Cornell Dots: Ultra-small Silica Nanoparticles as Probes for Image-Driven Clinical Applications

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The Wiesner Research Group

Organic (Polymer)-Inorganic Hybrids with Nanoscale Structures

Aim: Understand the fundamental chemical, thermodynamic and kinetic formation principles enabling general and relatively inexpensive wet-polymer chemistry methodologies for the efficient creation of nano- to multiscale functional materials with novel property profiles

Targeted applications (with collaborators)

diagnostics & nanomedicine

clean water

energy conversion & storage

Overview

The Problem: Lack of Visualization during Cancer Surgery

A Solution: Cornell Dots (C Dots), a Fluorescent Silica Nanoparticle Imaging (Diagnostic) Platform

First inorganic particle of its class and properties to be approved as a an investigational new drug (IND) for clinical use

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Clinical Imaging
Whole body mapping

MRI

CT

PET

Large & expensive (10^6-10^7) screening devices
Preoperative/limited intraoperative settings

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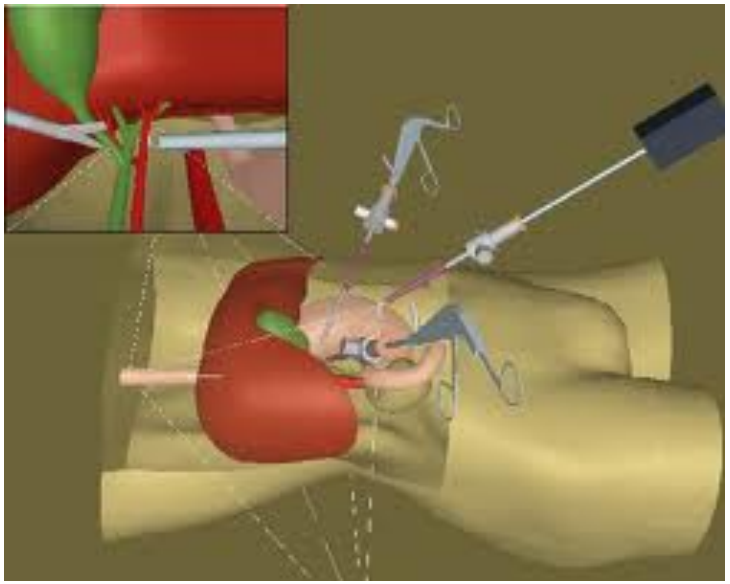
Minimally Invasive Surgery

Cheap, miniaturized optical imaging equipment available



Optical imaging can be integrated with endoscopes, other hand-held devices (PET gamma/beta probes)

What is missing: optical (fluorescent) probes for use in humans

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A solution: What we did differently

1. **Use of silica as a material:** **Safe to use**

2. **Use of extremely small (< 10 nm) particles:** **“Target or clear”**

Memorial Sloan-Kettering Cancer Center

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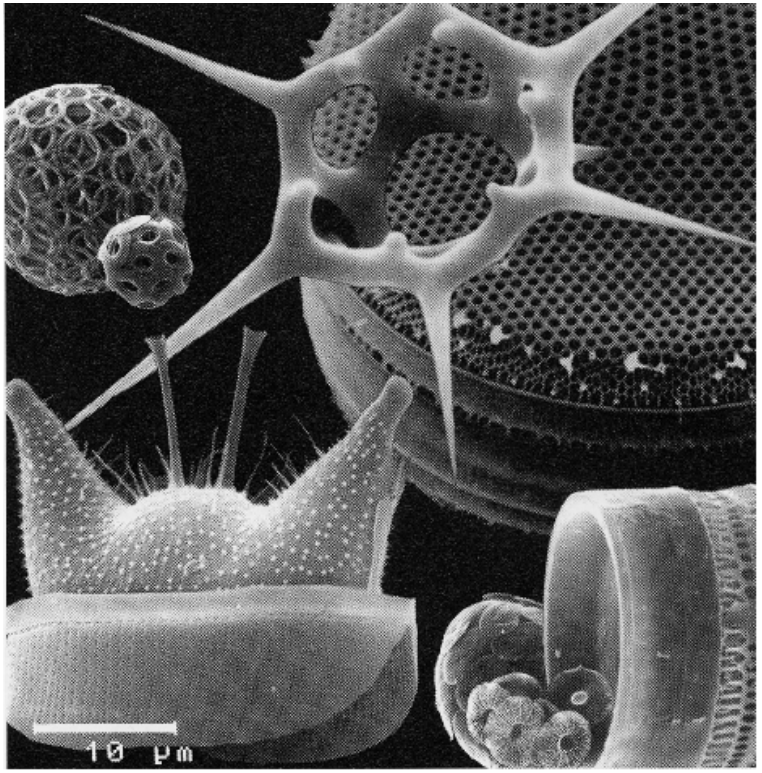
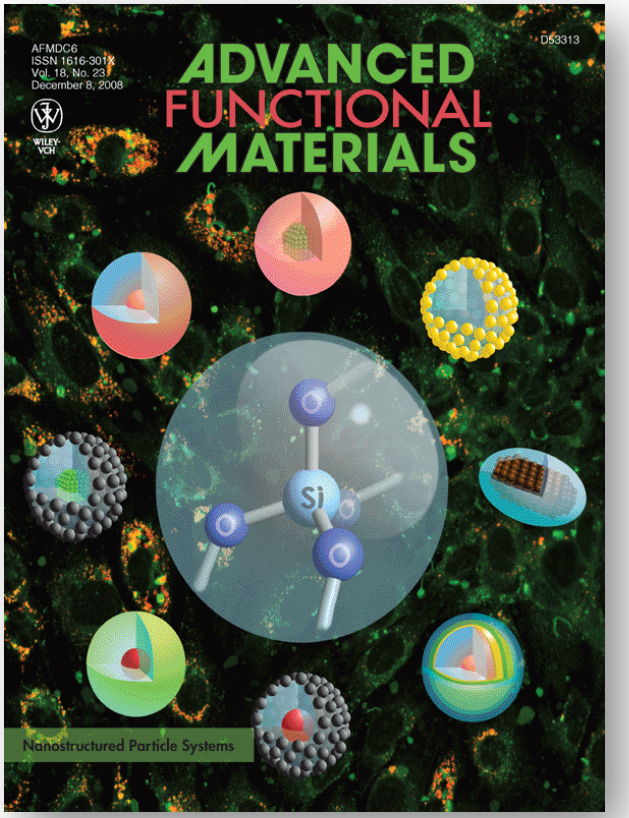
Silica as a biocompatible materials platform

Part of the oldest living organisms on this planet



silica nanoparticle platform



Science **278** (1997), 1795

Science **330** (2010), 214

Science **340** (2013), 337

Nature Mater. **6** (2007), 156

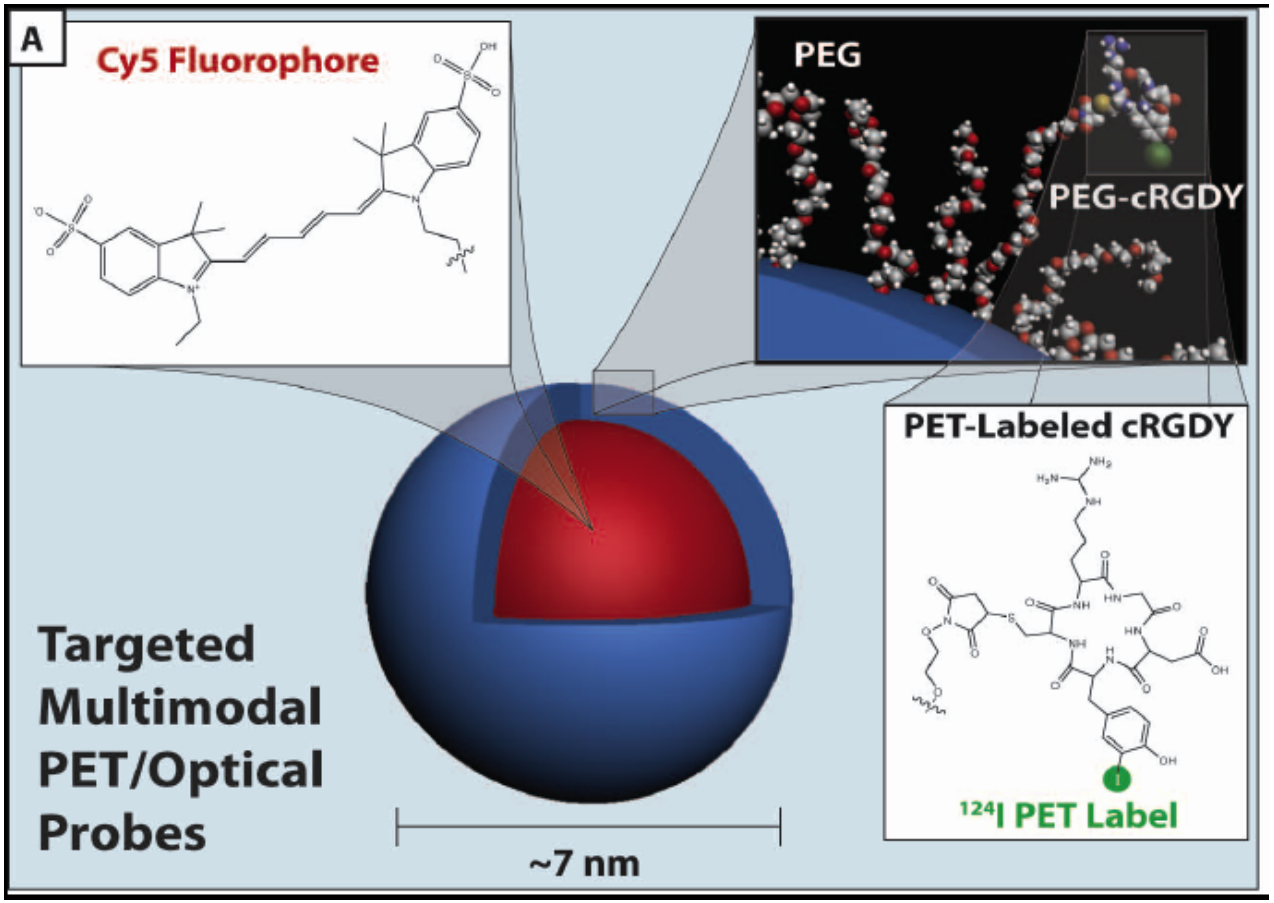
Nature **460** (2009), 1110

Y. Piao, U.W. *et al., Adv. Func. Mater.* **18** (2008), 3745

Cornell dots (C dots): "Target or Clear"

M. Bradbury

Kai Ma



molecular targeting group for melanoma

PET label

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J. Clin. Invest. **121** (2011), 2768
Nano Letters **5** (2005), 113

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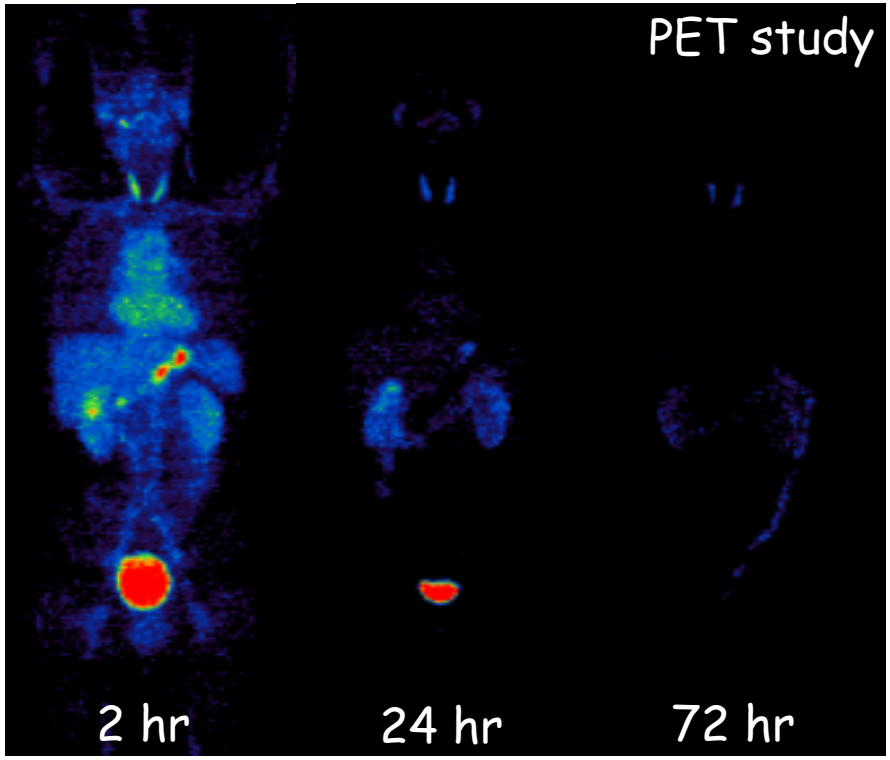
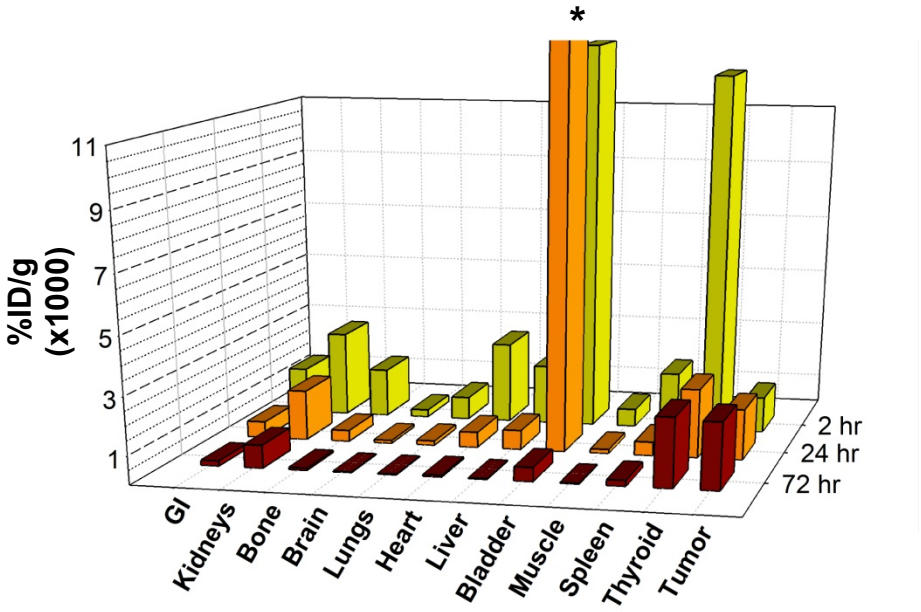
First Human Clinical C dot Trial: Melanoma

0 Phase Trial with 5 Patients: Safety Study





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M. Bradbury, U.W. *et al.* (2014), submitted

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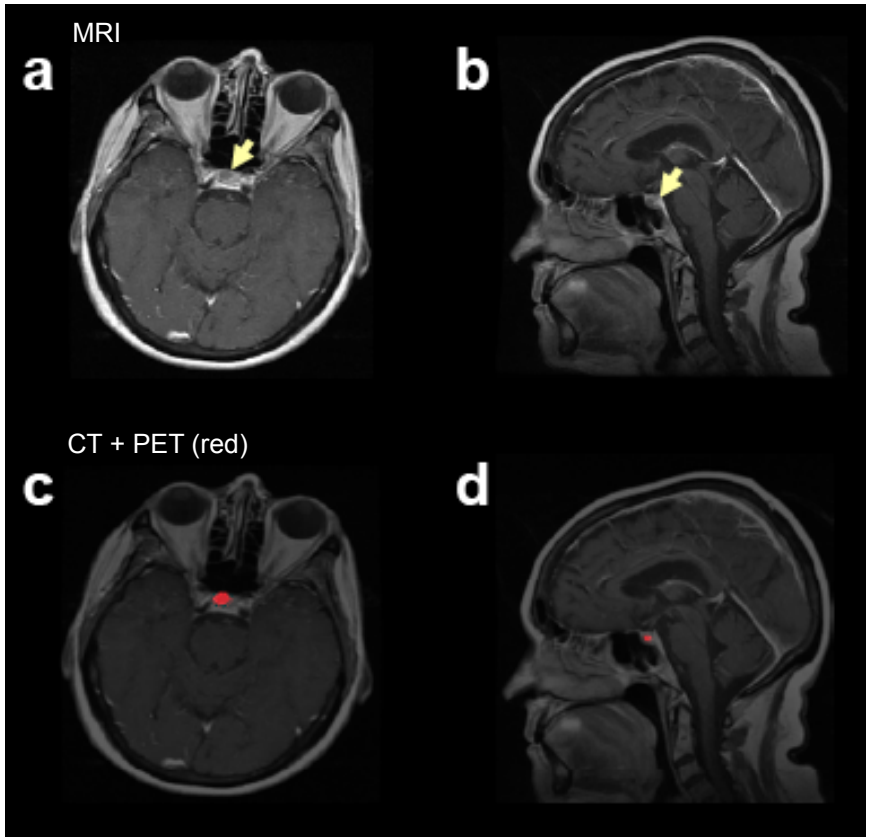
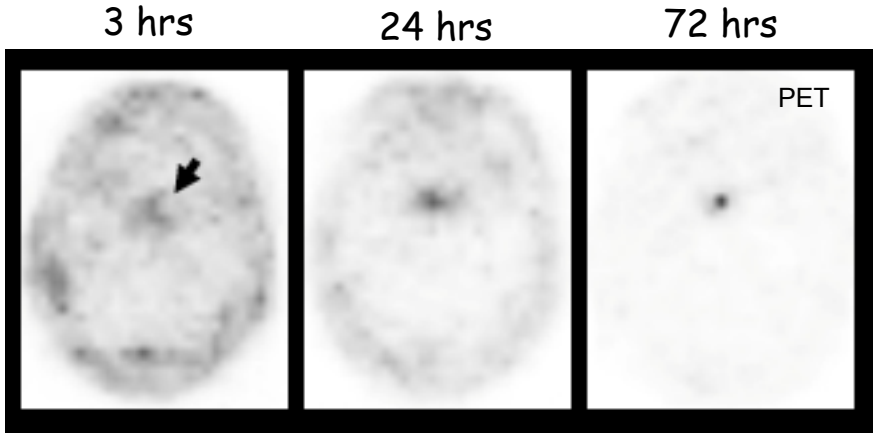
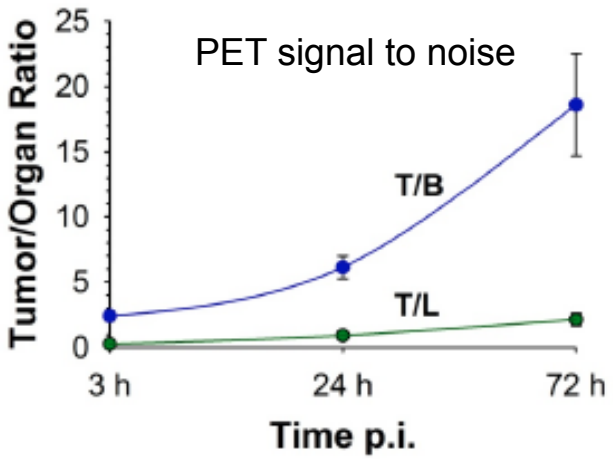
Lesion targeting with C dots







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M. Bradbury, U.W. *et al.* (2014), submitted

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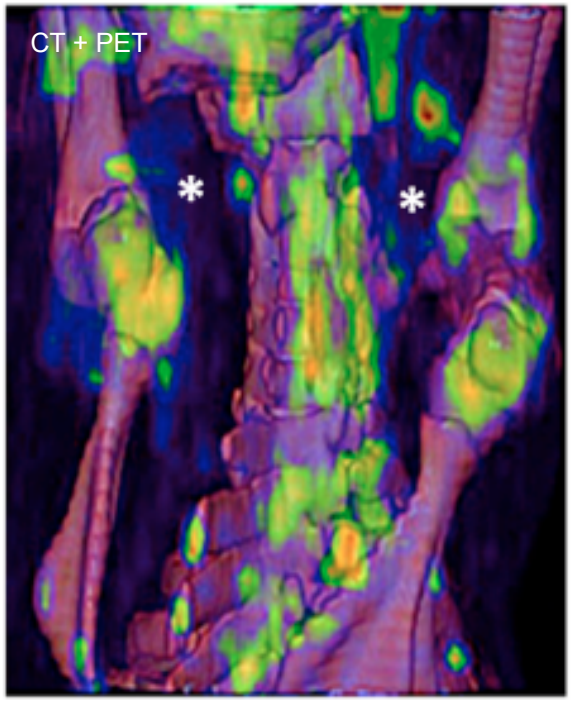
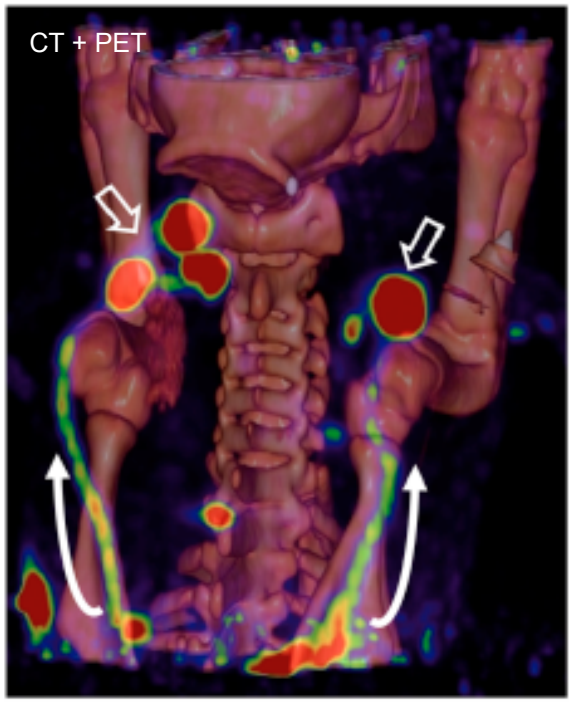
First C dot Application: SLN Mapping

mini-swine whole body CT + PET imaging

^{18}F-FDG



^{124}I-cRGDY-PEG-C-dots



Next IND just approved by FDA

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Integr. Biol. **5** (2013), 74

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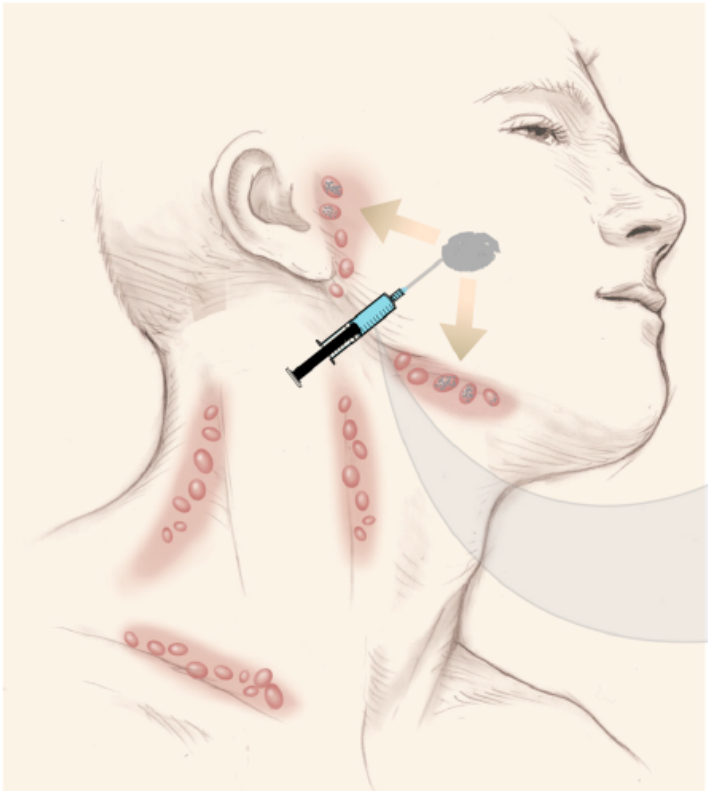
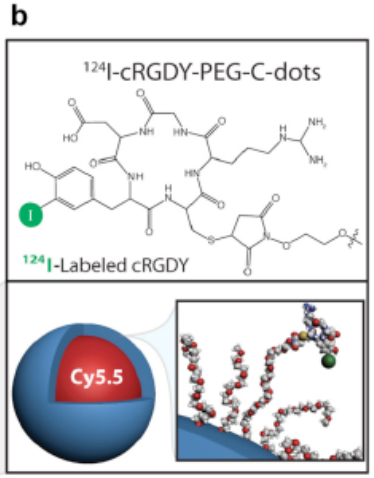
Next clinical trial: Head & neck nodal mapping

Advances in probe & imaging technology to improve patient care



melanoma patient



Handheld fluorescent camera systems:
ArteMIS™

Integration of multiple technologies for next generation diagnostics

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M. Bradbury, U.W. *et al. Integr. Biol.* **5** (2013), 74

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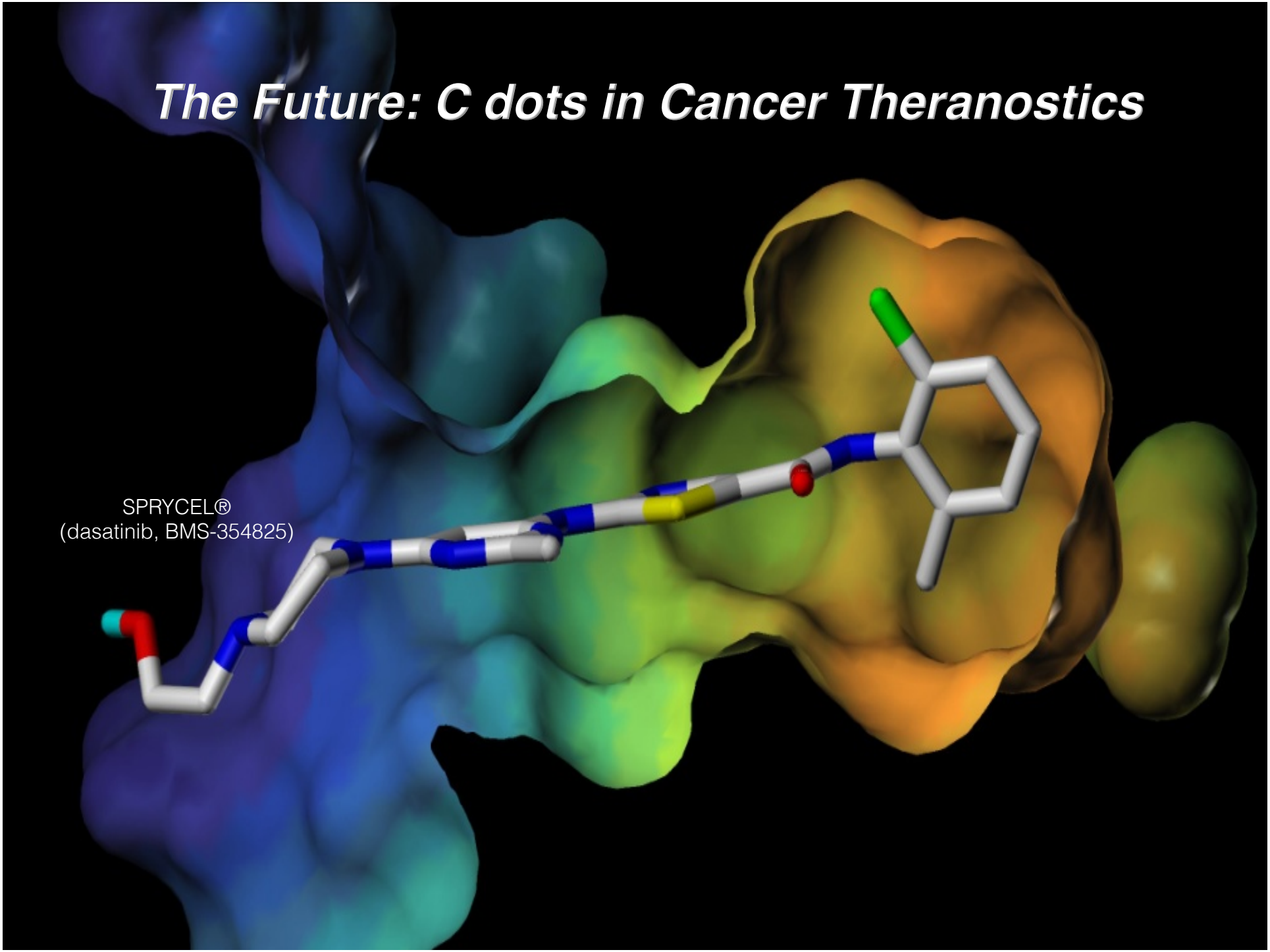
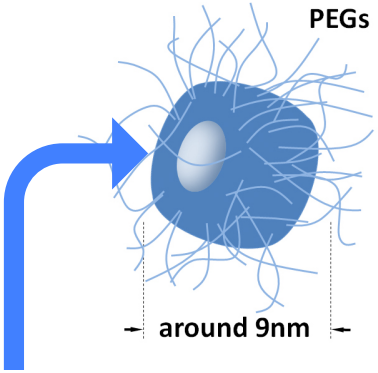
The Future: C dots in Cancer Theranostics



SPRYCEL®
(dasatinib, BMS-354825)

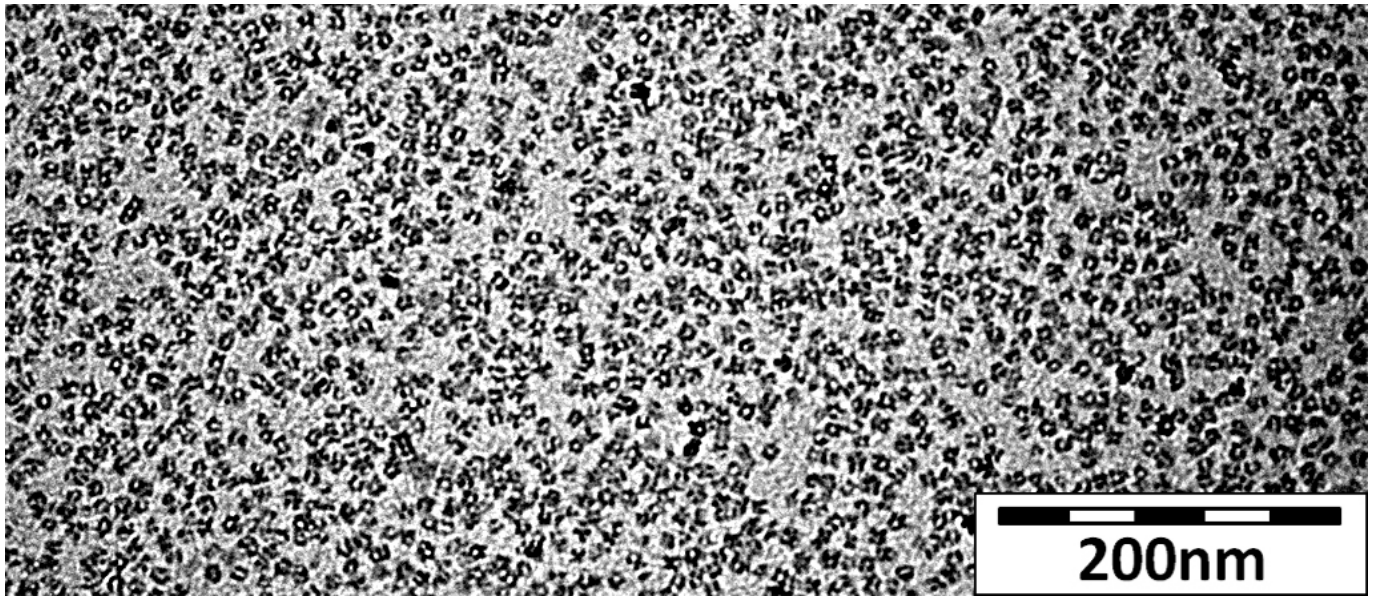
New Particle Platform: Single Pore Cornell Dots

Single-pore sub-10 nm fluorescent silica NPs that can load drugs



drug will be hidden inside

Kai Ma



Precise control over particle architecture and size

K. Ma, H. Sai and U.W. *JACS* **134** (2012), 13180
K. Ma, U.W. et al. *Chem. Mater.* **25** (2013), 677

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Start- up:

Claymore Technologies

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Steve Larson, MD (MSKCC)
Ulrich Wiesner, PhD (Cornell)