DNA bases in rare tautomeric forms are cause of an untargeted ultraviolet mutagenesis

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Untargeted mutations are one of the features of cancer. Untargeted mutagenesis is called brush of SOS mutagenesis, when mutations arise on, as postulated, undamaged sites. The lesion-bypass DNA polymerase such as DNA polymerase IV and V *E. coli* are involved in untargeted SOS mutagenesis. The generally accepted paradigm rests upon the idea that mutations are conditioned by sporadic errors of DNA polymerases exclusively. However, such an approach can't explain some phenomena of UV mutagenesis and contradicts some experimental facts [1, 2]. Mutations occur frequently opposite the dimers (the targeted mutagenesis). Sometimes they originate in a small vicinity of dimers (the untargeted mutagenesis). Therefore the polymerase-tautomer model of UV-mutagenesis is developed [1-4]. Three mechanisms of untargeted mutations formation are proposed.

First, the source of untargeted mutations may be such G-C pairs, when here occurs the double protonic transitions (G*-C*), they are stable. They may give only G-C→A-T transitions or G-C→C-G homologous transversions [3].

Second, untargeted mutations may form when mutagenic *cis-syn* cyclobutane pyrimidine dimers are in both strands of DNA in small vicinity each others. It is shown that only such *cis-syn* cyclobutane pyrimidine dimers are mutagenic, one or both bases in which are in rare tautomeric forms [1, 2]. The sources of untargeted mutations in this case are adenines in one of 5 rare tautomeric forms, or guanines in one of 7 rare tautomeric forms. These potential untargeted mutations may result in transitions, transversions or give one-nucleotide gaps [4].

Third, the sources of untargeted ultraviolet mutations may be any of the possible 5 pair of the bases A_i^*-T_i^* [1] or any of the possible 7 pair of the bases G_i*-C_i*, when they form in the small vicinity of any photodimer. Since in a close vicinity of photodimer the DNA strand becomes curved, then, consequently, the hydrogen bonds between bases of that strand and complementary bases of another strand are broken. In this case, the newly formed rare tautomeric states of bases will be stable. Under error-prone or SOS synthesis they may give any untargeted bases substitution mutations or one-nucleotide gaps.

1. Grebneva, H. A. J. Mol. Struct. 2003, V. 645, 133-143.
2. Grebneva, H. A. Environ. Mol. Mutagen. 2006, V. 47, 733-745.
3. Grebneva, H. A., Ivanov M. O. Biopolym. Kletka 2001, V. 17, 388-395.
4. Grebneva, H. A. Biopolym. Kletka 2002, V. 18, 394-400.