Nanotechnology in Cancer Diagnosis and Therapy

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MACRO

PERSON (~6ft tall)  
2 billion nm

APPLE (~8cm)  
80 million nm

ANT (~5mm)  
5 million nm

MICRO

diameter of a HUMAN HAIR  
75,000 nm

smallest the EYE CAN SEE  
10,000 nm

e. coli  
BACTERIA  
2,000 nm

NANO

BUCKYBALL  
1 nm

DNA  
2 nm

diameter of a CARBON NANOTUBE  
1.3 nm
Nanotechnology Cancer Research

- Improved cancer diagnosis
  - Imaging
  - Blood and tumor-specific tests
- Tissue engineering
- Drug and biologic agent delivery
- Nanoparticles as therapeutic agents
Cancer Diagnosis

Carbon nanotubes with Gadolinium
Gold-SPIO nanoshells for MR visibility

Direct injection of 1cc Au-SPIO into mouse xenograft

FCSI T2* (∆T2* = 11.7 ± 3.0 ms) FCSI MRTI

FCSI can potentially be used to more effectively guide emerging therapies, such as light activated nanoshells. Here, in addition to temperature monitoring, the T2* can be related to concentration of nanoparticles and used for treatment planning.
Cancer Diagnosis
Cancer Diagnosis

Quantum
Cancer Diagnosis
Cancer Diagnosis
Tissue Bioengineering

Design of Engineered Biologics

Nano-chemistry, structure, and mechanics of the biologically derived material can be designed per complex patient-specific clinical need, architecture, and design.

Endothelial Cell Anchored to Engineered Biologic

Nano-fiber diameter: 97.2±2.7 nm

In Vivo Regeneration of Tissues

Regeneration of Critical–Sized Bone via Engineered Biologics in an in vivo sheep model similar to the clinically used bone graft by 84 days. (Rios et al 2009)

Regeneration of Critical–Sized Abdominal Wall Musculofascia via Engineered Biologics in an in vivo guinea pig model results in similar gross appearance as the Normal Native Abdominal Wall after 4 weeks. (Gobin, Butler, Mathur 2006)
Drug and Biologic Agent Delivery
Drug and Biologic Agent Delivery
Drug and Biologic Agent Delivery

Carbon

Gold
Nanoparticles in Clinical Trials

• 30 nm Au nanoparticles for drug delivery/reduction of toxicity- TNF arrayed on surface, phase I
• 150 nm Au nanoshells, non-targeted delivery- near infrared laser stimulation (plasmon resonance) to treat oropharyngeal cancer, phase I
• Nanoparticles in Cancer Therapy
Tunable gold nanoshells for photothermal therapy

- Extinction (Arb. Units)
- Wavelength (nm)
- Gold Colloid 20 nm 10 nm 7 nm 5 nm
- Absorption Coefficient
- Tissue Optical Window
- Whole Blood
- Epidermis
- 75% Water
- TEM of nanoshells

Mouse: Balb/c with CT26 xenograft
Laser: 808 nm, 3 min. @ 4W/cm²
Passive extravasation of gold nanoshells

Gold-silica shell (150 nm)

NIR LASER (0.6 W/cm² for 20 min at 808-nm)
History: Thermal Cancer Therapy

- Hot oil treatment of tumors described in 5000 year old Egyptian papyrus
- Tumor “cautery” used for numerous cancer types over past 400 years
- Electrocautery destruction of superficial and endothelial malignancies over past 120 years
- More recently, cryoablation, laser photocoagulation, radiofrequency ablation, and microwave coagulation
Cancer Cautery
Radiofrequency Ablation

- New treatment first pioneered at M.D. Anderson beginning in 1995: based on our clinical research RFA was approved by the FDA in 2001
- Radiofrequency ablation (RFA) is a thermal (heat) treatment technique which produces localized tumor destruction
- RFA kills cancer cells around the needle placed directly into the tumor
Radiofrequency Ablation
Status in 2010

• Can treat cancers in the:
  - liver
  - kidneys
  - lungs
  - prostate
  - bone
  - breast

• Problems with current types of RFA:
  Can only treat a few tumors
  Invasive
  Damages normal tissue
  Incomplete killing of cancer cells
External RF Treatment

• The idea: Non-invasive, no needles placed into tumors

• Could be used to treat many kinds of cancer: liver, lung, prostate, kidney, thyroid, lymphoma, brain, melanoma, sarcoma, adrenal, bone, etc.

• Collaboration between the M.D. Anderson Cancer Center and Rice University
Noninvasive Radiofrequency (RF) Field Generator
SWNTs are 1 nm in diameter, 50-1000 nm long
RF-induced heating of soluble SWNTs
RF-induced heating of soluble SWNTs
Gold Nanoparticles (GNPs)

- 5 nm in diameter
- Excellent metallic conductor
- Known to be nontoxic to mammalian cells
- Gold is already FDA-approved in humans
- Possible to modify and add chemical side groups that may be used to target cancer cells
Heating rates of Au nanoparticles in a 13.56 MHz RF Field
Heating rates of Au nanoparticles in a 13.56 MHz RF Field

![Graph showing heating rates of Au nanoparticles in a 13.56 MHz RF Field](image-url)
Human Cancer Cell Lines

- Hepatocellular cancer: Hep3B and HepG2
- Pancreatic adenocarcinoma: Panc-1 and L3.6
- Colorectal adenocarcinoma: HT-29 and SW-620
Cell Proliferation Data

MTT - Gold Nanoparticles

<table>
<thead>
<tr>
<th>GNP concentration</th>
<th>Absorbance @ 570 nm</th>
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<tr>
<td>DMEM</td>
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<tr>
<td>1uM</td>
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<tr>
<td>10uM</td>
<td>L3.6</td>
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<td>67 uM</td>
<td>PANC-1</td>
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<td>Hep3B</td>
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<tr>
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<td>HepG2</td>
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SWNT or GNP Containing Cell Culture - RF Exposure

- SWNTs or GNPs added 24 hours prior to RF exposure
- Other cell cultures were treated with media alone
- Parameters:
  - 13.56 MHz
  - spacing 10 cm
  - continuous RF field
  - variable exposure time
- Cells returned to incubator for 24 hours
- PI FACS to assess cell viability
Shortwave RF Field Generator

- Totally noninvasive
- No wires or capacitor plates required for sample
SWNT Dose-Related Cytotoxicity With RF Field Treatment

Hep 3B cells
Hep G2 cells
Panc-1 cells
Human Pancreatic Cancer Cell Line with GNPs

RF

No RF
RF and SWNTs in vivo

- NZW rabbits bearing 1-1.5 cm hepatic VX2 tumors
- Tumors directly injected with 1.0 ml of functionalized SWNTs or with control solutions (no SWNTs)
- Animal treated with external RF 400W for 2 minutes
- Tissue temperatures were monitored during the RF treatment
- Tumors harvested 48 hours later
RF and SWNTs in vivo

- During RF, thermistors adjacent to tumor showed temperature increase.
- Thermistor in liver 2 cm away showed no temperature increase.
- Tumors injected with functionalized SWNTs were necrotic at 48 hours by H&E and NADH staining.
- Tumors injected with control solutions were completely viable.
Near Infrared Microscopy

Multiple SWNTs in Rabbit Liver
VX2 controls, RF no SWNTs

Tumor cells all viable after 2 min. RF
VX2 tumor treated with SWNTs

No viable cancer cells, all inflammatory cells (PMNs, etc.)
Targeted Gold Nanoparticles
Western Blot for EGFR

- PANC-1
- SN12PM6
- DiFi
- CAMA-1
- AsPC-1

**EGFR**
- 170 kDa
- 55 kDa
- 40 kDa

**β-Actin**
The So What Questions

• Are there long-term toxicities associated with nanoparticles?
• Can we reliably attach cancer-targeting molecules to the nanoparticles?
• Can we specifically target a variety of different cancer types, in a variety of individual patients?
• Will nanotechnology approve our ability to diagnose and treat cancer patients?
Thank You!