Well-defined Spiky Gold Nanoparticles for Effective Photothermal Cancer Therapy in the Second NIR Window

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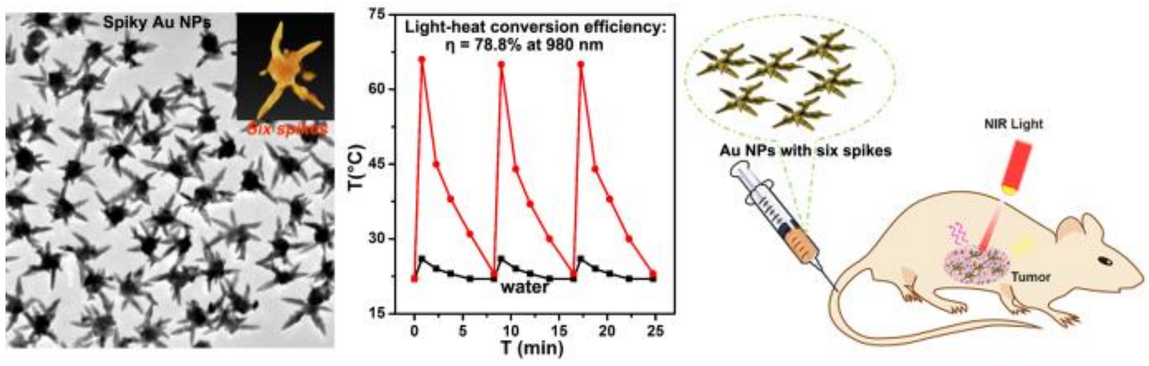
Abstract: In this work, we successfully prepared spiky gold nanoparticles (spiky Au NPs) with a controlled number of. Their overall size and morphology were judiciously adjusted to render their maximum SPR peaks locate in the second NIR window and also achieve a higher absorption to scattering ratio. As a result, the spiky Au NPs exhibited the highest light-heat conversion efficiency (78.8%) under irradiation of 980 nm light. After surface PEGylation and conjugation with lactoferrin (LF) ligand on the resulting spiky Au NPs, they displayed long circulation time (blood circulation half-life of ~ 600 min) and high tumor accumulation in vivo after intravenous injection, allowed complete ablation of tumors without recurrence after 3 min light irradiation at 980 nm.

Introduction



Photothermal (PT) therapy has been intensively developed as a minimally invasive approach for cancer treatment. Near-infrared (NIR) light especially in the wavelength range of 900 – 1400 nm, known as second NIR (NIR-II) window, is more favourable for PT therapy, because the light in NIR-II window can penetrates into deep tissues (up to 10 mm), in comparison with the light in traditional first NIR window (700-900 nm). Thus, the key component of PT therapy, the PT transducer, should have high conversion efficiency of light in NIR-II window, i.e. 980 nm rather than 808 nm, into heat. Taking into account the applicability for *in vivo* PT therapy, the overall size of spiky Au NPs should be controlled in the range of 50-200 nm, which is a prerequisite for cancer accumulation based on the well-known enhanced permeability and retention (EPR) effect. Therefore, a design of spiky Au NPs with controlled morphology is necessary, which have controlled number (<10) of spikes on a small core with diameter less than 60 nm as well as their overall size below 200 nm.

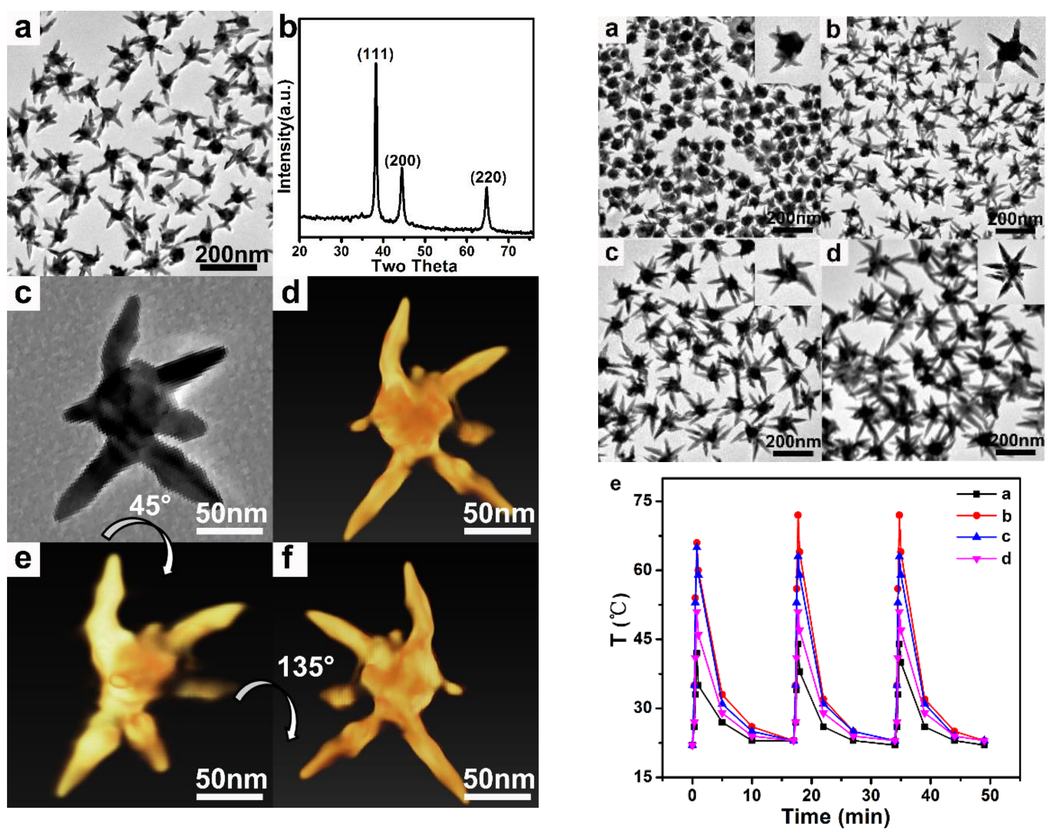


Fig.1 Morphology and photothermal effect of spiky Au NPs.

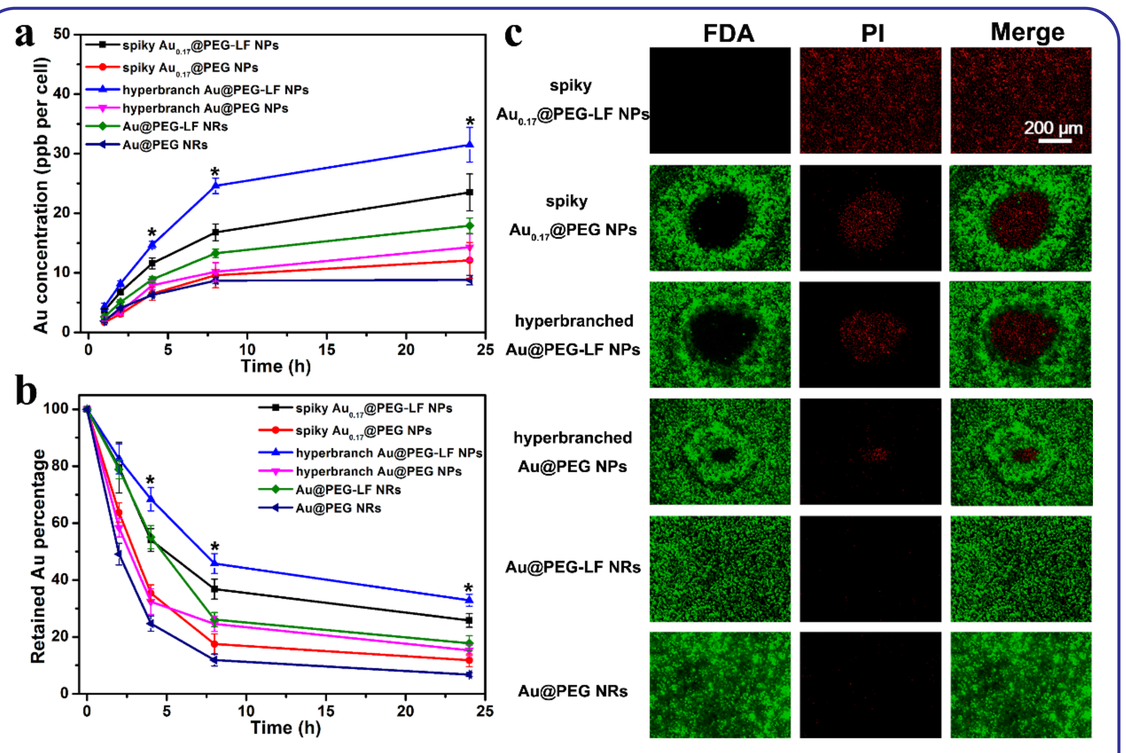


Fig. 2 (a) Amount of Au NPs ingested by HepG2 cells. (b) The percentage of the remaining Au NPs in the cells after they are exposed to different Au NPs for 24 h. (c) HepG2 cells incubated with spiky $Au_{0.17}$@PEG-LF NPs (Row 1), spiky $Au_{0.17}$@PEG NPs (Row 2), hyperbranched Au@PEG-LF NPs (Row 3), hyperbranched Au@PEG NPs (Row 4), Au@PEG-LF NRs (Row 5), and Au@PEG NRs (Row 6), then recieved irradiation by 980 nm NIR light (0.5 W/cm^2) for 2 min.

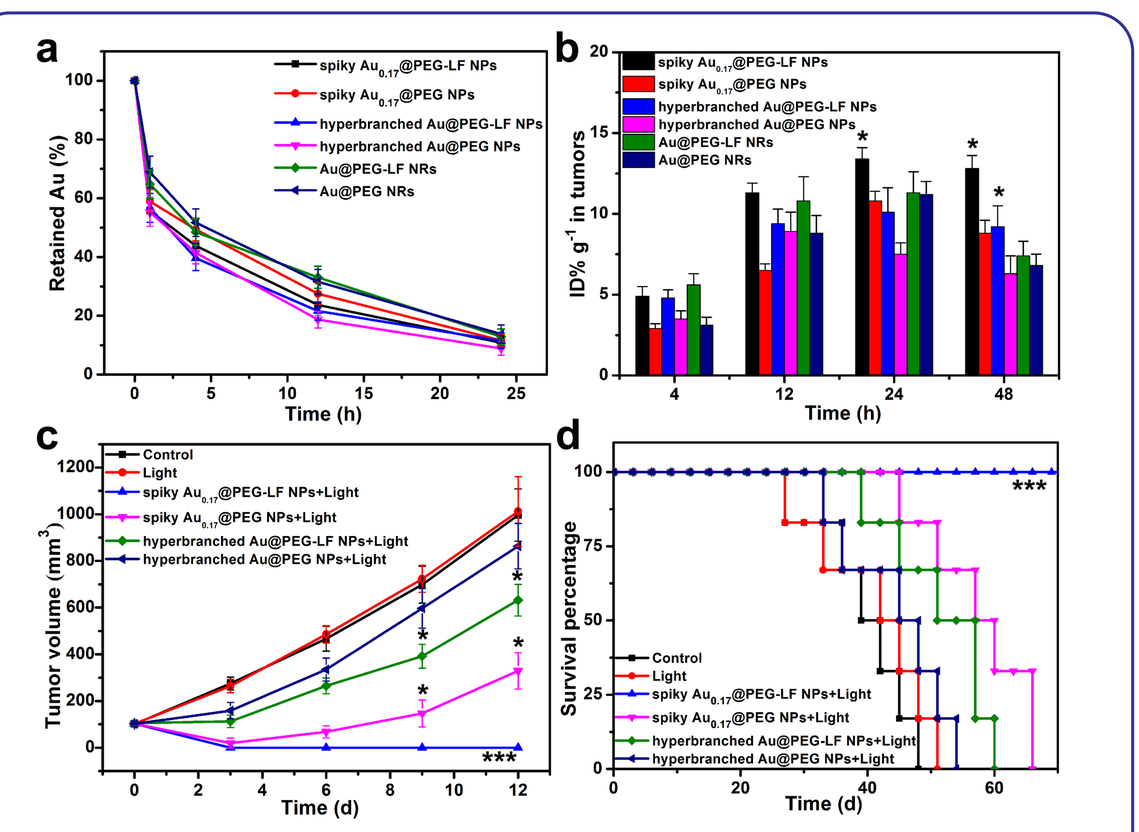


Fig. 3 (a) Plot of the amount of different Au NPs in mice blood versus circulation time after intravenous injection. (b) Histograms of the tumor concentration of different Au NPs after various times post intravenous injection. ID stands for normalized injection dosage. (c) *In vivo* tumor growth inhibition curves for mice received different Au NPs and 3 min 980 nm light irradiation (0.5 W/cm^2, n = 5 for each group). (d) Kaplan-Meier plots showing the percentage of animals remaining in the study as a function of time. * and *** indicate significant difference at $p < 0.05$ and $p < 0.001$ level.

Conclusions

We successfully prepared spiky Au NPs exhibit a light-heat conversion efficiency as large as 78.8% under irradiation of 980 nm light, which is the best for currently accessible gold-based PT transducers. After their surfaces are PEGylated and then conjugated with lactoferin, the spiky Au@PEG-LF NPs display long circulation time and high tumor accumulation in vivo after intravenous injection. Tumors can be completely ablated without recurrence by the spiky Au@PEG-LF NPs together with 3 min light irradiation at 980 nm.

Acknowledgement

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References

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