Supporting Information

Surfactant-Free Preparation of Au@Resveratrol Hollow Nanoparticles with Photothermal Performance and Antioxidant Activity

Wenjing Wang,[†] Qi Tang,[‡] Tianrong Yu,[§] Xing Li,[‡] Yang Gao,[§] Jing Li,[†] Yi Liu,[†] Li Rong,[∥,*] Zhigang Wang,[§,*] Hongchen Sun,[‡,*] Hao Zhang,[†,*] and Bai Yang

[†]State Key Laboratory of Supramolecular Structure and Materials, College of Chemistry, Jilin University, Changchun 130012, P. R. China

[‡]School of Stomatology, Jilin University, Changchun 130041, P. R. China

[§]Institute of Atomic and Molecular Physics, Jilin University, Changchun 130012, P. R. China

[∥]First Hospital of Jilin University, Jilin University, Changchun 130021, P. R. China.

[*]Address correspondence to hao_zhang@jlu.edu.cn; hcsun@mails.jlu.edu.cn; wangzg@jlu.edu.cn; rongli6262@hotmail.com.

Figure S1. TEM image (a), UV-vis absorption spectrum (b), and hydrated diameter statistics (c) of the sacrificial Ag seeds.

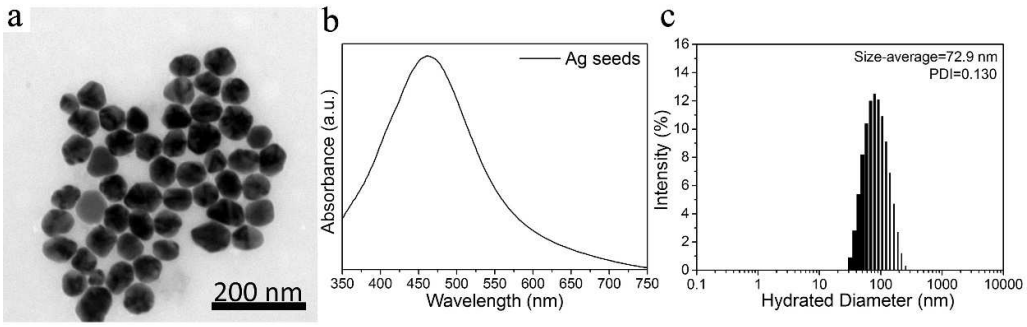


Figure S2. The scheme for the preparation of Au@Res HNPs. (a) $HAuCl_4$ aqueous solution. (b) $HAuCl_4$ solution with the addition of resveratrol for 15 min. (c) The further addition of Ag seeds to produce Au@Res HNPs. The amount of $HAuCl_4$, resveratrol, and Ag seeds is 100, 60, and 1200 μL. The preparation is operated at room temperature.

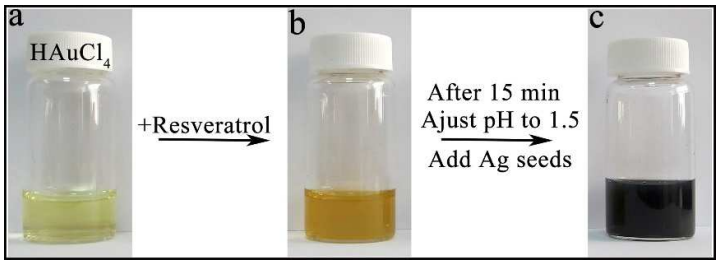


Figure S3. Hydrated diameter statistics of Au@Res HNPs by DLS measurement. The PDI is 0.105, indicating the good monodispersity of Au@Res HNPs.

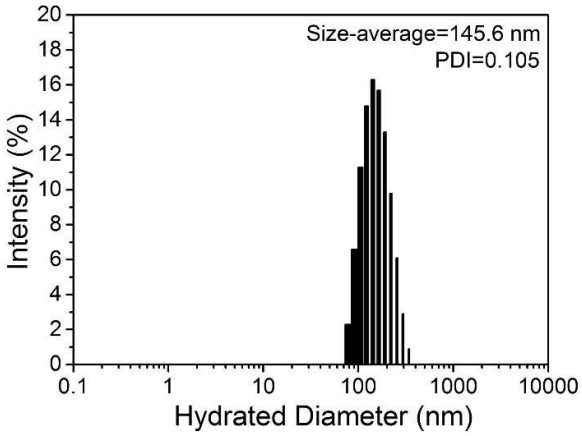


Figure S4. EDX spectrum of Au@Res HNPs, which reveals that the Au@Res HNPs are solely composed of Au element without Ag. This means that only Au is reduced by resveratrol.

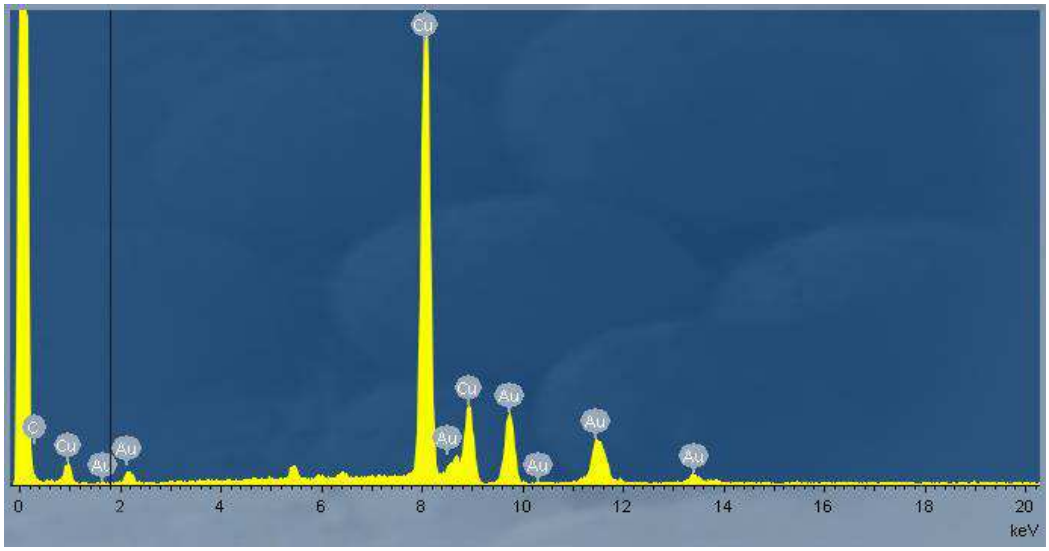


Figure S5. (a) XPS analysis of Au@Res HNPs and resveratrol. The Au 4f (b) and C 1s (c) spectra are also shown. The XPS spectra proves the existence of C=C and C-O bond.

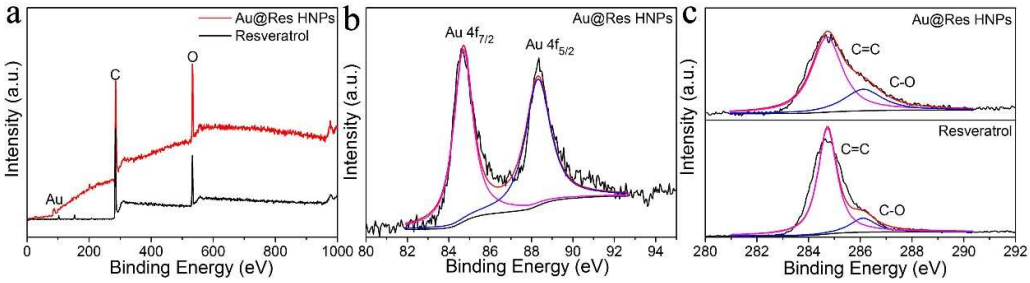


Figure S6. TGA of Au@Res HNPs. The amount of resveratrol shell is calculated as 8 wt%.

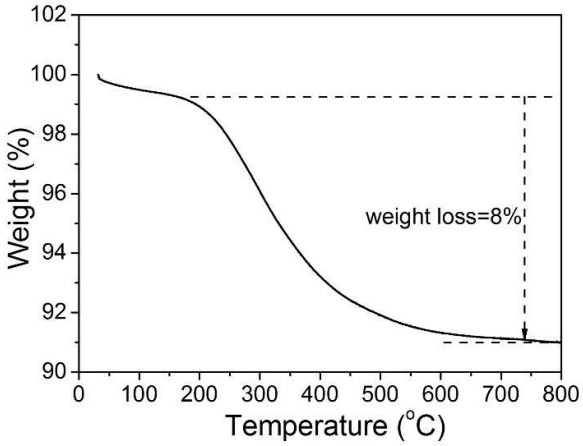


Figure S7. UV-vis absorption spectra of resveratrol (black), acidic ammonium persulfate (red), and the mixture of resveratrol and acidic ammonium persulfate (green). The resveratrol is oxidized by acidic ammonium persulfate, represented by the decrease of 314 nm absorption and the appearance of 284 nm absorption.

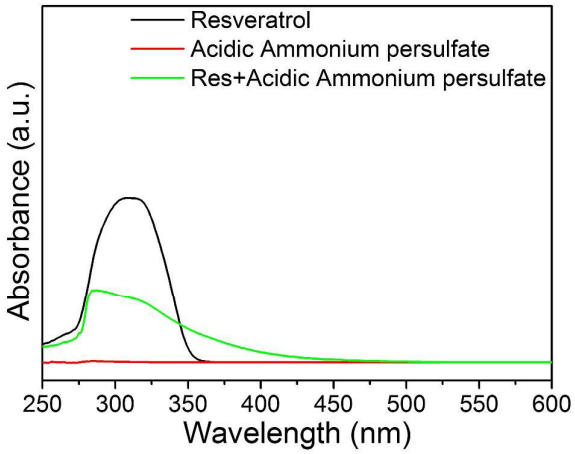


Figure S8. TEM image of small gold nanoparticles, which are prepared by mixing $HAuCl_4$ and resveratrol for 28 min.

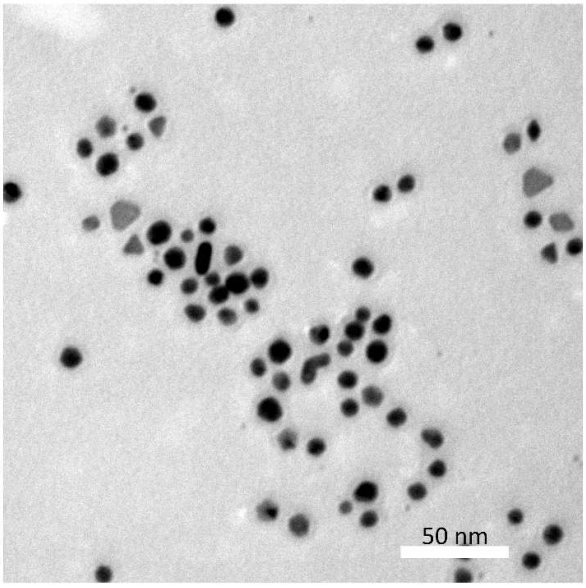


Figure S9. TEM image (a), and EDX spectrum (b) of the dendritic nanoparticles. EDX result shows that the component of the dendritic nanoparticles is gold.

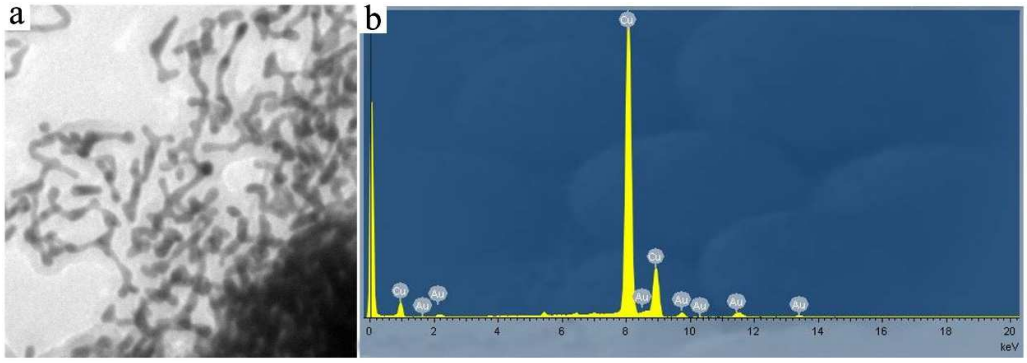


Figure S10. Additional experiments to prove the mechanism of the formation of dendritic nanoparticles. TEM images (a, c) and EDX spectra (b, d) of dendritic and quasi-spherical nanoparticles are compared. The nanoparticles are prepared by mixing $HAuCl_4$ and resveratrol with 0 (a) and 15 min (c) pre-reaction at room temperature, then the growth of nanoparticles is trigged by adding $AgNO_3$ instead of Ag seeds. The amount of $HAuCl_4$, resveratrol, and $AgNO_3$ is 100, 60 and 36 μL of 0.1 M aqueous solution.

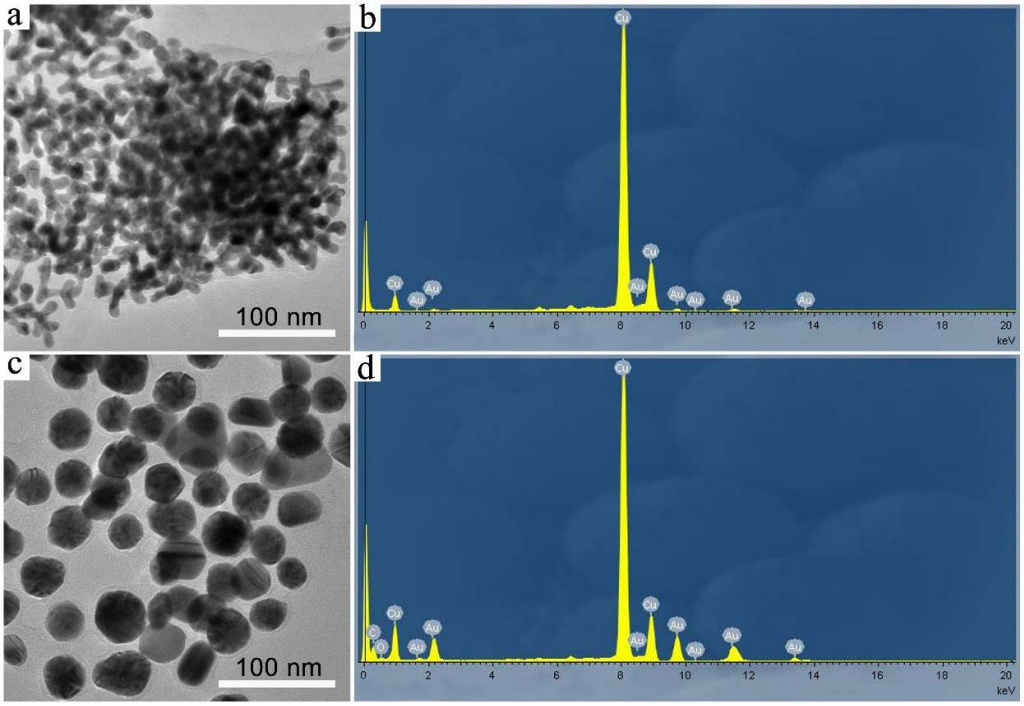


Figure S11. The photograph of the mixed solution of resveratrol and $AgNO_3$. The amount of resveratrol and $AgNO_3$ is 60 and 36 μL of 0.1 M aqueous solution. The white precipitate is resveratrol. This excludes the redox reaction between Ag^+ and resveratrol.

Figure S12. TEM images (a-e) and UV-vis absorption spectra (f) of Au@Res HNPs that are prepared by altering the dosage of resveratrol from 20 (a), 40 (b), 60 (c), 80 (d) to 100 μL (e). While the concentration of $HAuCl_4$ and Ag seeds are 100 and 1200 μL. The incubation duration and solution pH are fixed at 15 min and 1.5. The scale bar is 100 nm.

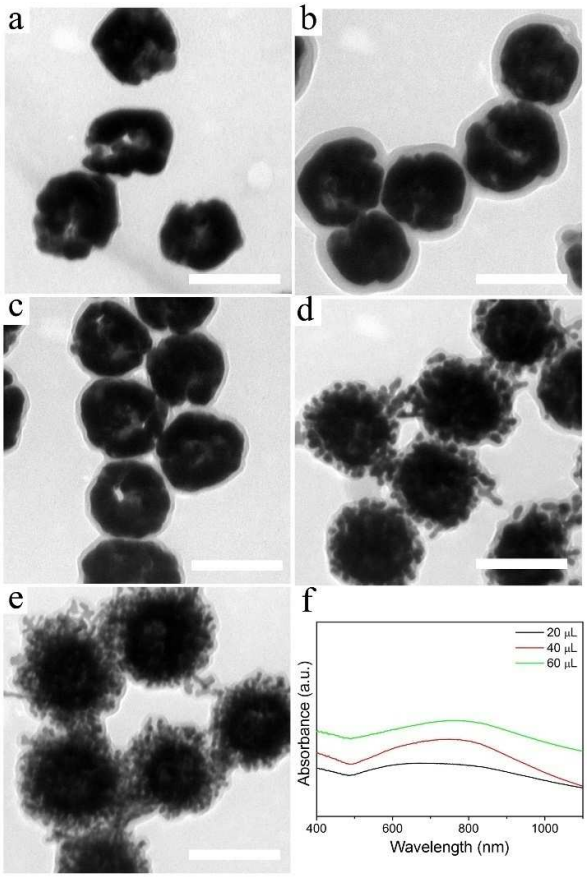


Figure S13. TEM images (a-e) and UV-vis absorption spectra (f) of Au@Res HNPs that are prepared by altering the dosage of Ag seeds from 400 (a), 800 (b), 1200 (c), 2400 (d), to 4000 μL (e). While the concentration of $HAuCl_4$ and resveratrol are fixed at 100 and 60 μL. The incubation duration and solution pH are fixed at 15 min and 1.5. The scale bar is 100 nm.

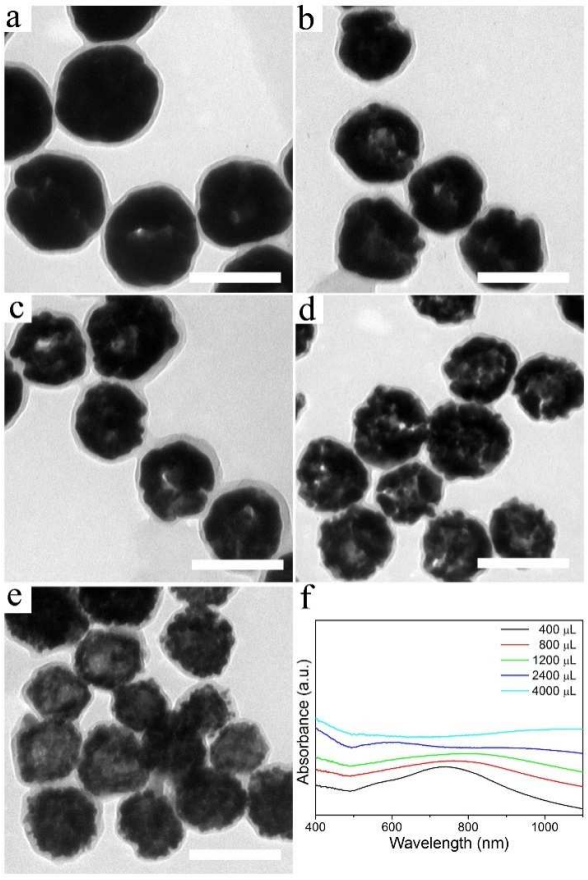


Figure S14. The UV-vis absorption spectrum of DPPH.

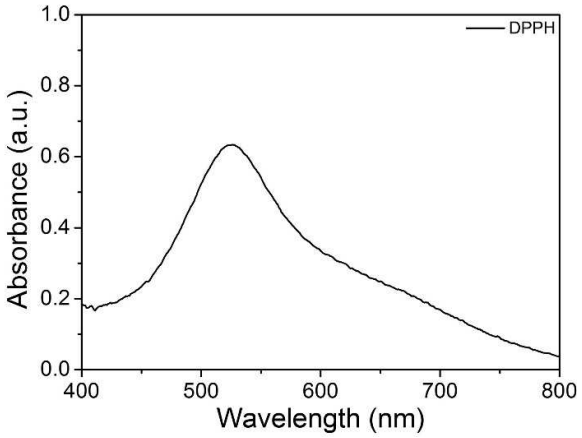


Figure S15. The UV-vis absorption spectra of Au@Res HNPs before and after irradiating with 2 W/cm^2 808 nm laser for 4 cycles.

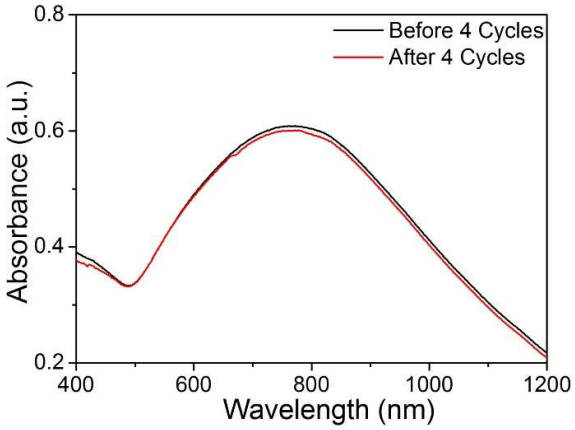
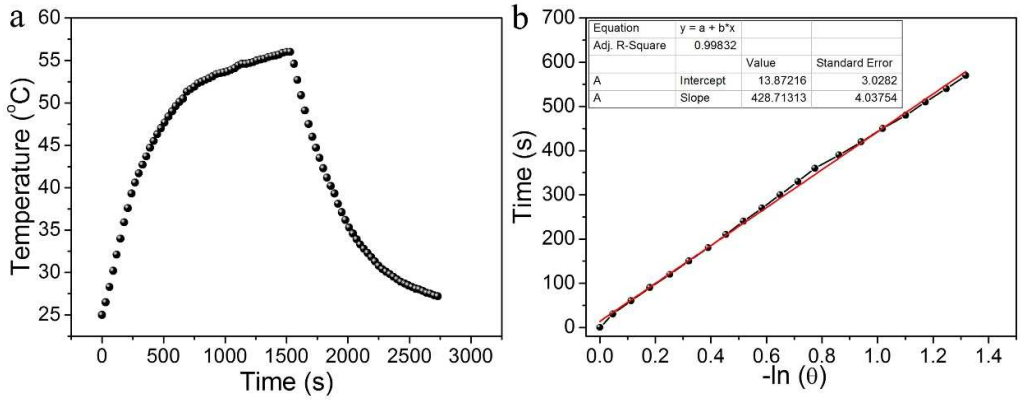


Figure S16. (a) The temperature variation of the Au@Res HNPs solution with the LSPR peak at 800 nm. The volume of solution is 2 mL. The solution is irradiated for 1500 s using a 2.0 W/cm^2 808 nm laser, and cooled to room temperature under ambient environment. (b) Time constant for heat transfer from system is calculated to be 428.7 s by applying the linear time data from cooling period *versus* negative nature logarithm of driving force temperature, which is obtained from Figure S16a.



Calculation S1. Calculation of the photothermal transduction efficiency (η) of Au@Res HNPs that are prepared using resveratrol as the reductant.

According to Roper's report, the energy transfer of system obeys the following equitation:[1]

$$\sum_i m_i C_{p,i} \frac{dT}{dt} = Q_{NP} + Q_0 - Q_{output} \quad (1)$$

where Q_{NP} is the heat generated by nanoparticles, Q_0 is the heat generated by water and quartz cell, and Q_{output} is the energy transferred from system to environment. m_i and $C_{p,i}$ is the mass and heat capacity of water and quartz cell, respectively. T is the solution temperature. The mass of water and quartz cell is 2.000 g and 5.603 g. The heat capacity of water and quartz cell is 4.200 J/g·K and 0.892 J/g·K.

$$Q_{NP} = P\eta_{Abs}\eta \quad (2)$$

$$\eta_{Abs} = 1 - \frac{I}{I_0} = 1 - 10^{-A_{808}} \quad (3)$$

where P is incident laser power, η_{Abs} is the efficiency of nanoparticles absorption at 808 nm, η represents the photothermal transduction efficiency, I_0 and I represent the light intensity of original source and transmittance, A_{808} is absorption intensity of nanoparticles at 808 nm.

The equation of energy transferred from system to environment is expressed as:

$$Q_{output} = hS(T - T_{surr}) \quad (4)$$

where h is heat transfer coefficient, S is the surface area of the container, and T_{surr} is the ambient temperature. When the system temperature reaches maximal value (T_{max}), a heat transfer equilibrium with the environment can be established and T is a

constant:

$$\frac{dT}{dt} = 0 \tag{5}$$

$$Q_{NP} + Q_0 = Q_{output} \tag{6}$$

Then η can be calculated by the following equation:

$$\eta = \frac{hS(T_{max} - T_{surr}) - Q_0}{P(1-10^{-A_{808}})} \tag{7}$$

However, hS is still unknown. In order to get hS, we introduce θ:

$$\theta = \frac{T - T_{surr}}{T_{max} - T_{surr}} \tag{8}$$

when the laser is shut down, $Q_{NP}+Q_0=0$. So

$$Q_{output} = -\sum_i m_i C_{p,i} \frac{dT}{dt} = hS(T - T_{surr}) \tag{9}$$

$$\frac{d\theta}{dt} = -\frac{hS}{\sum m_i C_{p,i}}\theta \tag{10}$$

$$t = \frac{\sum m_i C_{p,i}}{hS} \ln\theta + b \tag{11}$$

Therefore, time constant for heat transfer from system is calculated to be $\frac{\sum m_i C_{p,i}}{hS}$ by applying the linear time data from cooling period *versus* negative nature logarithm of driving force temperature. According to Figure S16a and b, the time constant is calculated as 428.7 s and η at 808 nm is 48.2 %.

Calculation S2. The calculation of molar extinction coefficient of Au@Res HNPs that are prepared using resveratrol as the reductant.

The molar extinction coefficient (ε) is calculated according to the following equation:[2]

$$\varepsilon = \frac{AV_{NP}\rho N_A V_0}{Lm_0} \quad (12)$$

A is the value of absorbance, V_{NP} (cm^3) is the volume of one Au@Res HNP, ρ (g/cm^3) is the density of gold, N_A is Avogadro's number, V_0 (mL) is the volume of solution, L is the path length (cm), and m_0 (g) is the mass of Au@Res HNPs in the solution. V_{NP} is calculated according to TEM observation (Figure 1a)

Figure S17. The UV-vis absorption spectra of Au@Res HNPs after 72 h of storage at room temperature in H_2O (a), PBS (b), and medium with (c) and without (d) 10% serum.

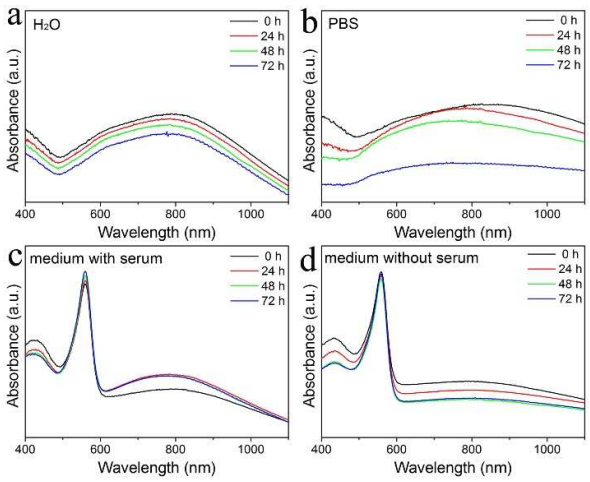


Figure S18. Bright field (a-b) and corresponding fluorescent images (c-d) of A375 cells with control group (a, c) and with incubation in 150 μg/mL Au@Res HNPs for 24 h (b, d). The dead cells are stained by EB with red color. The scale bar is 100 μm. As shown in Figure S18, there is almost no cell death with incubation in 150 μg/mL Au@Res HNPs for 24 h.

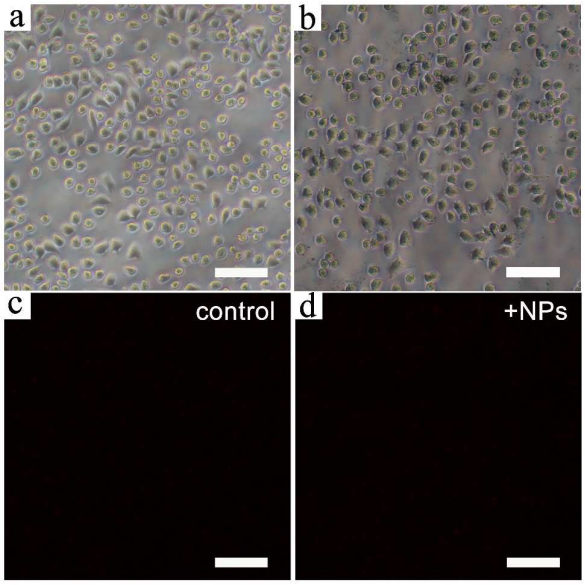


Figure S19. (a) Cellular uptake of Au@Res HNPs per well by A375 cells at 0.5, 1, 3, 6, and 24 h referring to the Au quantity. (b) The uptake percentage per well at 0.5, 1, 3, 6, and 24 h. The error bar means ±S.E. of three independent experiments.

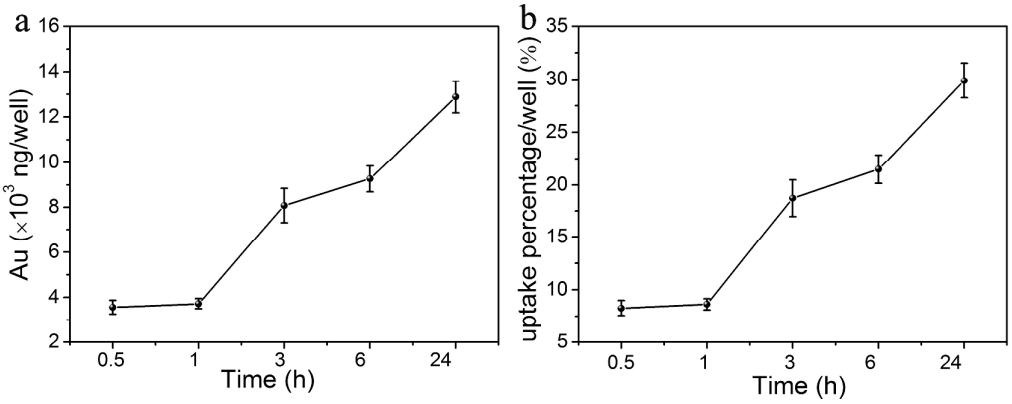
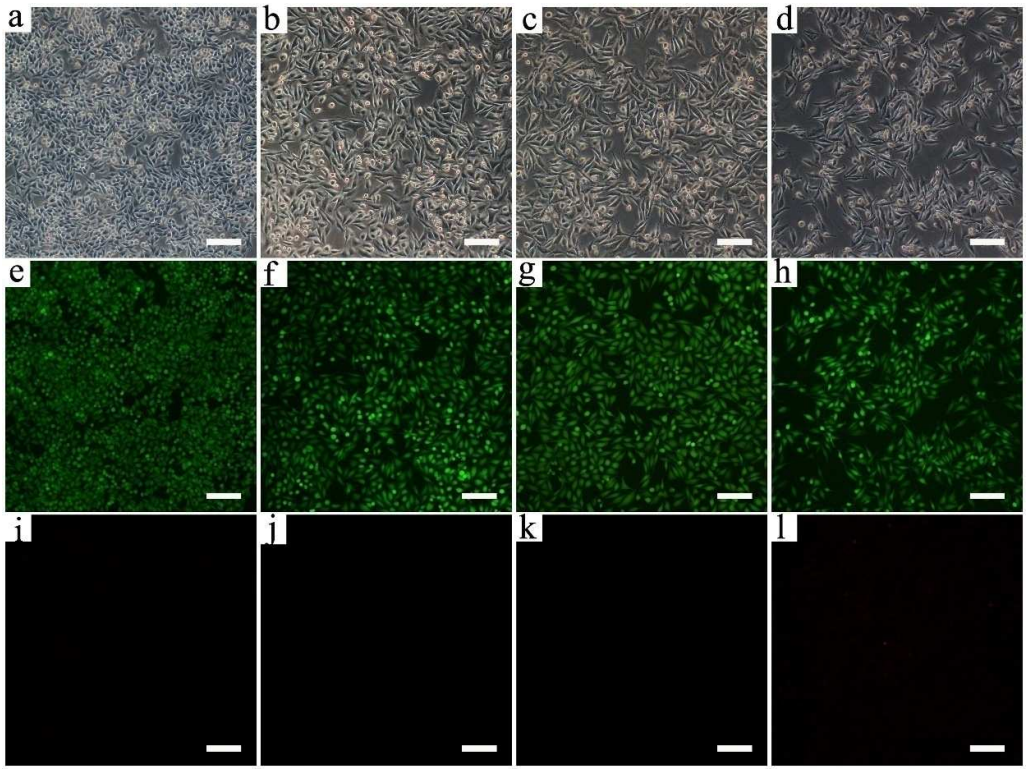


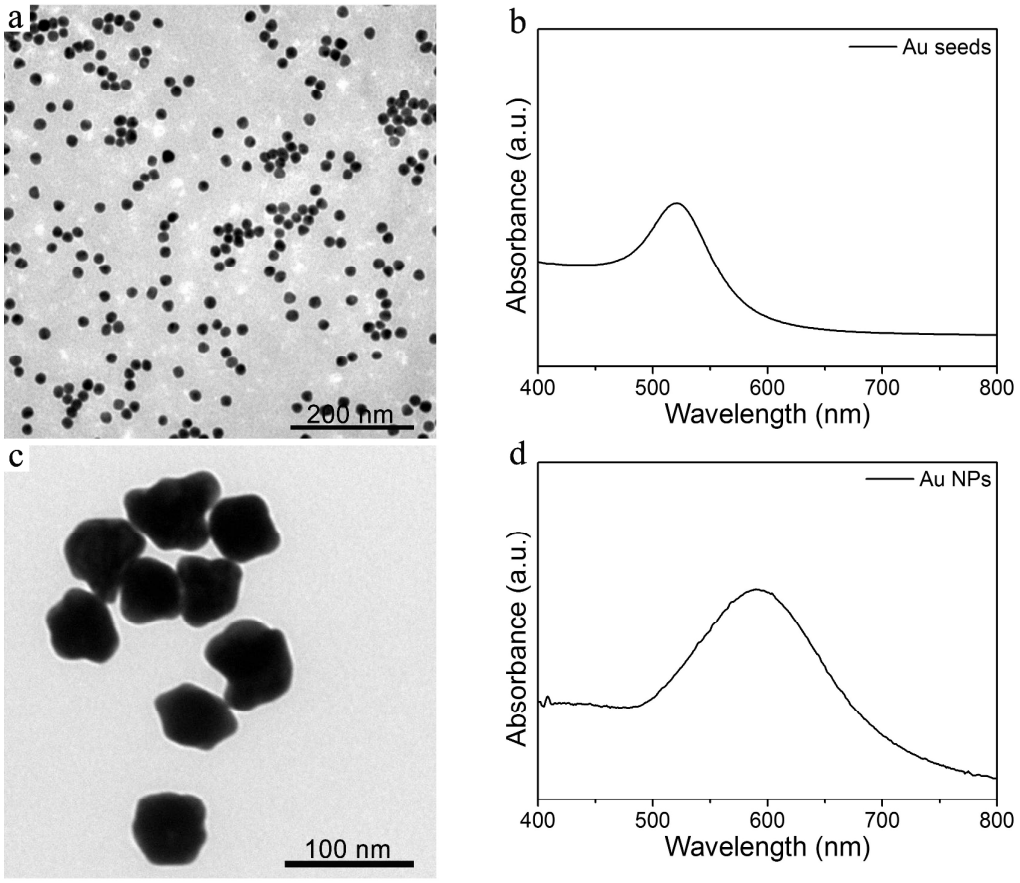
Figure S20. Bright field (a-d) and corresponding fluorescent images (e-l) of A375 cells after incubating with 0 (a, e, i), 8 (b, f, j), 12 (c, g, k) and 16 μg/mL (d, h, l) resveratrol for 24 h. The living cells are stained by FDA with green color and the dead cells were stained by EB with red color. The scale bar is 100 μm.



In order to demonstrate that the resveratrol apoptosis detection results are not conflict with the result determined by MTT assay, we do the following experiments. The A375 cells are incubated with different concentration of resveratrol, and then the living and dead cells are detected by staining with FDA and EB (Figure S20). With the increase of resveratrol concentration, the cell number decreases (Note that the cells in pictures are taken from nearly same location of 12-wells). But there is just little cell death when the concentration is 16 μg/mL (Figure S20d-l). So, the lowered cell viability detected by MTT assay within 24 h results from cell number decrease,

not all for the cell death.

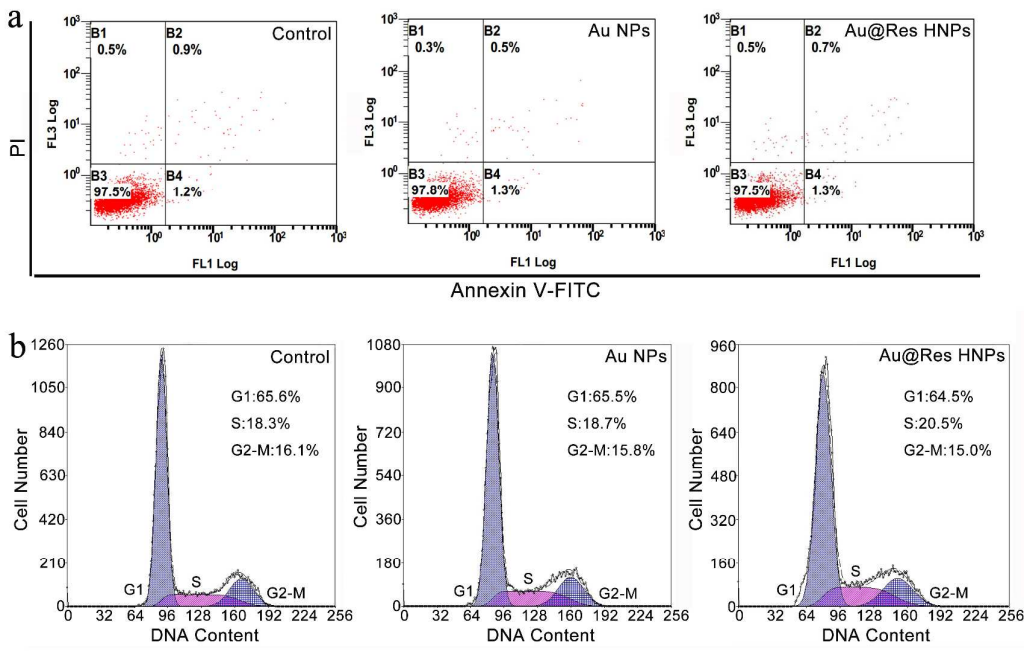
Figure S21. TEM images (a, c) and UV-vis absorption spectra (b, d) of Au seeds (a, b) and the as-prepared Au NPs with an average diameter of 53±6 nm (c, d).



The Au NPs are prepared through a seed-mediated method.[3] The spherical Au seeds were foremost synthesized according to the citrate reduction approach.[4] A 75 μL $HAuCl_4$ solution was put into a flask with 30 mL deionized water under vigorous stirring and heated to boil. As soon as the solution was boiling, 900 μL 1 w/v% sodium citrate aqueous solution was added and kept at boiling until the solution became wine red in color. This solution was used as a seed solution. In order to decrease the cytotoxicity of Au NPs, the preparation of Au NPs was modified based on the method reported by Murphy *et al.*[3] In a typical preparation, 100 μL 0.1 M $HAuCl_4$ was put into 9.2 mL deionized water under vigorous stirring. Subsequently,

200 μL Au seeds and 500 μL 0.1 M ascorbic acid aqueous solution were added. After 20 min, the Au NPs solution was purified by centrifugation at 5000 rpm for 5 min and then dissolved in deionized water.

Figure S22. Flow cytometric analysis of apoptosis (a) and cell cycle analysis by staining the DNA in A375 cells with PI (b) induced by 24 h post incubation with 150 μg/mL Au NPs and 150 μg/mL Au@Res HNPs, respectively. The results mean that the influence of Au NPs on cell apoptosis process and cell cycle is not obvious.



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4. Zhang, H.; Wang, D. Controlling the Growth of Charged-Nanoparticle Chains through Interparticle Electrostatic Repulsion. *Angew. Chem. Int. Ed.* **2008**, *47*, 3984-3987.