



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

***Transformative Technology Support  
from the NCI:  
the Innovative Molecular Analysis  
Technologies (IMAT) Program***

**ASME NEMB 2013 Annual Meeting**

**Tony Dickherber, Ph.D.**

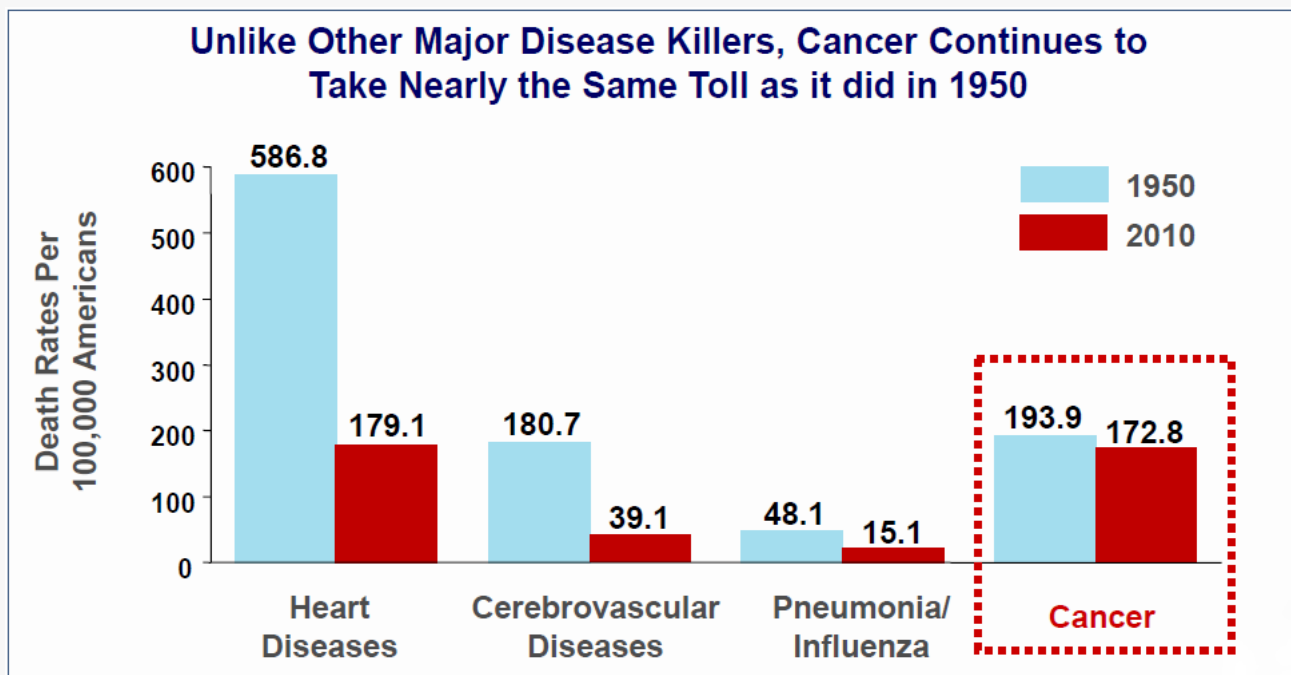
**Center for Strategic Scientific Initiatives  
National Cancer Institute**

# In the U.S., Cancer Continues to Represent an Enormous Burden



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

- **571,950** Americans died of cancer in 2011
- **1,638,910** Americans will be diagnosed with cancer this year
- **\$124.6B** in 2010 for cancer-related healthcare costs

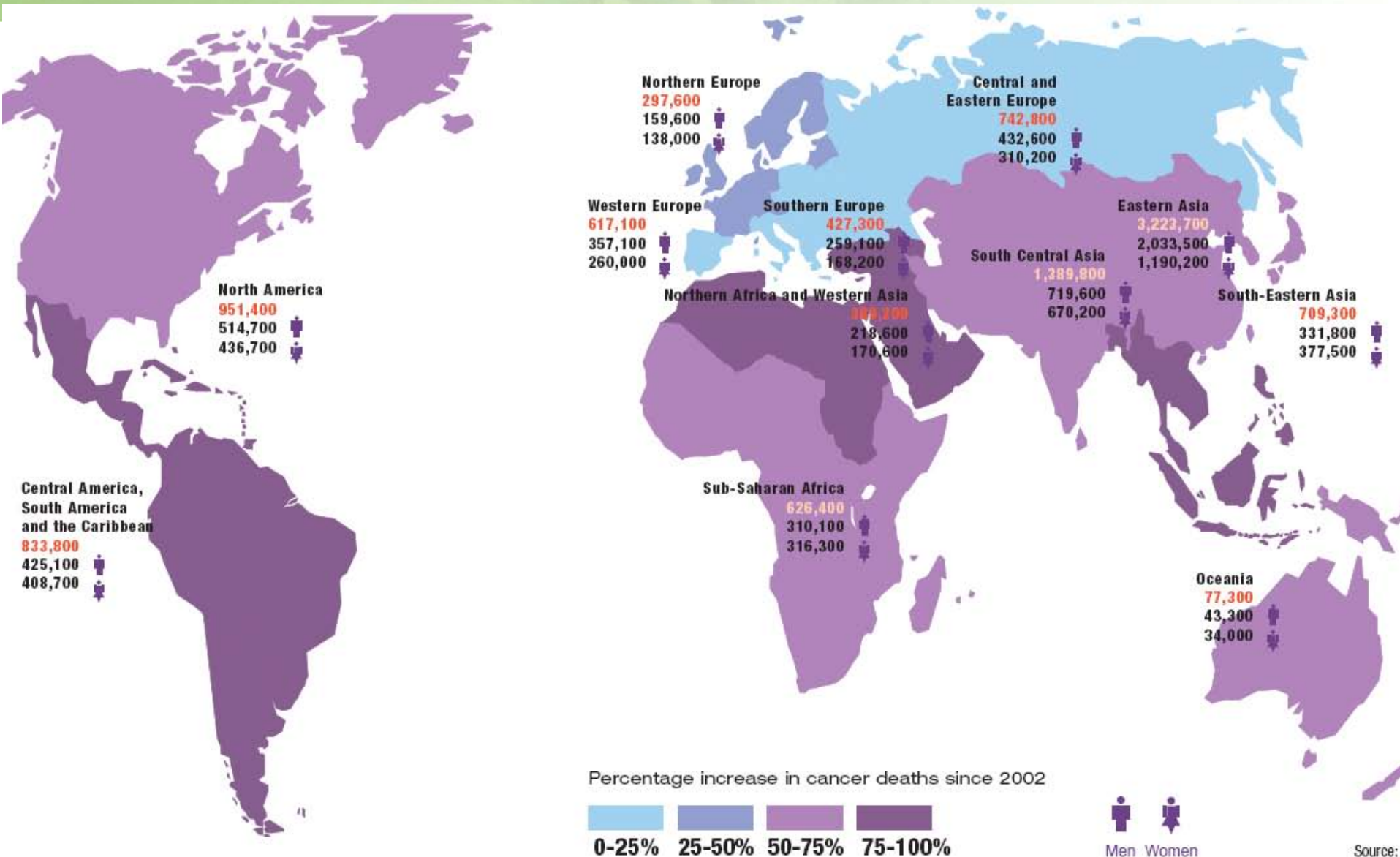


Source for 2011 deaths and diagnoses: American Cancer Society (ACS) 2011 Cancer Facts & Figures; Atlanta, GA  
Source for 2010 age-adjusted death rate: National Center for Health Statistics, NCHS Public-use file for 2010 deaths.

# Globally: By 2020, cancer mortality 10 M/yr (incidence 16 M/yr)



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

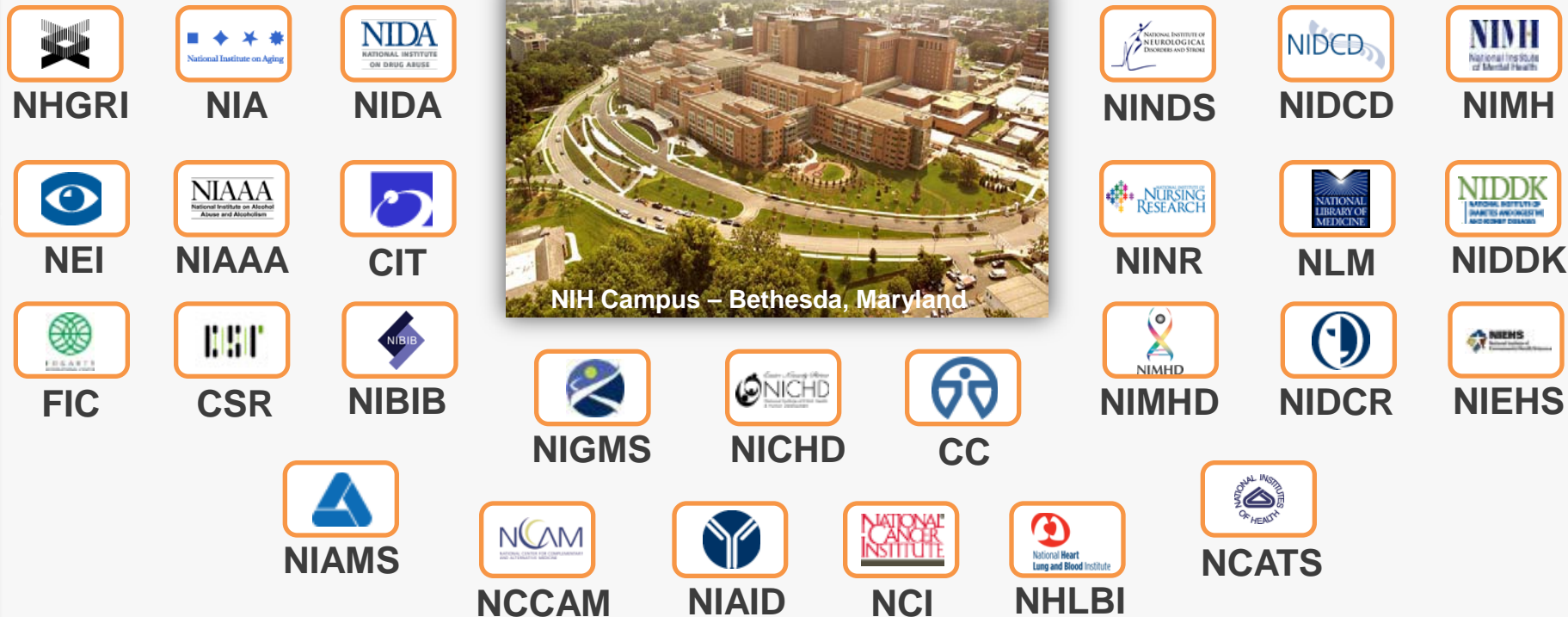


Source:

# National Institutes of Health (NIH): 27 Institutes and Centers



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES



**NIH Budget ~ \$30.63 Billion (FY11)**

- ~82% for extramural support
- ~64,000 grants and contracts

**NCI Budget ~ \$ 5.06 Billion (FY11)**

- ~ 76% for extramural support
- ~8,000 grants and contracts



# National Cancer Institute: Organization



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES



**Director**  
Harold Varmus, MD

**National Cancer Institute**

**\$5.07B**  
(FY12)



**Deputy Director**  
Douglas Lowy, MD

**Office of the  
Director**

**CSSI**

**CCG**

~\$190 M (~4%)

**Center for  
Cancer  
Research**

**Division of  
Cancer  
Epidemiology  
and Genetics**

**Division of  
Cancer  
Treatment and  
Diagnosis**

**Division of  
Cancer  
Biology**

**Division of  
Cancer Control  
and  
Population  
Sciences**

**Division of  
Cancer  
Prevention**

**Division of  
Extramural  
Activities**

**Conducting – Intramural**

**Funding – Extramural**

# NCI Center for Strategic Scientific Initiatives (CSSI): Concept Shop



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES



**Director**  
Douglas Lowy, MD



~\$190M (FY12)



**Deputy Director**  
Jerry S.H. Lee, PhD



**Office of Cancer Clinical  
Proteomics Research**

**Director**  
Henry Rodriguez, PhD, MBA



**Office of Physical Sciences-  
Oncology**

**Director**  
Larry A. Nagahara, PhD



**Office of Cancer Nanotechnology  
Research**

**Director**  
Piotr Grodzinski, PhD

**Office of Cancer Genomics**

**Director**  
Daniela S. Gerhard, PhD



**The Cancer Genome Atlas  
Program Office**

**Director**  
Kenna M. Shaw, PhD



# NCI Center for Strategic Scientific Initiatives (CSSI): Concept Shop



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES



**Director**  
Douglas Lowy, MD



~\$190M (FY12)



**Deputy Director**  
Jerry S.H. Lee, PhD

## Mission

“...to create and uniquely implement exploratory programs focused on the development and integration of advanced technologies, trans-disciplinary approaches, infrastructures, and standards, to accelerate the creation and broad deployment of data, knowledge, and tools to empower the entire cancer research continuum in better understanding and leveraging knowledge of the cancer biology space for patient benefit...”



2003, 2007, 2011



2005, 2010



2008



2011



2004, 2008



2005, 2008



2010

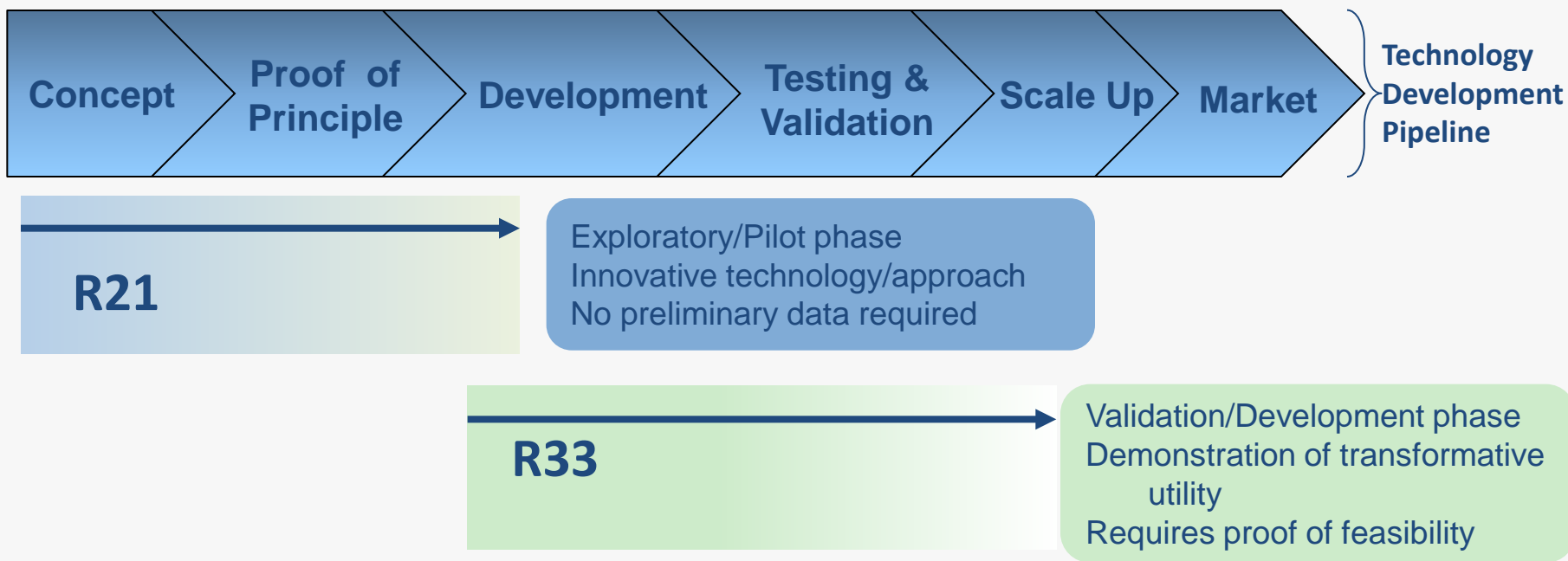
# Innovative Molecular Analysis Technologies (IMAT) Program



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

## Program Mission:

*To support the development, maturation, and dissemination of novel and potentially transformative next-generation technologies through an approach of balanced but targeted innovation in support of clinical, laboratory, or epidemiological research on cancer.*





# Diversity of IMAT-supported technologies



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

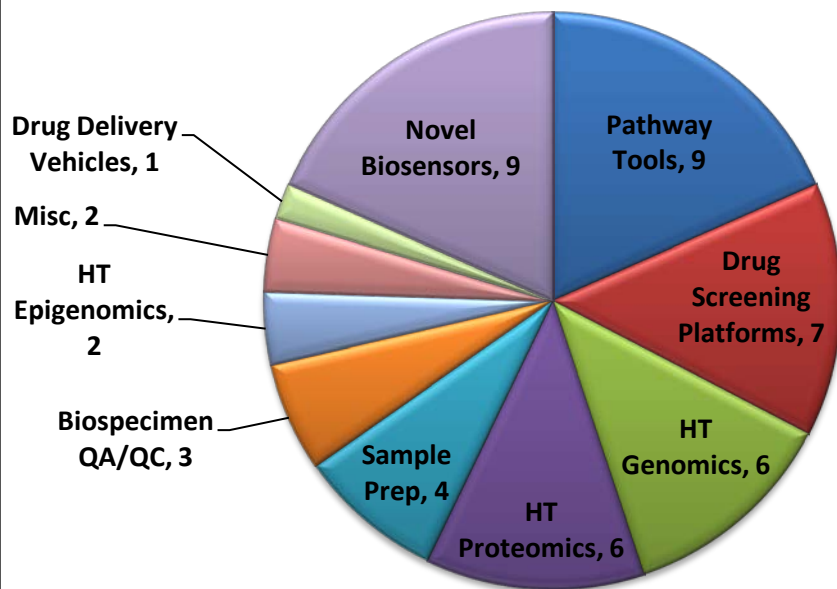
## Innovative Technologies for Molecular Analysis of Cancer (R21)

- Proof-of-concept
- Milestone driven (no biology)

## Application of Emerging Technologies for Cancer Research (R33)

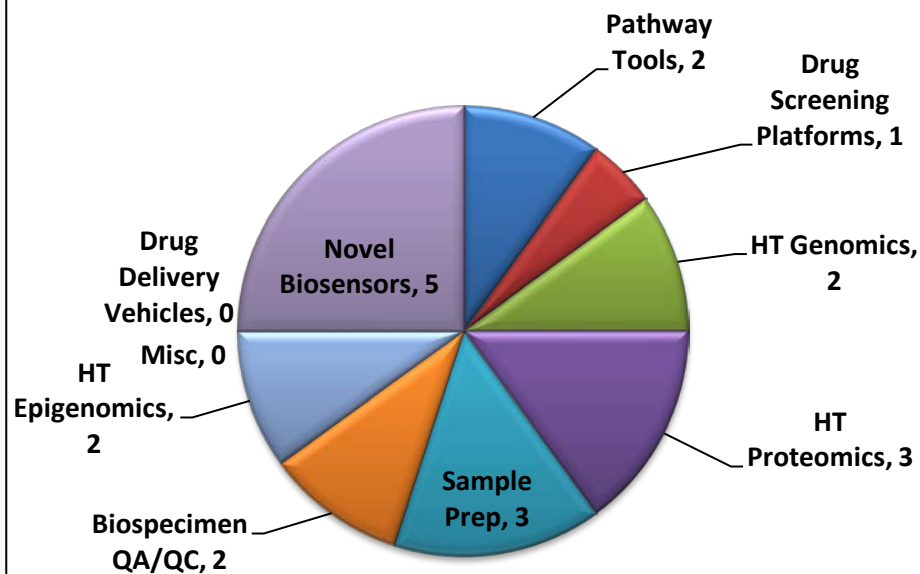
- Validation
- Demonstration of impact on basic and/or clinical research

**Current IMAT R21 Portfolio (49 Active Projects)**



HT = High throughput

**Current IMAT R33 Portfolio (20 Active Projects)**



# IMAT credits thus far...



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

## Older

- **ICAT** by Applied Biosystems [2001]
- **Mudpit**, licensed by the Scripps Research Institute [2001]
- **Rolling Circle Amplification**, available from Amersham Biosciences (now GE Healthcare), [2002]
- **Affymetrix GeneChip® CustomSeq®** arrays [2002]
- **Illumina Bead** technology (**BeadChip**, **Beadstation**, and **Sentrix BeadArray**) [2004]
- **Quantum Dots**, purchased by Invitrogen [2005]
- **MELT®** & **RNALater®** by Ambion [2005 and 2008, respectively]

## Newer

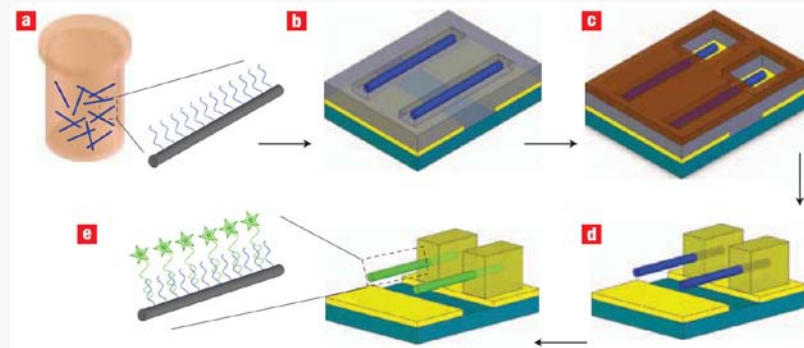
- **Microfluidic Genetic Analysis** platform, licensed by both Lockheed Martin and MicroLab Diagnostics [2008]
- Raindance® **RDT-1000** (oil nanodroplet technology) [2009]
- **COLD-PCR**, licensed by TransGenomic [2010]
- **TriP-Chip** Technology, licensed by OceanRidge Biosciences [2010]
- **NanoTrap** Biomarker Discovery Platform, licensed by Shimadzu Scientific [2010]
- **IUVO™** cell isolation platform from Bellbrook Labs, exclusively licensed by ThermoFisher [2012]
- CellASIC **ONIX** microfluidic perfusion system, acquired by EMD-Millipore [2012]

# NEMS-based RNA Sensor



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

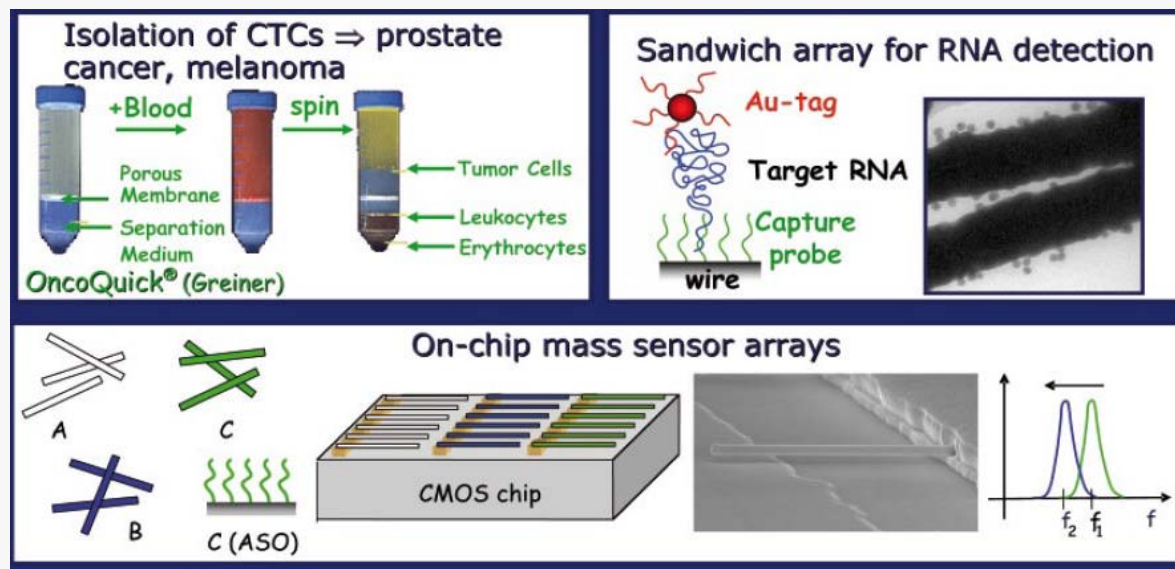
- Bottom up assembly offers superior sensitivity with simplified cost-effective fabrication and assembly
- Multi-analyte RNA sensor chip for CTC marker detection
  - Utilize OncoQuick® to isolate cells then extract RNA for exposure to sensor chip
  - Demonstrated positive frequency shifts for 2 binding events on a single nanowire



PENNSSTATE



PI: Gary Clawson, MD  
Anatomic & Clinical Pathologist  
Penn State



\*Li *et al*, Nature Nanotech 3(2) p88-92, Feb 2008

\*\*Clawson *et al*, Bioforum Eur 13(1-2) 10-11, Feb 2009

# Raindance<sup>®</sup> Microfluidic RDT-1000

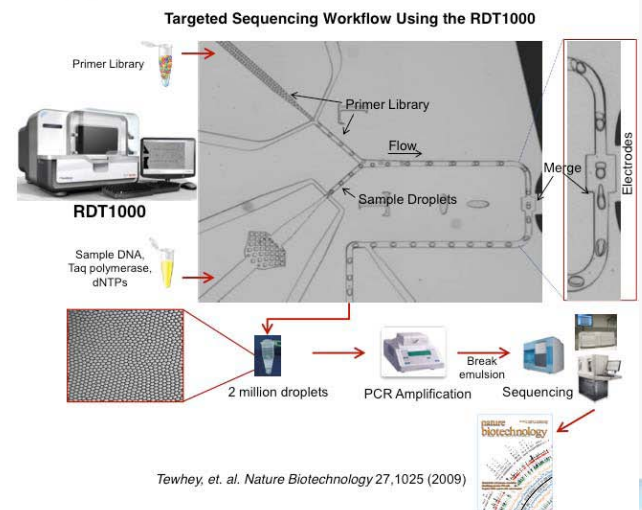
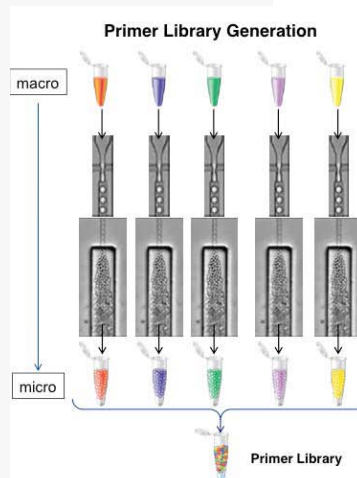


INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

- Platform for isolating nanoliter volumes of solution using oil droplets at rate of 10 million/hour at varying size. Allows isolation of target analytes for single-cell analysis, high-throughput sequencing, etc
- Runner-up for 2009 Innovation of the Year, *Association for Laboratory Automation*
- Commercialized by Raindance<sup>®</sup> (2009). Currently collaborating with Ambry Genetics on ADMESeq<sup>™</sup>



PI: Darren Link, PhD  
Co-founder and VP of R&D  
Raindance Technologies





# NanoTrap<sup>®</sup> Biomarker Discovery Platform

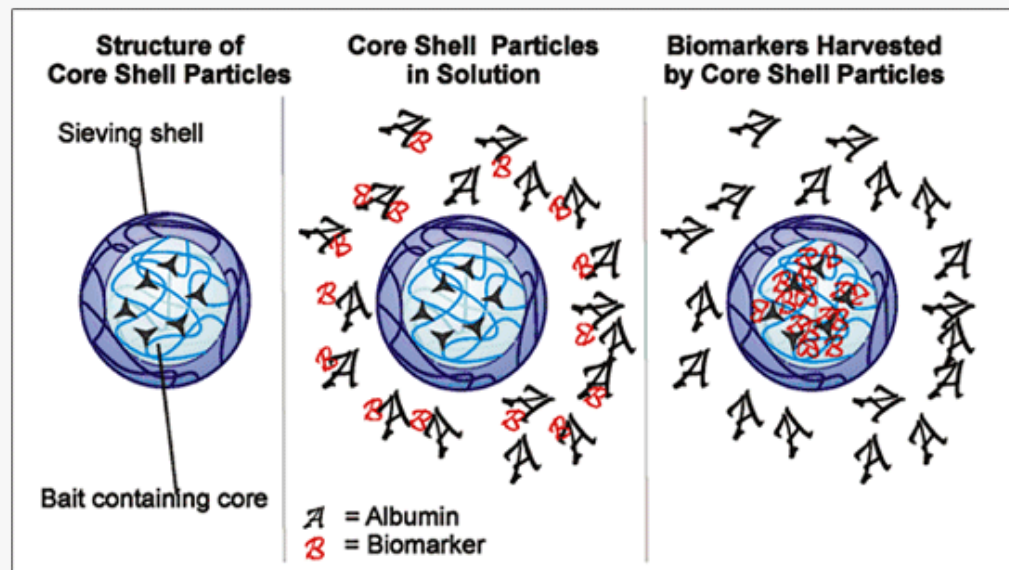


INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

- Porous core shell hydrogel nanoparticles with affinity via “bait chemistry” and size exclusion for selection of biomolecular target
- Allows for immediate preservation and conservation of low-abundance target biomarkers in complex solutions, including whole blood
- Licensed by Shimadzu Scientific [2010] and made available in partnership with Ceres Nanosciences and Nonlinear Dynamics



PI: Lance Liotta, MD, PhD  
Co-Director, Center for Applied  
Proteomics and Molecular Medicine  
George Mason University



# DNA-Catalyzed Molecular Biomarker Imaging Amplification (DC-MBIA)



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

- Dynamic DNA based programmable imaging probes
  - Highly multiplexed and reiterative immuno-fluorescence imaging capability for *in situ* studies
- Enzyme-free, isothermal, programmable, and regenerative system uses no harsh chemicals
- Multiplex imaging with 10-min to label and 10-min to erase



THE UNIVERSITY OF TEXAS  
**MDAnderson**  
~~Cancer~~ Center

PI: Michael Diehl, PhD  
Asst. Professor of Bioeng/Chemistry  
Rice University

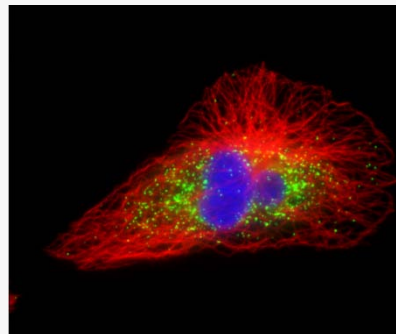
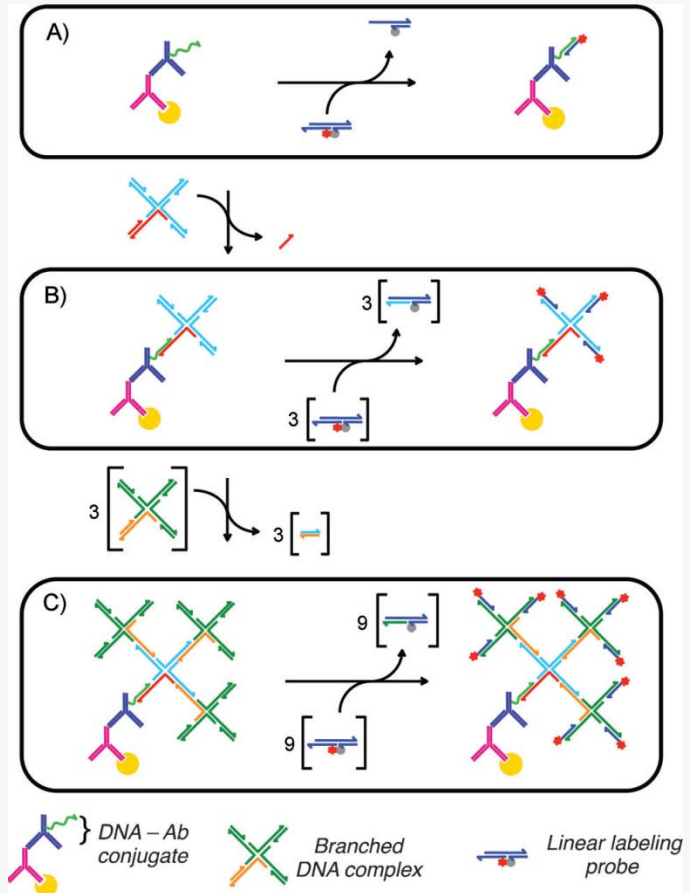


Image from <http://diehl@lab.rice.edu>



Diehl et al, ChemBioChem 2012, 13, 2722-8

# Active IMAT Funding Opportunities



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

**Early-Stage Innovative Molecular Analysis Technology Development for Cancer Research [R21]**

**RFA-CA13-001**

**Advanced Development and Validation of Emerging Molecular Analysis Technologies for Cancer Research [R33]**

**RFA-CA13-002**

**Innovative Technologies for Cancer-Relevant Biospecimen Sciences [R21]**

**RFA-CA13-003**

**Advanced Development and Validation of Emerging Technologies for Cancer-Relevant Biospecimen Sciences [R33]**

**RFA-CA13-004**

# Unique Attributes of IMAT Program



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

- Emphasis on ***innovative technology with transformative potential*** (*i.e.* high-risk, high-impact)
  - Focus on technology development (*NOT hypothesis-driven research*)
- ***Milestone-based*** applications that *quantitatively* assess the performance capacities of the technology (such as specificity, sensitivity, and speed) and characterize the improvement over state-of-the-art
- 100% ***investigator-initiated*** research grants



# Non-responsive applications



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

- Projects focused on a biological or clinical hypothesis for which the novelty resides in the biological or clinical question being pursued (i.e. traditional biological-hypothesis driven research);
- Projects that propose to use existing technologies (for which proof of concept has already been obtained) that may be ready for the targeted applications without substantial further developmental efforts;
- Projects that propose to develop only incremental technical advances to existing technologies projects that will have low potential for transforming cancer research;
- Technologies for whole-body or *in vivo* imaging methods;
- Projects involving clinical trials or toxicology studies;
- Projects focused on biomarker discovery or biomarker validation;
- Projects focused on development of specific contrast agents;
- Projects focused on development of specific drugs or therapies;
- Projects focused primarily on software/informatics solutions, database development, data mining, statistical tools, and computational/mathematical modeling (including those applicable to drug and/or patient responses) with the exception of projects which include software development for embedding in new devices or limited amounts of computational efforts as might be needed to develop new devices or methods;
- Applications that may have appropriate scientific scope but do not include the required specific components (Statement of Impact and Quantitative Milestones) will also be considered non-responsive to this FOA and will not be reviewed.

# Application Information



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

<b>Funding Instrument</b>	<b>R21 &amp; R33 Grants</b>
<b>Application Types Allowed</b>	New Resubmission
<b>Award Budget</b>	<p><u>R21</u>: Direct costs are limited to \$200,000 in any single year, with no more than \$500,000 in all direct costs over a 3-year period</p> <p><u>R33</u>: Direct costs are limited to \$300,000 per year, and \$900,000 in all direct costs over a 3-year period.</p> <p><u>Application budgets must reflect actual needs of the proposed project</u></p>
<b>Award Project Period</b>	The total project period is allowed for up to, but may not exceed, <u>3 years</u> for all awards
<b>Letter of Intent Due Date</b>	January 20, 2013; April 20, 2013; August 20, 2013
<b>Application Due Date(s)</b>	February 20, 2013; May 20, 2013; September 20, 2013, by 5:00 PM local time of applicant organization.
<b>Earliest Start Date(s)</b>	December 2013; April 2014; July 2014

# Opportunities



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

- CSSI: [http://cssi.cancer.gov/resources-current\\_funding.asp](http://cssi.cancer.gov/resources-current_funding.asp)
- NCI: <http://www.cancer.gov/researchandfunding/funding/announcements>
- NIH: <http://grants.nih.gov/grants/guide/>



# Thank You!

# Questions?

Contact info:

<http://innovation.cancer.gov>

301.547.9980

[dickherberaj@mail.nih.gov](mailto:dickherberaj@mail.nih.gov)