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.

Typical NIH barrier for technology

- **R21**: ≤$400k over 3 years direct cost support
  - Feasibility/Proof-of-principle study
  - Highly innovative technology
  - No preliminary data required

- **R33**: ≤$900k over 3 years direct cost support
  - Advanced development & validation phase
  - Demonstration of transformative utility
  - Requires proof of feasibility

- **R43**: ≤$225k over 6m total cost support
  - Feasibility study
  - Clear commercial potential

- **R44**: ≤ $1.5M over 2 years total cost support
  - Development & (regulatory) validation
  - Manufacturing & marketing plan
  - Requires proof of feasibility and commercialization plan
  - Demonstration of transformative utility
**Active IMAT Funding Opportunities**

### Molecular/Cellular Analysis Tools

- **[R21] Early-Stage Innovative Molecular Analysis Technology Development for Cancer Research**
  - FOA#: RFA-CA-16-001
  - Budget: $400k/3yrs (direct cost cap)

- **[R33] Advanced Development and Validation of Emerging Molecular Analysis Technologies for Cancer Research**
  - FOA#: RFA-CA-16-002
  - Budget: $900k/3yrs (direct cost cap)

### Sample QA/QC Tools

- **[R21] Innovative Technologies for Cancer-Relevant Biospecimen Sciences**
  - FOA#: RFA-CA-16-003
  - Budget: $400k/3yrs (direct cost cap)

- **[R33] Advanced Development and Validation of Emerging Technologies for Cancer-Relevant Biospecimen Sciences**
  - FOA#: RFA-CA-16-004
  - Budget: $900k/3yrs (direct cost cap)
2015 IMAT PI Meeting Agenda:

Session 1 – Cancer Imaging
Session 2 – Liquid Biopsy Platforms
Session 3 – Biomarker Discovery Tools
Session 4 – Detection and Diagnosis Tools
Session 5 – Drug Development and Improved Treatment Technologies
Session 6 – Novel Biosensors
Session 7 – Cancer Modeling
Session 8 – Improving Sample Preparation and Preservation
Emerging Platforms: Genomic Screening

**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

**Oligonucleotide Selective Sequencing (OS-Seq)**

A novel targeted resequencing technology that substantially accelerates and improves targeted detection of genomic variants, including mutations and structural variations.

Hopmans et al, Nucl Acid Res, 2014

Hanlee Ji, MD
Division of Oncology
Stanford School of Medicine
Emerging Platforms: Epigenetic Screening Tools

Sensor-Seq
A genome-wide biological measure of miRNA activity

Differential Allele-Specific Expression (DASE) by RNA-ISH
DASE as a functional index for cis-acting variants and pathogenic mutations, and global profiling of DASE in breast cancer precursor tissues to identify novel causative alleles for breast cancer susceptibility.

Andikyan et al, Adv in Genet & Genom, Oct 2015

Brian D Brown, Ph.D
Genetics and Genomic Sciences
Mount Sinai Hospital

Ravi Sachidanandam, Ph.D
Oncological Sciences
Mount Sinai Hospital

Xiaowei Chen, PhD
Cancer Epigenetics Research Program

Temple Health
Fox Chase Cancer Center
Mount Sinai Hospital
Emerging Platforms: Epigenomic Screening Tools

Microfluidic oscillatory washing–based ChIP-seq (MOWChIP-seq)

Microfluidic ChIP assays for studying transcriptional regulation, allowing genome-wide analysis of histone modifications using as few as 100 cells.

Cao et al, Nat Meth 2015
Emerging Platforms: Quantitative Redox Proteomics

Chemical reagents for site-specific imaging of sulfenic acid (-SOH) modifications via mass spectrometry (MS) technologies.

SILAC labeling: Lys8, Arg10

<table>
<thead>
<tr>
<th></th>
<th>Heavy</th>
<th>Light</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCC-61</td>
<td>2 Gy</td>
<td>0 Gy</td>
</tr>
<tr>
<td>rSCC-61</td>
<td>0 Gy</td>
<td>2 Gy</td>
</tr>
</tbody>
</table>

Capture by 1,3-dicarbonyl probe BP1

Lyse Label Cys-SOH with BP1

Cellular proteins (live cells)

1. precipitation
2. enrichment

nanoLC-MS for redox-regulated protein IDs

Emerging Platforms: Macromolecular Interaction Tools

Protein Paint

Native interacting proteins are painted with a pulse of dyes. Dyes block trypsin cleavage sites

Proteins are dissociated and linearized; dyes remain bound to linearized proteins

Mass spectrometry analysis yields peptides uniquely from the interface area

* dye (paint) molecules
\| blocked cleavage sites
\| available cleavage sites

Luchini et al, Nat Comm 2014

Lance Liotta, MD, PhD  Virginia Espina, PhD  Alessandra Luchini, PhD
Center for Applied Proteomics and Molecular Medicine
Emerging Platforms: Advanced Microscopy

Molecular Ion Beam Imaging

Stain tissue section with antibodies labeled with elemental isotopes

Measure spatial distribution of N elemental isotopes quantifying 7 masses per scan

Garry Nolan, PhD
Microbiology & Immunology

Michael Angelo, MD, PhD
Dept of Pathology

Richard Levenson, MD, FCAP & Alexander Borowski, MD
Center for Comparative Medicine
http://innovation.cancer.gov

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.

Funding Opportunities

The NCI is very pleased to announce that the IMAT program has approved reissuance for funding opportunity announcements through calendar year (CY) 2015.

Please use the links below for examples of past funding opportunities. New funding opportunities will be linked once posted.

Recent News and Upcoming Events

FDA holding workshop on NGS.

The Food and Drug Administration (FDA) is announcing a free public workshop to be held on the NIH campus on Feb. 20, 2015 entitled: "Optimizing FDA’s Regulatory Oversight of Next Generation Sequencing Diagnostic Tests.” The purpose of this workshop is to discuss and receive feedback from the community on FDA’s regulatory approach to diagnostic tests for human genetics or genomics using Next Generation Sequencing (NGS) technology. The meeting will be webcast for those not able to attend in person. Please register here if you wish to attend.

New 2015 IMAT RFAs now open!

Cancer Detection, Diagnosis, and Treatment Technologies for Global Health (UH2/UH3)

The NCI has issued a new solicitation to support the development of cancer-relevant technologies suitable for use in low- and middle-income countries (LMICs). Specifically, the FDA solicits applications for projects to adapt, apply, and validate existing or emerging technologies into a new generation of user-friendly, low-cost devices or assays that are clinically comparable to currently used technologies for imaging, in vitro detection/diagnosis, or treatment of cancers in humans living in LMICs. more →

IMAT support leads to new commercial glycan tagging kit from Cambridge Isotope Laboratories.

Congratulations to the Muddiman group (NCI) for commercial launch of their INLIGHTTM glycan tagging kit, an important new tool for enabling mass spectrometry-based glycomic research. more →
http://innovation.cancer.gov

Innovative Molecular Analysis Technologies

CENTERS FOR STRATEGIC SCIENTIFIC INITIATIVES

About IMAT  Program Areas  Funding Opportunities  Applicant Resources

History  Mission  Center for Strategic Scientific Initiatives  Management Team  Scope of Supported Technologies  Outputs and Achievements  News Archives  Annual PI Meetings  Grants Awarded

Funding Opportunities

The NCI is very pleased to announce that the IMAT program has approved reissuance for funding opportunity announcements through calendar year (CY) 2015.

Please use the links below for examples of past funding opportunities. New funding opportunities will be linked once posted.

http://innovation.cancer.gov

Innovative and Applied Emerging Molecular Analysis Technologies in Cancer Research

Innovative and Applied Emerging Technologies in Biospecimen Science

Recent News and Upcoming Events

FDA holding workshop on NGS.

The Food and Drug Administration (FDA) is announcing a free public Workshop to be held on the NIH campus on Feb 20, 2015 entitled: “Optimizing FDA’s Regulatory Oversight of Next Generation Sequencing Diagnostic Tests.” The purpose of this workshop is to discuss and receive feedback from the community on FDA’s regulatory approach to diagnostic tests for human genetics or genomics using Next Generation Sequencing (NGS) technology. The meeting will be webcast for those not able to attend in person. Please register here if you wish to attend.

New 2015 IMAT RFAs now open!

Cancer Detection, Diagnosis, and Treatment Technologies for Global Health (U01/UH2)

The NCI has issued a new solicitation to support the development of cancer-relevant technologies suitable for use in low- and middle-income countries (LMICs). Specifically, the FDA solicits applications for projects to adapt, apply, and validate existing or emerging technologies into a new generation of user-friendly, low-cost devices or assays that are clinically comparable to currently used technologies for imaging, in vitro detection/diagnosis, or treatment of cancers in humans living in LMICs. more

IMAT support leads to new commercial glycans tagging kit from Cambridge Isotope Laboratories.

Congratulations to the Muddiman group (NCU) for commercial launch of their INLIGHTTM glycans tagging kit, an important new tool for enabling mass spectrometry-based glycomics research. more

IMAT, ERIC BARD
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.


<table>
<thead>
<tr>
<th>Award Type</th>
<th>Project #</th>
<th>Year of Award</th>
<th>PI Name(s)</th>
<th>Institution</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>R21</td>
<td>CA186853</td>
<td>2014</td>
<td>CHEN, XIAOWEI</td>
<td>RESEARCH INST OF FOX CHASE CAN CTR</td>
<td>A Novel Allele-Specific RNA-ISH For Differential Allele-Specific Expression</td>
</tr>
<tr>
<td>R21</td>
<td>CA186796</td>
<td>2014</td>
<td>CHIU, DANIEL T</td>
<td>UNIVERSITY OF WASHINGTON</td>
<td>Ultra-Bright Probes With Ultra-Narrow Emission For Molecular And Cellular Analysis</td>
</tr>
<tr>
<td>R21</td>
<td>CA177391</td>
<td>2014</td>
<td>QIMA, MICHAEL J</td>
<td>MASSACHUSETTS INSTITUTE OF TECHNOLOGY</td>
<td>Implantable Device For High-Throughput In Vivo Drug Sensitivity Testing</td>
</tr>
<tr>
<td>R21</td>
<td>CA182336</td>
<td>2014</td>
<td>ISSADORE, DAVID AARON</td>
<td>UNIVERSITY OF PENNSYLVANIA</td>
<td>A Micro Hall Chip For Circulating Microvesicle Based Cancer Monitoring</td>
</tr>
<tr>
<td>R21</td>
<td>CA174573</td>
<td>2014</td>
<td>KUMAR, SANJAY</td>
<td>UNIVERSITY OF CALIFORNIA BERKELEY</td>
<td>Molecular Analysis Of Physical Microenvironmental Control Of Tumor Cell Invasion</td>
</tr>
</tbody>
</table>