Comparative study of radiosensitizing effects of gold and aluminum nanoparticles; does atomic number matter?

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Heavy metal-based nanoparticles are being investigated as radiosensitizers to enhance radiotherapy. Although a couple of nano-radiosensitizers have progressed to the clinic, their mechanisms of action are yet to be elucidated [1]. While the conventional theory emphasizes the physical interactions between the nanoparticles and X-rays; we have recently shown that gold nanoparticles (AuNPs) downregulate the enzyme required for DNA damage repair, following radiotherapy [2]. This discovery spurred us to further investigate the radiosensitizing mechanisms of AuNPs compared to immunogenic aluminum nanoparticles (AlNPs) [3].

The bespoke AlNPs and AuNPs were synthesized and characterized in our laboratories. Next, their toxicity to 4T1 murine breast cancer cells was assessed, to identify biologically relevant concentrations at which the NPs induce minimal, moderate, and maximal toxicity. Next, their ability to attract RAW264.7 murine macrophages to 4T1 cells using a dual-chamber transwell system as well as induce phenotypic changes to the macrophages was studied. Their effects on the invasiveness of the 4T1 cells were also quantified using Matrigel® invasion assay. Finally, their radiosensitizing effects to 4T1 cells was investigated using the clonogenic assay following irradiation with 160 keV X-radiation.

Both nanoparticle types significantly increased the migration of RAW264.7 cells and induced morphological changes characterized by enlarged and hypervacuolized cells. While AuNPs significantly reduced the invasion of 4T1 cells with a dose-dependent trend, AlNPs surprisingly increased the invasiveness at the minimally toxic concentration and reduced at the other two concentrations. Finally, both NPs significantly increased the number of aborted colonies and reduced colony sizes compared to the untreated 4T1 cells with or without the lowest radiation dose (Figure 1).

These findings suggest that biological interactions between NPs and cells also plays an important role in radiosensitization, as well as the physical interactions between x-rays and nanoparticles. Therefore, high atomic number of a nanoparticle may not be essential for it to act as a radiosensitizer which has been validated in vivo, as well.

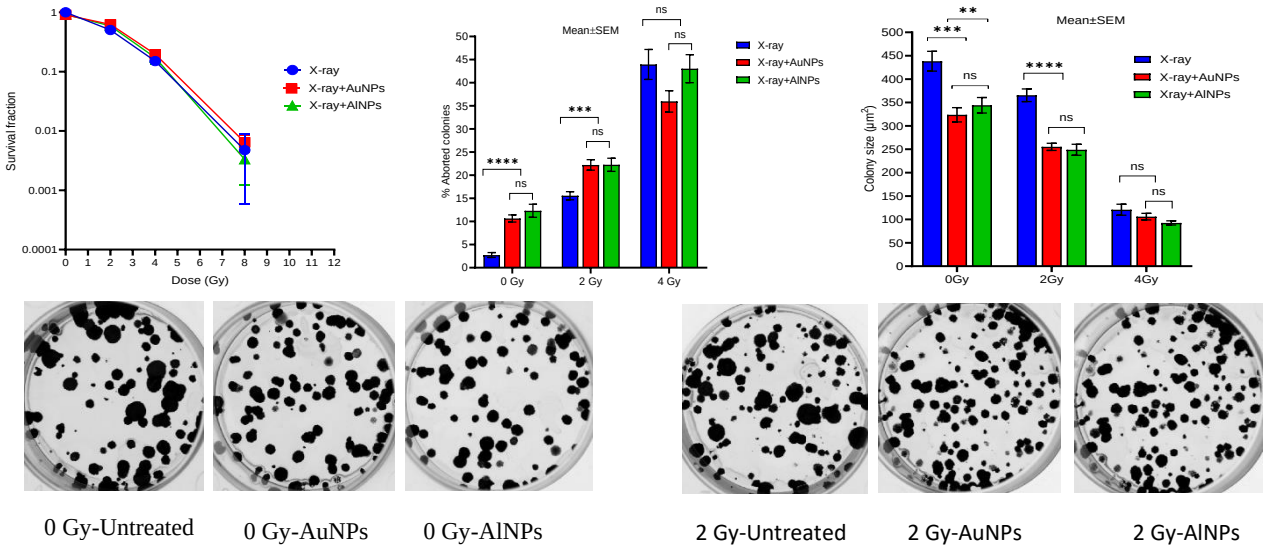

Figure 1: Examining radiosensitizing effects of AuNPs (0.5 nM) and AlNPs (2 µg/mL) at equivalently minimally toxic concentrations with 4T1 cells. The treatments did not significantly alter survival fraction but increase the number of aborted/small colonies at the lowest X-ray dose (2 Gy),
NS: not significant, **: P<0.01, ***: P<0.001, ****: P<0.0001.

References:

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