Kinetics of base pair opening-closing process in DNA duplex containing oxoG:C pair and oxoG:A mismatch

Ovcherenko Sergey S.,[1,3*] Shernyukov Andrey V.,[1] Nasonov Dmitry M.,[1,3]
Endutkin Anton V.,[2] Zharkov Dmitry O.,[2,3] Bagryanskaya Elena G.[1]

[1] *N.N. Vorozhtsov Novosibirsk Institute of Organic Chemistry SB RAS, Lavrentiev 9, 630090, Novosibirsk, Russia*

[2] *Institute of Chemical Biology and Fundamental Medicine SB RAS, Lavrentiev 8, 630090, Novosibirsk, Russia*

[3] *Novosibirsk State University, Pirogova 1, 630090, Novosibirsk, Russia*

* *E-mail: ovcheren@nioch.nsc.ru*

8-oxoguanine is known to be one of the most common and major DNA lesions resulting from the reactive oxygen species modifying guanine. When this lesion is located opposite to adenine in a base pair, the change from 8-oxoguanine's anti- to syn-conformation leads to the formation of a Hoogsteen base pair with adenine. The repair of this lesion is initiated by specific enzymes, namely 8-oxoguanine glycosylases, which locate and excise the damaged base by means of flipping it outside DNA double helix to the enzyme's active site. There are several models of how DNA glycosylase locate a damaged base and the role of the base pair opening-closing kinetics in this process [1]. However, there is no exact match in the literature that confirms one model and refutes the others [2].

NMR spectroscopy provides the exact experimental detection of DNA base pair opening-closing rate constants at the single base pair level through the analysis of the water-iminoproton exchange rate. Iminoproton exchange with water occurs in two steps, namely opening of a base pair followed by proton exchange from the open conformation. The application of water magnetization transfer technique permits determination of exchange rate constants in the range that is most common for iminoprotons of a normal DNA duplex.

As a part of the study of the role of the opening-closing kinetics of 8-oxoG:A and 8-oxoG:C DNA base pairs in the recognition of 8-oxoguanine lesion by formamidopyrimidine-DNA glycosylase in the current work in the absence of the enzyme we obtained the kinetics constants for the base pair opening-closing process in DNA duplexes containing 8-oxoG:A and 8-oxoG:C base pairs in two different sequence contexts and compare them with the values for the canonical G:C base pair in the same sequence contexts. The results obtained by NMR spectroscopy using water magnetization transfer technique [3] will be presented and discussed.

This work was supported by the Russian Science Foundation (21-14-00219)

[1] C. Cao et al., *Nature Struct. & Molec. Biol.* **2004**, *11(12)*, pp. 1230-1236.

[2] R. Li, C. H. Mak. *The J. of Phys. Chem. B* **2020**, *124(27)*, pp. 5559-5570.

[3] T. L. Hwang et al. *Journal of biomolecular NMR* **1998**, *11(2)*, pp. 221-226.