Our process

- Jacks/Sharp/Langer
- Group of 12
- Meetings every Wednesday at 5:00 pm plus email communication
- Proposal

Projects overview

The CCNE supports the following Projects and Cores:

- Project 1: Targeted polymeric nanoparticles for cancer therapeutic applications
- Project 2: Treatment of cancer with siRNA delivered by nanoparticles
- Project 3: Development of targeted magnetic nanoparticles for imaging
- Project 4: Discrete sensor devices for determining cancer targets
- Project 5: Novel semiconducting nanocrystals for cancer detection
- Toxicity core
- Mouse model core

Additional Funds are also available to fund Pilot Project Studies:

- Hybrid integrated circuit/microfluidic chips for the manipulation of cells
- Linear-dendritic diblock copolymers functionalized with an engineered scFv for targeted, tumor-selective gene delivery and toxin potentiation

Faculty members leading core or pilot projects include:

- Nobel Prize winner
- Draper Prize (Engineering Nobel Prize Equivalent) winners
- MacArthur Prize winner
- 3 women
- 1 minority
- 4 members of NAS; 1 member of the NAE
- Assistant Professors→ Institute Professors

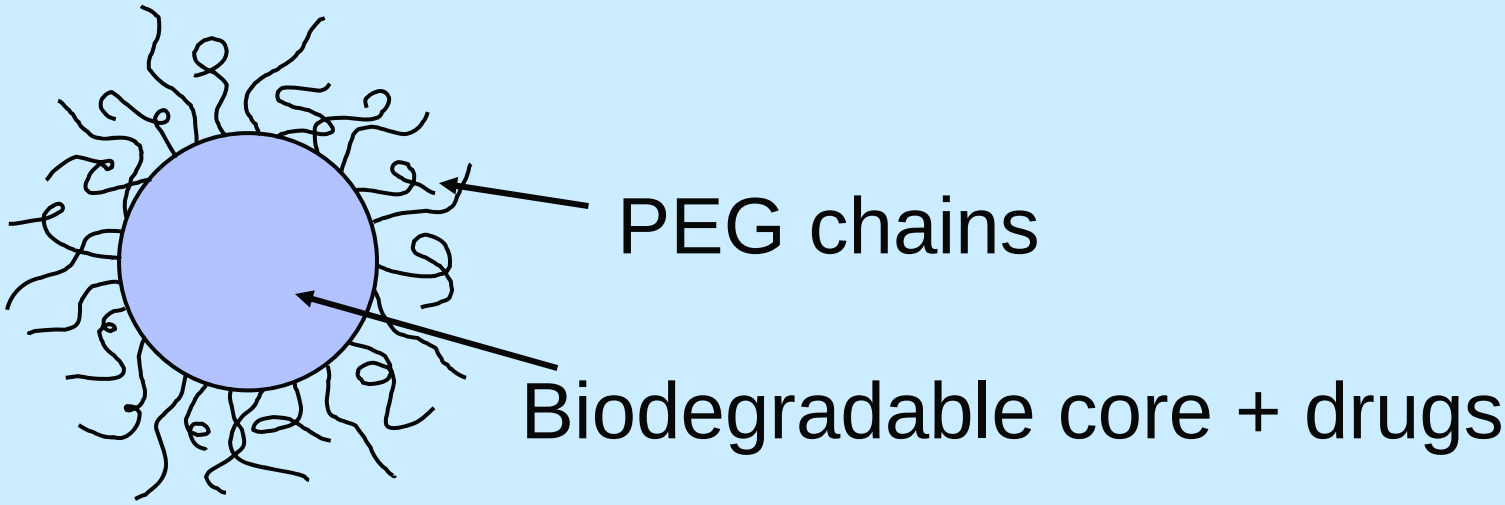
Overview of targeted therapies

Technology	**Example**	**Approved drugs**	**Payload**
Naked ligands	Humira, Macugen	18	none
Fusion proteins	Ontak	1	enzyme
Radioimmuno-conjugates	Zevalin, Bexxar	2	radioisotope
Chemoimmuno-conjugates	Mylotarg	1	2-8 molecules
Nanoparticle conjugates		0	10^3 - 10^5 molecules

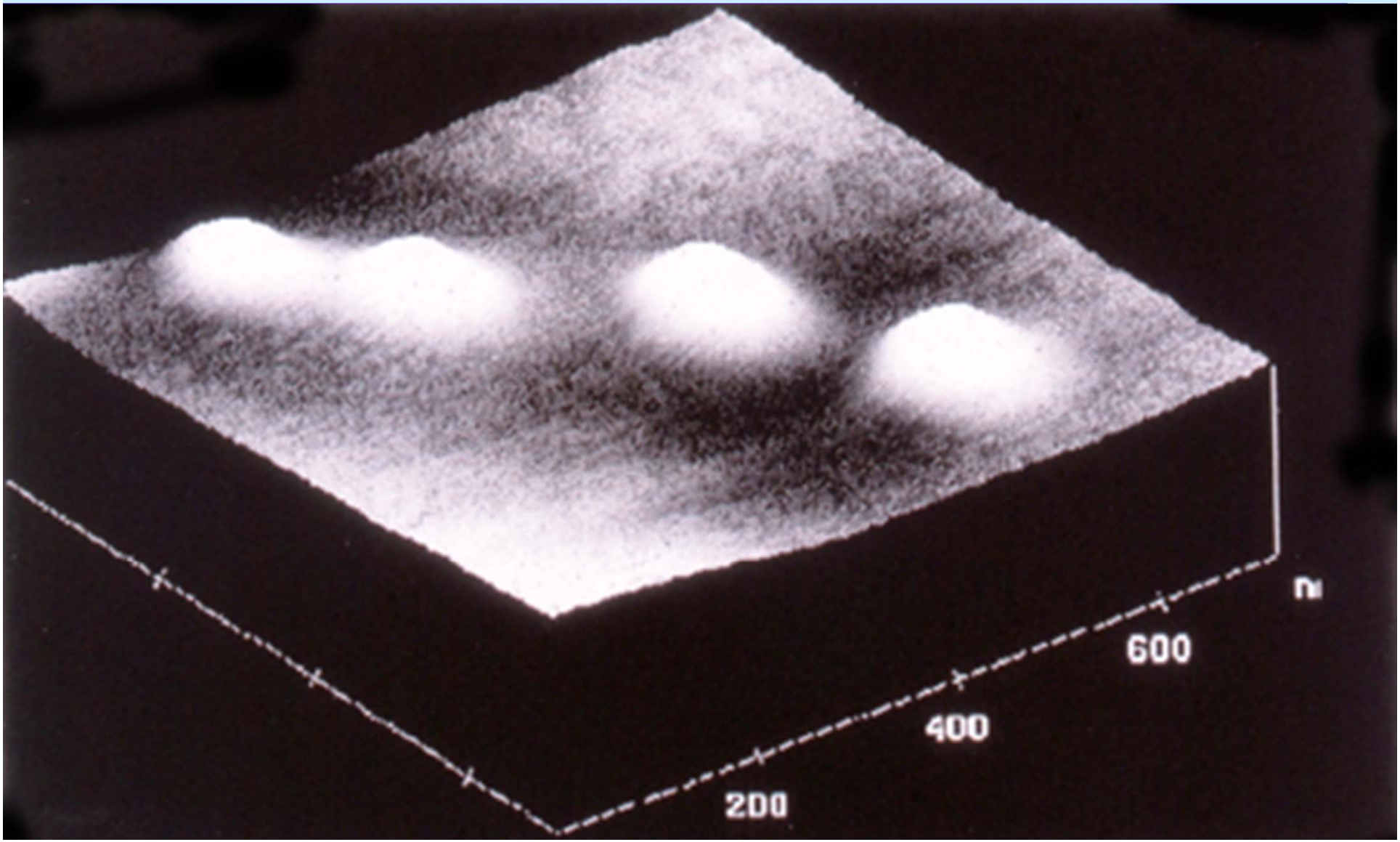
Desired nanoparticle characteristics

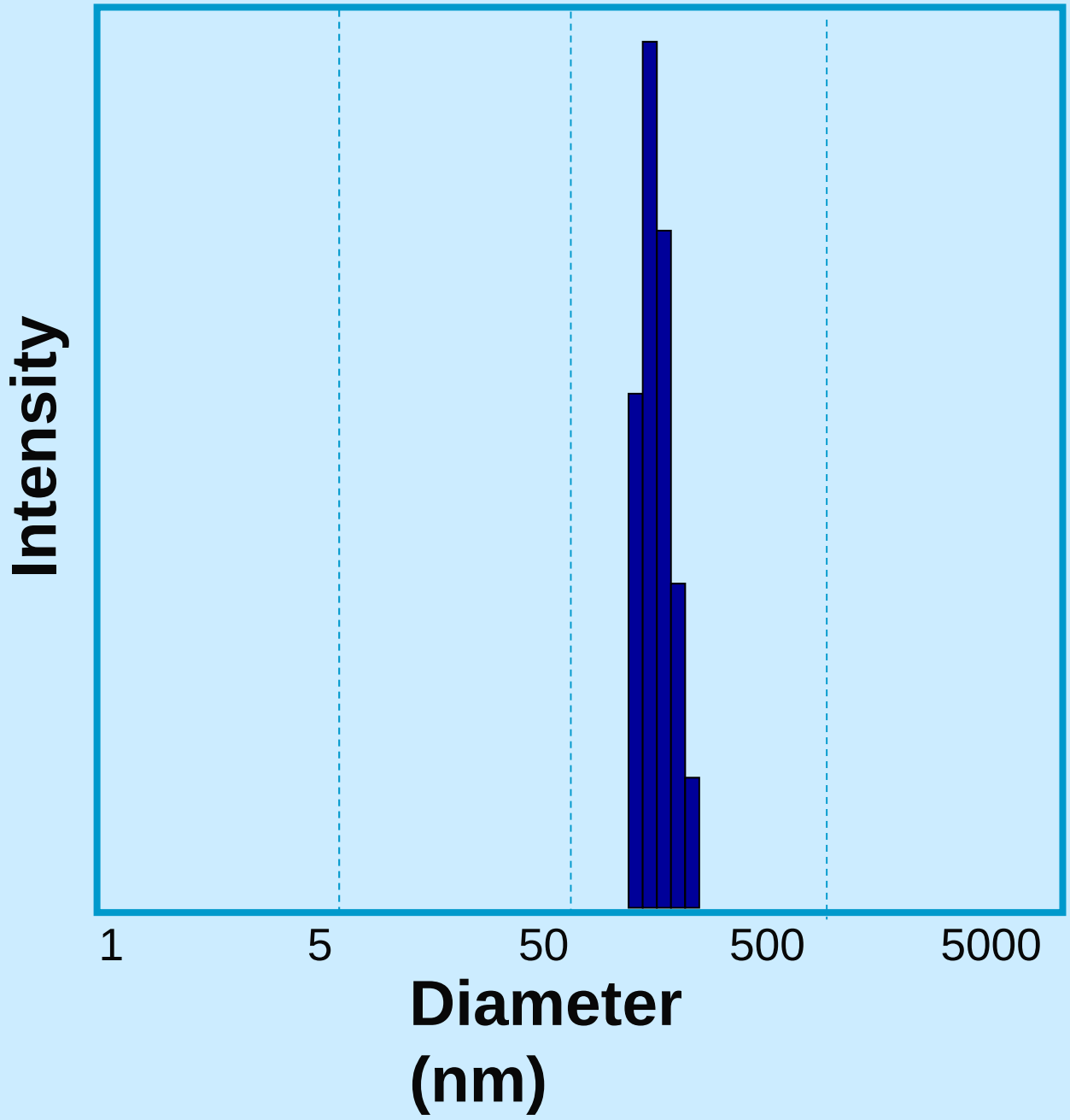
- High encapsulation amount (> 30%)
- High encapsulation efficiency (> 80%)
- Can be freeze dried
- No aggregation
- Degradable
- Small (200 nm or less)
- Not rapidly cleared

Coating nanoparticles with polyethylene glycol (PEG)



Atomic force microscope shows spherical shape nanoparticles



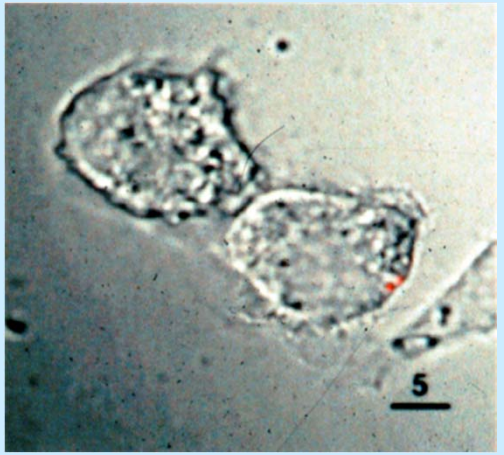

Intensity
1
5
50
500
5000
Diameter
(nm)

In vitro phagocytosis of surface-modified polymeric particles

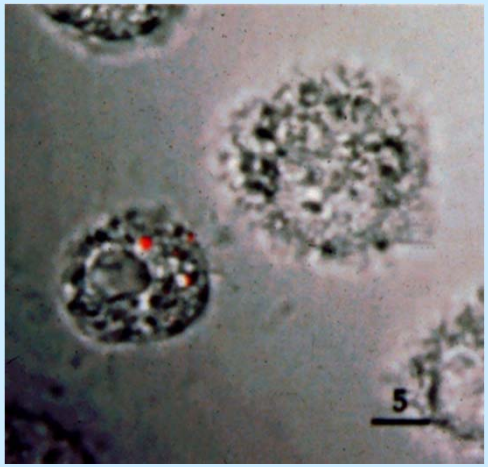
Rat alveolar macrophages - 1hr

Polymeric particles without PEG

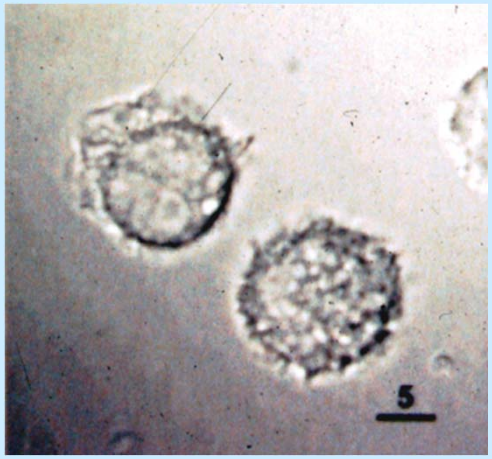
PEG (5000 M.W. Single chain)

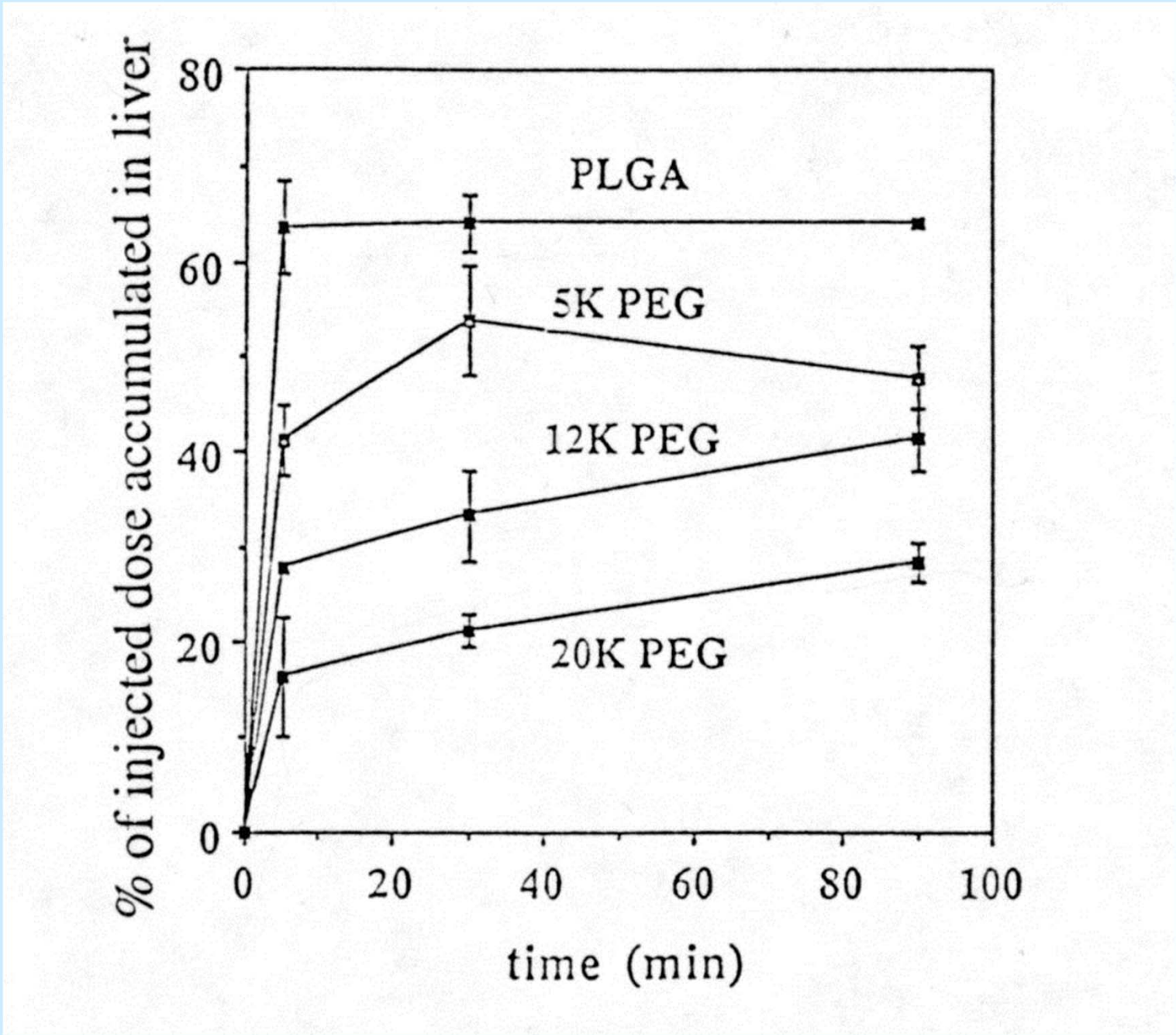


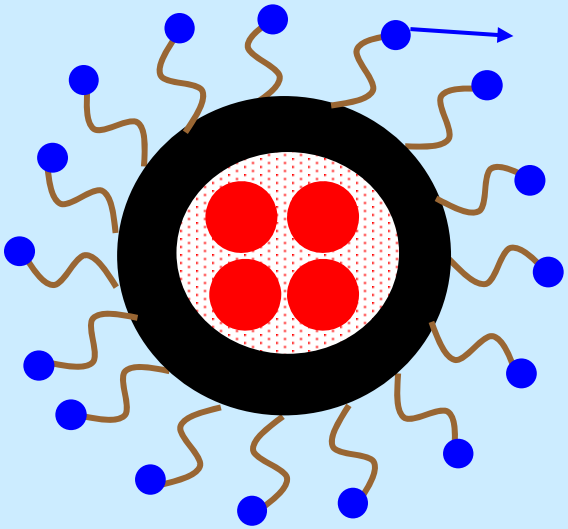
PEG (20,000 M.W. Single chain)

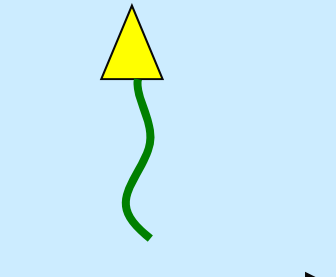


PEG (5000 M.W. Triple chain)

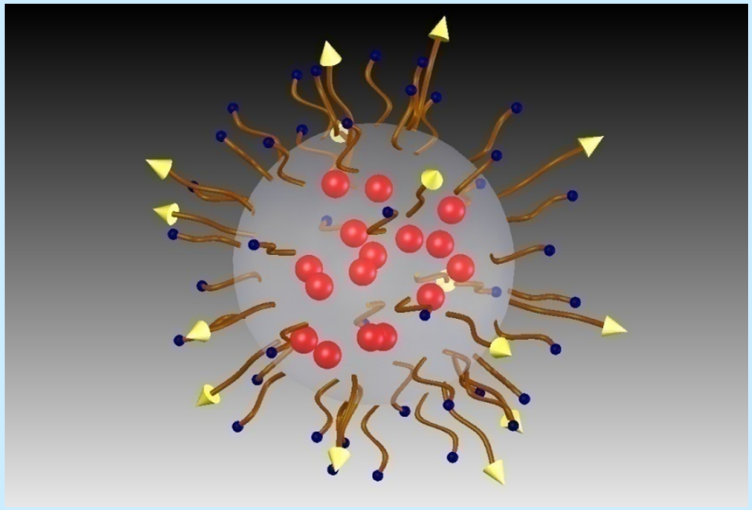


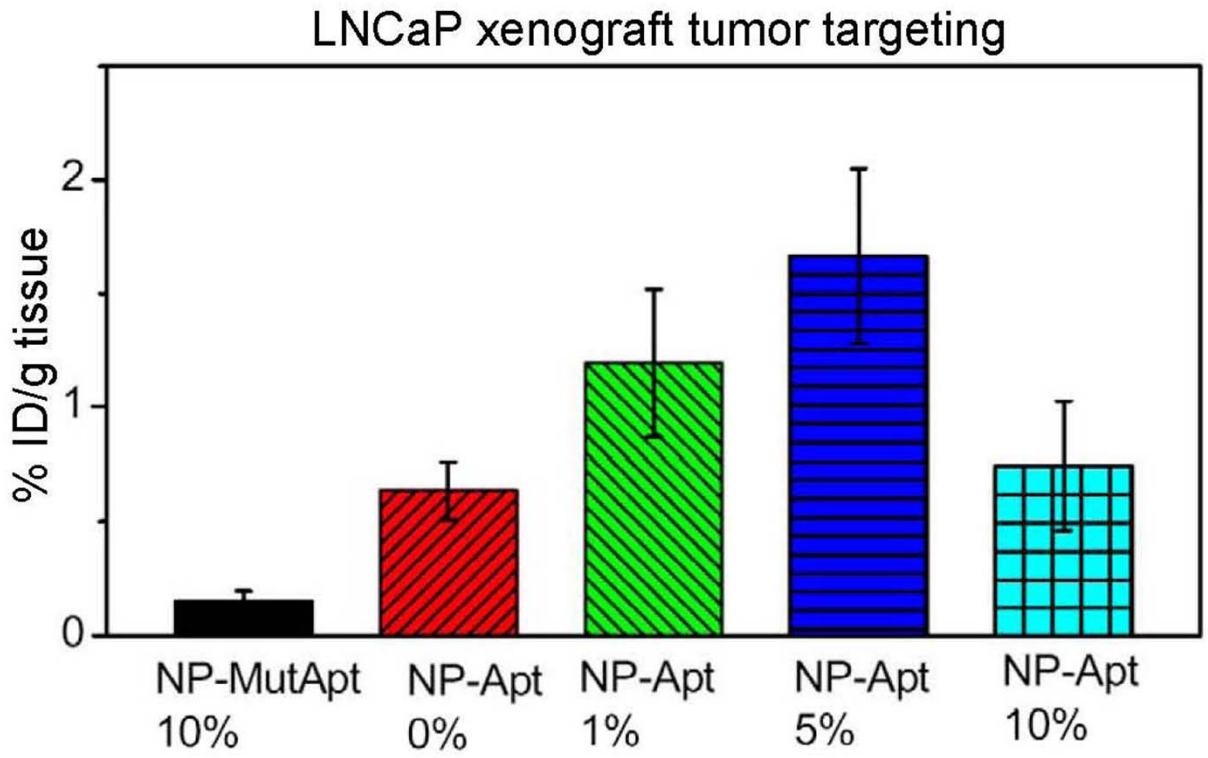

% of injected dose accumulated in liver
80
60
40
20
0
PLGA
5K PEG
12K PEG
20K PEG
0
20
40
60
80
100
time (min)



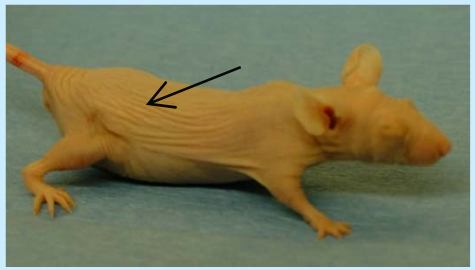


Targeting
molecule

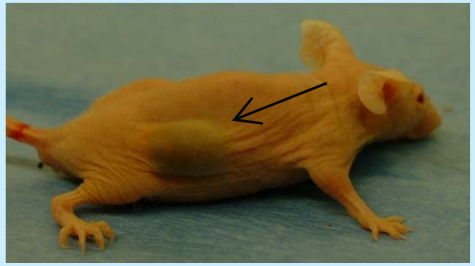


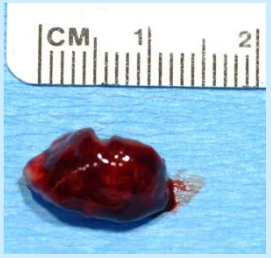

LNCaP xenograft tumor targeting
% ID/g tissue
0
1
2
NP-MutApt 10%
NP-Apt 0%
NP-Apt 1%
NP-Apt 5%
NP-Apt 10%

Targeted NP

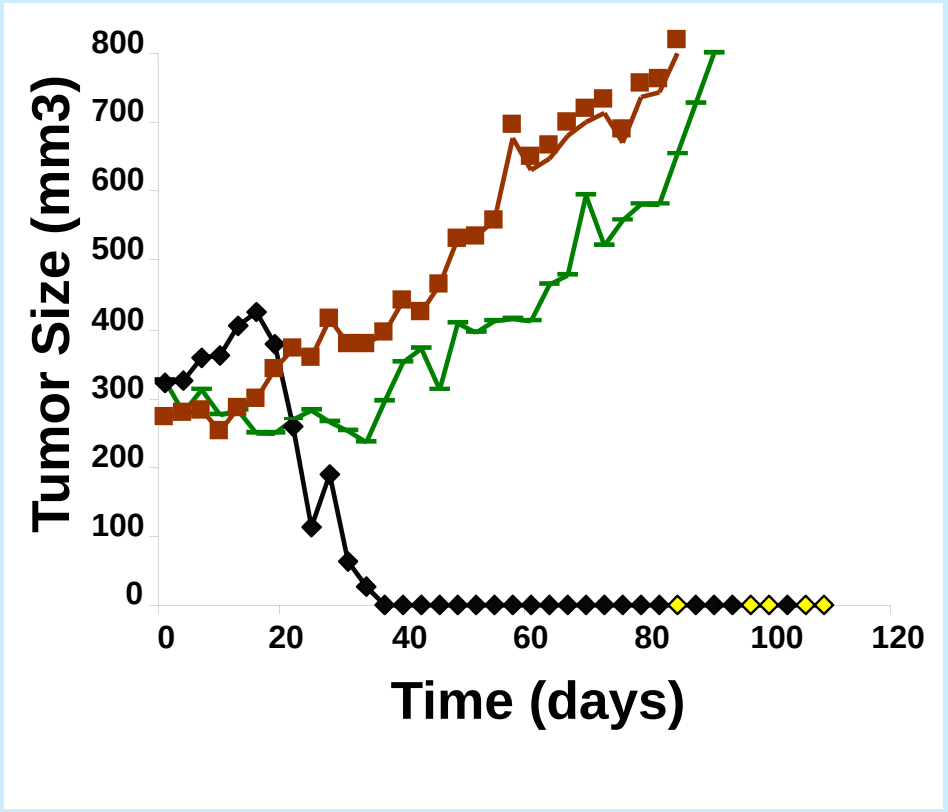


Decetaxel

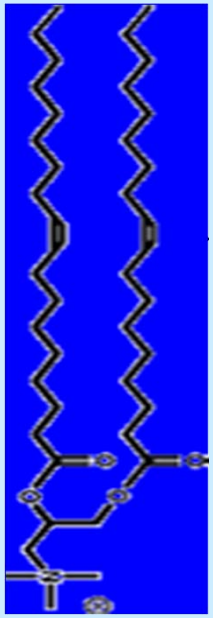


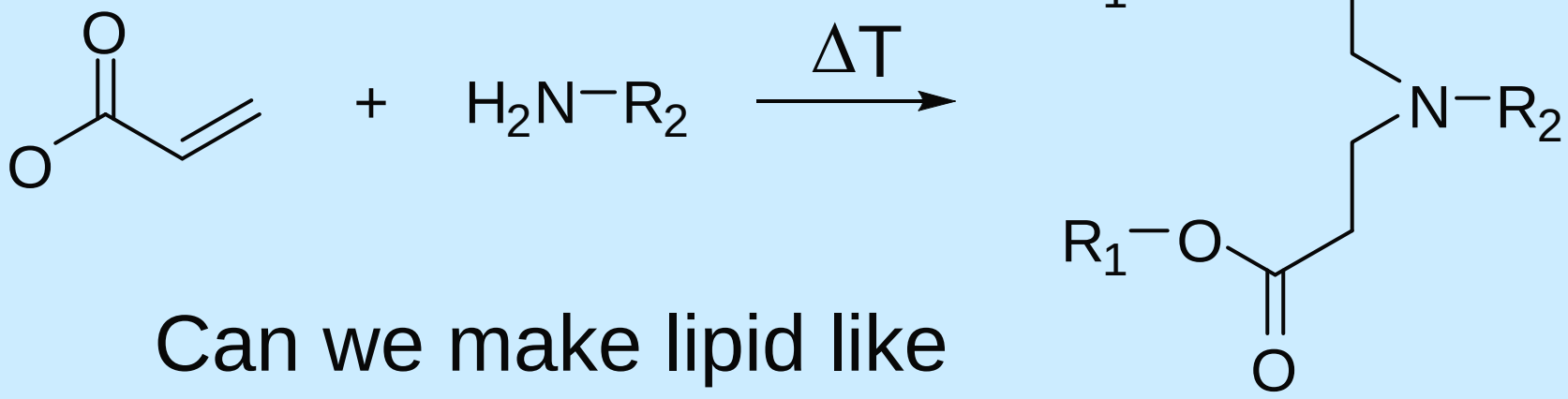


Control NP



Lipid-like "lipidoid" materials for drug delivery





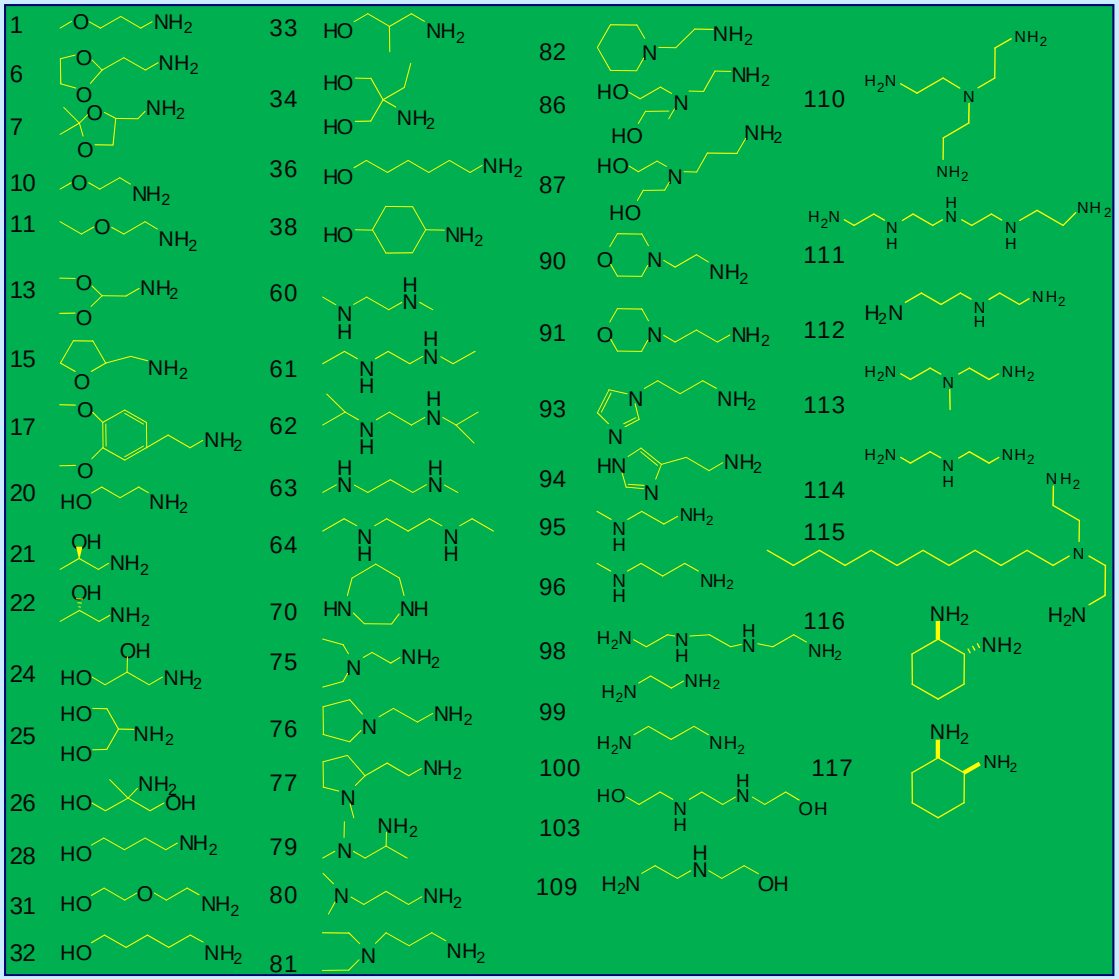
Can we make lipid like materials?

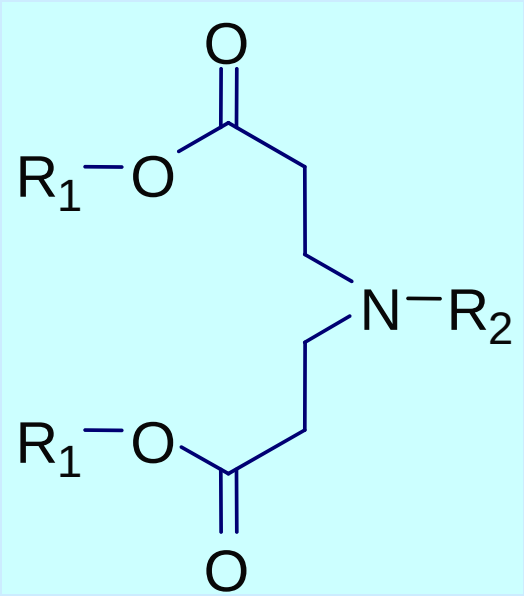
Ad*vantages:*

- Commercially available starting materials.
- Polymerization accomplished in a *single synthetic step*.
- No byproducts.
- No protection/deprotection steps.

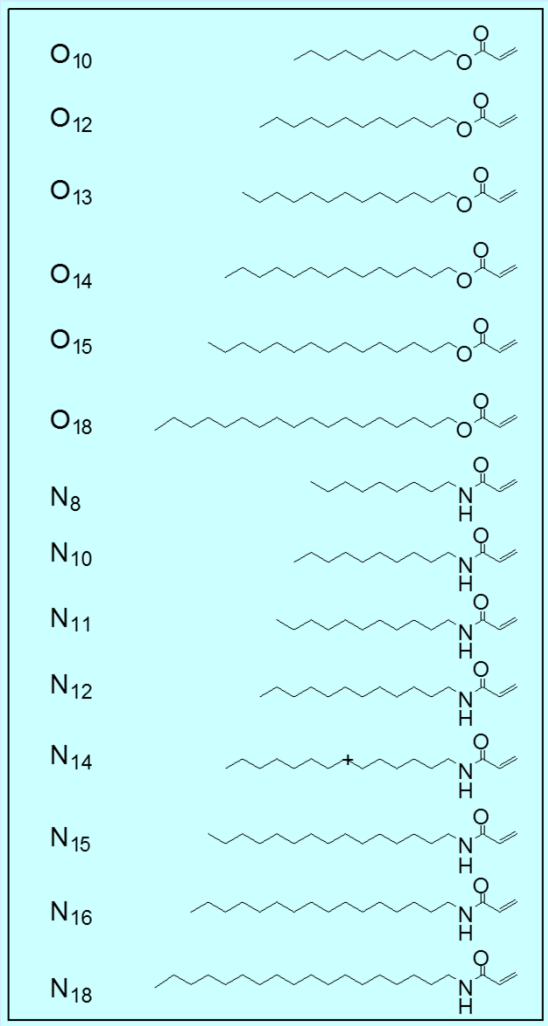
POTENTIAL FOR HIGH THROUGHPUT

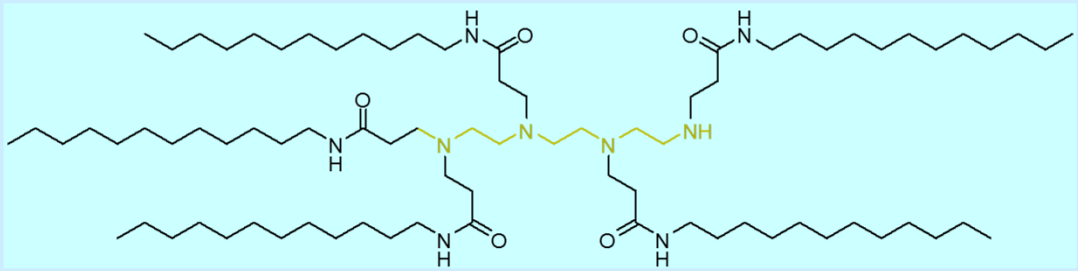
Large variation in R group

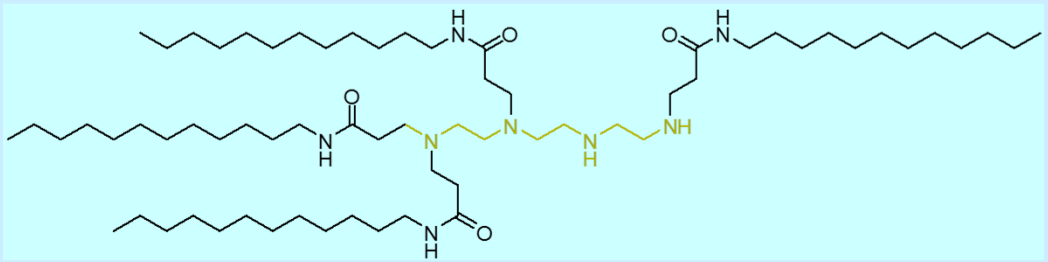


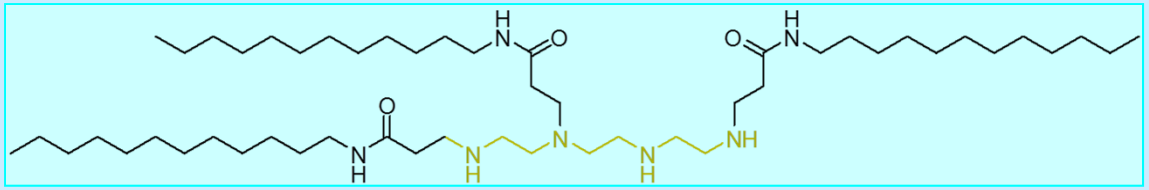


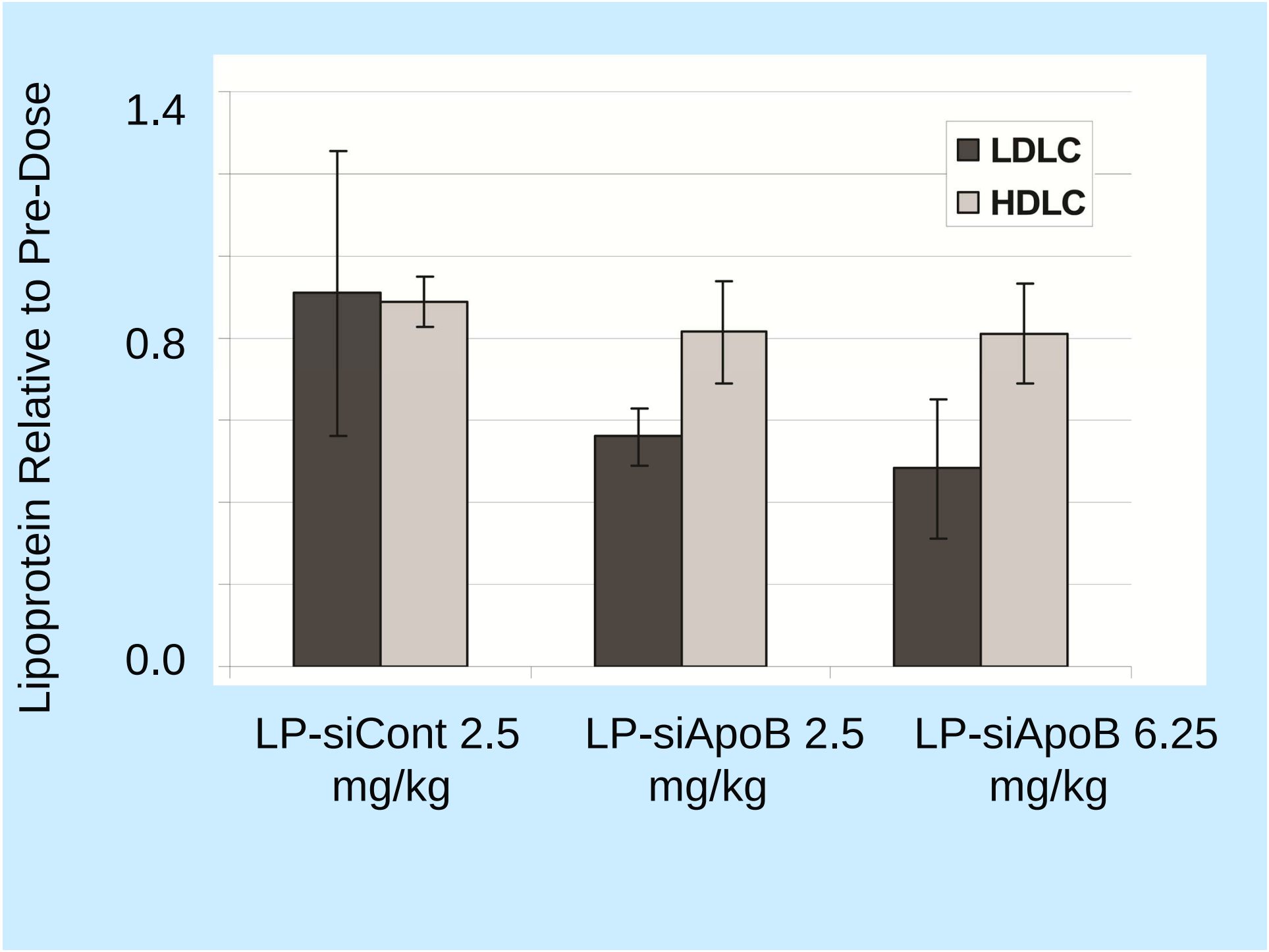
Variable tail length and number of tails



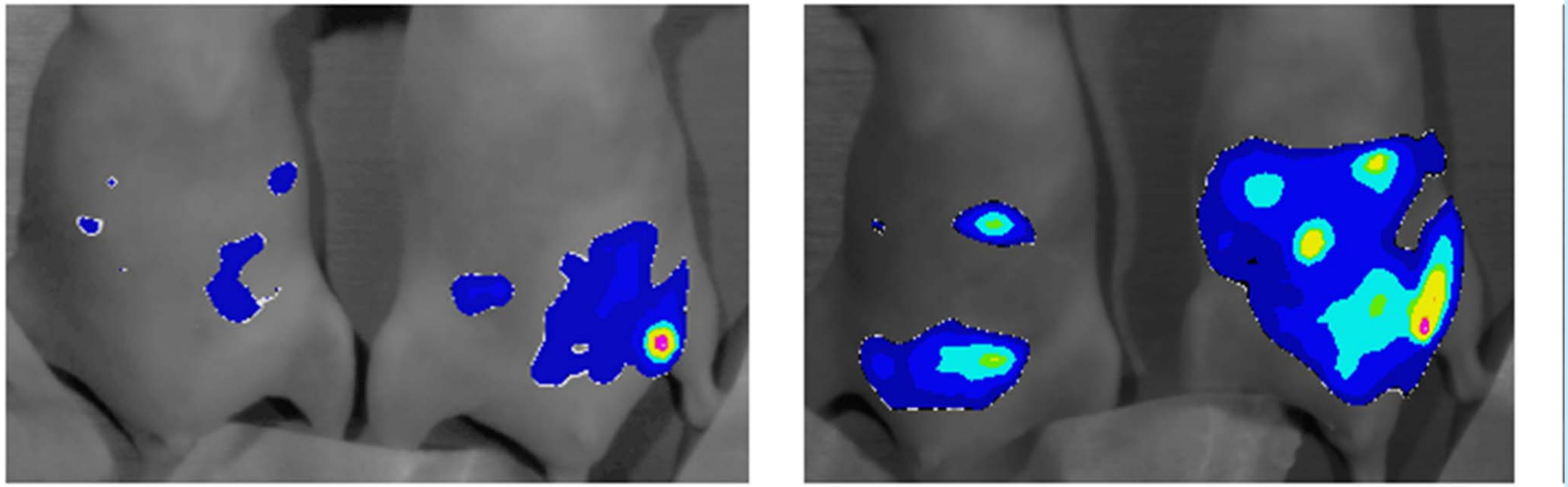






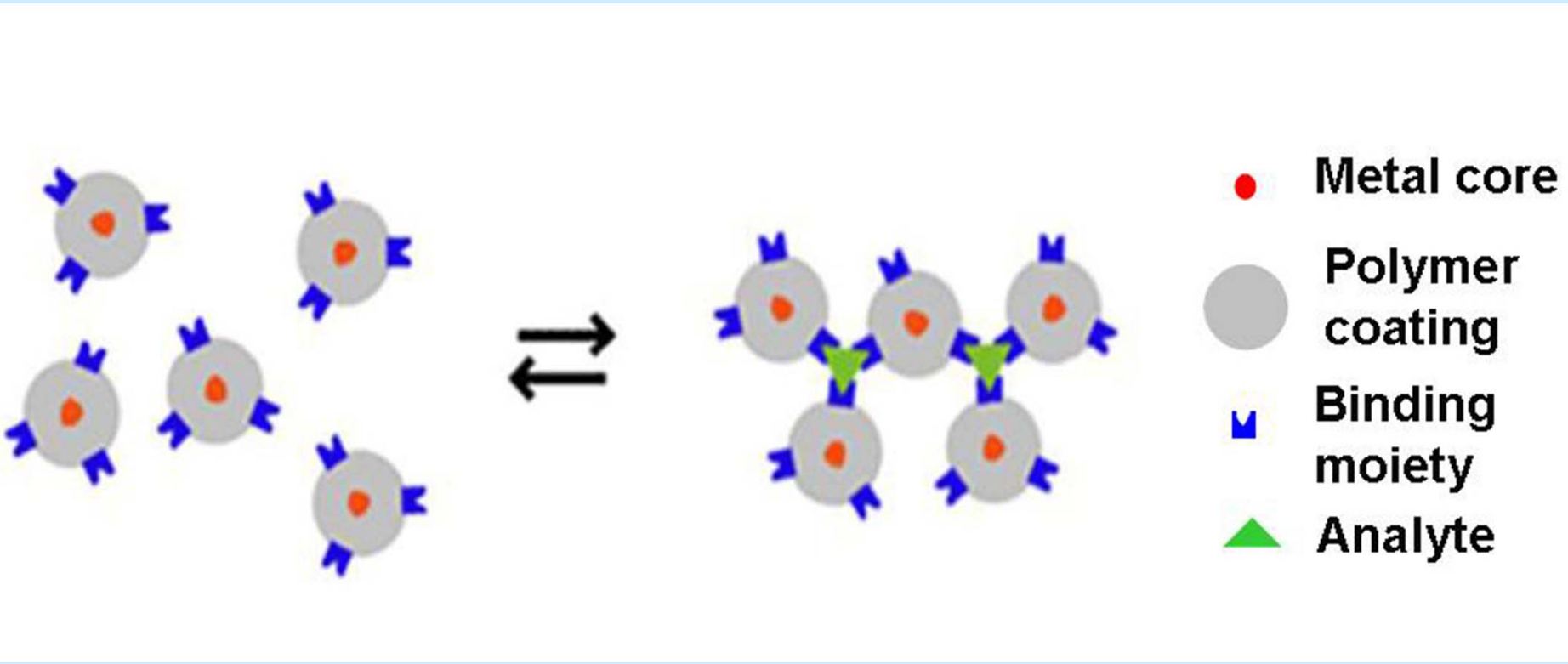

Lipoprotein Relative to Pre-Dose
1.4
0.8
0.0
LDLC
HDLC
LP-siCont 2.5 mg/kg
LP-siApoB 2.5 mg/kg
LP-siApoB 6.25 mg/kg

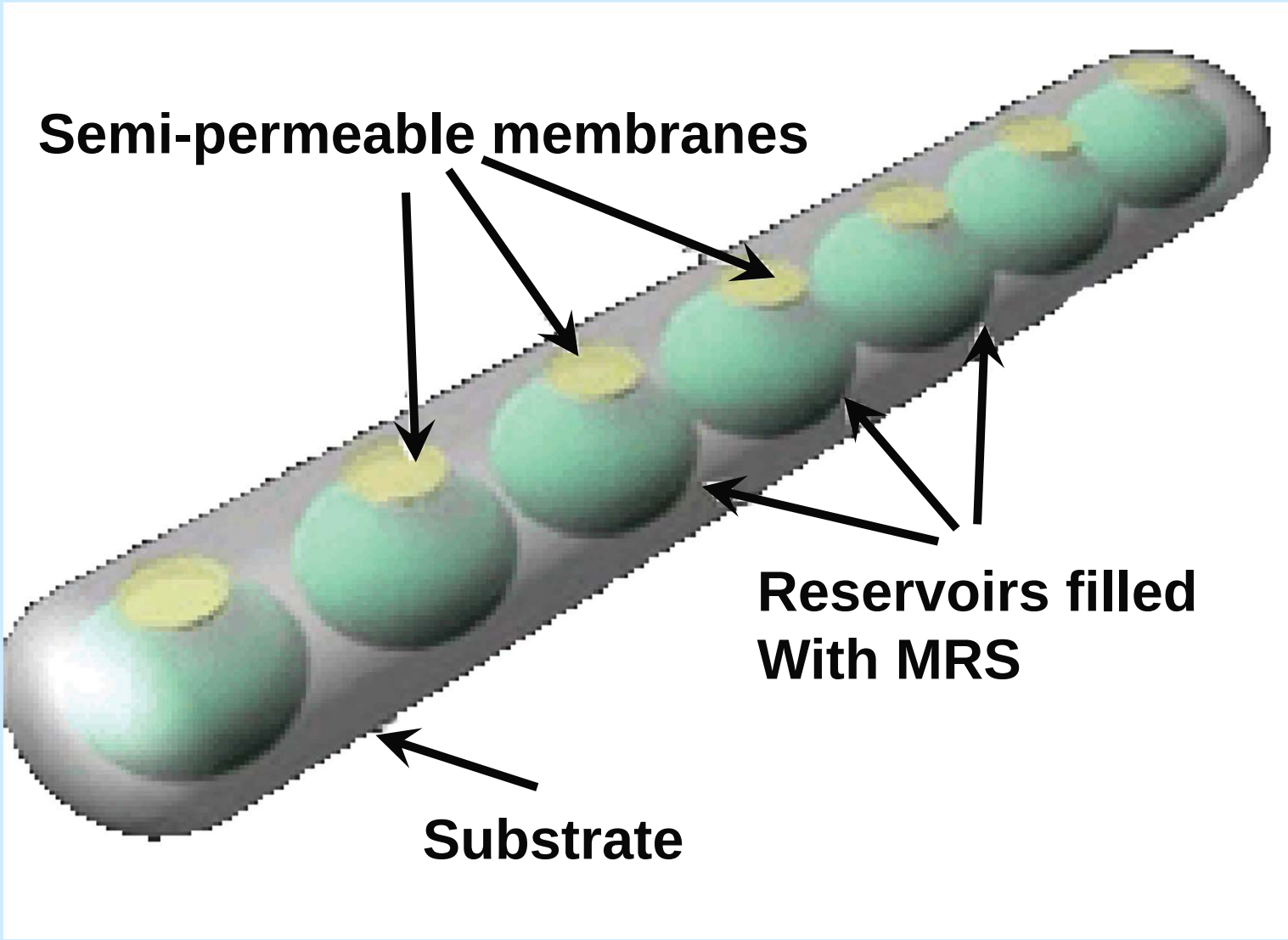
Lipidoid-formulated siLuc (left) and siCont (right)



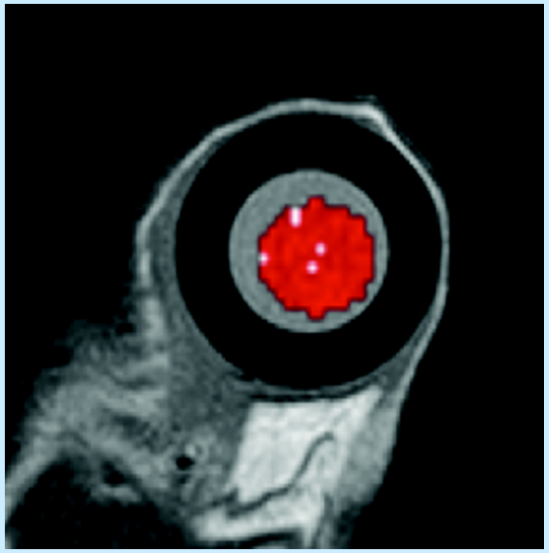
IP injections were administered at 5 mg/kg following 10 days of tumor growth

Cell type = mT2K, mouse strain = nude mice)

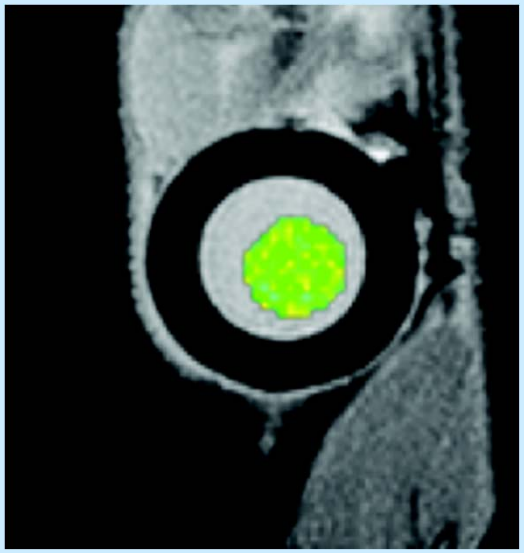

Metal core
Polymer coating
Binding moiety
Analyte


Semi-permeable membranes
Reservoirs filled
With MRS
Substrate

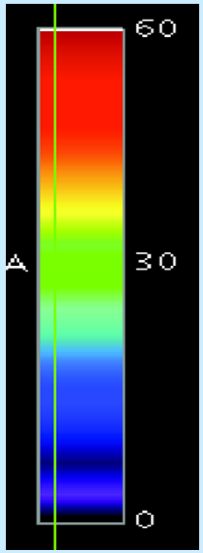
Device-based sensing: In vivo



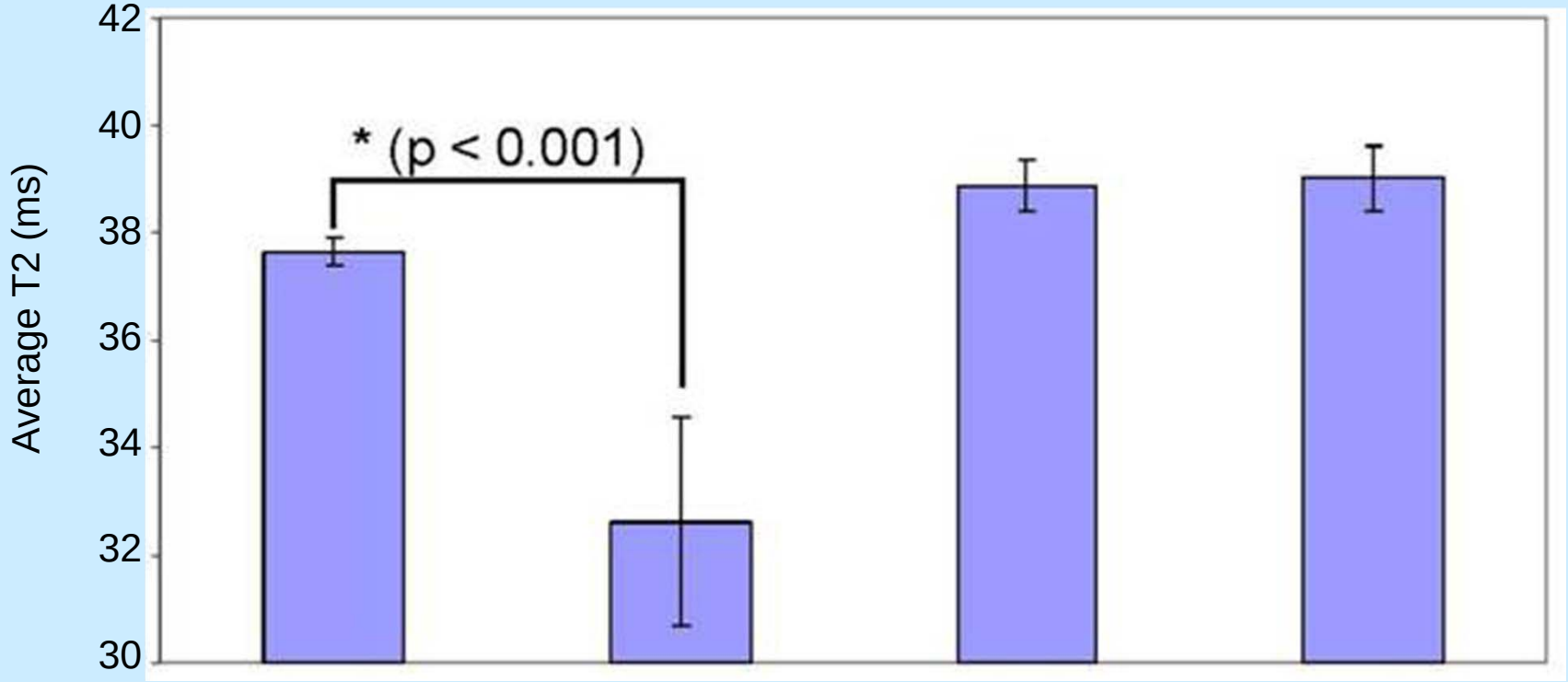
Control
Device
(no tumor)



Sample Device
(tumor)



T_2
(4.7 Tesla
MRI)



Tumor present	No	Yes	No	Yes
NP functionalized for hCG	Yes	Yes	No	No

CCNE community

Monthly Meetings

Attended by all CCNE participants and all Koch Institute members are now invited to further foster collaboration. Many presentations given by post-doctoral associates to encourage peer review. Meetings are growing with popularity and are a continued success.

Cores

Toxicity Core, Mouse Model Core and CCR's Core Facilities, serve as hubs for fostering interactions between Projects and other institutions (UCSD, Washington University, and Northeastern)

Koch Institute Nano Symposium

On June 27th, our cancer institute will host Alliance member James Heath, as well as NCI funded scholars Rebecca Richards-Kortum, Mark Davis and Charles Lieber at our annual Symposium. Dr. Piotr Grodzinski will also be speaking.

Education and outreach

Bhatia Lab outreach work: The Bhatia Lab continues to host middle school girls in their lab through the MIT KEYs program.

Langer Lab: The FIRST Lego Robotics Team (middle school students from Lincoln, MA) visited the Langer Lab and met with various researchers to discuss building a robot that would involve molecular motors, smart fabrics and cancer delivery systems.

Belcher Lab's NanoSleuths:

This year the Belcher lab hosted about 30 students in the nanotech hands-on modules at MIT. Prof Belcher also worked with and visited over 50 students outside MIT in MA, NH and CT and over 20 teachers on developing nano content for teaching high school students. This summer she expects 3 high school students in the lab working on CNI related projects.

New funding which leveraged CCNE work

The work supported by this CCNE has led to many new funding opportunities for many participants. Additionally, MIT received a gift from David Koch:

Koch made a $100 million gift to establish the David H. Koch Institute for Integrative Cancer Research and to build a $280 million state-of-the-art research facility. The new building will house faculty from 10 departments and Institutes and 4 hospitals.

The Koch Institute broke ground for the new building on March 7th, 2008.

MIT-Harvard CCNE facts

A few quick facts about the MIT-Harvard CCNE:

- 83 publications in the past year
- 67 people are supported by the grant
- 26 patents have been applied for the past year (at least 4 companies started by major licenses)
- Every CCNE PI at MIT offers courses through MIT's Open Courseware Initiative
- Washington University, UCSD and Northeastern are among the other Alliance CCNE's we work with through our Toxicity Core