Cancer Nanotechnology: Design of Multimodal Gold Nanoparticle-based Chemotherapeutics

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Introduction

Gold nanoparticles exhibit great potential for anticancer applications due to their biocompatibility, tuneable optical properties, and advanced surface functionalisation[1]. Nanomaterials exposed to biological fluids may generate a coating of biomolecules, if not prevented by surface chemistry design, known as 'biomolecular corona' which confers biological identity of nanoparticles[2]. Therefore analysing the bio-nano interactions can be challenging and requires multidisciplinary approaches. Various routinely available particle characterisation techniques result in biased and often limited results[3]. Routinely available assays for drug screening require adaptation to account for often complex physico-chemical properties of nanoparticle-drug carries and offer a realistic assessment of the *in situ* biomolecule-nanoparticle interactions[4].

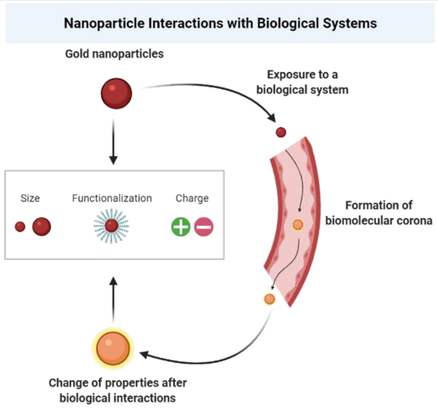

Figure 1. Interaction of gold nanoparticles with biological fluids.

Gold Nanoparticles

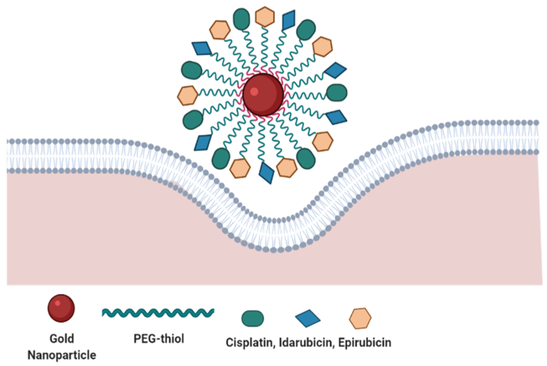

Figure 2. Conjugation of several chemotherapy drugs with PEG-thiol GNPs.

Our research focuses on the design of multimodal GNPs containing multiple functionalities within the nanoparticle ligand shell conferring advanced particle functionality

- Use of the functional PEG-thiols to ensure colloidal stability
- Use of anticancer drugs for improved drug delivery
- Generation of novel nanoparticle-based therapeutic tools for enhanced X-ray radiation dose enhancement

Multimodal Gold Nanoparticles

Multimodal nanoparticles by design offer advanced therapeutic approaches [5]:

- Theranostic function (treatment and detection in one platform)
- Customisable precision medicine
- Targeted drug-delivery
- Minimised side effects
- Increased X-ray radiation dose delivered

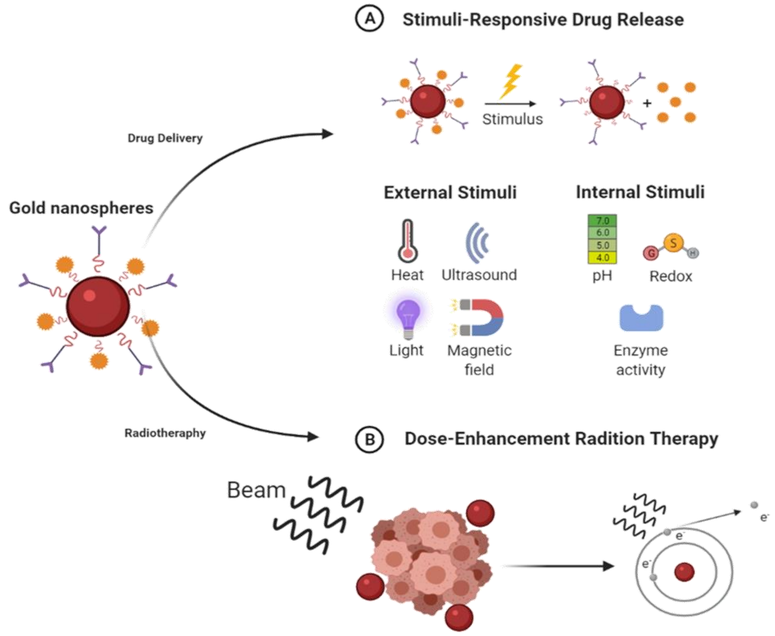

Figure 3. Gold nanoparticle application as multimodal targeted drug delivery and radiation dose delivery..

Differential Centrifugal Sedimentation (DCS)

One of the most significant steps towards the designation of multimodal GNPs is an accurate characterisation of particles. Differential Centrifugal Sedimentation (DCS) offers high-resolution sizing of functionalised nanoparticles and *in situ* characterisation of the bio-nano interface[6].

Advantages of DCS:

- High resolution, accuracy & precision
- Sensitivity
- Dynamic range
- Analysis of the entire sample with rapid detector response

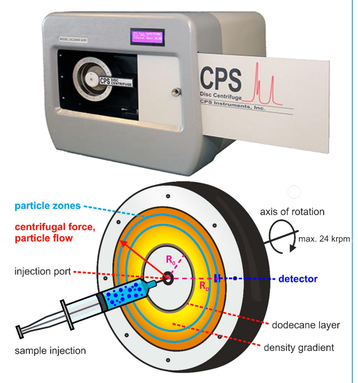

Figure 4. DCS machine and its mechanism of action.

High-Resolution Sizing of Gold Nanoparticles

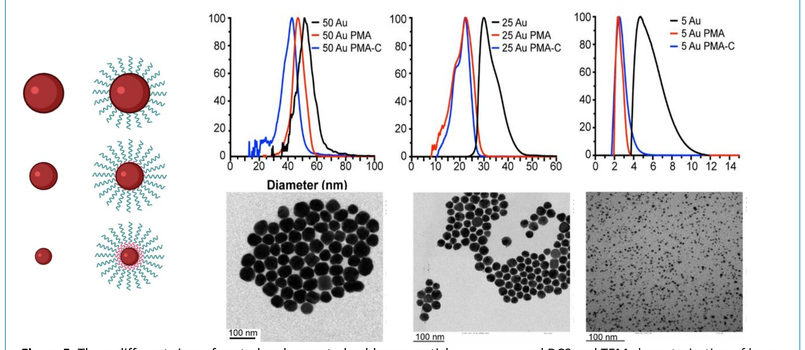

Figure 5. Three different sizes of coated and uncoated gold nanoparticles are prepared DCS and TEM characterisation of bare and polymer coated 5 nm, 25 nm, and 50 nm GNPs [7].

Characterisation of biomolecular corona formation

After sizing of both uncoated and coated GNP, the DCS can is evaluated whether it provide meaningful information on the colloidal stability of particles after the presence in a complex biological fluid, such as human plasma, in order to characterise the gold-biomolecular corona complexes (Au-PMA-C). To achieve this goal, NP-biomolecular corona complexes "in situ" is characterised with DCS, after incubation in blood plasma.

A shift is observed between the PMA coated particles and the uncoated gold (blue and black lines) and another shift after the particles *in situ* in blood plasma were incubated (red and blue), confirming the presence of the biomolecular corona with DCS [7].

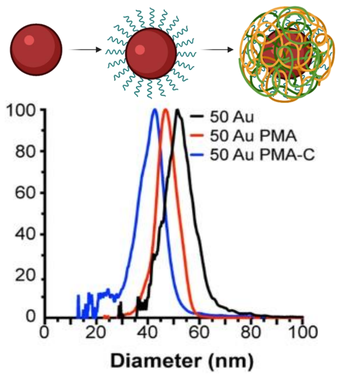

Figure 6. DCS and TEM characterisation of bare and polymer coated 5 nm, 25 nm, and 50 nm GNPs [5].

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