Nanotechnology and Novel Cancer Therapies
View from the NCI Alliance for Nanotechnology in Cancer

Washington, DC, Nov 5

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Office of Cancer Nanotechnology Research, NCI
In the U.S., Cancer Continues to Represent an Enormous Burden

- **576,691** Americans died of cancer in 2011 (**589,430** projected for 2015)
- **1,658,370** Americans will be newly diagnosed with cancer in 2015 (projected)
- **$157 billion** in 2010 for cancer healthcare costs (**$173 billion** projected in 2020)

Unlike Other Major Disease Killers, Cancer Continues to Take Nearly the Same Toll as it did in 1950

![Death Rates Per 100,000 Americans](chart)

<table>
<thead>
<tr>
<th>Disease</th>
<th>1950</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Diseases</td>
<td>169.8</td>
<td>163.2</td>
</tr>
<tr>
<td>Cerebrovascular Diseases</td>
<td>180.7</td>
<td>36.2</td>
</tr>
<tr>
<td>Pneumonia/Influenza</td>
<td>586.8</td>
<td>48.1</td>
</tr>
<tr>
<td>Cancer</td>
<td>193.9</td>
<td>15.9</td>
</tr>
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</table>
Combine power of innovation in nano-materials and cancer biology to develop new solutions in cancer

Detect Disease *Before* Health Has Deteriorated
- Sensors
- Imaging

Deliver Therapeutics
- Local delivery
- Improved efficacy
- Post-therapy monitoring

Develop Research Tools to Enhance Understanding of the Disease
Nanoparticles in Medicine

How Long Does it Take for a New Field to Yield Clinically Approved Interventions?

It took ~20 years for monoclonal antibody therapies to move from the lab to the clinic – majority of FDA approvals occurred after year 2000.

How much time does nanotechnology need?
Multifunctional Nanoparticle Delivery Vehicles


CCR 20th Anniversary Commentary: Prospects and Challenges of Therapeutic Nanoparticles in Cancer

Mohammad Aminur Rahman and Dong M. Shin
Cellular Uptake of Nanoparticles

Yameen, Farokhzad et al., J. Controlled Release (2014) 190, 485–499
Nano-therapy Strategies

Delivery of chemotherapeutics


Delivery of siRNA


Hyperthermia

Photothermal


RF-heated

A. Ito et al., J. of Bioscience and Bioeng. (2005 100: 1)
**Integrated Biobarc ode Microfluidic Chip**

**In vitro diagnostics and nanotechnology**

- Modular diagnostics – work with bodily fluids, such as blood, serum, urine, or saliva
- Multiplexing – interrogate several biomolecular signatures at the same time
- Techniques to monitor and capture circulating tumor cells from blood
- Multifunctional capabilities – one platform capable of detecting nucleic acid and protein

- IBBC - microfluidic device for multiplexed detection of proteins in whole blood sample
- DEAL - single-strain (ss) DNAs bound to antibodies that are labeled with complementary ssDNA oligomers
- Currently tested for molecular and functional analysis of prostate, breast, melanoma, and glioblastoma
- Less than 10 min working time

Multiplexed protein measurements of clinical patient sera, (a) Layout of the barcode array used in this study, (b) Representative fluorescence images of barcodes used to measure the cancer marker PSA and 11 cytokines from cancer patient serum samples. B - samples from breast cancer patients; P - samples from prostate cancer patients, (c) Distribution of estimated concentrations of PSA, TNF-α and IL-1β in all serum samples. The horizontal bars mark the mean values.
Monitor secretion of proteins from individual cells to assess effectiveness of therapies

Shin, et al., *ChemPhysChem* 2010 (molecular patterning for these chips)
Shin, et al., *Biophys J* 2011 (macrophage secretome, information theory)
Ma, et al., *Nature Medicine*, 2011 (applied to melanoma immunotherapy patients)
**Spherical Nucleic Acids (SNAs)**

- highly resistant to nuclease degradation
- enter a variety of cell types, including “hard-to-transfect” primary cells without the use of auxiliary reagents
- induce less activation of the innate immune response

Can attach other functional groups to oligonucleotides:
- dye molecules
- quenchers
- modified bases
- drugs

**Detection and regulation of mRNA expression**
- Anti-glioma therapeutics
- Scanometric detection of low level miRNAs

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Thaxton et al., *ACS Nano*, (2009)
Circulating Tumor- Shed Material: What is it?

- Circulating Tumor Cells (CTCs) discovered 1869
- Incredibly rare cells in blood (only 1 in every 1,000,000,000 normal cells on average)
- Passively and Actively (metastatic) shed from primary tumor site
- Hard to detect and capture
- Do carry genetic information about tumor-type and molecular sub-type
- CTCs are not only material from tumor in blood (ctDNA, etc.), but contain much information that is clinically relevant in one package
- Known to come from all solid tumor types
Liquid Biopsy: Circulating Tumor DNA

TCGA: Connecting Multiple Standardized Sources, Experiments, and Data Types

Three Cancers - Pilot

- glioblastoma multiforme (brain)
- squamous carcinoma (lung)
- serous cystadenocarcinoma (ovarian)

Multiple data types

- Clinical diagnosis
- Treatment history
- Histologic diagnosis
- Pathologic status
- Tissue anatomic site
- Surgical history
- Gene expression
- Chromosomal copy number
- Loss of heterozygosity
- Methylation patterns
- miRNA expression
- DNA sequence
A New Initiative on Precision Medicine
Francis S. Collins, M.D., Ph.D., and Harold Varmus, M.D.

“Tonight, I’m launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes — and to give all of us access to the personalized information we need to keep ourselves and our families healthier.”
— President Barack Obama, State of the Union Address, January 20, 2015

Focus Areas:
• NCI Clinical Trials to Advance Precision Medicine
• Overcoming Drug Resistance in Cancer Treatment
• Knowledge System to Support Precision Medicine

NCI Existing Efforts:
• Translational and Therapeutic Studies
• Genomics and Cancer Biology Research
• Immunology and Immunotherapy Research
• Cancer Imaging Research
NIH Nanotechnology Funding

Millions of Dollars

0 100 200 300 400 500

NNI begins
Translational Support

**Nanotechnology Characterization Laboratory (NCL)**
- Pre-clinical characterization of nanomedicines
- 3 way agreement of NCI, FDA, and NIST
- Supports extramural community
- Characterized over 300 nanoparticle submissions
- Assisted with characterization leading to 9 IND or IDE filings with FDA

**Translation of Nanotechnology in Cancer Consortium (TONIC)**
- Public–private partnership
- 16 industry members (e.g. Janssen, AstraZeneca, Onyx Pharma, Teva), 3 patient advocacy group members
- Discussion forum on promising nanotechnologies and strategies on their translation to clinic
  - Workshops
  - Showcasing of technologies
  - Joint, pre-competitive projects
Spin-off Companies Collaborating with NCI Alliance Investigators

**Diagnostics**
- Biomarker Assays
  - Affinity Biosensors
  - MagArray
  - MDxHealth
  - Nanogen
  - Nanolink
  - Nanosphere
  - Omnis
- Imaging Contrast Agents
  - Carestream
  - ImaginAb
  - Sophie Biosciences
  - Visual Sonics
- Multimodality Imaging
  - CellSight Technologies
  - Endra, Inc.
- Hardware and Optics
  - American BioOptics
  - Lumicell Diagnostics, Inc.
  - NanoSonix
  - Nine Point Medical
  - Xinfar Systems
  - Xintek
- Single Cell Analysis
  - Integrated Diagnostics
  - Nodality
  - PixelEXX Systems
- In Vitro Imaging
  - DiagNano
  - Vivonetics

**Therapeutics**
- Nanoparticles
  - Blend Therapeutics
  - BIND Biosciences
  - Cerulean Pharma
  - Coordination Therapeutics
  - Kala Pharmaceuticals
  - Leonardo Biosystems
  - Liquidia Technologies
  - Molecular Therapeutics
  - NanoMed Pharmaceuticals, Inc.
  - PreDx
  - Qualiber, Inc.
  - SignPath Pharmaceuticals
  - SoluBest
  - Valence Therapeutics
- Nanotheranostics
  - Kereos
  - Nanoparticle Biochem, Inc.
  - Nvigen
  - Pharocore
- Nucleic Acid
  - Alnylam Pharmaceuticals
  - Aurasense Therapeutics
  - B3 Biosciences
  - Bio-Path Holdings
  - Calando Pharmaceuticals
  - Kylin Therapeutics
- Immunotherapy
  - Aduro BioTech
  - CellDex Therapeutics
  - CytomX Therapeutics
  - Immune Design Corporation
  - Memgen
  - Selecta Biosciences
- Ablation
  - Consegna
  - Nanospectra Biosciences, Inc.

**Support**
- Implantable Devices
  - MicroCHIPS, Inc.
  - NanoMedical Systems
- Resistance/Barriers/Metastasis
  - Arrogene
  - Grzybowski Scientific Inventions
  - Nemucore Medical Innovations
- Antibodies and Proteomics
  - Adimab, Inc.
  - AM Biotechnologies
  - Applied Proteomics
- Incubators and Research Services
  - Arrowhead Research Corporation
  - Enlight Biosciences
  - Molecular Biomarkers
  - Regis Technologies
  - Tactic Pharma
- Materials
  - Calhoun Vision
  - Micromod
  - Ocean Nanotech, LLC
  - ProChimia Surfaces


NCI SBIR Awards: BIND Therapeutics, ImaginAb, Liquidia Technologies, MagArray, Nanoparticle Biochem, Nanospectra Biosciences, Nemucore, Ocean Nanotech, Qualiber Inc., Zymera
Office of Cancer Nanotechnology Research

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Natalie Abrams

Chris Hartshorn

Christina Liu

Consultants:
Subhas Malghan – FDA
Uma Prabhakar – formerly J&J

http://www.nano.cancer.gov/