Conference

Free radicals induced DNA damage: Chemical, Analytical, Biological, and Diagnostic Aspects.

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DNA damage caused by free-radicals includes a large variety of base and sugar lesions leading to DNA breaks and DNA-protein cross-links. Among free radicals, the diffusible hydroxyl radicals ($HO^{\cdot}$) are key oxidant species responsible for reacting with DNA either by hydrogen abstraction from 2-deoxyribose units or by addition to the base moieties. The purine 5',8-cyclo-2'-deoxynucleosides (cPu) are an important class of lesions exclusively generated by the $HO^{\cdot}$ attack to DNA purine nucleotides, forming C5' radicals followed by an internal cyclization giving 5',8-cyclo-2'-deoxyadenosine (cdA) and 5',8-cyclo-2'-deoxyguanosine (cdG) identified as products, in two possible diastereomeric forms, 5'*R* and 5'*S* (Fig. 1).[1,2]

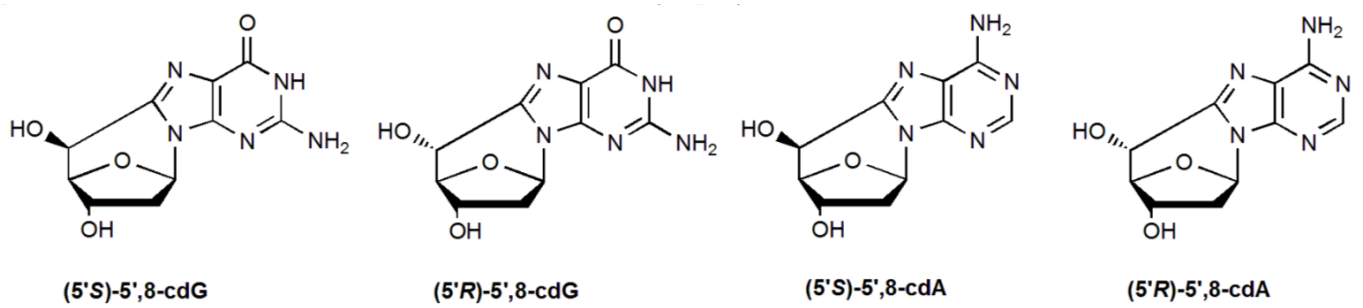

Fig. 1

These lesions are exclusively repaired by the Nucleotide Excision Repair pathway (NER) with low efficiency in comparison with other bulky DNA lesions.[3]

Nowadays cPu are used as radical stress biomarkers of DNA damage thanks to their specific formation mechanism and their chemical stability during work-up.

The diastereomeric 5'*S*- and 5'*R*-cPu are discussed in terms of:

(i) Synthetic and analytical protocols for the availability and characterization of the diastereoisomeric 5'S- and 5'R-cPu lesions, also as isotopic labelled references;
(ii) Physical-chemical studies on specific oligonucleotide models as: MD simulations, NMR, Melting Temperature;
(iii) Biological and Clinical studies for the investigation of the relationships between the levels of lesions and human health, disease, and aging is a matter of investigation.[4]

References

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