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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.

Experts
Joe Landolina
Cresilon
Mark Jones
Dow Chemical

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October 9, 2016

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

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Darren Griffin, Professor of Genetics, University of Kent

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**2016 Material Science Series**

“Treating Cancer with Nanoparticles Powered by the Sound of Light”

Justin Harris
Lead Research Scientist, NanoHybrids

Mark Jones
Executive External Strategy and Communications Fellow, Dow Chemical

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Chemistry of Life:
Treating Cancer with Nanoparticles Powered by the Sound of Light

Dr. Justin Harris – NanoHybrids Inc.

Photoacoustic Theranostics
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

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

Photoacoustic Imaging

\[ P(\lambda) \propto \Gamma F \mu_a(\lambda) \]

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

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

- Ultraviolet
- Visible
- Near-Infrared
- Infrared

Endogenous vs Exogenous

“Tissue Optical Window”

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

Absorption Modes

Molecular Absorption

Image Source: Dr. van Duyne (Northwestern University)

Surface Plasmon Resonance

Plasmonic Nanoparticles

Gold NanoSpheres

– Diameter from 5 – 150 nm
– Tunable peak absorption
– 510 – 650 nm
Tuning in the NIR

**Gold NanoRods**

- Aspect ratio adjusts $\lambda$
- 2 SPR modes
- Silica-coating stabilizes
- 600 – 1400 nm

![](image1)

USPA Imaging

Combined Ultrasound and Photoacoustic (USPA) Imaging

![Image of USPA Imaging](image2)

Exogenous Contrast via EPR

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

Molecular Imaging with USPA

Molecularly specific nanoparticle probes + Multimodal imaging technique

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

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

Molecular Targeting

No Contrast Agent | Non-Targeted Contrast Agent | Targeted Contrast Agent

Non-Targeted Liposomes | FRβ Targeted Liposomes

M1 Activated | M2 Activated | Non-Activated

M1 Activated | M2 Activated | Non-Activated
In Vivo Studies

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

Theranostic Nanoparticles

Theranostics = Therapy + Diagnostics
Photothermal Therapy (PTT)

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](image.png)

** 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
Photothermal Therapy (PTT)

0 sec 60 sec 180 sec

US / PA
Thermal

C[NP] > 50%
0°C ΔT 15°C

Maximum ΔT (°C)
Time (min)

0 1 2 3 4 5

0°C 10°C 20°C

US / PA Guided Drug Delivery

Lipo-ICG

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

Phospholipid
Cholesterol
Targeting Moiety
PEG
J-Aggregated ICG
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!

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
Patents and References

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