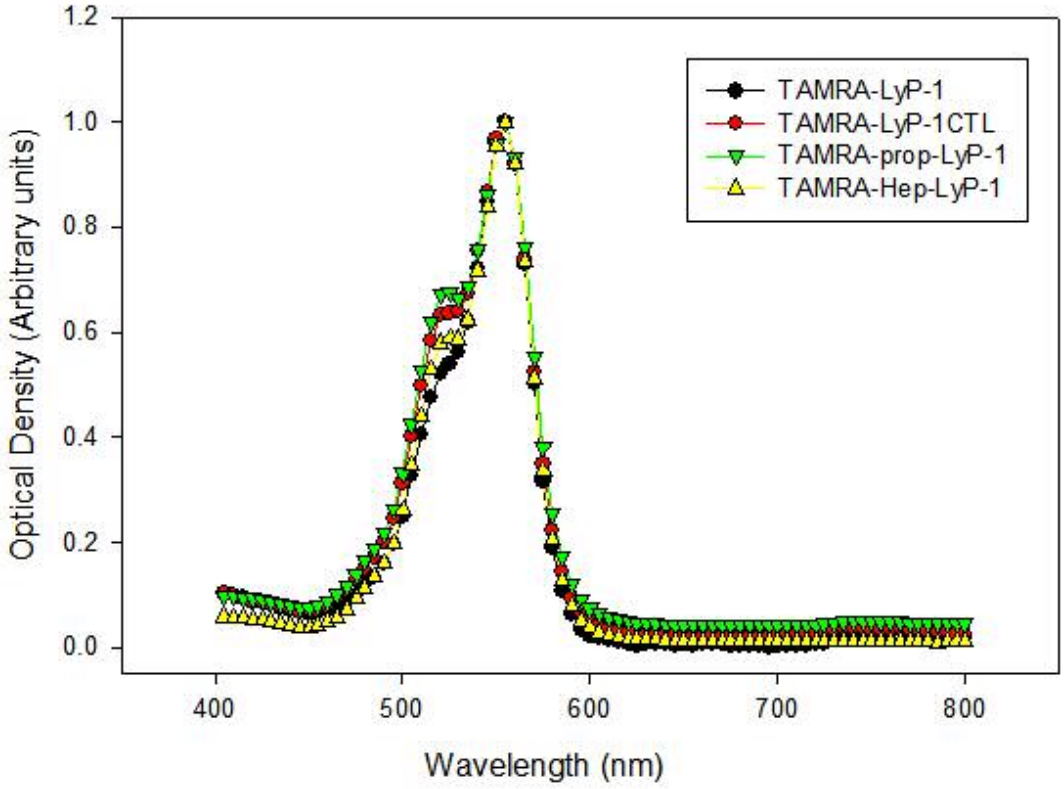
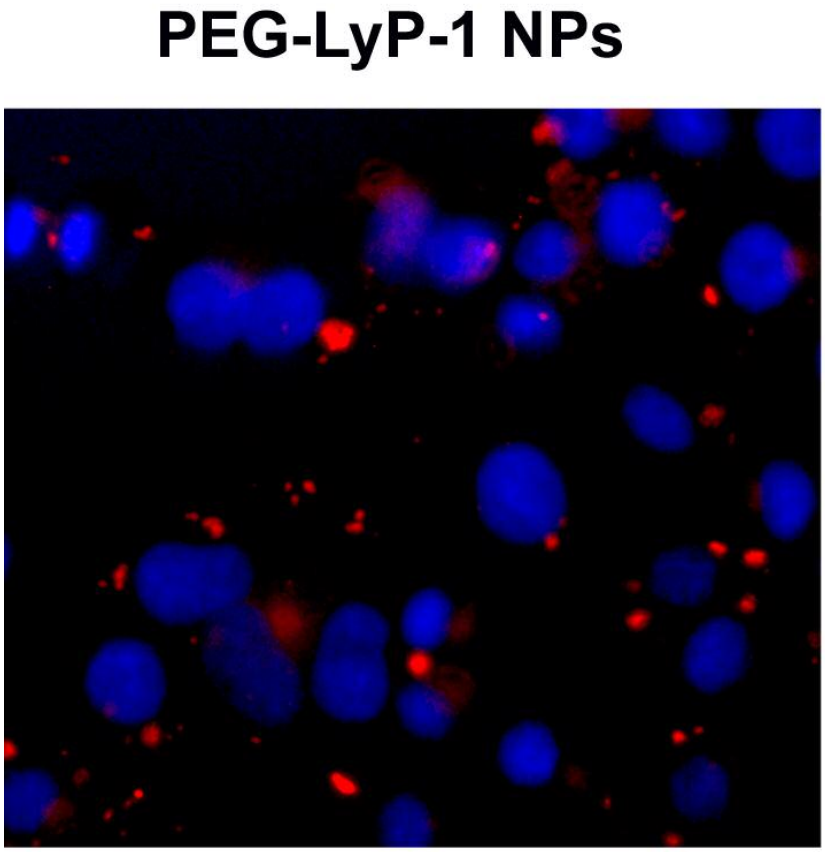
	Degree of Functionalization	
Catalyst [mM], Time	Propargylglycine-Lyp1	Heptynoic Acid-Lyp1
CuSO4 [1mM], 24 h	44%	48%
CuSO4 [1mM], 72 h	80%	82%
CuSO4 [10mM], 24h	0%	0.5%
CuSO4 [10mM], 72h	0%	13%
CuI [1mM], 24 h	70%	70%
CuI [1mM], 72 h	76%	95%
CuI [10mM], 24 h	68%	76%
CuI [10mM], 72 h	77%	100%
CuI [100mM], 24 h	75%	83%
CuI [100mM], 72 h	79%	89%
No Catalyst, 72h	0%	0%

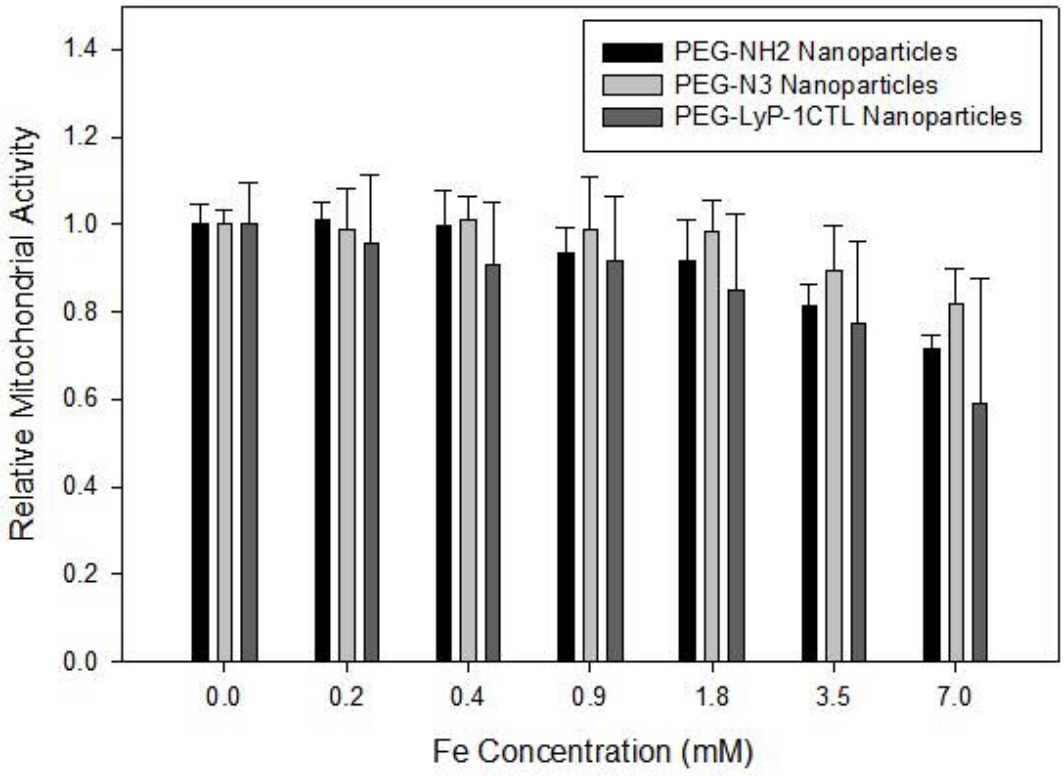
Table S1. Optimization of the "click" reaction. The rate of product conversion in the "click" reaction is measured as a function of product formation in HPLC. The reaction is performed in various catalysts (CuSO4 or CuI) and concentrations, in 24h or 72h reactions, using LyP-1 peptides bearing either propargylglycine or 6-heptynoic-acid.



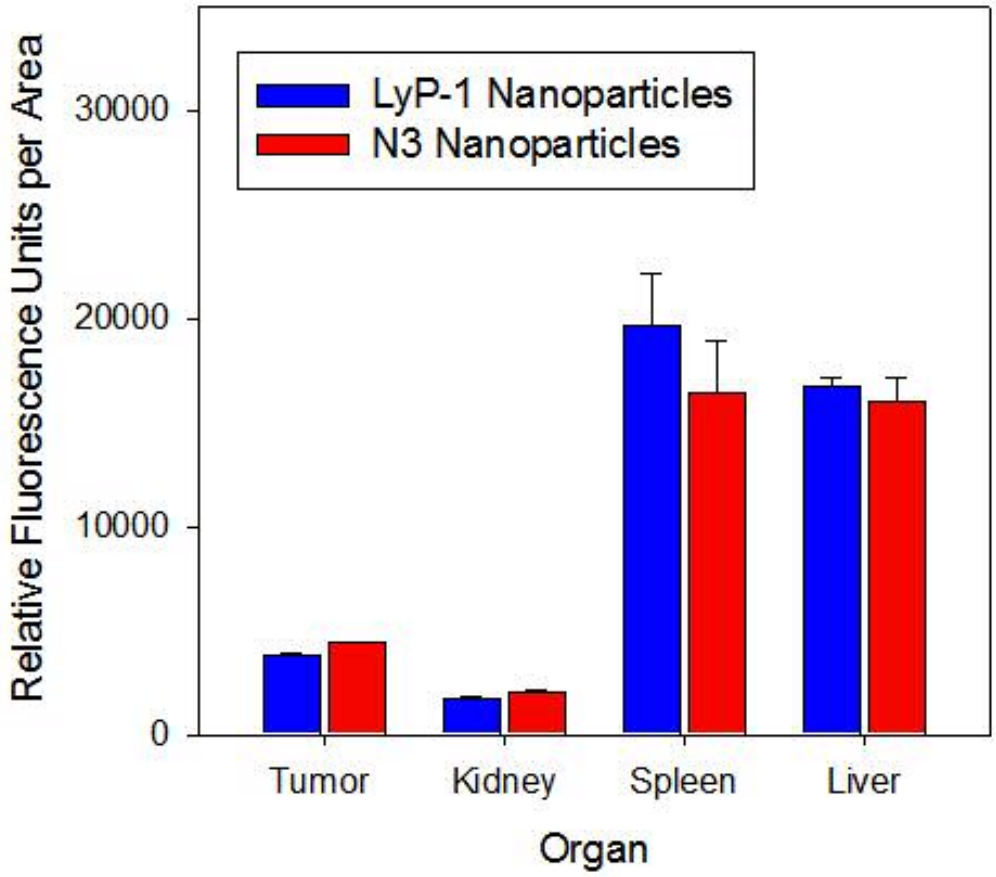
Supplementary Figure 1. *Fluorophore-labeled LyP-1 Peptide Spectra.* UV-Vis spectra for LyP-1 and LyP-1CTL peptides synthesized with varying pendant alkyne groups (prop= propargylglycine; Hep=heptynoic acid)



Supplementary Figure 2. LyP-1-nanoparticles target MDA-MB-435 cancer cells and become localized in endosome-like compartments over 24hrs in vitro. Cells were incubated with LyP-1-nanoparticles for 30min, washed, and incubated for 24hrs before nuclear staining and imaging. PEG-LyP-1 nanoparticles no longer show diffuse membranous staining, but have become localized into punctuate compartments, implying endosomal sequestration away from cell surface.



Supplementary Figure 3. *Probing "Click" Nanoparticle Cytotoxicity to Human Cell Cultures.* Human HeLa cervical cancer cells were incubated with parent NH2-PEG-NPs, PEG-N3-NPs, or PEG-LyP-1CTL-NPs at varying concentrations for 24 hrs, rinsed, and incubated with media containing thiazolyl blue tetrazolium bromide (MTT reagent) at 0.5mg/ml. After 3hr, blue precipitates begin to form within cells as a result of mitochondrial activity. Quantitaion of cellular viability via absorbance of DMSO:isopropanol-solubilized MTT reagent showed that all three NP peparations have TC_{50} values of greater than 7mM, which is over 35-times that used in vitro here (100nM NPs used in cell culture and FACS expts = 0.2mM Fe) and greater than sixteen times the maximum blood concentrations during *in vivo* experiments (200nM NP concentration in blood immediately after injection = 0.4mM Fe).



Supplementary Figure 4. *Near-Infrared Fluorescence Analysis of LyP-1- and Azido-Nanoparticle Tumor Accumulation.* Near-infrared fluorochrome-labeled nanoparticles bearing terminal azide groups (red) or LyP-1 peptides (blue) were injected intravenously via the tail vein into mice bearing human MDA-MB-435 cancer xenografts (4 mice). After particles had cleared the systemic circulation (24hrs), mice were sacrificed and tumor, liver, spleen, and kidneys were fluorescently imaged for nanoparticle accumulation (LI-COR Odyssey). As expected for nanoparticles above the renal filtration limit, clearance was predominately via reticuloendothelial system uptake (liver and

spleen). Nanoparticle accumulation in tumors was slightly decreased for peptide-modified nanoparticles, likely due to a decrease in the particle circulation time following cationic peptide attachment and concomitant decrease in the passive targeting.