National Cancer Institute



13th Annual Innovative Molecular Analysis Technologies (IMAT) Program Principal Investigators (PI) Meeting

November 27-28, 2012

The Methodist Hospital Research Institute Houston, Texas

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES National Institutes of Health

Program Overview

Welcome to the 13th Annual Innovative Molecular Analysis Technologies (IMAT) Program Principal Investigators (PI) Meeting. As many of you already know, this annual meeting is organized to address two important aims of the IMAT program: (1) to provide NCI program staff a chance to interact directly with PIs and receive an update on progress to date with supported research and (2) to provide an opportunity for interactions and exchange of ideas among meeting participants. This latter aim is a critical opportunity for sparking potentially transformative project collaborations, receiving critical feedback and guidance from the community, as well as for fostering dissemination of the exciting technologies emerging from IMAT-supported researchers.

The overarching theme for this year's meeting is to *emphasize the importance of engaging technology end-users*, and so the meeting includes various mechanisms for facilitating that communication. To that end, each of the speaker sessions will be chaired by a prominent researcher or clinician engaged in a field relevant to the session topic. They have been asked to provide a brief overview of the various basic and/or clinical research challenges associated with the topic that represent unmet opportunities for innovative technology solutions. Further, our IMAT success story overviews a dissemination path that did not require commercialization of the platform to have a significant impact on cancer research.

As there are more exciting active research projects in the IMAT portfolio than we could possibly allow sufficient speaking time for, we are repeating the "Poster Highlights" session that was piloted last year, in which a number of investigators will give short overview talks on their research posters. An additional change to this year's meeting spurred by our theme is to open the meeting on the afternoon of the first day to all interested local area researchers and clinicians, which will overlap with the Poster Highlights session, and the subsequent poster session in the atrium.

In addition to the agenda and presentation abstracts, a list of resources and funding opportunities that we thought might be of interest to participants are included toward the back of the book. On behalf of the NCI program staff and everyone involved in the planning for this meeting, I thank you for your participation, your interest, and the important work you all do to assist in our collective mission against cancer. I look forward to an exciting and productive meeting.

Sincerely,

Tony Dickherber, Ph.D. Program Director Center for Strategic Scientific Initiatives Office of the Director National Cancer Institute

Agenda

Day 1: Tuesday, November 27

8:00 a.m 8:45 a.m.	Registration and Continental Breakfast
	Poster Session Setup
8:45 a.m 9:00 a.m.	Welcome Auditorium Tony Dickherber, Ph.D., Program Director Innovative Molecular Analysis Technologies Program National Cancer Institute, NIH
9:00 a.m 10:10 a.m.	Panel Session: Novel Biosensors I Chair: Steven Shen, M.D., Ph.D. The Methodist Hospital Research Institute
9:10 a.m 9:30 a.m.	<i>Measuring Kinase Activity in Intact Cells Using Surface-Enhanced Raman</i> <i>Spectroscopy Nanosensors</i> Alyssa Garrelts, Ph.D. Purdue University
9:30 a.m 9:50 a.m.	Nanoelectrode and Nanofluidic-Based Assay of Mitochondria Membrane Potential and Apoptosis Peter J. Burke, Ph.D. University of California, Irvine
9:50 a.m 10:10 a.m.	<i>Multiplex Cancer Cell Purification With Magnetic Sifters</i> Shan X. Wang, Ph.D. Stanford University
10:10 a.m 10:30 a.m.	Break
10:30 a.m 12 noon	Panel Session: Novel Biosensors II Chair: Rebecca R. Richards-Kortum, Ph.D. Rice University
10:40 a.m 11:00 a.m.	Quantifying RNA-Protein Interactions In Situ Using Modified-MTRIPs and Proximity Ligation Philip J. Santangelo, Ph.D. Georgia Institute of Technology and Emory University
11:00 a.m 11:20 a.m.	<i>Highly Multiplexed, Spatially Delineated Molecular Imaging in Cancer</i> Michael R. Diehl, Ph.D. Rice University
11:20 a.m 11:40 a.m.	An Integrated Platform for Quantifying Gene Expression in Co-Cultured Cells David J. Beebe, Ph.D. University of Wisconsin

11:40 a.m 12 noon	Rapid and Sensitive Multiplex Sequencing of Actionable Cancer Genes in Clinical Samples Stephen Salipante, M.D., Ph.D. University of Washington
12 noon - 1:00 p.m.	Lunch (on your own)
1:00 p.m 2:00 p.m.	Success Story: Collaboration Versus Commercialization to Disseminate Your Technology William C. Hahn, M.D., Ph.D. Dana-Farber Cancer Institute
	David E. Hill, Ph.D. Dana-Farber Cancer Institute
2:00 p.m 3:50 p.m.	Poster Highlights Session
	Activatable BRET Probes for MMP Enzymatic Activity Detection Jianghong Rao, Ph.D. Stanford University
	Development of a Methylation-Based Diagnostic Assay for Malignant Melanoma: Defining the Factors Affecting Marker Selection and Assay Performance Sharon N. Edmiston The University of North Carolina at Chapel Hill
	<i>FRET-Based Biosensors to Monitor Redox in Cell Cycle Regulation</i> Vladimir Kolossov, Ph.D. University of Illinois, Urbana-Champaign
	<i>Microfluidic Sorting of Blood Cells for SPR and Fluorescence Analysis</i> Nathaniel C. Cady, Ph.D. University at Albany
	Application of an Innovative Technology to Develop Low-Toxicity Kinase Inhibitors Xiang Li, Ph.D. University of Maryland, Baltimore County
	<i>Multiple Reaction Monitoring to Profile Biosensor Phosphorylation in Leukemia</i> Laurie L. Parker, Ph.D Purdue University
	Probing Cancer Cell Chemoinvasion Strategies Using 3D Microfluidic Models Mingming Wu, Ph.D. Cornell University
	Specific and Reversible Binding of DNA Nanoparticles to Cancer Cells Bradley T. Messmer, Ph.D. University of California, San Diego

2D-PCR for Spatially Mapping Gene Changes in Tumor Sections

Daniel Gowetski, Ph.D. University of Maryland

Discovery Platform for Cancer Antigens

Kevin Claffey, Ph.D. University of Connecticut Health Center

Digital Analysis of Proteins Through End Sequencing (DAPES) Tom Cohen, Ph.D.

Washington University in St. Louis

Molecular Diagnostic Tests to Augment Cytomorphologic Diagnosis of Lung Cancer James C. Willey University of Toledo

Method for Detection of Secreted Proteins in Single-Cell Assays Henryk Szmacinski, Ph.D. University of Maryland

3:50 p.m. - 6:00 p.m.

Poster Session

First Floor Lobby

Day 2: Wednesday, November 28

8:00 a.m 8:15 a.m.	Recap of Day One and Overview of Day TwoAuditoriumTony Dickherber, Ph.D.Innovative Molecular Analysis Technologies ProgramNational Cancer Institute, NIH
8:15 a.m 8:45 a.m.	Host Welcome Mauro Ferrari, Ph.D. The Methodist Hospital Research Institute
8:45 a.m 9:30 a.m.	Keynote Address Joshua LaBaer, M.D., Ph.D. The Biodesign Institute Arizona State University
9:30 a.m 10:40 a.m.	Panel Session: Pathway Tools - 1 Chair: TBD
9:40 a.m 10:00 a.m.	VEC³-Valve Enabled Cell Co-Culture Platforms for Cancer Biology Study Deyu Li, Ph.D. Vanderbilt University
10:00 a.m 10:20 a.m.	Translational Control Analysis by Translationally Active RNA Capture/Microarray Analysis (TrIP-Chip) Jingfang Ju, Ph.D. Stony Brook University
10:20 a.m 10:40 a.m.	Scanning Correlation Microscopy Methods for Quantifying DNA Repair Kinetics Georgios Alexandrakis, Ph.D. The University of Texas at Arlington
10:40 a.m 11:00 a.m.	Break
11:00 a.m 12:30 p.m.	Panel Session: Biomarker Preservation and Discovery Chair: Ignacio Wistuba, M.D. The University of Texas MD Anderson Cancer Center
11:10 a.m 11:30 a.m.	Genome-Scale DNA Methylation Profiling in the Developing Colon and the Impact of Diet Lanlan Shen, M.D., Ph.D. Baylor College of Medicine
11:30 a.m 11:50 a.m.	Detection of Low-Prevalence Mutations in Solid Tumors via Ultra-Deep Targeted Sequencing Olivier Harismendy, Ph.D. University of California, San Diego

11:50 a.m 12:10 p.m.	<i>Tissue Is Alive: Preserving Biomolecules and Tissue Morphology in</i> <i>Clinical Trial Samples</i> Lance A. Liotta, M.D., Ph.D. George Mason University
12:10 p.m 12:30 p.m.	Sentinel RNAs as a Measure of mRNA Integrity in Clinical Biospecimens Curt H. Hagedorn, M.D. University of Utah
12:30 p.m 1:30 p.m.	Lunch (on your own)
1:30 p.m 2:40 p.m.	Panel Session: Pathway Tools - 2 Chair: Stephen Wong, Ph.D. The Methodist Hospital Research Institute
1:40 p.m 2:00 p.m.	Development and Application of Novel Glycan-Specific Reagents to Facilitate Early Detection of Epithelial Ovarian Cancer David C. Muddiman, Ph.D. North Carolina State University
2:00 p.m 2:20 p.m.	<i>Targeted Selection, Sequencing, and Analysis of Human Telomere and</i> <i>Subtelomere DNA in Cancer</i> Harold C. Riethman, Ph.D. The Wistar Institute
2:20 p.m 2:40 p.m.	Application of Next-Generation Sequencing to Cancer Epigenomics Huidong Shi, Ph.D. Georgia Health Sciences University
2:40 p.m 3:00 p.m.	Break
3:00 p.m 4:50 p.m.	Panel Session: Technologies to Assist With Drug Screening and Delivery Chair: Melissa D. Landis, Ph.D. The Methodist Hospital Research Institute
3:10 p.m 3:30 p.m.	<i>Magnetorotation: A Rapid Assay for Single Cell Drug Sensitivity of Cancer</i> <i>Cells</i> Raoul Kopelman, Ph.D. University of Michigan
3:30 p.m 3:50 p.m.	Scaffolds for Delivering Deoxycytidine Kinase to HER2 Positive Cancer Cells Brian K. Kay, Ph.D. University of Illinois at Chicago
3:50 p.m 4:10 p.m.	384-Well Cell Migration Assay Suitable for High-Throughput Screening (HTS) of Chemical Libraries for Cancer Therapeutics Andreas Vogt, Ph.D. University of Pittsburgh Drug Discovery Institute

4:10 p.m 4:30 p.m.	<i>Hyperspectral and Structural Microscopy Platform for Therapy of Resistant</i> <i>Cancer</i> Conor L. Evans, Ph.D. Harvard University
4:30 p.m 4:50 p.m.	Ultra-Throughput Multiple Reaction Monitoring Mass Spectrometry for Large-Scale Cancer Biomarker Validation Xudong Yao, Ph.D. University of Connecticut
4:50 p.m 5:00 p.m.	Closing Remarks and Adjournment Tony Dickherber, Ph.D. Innovative Molecular Analysis Technologies Program National Cancer Institute, NIH

Speaker Abstracts

Speaker	Abstract Title	Page Number
Alyssa Garrelts	Measuring Kinase Activity in Intact Cells Using Surface-Enhanced Raman Spectroscopy Nanosensors	9
Peter J. Burke	Nanoelectrode and Nanofluidic-Based Assay of Mitochondria Membrane Potential and Apoptosis	11
Shan X. Wang*	Multiplex Cancer Cell Purification With Magnetic Sifters	13
Philip J. Santangelo	Quantifying RNA-Protein Interactions In Situ Using Modified-MTRIPs and Proximity Ligation	14
Michael R. Diehl*	Highly Multiplexed, Spatially Delineated Molecular Imaging in Cancer	16
David J. Beebe	An Integrated Platform for Quantifying Gene Expression in Co- Cultured Cells	17
Stephen Salipante	Rapid and Sensitive Multiplex Sequencing of Actionable Cancer Genes in Clinical Samples	18
Jianghong Rao*	Activatable BRET Probes for MMP Enzymatic Activity Detection	19
Sharon N. Edmiston	Development of a Methylation-Based Diagnostic Assay for Malignant Melanoma: Defining the Factors Affecting Marker Selection and Assay Performance	20
Vladimir Kolossov	FRET-Based Biosensors to Monitor Redox in Cell Cycle Regulation	21
Nathaniel C. Cady*	Microfluidic Sorting of Blood Cells for SPR and Fluorescence Analysis	22
Xiang Li*	Application of an Innovative Technology to Develop Low-Toxicity Kinase Inhibitors	23
Laurie L. Parker*	Multiple Reaction Monitoring to Profile Biosensor Phosphorylation in Leukemia	24
Mingming Wu*	Probing Cancer Cell Chemoinvasion Strategies Using 3D Microfluidic Models	26
Bradley T. Messmer*	Specific and Reversible Binding of DNA Nanoparticles to Cancer Cells	27
Daniel Gowetski*	2D-PCR for Spatially Mapping Gene Changes in Tumor Sections	28
Kevin Claffey*	Discovery Platform for Cancer Antigens	29
Tom Cohen*	Digital Analysis of Proteins Through End Sequencing (DAPES)	30
James C. Willey*	Molecular Diagnostic Tests to Augment Cytomorphologic Diagnosis of Lung Cancer	31
Henryk Szmacinski*	Method for Detection of Secreted Proteins in Single-Cell Assays	32
Deyu Li*	VEC ³ -Valve Enabled Cell Co-Culture Platforms for Cancer Biology Study	33

*Abstracts that are also part of the poster session.

Speaker	Abstract Title	Page Number
Jingfang Ju	Translational Control Analysis by Translationally Active RNA Capture/Microarray Analysis (TrIP-Chip)	34
Georgios Alexandrakis	Scanning Correlation Microscopy Methods for Quantifying DNA Repair Kinetics	35
Lanlan Shen*	Genome-Scale DNA Methylation Profiling in the Developing Colon and the Impact of Diet	37
Olivier Harismendy*	Detection of Low-Prevalence Mutations in Solid Tumors via Ultra- Deep Targeted Sequencing	38
Lance A. Liotta*	Tissue Is Alive: Preserving Biomolecules and Tissue Morphology in Clinical Trial Samples	39
Curt H. Hagedorn*	Sentinel RNAs as a Measure of mRNA Integrity in Clinical Biospecimens	40
David C. Muddiman*	Development and Application of Novel Glycan-Specific Reagents to Facilitate Early Detection of Epithelial Ovarian Cancer	41
Harold C. Riethman	Targeted Selection, Sequencing, and Analysis of Human Telomere and Subtelomere DNA in Cancer	43
Huidong Shi*	Application of Next-Generation Sequencing to Cancer Epigenomics	44
Andreas Vogt	384-Well Cell Migration Assay Suitable for High-Throughput Screening (HTS) of Chemical Libraries for Cancer Therapeutics	45
Raoul Kopelman*	Magnetorotation: A Rapid Assay for Single-Cell Drug Sensitivity of Cancer Cells	46
Conor L. Evans	Hyperspectral and Structural Microscopy Platform for Therapy of Resistant Cancer	47
Xudong Yao*	Ultra-Throughput Multiple Reaction Monitoring Mass Spectrometry for Large-Scale Cancer Biomarker Validation	48
Brian K. Kay	Scaffolds for Delivering Deoxycytidine Kinase to HER2 Positive Cancer Cells	49

Resources

- TCGA Data Portal (<u>https://tcga-data.nci.nih.gov/tcga/tcgaHome2.jsp</u>) provides a platform for researchers to search, download, and analyze datasets generated by TCGA. It contains clinical information, genomic characterization data, and high-throughput sequencing analysis of the tumor genomes.
- NCI Proteomics Data Portal (<u>https://cptac-data-portal.georgetown.edu/cptacPublic/</u>) provides proteomics datasets of breast, ovarian, and tumor tissue that have also been genomically characterized by TCGA datasets.
- The Antibody Characterization Laboratory (<u>http://Antibodies.cancer.gov</u>) provides access to a large number of
 reagents and accompanying characterization data. Antigens and antibodies are expressed, purified, and
 characterized using standard operating procedures, with all accompanying protocols and data.
- NCI Best Practices for Biospecimen Resources guiding principles define state-of-the-science biospecimen resource practices, promote biospecimen and data quality, and support adherence to ethical and legal requirements (<u>http://biospecimens.cancer.gov/practices/default.asp</u>).

Funding Opportunities

- Innovative Molecular Analysis Technologies (IMAT) reissuance
 - Early-stage innovative molecular analysis technologies for cancer research (R21, up to 3 years and \$500k in direct costs) RFA-CA-13-001
 - Advanced development and validation of emerging molecular analysis technologies for cancer research (R33, up to 3 years and \$900k in direct costs) – RFA-CA-13-002
 - Early-stage innovative technologies for biospecimen science (R21, up to 3 years and \$500k in direct costs)
 RFA-CA-13-003
 - Advanced development and validation of emerging technologies for biospecimen science(R33, up to 3 years and \$900k in direct costs) – RFA-CA-13-004
- NCI Provocative Questions (PQ) initiative (<u>http://provocativequestions.nci.nih.gov/</u>), to support research
 projects designed to use sound and innovative research strategies to solve specific problems and paradoxes in
 cancer research
 - Group A covered by RFA-CA-12-015 (R01) and RFA-CA-12-016 (R21) that generally relates to cancer prevention and risk
 - Group B covered by RFA-CA-12-017 (R01) and RFA-CA-12-018 (R21) that generally relates to mechanisms
 of tumor development or recurrence
 - Group C covered by RFA-CA-12-019 (R01) and RFA-CA-12-020 (R21) that generally relates to cancer detection, diagnosis, and prognosis
 - Group D covered by RFA-CA-12-021 (R01) and RFA-CA-12-022 (R21) that generally relates to cancer therapy and outcomes
- Informatics Technology for Cancer Research (ITCR) program (<u>http://itcr.nci.nih.gov</u>)
 - Early-stage development including initial development (prototyping) and modification of existing methods for new applications: collaborate with NCI grantees and target naïve users for up to \$150k DC/yr for 2 years -PAR-12-286[R01 supplement], PAR-12-290[P01 supplement], PAR-12-289[U01 supplement]
 - Early-stage development (U01) at the prototyping and hardening stages, for up to \$250k DC/year for 3 years PAR-12-288
 - Advanced development (U24) at the enhancement, dissemination, and maintenance stages: target both naïve users and power users, for up to \$500k DC/year for 5 years - PAR-12-287

- NCI Small Business Innovation Research Development Center offers an array of grant and contract awards and other resources for the cancer research community. Find out more at <u>http://sbir.cancer.gov</u>
- Bioengineering Research Grants program (<u>http://www.nibib.nih.gov/Funding/Bioengineering</u>)
 - Multidisciplinary research that applies an integrative, systems approach to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease or to understand health and behavior. Exploratory BRG (R21, up to \$275k DC/2 years), BRG (R01), and BRP (large partnerships R01).
- Research Supplements to Promote Diversity in Health Related Research
 - Research supplements to support and recruit students, postdoctorates, and eligible investigators from groups that have been shown to be underrepresented in cancer and cancer health disparities research (PA-12-149)
- Other Current NCI FOAs
 - PA-11-158 & -159 Biomarkers of Infection-Associated Cancers (R01 and R21, respectively)
 - PA-12-213 & -214 Identifying Non-coding RNA Targets for Early Detection of Cancer (R01 and R21, respectively)
 - PA-12-221 & -220 Biomarkers for Early Detection of Hematopoietic Malignancies (R01 and R21, respectively)
 - PAR-12-039 Small Grants Program for Cancer Epidemiology (R03)
 - PA-11-297 & -298 Pilot studies in Pancreatic Cancer (R21 and R03, respectively)
 - PA-10-290 & -291 Research on Malignancies in the Context of HIV/AIDS (R01 and R21, respectively)
 - PA-11-073 & -074 Mitochondria in Cancer Epidemiology, Detection, Diagnosis and Prognosis (R01 and R21, respectively)
 - PA-11-151 Strategic Partnering to Evaluate Cancer Signatures (SPECS II) (U01)
 - PA-12-013 & -014 Validation of Molecular Diagnostics to Predict Patient Outcomes Using Specimens from Multi-Site Cancer Trials (R01 and R21, respectively)
- Coming soon (approved but no FOA assigned by time of printing)
 - Bridging the gap between cancer mechanism and population research: brings together systems biology + epidemiology to connect mechanism to population outcomes
 - Collaborations with the Integrative Cancer Biology Program (ICBP): multi-PI U01s, one from within ICBP one from outside ICBP to collaborate on anything related to cancer systems biology
 - Pending challenge/prize topics on BIG DATA from the NIH Common Fund in the next year or so
- And please always check the following for opportunities
 - NCI Center for Strategic Scientific Initiatives @ <u>http://cssi.cancer.gov/resources-current_funding.asp</u>
 - NCI Research Funding Opportunities @ http://www.cancer.gov/researchandfunding/funding/announcements
 - NIH Common Fund Initiatives @ <u>http://commonfund.nih.gov</u>, especially the "High-Risk Research" programs @ <u>http://commonfund.nih.gov/highrisk/index.aspx</u>