

Nanomedicines to Improve the Therapeutic Index of Precision Medicines

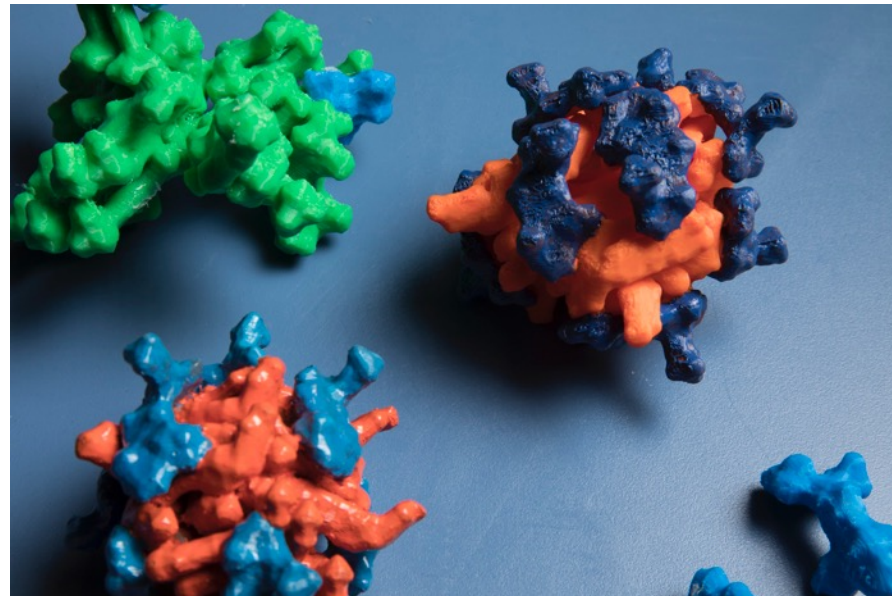
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Head, Cancer Nanomedicine Laboratory

Bristol-Myers Squibb/James D. Robinson III Junior Faculty Chair

Associate Member, Memorial Sloan Kettering Cancer Center

Associate Professor, Weill Cornell Graduate School of Medical Sciences



16th US-Korea Forum
September 23, 2019



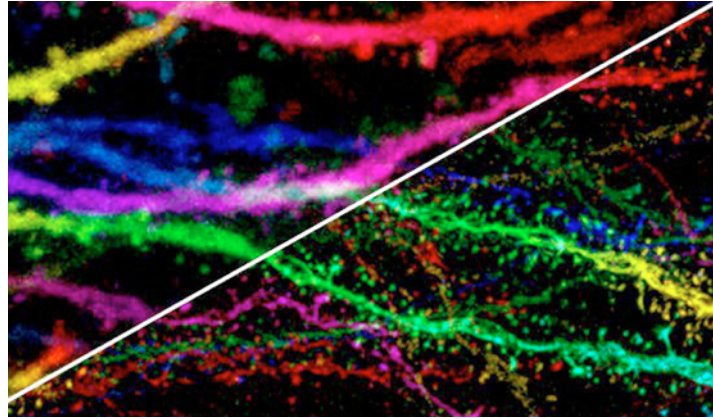
Memorial Sloan Kettering
Cancer Center™

Nanotechnologies at Memorial Sloan Kettering Cancer Center and Weill Cornell Medicine

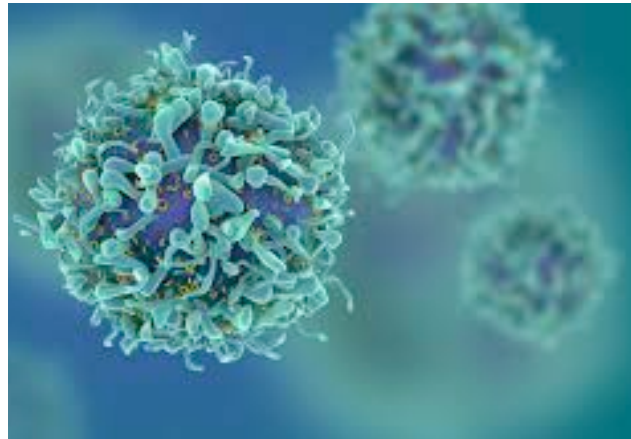


Nanotechnologies to Address Disease

Biomedical Research Tools



Drug Delivery



Drug Discovery Tools

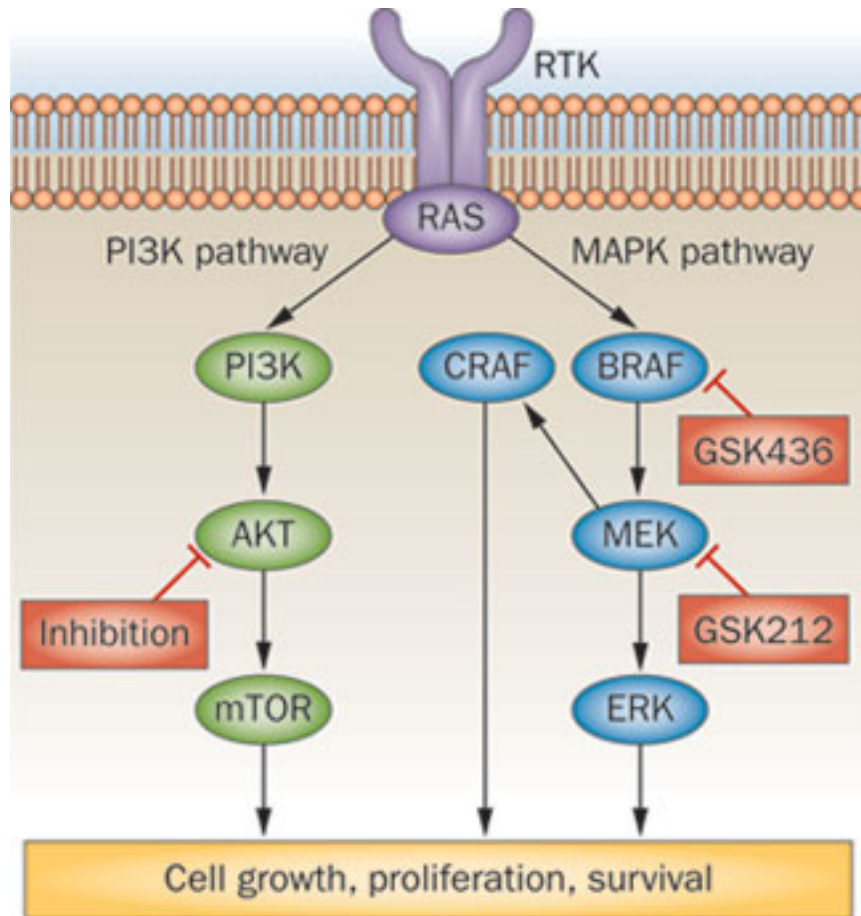


Imaging/Diagnostics

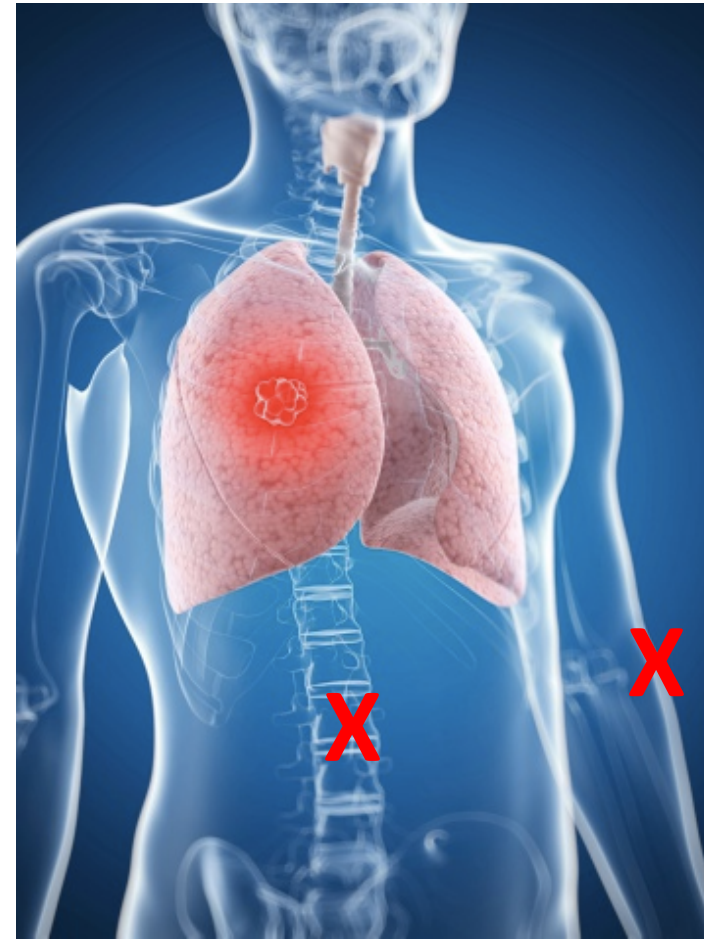


Targeting Targeted Therapies

Targeting the Pathway

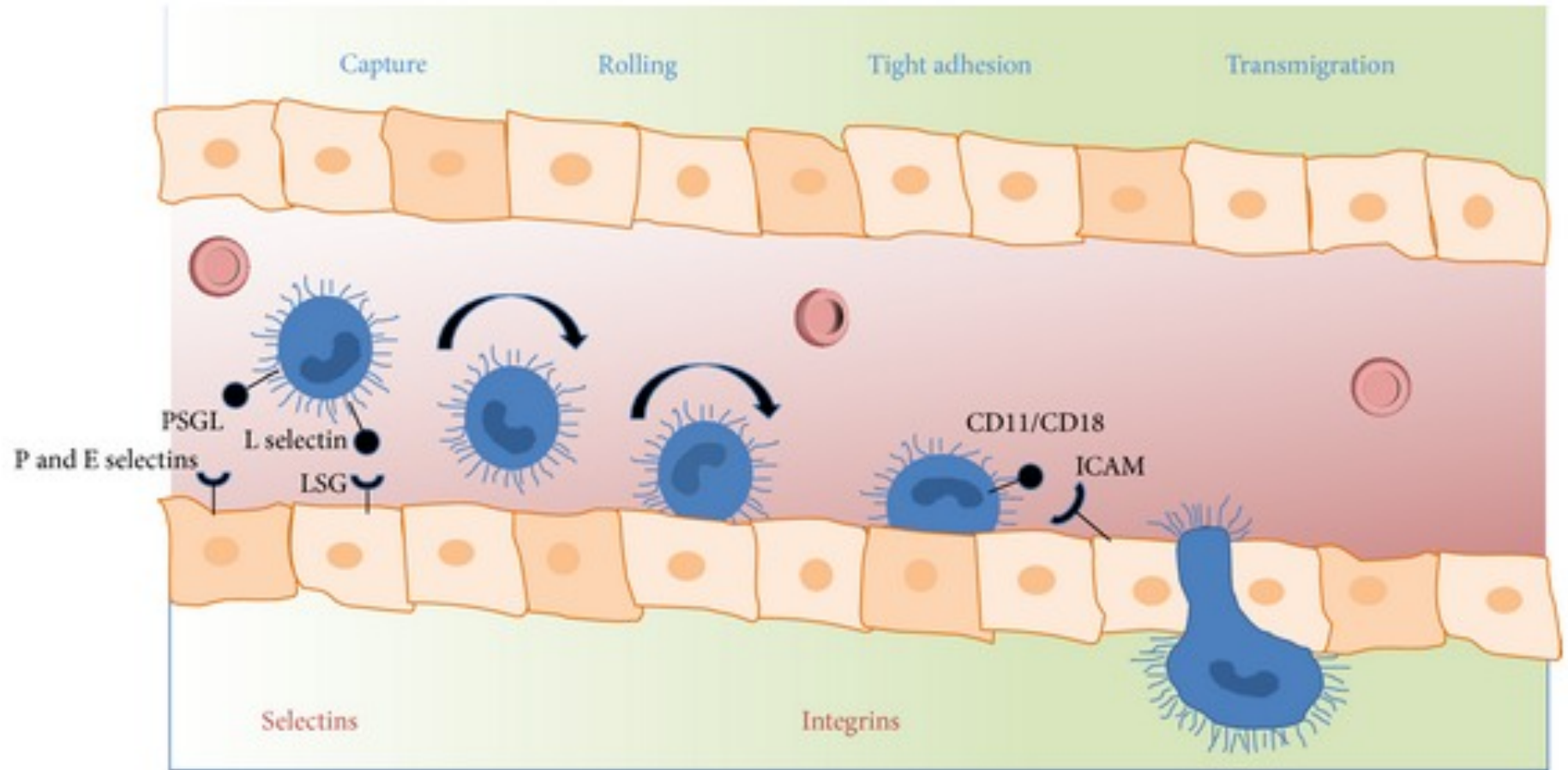
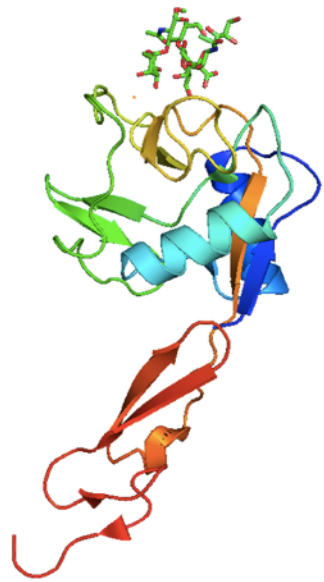


Targeting the Location

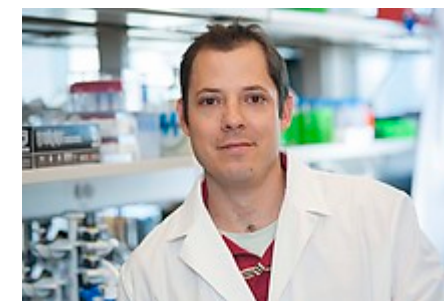
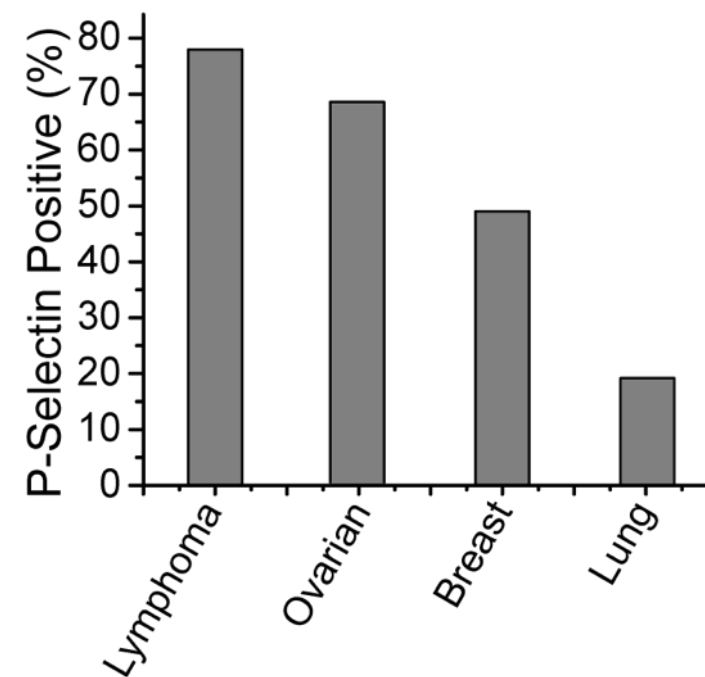
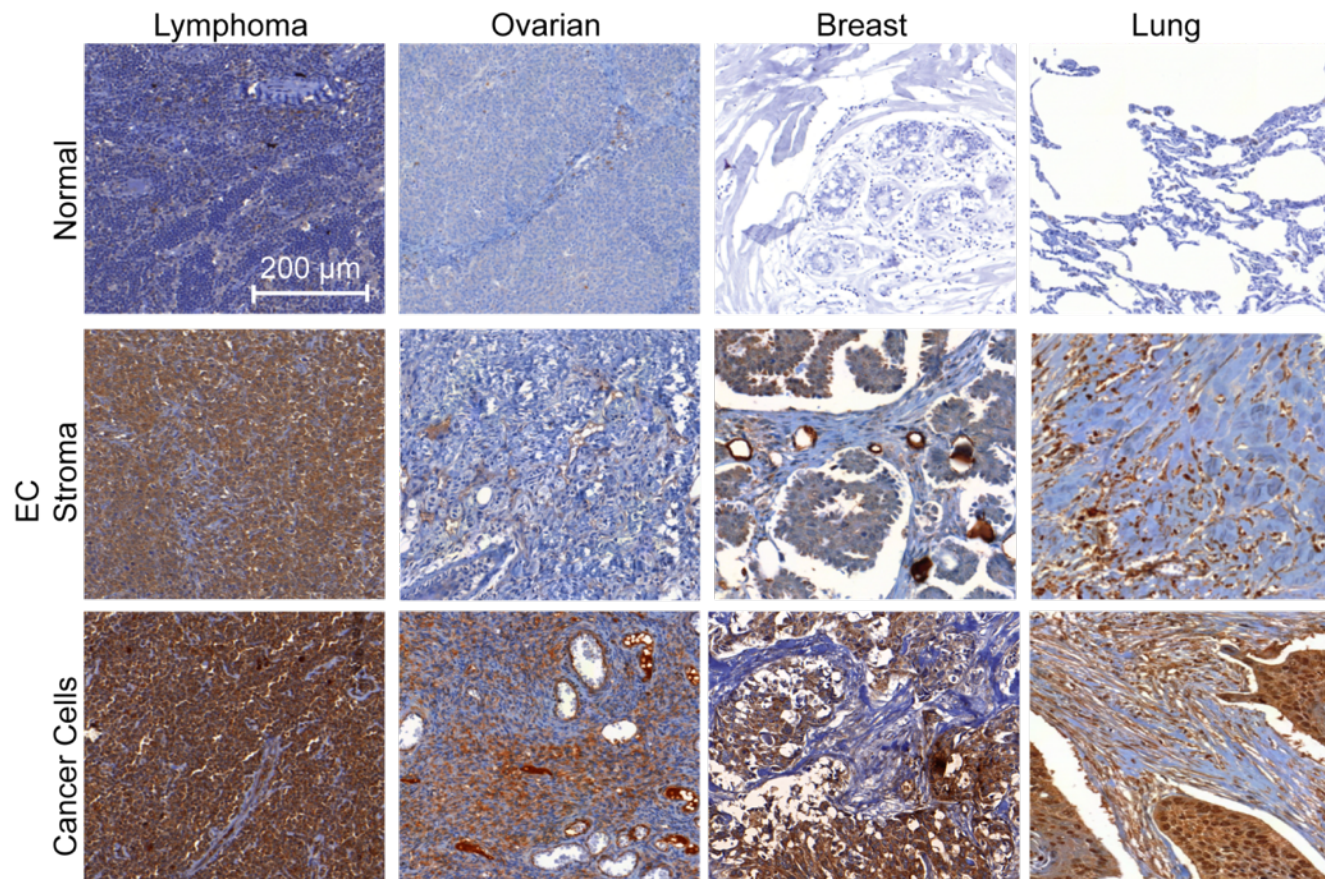


Avoiding Problem Tissues

P-selectin is Released to the Surface of Activated Endothelial Cells

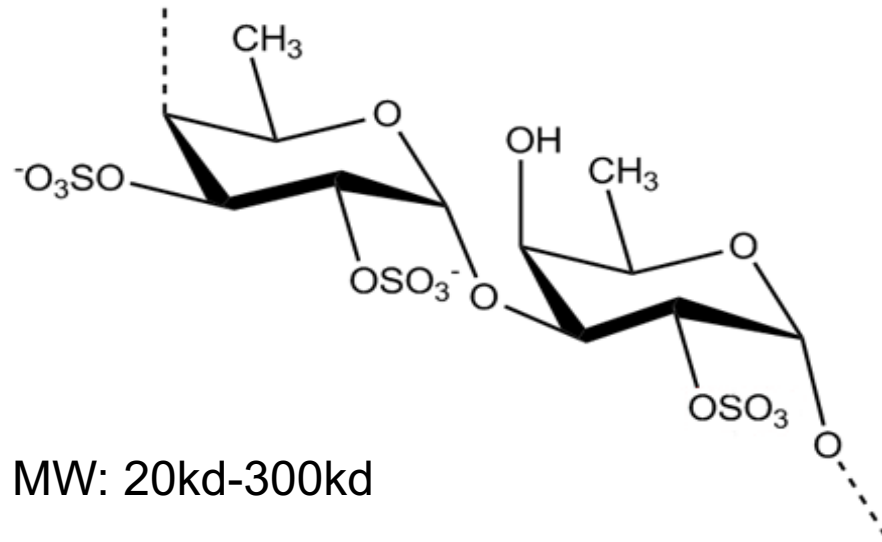


P-selectin is Expressed in Human Cancers on Blood Vessels, Stroma, and Cancer Cells



Yosi Shamay

Fucoidan, a Fucosylated, Sulfated Polysaccharide Binds P-Selectin



MW: 20kd-300kd



-High affinity to P-selectin (~20nM)

-Structural element for building nanoparticles

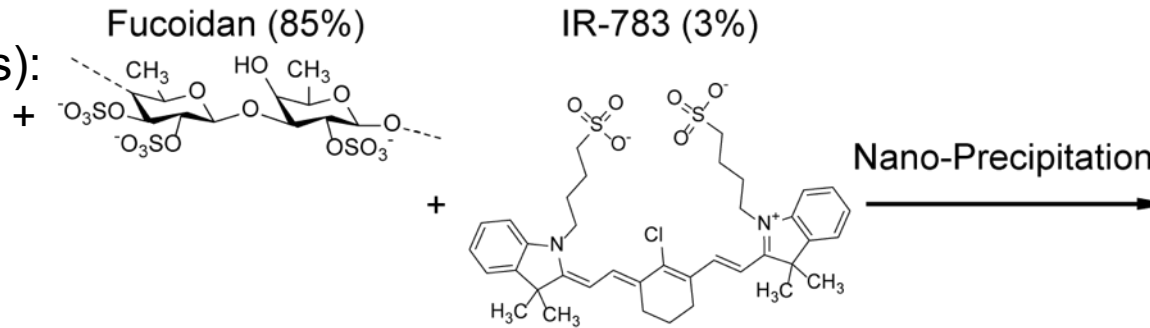
Rouzet, Journal of Nuclear Medicine (2011)

Cho, Carbohydrate Polymers (2012)

Nanoparticle Synthesis

Drug compound
(wide range of drug classes):

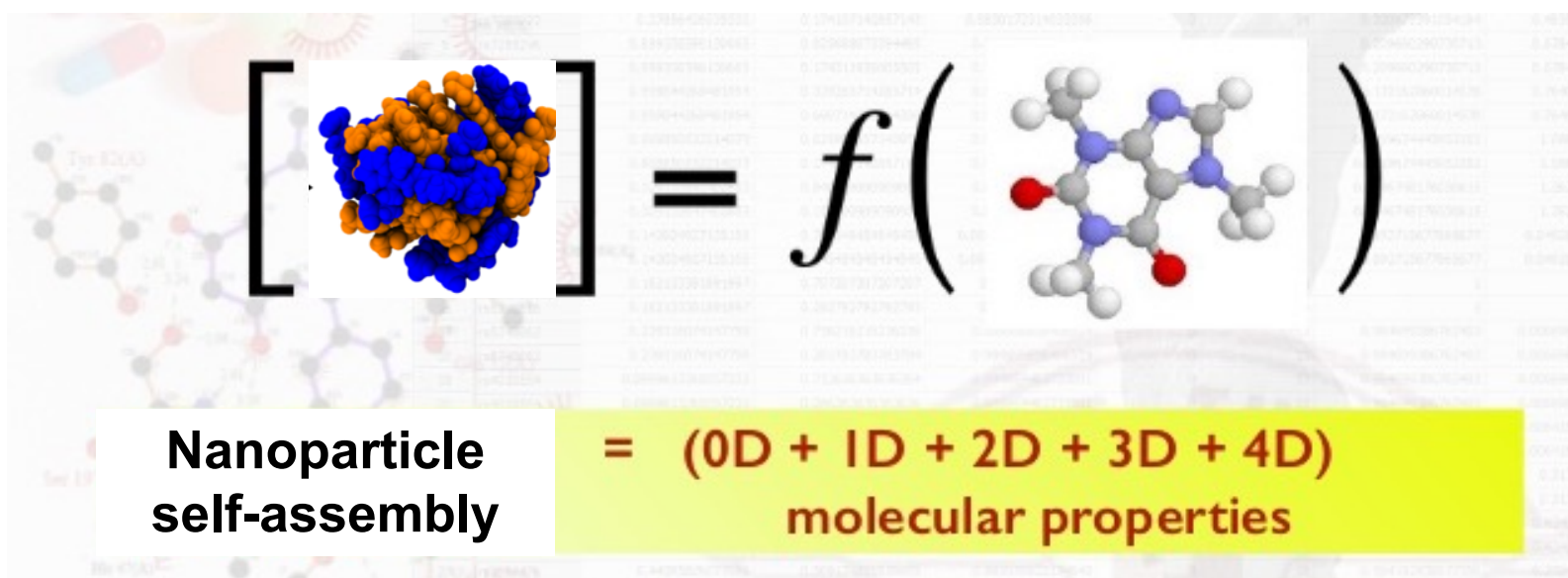
Paclitaxel - FiPAX
MEK 162 – FiMEK
Trametinib -- FiTRAM
Sorafenib – FiSOR
BYL719 – FiBYL719
Others...



Fi-(Drug)

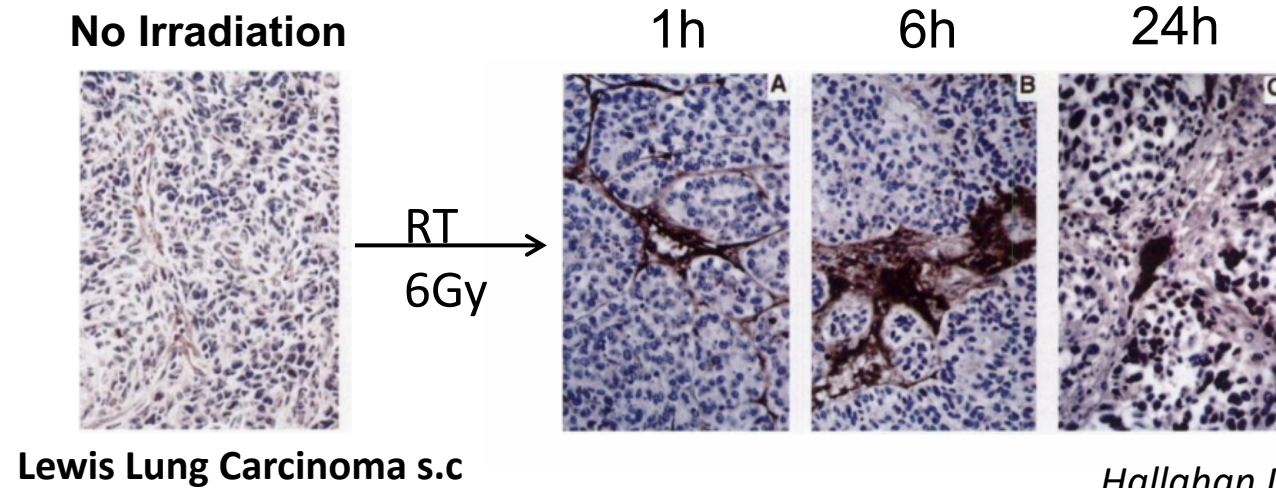
Dex-(Drug)

Machine Learning and QSAR Facilitate Nanoparticle Synthesis with Diverse Drugs

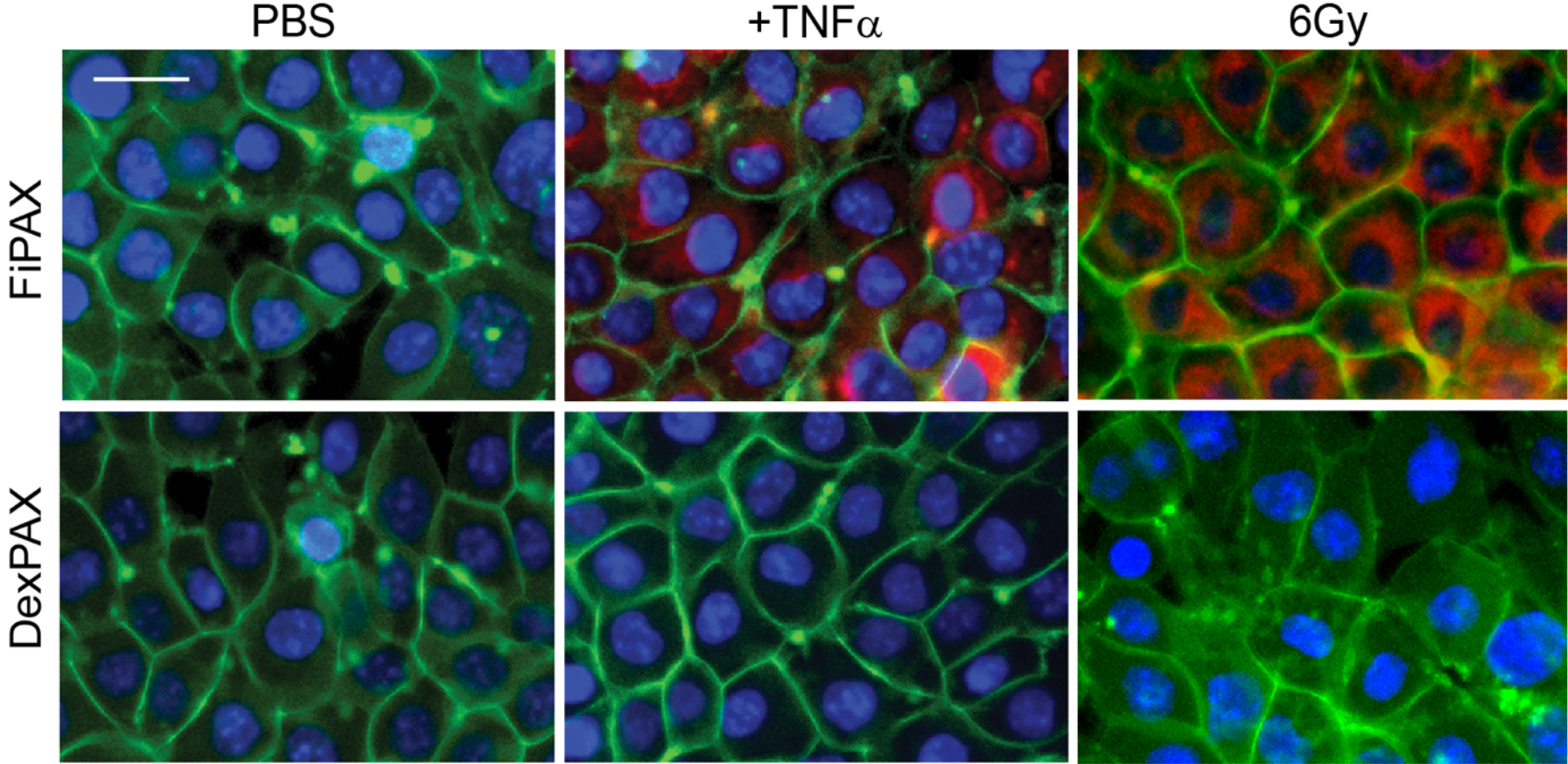


Quantitative Structure-Nanoparticle
Assembly Prediction (QSNAP)

Radiotherapy Induces P-selectin Expression in Vasculature

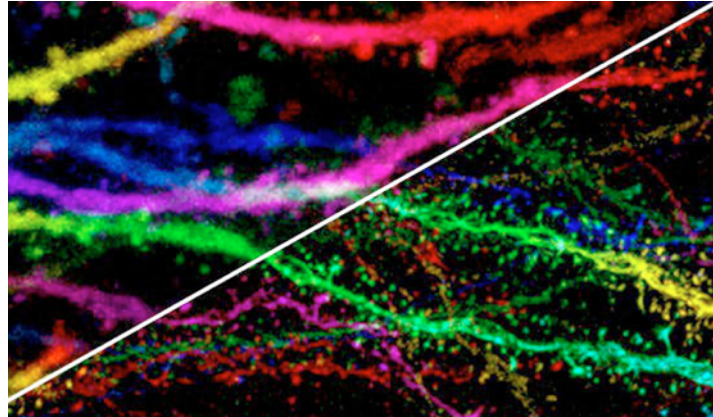


Nanoparticles Bind to Irradiated Endothelial Cells

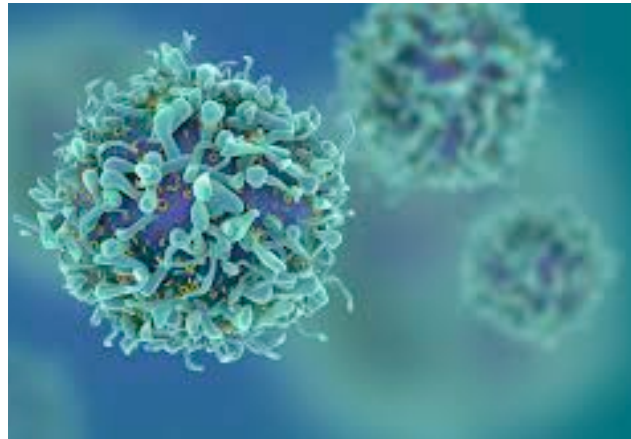


Nanotechnologies to Address Disease

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Drug Delivery



Drug Discovery Tools

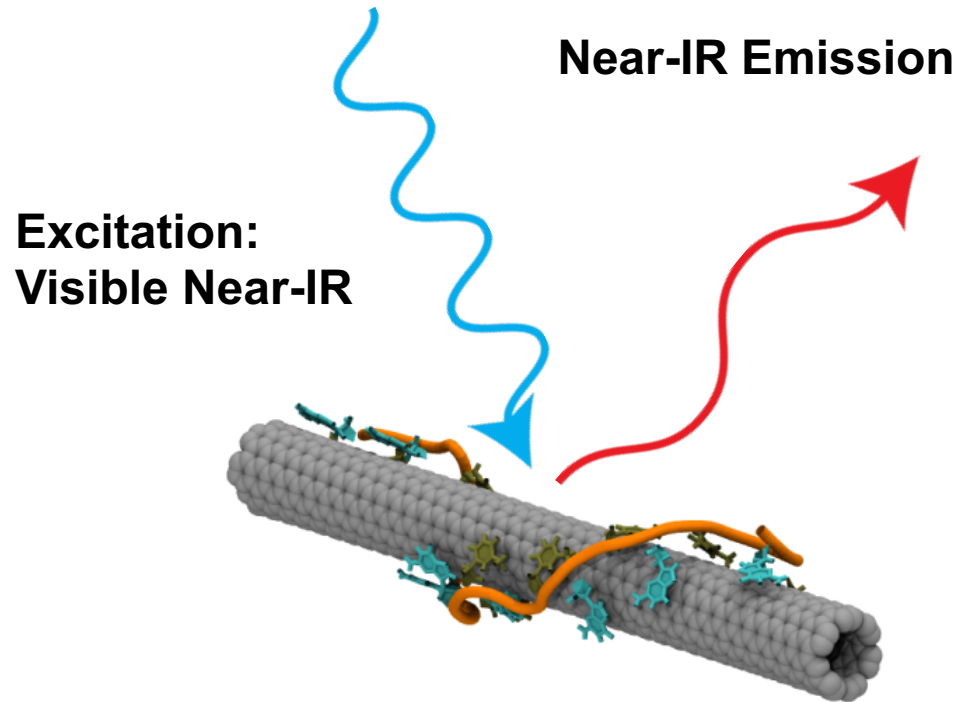
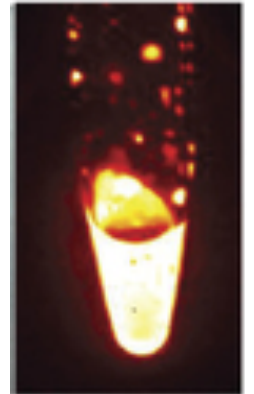
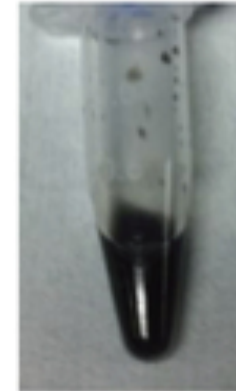


Imaging/Diagnostics



Fluorescent Reporters from Carbon Nanotubes

Tissue-Penetrating Signal

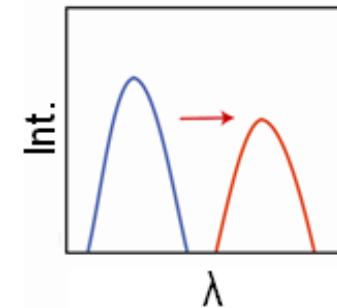
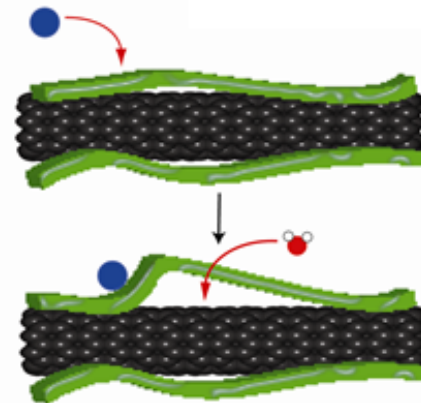


Excitation:
Visible Near-IR

Near-IR Emission

DNA/Polymer-Encapsulated
Carbon Nanotube

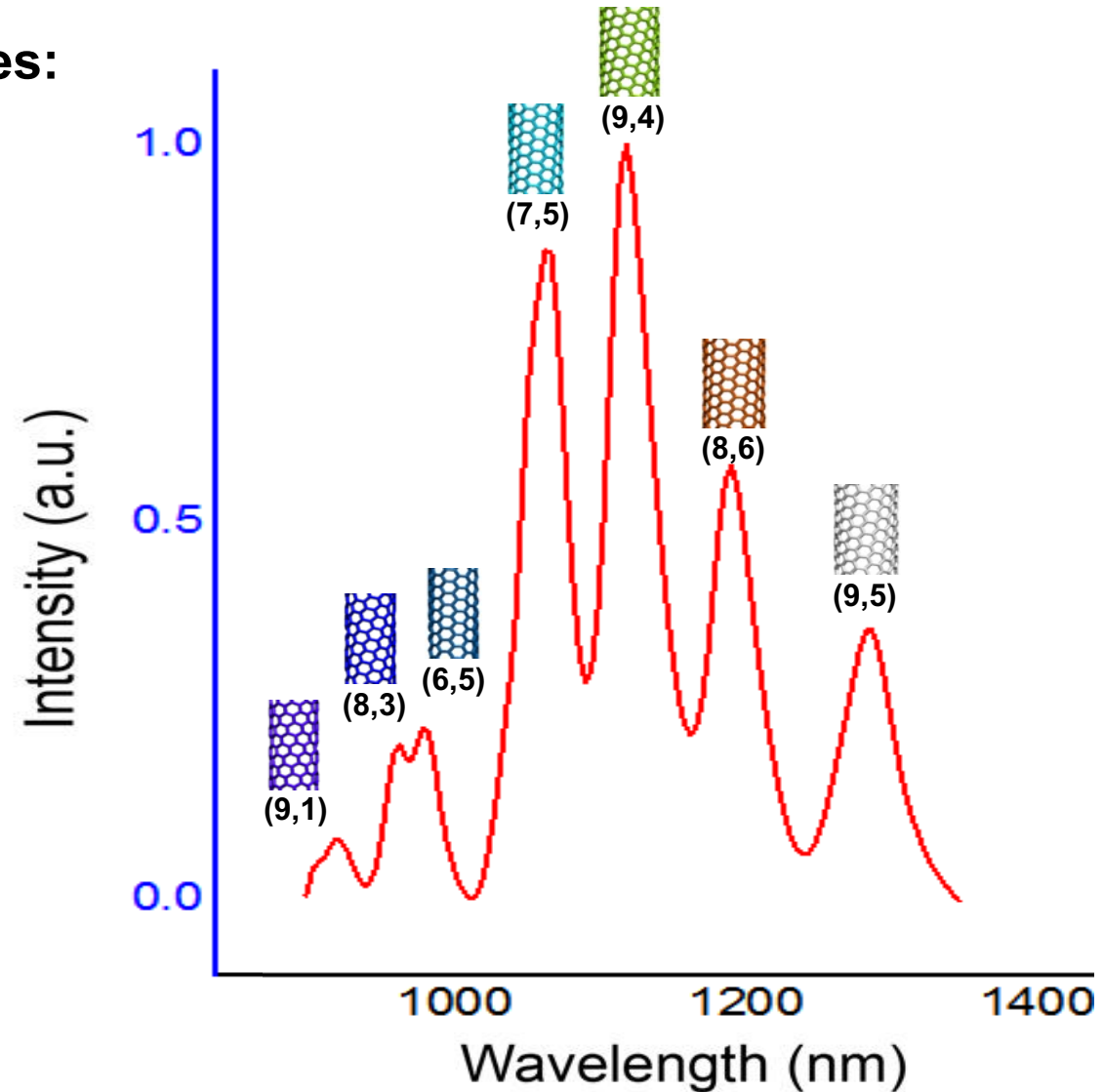
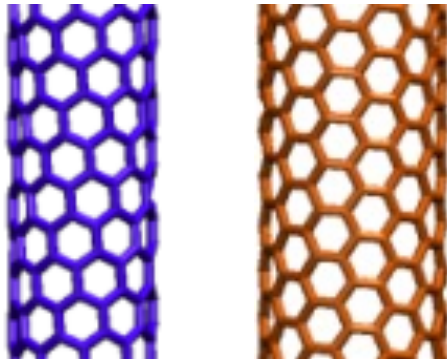
Respond to Local Solvent Environment



Carbon Nanotube Near-Infrared Fluorescence is Structure-Dependent

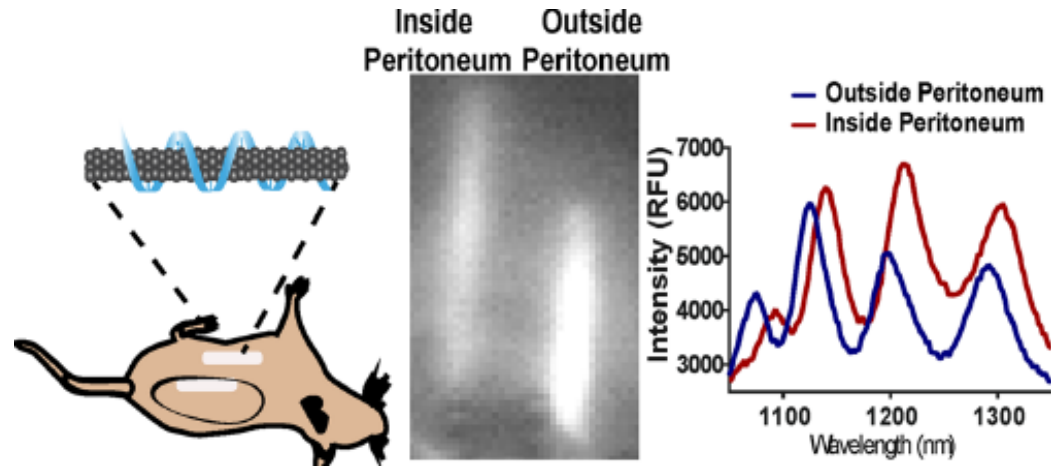
Semiconducting Nanotubes:
Near-Infrared Emission
900-1600 nm

Narrow Band Emission
Structure/Diameter-
Dependent



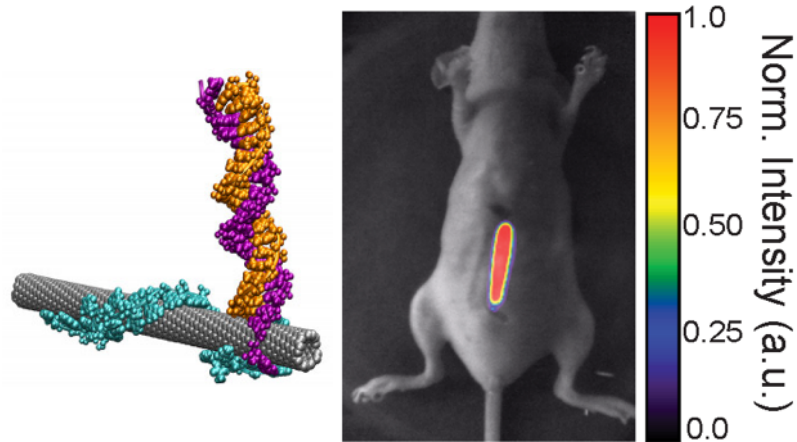
Tools for Research, Drug Discovery, and Diagnosis

Sensor Implant to Measure Drug PK



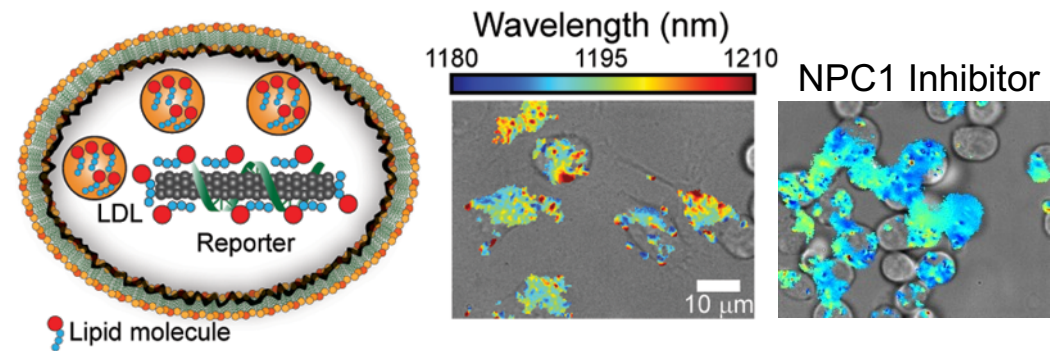
Harvey, *Nano Lett* (2019)

Nanosensor Implant for Non-Invasive Detection of miRNA



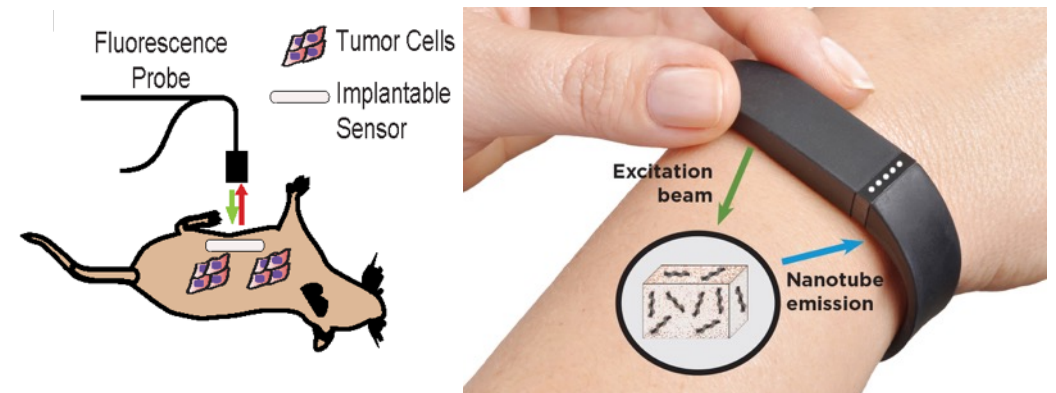
Harvey, *Nat Biomed Eng* (2017)

Live Cell Reporter of Endolysosomal Lipids

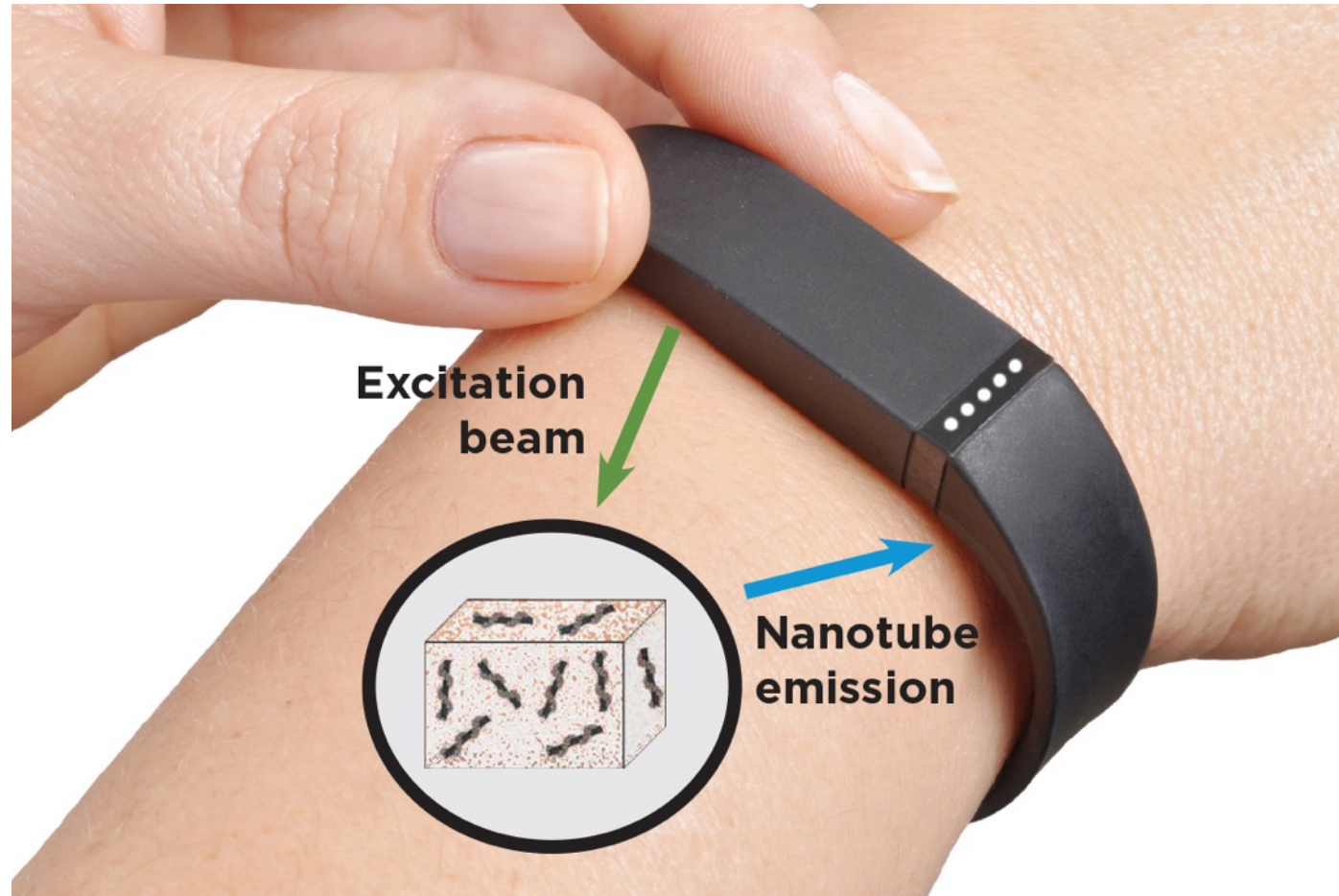


Jena, *ACS Nano* (2017)

Detection of HE4 in Ovarian Cancer

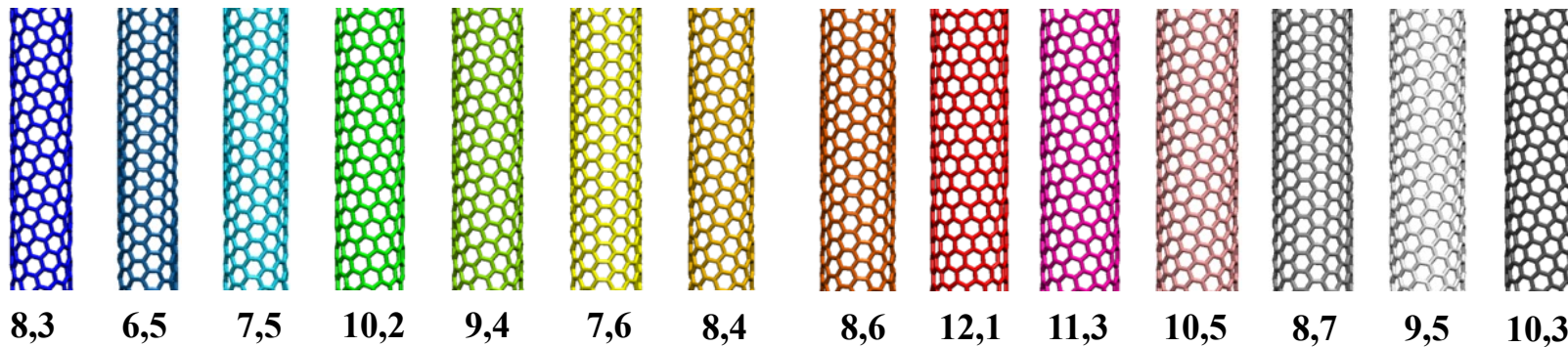
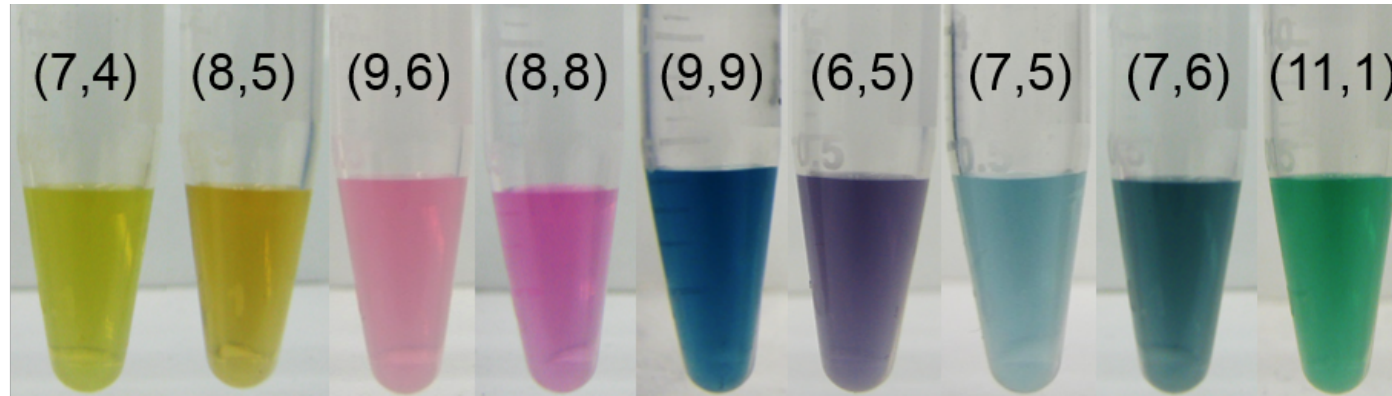


Williams, *Sci Adv* (2018)



Harvey, et. al., *Nature Biomedical Engineering* 2017
Williams et al. *Science Advances*, 2018

CNTs: Optical Materials in Need of Outreach



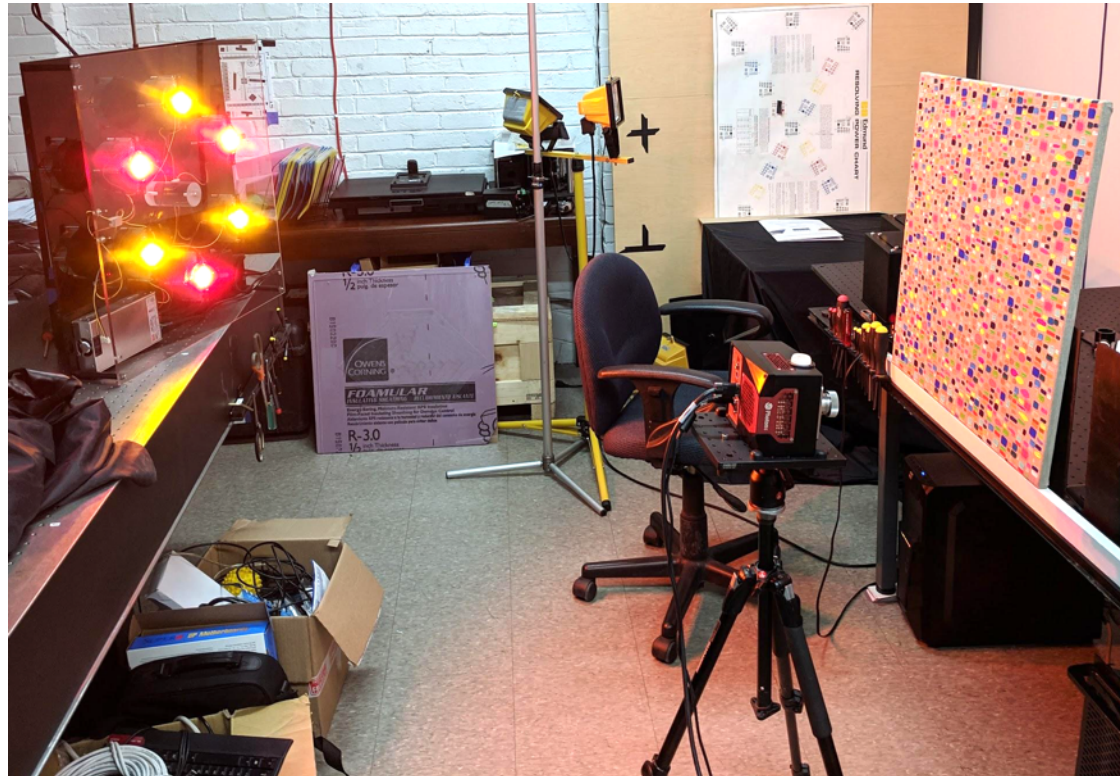
Ao, et. al., J. Am. Chem. Soc., 2016, 138 (51), pp 16677–16685

Bring in the Artists?



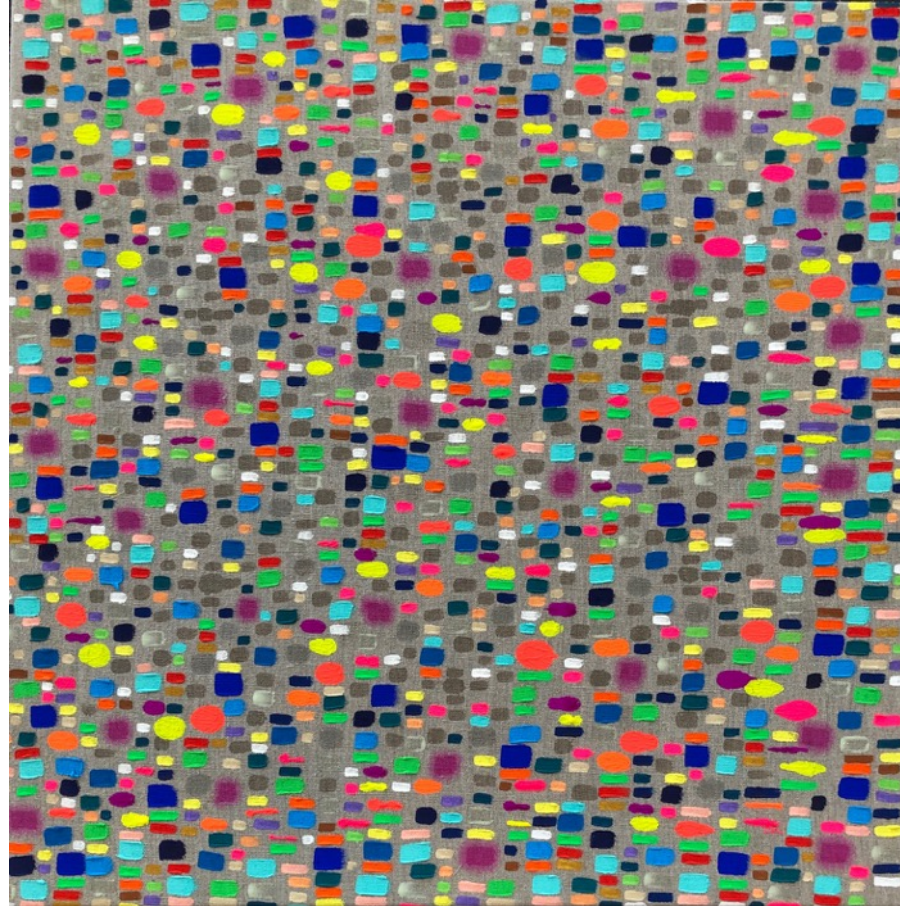
Joseph Cohen

NanoArt Out of the Lab



w/ Bruce Weisman, Photon Etc.

The Mind's Eye

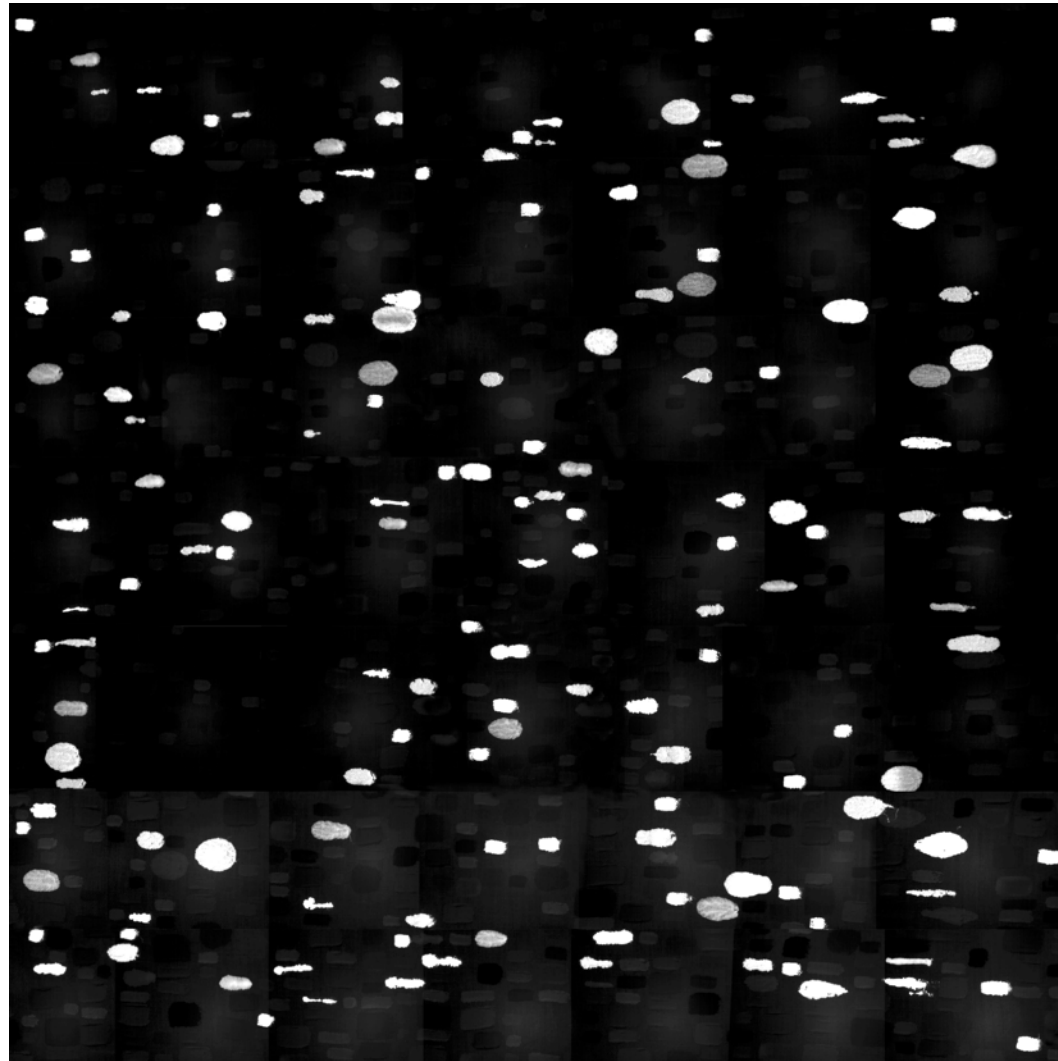


Joseph Cohen (American, b.1982)

MSP-001 (Multi-Spectrum Painting), 2019

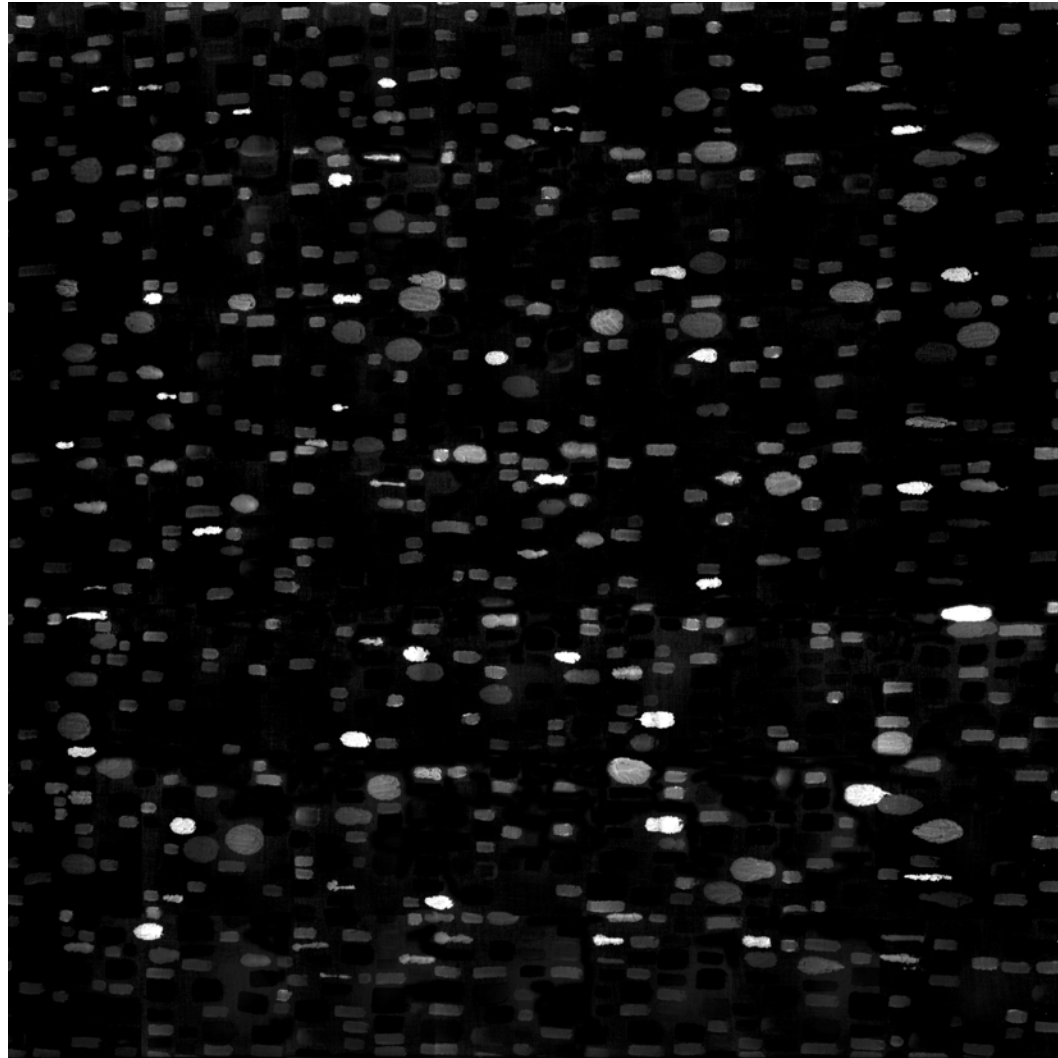
Enriched carbon nanotubes, separated carbon nanotubes, sodium deoxycholate, WBV™, tracer dyes and phosphorescent pigments on linen

24 x 24 inches



SWIR (Excitation: 590 nm 3 x 30 w LED)

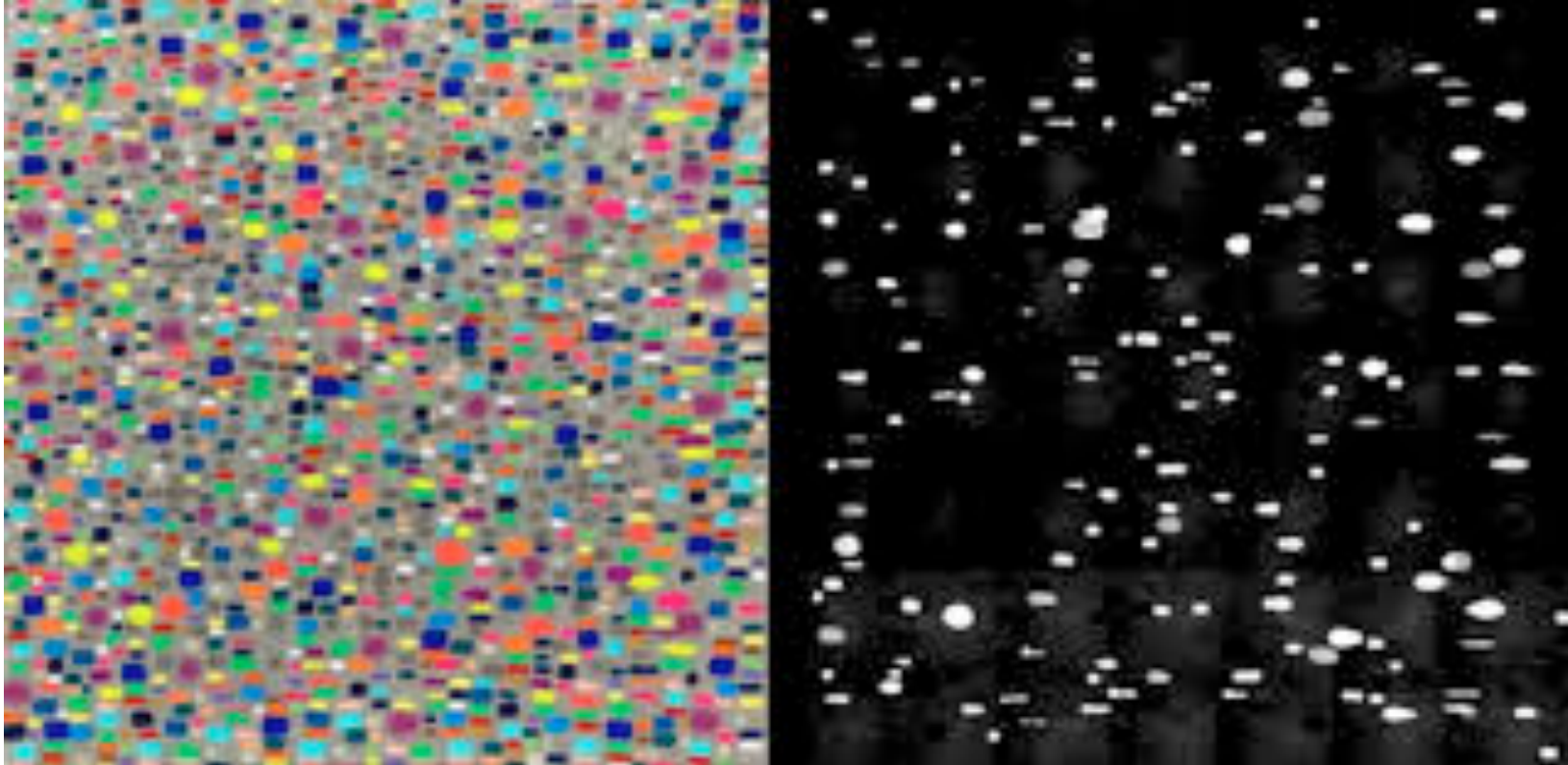
InGaAs Array Camera



SWIR (Excitation: 630 nm 3 x 30 w LED)

InGaAs Array Camera

The Mind's Eye



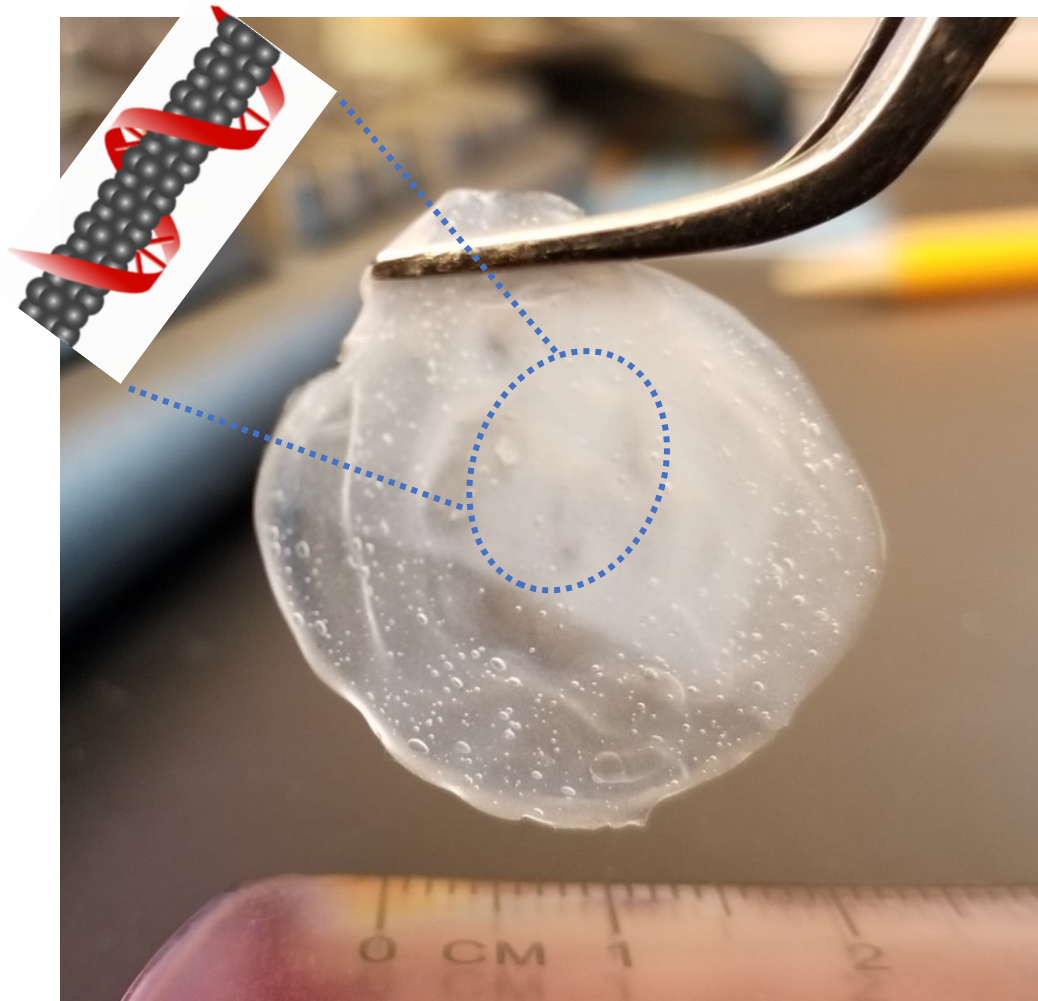
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MSP-001 (Multi-Spectrum Painting), 2019

Enriched carbon nanotubes, separated carbon nanotubes, sodium deoxycholate, WBV™, tracer dyes and phosphorescent pigments on linen

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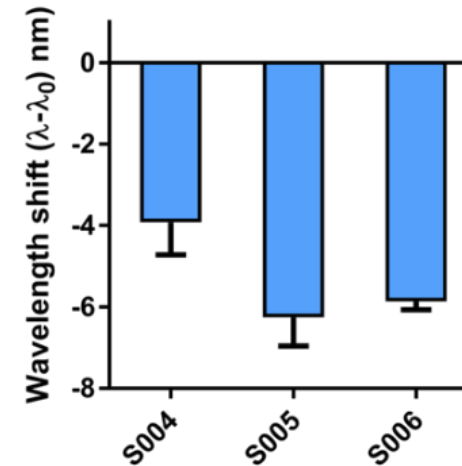
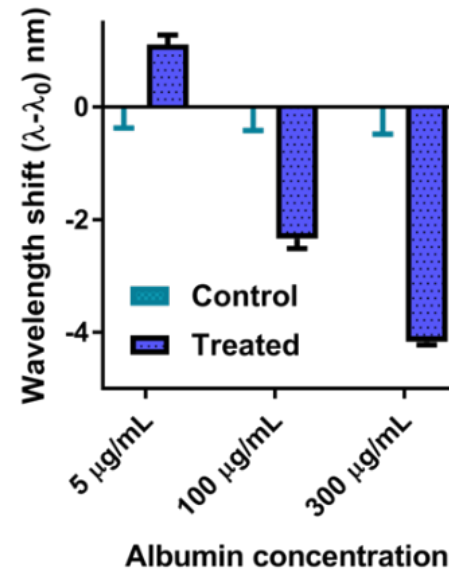
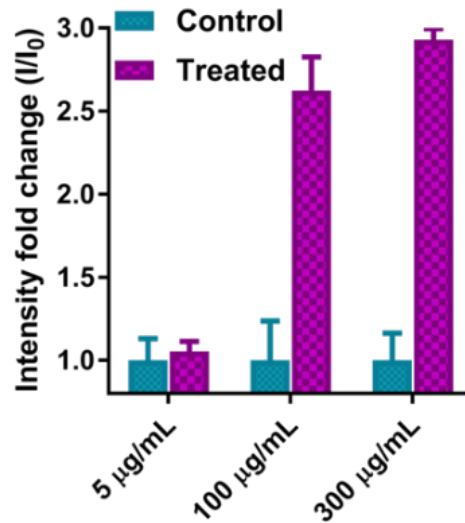
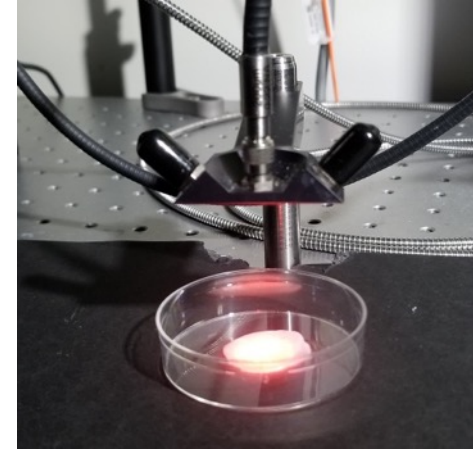
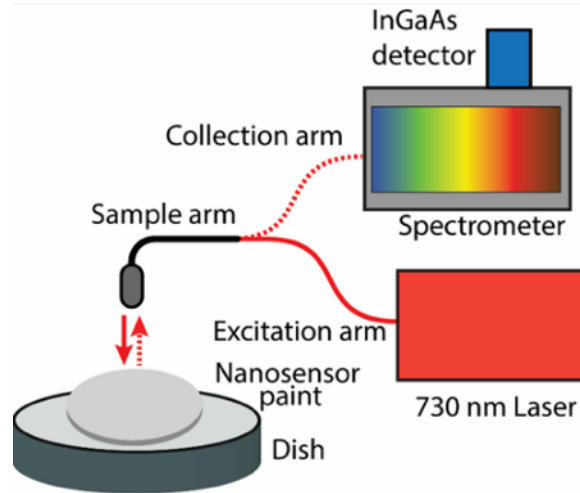
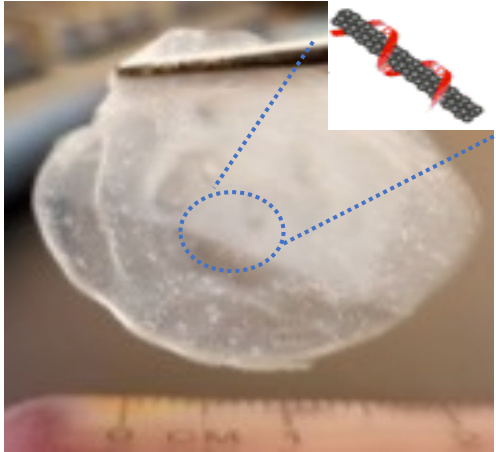
Nanosensor Paint



Applied on glass surface

Free-standing film

Nanosensor Paint for Microalbuminuria

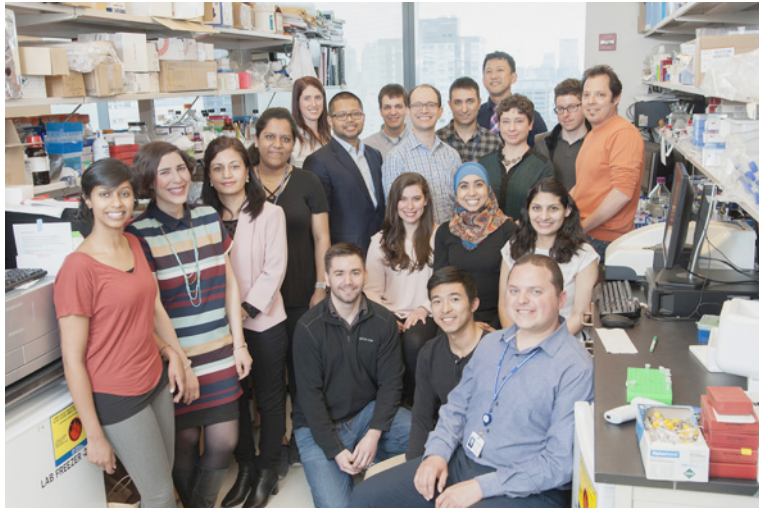




Acknowledgements



Memorial Sloan Kettering
Cancer Center™



Cancer Nanomedicine Lab

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Metastasis and Tumor Ecosystems Center,
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Collaborators

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Anand Jagota

Yoona Yang

Jeetain Mittal

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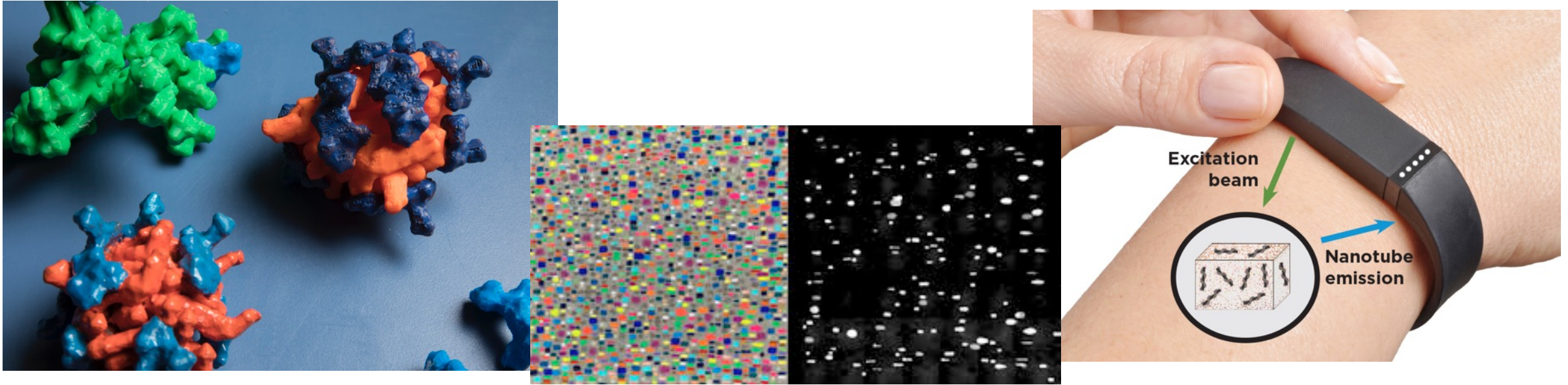
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Thank You



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 **@HellerLab**

@ Nanocarbons

Shamay, et al. *Sci Transl Med*, 2016

Mizrachi, et al., *Nat Comms*, 2017

Shamay, et al., *Nat Mater*, 2018

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Williams, et al., *Sci Adv*, 2018

Galassi, et al., *Sci Transl Med*, 2018

Budhathoki-Uprety, et al., *Nat Commun*, 2019