Hyaluronic acid- modified gold nanoparticles with different morphologies for tumor diagnosis and photothermal therapy

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Introduction

Multifunctional nanoprobes in tumor diagnosis and therapy drew more and more attention, but simple and effective preparation of the theranostic nanoplatforms is still a urgent task. In this study, we reported the synthesis of fluorescence labelled thiol-HA(NB-HA-SH) coating gold nanorod(AuNR) and gold nanosphere(AuNS). [1] HA could significantly increase biocompatibility, stability and enhance endocytosis rate of some tumor cells by specific combine the over-express CD44 receptors. [2] The fluorescence molecules (nile blue) quenched on the surface of gold nanoparticles due to fluorescence resonance energy transfer(FRET) and recovered after the HA degrade by the ROS or HAdase in the cells. Notably, the AuNR could effectively generate photothermal therapy effect by strong absorption of near-infrared(NIR) light.[3] Different morphologies of gold nanoparticles for tumor diagnosis and photothermal therapy performances were also investigated.

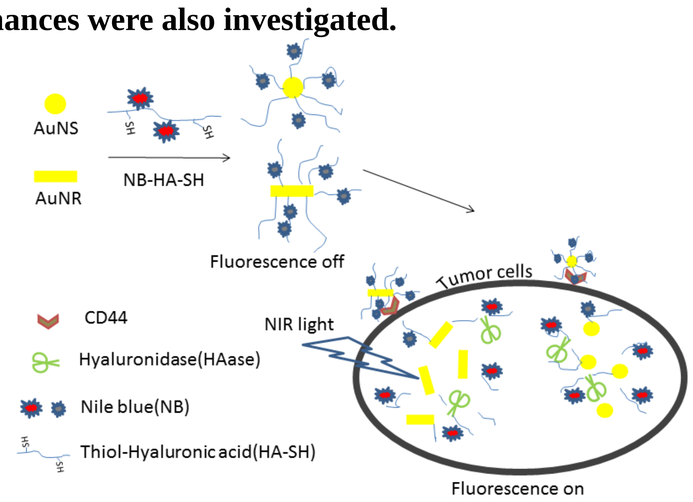

Fig. 1 Illustration of hyaluronic acid modified gold nanoparticles with different morphologies and their cellular behaviours.

Results & Discussion

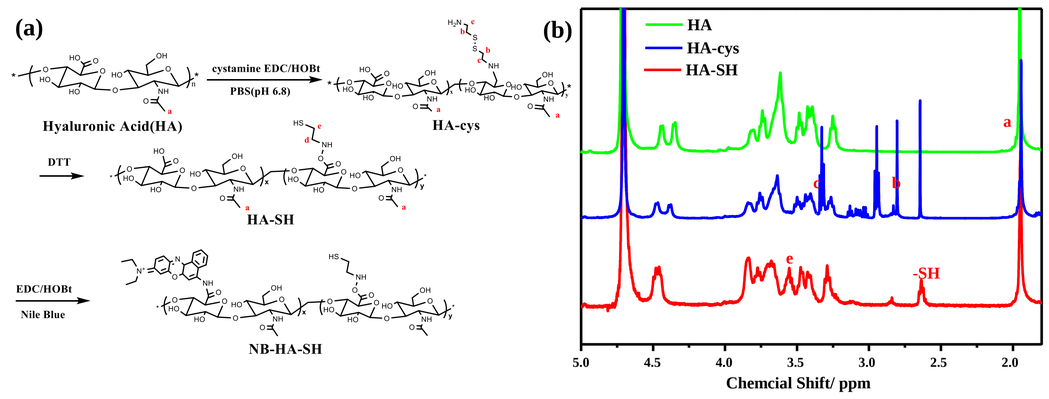

Fig. 2 (a) Synthesis process of NB-HA-SH and (b) ^{1}H NMR HA-SH

➢HA-SH were successfully synthesized according to ^{1}H NMR and thiol grafting degree to the repeat units of HA is 13%.

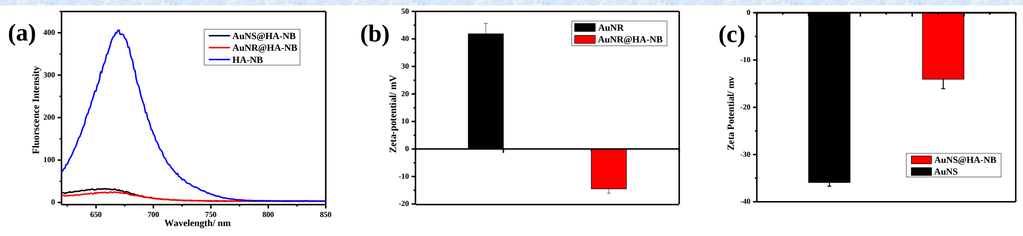

Fig. 3 (a) Fluorescence intensity change, zeta-potential change of (b)AuNR and (c)AuNS after coating with NB-HA-SH.

➢The fluorescence dramatically quenched on the surface of gold nanoparticles due to the FRET. The zeta-potential of AuNR and AuNS strongly changed after coating with NB-HA-SH.

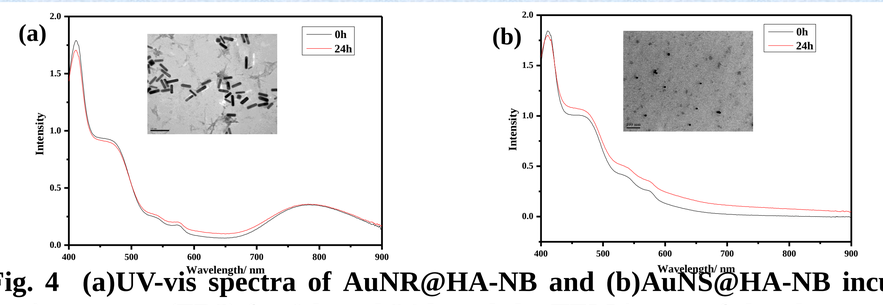

Fig. 4 (a)UV-vis spectra of AuNR@HA-NB and (b)AuNS@HA-NB incubated with fetal bovine serum (FBS) for 0 h and 24 h and the TEM image of the above particles incubated with FBS for 24 h.

➢HA modified AuNR and AuNS showed excellent stability in FBS environment.

➢TEM images confirmed the gold nanoparticles kept their morphologies with FBS.

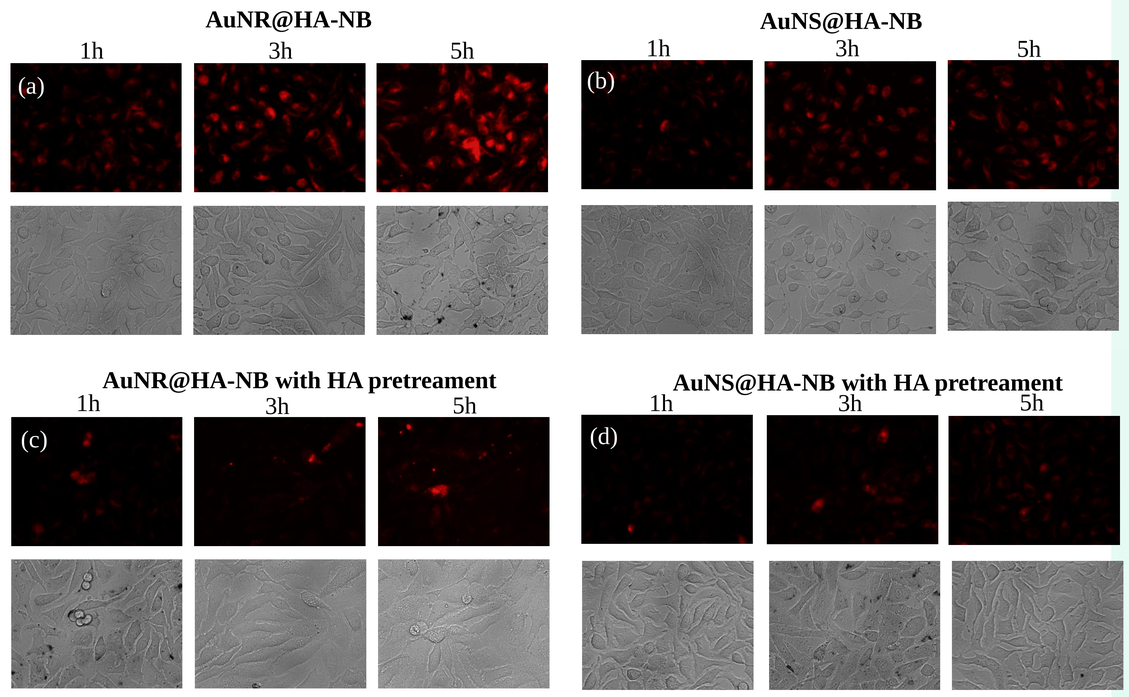

Fig. 5 Fluorescence images of MCF-7 cells incubated with (a) AuNR@HA-NB and (b) AuNS@HA-NB and (c) (d) corresponding control groups with HA pretreatment for 4 h.

➢Fluorescence intensity enhanced over time because of the fluorescence recoverd after HA degradation and accumulation of the dye molecules. AuNR@HA-NB performance better than AuNS@HA-NB in the same time probably due to the larger load capacity and the rod shape. Pretreating with HA can effectively inhabited the MCF-7 cells endocytosis of HA-NB coated gold nanoparticles for the reason that the CD44 receptors were inhabited by free HA.

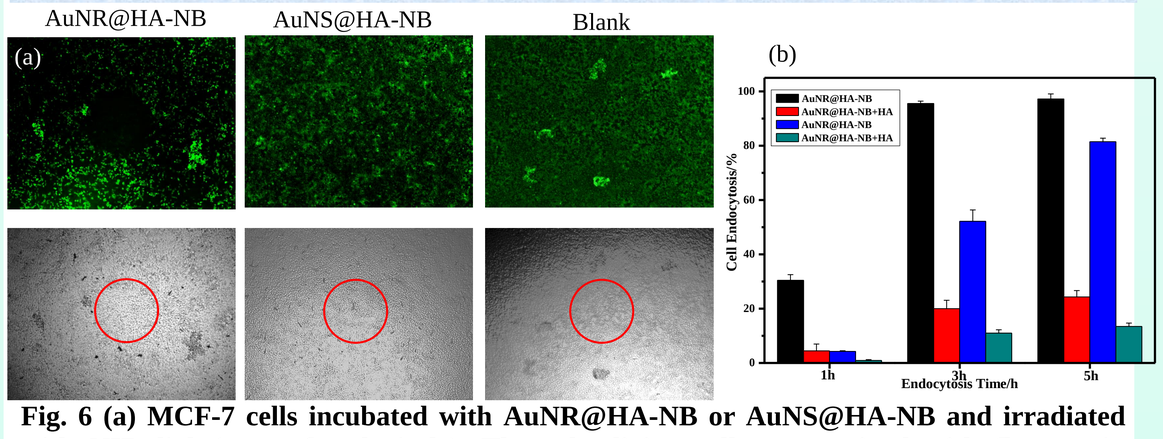

Fig. 6 (a) MCF-7 cells incubated with AuNR@HA-NB or AuNS@HA-NB and irradiated with NIR light(area of red circle). Then the living cells was stained with fluorescein diacetate(FDA). (b) Flow cytometry result of MCF-7 incubated with different shape of nanoparticles with or without HA pretreatment.

➢AuNR could kill MCF-7 cells under NIR irradiated while the AuNS cannot.

➢ Flow cytometry result reconformed the target ability of AuNR@HA-NB and AuNS@HA-NB to MCF-7 cells and the morphologies of the nanoparticles could affect endocytosis behavior.

Conclusion

In summary, owing to the excellent biocompatibility and biodegradability of HA, the combined nanoparticles remained stable in the serum treatment. Moreover, the targeting ability of HA to CD44 receptor-overexpressing cancer cells was also verified via competitive inhibition experiment. Interestingly, compared with the spherical nanoparticle, the rod-shaped nanoparticle appeared fluorescence more quickly for the reason that the large size affords the AuNR ability to carry more fluorescent molecules in a single nanoparticle. Also, the AuNR can easily absorb and produce heat which result the photothermal therapy effect. Small, stable, versatile nanoparticles provided additional possibilities to cell imaging and targeting tumor medication.

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References

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