An Effective Drug-Delivery-Mechanism-Based Approach to Clinical Radiosensitization

Kanneganti, Lavanya

As of 2015, it has been estimated that over fifty percent of all cancer patients will receive radiation therapy during some phase of their treatment. Despite clinical potential, the therapy's undirected application gives significant room for secondary tumor formation. In fact, for certain forms of cancer, there are just as many dying from the radiation therapy treatment as there are from the initial diagnosis itself. Within the last decade, there has been an augmentation in the evidence to suggest that three of the top five most diagnosed cancer types express nucleolin on their surface. As the first anti-cancer and nucleolin-binding oligonucleotide to reach clinical trials, AS1411 has promising evidence to suggest therapeutic application to focus radiation therapy. A 5nm drug-release mechanism with a gold core and citrate shell was developed to take advantage of the aptamer's thiol bond and transmit the drug into the tumor, which would engulf the mechanism using macro-pinocytosis after bonding. Radiation of the targeted site would then release the drug and remove the citrate shell, exposing the gold core, which, because of its high atomic number and passivity, would increase the drug's pharmacology. In vitro analysis in Triple-Negative Breast Cancer cells shows significant reduction in breast cancer after seventy-two hours of treatment. AS1411 binding to the tumor was verified through in vivo analysis of a synthesized cytosine-rich aptamer sequence of identical length. The difference in the effects of both drugs suggests that the AS1411's G-rich structure forms a stable quadruplex to effectively bind to the targeted cancer. Results suggest that this aptamer-based mechanism has potential to reduce risk of tumor reformation and lower treatment time for patients.