Radiation-induced formation of tandem lesions: mechanistic aspect.

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During the last three decades considerable efforts have been made to determine the nature and quantify the amount of lesions produced in double stranded (ds)DNA exposed to oxidative stress. Nowadays, an almost complete decomposition pathway of the four DNA bases mediated by hydroxyl radicals and one electron-oxidation, the two damaging species of such a stress, is available. About 70 different DNA lesions have been identified and some of them have been quantified in cells exposed to ionizing radiations.
Regarding the chemical aspects of formation of these lesions, most of the reactions identified at the nucleoside level were also found to occur in double stranded (ds)DNA. However, differences exist and some modifications were found to be generated specifically in dsDNA. This highlights the fact that the 3D structure of DNA somehow plays an important role in the decomposition of the initially generated radicals.
Attention will be focused during the presentation on the formation of complex DNA lesions that could be significantly generated through a single oxidation event. Such damages are different to so-called locally multiple damage sites that are produced specifically by radiations as a consequence of multiple ionization processes. These include tandem DNA lesions generated through peroxidation reactions and also intra- and inter-strand crosslinks. These examples indicate that the described mechanisms of decomposition of the DNA bases could be different in dsDNA compared to that observed for free nucleosides. Moreover, this also indicates that in a cellular environment, biomolecules surrounding DNA could also play a role in the mechanisms of decomposition of initially produced DNA radicals.
To further delineate the mechanisms of radiation-mediated decomposition of DNA bases in dsDNA both experimental and theoretical approaches are required.