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Low-Energy Electron Damage to Plasmid DNA in Thin Films: Experimental parameters and DNA radiosensitization by terpyridine-Pt

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The interaction of low-energy electrons (LEEs) with DNA plays a significant role in the mechanisms leading to biological damage induced by ionizing radiation, particularly in radiotherapy, and its sensitization by chemotherapeutic drugs and nanoparticles [1]. Plasmids constitute the form of DNA found in mitochondria and appear as a suitable model of genomic DNA [2]. In a search for the best LEE targets, the films were deposited on oriented graphite or polycrystalline tantalum, with or without DNA auto-assembly via diaminopropane (Dap) intercalation. The damages were induced to thin plasmidfilms in vacuum, by 6, 10 and 100 eV electrons under single collision conditions. The yields of single and double strand breaks (SSBs and DSBs), other cluster damages (NDCD), isolated base lesions (BDs),crosslinks (CLs)and loss of supercoiled (LS) were measured by electrophoresis and enzyme treatment. Yields were correlated to the influence of vacuum, film uniformity and surface density, substrate and DNA environment. The lyophilized Dap-DNA films were found to be the most practical high-quality targets for the investigation of LEE interaction [3]. These studies pave the way to the fabrication of LEE target-filmscomposed of plasmids intercalated with other biomolecules that could mimic the cellular environment, e.g., as a first step, by replacing Dap with an amino acid.

Terpyridine-platinum (Tpy-Pt), whichbind preferentially to guanine-quadruplexes in telomeres hasrecently emerged as a drug having considerable potential for usein cancer chemoradiation therapy [4].Our new results indicate that the introduction of Tpy-Pt in plasmid DNA significantly enhance LEE-induced DNA damages, especially CLs,BDsand potentially lethal cluster damages. The magnitude of these enhancements suggests that LEEs play an important role in theradiosensitization mechanism of Tpy-Pt at molecular level.Some of these results will be presented at the conference with corresponding amplification factors caused by binding Tpy-Pt to plasmid DNA.

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