Oxidative DNA Damage and Repair: Mechanistic and Diagnostic Insights of the Purine lesions

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Abstract: 5′,8-Cyclopurine-2′-deoxynucleosides (cPu) are solely generated by the attack of HO• radicals on purine moiety *via* C5′-radical chemistry resulting in the formation of an additional C5′−C8 covalent bond; the structures of the four cPu are shown in the Figure. cPu can be removed only by the nucleotide excision repair (NER) pathway and different repair efficiency of the *R* and *S* diastereoisomers has been detected. On the other hand, the well-known 8-oxo-purines (8-oxo-Pu) lesions (see Figure for the structures), derive from the oxidation at the C8 position of adenine and guanine by a variety of reactive oxygen species (ROS), and can be repaired by the base excision repair (BER).

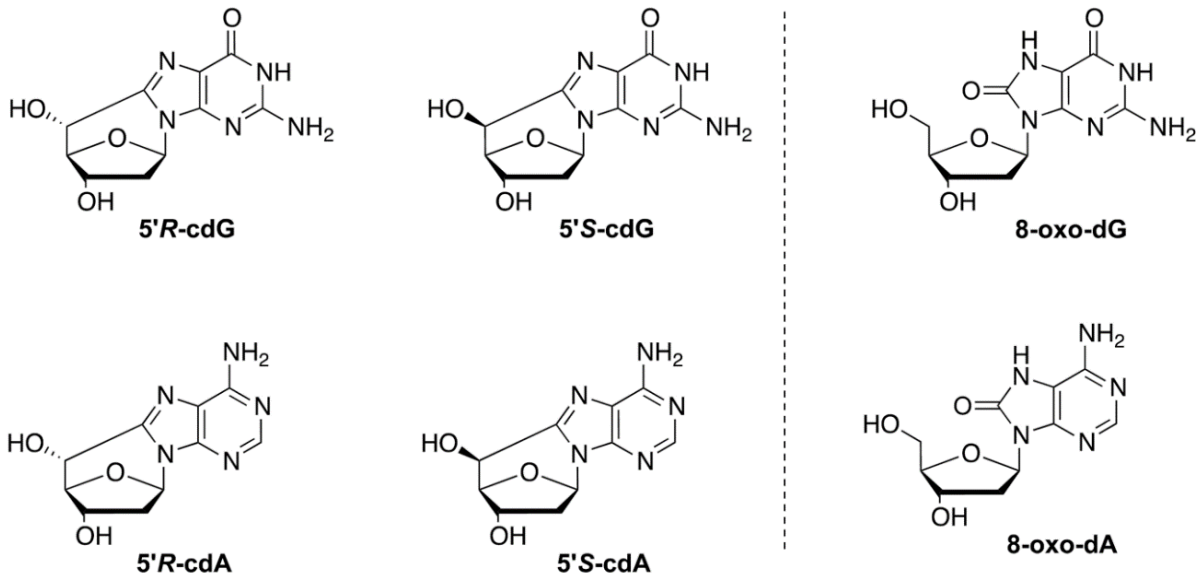

Figure. Structures of 5′,8-cyclo-2′-deoxyguanosine (cdG) and 5′,8-cyclo-2′-deoxyadenosine (cdA) in their 5′*R* and 5′*S* diastereomeric forms (left) and 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxo-dG) and 8-oxo-7,8-dihydro-2′-deoxyadenosine (8-oxo-dA) (right).

In this lecture we will discuss our most recent results on these purine lesions: (i) Radical-based synthetic strategies and Mechanistic insights; (ii) Analytical protocol based on LC-MS/MS method for quantification of these lesions in DNA; (iii) Comparison of analytical method efficiencies using irradiated samples of calf thymus DNA; (iv) Detection of purine lesions in mammalian cell cultures, human fluids and animal tissues; (v) Recognition of DNA damage by repair enzymes and mutagenic potential.

Recent selective publications

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