Gold nanoparticles and their coatings, their effect on cells and their interaction with radiation

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Synopsis Two nanometre gold nanoparticles (AuNPs), bearing sugar moieties and/or polyethylene glycolamine (PEG-amine), were synthesised and evaluated for their in vitro toxicity and ability to radiosensitise cells with 220 kV and 6 MV X-rays, using four cell lines representing normal and cancerous skin and breast tissues. In addition to the observed intrinsic cancer-selective chemotoxicity, these AuNPs acted as radiosensitisers in combination with 220 kV or 6 MV X-rays. The ability of AuNPs bearing simple ligands to act as cancer-selective chemoradiosensitisers is a novel discovery that holds great promise in developing low-cost cancer nanotherapeutics

Radiotherapy is currently used in around half of all cancer treatments. Although generally effective, it is damaging to surrounding healthy tissues and needs to be improved by better targeting of cancer cells. One promising approach is to use nanoparticles composed of high atomic number elements, such as gold, hafnium, gadolinium, platinum or iron, which have large X-ray photon capture cross-sections, and can therefore locally increase the energy deposition near the nanoparticle through secondary electron emission from the nanoparticles [1]. Because of their biocompatibility and amenability to surface modification for tumour targeting, gold nanoparticles (AuNPs) have predominantly been used for tumour radiosensitisation studies [2]. AuNP radiosensitisation with external beam sources is more effective when using kilovoltage X-ray photons than with megavoltage X-ray photons, although megavoltage is preferable due to its deeper tissue penetration.

AuNPs are generally non-toxic, except at high concentrations where they generate appreciable levels of reactive oxygen species (ROS) [3]. AuNPs smaller than 6 nm are preferable for therapeutic applications, since these can be excreted from the body by renal clearance, reducing long-term exposure to other organs [4].

Chemoradiosensitisers are dual-action drugs that are directly toxic to cells and also render the DNA more susceptible to radiation-induced damage. They include inhibitors of topoisomerase I, poly ADP-ribose polymerase (PARP), histone deacetylase (HDAC) and heat-shock protein 90 (Hsp90). However, current chemoradiosensitisers lack the ability to locally increase the deposited dose of radiation within cells. With that goal in mind, we have designed novel 2 nm gold nanoparticles coated with sugar ligands to improve aqueous solubility [5], and PEG-amine to improve biocompatibility [6] and cellular uptake [7]. Although originally envisaged as radiosensitising platforms to co-deliver anti-cancer drugs, these novel AuNPs were found to be selectively toxic for cancer cells at nanomolar concentrations and also act as radiosensitisers.

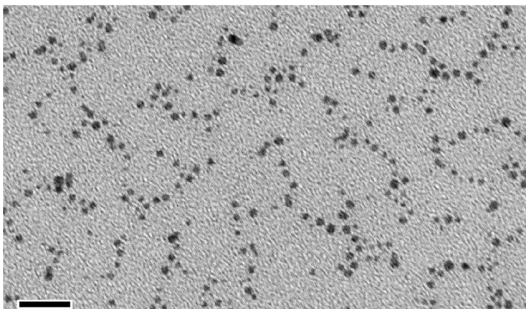

Figure 1. Representative TEM image, showing 50:50 βGlc:PEG-amine. Scale bar is 20 nm.

References

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