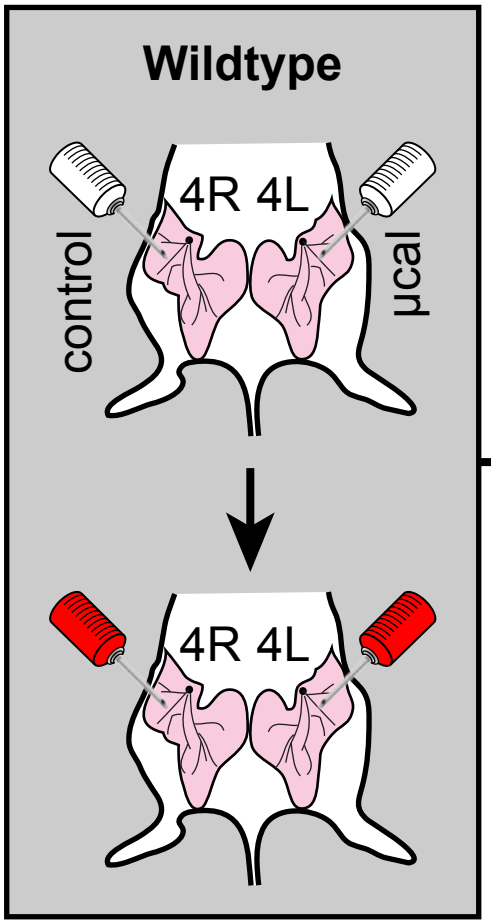
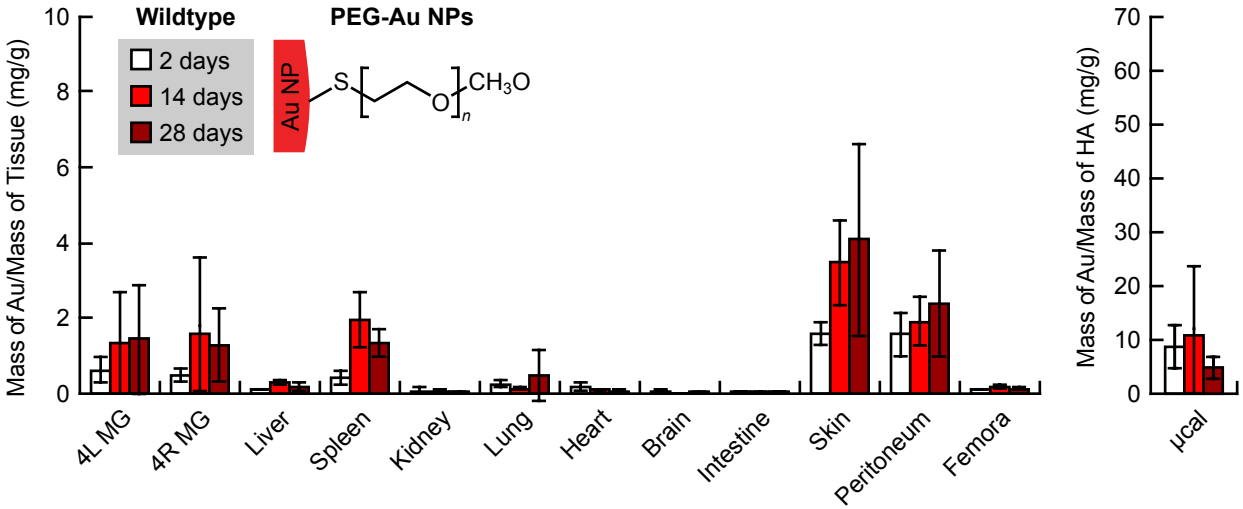
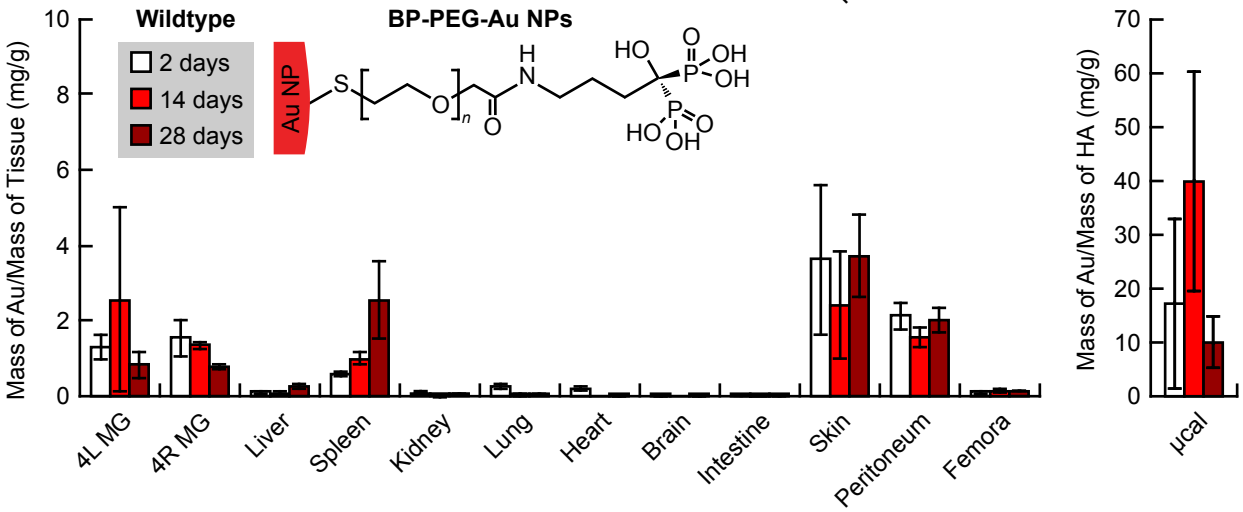
Biodistribution of PEG- & BP-PEG-Au NPs







Cole et al., Acta Biomaterialia, 2018

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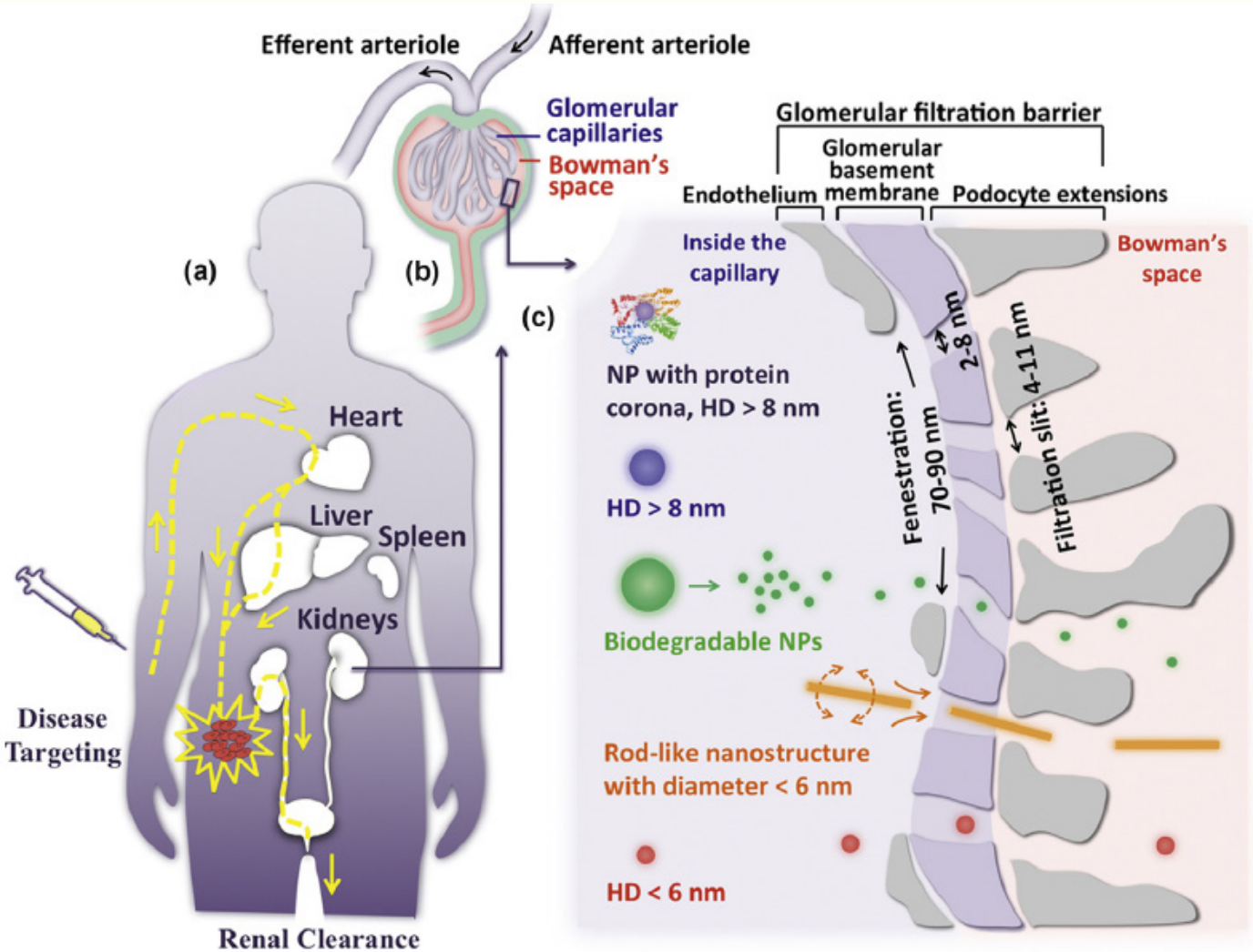
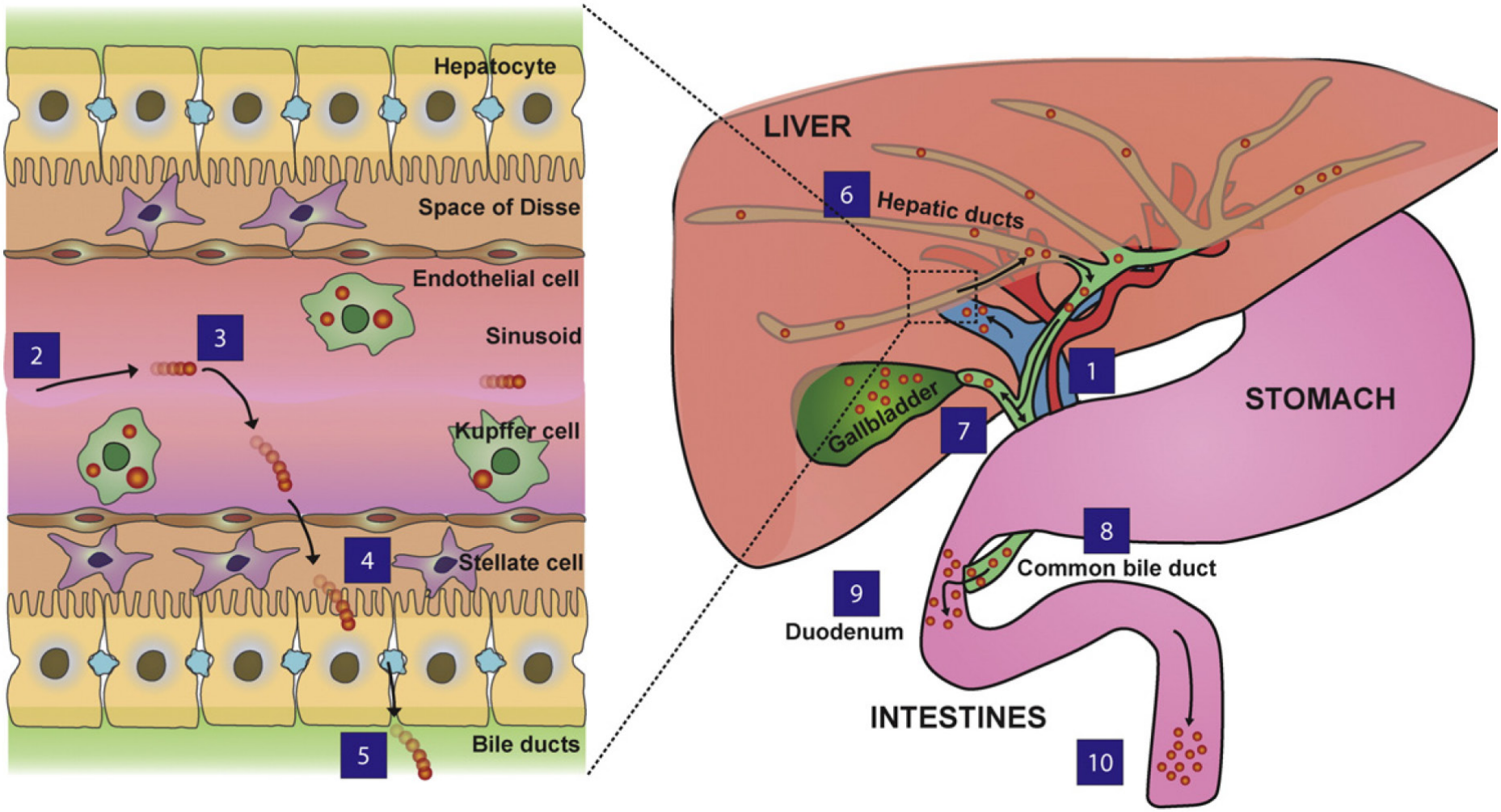
Renal Clearance (Glomerular Filtration)



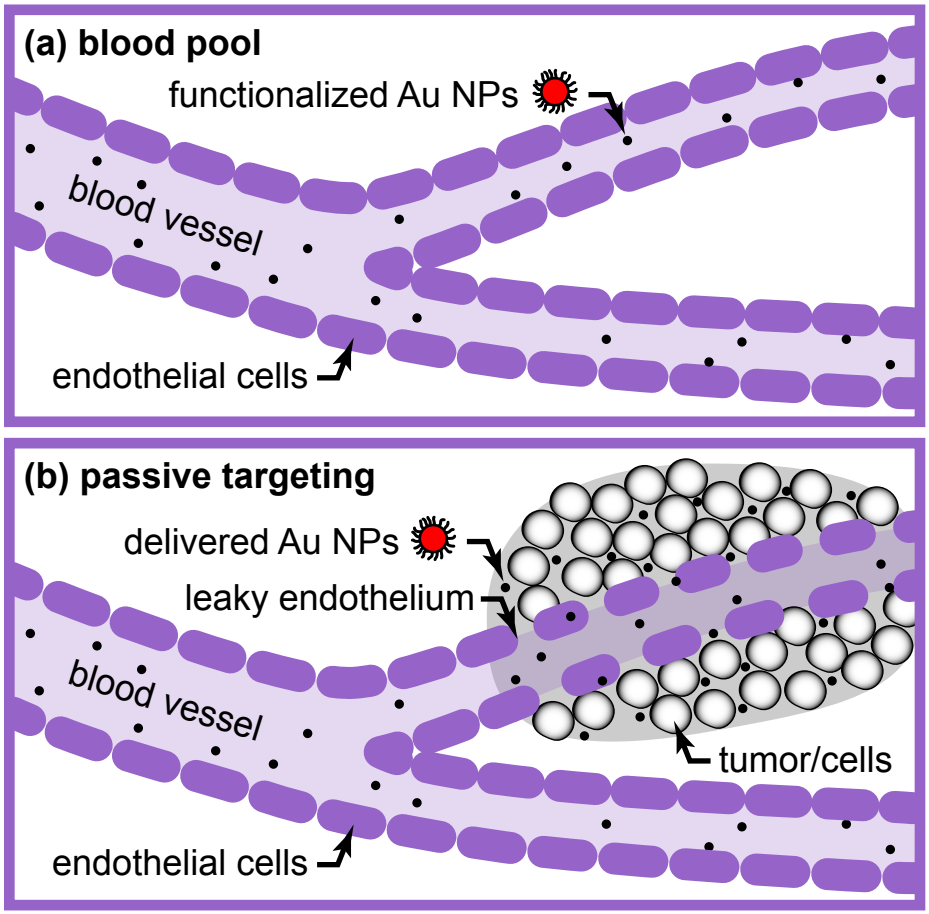
Liu *et al.*, *Mater. Today*, 2013

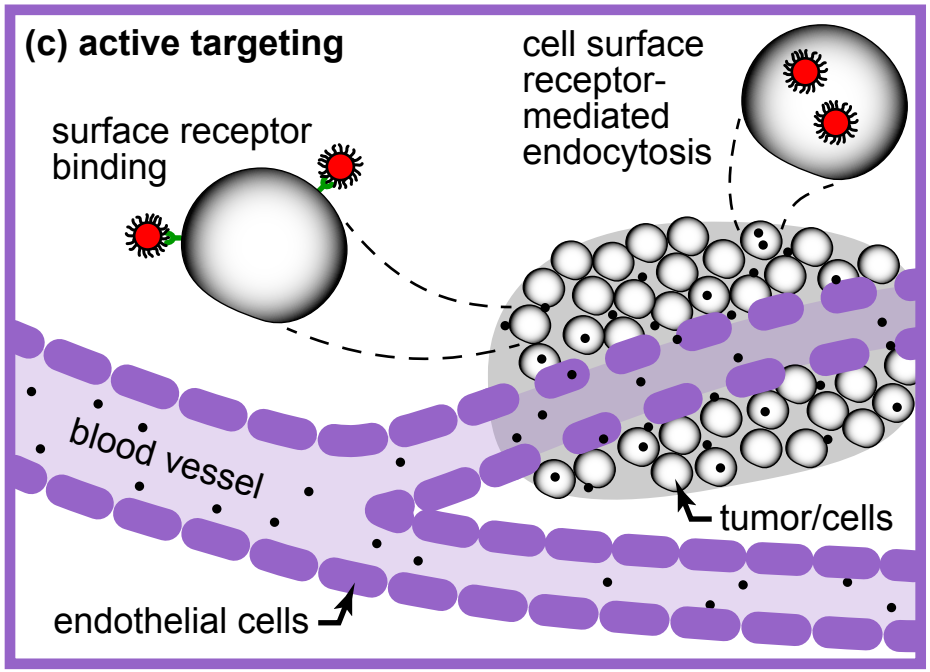
Hepatobiliary Clearance



Zhang *et al.*, *J. Controlled Release*, 2016

Passive Versus Active Targeting



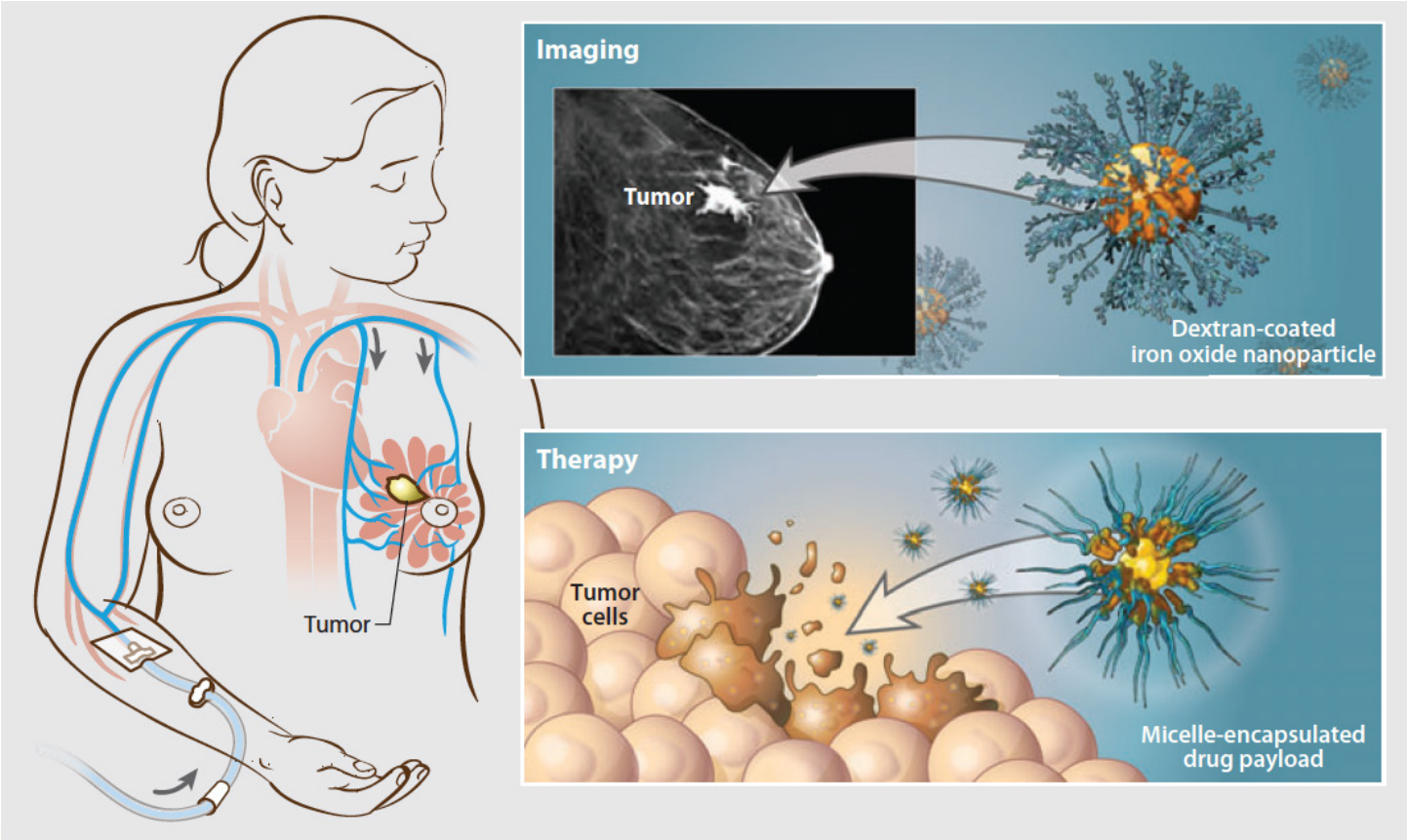


Cole et al., Nanomedicine, 2015

Targeting Nanoparticles

Passive Targeting: accumulation of NPs due to physiological effects

- size, molecular weight
- enhanced permeation and retention (EPR) effect

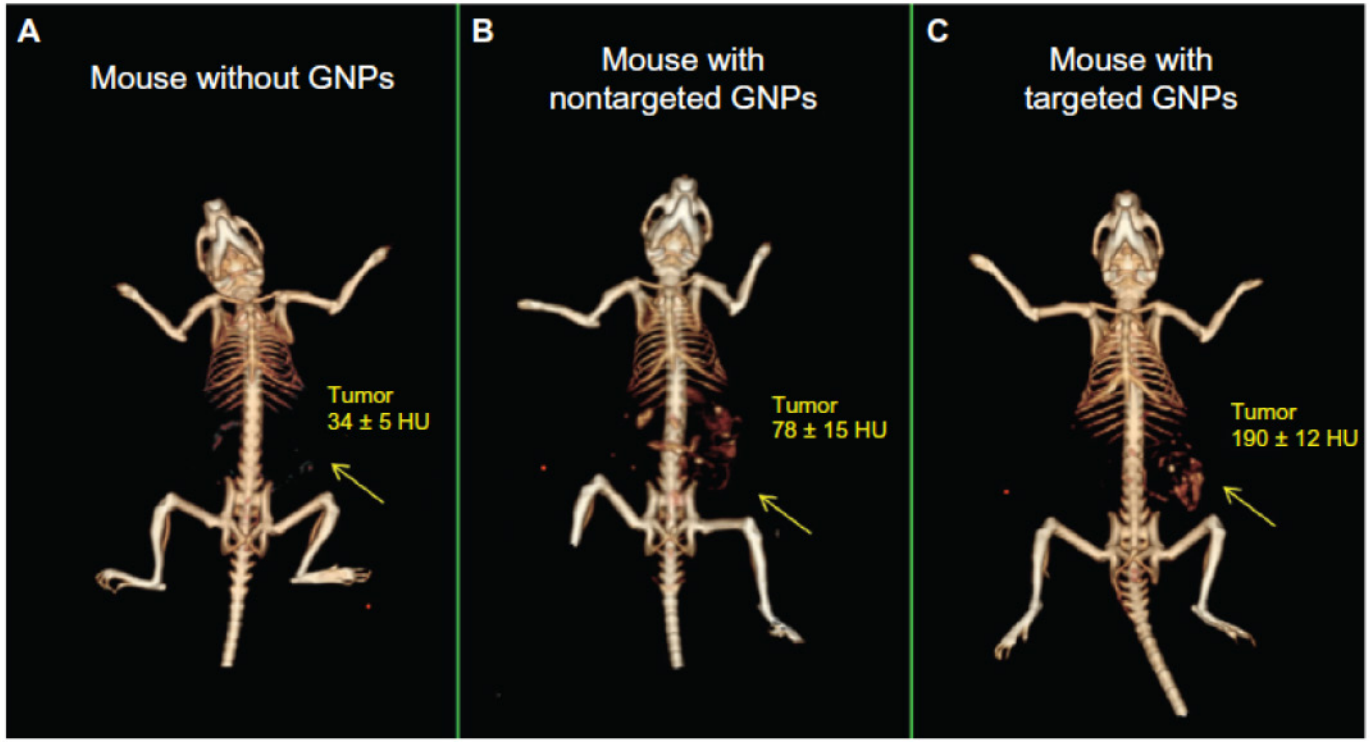


Albanese et al., Annu. Rev. Biomed. Eng., 2012

Targeting Nanoparticles

<u>Active Targeting</u>: binding of a functional molecule to specific sites

- ligands (e.g., -COOH, $-NH_2$, $-PO(OH)_2$, etc.)
- biomolecules (e.g., folic acid, heparin, bombesin, insulin, etc.)
  - antibodies (e.g., anti-HER, anti-EGFR, anti-CD4, etc.)

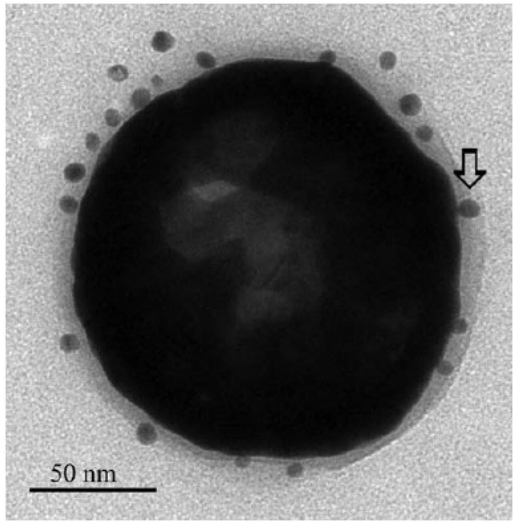


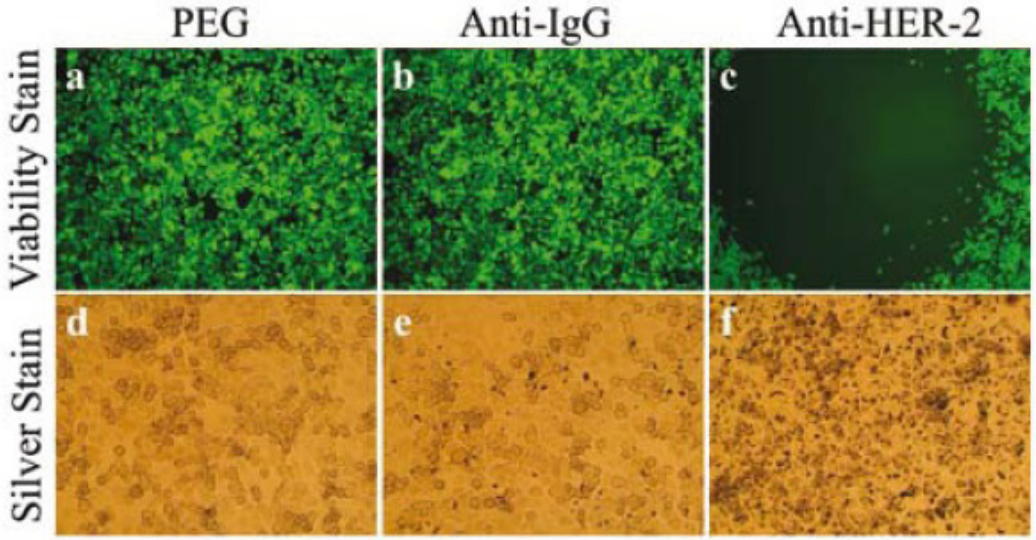
Reuveni et al., Int. J. Nanomed., 2011

Targeting Nanoparticles

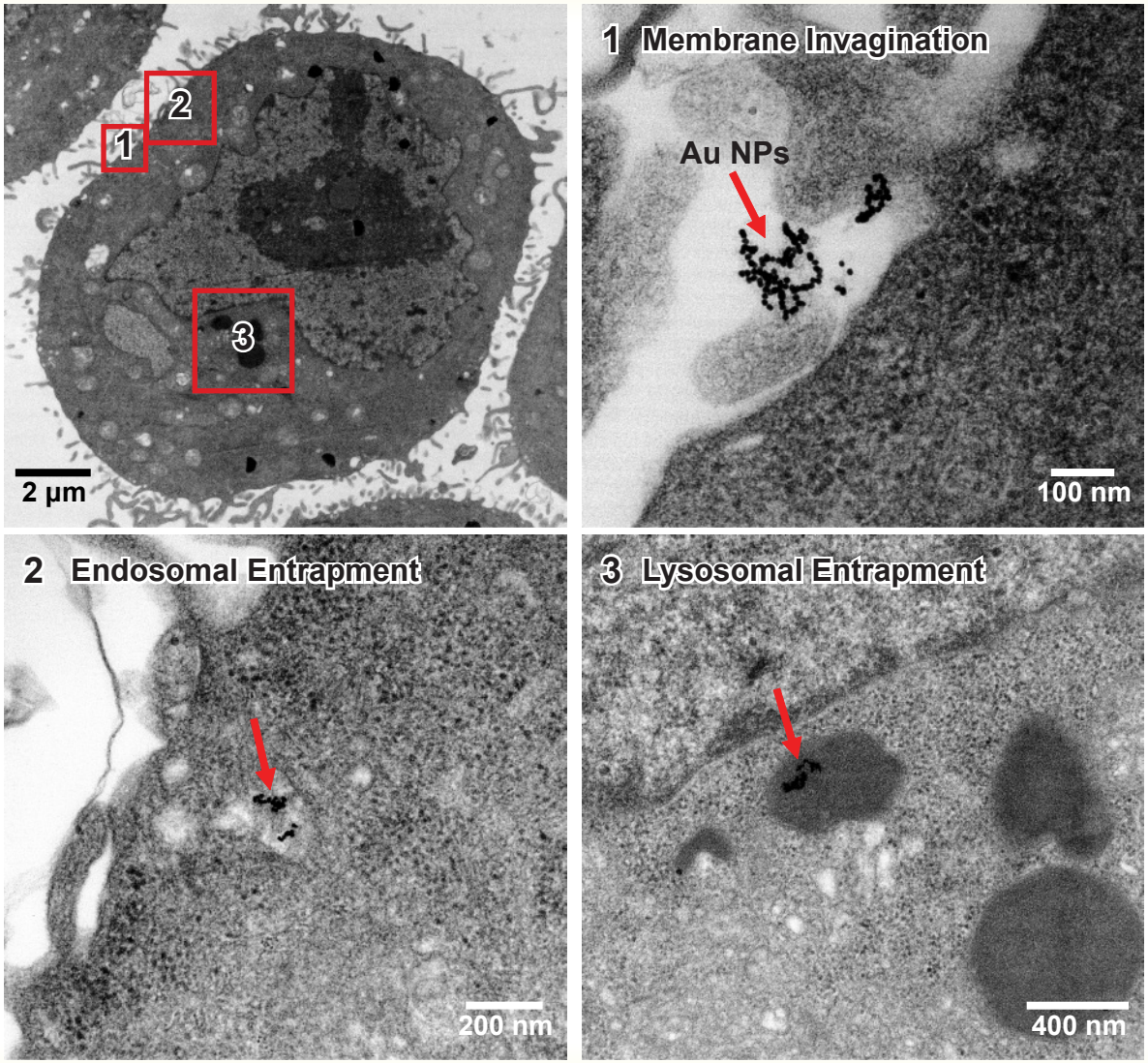
<u>Active Targeting</u>: binding of a functional molecule to specific sites

- ligands (e.g., -COOH, $-NH_2$, $-PO(OH)_2$, etc.)
- proteins
- antibodies e.g., SiO_2 coated Au nanoshells functionalized with anti-HER-2 to target surface receptors overexpressed in breast cancer cells for photothermal ablation
  Lowery et al., Int. J. Nanomed., 2006



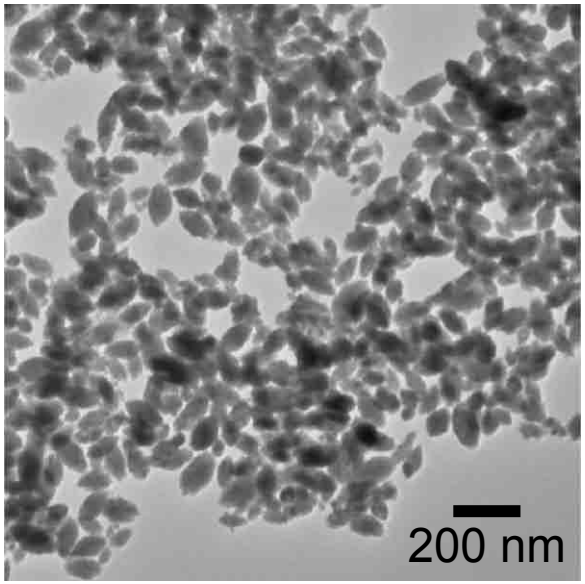


Cellular Uptake of Au NPs

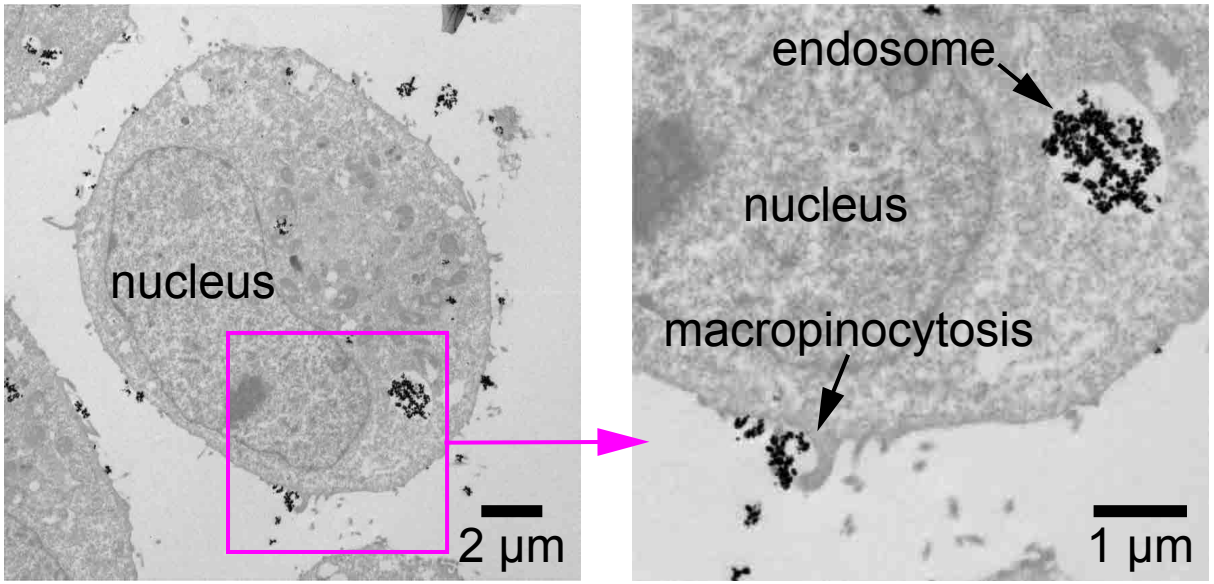


Cellular Uptake of HfO_2 NPs

As-prepared HfO_2 NPs



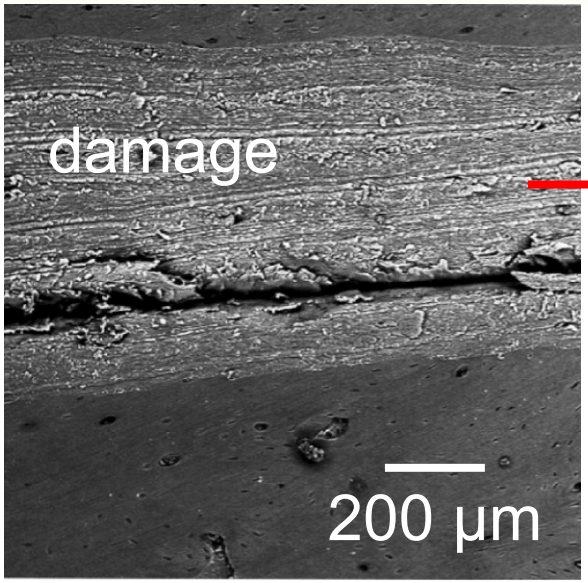
Uptake in HeLa cells by macropinocytosis

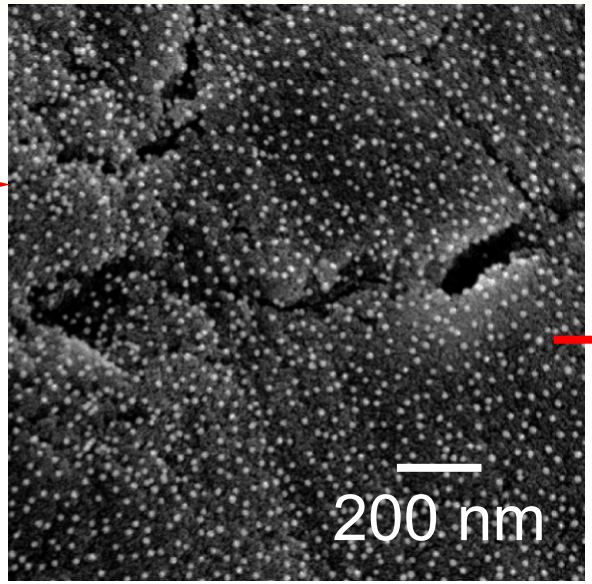


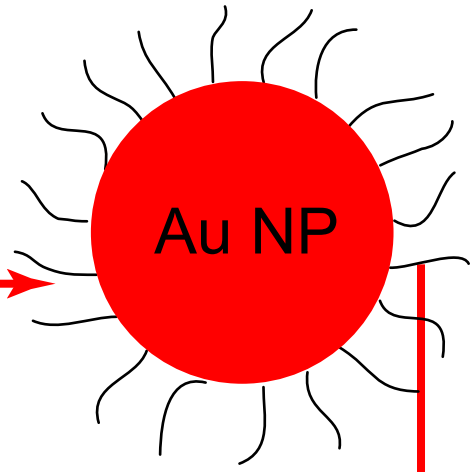
McGinnity *et al., J. Biomed. Mater. Res B*, in review

Targeted Labeling of Damaged Bone Tissue

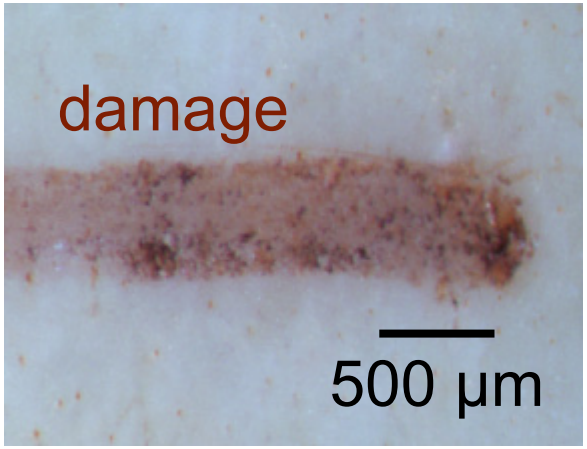
SEM-BEI

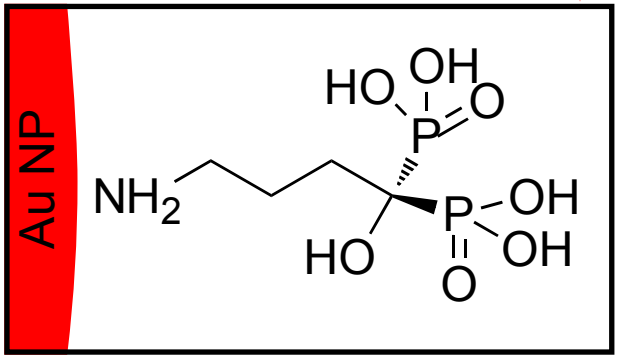






Optical





Ross *et al.*, *J. Biomed. Mater. Res.*, 2011, *JNR*, 2012

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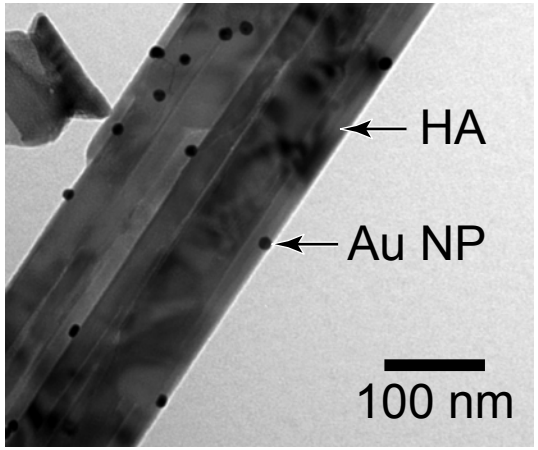
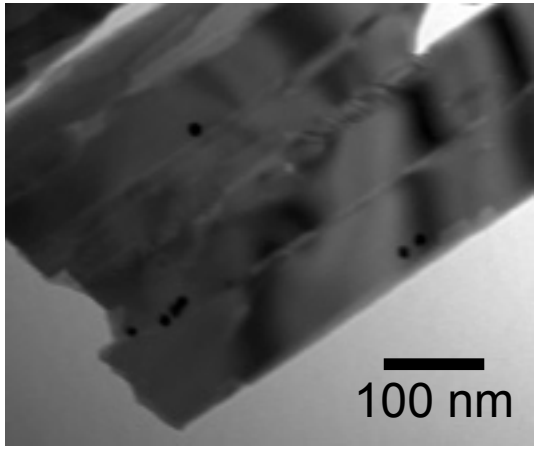
Functionalized Au NP Binding to HA

- used single crystal HA whiskers, 5.63 m^2/g (BET) *Roeder et al., 2006*
- incubated in functionalized Au NP solutions for varying time, concentration, and media (DI H_2O, PBS, FBS)
- measured supernatant [Au] using ICP-OES
- modeled Langmuir binding isotherms

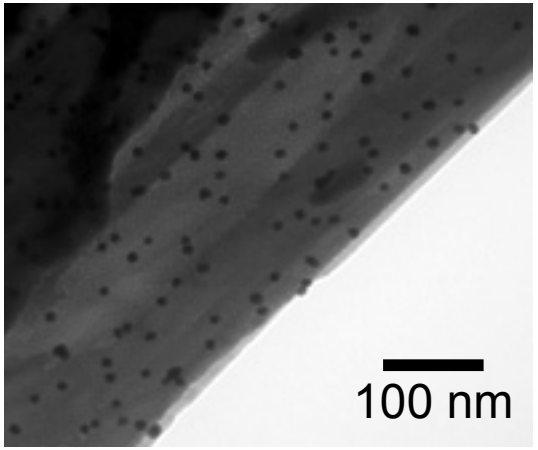
GA-Au NPs



PA-Au NPs

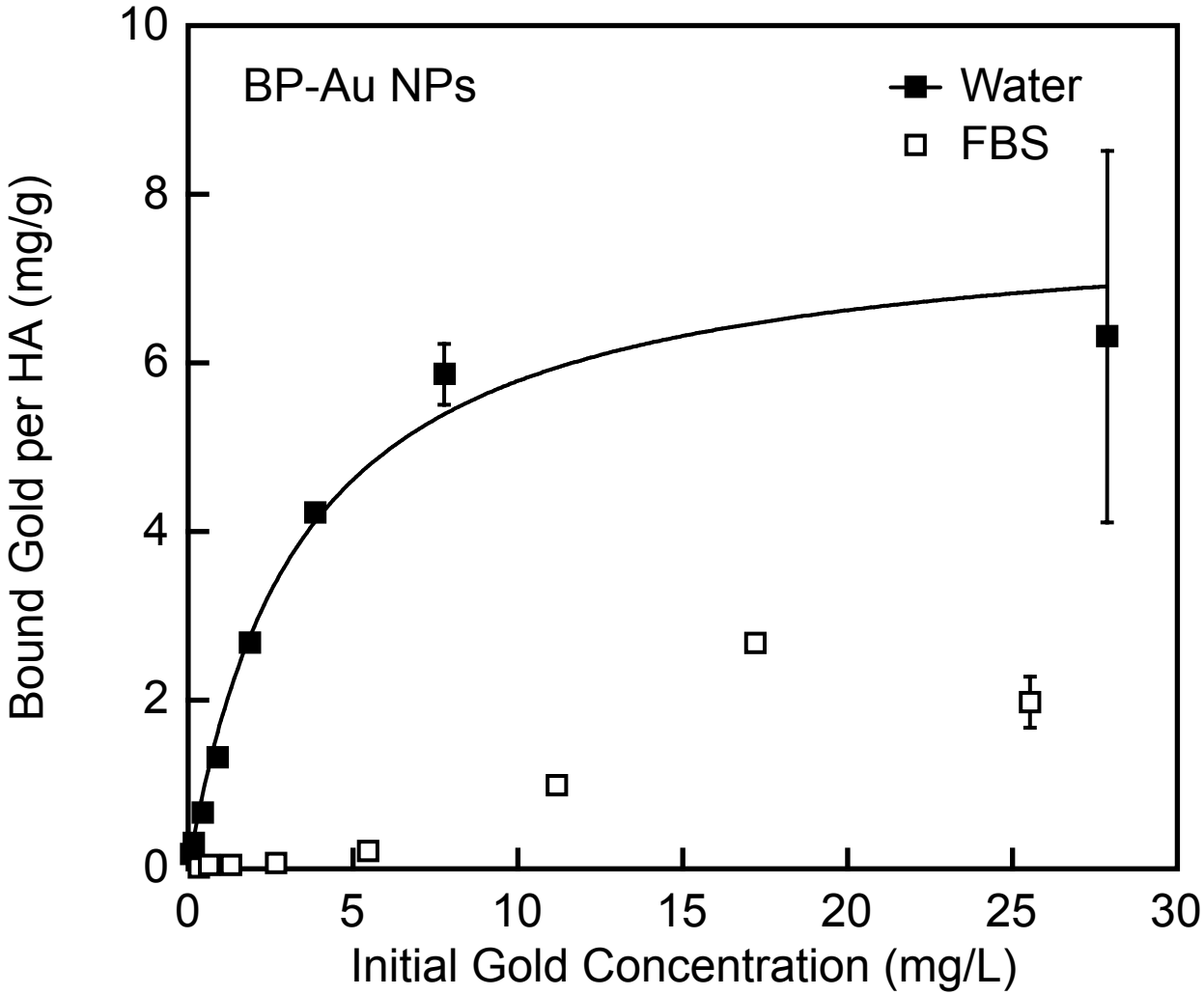


BP-Au NPs



Ross *et al., J. Biomed. Mater. Res.*, 2011

Binding Affinity to HA



Ross *et al., J. Biomed. Mater. Res.*, 2011

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Functionalized Au NP Binding to HA

binding constants in DI water determined from Langmuir isotherms

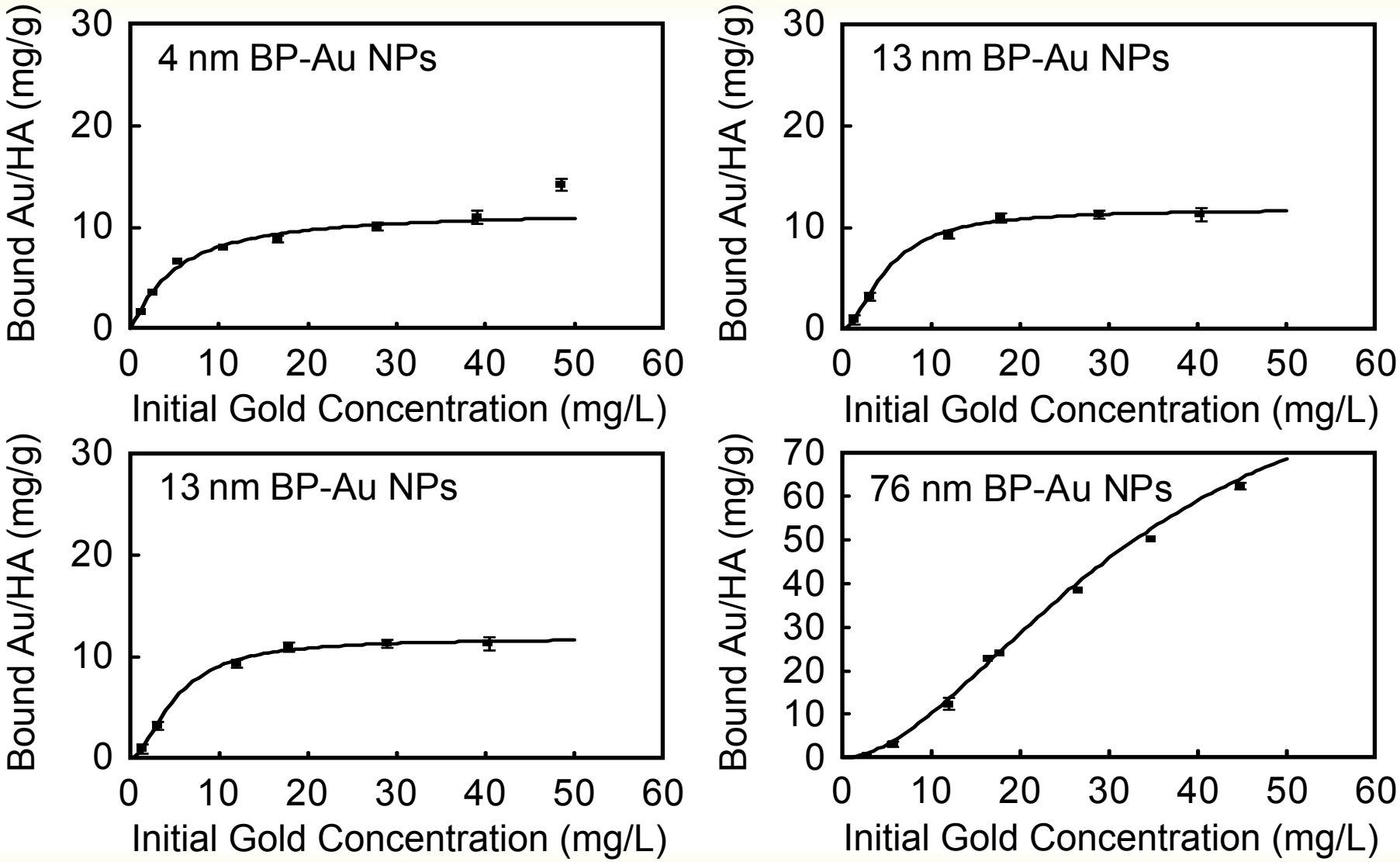
$$V = \frac{V_{max} \cdot [S]}{K + [S]}$$

Group	K (mg/L)	V_{max} (mg/g)	V_{max}* (mg/m^2)	R^2
GA-Au NPs	0.69	1.20	0.21	0.88
PA-Au NPs	0.25	0.48	0.09	0.69
BP-Au NPs	3.40	7.75	1.38	0.95
Au NPs	2.14	0.39	0.07	0.75

Recall that BP exhibited ~50% lower surface density on Au NPs compared to GA and PA.

Ross *et al., J. Biomed. Mater. Res.*, 2011

BP-Au NP Binding Affinity to HA



Ross *et al., Chem. Mater.*, 2014

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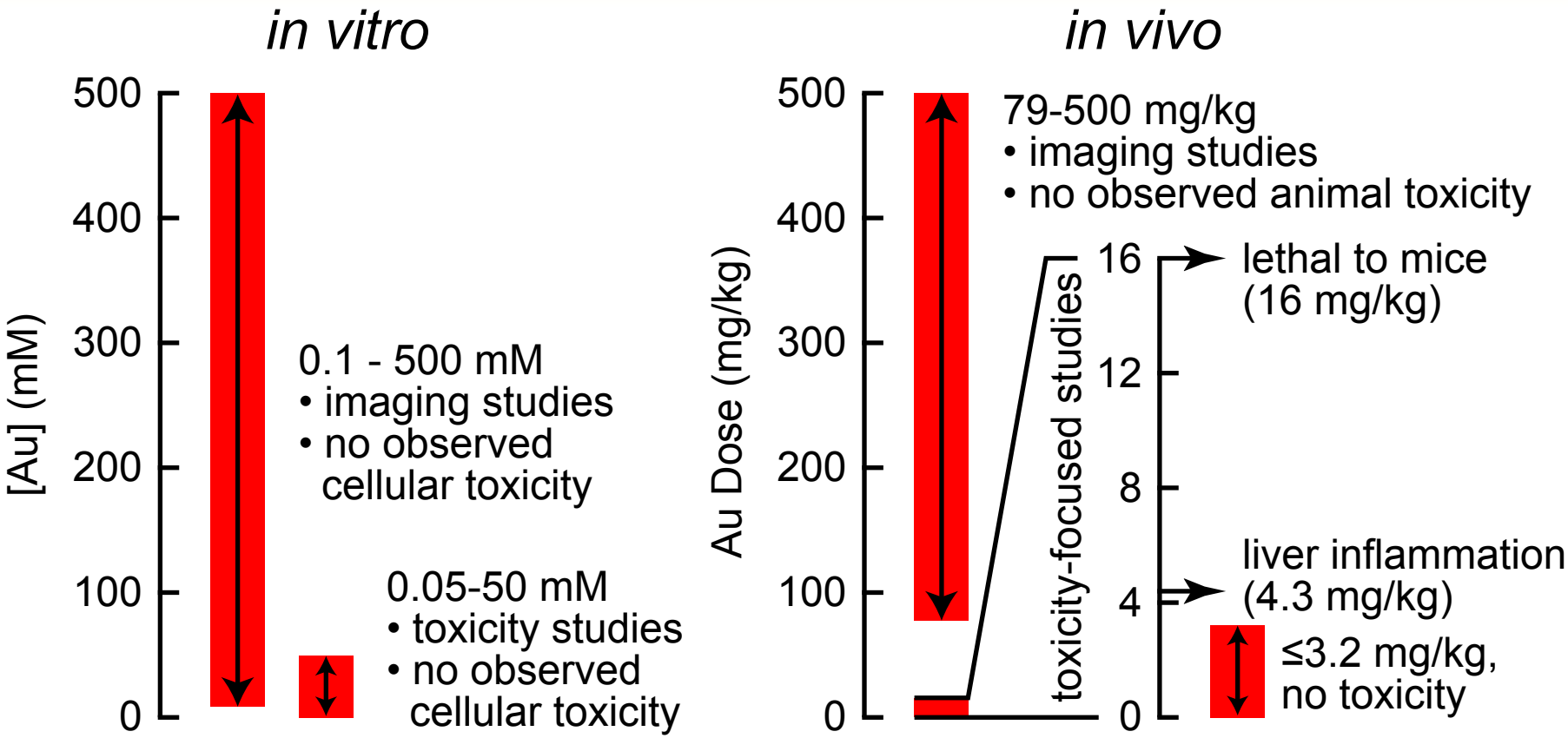
Effects of Au NP Size

	Reference	Size (nm)	# Au NPs/cell	ng Au NPs/cell
Passive targeting to cells	*Chithrani et al.* 2006 Citrate-stabilized Au NPs HeLa cells	14	$3 \cdot 10^{3}$	$8.31 \cdot 10^{-8}$
		30	$4.5 \cdot 10^{3}$	$1.23 \cdot 10^{-6}$
		50	$\mathbf{6 \cdot 10^{3}}$	$7.58 \cdot 10^{-6}$
		74	$4 \cdot 10^{3}$	$1.64 \cdot 10^{-5}$
		100	$2 \cdot 10^{3}$	$\mathbf{2.02 \cdot 10^{-5}}$
	Xu *et al.* 2009 2-mercaptosuccinic acid stabilized Au NPs HeLa cells	4	$\mathbf{1 \cdot 10^{7}}$	$6.46 \cdot 10^{-6}$
		20	$1 \cdot 10^{5}$	$8.08 \cdot 10^{-6}$
		40	$2 \cdot 10^{4}$	$1.29 \cdot 10^{-5}$
		60	$1 \cdot 10^{4}$	$\mathbf{2.18 \cdot 10^{-5}}$
Active targeting to mineral substrate	Reference	Size (nm)	# Au NPs/g mineral	mg Au NPs/g mineral
	Ross *et al.* 2014 Bisphosphonate functionalized Au NPs	5	$\mathbf{9.3 \cdot 10^{15}}$	11.0
		13	$5.1 \cdot 10^{14}$	11.3
		35	$7.0 \cdot 10^{13}$	29.3
		76	$1.6 \cdot 10^{13}$	**62.5**

Cole *et al.*, *Nanomedicine*, 2015

Au NP (Non-)Toxicity



Dosing studies are critical to determine the minimum dose required to enhance contrast without inducing cytotoxicity.

Cole *et al.*, *Nanomedicine*, 2015

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