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S E M I N A I R E

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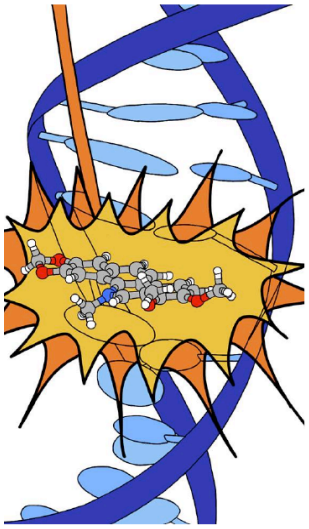
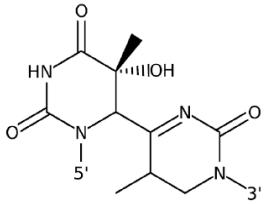
"DNA damages: the birth, life and death of nucleobases lesions"

What is the common denominator between aging, cancers, inflammations, tanning and cellular life? One answer involves molecular processes occurring deep inside our cells nucleus, DNA damaging and repairing. Since these phenomena have direct medical and societal impacts, it appears crucial to understand every steps of the DNA lesion evolution, from the chemical mechanisms that produced the damage, to the influence on its environment, mainly the modification of the DNA double helix structure and finally how efficiently it is repaired by our biological protecting mechanisms.

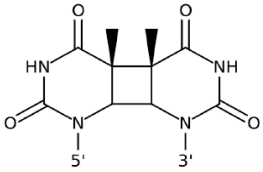
In this contribution I will present the use of hybrid QM/MM methods and extensive molecular dynamics to help understand each steps of a DNA lesion lifetime. First I will focus on the photosensitizing processes triggered by the photo-excitation of endogenous light sensitive molecules interacting with DNA: mainly electron transfer [1], Triplet-Triplet Energy Transfer (TTET), or hydrogen abstraction. I will then provide an analysis of the structural modifications in the DNA double strand containing either Cyclo-Pyrimidine dimers (CPD), 6-4 photoproducts (64PP) or abasic sites [2], allowing a rationalization of their relative toxicity. This aspect will also be treated by explicitly studying the interaction of human and bacterial repairing proteins with DNA and in particular the influence and sequence specificity of several clustered lesions on the efficiency of the repairing process [3].



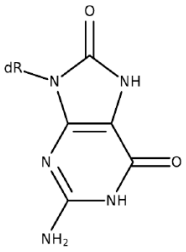
CPD



64PP



8oxoG



[1] Hugo Gattuso et al., Scientific Reports, **2016**, 6(28480)
[2] Hugo Gattuso et al., Nucleic Acids Res, **2016**, 44(18), 8588-8599
[3] Hugo Gattuso et al., J. Phys.

Chem. Lett., **2016**, 7(19), 3760-3765