Hot Topic Discussion

A framework for designing delivery systems

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Why is this a hot topic?

Median delivery efficiency **0.7%** of an injected dose of NPs in tumor

2017

Dominant mechanism of extravasation of NPs into solid tumors through **endothelial transcytosis**.

2016

Tumor delivery increased up to 150 times, but only achieved **2% median**

2020

Wilhem, S. *Nature*. **1**, 16014 (2016).

Tavares, A.J. et al. *PNAS*. **114**, 10871–10880 (2017).

Sindhwani, S. *et al. Nature Materials*. **19**, 566–575 (2020).

Ouyang, B. *et al. Nature Materials* (2020).

Poon, W. *et al. Nature Nanotechnology* **15**, 819-829 (2020).

How tumor biology impacts NP delivery

EPR effect
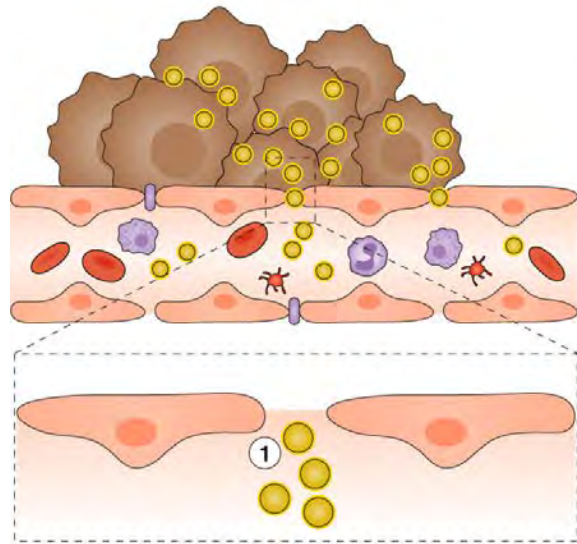
Transcytosis
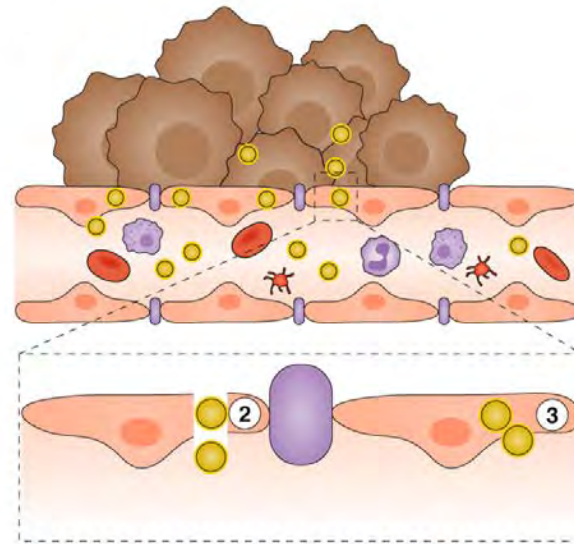
Dose threshold for improving NP tumor delivery
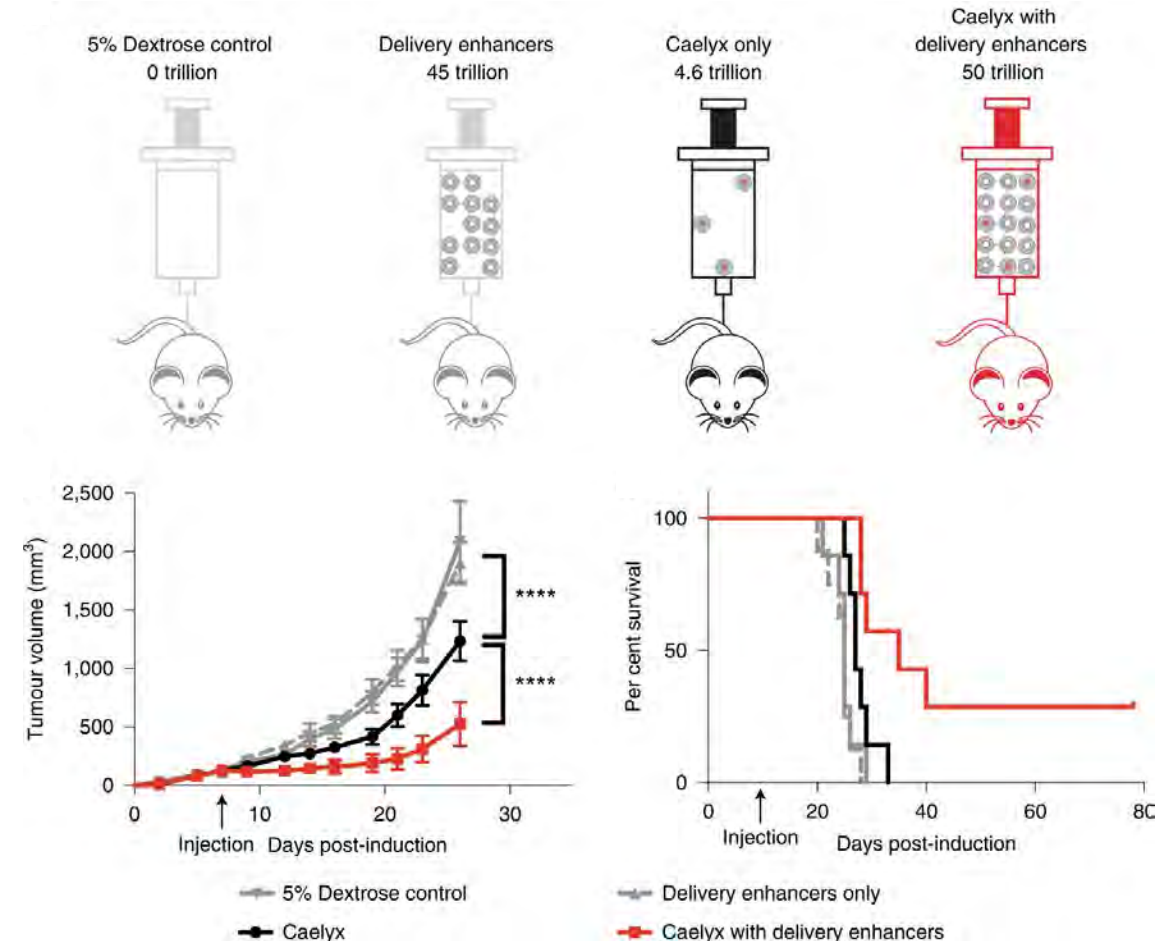
Sindhwani, S. *et al. Nature Materials.* **19**, 566–575 (2020).
Ouyang, B. *et al. Nature Materials* (2020).

The biology of delivery barriers

Poon, W. *et al. Nature Nanotechnology* **15**, 819-829 (2020).
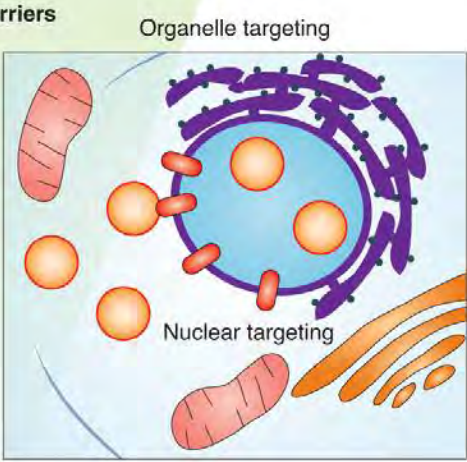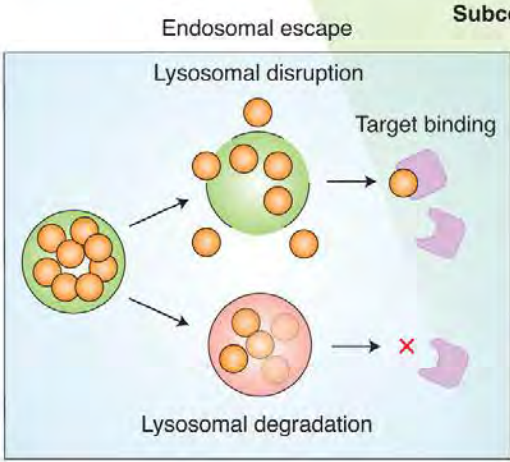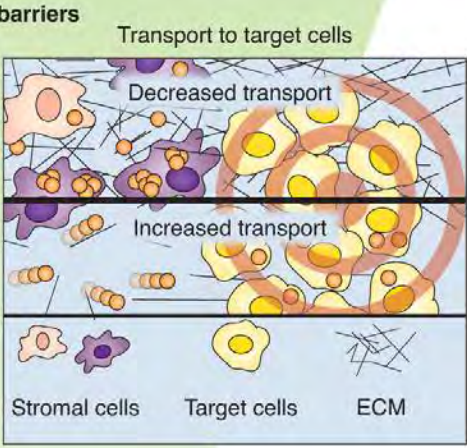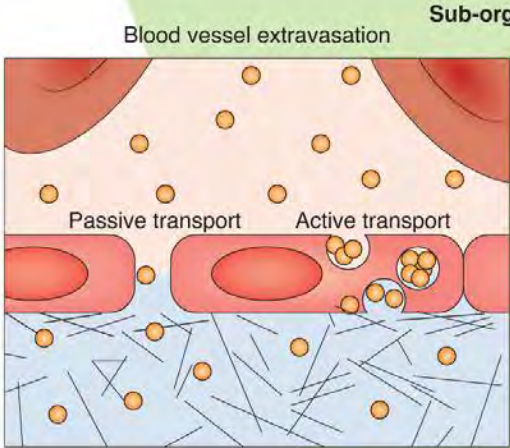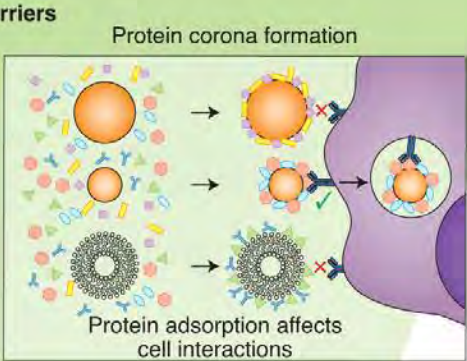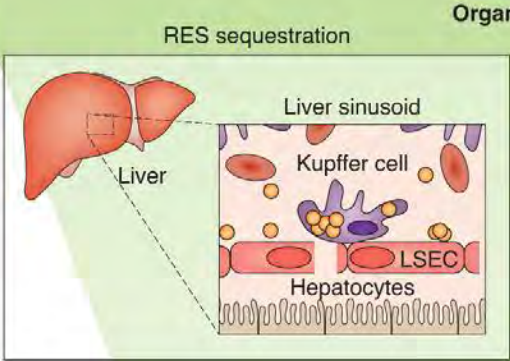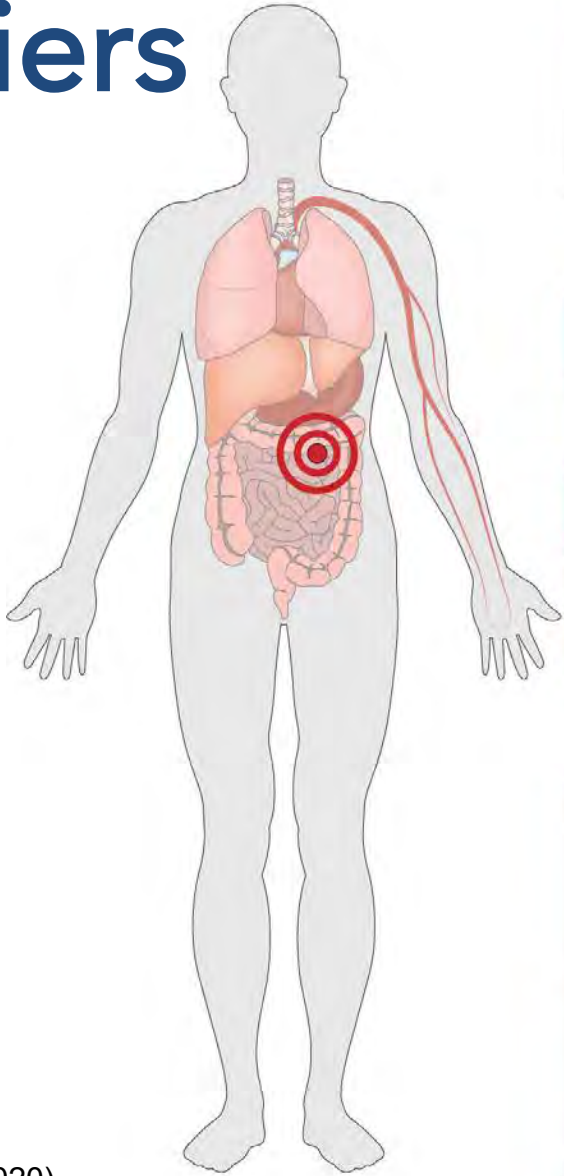
Modeling NP delivery to tumor cells

Poon, W. *et al. Nature Nanotechnology* **15**, 819-829 (2020).

How do we identify the ideal NP?

Classically
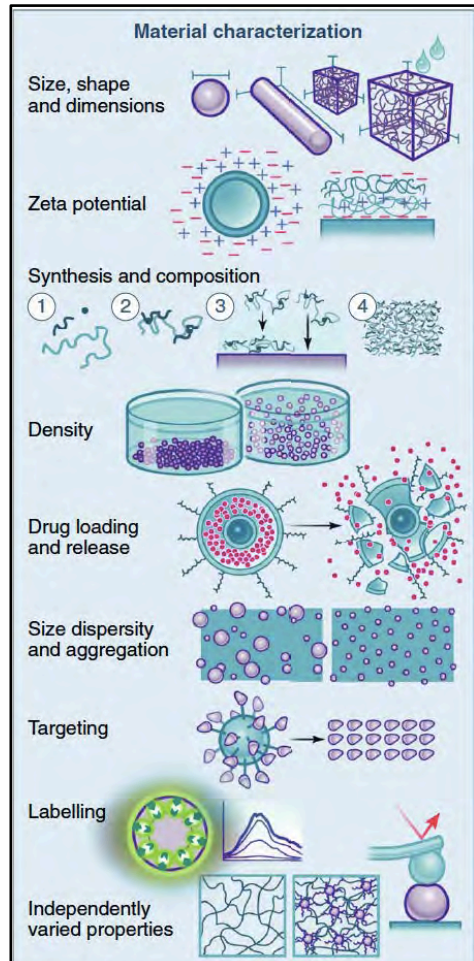
Collect nano-bio interaction data from *in vitro* + *in vivo* studies

Proposed framework

Faria, M., *et al. Nature Nanotechnology* **13**, 777-785 (2018).
Poon, W. *et al. Nature Nanotechnology* **15**, 819-829 (2020).
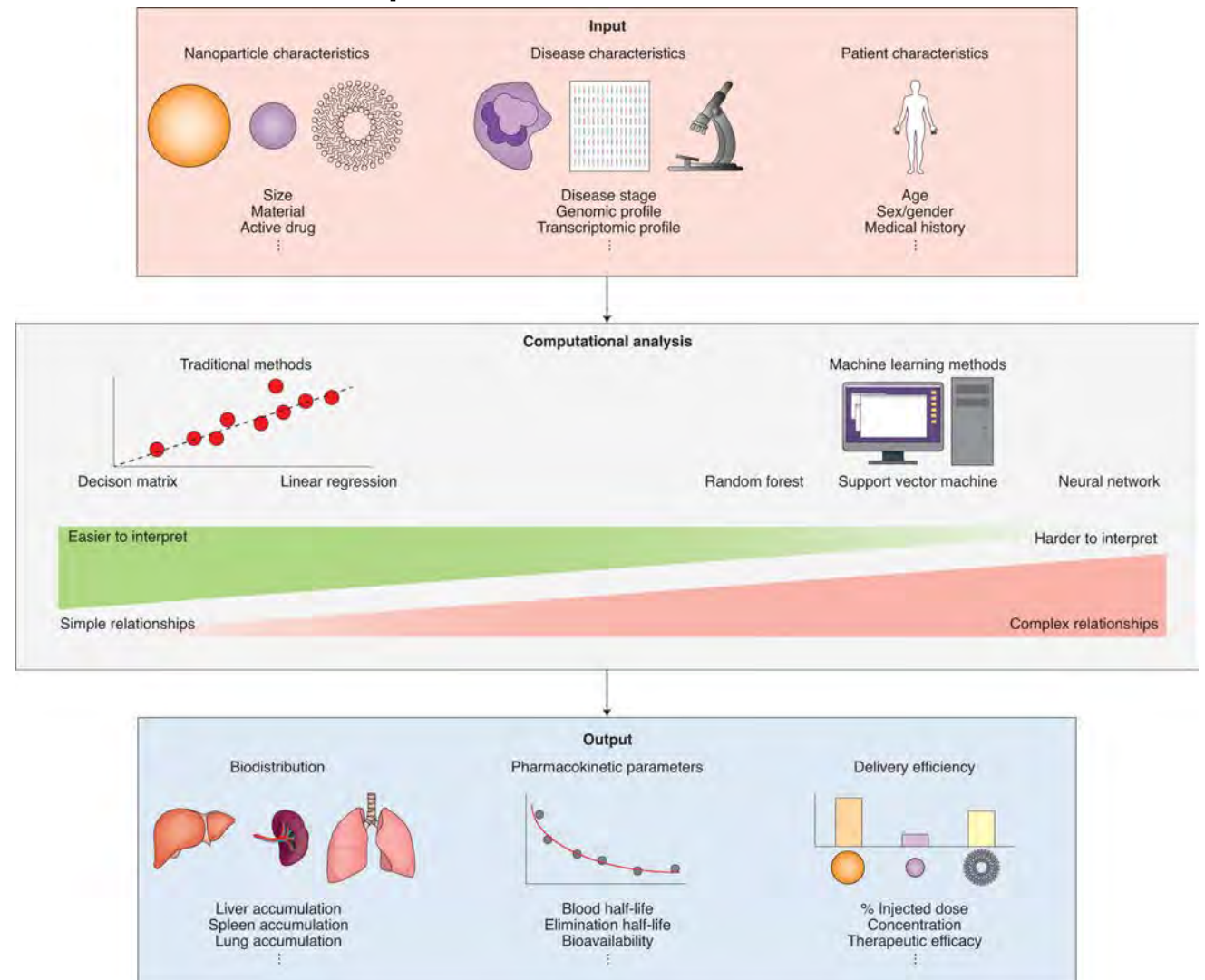
Computational approaches for understanding nano–bio interactions
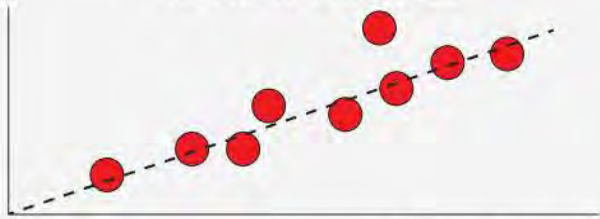
Challenges of using computational approaches:
- Need for large datasets
- Multidisciplinary team of experts including computer science
- Broad algorithms that work across a large variety of nanoparticle formulations or biological applications.

Poon, W. *et al. Nature Nanotechnology* **15**, 819-829 (2020).

Workflow for the development of NP for clinical applications

Poon, W. *et al. Nature Nanotechnology* **15**, 819-829 (2020).
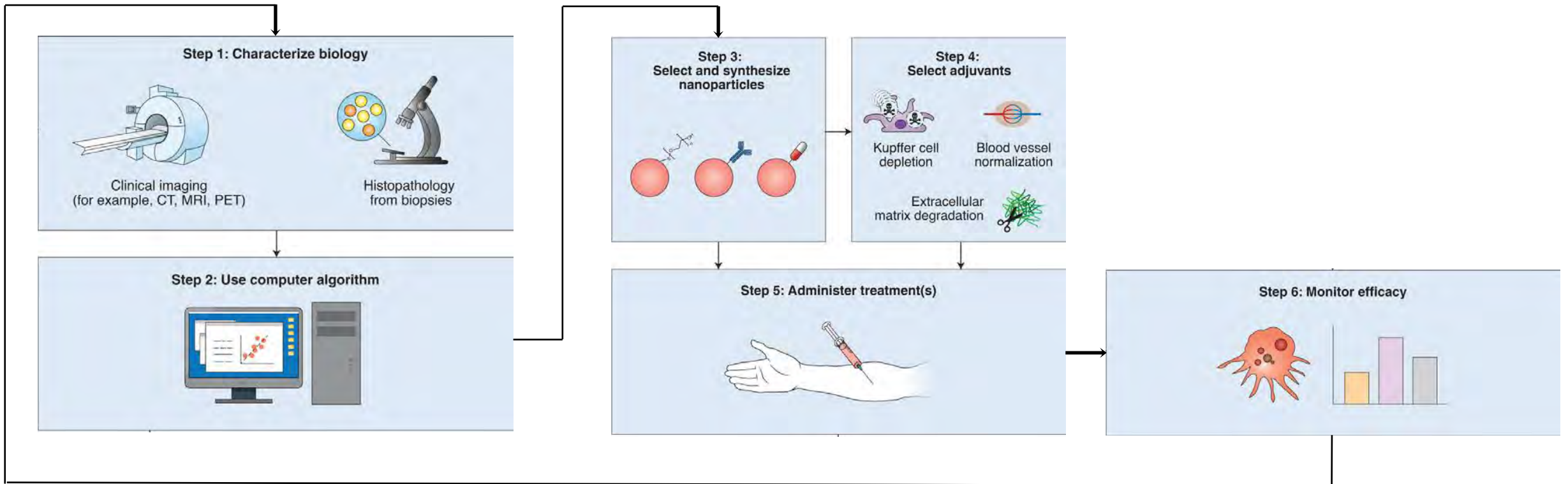
Proposed questions for designing nanoparticle delivery systems

Question	Rationale for the question
(1) Where is the delivery target?	The specific biological target (organ or tissue, cell type and subcellular location) defines design of the nanoparticle strategy.
(2) What is the cargo or active agent that needs to be delivered to the target location?	This defines the chemistry for incorporating the agents into the nanoparticle for delivery.
(3) Where is the site of administration?	The location of administration and the delivery target location define the delivery pathway.
(4) What are the specific organs, tissues and cells encountered along the delivery pathway?	This defines the barriers that the nanoparticle will encounter.
(5) What are the interactions between the nanoparticle carrier and the body in each of these biological environments along the delivery pathway?	These interactions will determine if the formulation is degraded or sequestered before it can reach its intended target location.
(6) What strategies are available to overcome the barriers at each step in the delivery pathway?	This allows the development of specific strategies to overcome the barriers.
(7) How will any administered components leave the disease site and be excreted from the body?	This helps to define locations of toxicity and elimination routes.

Where to get started?

Right here!

Marble Center and other KI colleagues

Swanson Biotech Center:
- High throughput sciences
- Genomics and bioinformatics (BioMicro Center)
- Nanotechnology materials

Across the street!

Whitehead Institute

Broad Institute

Many KI faculty also have Broad affiliation for easy collaborations

Discussion Questions

1. What about high-throughput techniques?

2. What other tools or experimental technique would you like to see applied to the advancement of nanomedicine?

3. Are there any examples out there of computing-enabled therapies that have been approved by FDA?