Nuclear Membrane-Targeted Gold Nanoparticles Inhibit Cancer Cell Migration and Invasion

Moustafa R. K. Ali [∞, ‡]; Yue Wu [∞, ‡]; Deepraj Ghosh [φ]; Brian H. Do [Δ]; Kuangcai Chen [σ]; Michelle R. Dawson [φ]; Ning Fang [σ, *]; Todd A. Sulchek [Δ, *]; Mostafa A. El-Sayed [∞, #, *]

Supporting information

[‡] *Equal contribution and listed alphabetically*

∞ Laser Dynamics Lab (LDL), School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, Georgia 30332-0400, and USA.

φ Department of Molecular Pharmacology, Physiology and Biotechnology, Brown University, Providence, Rhode Island 02912, USA.

Δ School of Mechanical Engineering, Georgia Institute of Technology, Atlanta, Georgia 30332-0400, USA.

σ Department of Chemistry, Georgia State University, P.O. Box 3965, Atlanta, Georgia 30302

 # Adjunct Professor, School of Chemistry, King Abdul Aziz University, SA.

** Corresponding author:*

* Mostafa A. El-Sayed, 901 Atlantic Drive, Atlanta, GA, USA, 30332-0400. E-mail: melsayed@gatech.edu

* Todd A. Sulchek, Atlanta, GA, 901 Atlantic Drive, 30332-0400, USA E-mail: tsulchek4@gatech.edu

* Ning Fang, Department of Chemistry, Georgia State University, P.O. Box 3965, Atlanta, GA, USA, 30302. Email: nfang@gsu.edu

1. **Figures and Tables**

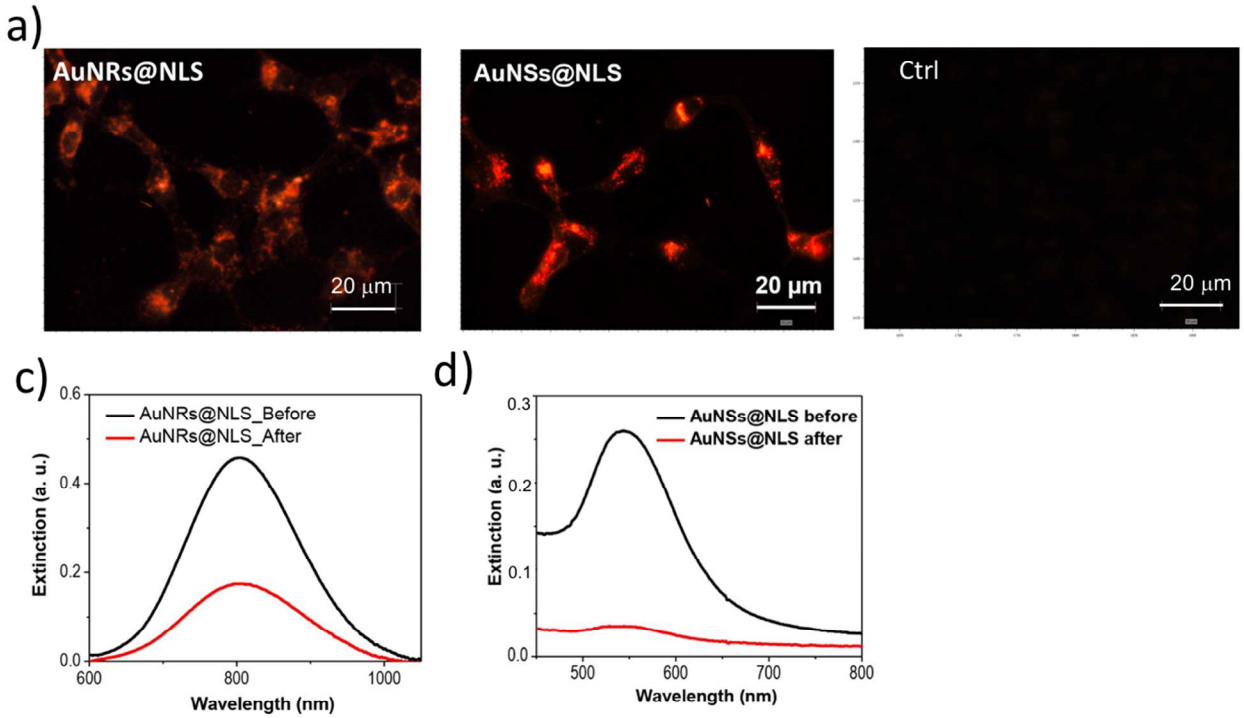


Figure S1. HEY A8 cell uptake of AuNRs@NLS and AuNSs@NLS. (a) Dark field images of cells without AuNPs incubation (Ctrl), with 2.5 nM of AuNRs@NLS and 0.1 nM of AuNSs@NLS incubation. (c) UV-Vis spectra of 2.5 nM of AuNRs@NLS or 0.1 nM of AuNSs@NLS (d) in culture media before incubation with cells (black spectrum), compared with the ones after 24 h cell incubation (red spectrum).

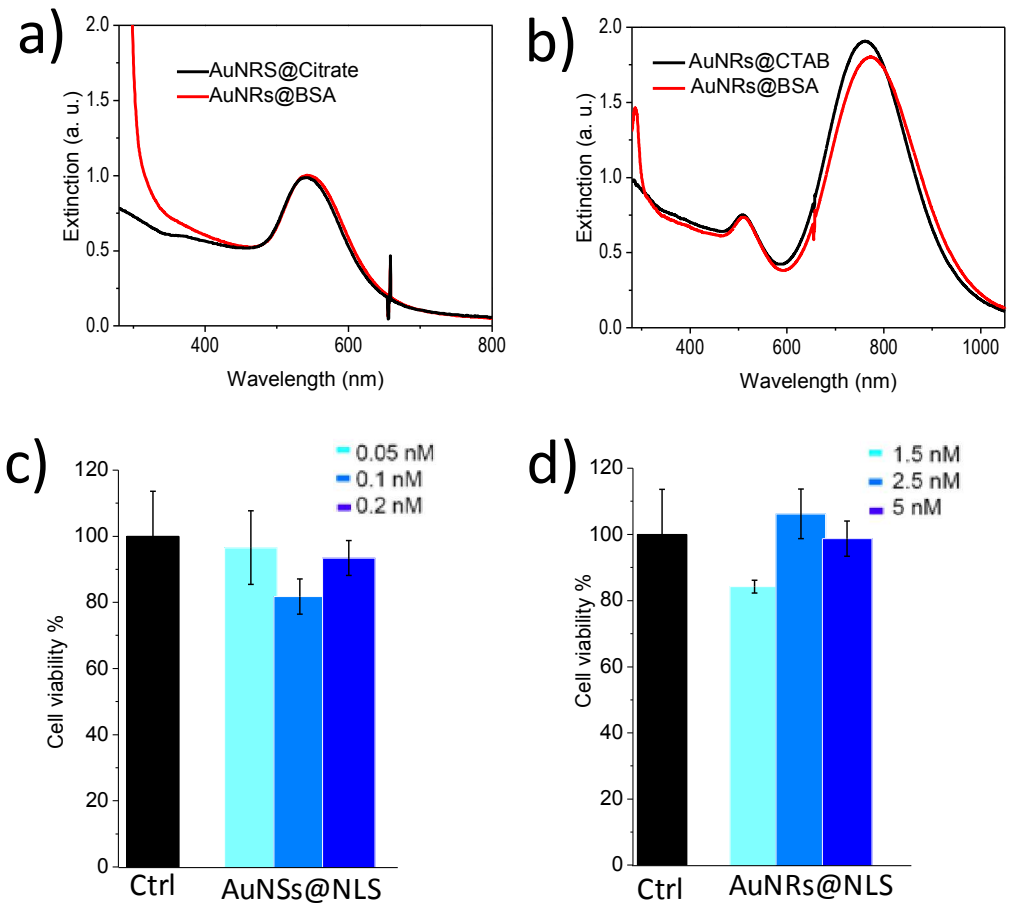


Figure S2. Characterization for AuNPs@BSA and HEY A8 cell uptake. (a) UV-Vis extinction spectra of the unconjugated AuNSs@Citrate (black spectrum) and AuNRs@BSA (red spectrum). (b) UV-Vis extinction spectra of the unconjugated AuNRs@CTAB (black spectrum) and AuNSs@BSA (red spectrum). (c) XTT assay of HEY-A8 cells after 24 h incubation with AuNSs@NLS at concentrations 0.05 nM (light blue), 0.1 nM (medium blue) and 0.2 nM (dark blue), n=3. (d) XTT assay for cells after 1.5 nM (light blue), 2.5 nM (medium blue) and 5 nM (dark blue) of AuNRs@NLS incubation with HEY-A8 cells for 24h (n=3).

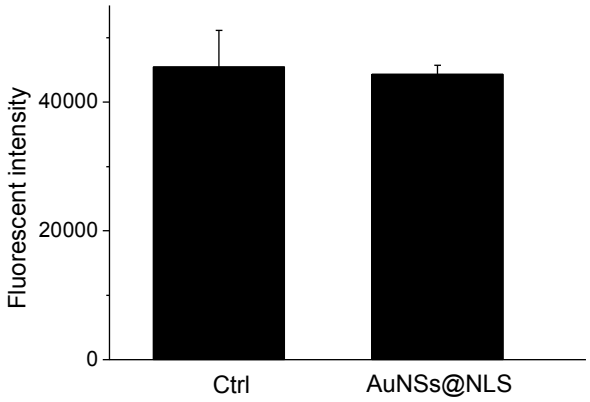


Figure S3. The introduction of Au nanoparticles in cells does not affect the Fluorescent intensity of Calcein AM (n=3).

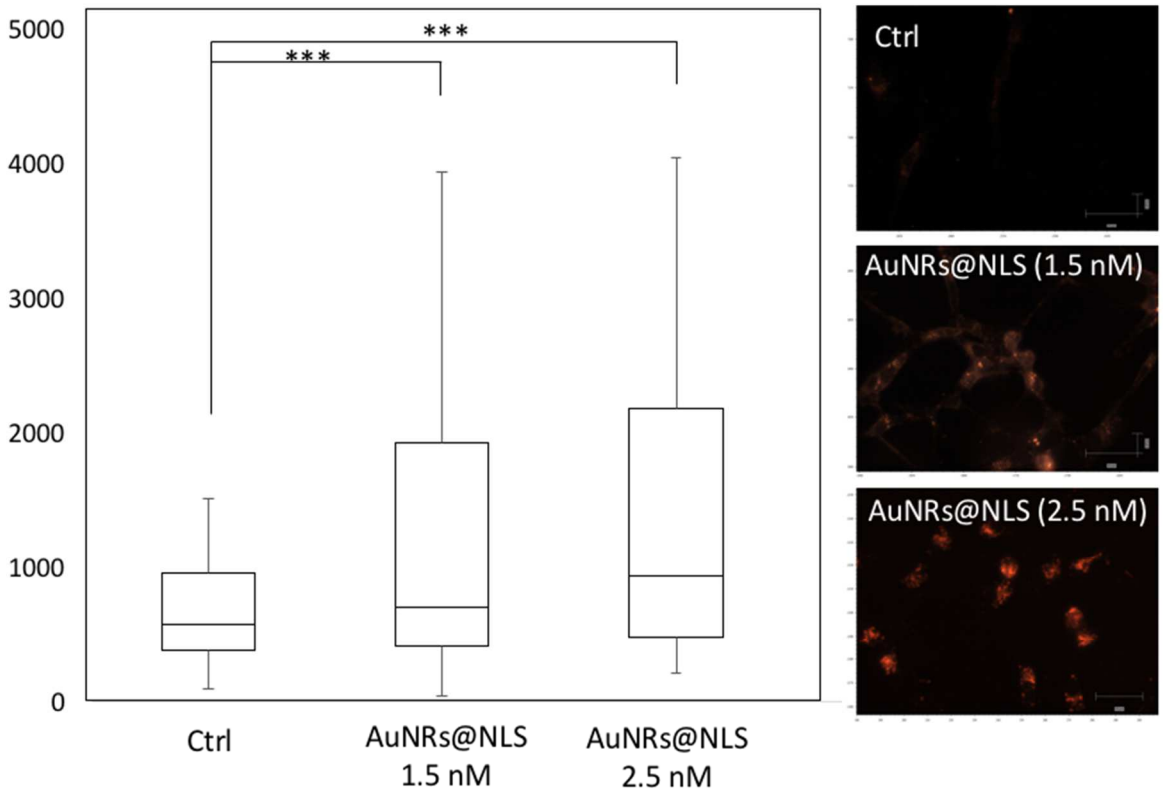


Figure S4. Nuclear stiffness increase with the increased quantity of AuNRs. AFM result (left) and dark field images (right) show the stiffness and the nanoparticle uptake of AuNRs under different nanoparticle concentrations, respectively. n=3, cell counts>20 for each sample.

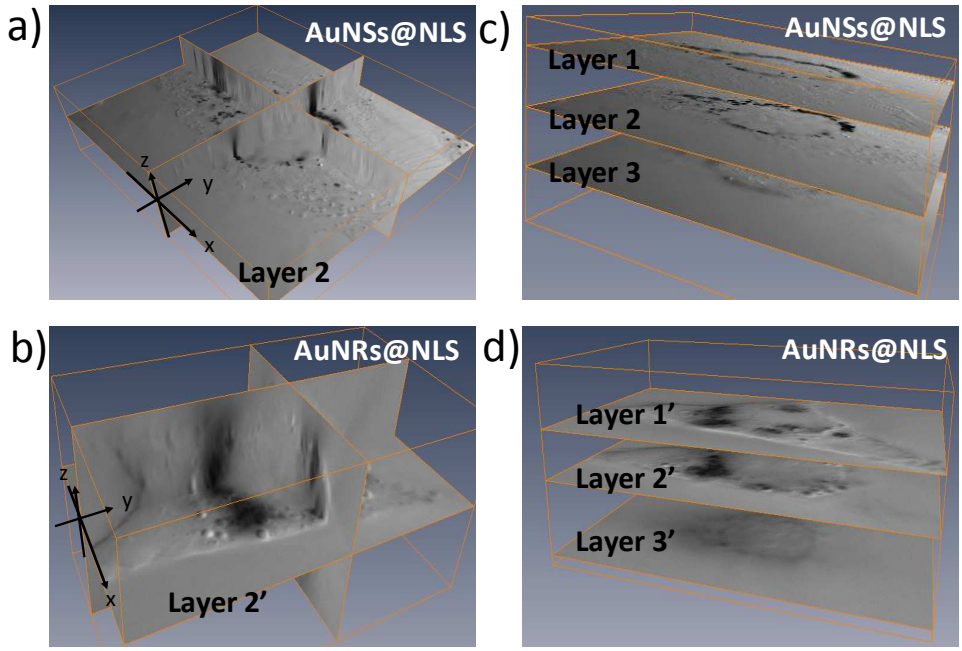


Figure S5. 3 dimensional (3D) view of HEY A8 cells incubated with AuNPs. (a and b) 3D figures of cells with 2.5 nM of AuNRs@NLS and 0.1 nM of AuNRs@NLS, showing xy, xz and yz planes (c and d) showing the z-stacking of 3 layers from the bottom of the cell (close to the attached glass surface as shown in the scheme), the middle of the cell, and the top of the cell, respectively, for AuNSs@NLS (c) and AuNRs@NLS (d).

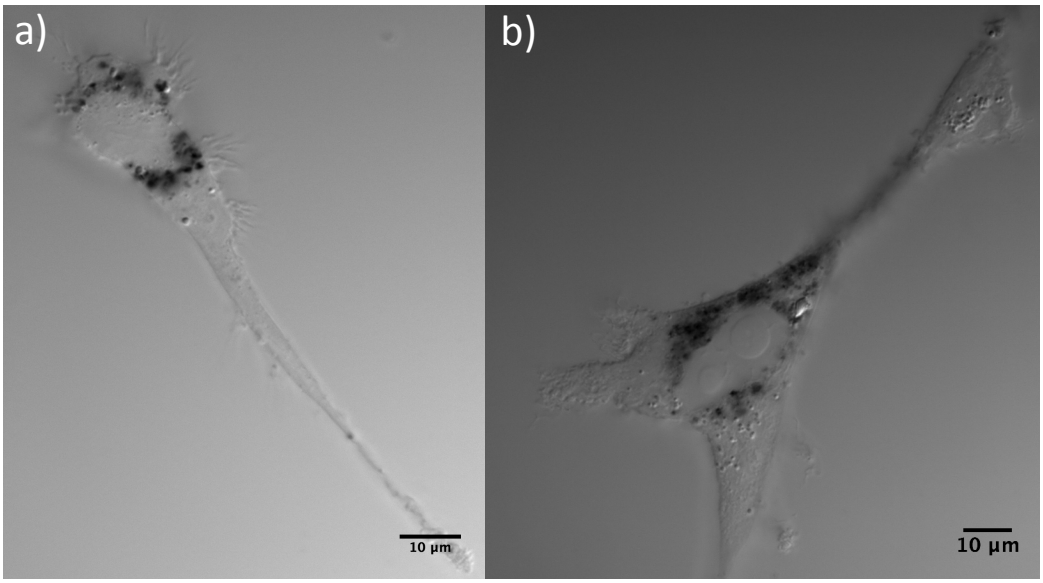


Figure S6. The nuclear membrane targeting for AuNRs@NLS indicated by differential interference contrast (DIC) images.

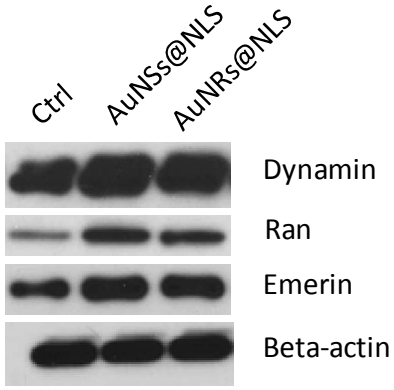
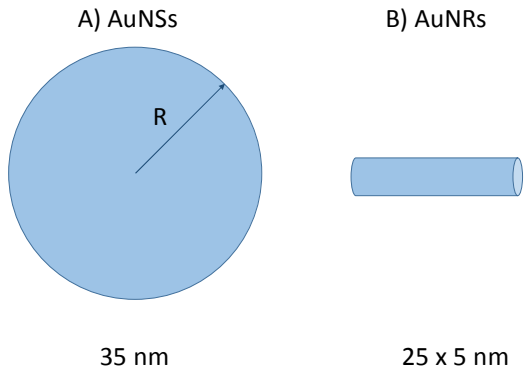


Figure S7. Western blot of expression levels of Dynamin, Ran, emerin proteins and beta-actin from HEY-A8 cells (without AuNPs), HEY A8 cells with 0.1 nM of AuNSs@NLS and 2.5 nM of AuNRs@NLS treatment for 24 h.

Table S1. Zeta potential of AuNPs with different surface ligands

Au nanoparticles with different surface ligands	Zeta potential (mV)
AuNRs@CTAB	50.9 ± 7.97
AuNRs@PEG	-13.6 ± 11.8
AuNRs@PEG@RGD@NLS	14.9 ± 3.13
AuNSs@Citrate	-29.7 ± 4.72
AuNSs@PEG	-12.1 ± 5.79
AuNSs@PEG@ RGD@NLS	18.3 ± 7.55
AuNRs@BSA	-19.6 ± 9.89
AuNSs@BSA	-15.2 ± 12.5

2. The Calculation of Mass Concentration Of AuNPs in the Cell Culture Media



$$\frac{C_{\text{AuNSs (g/L)}}}{C_{\text{AuNRs (g/L)}}}=\frac{M_{w(Au)}\rho_{(Au)}V_{AuNSs}C_{AuNSs}}{M_{w(Au)}\rho_{(Au)}V_{AuNRs}C_{AuNRs}}=\frac{V_{AuNSs}C_{AuNSs}}{V_{AuNRs}C_{AuNRs}}=\frac{{}^{4}/_{3}\pi R^{3}C_{AuNSs}}{\pi(\frac{w}{2})^{2}lC_{AuNSs}}=0.92\approx 1 \qquad \text{(Equation 1)},$$

where $C_{AuNSs(g/L)}$ or $C_{AuNRs(g/L)}$ is the mass concentration (in gram of gold/L), $M_{w(Au)}$ is the molar mass of gold, $\rho_{(Au)}$ is the density, V_{AnNSs} or V_{AuNRs} is the volumn of the gold nanoparticles (AuNSs or AuNRs), C_{AuNSs} or C_{AuNRs} is the molar concentration of the gold nanoparticles (AuNSs or AuNRs), R is the average radius of the AuNSs, w and l are the width and length in the AuNRs.