The Influence of Surface Protein Adsorption on Gold Nanoparticle Intratumoral Distribution and Retention

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Background/Introduction

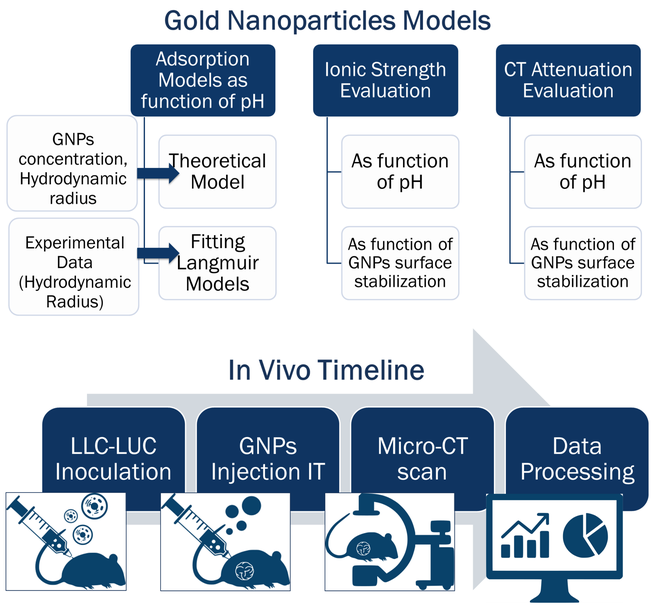
The biological effects of GNPs in the tumor microenvironment, including the particle-protein interaction and the consequent impact on cellular pathways and contrast enhancement remain unclear [1]. In this regard, further investigations regarding the effects of GNP-surface passivation on X-ray attenuation as well as in vivo biodistribution will clarify several aspects still under discussion from the scientific community, which so far have limited the clinical translation of their theranostics applications cancer-related [2-4].

Purpose/Objectives/Hypothesis

- Evaluate the influence of protein surface adsorption on the GNP biodistribution in Lewis Lung Carcinoma (LLC) tumor-bearing mice using high resolution Computed Tomography (CT) preclinical imaging.

- Hypothesis: the adsorption of proteins on the GNP surface can influence the intratumoral distribution and retention of the particles.

Methods



Result

Figure 1. GNPs Characterization and In Vitro Study. Absorbance peak in the UV-Vis spectrum of the gold nanoparticles citrate stabilized and functionalized with bovine serum albumin as well as their size and shape captured by electronic microscopes (A). The pH influence on the adsorption of proteins on GNPs with a transition from monolayer to multilayer structures (B). GNPs presents higher X-ray attenuation properties compared to a standard contrast agent (C). In vitro study to evaluate the uptake of GNPs by Lewis lung carcinoma cells: optical and electronic microscopy images of treated cells and incubated for 24h (D) and trypan blue assay for cytotoxicity (E). Significance (p*<0.05) in the internalization depending on the surface functionalization.

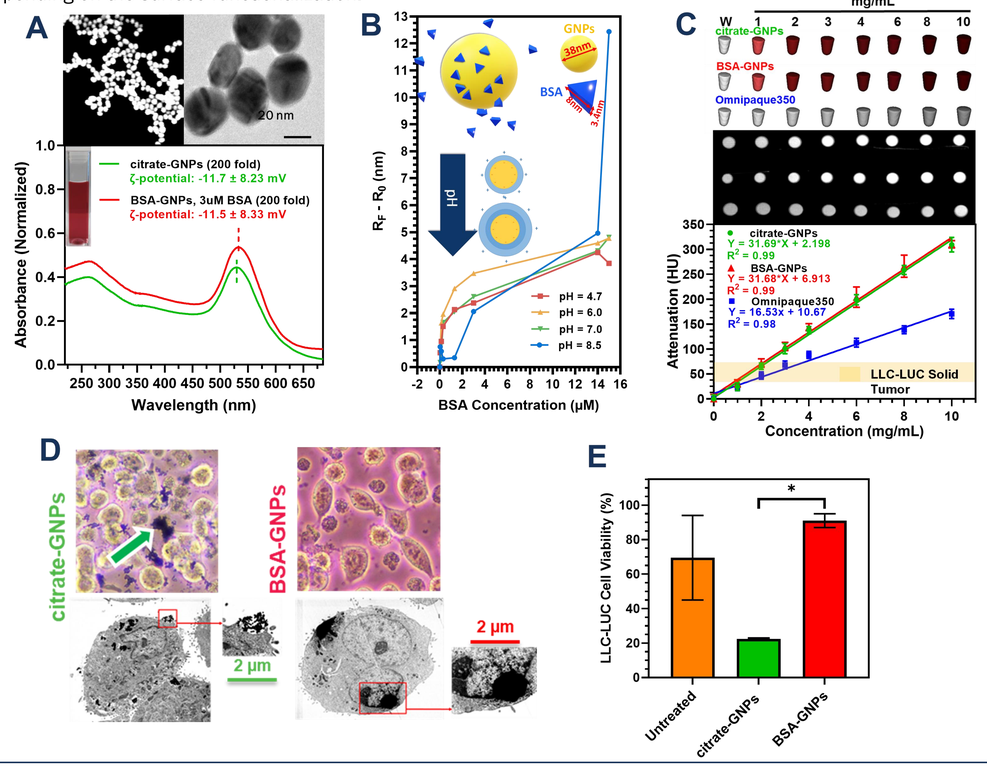
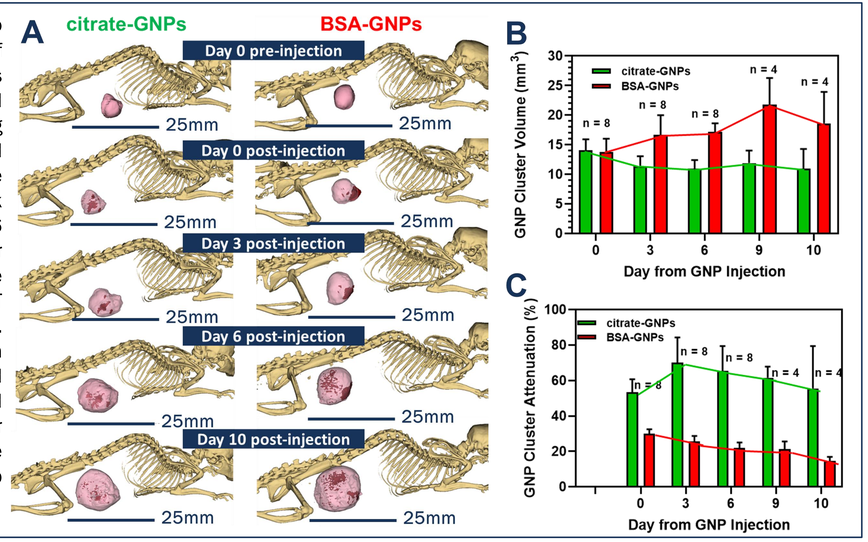


Figure 2. In Vivo Study. 3D Rendering of concentrated GNPs intratumorally injected into Lewis Lung Carcinoma solid tumors grown on the right flank of 6-week old female C57BL/6 mice (A). GNP cluster volume over time calculated using CT follow-up images (B). Mean attenuation values in Hounsfield Units (HU) calculated within the GNP cluster volume over time using CT follow-up images (C).



Results/Implications

- Intratumoral biodistribution of GNPs is dependent on surface passivation.
- BSA-GNPs perfusion along the tumor periphery with few depositions throughout the entire tumor volume diverges from that obtained after unpassivated, citrate-GNP intratumoral injections.
- This response can be explained by the abnormal and heterogeneous vascular structure of the LLC tumor, suggesting perfusion rather than permeability as the limiting factor for tumor accumulation of the GNPs.

Conclusions

Outcomes of the research: surface passivation of GNPs is able to influence the mechanism of cellular uptake in vitro and their in vivo intratumoral diffusion.

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References

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