

# Johns Hopkins Engineering

## Immunoengineering

**Immunoengineering: Biomaterials and Tissue Engineering**

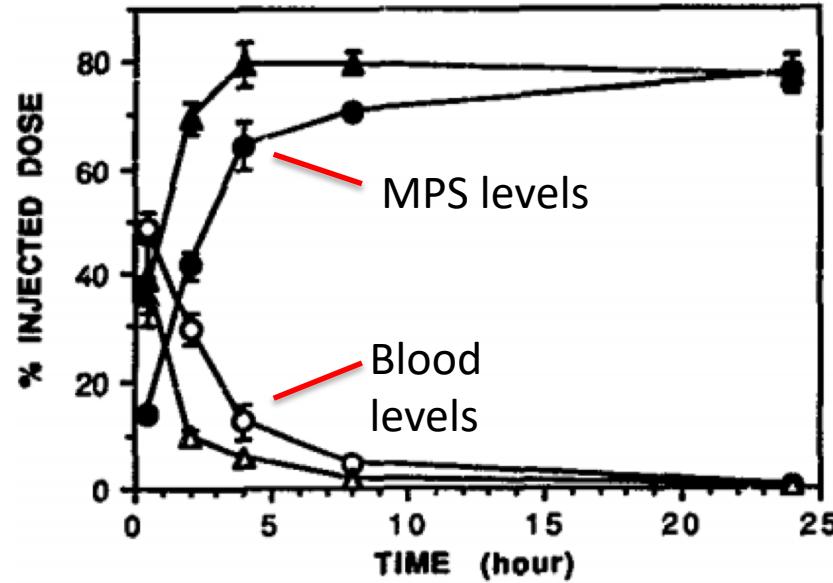
**Immune Recognition of Nanoparticles**



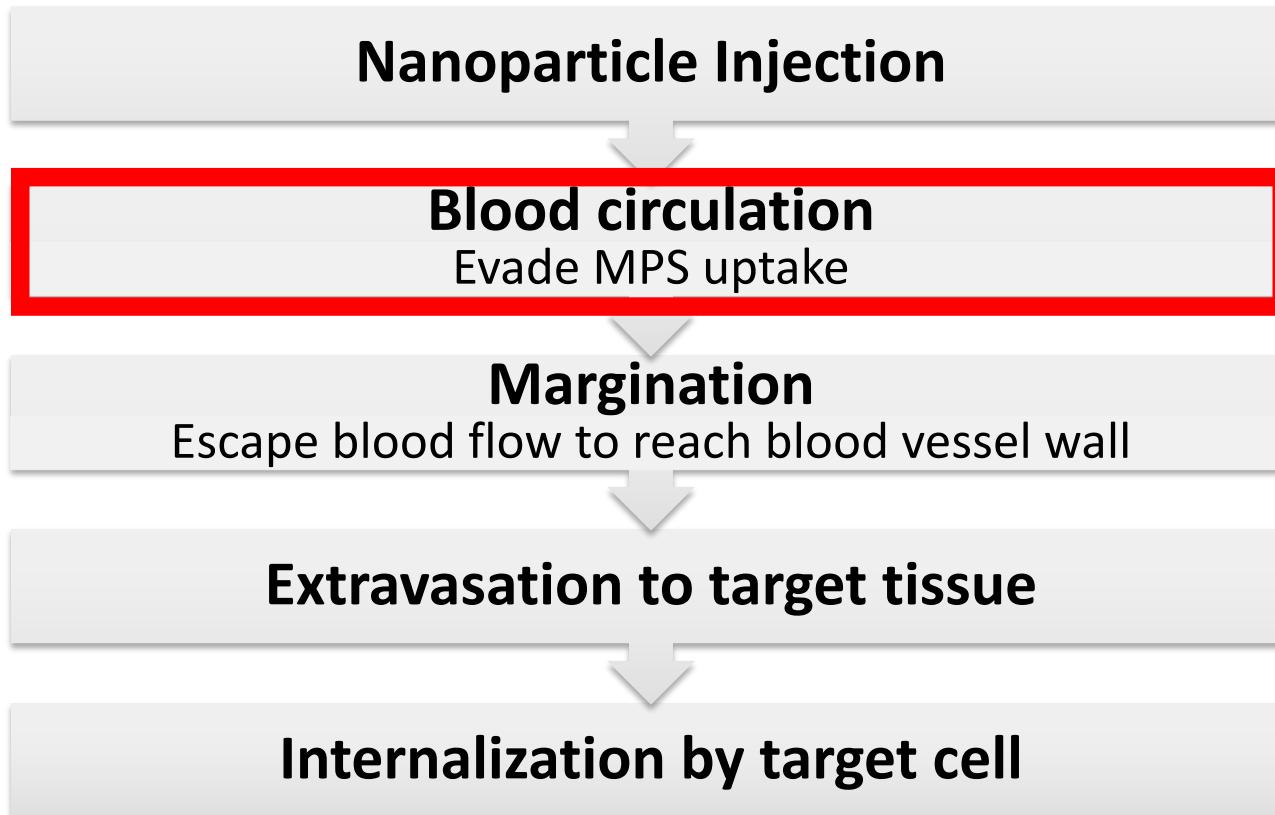
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# Nanoparticle Clearance

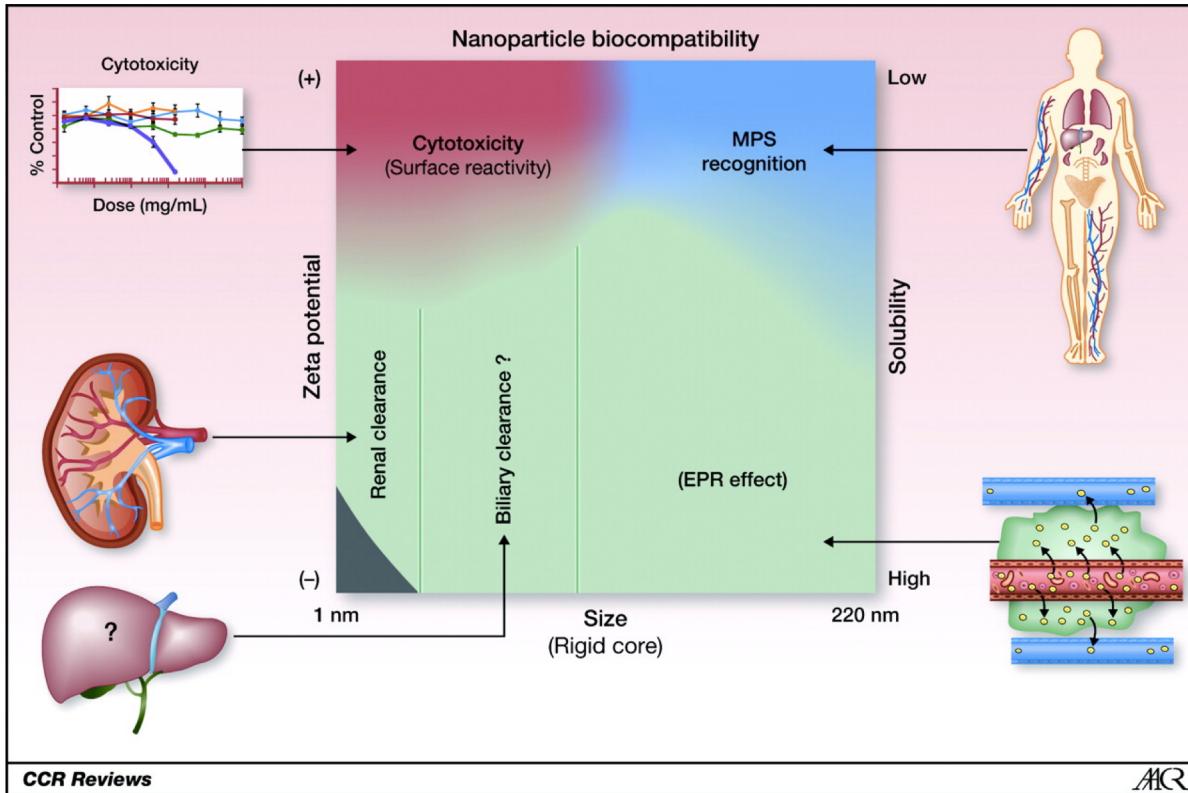
- NPs cleared by mononuclear phagocyte system (MPS), also known as reticuloendothelial system (RES)
  - Monocytes and macrophages in the LNs and spleen
  - Kupffer cells in the liver
- For most drug delivery applications, goal is to prolong NP circulation time
  - Avoid recognition by MPS



# Nanoparticle journey *in vivo*



# Nanoparticle Design Parameters

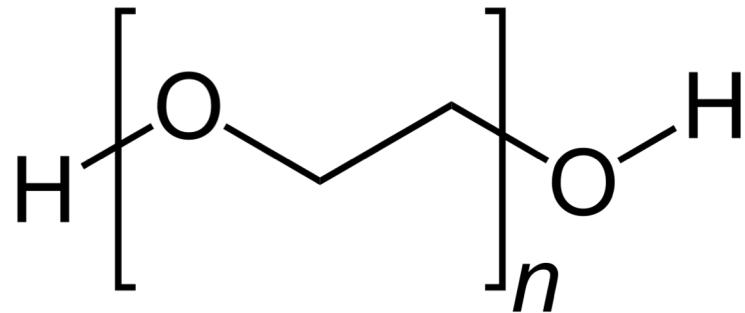


# Mechanisms to avoid macrophage uptake

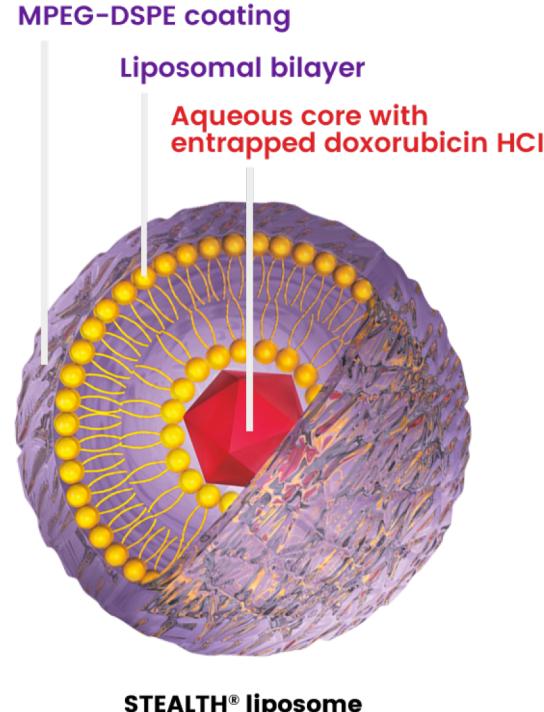
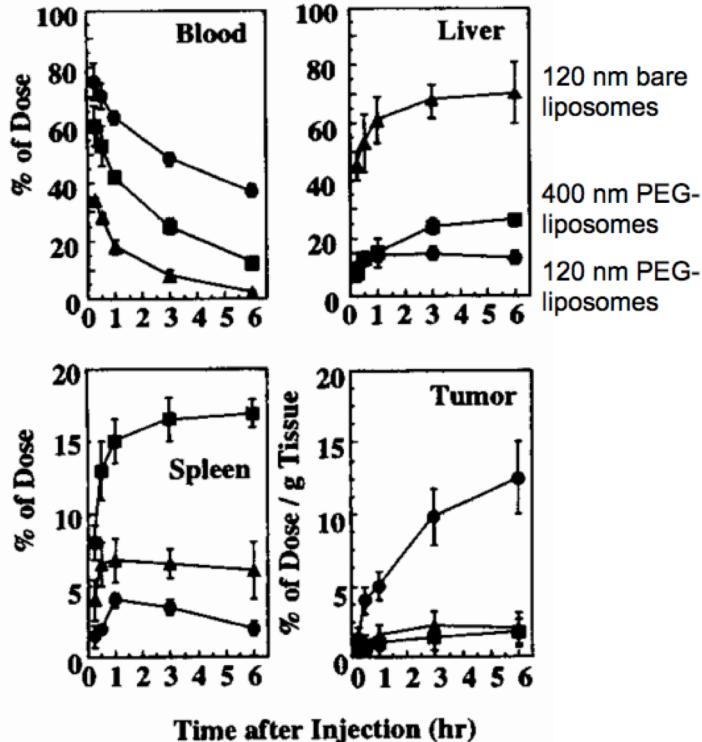
- PEGylation
- “Self” peptide conjugation
- Membrane coating
- Shape modulation

# PEGylated nanoparticles

- Gold standard—most widely used “stealth” technique
- Hydrophilic polymer
- Conjugated to particle surface
- Reduces serum protein binding
  - Steric hindrance



# PEGylated liposomes



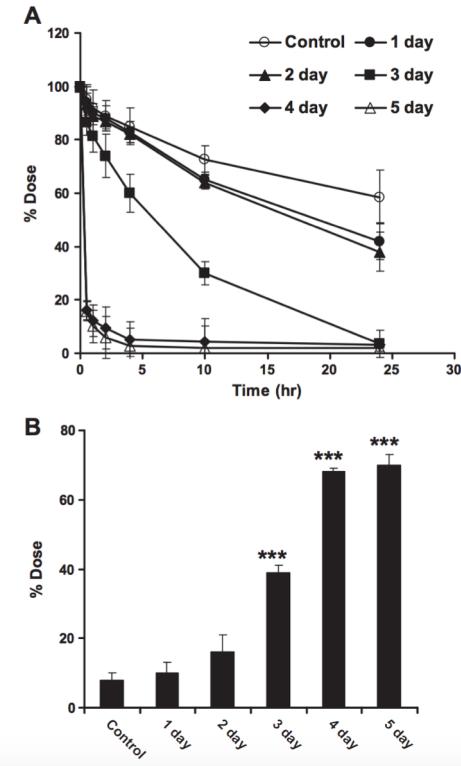
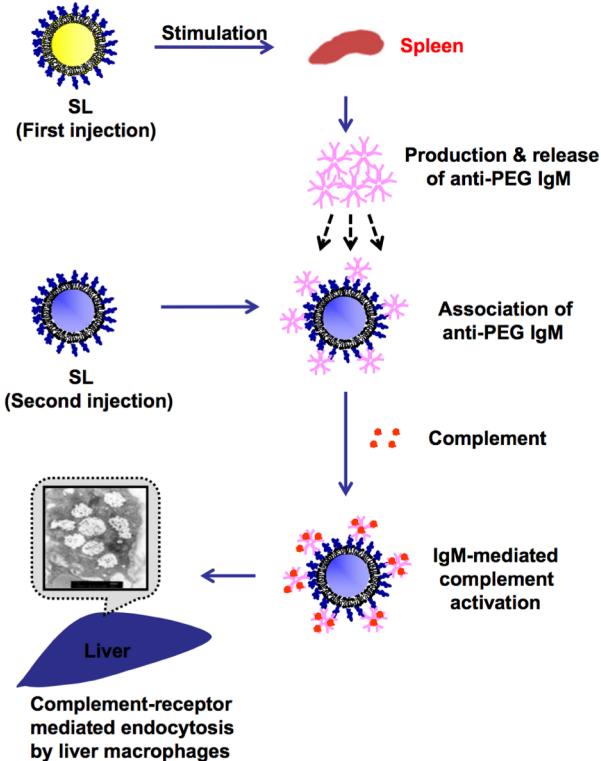
STEALTH® liposome

<https://www.doxil.com/hcp/mechanism-of-action/>  
Ishida et al. "Size-dependent extravasation and interstitial localization of polyethyleneglycol liposomes in solid tumor-bearing mice" *International Journal of Pharmaceutics*, 190 (1999): 49-56

# Disadvantages of PEG

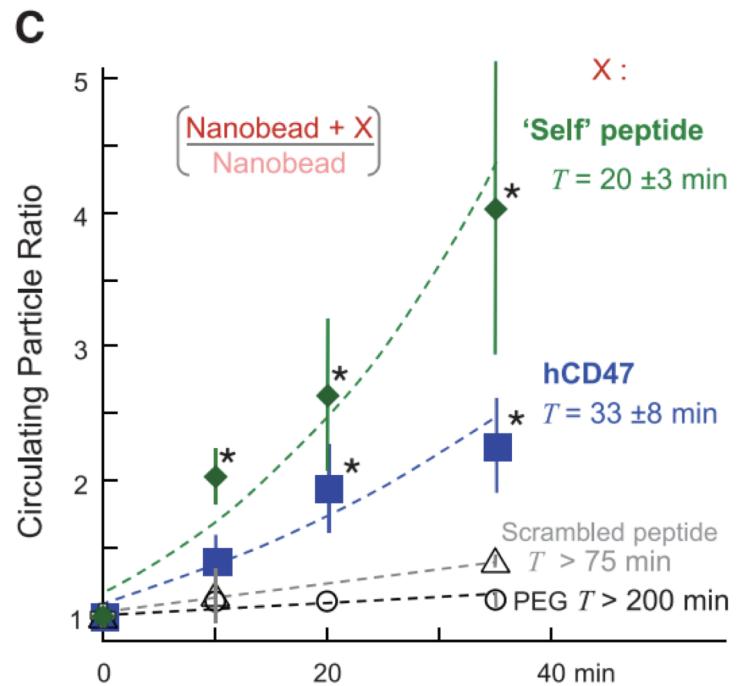
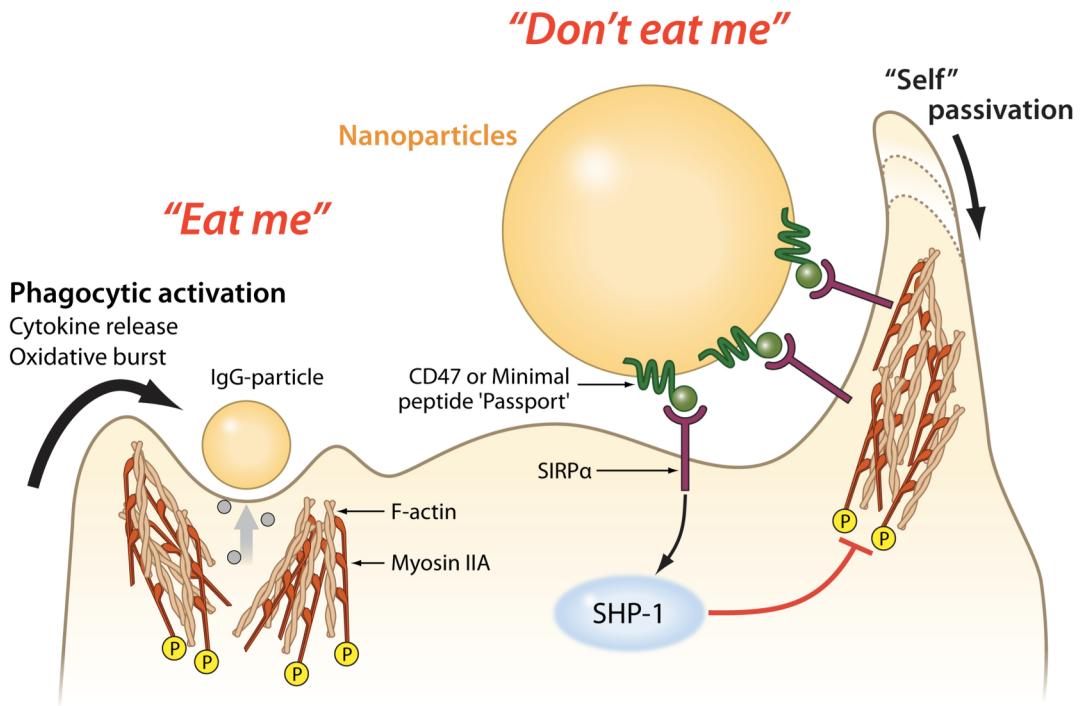
- Limited efficacy
  - Even for highly optimized NPs, 50% of injected dose end up in liver and spleen after 48 hours
- Can also reduce uptake by target cells
- May induce immune responses
- Anti-PEG antibodies develop
  - Accelerated blood clearance (ABC) upon subsequent injections

# ABC Phenomenon

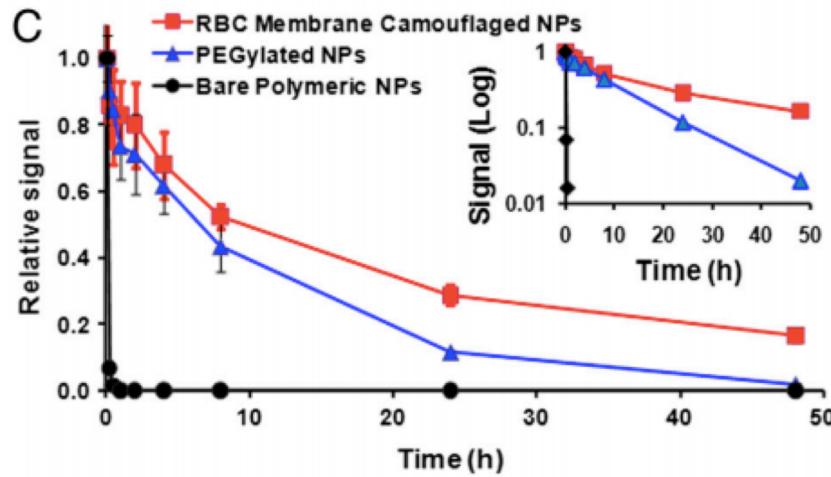
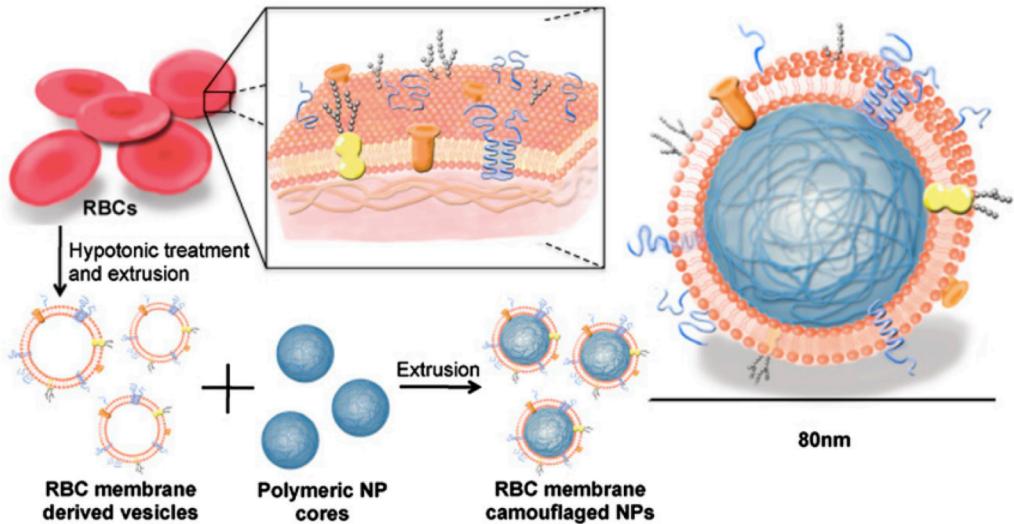


Lila et al. "The accelerated blood clearance (ABC) phenomenon: Clinical challenge and approaches to manage" *Journal of Controlled Release* 172, (2013): 38-47.

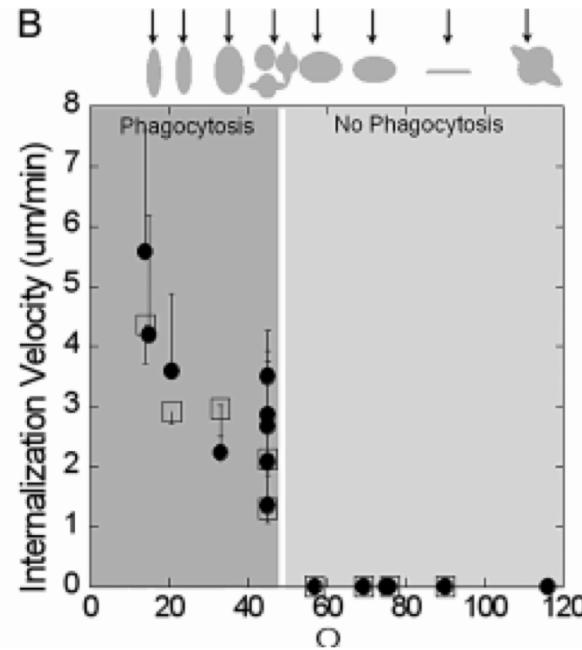
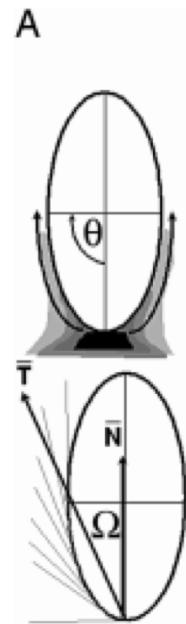
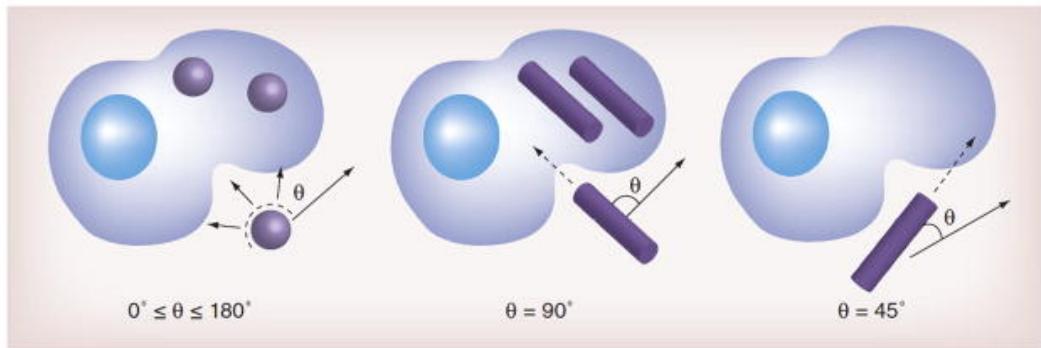
# “Self” peptide conjugation



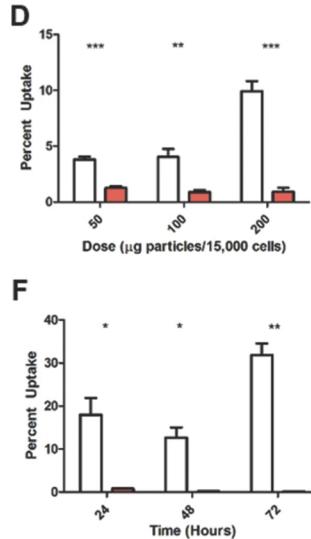
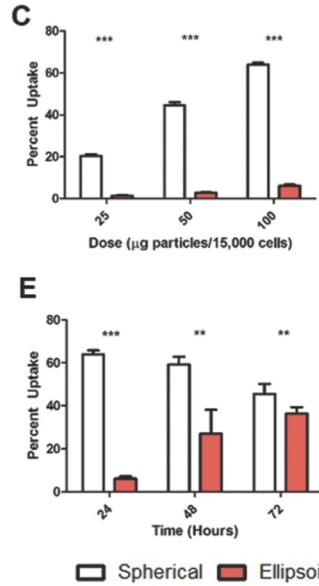
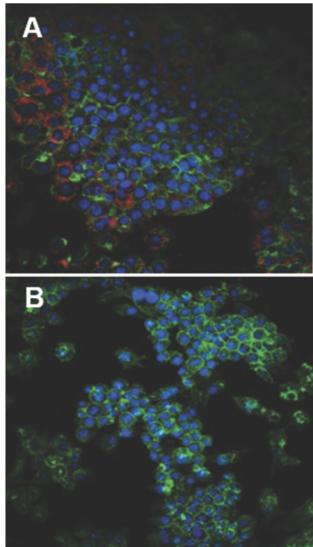
# Cell Membrane Coating



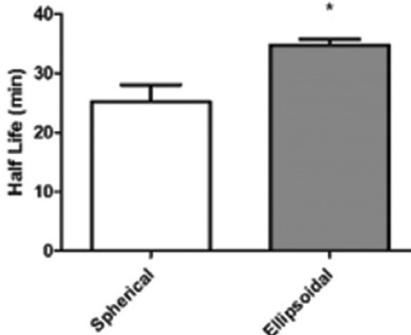
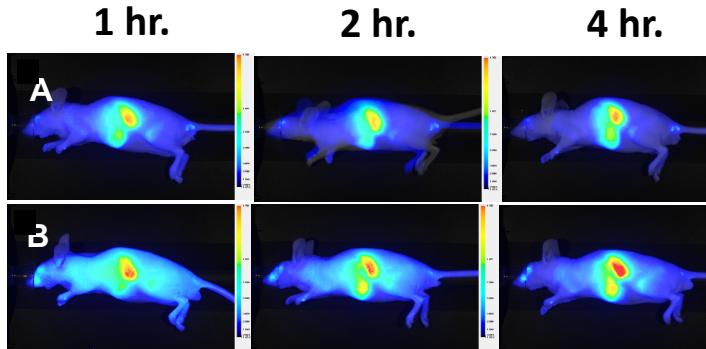
# Particle Shape



# Particle shape affects macrophage uptake



**Spherical**  
**Ellipsoidal**





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