



CENTER *for*  
STRATEGIC  
SCIENTIFIC INITIATIVES



# INNOVATIVE MOLECULAR ANALYSIS TECHNOLOGIES

Tony Dickherber, Ph.D.

Program Director

Center for Strategic Scientific Initiatives (CSSI)  
Office of the Director, National Cancer Institute (NCI)  
National Institutes of Health (NIH)



NCI Alliance for  
**Nanotechnology**  
in Cancer



INNOVATIVE MOLECULAR  
ANALYSIS TECHNOLOGIES

*Provocative*  
Questions  
Initiative



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



**Director**  
Douglas Lowy, MD

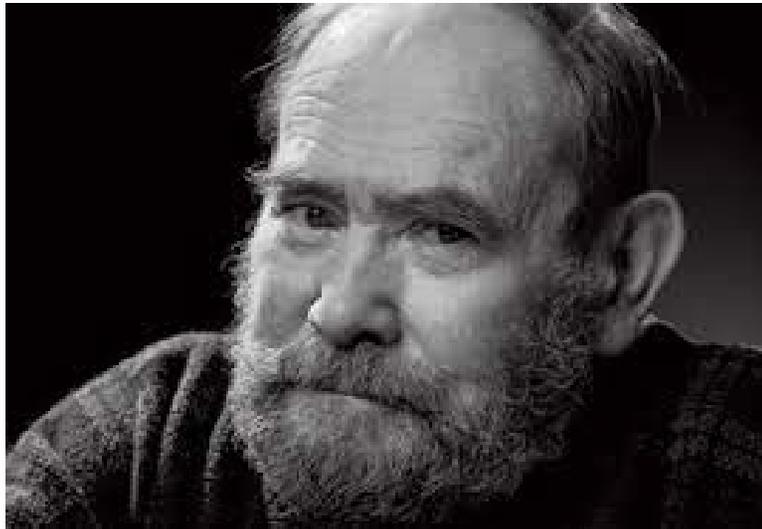


**Deputy Director**  
Jerry S.H. Lee, PhD

## 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...”





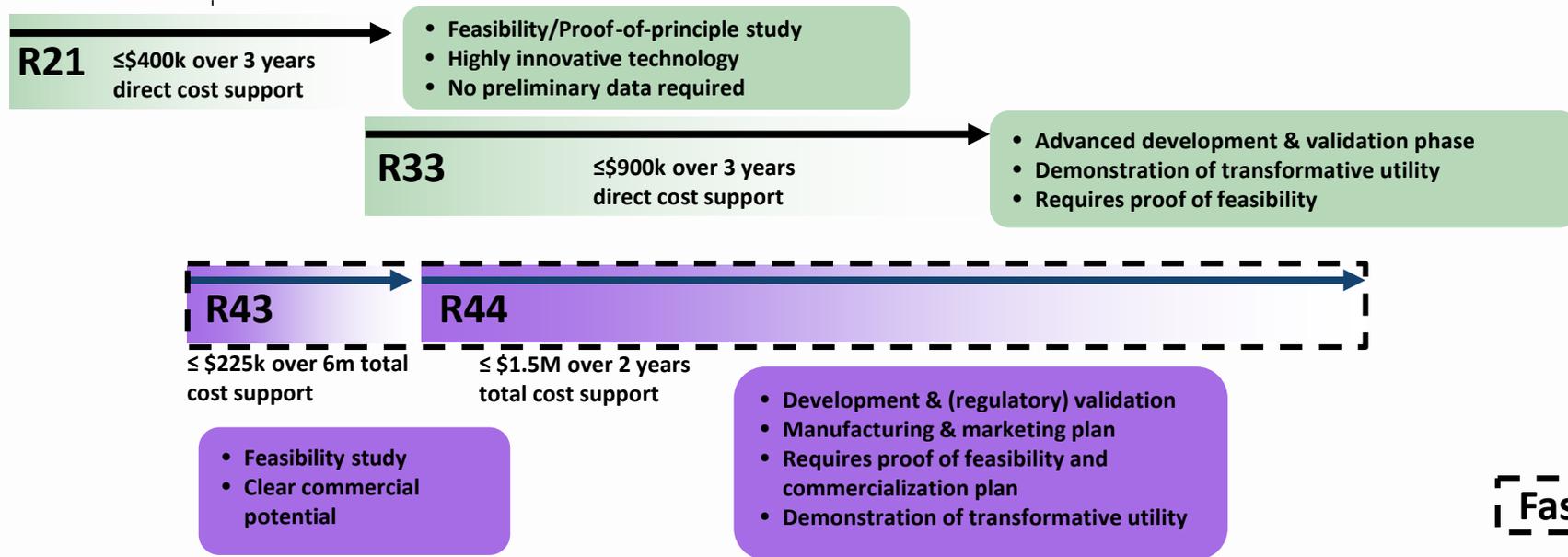
"Progress in science depends  
on new techniques, new  
discoveries and new ideas;

-Sydney Brenner

# Innovative Molecular Analysis Technologies (IMAT) Program

## 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.*



**Fast-Track**

# Unique Attributes of IMAT

## ■ Solicitation:

- Emphasis on ***innovative technology with transformative potential*** (*i.e.* high-risk, high-impact)
- Focus exclusively on ***technology development*** (*NOT biological/clinical hypothesis-driven research*)
- 100% ***investigator-initiated*** research grants

## ■ Review:

- ***Special emphasis panels*** recruited based on focus of submissions, drawing heavily from former IMAT grantees
- ***Milestone-based*** applications to *quantitatively* assess the capabilities of the technology (*e.g.*, specificity, sensitivity, and speed) and characterize the improvement over state-of-the-art

# Active IMAT Funding Opportunities

## Molecular /Cellular Analysis Tools

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

- FOA#: **RFA-CA-15-002**
- Budget: **\$400k/3yrs (direct cost cap)**

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

- FOA#: **RFA-CA-15-003**

***Remaining due dates: May 26, 2016 & September 26, 2016***

## Sample QA/QC Tools

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

- FOA#: **RFA-CA-15-004**
- Budget: **\$400k/3yrs (direct cost cap)**

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

- FOA#: **RFA-CA-15-005**
- Budget: **\$900k/3yrs (direct cost cap)**

# IMAT Awards for Small Business



**Molecular  
/Cellular  
Analysis  
Tools**

***Open to small business entities only***

**Innovative Molecular Analysis Technology  
Development for Cancer Research and Clinical Care  
[FOA# PAR-13-327]**

- **R43**
  - Time: 6 months
  - Budget: \$150k (total cost cap)
- **R44**
  - Time: 2 years
  - Budget: \$2M (total cost cap)

**Sample  
QA/QC  
Tools**

***Remaining due date: May 27, 2016***

# What is “Biospecimen Science”?

- **Sample Quality Control** (*e.g.*, RNALater)
  - Focus on preserving the biological integrity of the molecular and cellular targets to be assessed
  - Spans the preanalytical time period from patient management variables, through sample procurement, immediate handling and preservation, and processing prior to analysis
- **Sample Quality Assessment** (*e.g.*, RIN)
  - Focus on verifying the biological integrity of the molecular and cellular targets to be assessed

# An Important Public Resource: the Biospecimen Research Database

The Biospecimen Research Database - Office of Biore...

Home Search Quick Search Simple Search Advanced Search Experimental Factor Search Suggest New Paper Curator Login

## Biospecimen Research Database

### Search the Biospecimen Network Repository (Quick Search)

To find research studies for a biospecimen type and platform click on a cell in the table below.

Analyte	Technology Platform	Biospecimen Locations					Neoplastic Tissue		Others
		Blood	Serum	Plasma	Urine	Saliva	Normal	Cancerous	
DNA	<a href="#">Array CGH</a>	1					2	13	2
	<a href="#">CGH</a>							6	5
	<a href="#">DNA Sequencing</a>	3				1	2	21	15
	<a href="#">FISH</a>	1					1	37	6
	<a href="#">In situ hybridization</a>						1	6	7
	<a href="#">PCR</a>	11	3	1	2	2	4	86	101
	<a href="#">Comet assay</a>	4							3
	<a href="#">Electrophoresis</a>	5	1			2	3	31	45
	<a href="#">Fluorometry</a>	9				1	1	6	15
	<a href="#">Real-time qPCR</a>	13	1	6		4	2	23	21
	<a href="#">SNP assay</a>	10				2	4	15	16
	<a href="#">Southern blot</a>	2					1	14	17
	<a href="#">Spectrophotometry</a>	9	2	1		5	4	29	31
<a href="#">Tissue microarray</a>						1	5		

<http://brd.nci.nih.gov>

Local intranet

# Diversity of IMAT



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

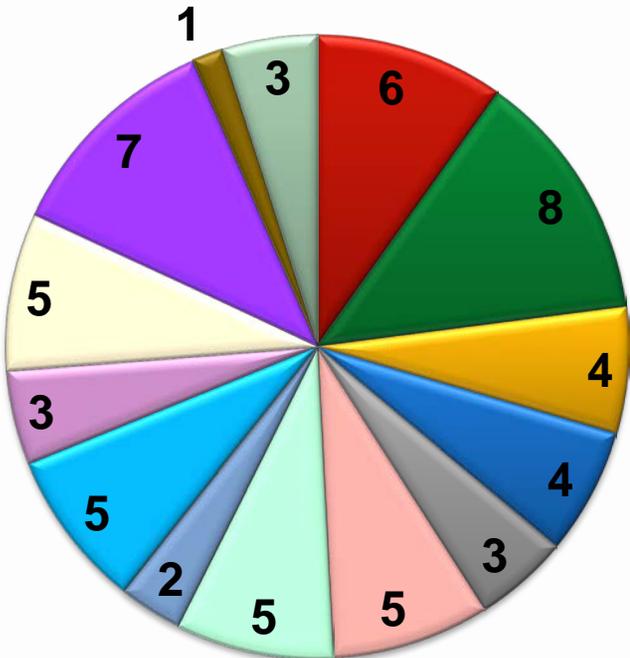
- Initial proof-of-concept
- Quantifiable milestone driven development plan



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

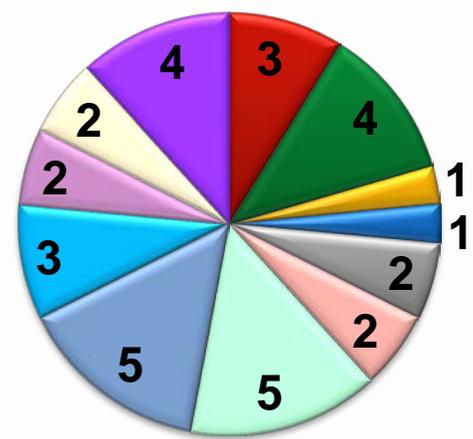
- Optimization/scaling or other further development
- Analytical/technical validation in biological context of use

### Current IMAT R21 Portfolio (61 Active Projects)



- Epigenomic Screening
- Novel Biosensor
- Drug Targeting/Delivery
- Drug Screening
- Advanced Microscopy
- Imaging Agents
- Liquid Biopsy Platform
- Genomic screening
- Cancer modeling
- Sample Preservation
- Sample Prep
- Proteomic screening
- Transcription screening
- Macromolecular Interaction Tools

### Current IMAT R33 Portfolio (34 Active Projects)

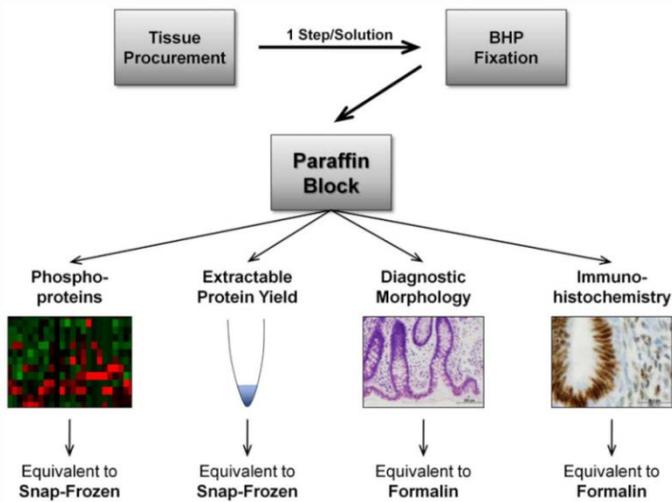


- Epigenomic Screening
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- Sample Prep
- Proteomic screening

# Basic research technology examples

## Novel Reagents: Biomarker & Histology Preservative

Validation of a novel tissue fixative as a replacement for formalin fixation, especially for the ability to preserve phosphoproteins.



GRACE BIO-LABS

Mueller *et al*, PloS One, Aug 2011

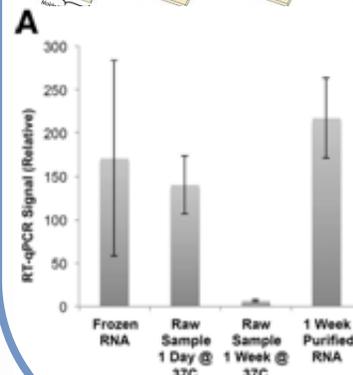
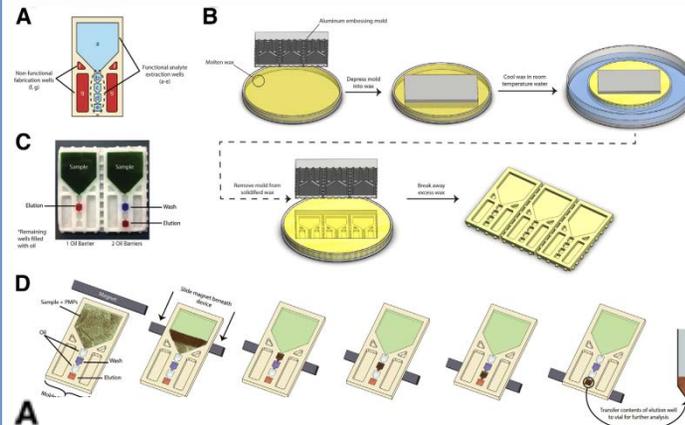


Lance Liotta, MD, PhD  
Center for Applied Proteomics and Molecular Medicine

GEORGE MASON UNIVERSITY

## Microfluidics: Exclusion-based Sample Prep

A seamless nucleic acid purification and amplification capability directly in line with a co-culture platform to examine intercellular interactions in heterogeneous patient specimens.



SALUS

WISCONSIN UNIVERSITY OF WISCONSIN-MADISON



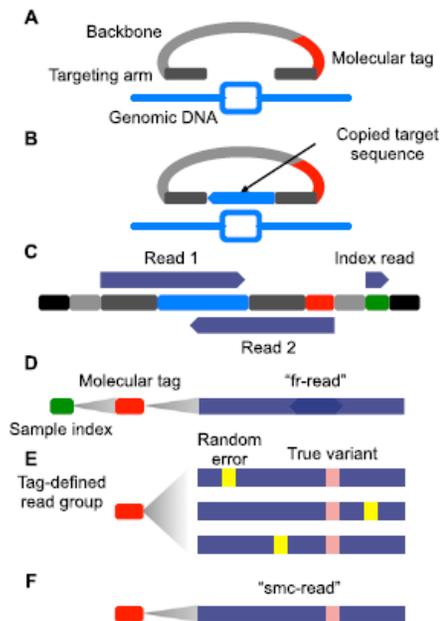
David Beebe, PhD  
Molecular & Cellular Pharmacology

Berry *et al*, J Mol Diag, May 2014

# Translational research project examples

## Chemical Methods: Single molecule Molecular Inversion Probes (smMIP)

More sensitive sequencing approach for detecting somatic mutations present at a frequency of 1 mutant copy among 100,000 wild type.



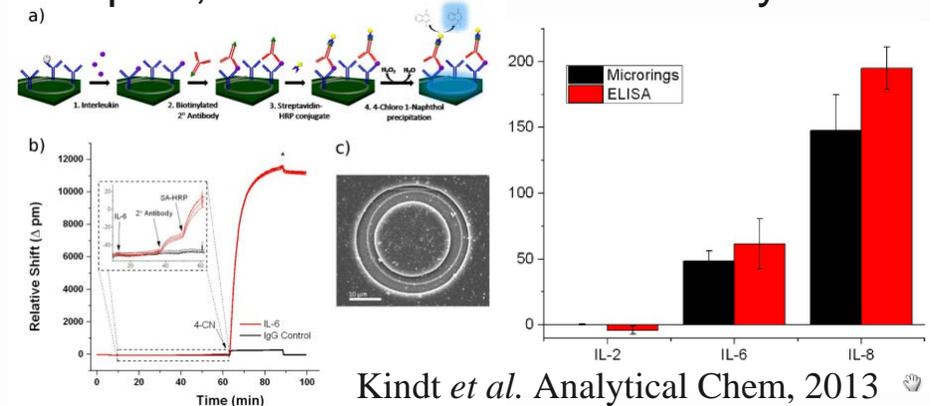
Jay Shendure, MD, PhD  
Stephen Salipante, MD, PhD  
Genome Sciences  
University of Washington



Hiatt *et al*, Gen Res Feb 2013

## Novel Sensors: Microring resonator-based biosensor array

Simultaneous, multiplexed profiling of miRNA and protein expression in clinical samples, with fM levels of sensitivity.



Ryan C. Bailey, PhD  
Associate Professor  
Department of Chemistry



ILLINOIS  
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN



Mark D Johnson, MD/PhD  
Assistant Professor of Surgery (HMS)  
Associate Surgeon (BWH)



# IMAT credits to date...



## Genomics

- **Digital Optical Chemistry**
- **Rolling Circle Amplification**
- Representational Oligonucleotide Microarray Analysis (**ROMA**)
- Multi-photon Intravital Imaging (**MPIVI**)
- **Recombomice**
- Pyrophosphorolysis Activated Polymerization (**PAP**)
- **Pair-end Sequencing** to screen structural rearrangements
- **Digital Transcriptome Subtraction**
- **Zinc Finger Nucleases** for targeted double-strand breaks
- **COLD-PCR** and derivatives

## Epigenomics

- Differential Methylation Hybridization (**DMH**)
- Methylation-Specific Amplification (**MSA**)
- Chromatin Immunoprecipitation with next gen Sequencing (**ChIP-Seq**)

## Clinical Diagnostics

- Paramagnetic chemical exchange saturation transfer (**ParaCEST**)
- **Near IR Probes** for in vivo diagnostics
- MicroSOL IEF (Invitrogen as **Zoom IEF Fractionator**)
- Microfluidic Genetic Analysis (**MGA**) chip
- **Oncomap** (a.k.a., **OncoPanel**)
- Mass Spec ImmunoAssays (**MSIA**) from Intrinsic Bioprobes
- **PhosphScan**® kits from Cell Signaling Technology, Inc
- Oligonucleotide-Selective Sequencing (**OS-Seq**)

## Proteomics

- Dynamic Range Enhancement Applied to Mass Spec (**DREAMS**)
- **Gateway** ORF Cloning Tool
- Multi-Dimensional Protein Identification Technology (**MuDPIT**)
- Isotope-Coded Affinity Tags (**ICAT**)
- **Synchrotron Protein Footprinting**
- Nanowire field effect transistors (**NWFETs**)
- **Proteolysis Targeting Chimera (PROTACs)**
- Deuterium exchange Mass Spec (**DXMS**)
- Nucleic Acid Programmable Protein Array (**NAPPA**)

## Sample Preparation

- **Magnetic Cell Sorting**, now available from Ikotech
- **RainDance** Oil Droplet Microfluidics
- Cryopreservation followed by culturing of CML cells
- **NanoVelcro**

## Drug Screening or Delivery

- One Bead One Compound (**OBOC**)
- Sleeping Beauty to genetically modify T-cells for treatment, targeting acute lymphoblastic leukemia
- **PI 3K inhibitor screening** platform from Echelon Biosciences (now Aeterna Zentaris)
- **ONIX** microfluidic perfusion cell toxicity screening system by CELLASIC Corp

# Non-responsiveness Criteria



- 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.

# R21 Milestones

- Should be quantitative and scientifically justified
- Critical components to include
  - Numerical performance targets (*what*)
  - Means by which they will be assessed (*how*)
- Important review consideration:
  - Means of judging the success of the aims
  - Provide proof-of-principle for justifying further developmental effort
    - *e.g.*, under a future R33 project

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Applicant Resources

“ The greatest problems of today cannot be solved at the same level of thinking with which they were created ”

## About IMAT

The Innovative Molecular Analysis Technologies (IMAT) program was established to support the development, technical maturation, and dissemination of novel and potentially transformative next-generation technologies through an approach of balanced but targeted innovation. In support of its mission, the IMAT program utilizes a variety of investigator-initiated research project grant mechanisms while retaining a strong commitment to diversity and to the training of scientists and clinicians in cross-cutting, research-enabling disciplines.

[Learn More About IMAT +](#)

## Recent News and Upcoming Events

NCI and NHLBI are offering a new contract funding opportunity to explore the impact of pre-analytical variables on markers of thrombosis in cancer patients. Proposals are due May 27, 2016. Please [click here](#) for more information.

The NCI is soliciting U01 applications for improved biomimetic tissue engineering platforms as part of a new cancer tissue engineering collaborative. Multiple due dates starting May 2016 through November 2018. Find out more [here](#).

Small business innovators should consider participating in the

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Next **application due date is set for May 26, 2016**. See [Funding Opportunities](#) for more information.



[Innovative and Applied Emerging Molecular Analysis Technologies in Cancer Research.](#)



[Innovative and Applied Emerging Technologies in Biospecimen Science](#)



[Small Business Funding Opportunities](#)

Funding opportunities in technology development are intended to support the inception, maturation, and subsequent dissemination of technically innovative and potentially transformative emerging technologies. These opportunities exist in parallel with various educational and training programs aimed at the recruitment, retention

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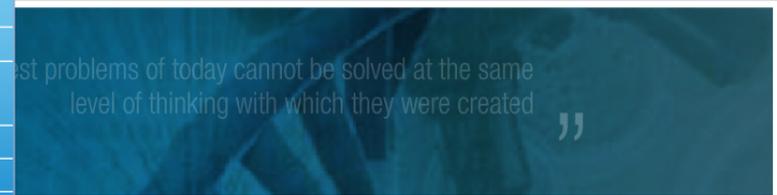
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Home Page > Awards: [Current Year Awards](#)

Click on any project title for a more detailed description of the project. For more information about any of these awards (e.g., PI contact information or associated publications), please use the corresponding project number to search for information at the NIH Reporter website. Consistent with NIH policy, abstracts are not available for projects receiving their first award within the past year, so descriptions provided below are from the NCI program director.

[Current Year](#) | [2014](#) | [2013](#) | [2012](#) | [2011](#) | [2010](#) | [2009](#) | [2008](#) | [2007](#) | [2006](#) | [2005](#) | [2004](#) | [2003](#) | [2002](#) | [2001](#) | [2000](#) | [1999](#)

Show/Hide All

Award Type	Project #	Year of Award	PI Name(S) All	Institution	Title
<b>Abstract Text (Official)</b>					
R21	CA186853	2014	CHEN, XIAOWEI	RESEARCH INST OF FOX CHASE CAN CTR	<a href="#">A Novel Allele-Specific RNA-ISH For Differential Allele-Specific Expression</a>
R21	CA186798	2014	CHIU, DANIEL T	UNIVERSITY OF WASHINGTON	<a href="#">Ultra-Bright Probes With Ultra-Narrow Emission For Molecular And Cellular Analysis</a>
R21	CA177391	2014	CIMA, MICHAEL J	MASSACHUSETTS INSTITUTE OF TECHNOLOGY	<a href="#">Implantable Device For High-Throughput In Vivo Drug Sensitivity Testing</a>
R21	CA182336	2014	ISSADORE, DAVID AARON	UNIVERSITY OF PENNSYLVANIA	<a href="#">A Micro Hall Chip For Circulating Microvesicle Based Cancer Monitoring</a>
R21	CA174573	2014	KUMAR, SANJAY	UNIVERSITY OF CALIFORNIA BERKELEY	<a href="#">Molecular Analysis Of Physical Microenvironmental Control Of Tumor Cell Invasion</a>

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ENABLING PROGRESS IN  
CANCER RESEARCH THROUGH  
ADVANCED TECHNOLOGIES,  
TRANS-DISCIPLINARY  
PROGRAMS

Tony Dickherber

[anthony.dickherber@nih.gov](mailto:anthony.dickherber@nih.gov)

(301) 547 - 9980

Timeline:

Select one or more offices to see events on timeline.

Offices:

- View All
- OD CSSI
- OBBR
- TCGA
- OCG
- OCCPR
- OCNR
- GPSO

Select level of detail in timeline.

Zoom Level:

- 1 Year
- 3 Years
- All Years

Timeline visualization showing various events from 2000 to 2012, represented by colored circles with icons.

RESOURCES

Current Resources

- Funding Opportunities
- Notices
- Useful Links

Archived Resources

- Funding Opportunities
  - 2013
  - 2012
- Notices

Current Resources

- CSSI Specific Funding Opportunities

Nanoscience and Nanotechnology in Biology and Medicine (R01)  
(PA-11-148)  
Application Receipt Date(s): [Standard dates](#) apply, by 5:00 PM local time of applicant organization.  
Expiration Date: May 8, 2014

- Relevant NCI Funding Opportunities

National Cancer Institute Program Project Applications (P01)