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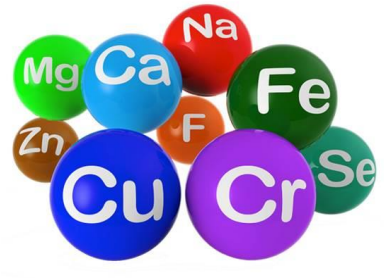

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#11 SERIES

Chemistry of Life: Instantly Treating Wounds with Hemostatic Gel

Joe Landolina shares progress being made with hemostatic gel that can stop the bleeding in seconds.

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National Nanotechnology Day: October 9, 2016

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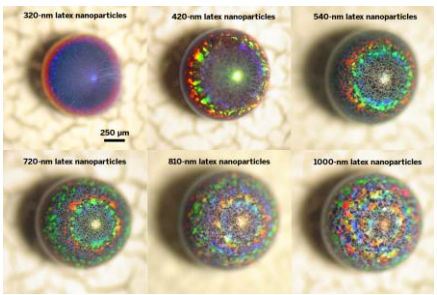

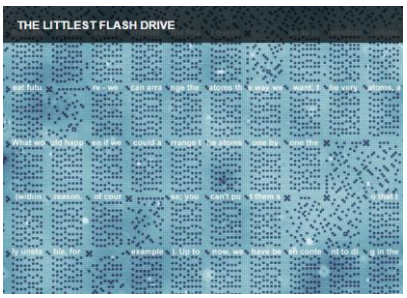

A joint project of the National Nanotechnology Coordinating Office and scientific societies, **National Nanotechnology Day** features a series of community-led events and activities on or around Oct. 9 to help to raise awareness of nanotechnology, how it is currently used in products that enrich our daily lives and the challenges and opportunities it holds for the future. The date pays homage to the nanometer scale, 10-9 meters!

www.acs.org/nano

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Upcoming ACS Webinars
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SPECIAL BROADCAST: Tuesday, October 11, 2016 @ 7pm ET

The Chemists' Code for Success: 3 Essential Skill Sets for Your Career

Patricia Simpson, Owner/Consultant, Game Changing Etiquette and Director of Academic Advising and Career Services, University of Illinois

Amanda Yarnell, Managing editor, editorial, *Chemical & Engineering News*

Thursday, October 13, 2016

Failure: Why Science Is So Successful

Stuart Firestein, Professor of Neurobiology, Columbia University

Darren Griffin, Professor of Genetics, University of Kent

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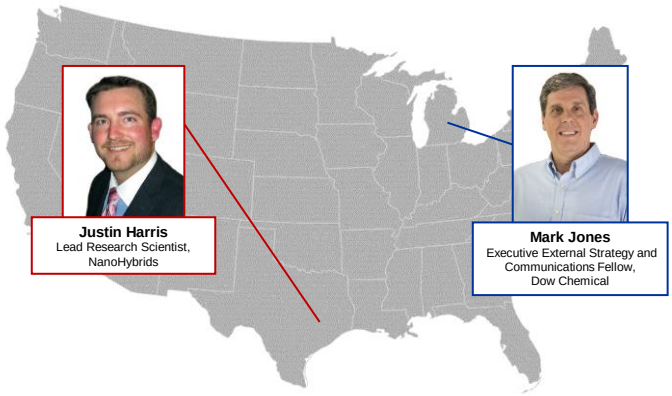
"Treating Cancer with Nanoparticles Powered by the Sound of Light"



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#10 SERIES

Chemistry of Life:

Treating Cancer with Nanoparticles Powered by the Sound of Light

Dr. Justin Harris – NanoHybrids Inc.



Photoacoustic Theranostics

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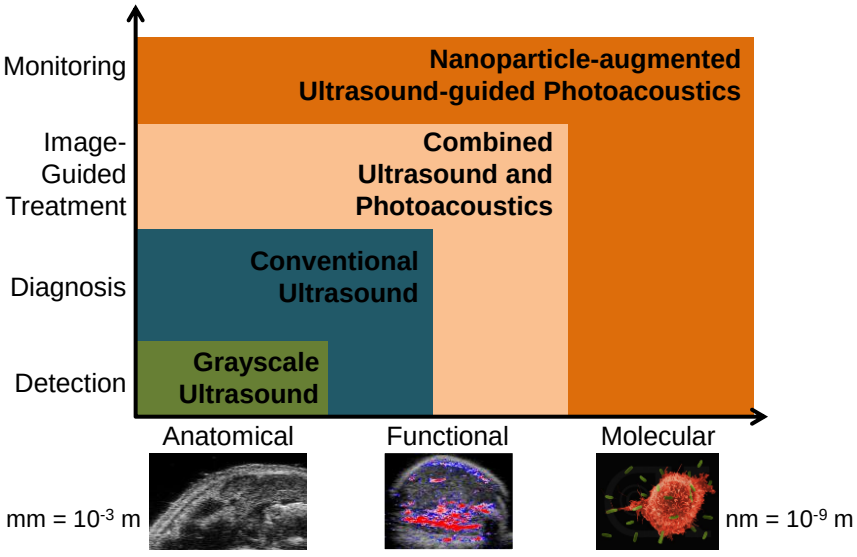

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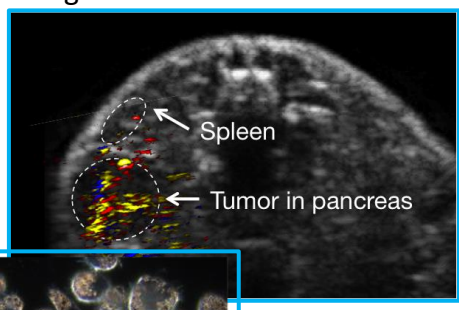
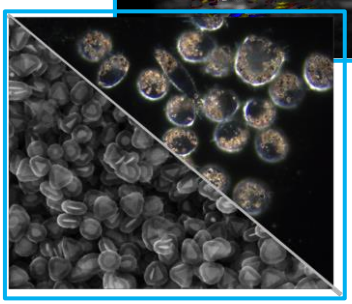
Agenda

- Photoacoustic imaging: an overview
- Generating contrast: endogenous vs exogenous
- Nanoparticle contrast agents
- EPR effect and imaging
- Molecular targeting and imaging
- Theranostics
  - Photothermal therapy
  - Drug delivery and sensing
  - Laser-triggered drug release
- Path to the Clinic





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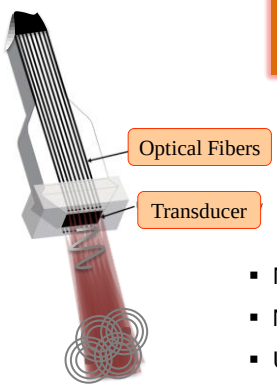
Photoacoustic Imaging

Photoacoustic signal is generated from agents with high optical absorption cross sections



Photoacoustic Effect

- Nanosecond pulses of laser light irradiate tissue
- Nanoparticles absorb light and thermoelastically expand
- Ultrasonic acoustic waves are produced

Image Source: Homan et al, "Combined Photoacoustic and Ultrasound Imaging of Metal Nanoparticles In Vivo," in Nanoimaging, Pan Stanford Publishing, Singapore (2010).

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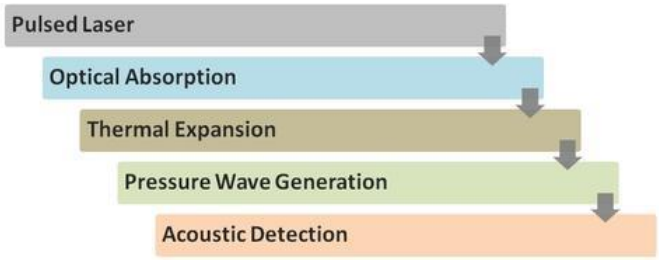
Photoacoustic Imaging

$$P(\lambda) \propto \Gamma F \mu_a(\lambda)$$

P = the received pressure
λ = optical wavelength
Γ = The Grüneisen parameter which accounts for the thermal/mechanical properties of the medium
F = light fluence (energy per cross-sectional area)
μ_a = net optical absorption



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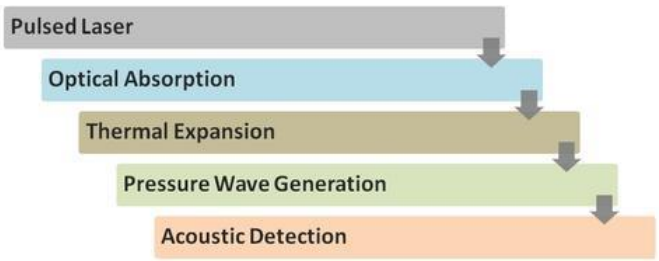
Photoacoustic Imaging

- No harmful ionizing radiation
- Sub-millimeter structure image resolution with high penetration depth
- Near real-time imaging capability
- Excellent contrast agents and molecular targeting at imaging depth
- Requires only modest floor-space and offers ultra-mobile units for point of care use
- Greater convenience at lower cost



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Audience Survey Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

What is the best light for maximum penetration and photoacoustic imaging resolution?

- Ultraviolet
- Visible
- Near-Infrared
- Infrared

Endogenous vs Exogenous

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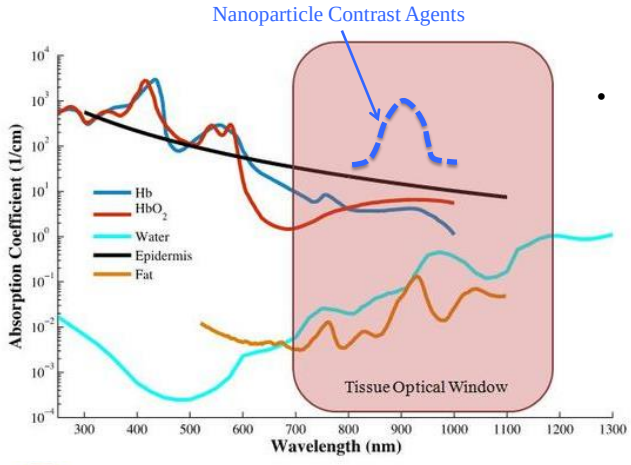


- "Tissue Optical Window"
  - Minimum absorption and scattering by tissue
  - Enables deeper penetration of light
  - Perfect zone to tune nanoparticle contrast agents!

Homan et al., "Prospects of molecular photoacoustic imaging at 1064 nm wavelength," Opt Lett 35(15), 2663-2665 (2010)

Absorption Modes

Molecular Absorption

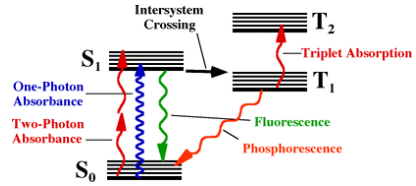
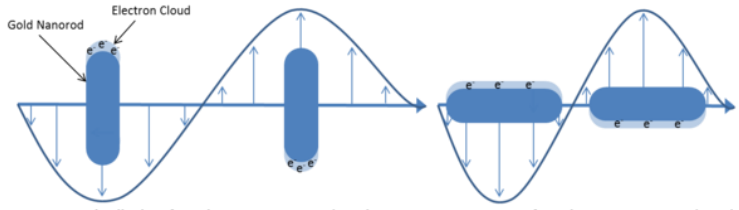


Image Source: Dr. Van Duyne (Northwestern University)

Surface Plasmon Resonance



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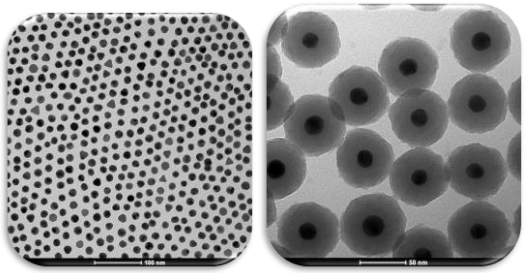
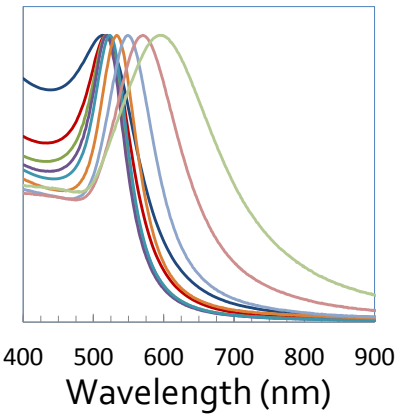
Plasmonic Nanoparticles

Gold NanoSpheres

- Diameter from 5 – 150 nm
- Tunable peak absorption
- 510 – 650 nm





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Tuning in the NIR

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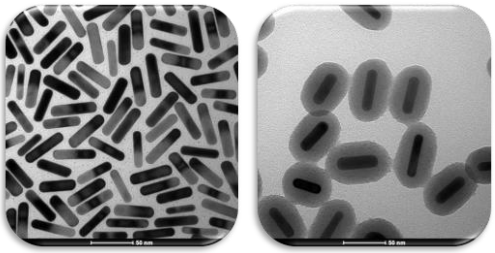
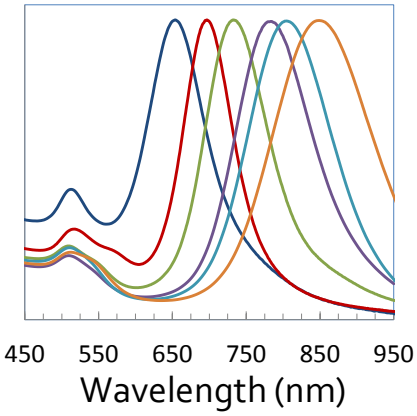
Gold NanoRods

- Aspect ratio adjusts λ
- 2 SPR modes
- Silica-coating stabilizes
- 600 – 1400 nm





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USPA Imaging

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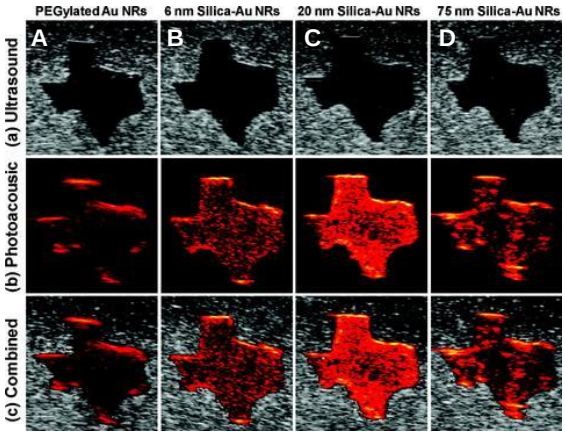
Combined Ultrasound and Photoacoustic (USPA) Imaging



Y. S. Chen, W. Frey, S. Kim, P. Kruizinga, K. Homan and S. Emelianov, "Silica-coated gold nanorods as photoacoustic signal nanoamplifiers," Nano Lett 11(2), 348-354 (2011)

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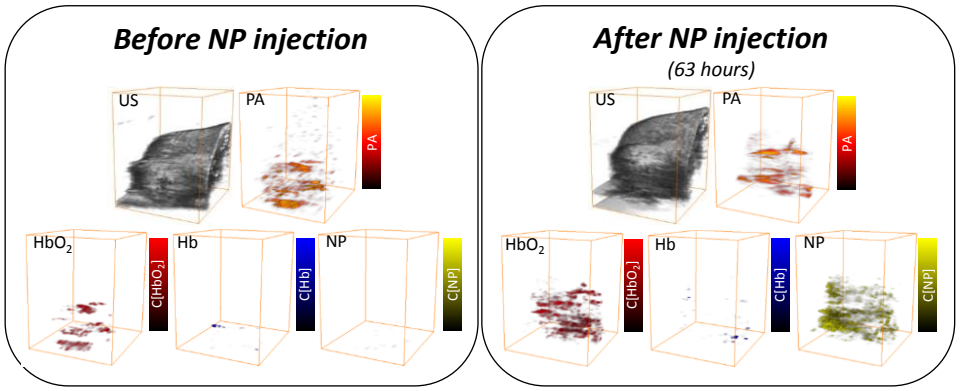
Exogenous Contrast via EPR



Nanoparticles accumulate via enhanced permeability and retention (EPR) effect in tumors

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Molecular Imaging with USPA

Molecularly specific nanoparticle probes

Multimodal imaging technique

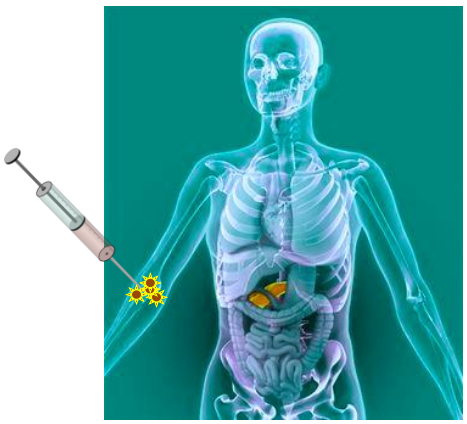

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Image: http://www.buzzle.com/articles/pancreatic-cancer-stages.html

Audience Survey Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

What is necessary to achieve molecular specificity for virtual histology with USPA imaging?

- Conjugate PEG to particle surface
- Utilize EPR effect
- Conjugate biospecific molecules to particle surface
- Nanobots

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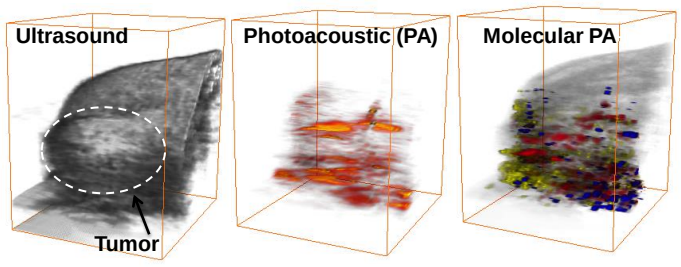
Virtual Histology

- Future of photoacoustics:
  - Molecular profiling in vivo using contrast agents
  - Longitudinal animal studies
    - Monitoring molecular responses to therapy
    - Decreasing animal sacrifice
    - Limiting the need for histology



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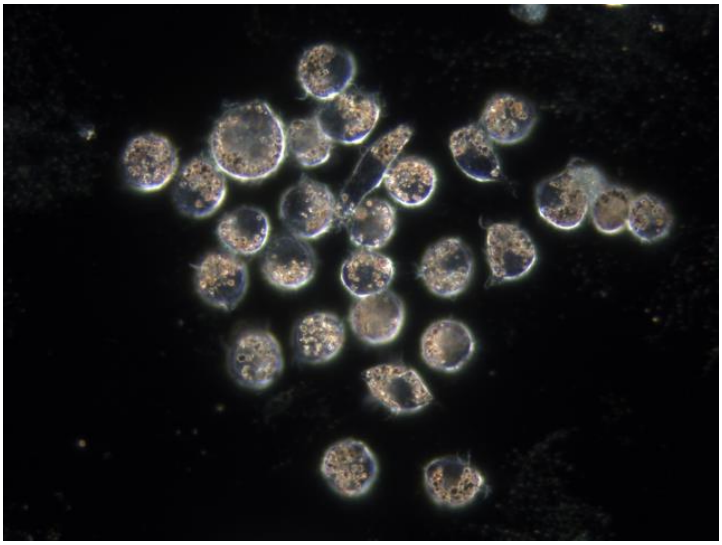
Molecular Targeting



Darkfield Microscopy of J774A.1 cells after 24 hour incubation with Ag nanoplates. Imaging is 10 hour time lapse, 6 images/hour, video at 2 fps

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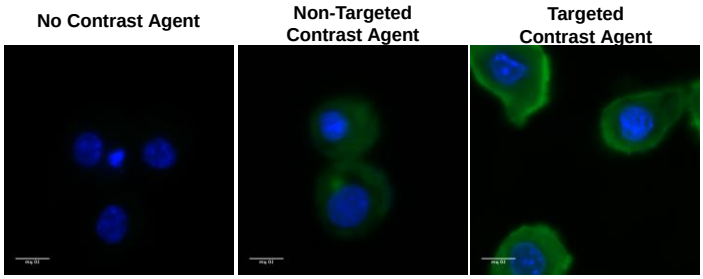
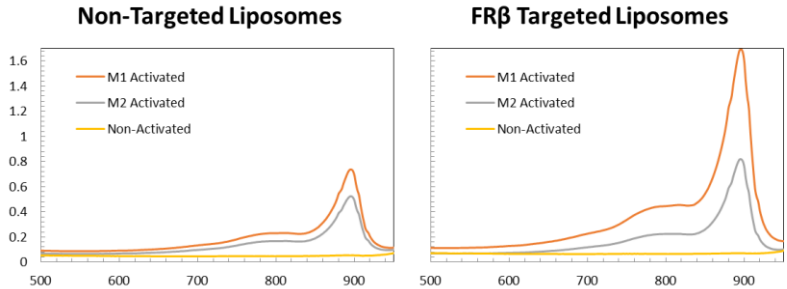
Molecular Targeting





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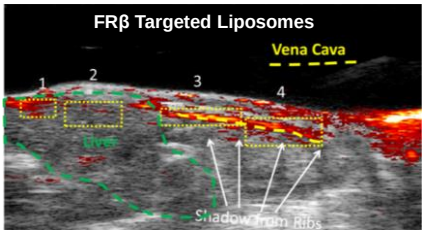
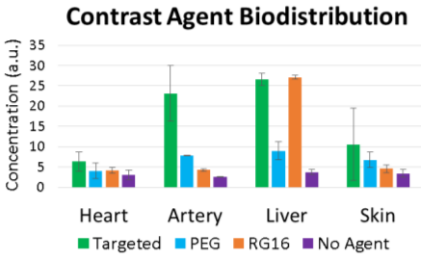
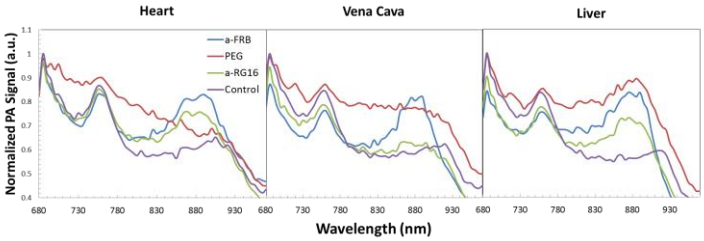
In Vivo Studies

Delivered anti-FRβ functionalized ICG-loaded liposomes systemically *in vivo* to apoE-deficient mouse models of atherosclerosis







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Theranostic Nanoparticles

Theranostics = Therapy + Diagnostics

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Photothermal Therapy (PTT)

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PTT is non-invasive, focal, and precise

- PTT provides selective destruction of cancer cells via hyperthermia
- How it works:
  - Cancer targeted nanorods are injected systemically and accumulate in the tumor
  - The nanorods bind preferentially to cancer cells
  - Irradiation with near-infrared light causes selective heating of the nanorods, inducing cancer cell death

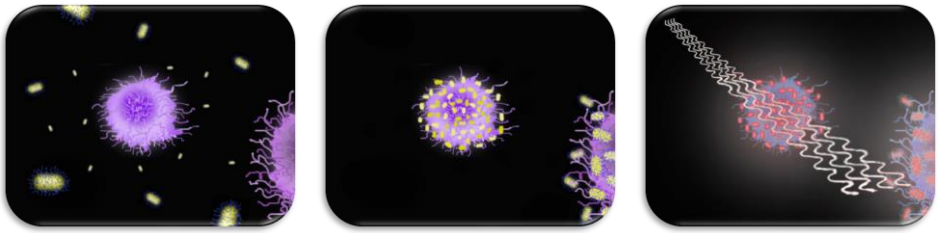

Image Credit: Yun-Sheng Chen

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Audience Survey Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT

What temperature is required to achieve cell death via hyperthermia?

- 35°C
- 40°C
- 50°C
- 60°C

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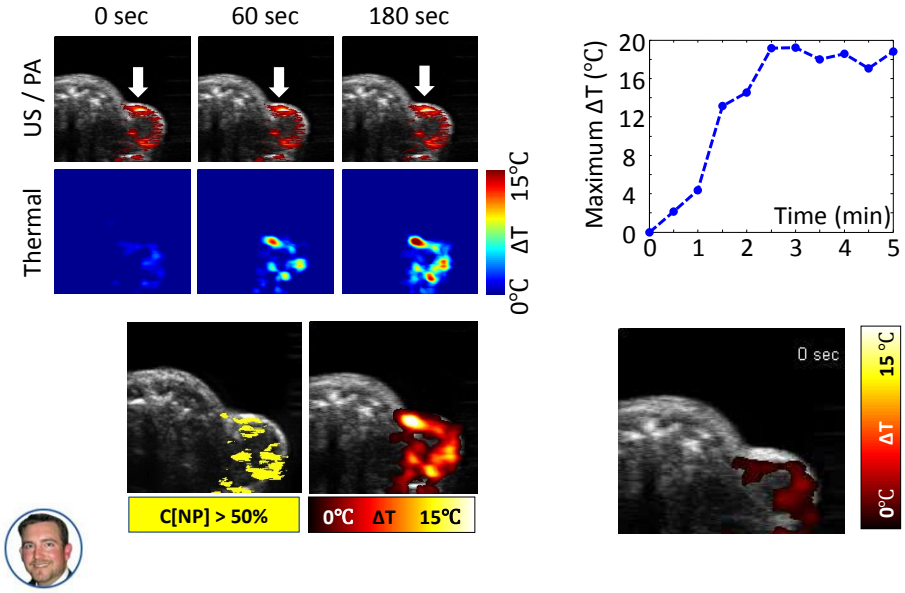
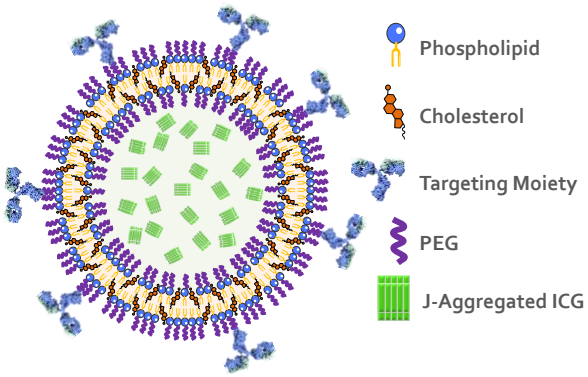
Photothermal Therapy (PTT)



USPA Guided Drug Delivery

Lipo-ICG

Liposomal encapsulation of ICG J-aggregates for use as a biological sensor and imaging agent.



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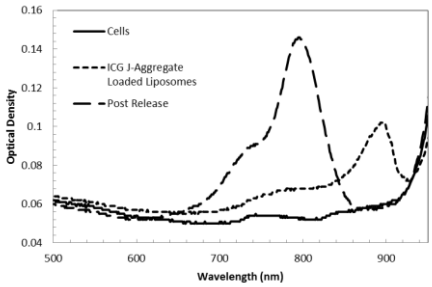
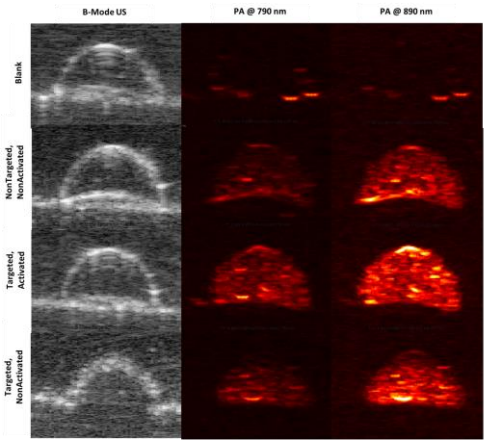
Sensor Capabilities

- Spectral shifts present upon uptake
  - Shift due to breakdown of J-aggregates
  - Observed in vitro via UV-Vis and PA imaging
  - USPA guided drug delivery!





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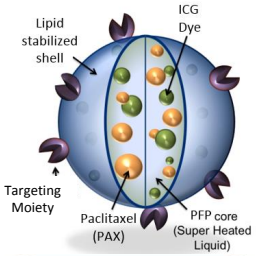
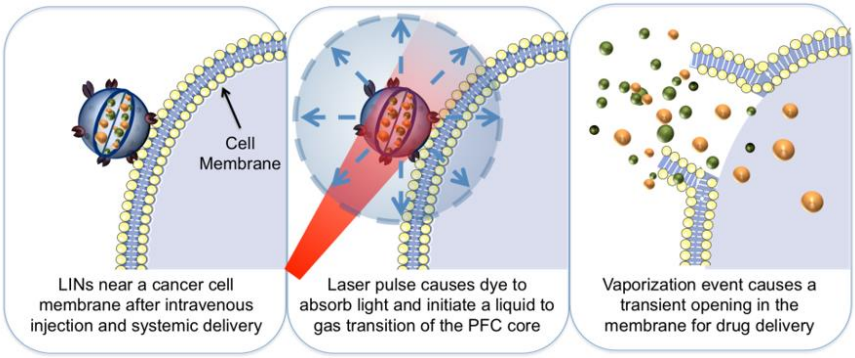
Triggered Drug Release

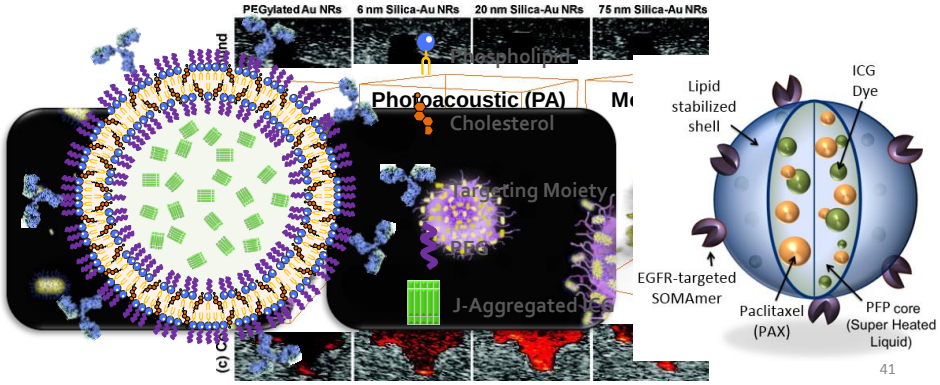
Laser-Initiated NanoSyringe (LINS)





Summary

- Photoacoustic imaging improves characterization of disease
- Contrast agents greatly aid in visualization
- Biofunctionalization enables molecular imaging and virtual histology
- Theranostic therapies combine therapy with diagnostics
- Novel particle design can enable targeted therapy



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Bringing Benchtop Science to the Clinic



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Patents and References

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- Yeager, D., Emelianov, S., *et al.* Intravascular photoacoustic imaging of exogenously labeled atherosclerotic plaque through luminal blood. *Journal of biomedical optics* **17**, 106016-106016 (2012).
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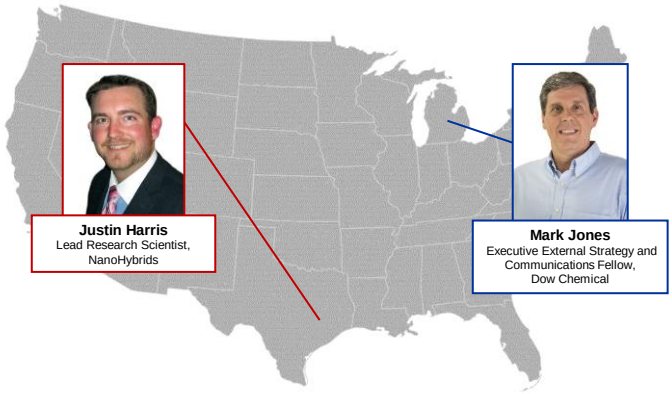
"Treating Cancer with Nanoparticles Powered by the Sound of Light"



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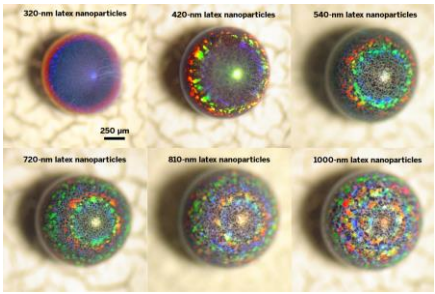
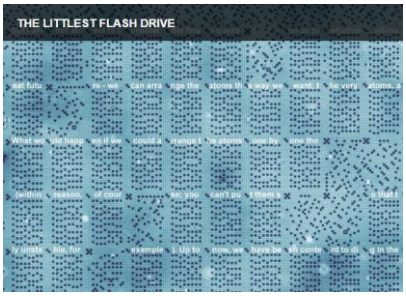
National Nanotechnology Day: October 9, 2016





A joint project of the National Nanotechnology Coordinating Office and scientific societies, **National Nanotechnology Day** features a series of community-led events and activities on or around Oct. 9 to help to raise awareness of nanotechnology, how it is currently used in products that enrich our daily lives and the challenges and opportunities it holds for the future. The date pays homage to the nanometer scale, 10-9 meters!

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Amanda Yarnell, Managing editor, editorial, *Chemical & Engineering News*

Thursday, October 13, 2016

Failure: Why Science Is So Successful

Stuart Firestein, Professor of Neurobiology, Columbia University

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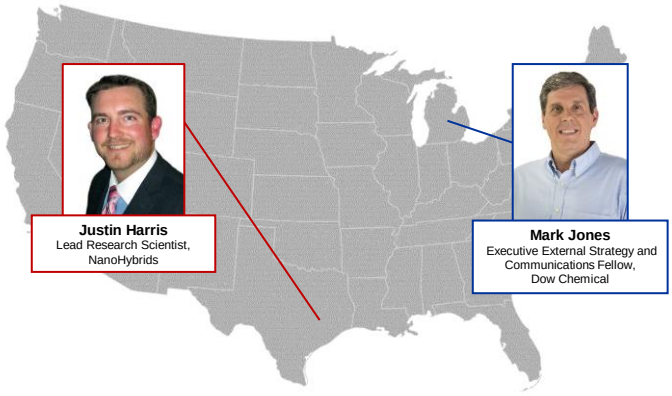

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