Reactions of Guanine Cation Radical in DNA-models

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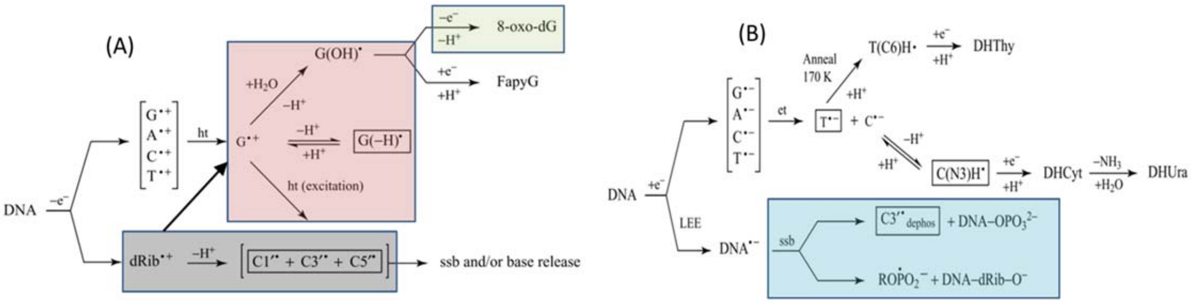
It has been widely accepted that the holes (or, the cation radical sites) are the major damaging entity in DNA radiation damage and much work has focused on the transfer and localization of the hole in DNA (scheme 1).[1-3] ESR studies at low temperatures have clearly established that, for the holes on the DNA bases, a fast hole transfer process from base cation radicals ($A\bullet^{+}$, $C\bullet^{+}$, $T\bullet^{+}$), and backbone cation radical ($[\text{sugar-phosphate}]\bullet^{+}$) localizes the hole preferentially to a nearby guanine base forming $G\bullet^{+}$ in agreement with the theoretically predicted ionization potential of guanine in the G:C base pair system (Scheme 1).[1-4] Prototropic equilibria critically influence (i) rate and distance of hole transfer and (ii) the final stabilization of the hole either at a G or Gn (n>1) site or another introduced hole acceptor.[1-4] In this talk, formation of $G\bullet^{+}$ by backbone-to-base hole transfer employing modified phosphates (e.g, phosphorothioates, phosphorodithioates),[3,4] the various reactions of $G\bullet^{+}$ in its ground state, e.g., prototropic equilibria, the nucleophilic addition of water at C-8 of $G\bullet^{+}$ leading to 8-oxo-G formation as well as the excited state reactions of $G\bullet^{+}$ that lead to sugar radical formation will be discussed.



Scheme 1. Radiation-induced ionization-mediated DNA-radical formation by (A) the oxidative electron-loss path and by (B) the reductive electron-gain path along with the subsequent reactions of these DNA-radicals. SSB denotes single strand break in both (A) and (B). Adapted from ref. 2.

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References

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