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Imaging and Magnetic Hyperthermia of Angiopepsin-2 Conjugated Titanium@Iron-Gold Alloy Nanoparticles for Glioma Theranostics

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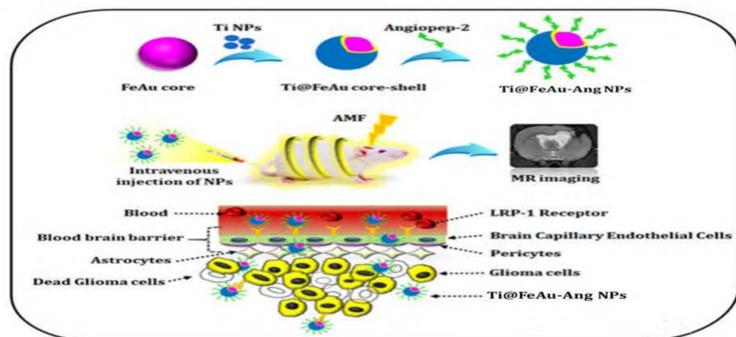


Abstract

Gliomas exhibit a low prognosis with death occurs within 15 month after diagnosis. Owing to the lower therapeutic window, ineffectiveness and greater cytotoxicity, primarily chemotherapy is inefficient to target and well cure glioma. In this study, we constructed Angiopepsin-2 conjugated Titanium@Iron-Gold nanoparticles (Ti@FeAu-Ang NPs) which allow to target the glioma and eliminate it with alternating magnetic field (AMF). The obtained results revealed that the Ti@FeAu-Ang NPs were super paramagnetic with improved T2 contrast image of glioma, and exhibited a 12°C temperature increase after AMF exposure, indicating the potential applications for hyperthermia therapy and MRI contrast agent. Cellular uptakes by C6 glioma cells were higher as compared to L929 fibroblasts, stating the well glioma targeting ability and elevated killing ability by cause of AMF. Further, histochemical analyses have shown the augmented necrosis led by Ti@FeAu-Ang NPs treatment. In conclusion, this study provides a novel application toward to nanomedicine and cancer theranostics for glioma.

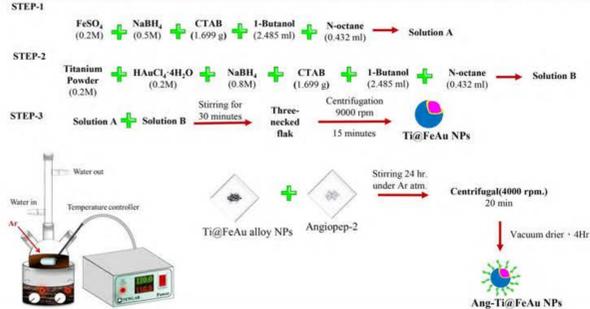
Key Words: Glioma, Hyperthermia, Magnetic resonance imaging, Angiopepsin-2.

Schematic Representation

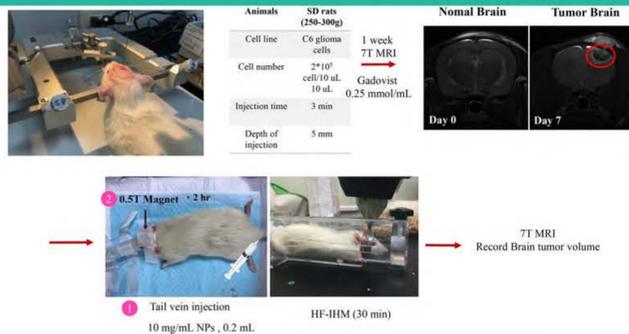


Experimental

Preparation of Ti@FeAu NPs and Ti@FeAu-Ang NPs

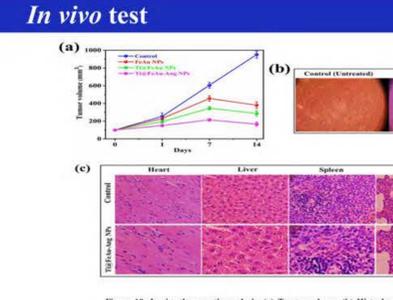
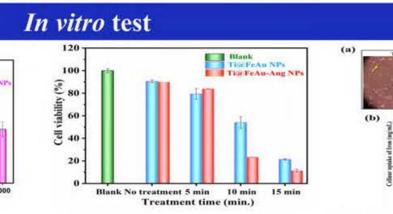
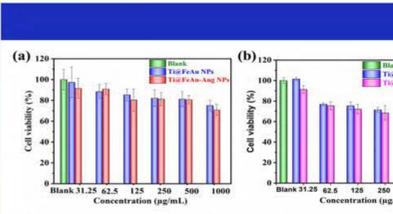
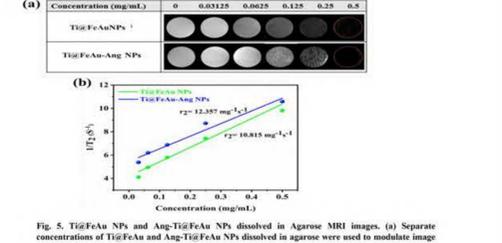
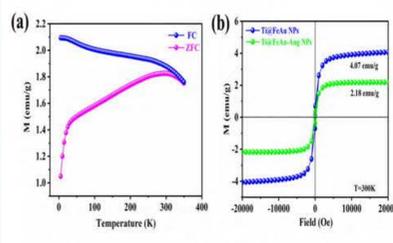
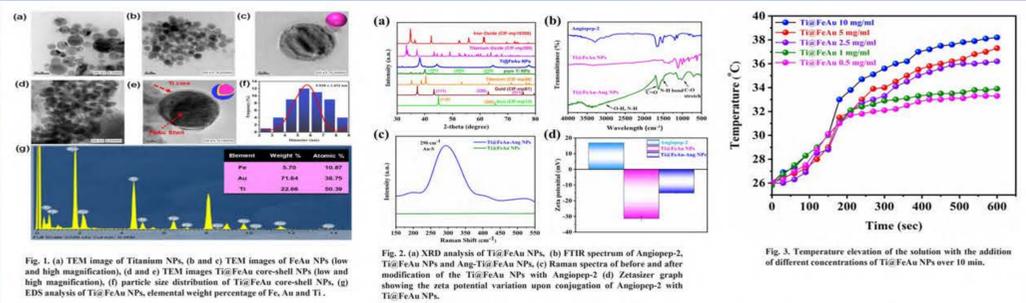


Brain tumor implantation and magnetic hyperthermia therapy



Results & Discussion

Characterization



Summary

- By FTIR and Raman spectroscopy, the results showed that Angiopepsin-2 was successfully modified on the surface of Ti@FeAu-Ang NPs.
- Upon exposure to AMF, Ti@FeAu-Ang NPs exhibited superparamagnetic behavior and produced sufficient heat in a concentration-dependent manner.
- Enhanced targeted delivery of Ti@FeAu-Ang NPs due to enhanced cellular uptake, and apoptosis was shown using an in-vitro model. Ti@FeAu-Ang NPs exhibited enhanced MRI imaging contrast.
- Moreover, the selective cellular uptake of Angiopepsin-2-conjugated Ti@FeAu NPs by glioma cells, make this a promising platform for in-vivo tumor therapy.
- In-vivo results confirmed that intravenous injection of Ti@FeAu-Ang NPs on rats effectively inhibited tumor growth with AMF stimulation without inflicting damage to major organs. Therefore, the CPP-conjugated core-shell NPs can serve as a new platform for simultaneous nanotheranostics and advanced imaging.



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