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Radiosensitization with Magnetic Nanoparticles

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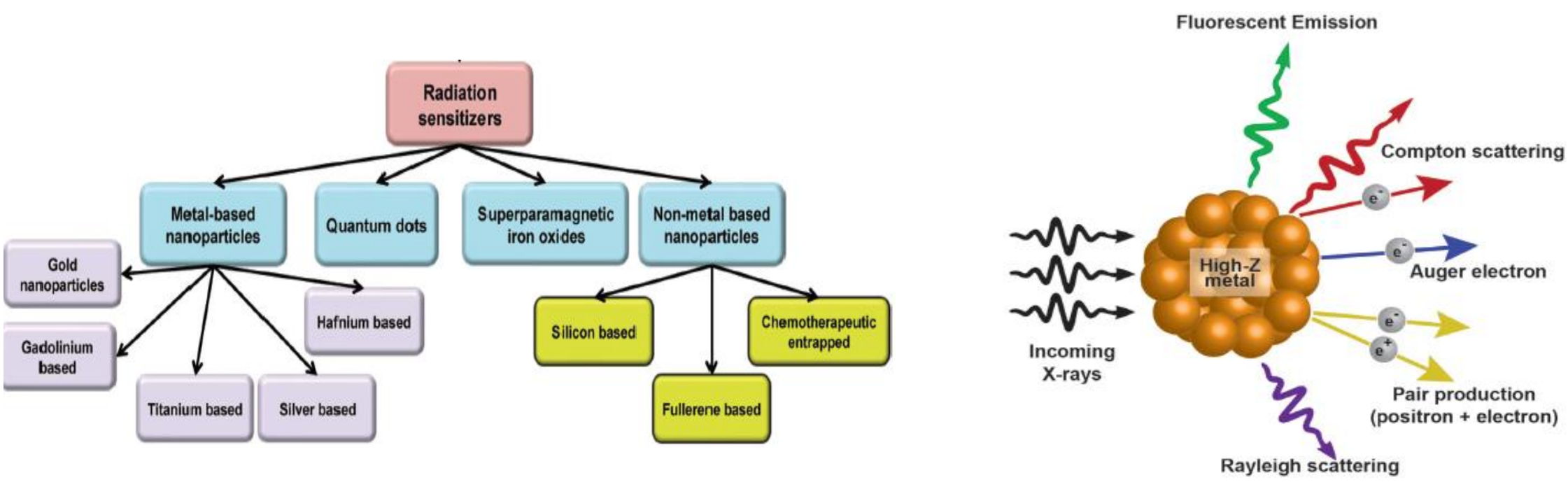
Radiation therapy, along with surgery and chemotherapy, are the major therapeutic strategies for cancer treatment. It involves the delivery of ionizing radiation with high accuracy to the tumor tissue, resulting in the death of tumor cells. Radiation sensitization is a process of enhancing the susceptibility of tumor tissues to injury by radiation exposure. Hence, radiation sensitizers are therapeutic or otherwise inert agents that enhance the effects of radiation therapy. Iron oxide nanoparticles, a type of magnetic nanoparticle (MNP), are amongst the nanomaterials which have been suggested as radiation sensitizers (Figure 1).[1] Hyperthermia is a type of cancer treatment in which tissue is exposed to elevated temperatures. Hyperthermia is almost always used with other forms of cancer therapy, such as radiation therapy and chemotherapy. Hyperthermia may make some cancer cells more sensitive to radiation. When hyperthermia and radiation therapy are combined, they are often given within an hour of each other. MNP can induce localized hyperthermia when exposed to an alternating magnetic field (AMF).[3,4] As MNP are potentially capable of producing two sensitization effects (x-ray interaction and hyperthermia generation) they are particularly attractive for this application.



(Kwatra 2013) (Kwatra 2013)

Figure 1: Left: Summary of various nanomaterial-based approaches for enhancing the radiosensitization in cancer cells. Right: Possible x-ray interactions with high Z materials. These interactions may result in the production of electrons, positrons or photons that may subsequently damage nearby DNA within cancer cells, resulting in cell death.[1]

Hypothesis: the combination of MNP and ionizing radiation increases the cytotoxicity of hyperthermia.

Cell lines: Chinese hamster ovary (CHO) and MTGB (a murine mammary adenocarcinoma cell line) will be incubated for 72 hrs with 1 mg/mL of MNP to allow for intracellular uptake (Figure 2). Each flask will be rinsed with PBS to remove extracellular MNP and given new media prior to irradiation. *Variables: CHO, MTGB.*

Fe_3O_4 Nanoparticles: MNP are promising materials for hyperthermia treatment, as well as radiation sensitizing agents. Relative to other nanoparticles considered for radiation sensitization, they are highly biocompatible, and well suited for adjuvant hyperthermia applications.[6] The particles used for these studies are BNF-Dextran plain, 84-00-102, (micromod GmbH, Rostock, Germany). These particles have a hydrodynamic radius of 100 nm, and are suspended in water at 25 mg/ml. *Variables: cell incubation +MNP, cell incubation -MNP.*

Irradiation: Cells will be irradiated with a Kubtec XCELL 50 kVP cell irradiator (Kubtec Scientific, Stratford, CT). *Variables: 0 Gy, 3 Gy, 6 Gy.*

Hyperthermia: Cells will be held at 45°C for 30 minutes either one hour before or one hour after irradiation with use of a water bath. *Variables: Hyperthermia before irradiation, Hyperthermia after irradiation, No hyperthermia.*

Cytotoxicity assays: Whether the cytotoxicity of is increased by the presence of MNP will be examined through the CCK-8 assay, the trypan blue assay, and colony forming assay to measure the cytotoxicity of MNP and hyperthermia.

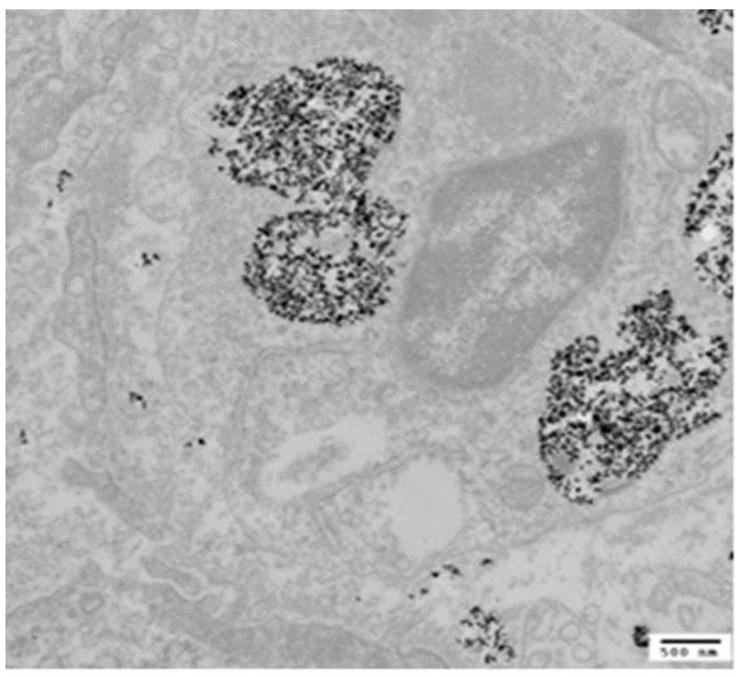


Figure 2: Transmission electron microscopy image of MNP located within an MTGB mouse mammary adenocarcinoma cell, following intratumoral injection. The clustering and intracellular uptake near nucleus may enhance the cytotoxicity of radiation therapy.

Future work: Magnetic nanoparticles are promising materials for hyperthermia treatment, as well as radiation sensitizing agents. If cytotoxicity is demonstrated in these studies, future work determine the mechanism of action. The subsequent studies will determine if reactive oxygen species (ROS) are increased with the combination of MNP, hyperthermia. By increasing the DNA damage due to ROS, MNP may have the potential to potentiate local radiation.

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