Supporting Information

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Gold Nanocarriers for Macrophage-Targeted Therapy of Human Immunodeficiency Virus

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Chemical optimization of nanocarriers

AuNP-drug conjugates sizing 10, 40, and 70 nm and the spacers polyethylene glycol (PEG), polyethylene imine (PEI), and citric acid were produced by an ease-of-use technique. Ultraviolet-visible spectroscopy (UV-Vis) demonstrated successful binding of stavudine to the carriers based on the peak of stavudine at 265 nm and that of the AuNP at 532 nm, as demonstrated by a representative UV-Vis spectrum for 40 nm sizing nanocarriers stabilized with citrate (**Figure S1A**). Zetapotential changes indicated successful coupling of stavudine to the AuNP, and drug loading efficacy, as determined from ultra-high pressure liquid chromatography (UHPLC) was plargest for the 10 and 40 nm sizing carriers (**Table S1**).

The drug release of stavudine from nanocarriers was, according to the UHPLC data, increased for all stabilizers under acidic conditions, and a burst release was noted during the first two hours. The largest extent of acidic release occurred when PEG was used as stabilizer, followed by citrate, whereas PEI had a strongly reduced release (**Figure S1B**). This rapid acidic discharge is highly desired to evoke release of stavudine inside macrophages since these cells transport all materials inside their endosome which subsequently becomes a lysosome also exhibits a similarly acidic pH of about 5.5 – a process which occurs in as little as two hours.[1]

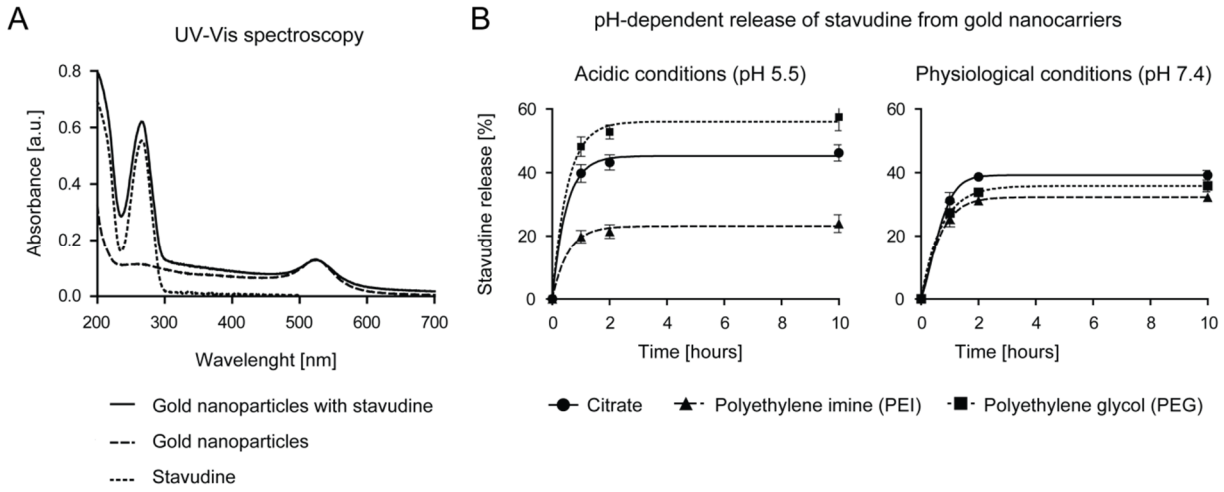

Figure S1. Characterization of gold nanoparticle-stavudine conjugates. (A) Coupling analysis of stavudine to citrate-stabilized gold nanoparticles by UV-Vis spectroscopy. (B) Release of stavudine from loaded AuNP stabilized with citrate (circles), polyethylene imine (PEI) (triangles), and polyethylene glycol (PEG) (squares) at 2.5 µg Au/mL in phosphate-buffered saline (PBS) at pH 5.5 and pH 7.4.

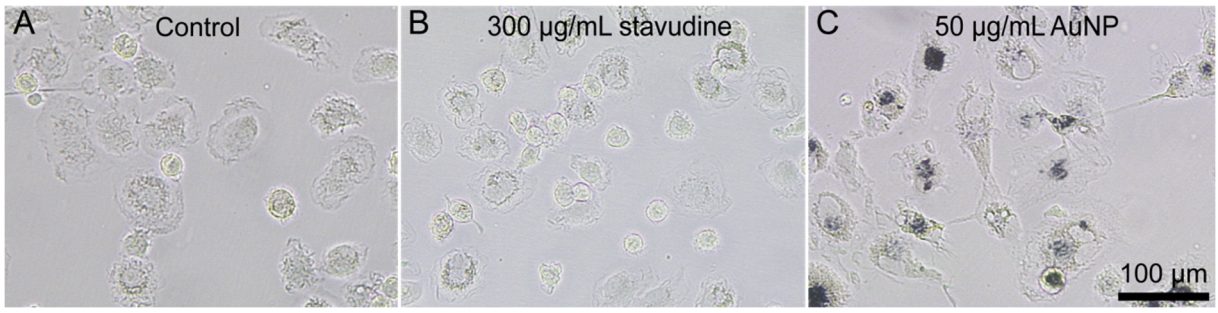

Figure S2. Effects of high concentrations of single components on macrophage morphology. Human primary macrophages were left untreated in cell culture medium for 24 hours (A), were added 300 µg/mL stavudine (B), or 50 µg/mL gold nanoparticles (C).

Table S1. Zetapotential and loading efficacy of gold nanocarriers before and after coupling of stavudine to the carriers. Gold nanocarriers exhibiting different sizes and the stabilizers citrate, polyethylene imine (PEI), and polyethylene glycol (PEG). Mean data ± SD.

Size [nm]	Stabilizer	Zetapotential [mV]	Conjugates [mV]	Coupled drug [mg/mL]	Loading efficacy [%]
10	Citrate	-45.03 ± 0.85	-27.30±6.07	0.765 ± 0.03	76.5 ± 3.1
40	Citrate	-51.63 ± 0.50	-28.30±8.84	0.729 ± 0.04	70.9 ± 4.3
40	PEI	66.70 ± 0.52	47.83±1.30	0.762 ± 0.05	75.4 ± 5.2
40	PEG	-5.19 ± 0.46	-36.10±1.52	0.734 ± 0.04	79.2 ± 4.1
70	Citrate	-64.30 ± 0.57	-28.67±9.24	0.569 ± 0.01	56.9 ± 1.5

References

[1] J. P. Luzio, P. R. Pryor, N. A. Bright, Nature reviews. Molecular cell biology 2007, 8, 622.