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Immunomodulatory Nanoradiopharmaceuticals As A New Paradigm in Cancer Therapy—Green Nanotechnology Toward the Development of MGF-198AuNPs Nanomedicine Agent

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The interrelationship of NF-κB and related signaling pathways involving NF-κB-related effector genes in adaptive radioresistance has attracted significant current interest toward the overall quest of developing more effective radiotherapeutic agents. Compelling evidence suggests that radiotherapy triggers several signaling pathways including NF-κB and related signaling vectors causing repopulation with radioresistant cancer stem cells—thus contributing to tumor radioresistance. Numerous pre-clinical and clinical data suggest the potentiation of radiation-induced therapy resistance is mediated solely by activation of NF-κB signaling pathway. Activated NF-κB in tumor cells is a key mechanism through which tumors acquire radioresistance and this tumor biological process has been linked to increased recurrence and failure of radiation therapy in cancer patients. It is, therefore, imperative to develop radiotherapeutic agents with dual immunomodulation while delivering radiotherapy site specifically to tumor sites. New radiotherapeutic agents must address targeting NF-κB transcription factors for cross talk between cell signaling and macrophage reeducation within the tumor microenvironment. Radiotherapeutic agents with capabilities to deliver effective radiation dose to tumor sites while suppressing NF-κB will provide the best means to treat myriad of human cancers effectively. This lecture focuses on the development of Mangiferin functionalized Au-198 nanoparticles (MGF-198AuNPs) as an innovative dual, NF-κB suppressing, radiation therapy with immunomodulatory effects. MGF-198AuNPs provides a desirable beta energy emission and half-life that destroys tumor cells/tumor tissue (βmax = 0.96 MeV; half-life of 2.7 days) while the presence of mangiferin suppresses pro tumor NF-κB signaling pathways. The penetration range of Au-198 (up to 4 mm in tissue or up to 1100 cell diameters) is sufficiently long to provide cross-fire effects to destroy tumor cells/tissue, but short enough to minimize radiation exposure to adjacent tissues. One particularly attractive feature of radioactive gold nanoparticles is that it does not have to be incorporated into every tumor cell to have a therapeutic effect. The path length of the emitted radiation is sufficient to allow effective therapy following uptake into a subpopulation of tumor cells.

This lecture will provide: (a) Scope and prospects of beta emitting radioisotopes in nanomedicine through the design and development of immunomodulatory radiotherapeutic agent: MGF-198AuNPs; (b) full in vivo investigations on therapeutic properties of MGF-198AuNP agent in treating prostate tumors; (c) Immunomodulatory effects of MGF-198AuNPs through targeting the tumor microenvironments and thereby suppressing NF-κB transcription factors while promoting antitumor M-2 macrophages; and (d) Estimation of the dose distribution delivered by radioactive gold nanoparticles (MGF-198AuNPs) to the tumor inside the human prostate as well as to the normal tissues surrounding the tumor using Monte-Carlo N-Particle code (MCNP-6.1.1 code). This lecture will highlight details on the importance of interaction of various types of cancer cells with immunotherapeutic nanoparticles for stopping the infiltrating aggressive tumor proliferating M2 type macrophages to achieve effective tumor therapy. The overall implications of Green Nanotechnology of MGF-198AuNPs as a therapeutic beta emitting nanomedicine immunomodulatory agent in oncology will be discussed.

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