PURDUE UNIVERSITY

Weldon School of Biomedical Engineering

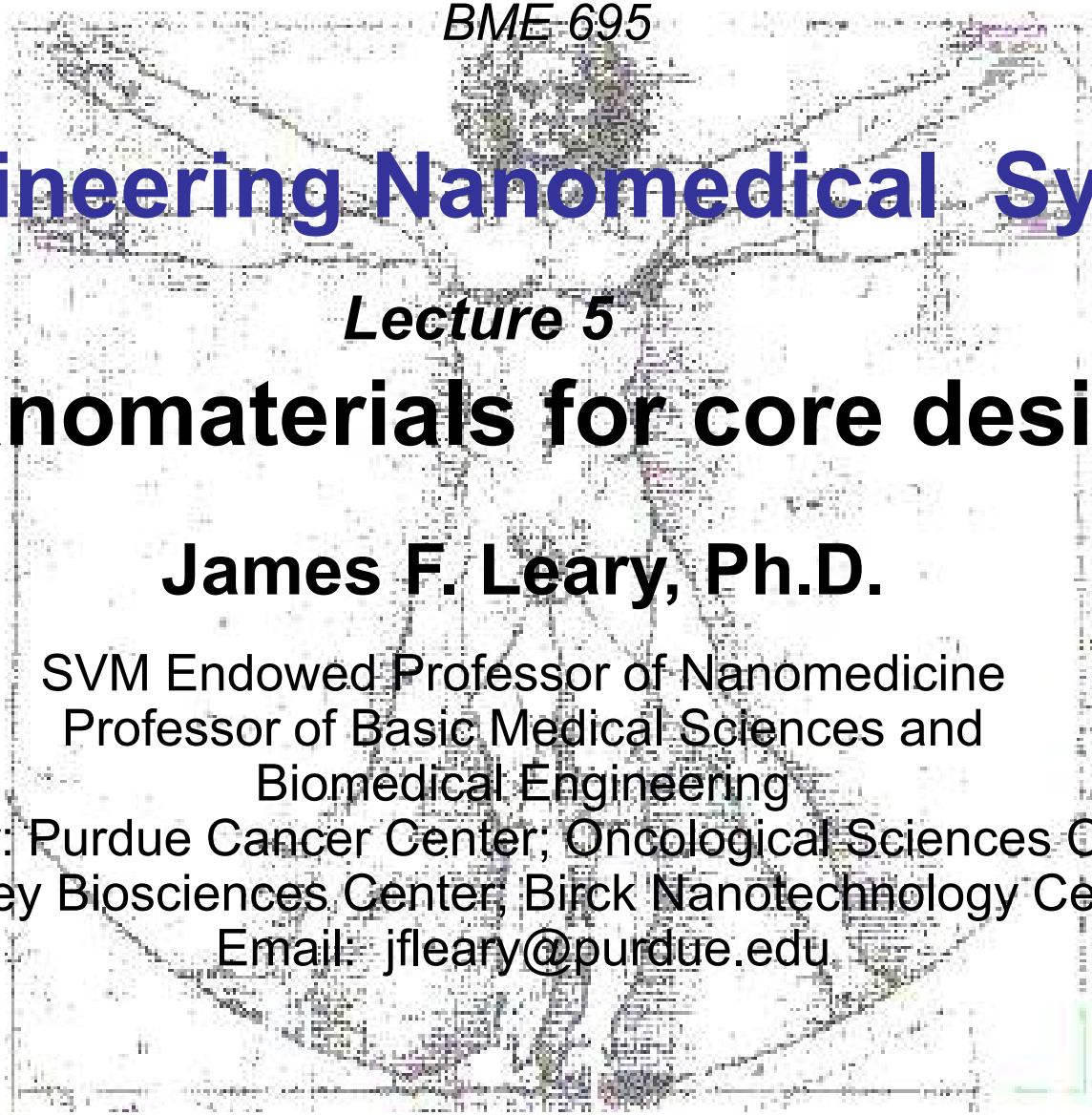
The Convergence of Differences, The Future of Excellence

BME 695

Engineering Nanomedical Systems

Lecture 5

Nanomaterials for core design



James F. Leary, Ph.D.

SVM Endowed Professor of Nanomedicine
Professor of Basic Medical Sciences and
Biomedical Engineering
Member: Purdue Cancer Center; Oncological Sciences Center;
Bindley Biosciences Center; Birck Nanotechnology Center
Email: jfleary@purdue.edu

5.1 Introduction

A. core building blocks

B. functional cores for theranostics

C. “functionalizing” the core surface chemistry to attach other molecules

Types of Core Materials and their detection

Core material	Detection
Iron oxide	x-ray, MRI, add fluorescent probe
C60 and carbon nanotubes	add fluorescent probe
Gold	surface plasmon resonance
Silver	surface plasmon resonance
Silica	add fluorescent probe
Quantum dots	intrinsic long-lifetime fluorescence
“Next generation”quantum dots	intrinsic fluorescence
Hybrid materials	mixture of detectable properties

5.2 Ferric oxide cores

A. paramagnetic cores

B. superparamagnetic cores

C. ferric nanorods

D. advantages and disadvantages

Ferric Oxide Nanospheres and Nanorods

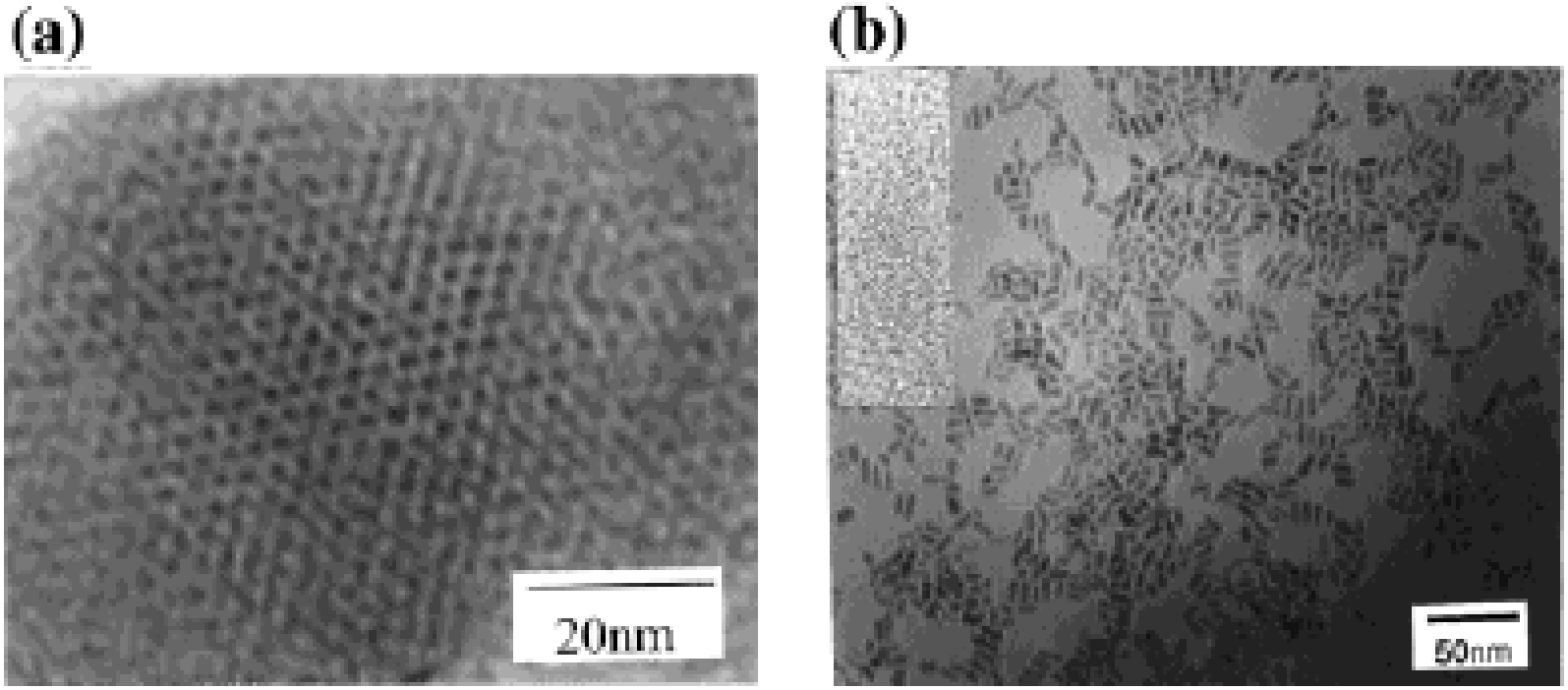


Figure 1. Transmission electron micrographs (TEM) of (a) spherical iron nanoparticles with diameters of 2 nm, and (b), rod-shaped iron nanoparticles with dimensions of 2 nm 11 nm, (Inset: High-resolution electron micrograph of a single nanorod) The images were obtained with a JEOL JEM-2000EX II instrument.
From: Park et al., J. Am Chem. Soc. 2000

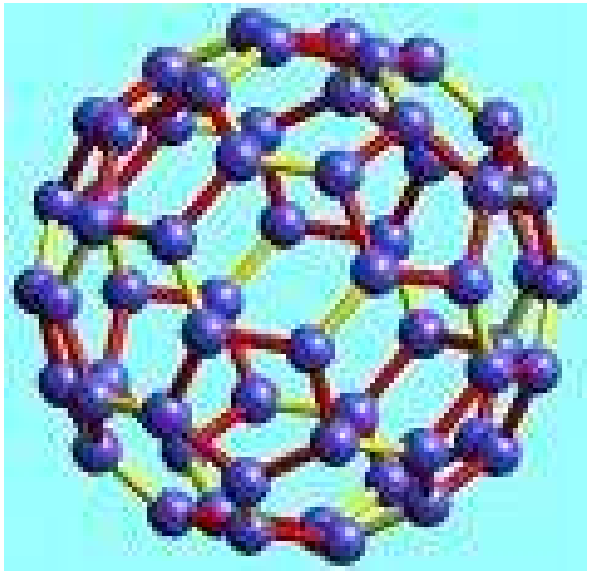
5.3 C60 and carbon nanotubes

A. size and structure of C60

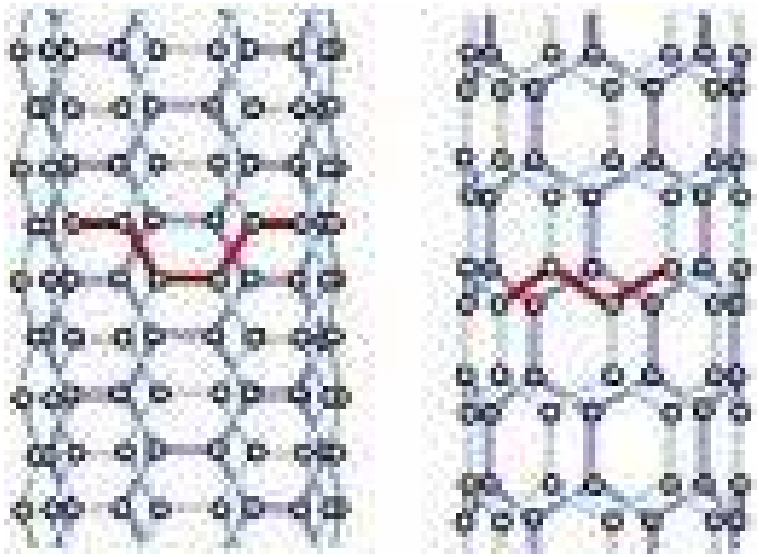
B. elongation of C60 into carbon nanotubes

C. advantages and disadvantages

C60 “Buckyballs” and Carbon nanotubes as drug carriers



http://www.ydae.edu

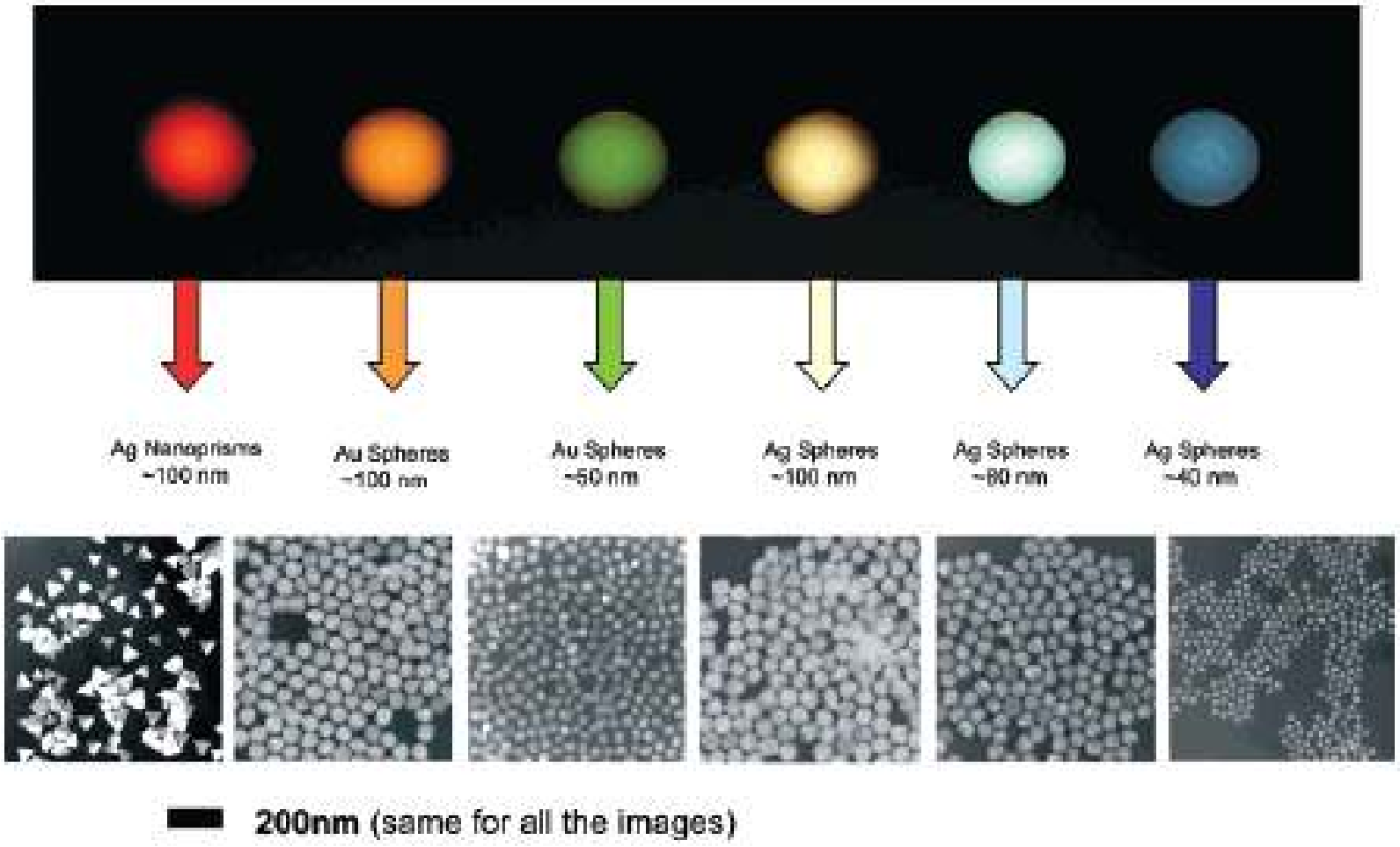


http://www.udel.edu

5.4 Gold cores

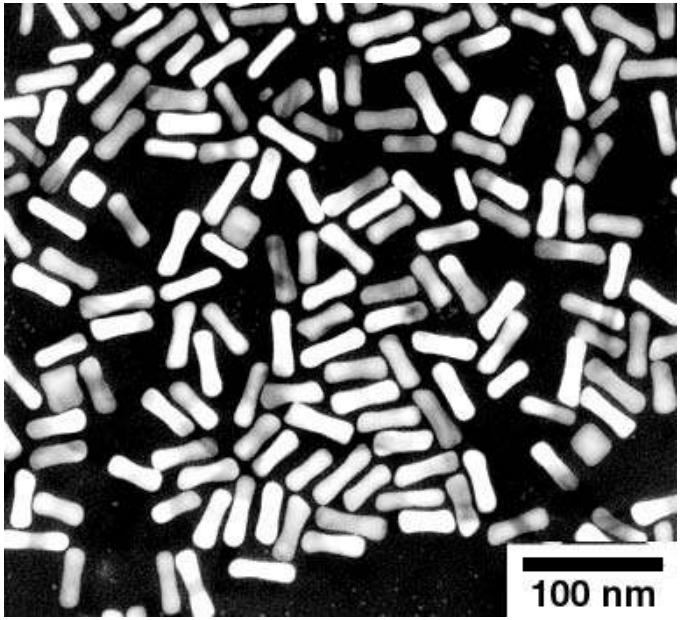
A. gold nanoparticles
B. gold nanorods
C. other shapes (e.g. "stars")
D. gold nanoshells
E. advantages and disadvantages

Gold and silver nanoparticles

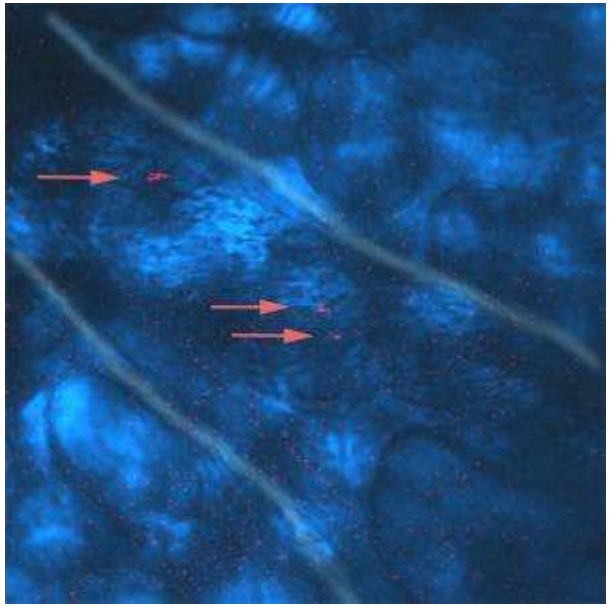


From: Rosi and Mirkin, 2005.

Gold nanorods for optical imaging



Courtesy: Alex Wei



Courtesy: Ji-Xin Cheng and Alex Wei

Gold nanorods, which fluoresce red, were photographed inside the blood vessels of a live mouse by researchers in Purdue's Weldon School of Biomedical Engineering and Department of Chemistry. The researchers have taken a step toward developing a new type of ultra-sensitive medical imaging technique that works by shining a laser through the skin to detect the tiny rods injected into the bloodstream. In tests with mice, the nanorods yielded images nearly 60 times brighter than conventional fluorescent dyes, including rhodamine, commonly used for a wide range of biological imaging to study the workings of cells and molecules. (Purdue University photo courtesy of Weldon School of Biomedical Engineering and Department of Chemistry)

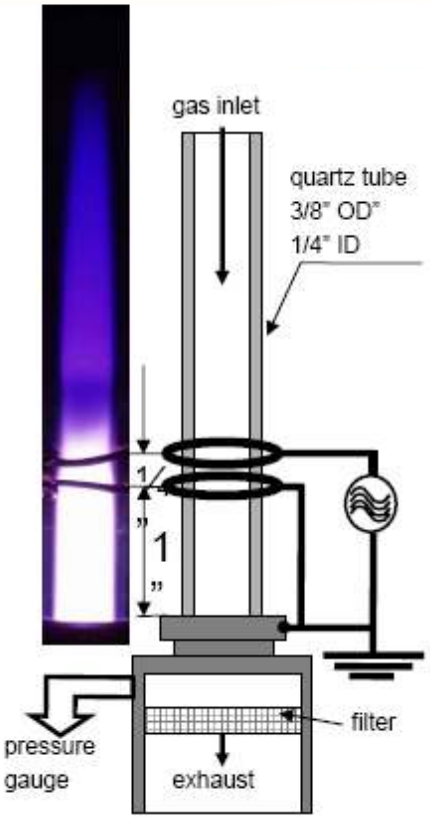
5.5 Silica cores

A. Silica nanoparticles

B. Embedding fluorophores to prevent photobleaching

C. Other advantages and disadvantages

Possibility of low toxicity silicon nanoparticles for in-vivo use? (Allison Hubel group and collaborators at Univ. Minnesota)



Achievements:

- **Scaleable high-yield synthesis approach for silicon quantum dots**

Mangolini et al., NanoLett **5**, 655, 2005

Achievements:

- **Organic surface passivation**
- **Photoluminescence quantum yield > 60%**

Jurbergs et al., Appl. Phys. Lett., June 5, 2006

Fundamental issues:

- Crystal formation in low-temperature plasmas
- Surface properties of quantum dots

Source: Research Highlights, Univ. Minnesota 2006

Silica nanoparticles can be easily made in different sizes and can embed conventional fluorescent molecules and prevent photobleaching

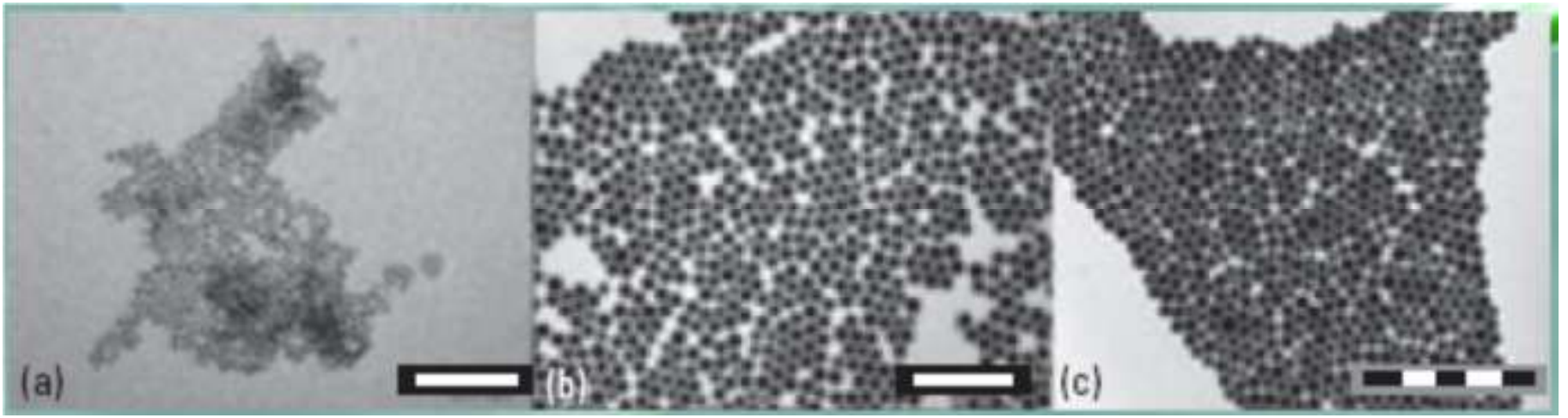


FIGURE 1. Transmission electron micrographs of different sizes of silica nanoparticles prepared in various microemulsion systems.

(a) 15-nm nanoparticles; (b) 40-nm nanoparticles; (c) 120-nm nanoparticles; scale bars are 200 nm, 200 nm, and 1 μm, respectively.

From Wang et al., 2006.

Use of fluorescent dye embedded silica nanoparticles

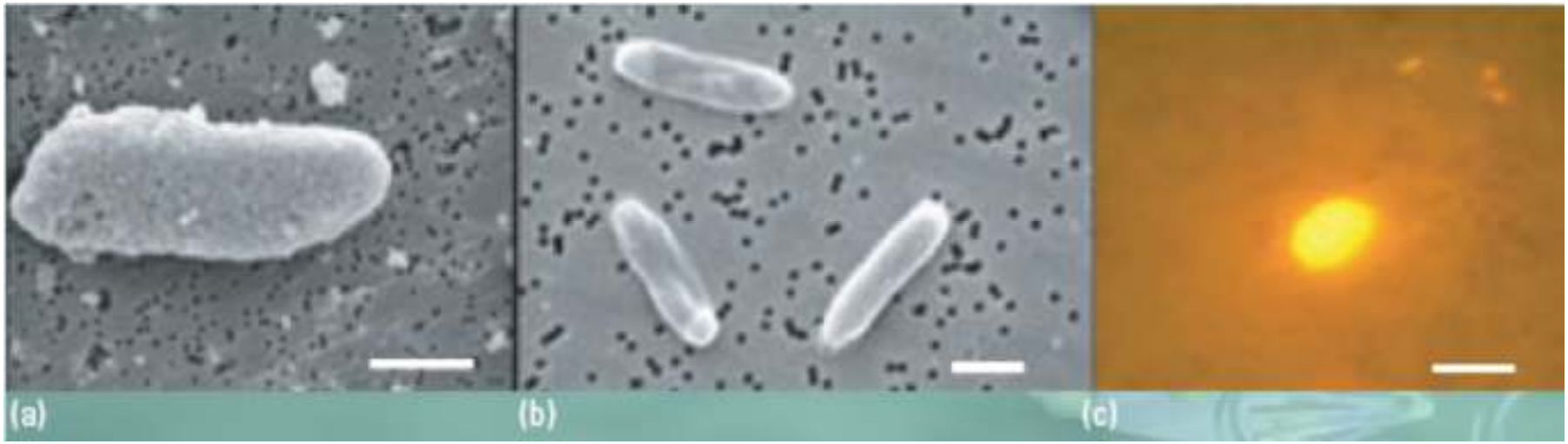
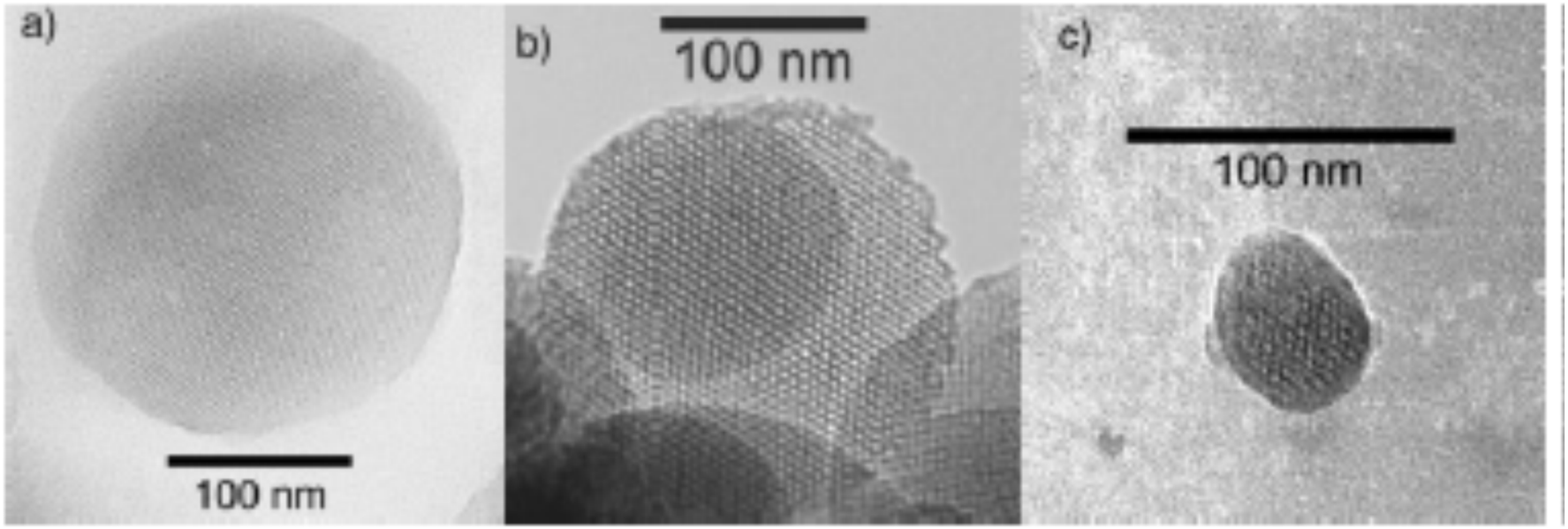


FIGURE 3. (a) SEM image of an E. coli O157:H7 cell incubated with nanoparticle–antibody conjugates, showing

nanoparticle binding to the target bacterium. Scale bar is 2.73 μm. (b) SEM image of an E. coli DH5a cell (negative control) incubated with nanoparticle–antibody conjugates, showing no nanoparticle binding. Scale bar is 1.5 μm. The black small dots in (a) and (b) are the pores on the surface of the filter membrane, and the white spots are unbound nanoparticles. (c) Fluorescence image of an E. coli O157:H7 cell after incubation with nanoparticle–antibody conjugates. Scale bar is 4 μm. The fluorescence intensity is strong, enabling identification of a single bacterial cell in aqueous solution.

From: Wang et al., 2006

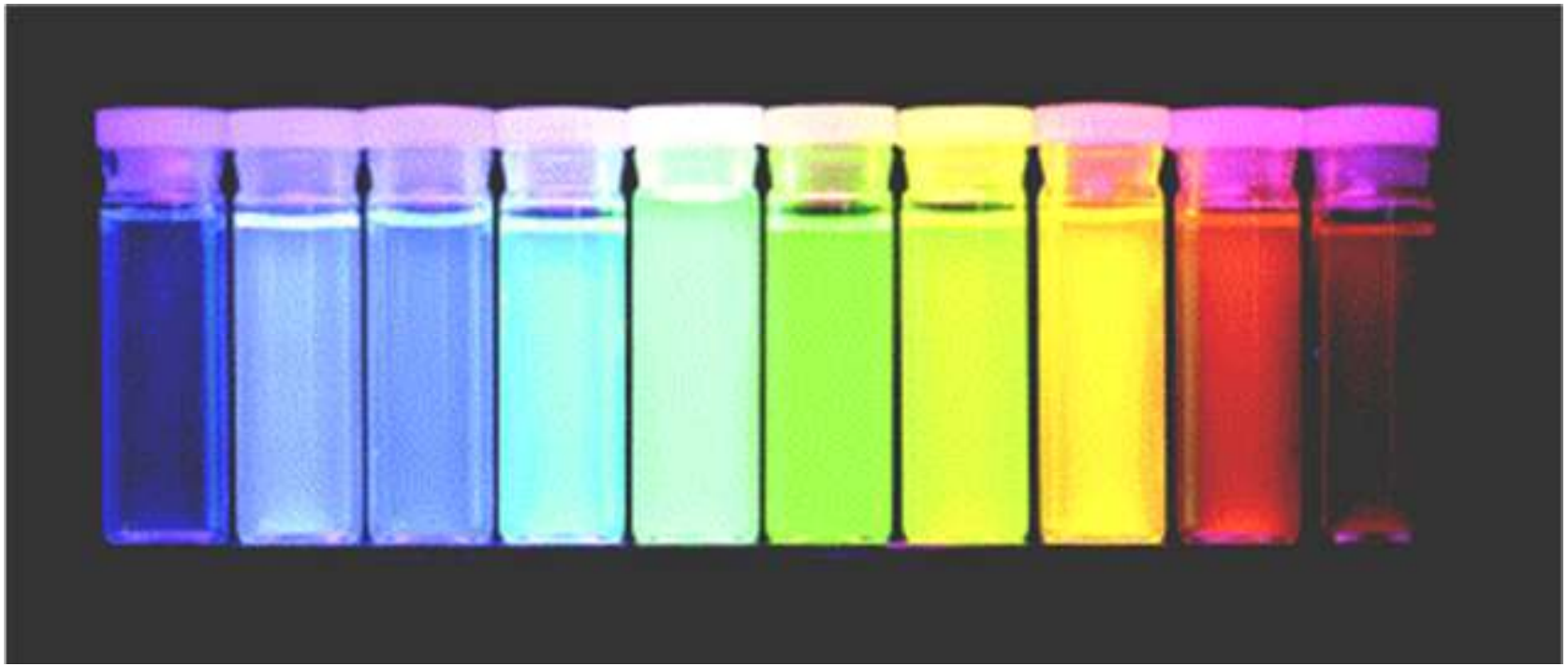
Mesoporous Silica NPs (MSNs) for drug release



Transmission electron microscopy images of three spherical MSNs with different particle and pore sizes: a) Particle size ca. 250 nm; pore diameter ca. 2.3 nm. b**)** Particle size ca. 200 nm; pore diameter ca. 6.0 nm. c**)** Particle size ca. 50 nm; pore diameter ca. 2.7 nm.

Original source: C.-Y. Lai, B. G. Trewyn, D. M. Jeftinija, K. Jeftinija, S. Xu, S. Jeftinija, V. S. Y. Lin, *J. Am. Chem. Soc.* **2003**, *125*, 4451

5.6 Quantum Dots



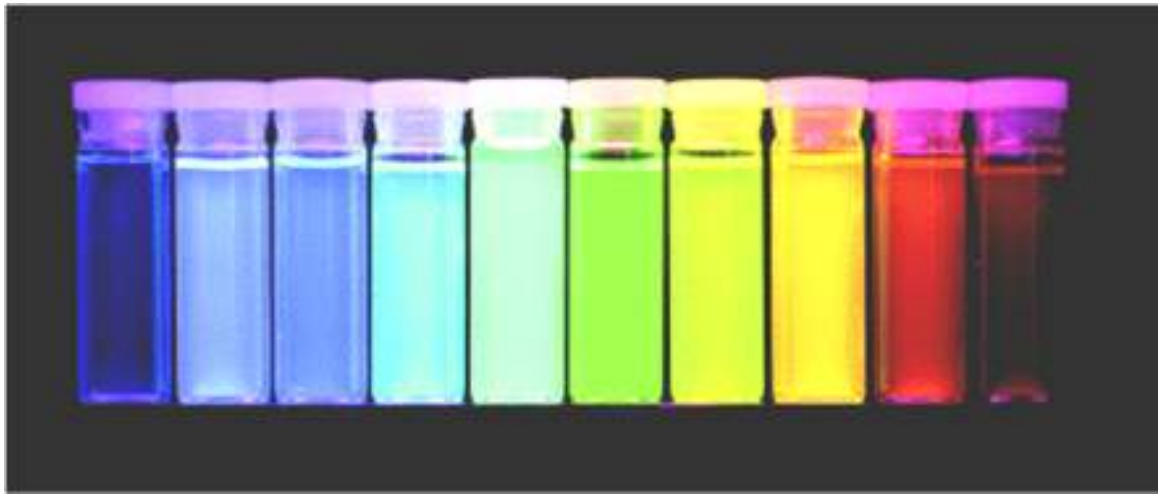
Increasing size →

4 nm 7 nm

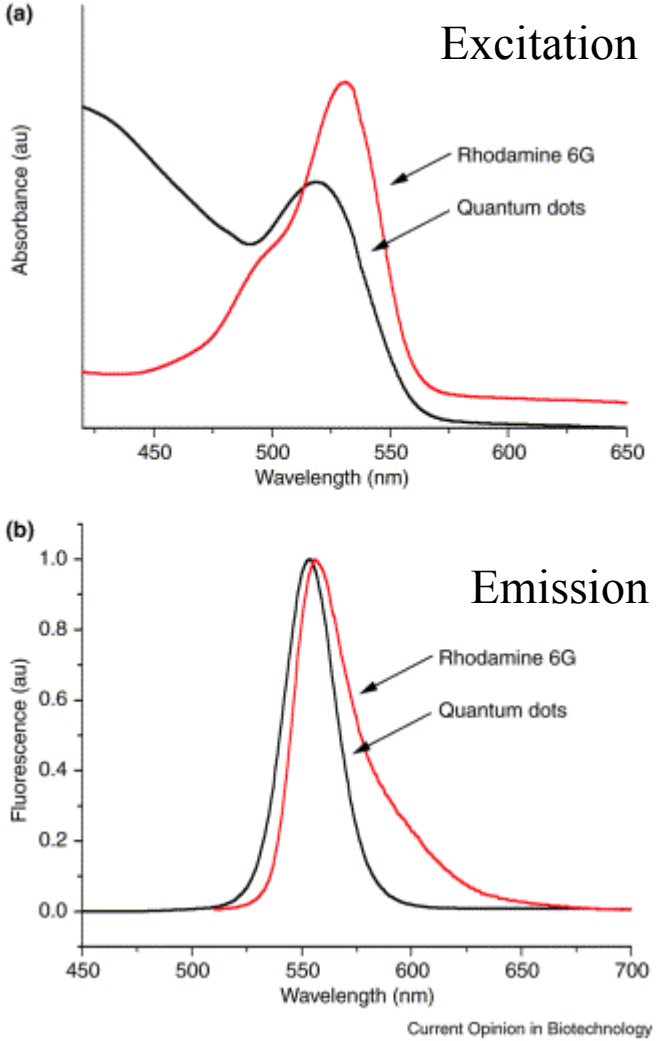
* Not including coatings

Quantum Dot Nanoparticles

- Excitation/emission spectra
- Photostability
- Size tunable
- Bioconjugation

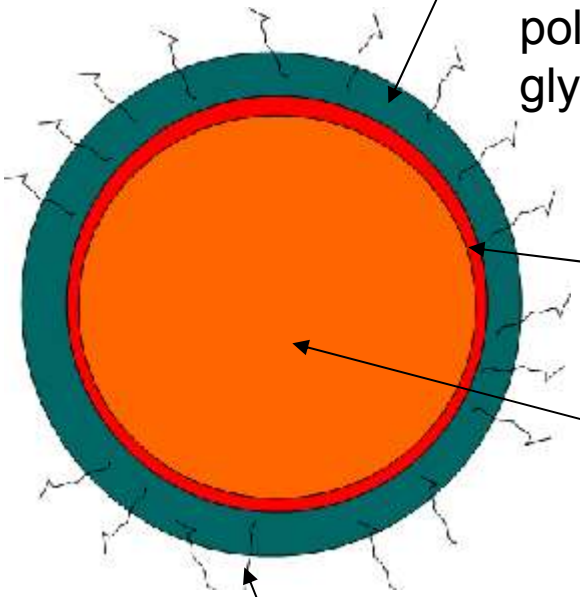


Increasing size



Comparison of quantum dot excitation and emission spectra to Rhodamine fluorescent dye.

Quantum Dot Nanoparticles

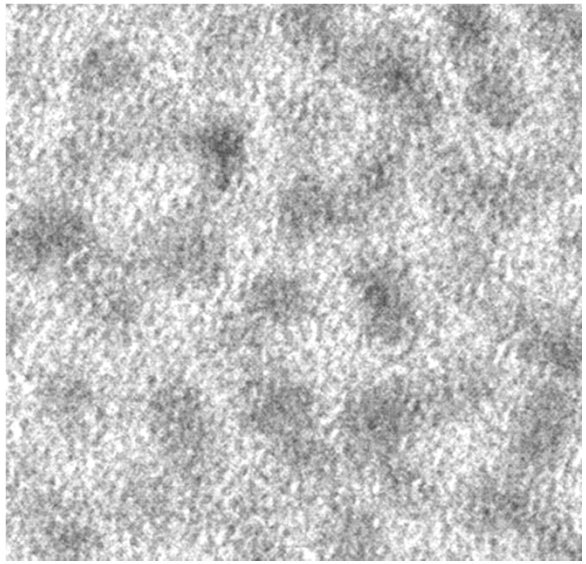


Biocoating to make hydrophilic and biocompatible (e.g. poly(ethylene glycol) or PEG)

ZnS cap

Semi-conductor core material (e.g. CdSe)

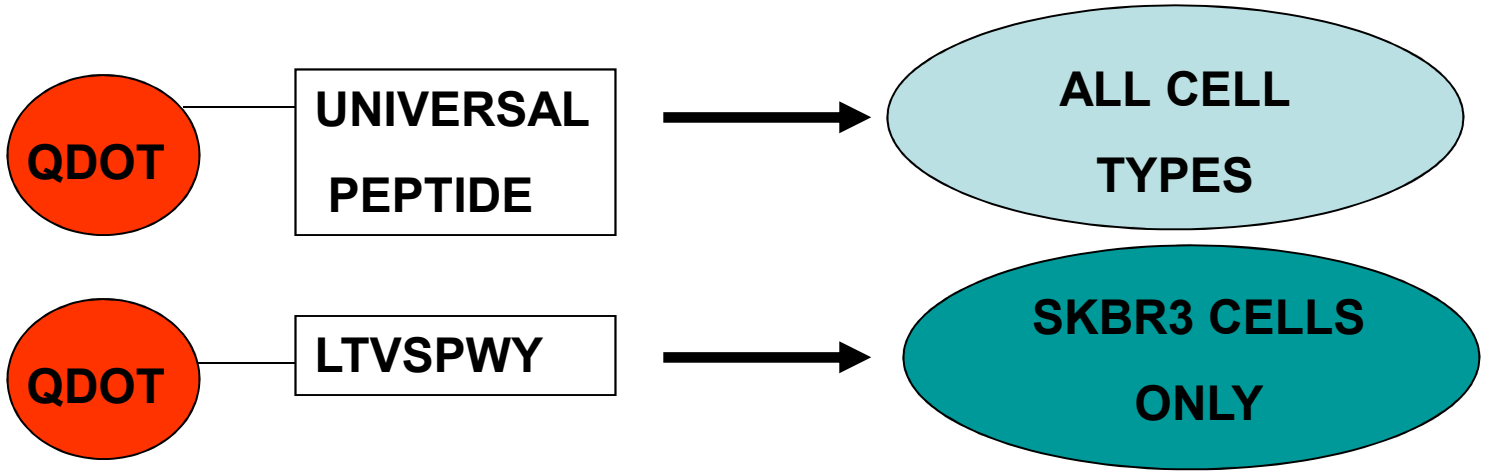
Surface group (e.g. $-NH_2$ or -COOH)



Transmission electron microscopy (TEM) image of amino-functionalized Qdots. Size was determined to be ~10 nm.

Biomolecular Targeting: Peptide

- Use of biomolecules offers advantages toward other uptake mechanisms: Cell receptor is targeted and functions normally
- Peptide offers ease of synthesis and well understood chemistry. These are also on the size order of the nanoparticles.
  - QTracker® Cell Labeling Kit (Invitrogen Corporation, Carlsbad, CA) offers Qdot nanoparticles conjugated to a universal peptide. This will enter all cell lines.
  - Specific peptides will enter only certain cell types; the focus of nanomedical approach to disease

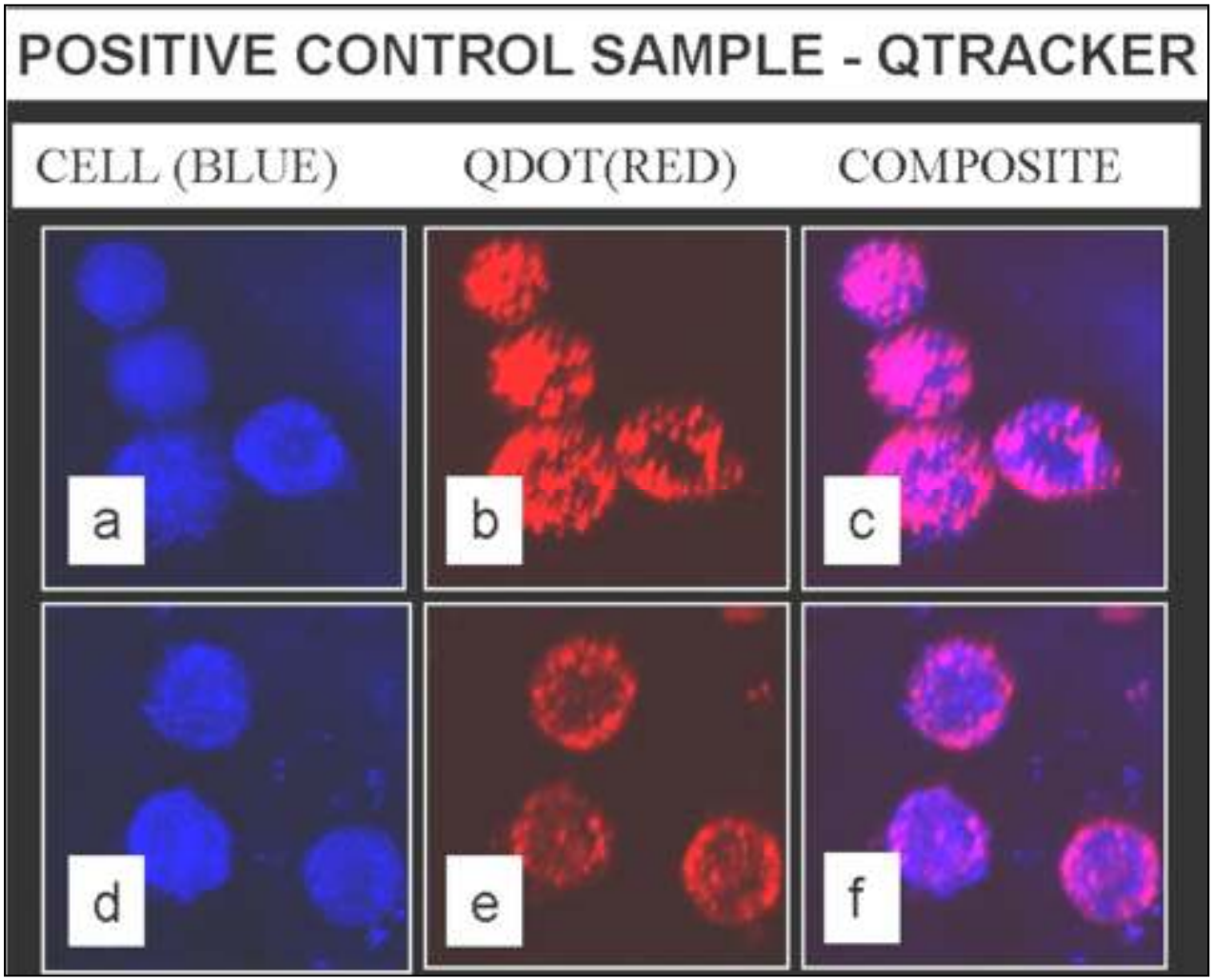


MCF-7

CONTROL

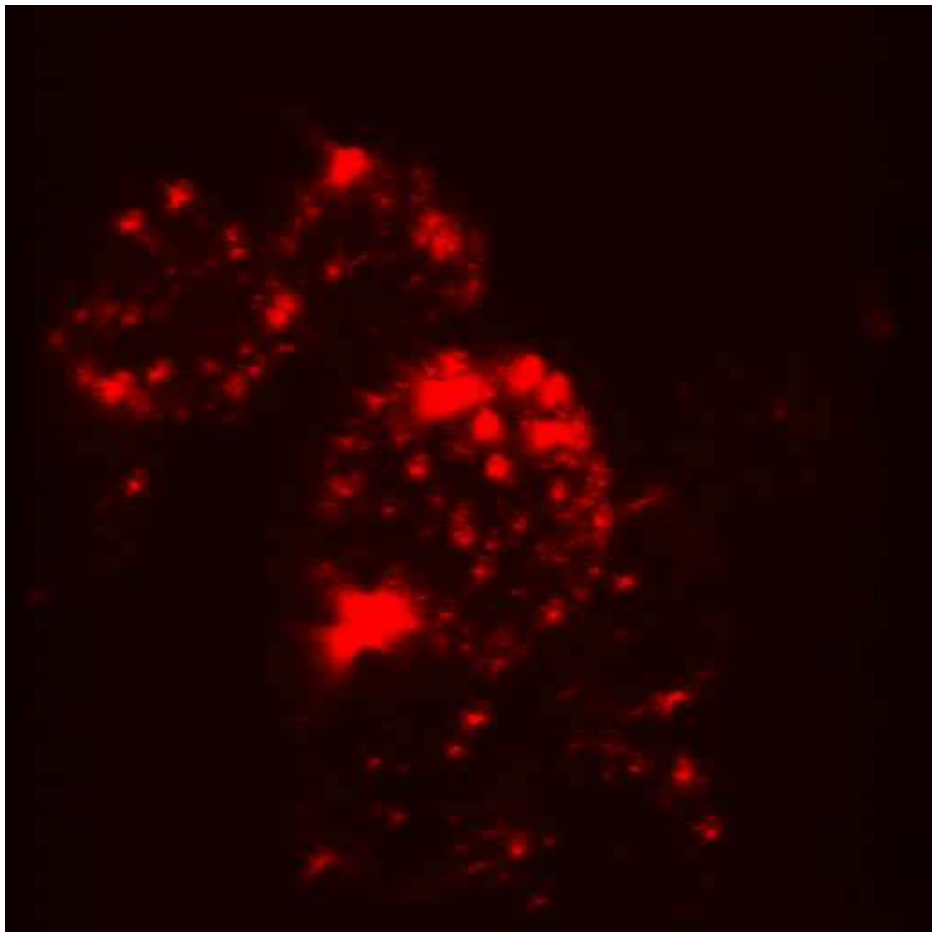
SkBr3

EXPERIMENTAL



QDOT — **UNIVERSAL PEPTIDE** → **ALL CELL TYPES**

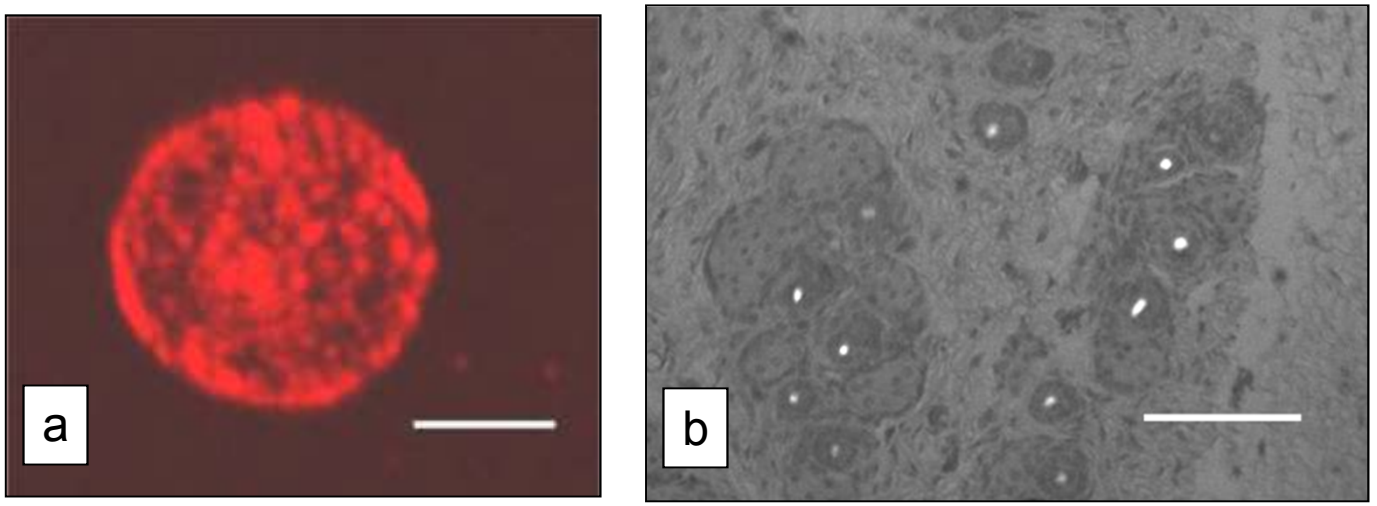
In vitro SkBr3 Study: Confocal Images



SkBr3 cells with application of Qdot-LTVSPWY complex

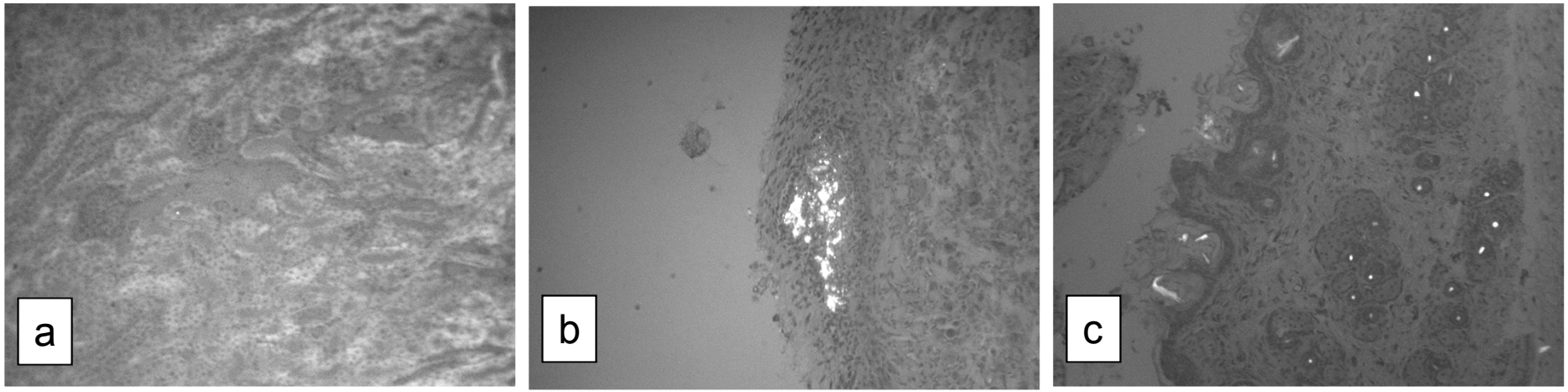
Quantum Dot Nanoparticles

- Agglomeration properties based on:
  - Chemistry of the Qdot; its properties, surface charge/molecules, elemental makeup, etc.
  - Chemical environment; for instance pH



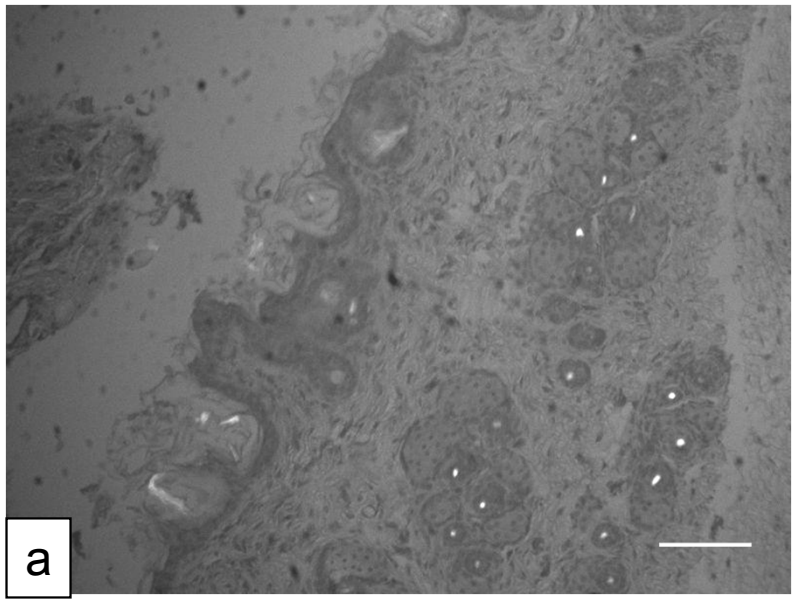
Qdots imaged in biological environments.
(a) *In vitro* Qdots in cell (Red, scale bar 5μm).
(b) *In vivo* Qdots within tissue (White, scale bar 100μm).

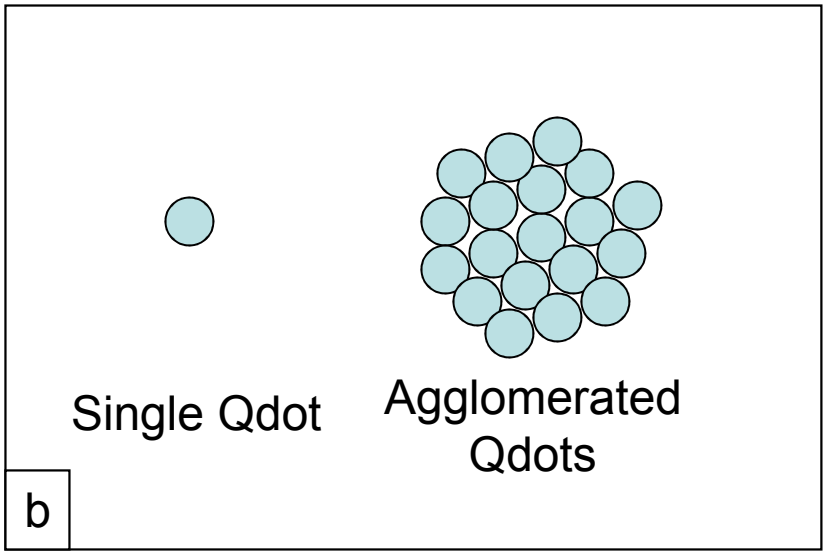
In vivo SkBr3 Tumor Study: Results



Fluorescent microscopy images of *in vivo* tumor tissue.
(a) Image of control kidney tissue, this sample did not receive any Qdots.
(b) Image of tumor tissue from a peritumoral injection.
(c) Image of tumor tissue from a tail vein injection.

Qdot Agglomeration





(a) *In vivo* tumor image. (b) Graphic representation of agglomerated Qdots.

NANOPARTICLE AGGLOMERATION:

~1000 - 2000 nm IN DIAMETER

APPROXIMATE: 50 – 100 NANOPARTICLES PER CLUSTER IN DIAMETER

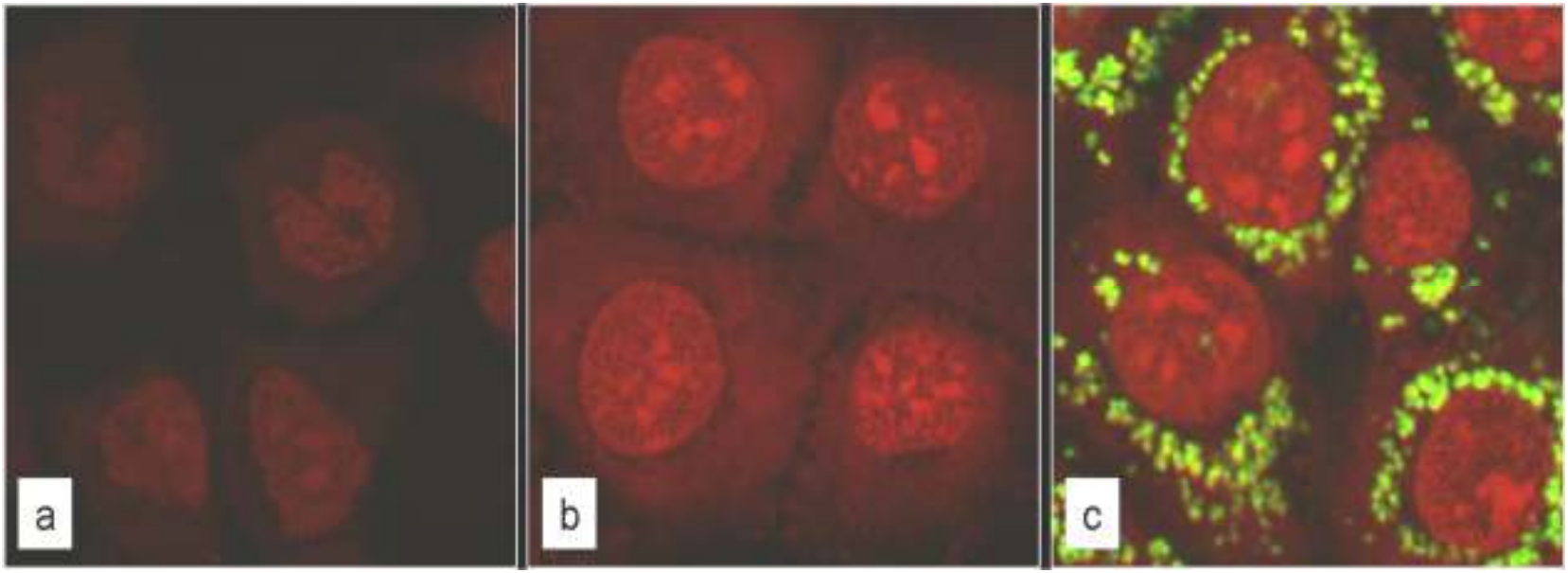
CONSIDERING THREE DIMENSIONS, THE NUMBER OF NANOPARTICLES PRESENT COULD BE BETWEEN 125,000 AND 10^6

Cytotoxicity: Some DNA damage!

- Confocal imaging
  - ROS are present normally in cells. Heightened presence indicates a state of cellular stress.
  - Detection of ROS was observed in the positive control sample and the QTracker® sample.

Dihydroethidium is shown in red QTracker® is shown in green.

(a) Control (b) H_2O_2 (c) QTracker®



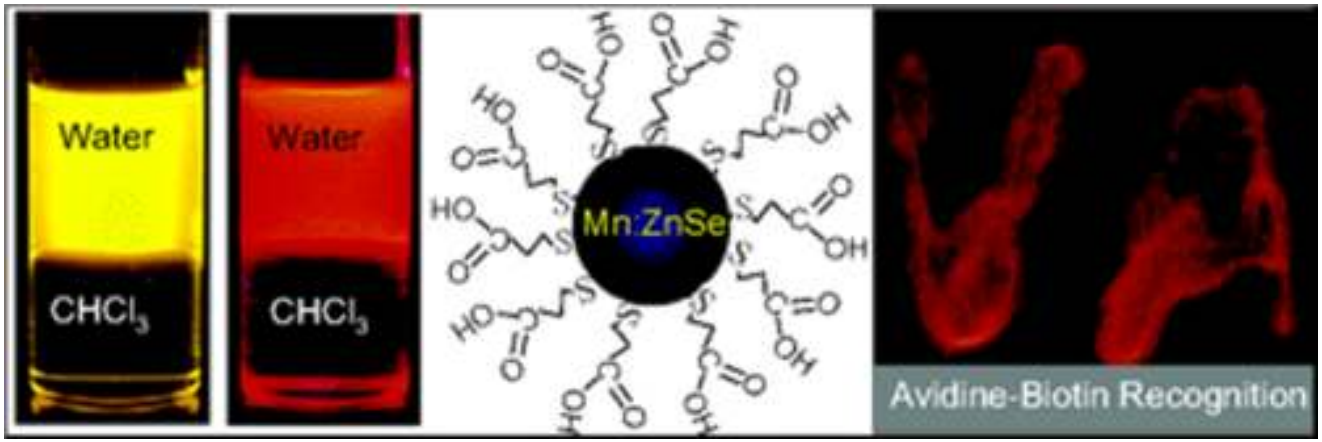
5.5 Next generation quantum dots

A. Water-Soluble Doped ZnSe Nanocrystal Emitters

B. Organic quantum dots

Future of Quantum Dots is Still being written…

- Concerns are arising over potential in-vivo toxicity of Cd based quantum dots
- But new less toxic “d-dots” are being developed



Efficient, Stable, Small, and Water-Soluble Doped ZnSe Nanocrystal Emitters as Non-Cadmium Biomedical Labels
Narayan Pradhan, David M. Battaglia, Yongcheng Liu, and Xiaogang Peng
Nano Lett.; **2007;** 7(2) pp 312 - 317; **(Letter)**

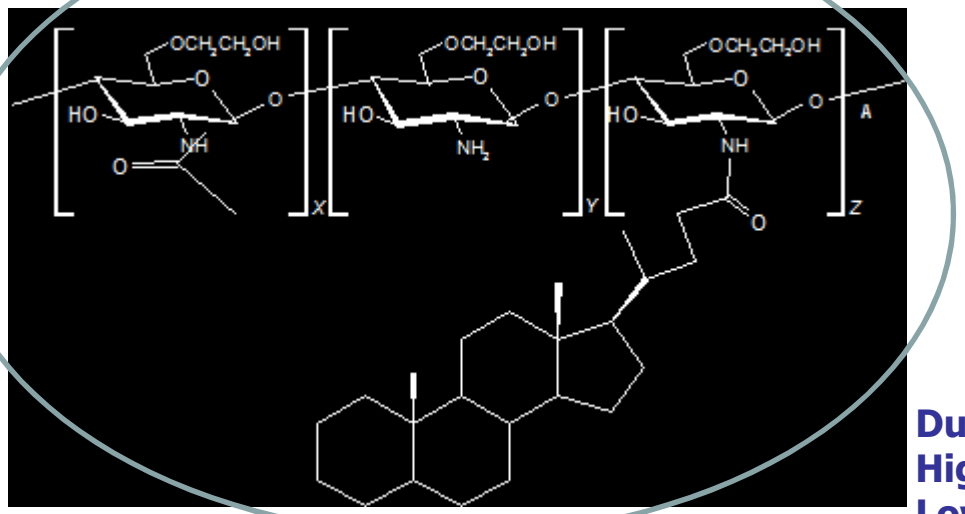
5.8 Hybrid material cores

A. Gold-ferric oxide nanoparticles and nanorods

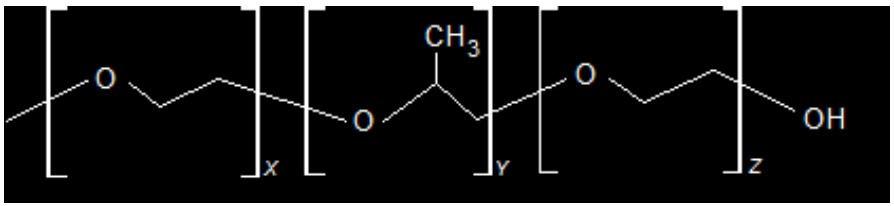
B. NIR fluorescent-chitosan polymer-iron oxide core hybrids

Polymers as vehicles for SPIO NPs

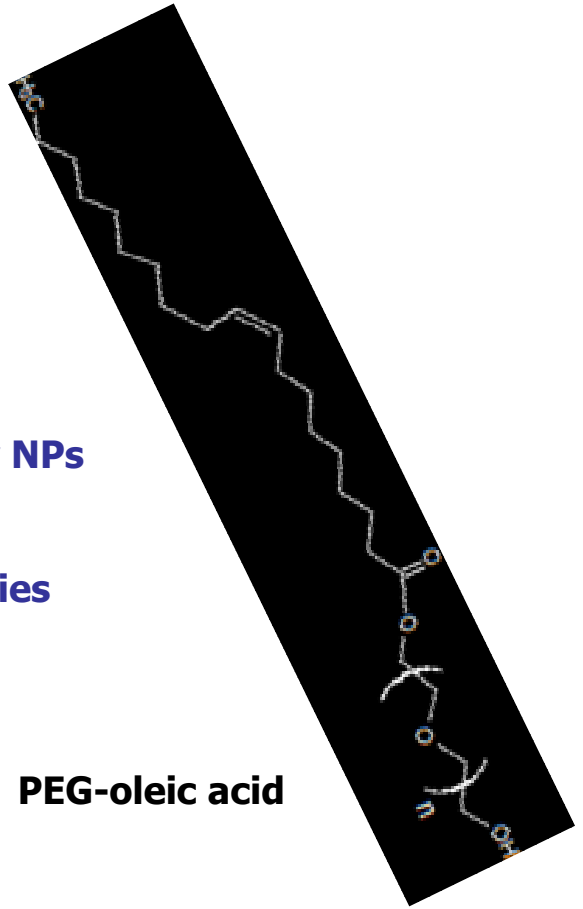
Glycol Chitosan



Dual Modality NPs
High stability
Low toxicity
Previous studies



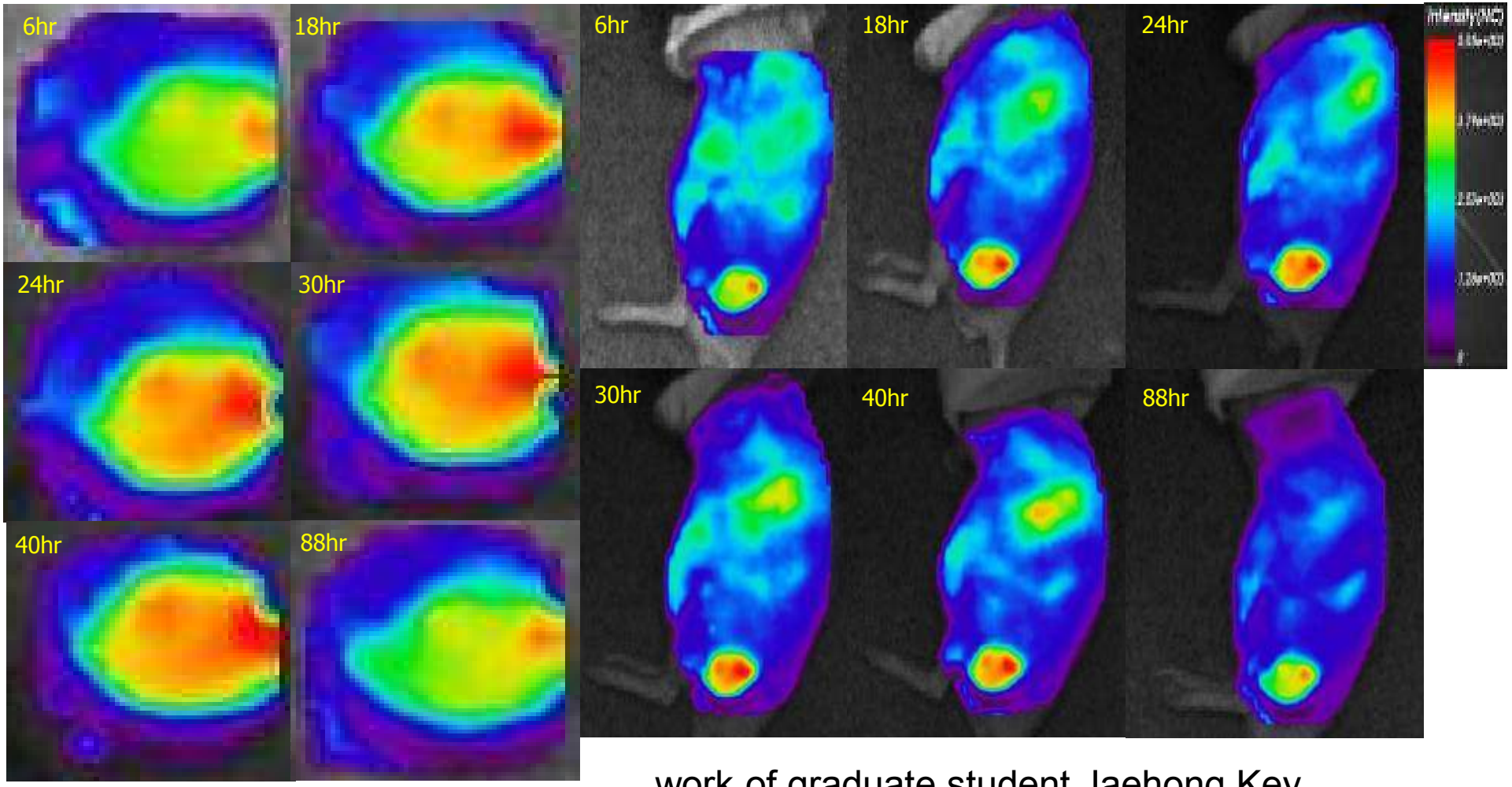
Pluronic



PEG-oleic acid

work of graduate student Jaehong Key

In-vivo fluorescent imaging (eXplore Optix) of NIR (Cy5.5) fluorescent chitosan-SPIO NPs



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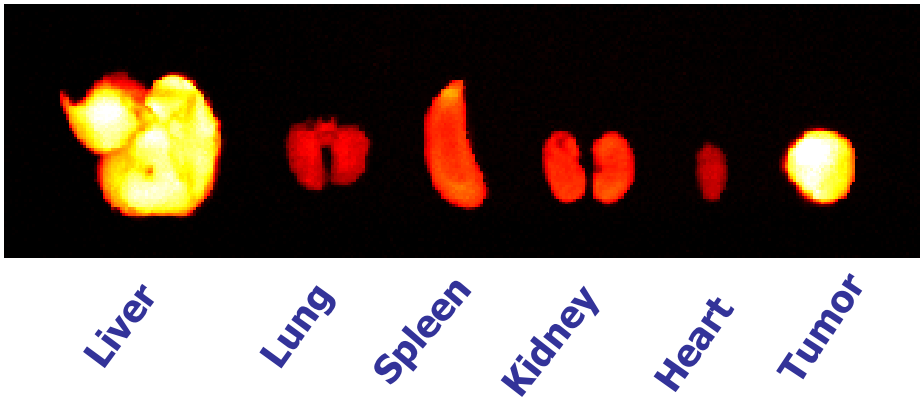
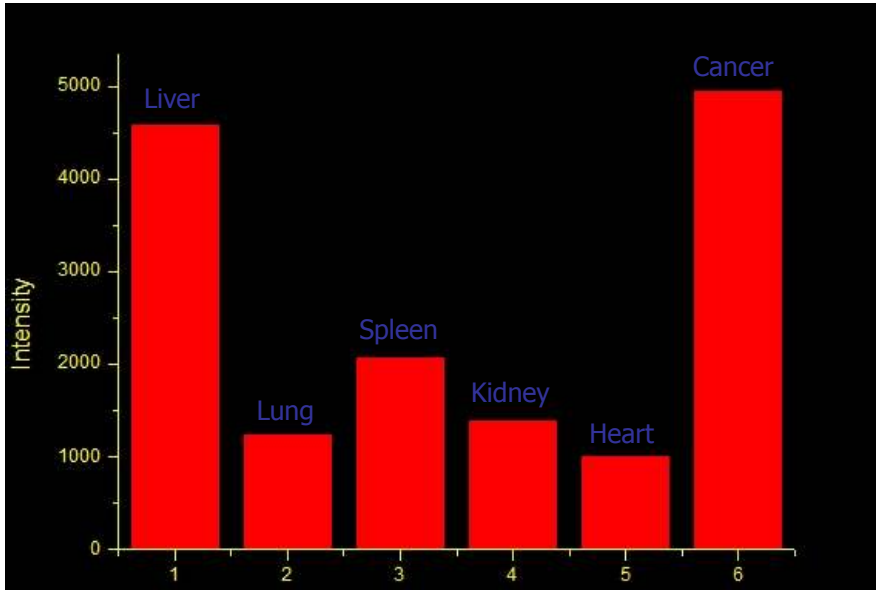
Ex-Vivo imaging of NIR (Cy5.5) fluorescent chitosan-SPIO NP labeled isolated mouse organs





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Lecture 5 References

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