent modifications of nucleic acids]

Beda NV, **Nedospasov AA**.

This review is devoted to chemical transformations of nucleic acids and their components under the action of nitrogen oxide metabolites. The deamination reaction of bases is discussed in the context of possible competing transformations of its intermediates (nitrosamines, diazonium cations, diazotates, triazenes, and diazoanhydrides) and mechanisms of crosslink formation with proteins and nucleic acids. The oxidation and nitration of bases by NO2 is considered together with the possibility of radical transfer to domains from the base stacks in DNA. Reduction of redox potentials of bases as a result of stacking interactions explains the possibility of their reactions within nucleic acids with the oxidants whose redox potential is insufficient for the effective reactions with mononucleotides. Modifications of nucleic acids with peroxynitrite derivatives are discussed in the context of the effect of the DNA primary structure and the modification products formed on the reactivity of single bases. The possibility of reduction of nitro groups within modified bases to amino derivatives and their subsequent diazotation is considered. The substitution of oxoguanine for nitroguanine residues may result; the reductive diazotation can lead to undamaged guanine. The intermediate modified bases, e.g., 8-aminoguanine and 8-diazoguanine, were shown to participate in noncanonical base pairing, including the formation of more stable bonds with two bases, which is characteristic of the DNA Z-form. A higher sensitivity of RNA in comparison with DNA to NO-dependent modifications (NODMs) is predicted on the basis of the contribution of medium microheterogeneity and the known mechanisms of nitrosylation and nitration. The possible biological consequences of nucleic acids NODMs are briefly considered. It is shown that the NODMs under the action of nitrogen oxide metabolites generated by macrophages and similar cells in inflammations or infections should lead to a sharp increase in the number of mutations in the case of RNA-containing viruses. As a result, the defense mechanisms of the host organism may contribute to the appearance of new, including more dangerous, variants of infecting viruses.

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