DNA DAMAGE BY IONIZING RADIATION: TANDEM DOUBLE LESIONS BY CHARGED PARTICLES*

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Oxidative damages by ionizing radiation are the source of radiation-induced carcinogenesis, damage to the central nervous system, lowering of the immune response, as well as other radiation-induced damages to human health. Monte Carlo track simulations [1] and kinetic modeling [2] of radiation damages to the DNA employ available molecular and cellular data to simulate the biological effect of high and low LET radiation to the DNA. While the simulations predict single and double strand breaks and base damages, so far all complex lesions are the result of stochastic coincidence from independent processes. Tandem double lesions have not yet been taken into account.

Unlike the standard double lesions that are produced by two separate attacks by charged particles or radicals, tandem double lesions are produced by one single attack. The standard double lesions dominate at the high dosage regime. On the other hand, tandem double lesions do not depend on stochastic coincidences and become important at the low dosage regime of particular interest to NASA. Tandem double lesions by hydroxyl radical attack of guanine in isolated DNA have been reported [3] at a dosage of radiation as low as 10 Gy. The formation of two tandem base lesions was found to be linear with the applied doses, a characteristic of tandem lesions. However, tandem double lesions from attack by a charged particle have not been reported.

Using the high end computing facility Columbia at NASA Ames Research Center, we have simulated the damages of guanine-cytosine base pair by charged particles using first principles calculations. The calculations established the formation of tandem double lesions to be a multi-step process. Guanine is first ionized by the charged particle. In the case when the ionized electron originates from an orbital with significant charge density along the N(1)-H bond, it leads to breaking of this bond (first lesion), releasing a proton. For proton energy above 3 eV, its interaction with the neighboring cytosine leads to cytosine ring opening (see Fig. 1), resulting in a second lesion. The present result shows that, analogous to the hydroxyl radical, charged particle interaction can also lead to tandem base damages.

The prediction from our model will be tested experimentally by Vercoutere et al. using the biological nanopore detector [4]. The data can also be used in Monte Carlo track simulation studies, particularly in the low dosage regime.

Figure 1. Left, normal cytosine configuration. Right, cytosine ring opening after attack by proton.

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REFERENCES