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Intracellular Retention and Redistribution of Gold Nanoparticles with Docetaxel

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Docetaxel (DTX) is an anticancer drug used in combination with radiotherapy to treat many cancers. Currently, Gold nanoparticles (GNPs) are being tested as novel radiosensitizers in radiotherapy. Addition of GNPs into this current protocol is expected to produce further therapeutic benefits. Our goal was to elucidate the behavior of GNPs in the presence of DTX since it can disturb the microtubule network affecting the vesicle transport of GNPs within cells. We tested our hypothesis using clinically feasible concentrations of DTX (50 nM) and GNPs (0.2 nM). Concurrent treatment of DTX and GNPs resulted in an over 80% increase in the retention of GNPs and forced them closer to the most important target, the nucleus. DTX appears to allow endocytosis while blocking exocytosis through restricting transport of vesicles to the cell surface, leading to an aggregation of GNPs surrounding the nucleus. This would cause more DNA damage from the extra short-range secondary electrons produced by GNPs during radiotherapy. DTX also prevents redistribution of GNPs into daughter cells by blocking cells in the G2/M phase of the cell cycle, already the most radiosensitive phase. The ability to trap GNPs at clinically feasible doses would lead to meaningful nanotechnology-based platforms in future combined therapy.

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