CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160497

Project Title:
Amplified gold nanoparticle-mediated radiosensitization of tumors

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Sequestering gold nanoparticles (GNPs) within tumors has gained prominence in recent years as a means to escalate radiation therapy (RT) dose to the tumor & improve the curability of locally advanced tumors. Current methods require large quantities of gold (clinically unachievable without direct injection into the tumor), low energy kilovolt x-rays (not used in the clinic for over half a century), immediate RT after GNP administration (since the gold is rapidly cleared by the kidneys & only remains in the tumor vasculature for a couple of minutes after intravenous administration), & re-administration of GNPs before each RT fraction (increasing cost and toxicity) – clinical translation is hindered by all of these constraints. We have developed engineered GNPs that surmount these challenges and, for the first time, shown that potent radiosensitization can be achieved via intravenous administration of thousand-fold lower concentrations (microgram/Kg instead of milligram/Kg), clinically relevant radiation beam energies (megavoltage RT using a clinical linear accelerator), a single injection before a course of fractionated RT, and the first radiation treatment occurring a day after intravenous administration of GNPs. We have characterized the molecular mechanisms of radiosensitization and we have now identified a simple technique to amplify the radiosensitization by dispersing clumped internalized GNPs within the cytoplasm so they do not shield the nucleus from secondary electron showers generated by neighboring GNPs. The overall goal of the proposed work is to test these paradigm-changing findings in a head & neck cancer (HNC) animal model that involves first-of-its-kind proof-of-principle studies prior to potential clinical translation. That will, in turn, catalyze the development of innovative next-generation strategies to not only improve RT for HNC but could also serve as a class solution for multiple other cancers treated with RT.