

Nano Congress 2019: Cancer nanotechnology: Gold nanostructures as a platform for combinational therapy in future cancer therapeutics - B. Devika Chithrani - University of Victoria

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The field of nanotechnology is currently undergoing explosive development on many fronts. The technology is expected to generate innovations and play a critical role in cancer therapeutics. Among other nanoparticle (NP) systems, there has been tremendous progress made in the use of gold nanostructures in cancer therapeutics. In treating cancer, radiation therapy and chemotherapy remain the most widely used treatment options and recent developments in cancer research show that the incorporation of GNPs into these protocols has enhanced tumor cell killing. These nanostructures further provide strategies for better loading, targeting, and controlling the release of drugs to minimize the side effects of highly toxic anticancer drugs used in chemotherapy and photodynamic therapy. In addition, the heat generation capability of gold nanostructures upon exposure to UV or near infrared light is being used to damage tumor cells locally in photothermal therapy. Hence, gold nanostructures provide a versatile platform to integrate many therapeutic options leading to effective combinational therapy in the fight against cancer. In this presentation, the recent progress in the development of gold-based nanostructures towards improved therapeutics will be discussed. A multifunctional platform based on gold nanostructures with targeting ligands, therapeutic molecules, and imaging contrast agents, holds an array of promising directions for cancer research.

Methods

Gold nanoparticles of size 10 nm were combined utilizing the citrate decrease strategy. The outside of The GNPs was changed with a peptide grouping (CKKKKKKGGRGDMFG) containing the RGD area and anticancer medication, bleomycin. Human bosom malignant growth cells (MDA-MB-231) were brooded with 0.3 nM grouping of GNP-sedate complex for 16 h before illumination with a 2 Gy single portion of 6 MV X-beams. After the treatment, cells were trypsinized and seeded in 60 mm dishes for clonogenic test. Harm to DNA was examined utilizing immunofluorescence measure.

Results

Malignant growth cells disguised with the GNP-tranquilize complex had a $32 \pm 9\%$ decline in cell endurance and measurably critical upgrade in DNA (deoxyribonucleic corrosive) harm when contrasted with control cells (lighted without any GNPs) in the wake of accepting a radiation portion of 2 Gy with 6 MV photons.

Conclusions

The trial results exhibit that GNP-interceded chemoradiation can possibly improve disease care soon through upgrade of the neighborhood radiation portion and controlled conveyance of anticancer medications.

Background

Malignant growth is one of the main sources of death in the worldwide and patients determined to have disease are relied upon to arrive at 22 million in the following two decades (Stewart and Wild 2014). The principle helpful modalities for malignant growth treatment other than medical procedure are chemotherapy and radiation treatment. In radiation treatment, vitality is stored in the objective zone, harming the disease cells or their vasculature instigating tumor demise or blockage of supplements (Hainfeld et al. 2006). In chemotherapy, cytotoxic chemotherapeutic medications are regulated to cause malignant growth cell demise through different systems relying upon the specific medication utilized (Crawford 2013). The joined utilization of radiation treatment and chemotherapy is being utilized in malignant growth treatment. Regardless of fruitful clinical utilization of joined radiation treatment and chemotherapy, the significant confinement of consolidating chemotherapy and radiation treatment is the ordinary tissue harmfulness, since either methodology can cause significant typical tissue poisonousness (Herscher et al. 1999; Ma et al. 2003). Symptoms of the treatment can be additionally limited through focused conveyance of anticancer medications and neighborhood improvement of the radiation portion. Gold nanoparticles (GNPs) can assume a noteworthy job in such manner, since GNPs can be utilized as radiation portion enhancers and anticancer medication transporters (Yohan and Chithrani 2014; Yang et al. 2016; Chithrani et al. 2010).

The utilization of high-Z components to improve radiation treatment results has extraordinarily expanded in the most recent decade, with an enthusiasm for GNPs. Early work by Hainfeld et al. 2004 indicated GNPs as radio sensitizers by showing regular tumor explicitness and considerable enhancements in tumor control in mice accepting kilo voltage radiotherapy minutes after intravenous infusion of GNPs. Past exploratory investigations indicated that GNPs upgrade radiation dosages in both the kV and MV go in vitro and in vivo (Chithrani et al. 2010; Hainfeld et al. 2004; Jain et al. 2011). In any case, more prominent radiation refinement was seen for cells lighted with lower vitality shafts (kV) than with higher

vitality bars (MV) (Chithrani et al. 2010; Rahman et al. 2009). Be that as it may, megavoltage vitality photons are commonly utilized in radiation treatment, since they can arrive at tumors found profound inside the patient. Consequently, in this examination, clinically important 6 MV vitality photons were utilized for radiation tests.

GNPs can likewise be utilized as an anticancer medication transporter (Ma et al. 2003; Jain et al. 2011). Bleomycin (BLM) has been picked as the anticancer medication for this examination. Bleomycin (BLM), utilized in this examination, is one of the most powerful normal enemy of tumor sedates and has been utilized for chemotherapeutic specialists in clinical medicines (Umezawa et al. 1980; Hecht 1986). The restorative adequacy, be that as it may, is restricted because of the reactions of the medication, most outstandingly aspiratory harmfulness (Georgelin et al. 2010). Bleomycin ties to the DNA and causes loosening up of the twofold helix and creates receptive oxygen radical species that causes DNA strand breaks (Siu and Malcolm 2005). The sulfate closure of bleomycin appends onto the outside of GNPs and this basic conjugation makes it a perfect medication to use in a combinational report test. The creators accept that NP-based stage talked about in this examination could be utilized later on for proficient and controlled conveyance inside the objective.

The utilization of GNPs as radiation portion enhancers and anticancer medication bearers has indicated promising outcomes as examined previously. The following legitimate advance was to test whether GNPs can give noteworthy improvement in consolidated chemoradiation. In this investigation, the GNP-intervened chemoradiation was tried just because with a clinically pertinent radiation wellspring of vitality 6 MV utilizing an in vitro bosom malignant growth cell model. MDA-MB-231 cells were utilized; since it has been researched in past gold nanoparticle (GNP) contemplates (Jain et al. 2011; Cui et al. 2014; Butterworth et al. 2010; Wang et al. 2015; Jain et al. 2014). This cell line has been seen to have moderately great GNP take-up and noteworthy

radiosensitization (McMahon et al. 2011). For instance, Jain et al. seen that the MDA-MB-231 cells had most prominent take-up of GNPs among the kind of cells (typical lung L132, prostate malignant growth DU145, bosom disease MDA-MB-231) utilized in take-up examines (Jain et al. 2011). MDA-MB-231 cells are additionally a triple negative cell line that are known to be progressively forceful, profoundly obtrusive with more awful visualization (Dai et al. 2017), in this manner chose to concentrate new choices to additionally improve the as of now utilized treatment modalities. What's more, MDA-MB-231 cells express elevated levels of integrins, including $\alpha\beta3$ receptors (Vloedgraven et al. 1997) and are focused by integrin-restricting proteins that will be utilized to adjust the outside of GNPs in this investigation.

It is likewise critical to think about the size of the GNP stage, since they extend from 1 to 100 nm. Littler GNPs include a superior entrance inside tumor network, despite the fact that the most elevated take-up at the cell level was seen as for GNPs of measurement 50 nm (Chithrani et al. 2006; Yohan et al. 2015; Gao et al. 2005). There have been endeavors made to improve the take-up of littler NPs. One of the methodologies is to conjugate NPs with a peptide succession containing integrin-restricting area, RGD (Yang et al. 2014). GNPs of distance across 10 nm was chosen for this examination, since their potential in a genuine tumor like condition is more prominent (Perrault et al. 2009).