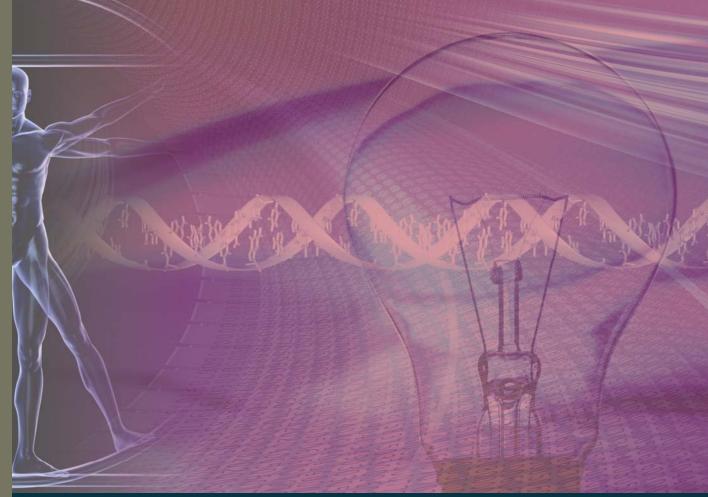
# National Cancer Institute



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

November 27-28, 2012

The Methodist Hospital Research Institute Houston, Texas

### **Program Overview**

Welcome to the 13<sup>th</sup> 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.	<i>Nanoelectrode and Nanofluidic-Based Assay of Mitochondria Membrane Potential and Apoptosis</i> 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.	<i>Quantifying RNA-Protein Interactions In Situ Using Modified-MTRIPs and Proximity Ligation</i> 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.	<i>An Integrated Platform for Quantifying Gene Expression in Co-Cultured Cells</i> 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
	<i>Application of an Innovative Technology to Develop Low-Toxicity Kinase Inhibitors</i> 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
	<i>Specific and Reversible Binding of DNA Nanoparticles to Cancer Cells</i> 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 TwoAuditoTony Dickherber, Ph.D.Innovative Molecular Analysis Technologies ProgramNational Cancer Institute, NIH	orium
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.	<i>VEC<sup>3</sup>-Valve Enabled Cell Co-Culture Platforms for Cancer Biology Stud</i> Deyu Li, Ph.D. Vanderbilt University	ly
10:00 a.m 10:20 a.m.	<i>Translational Control Analysis by Translationally Active RNA Capture/Microarray Analysis (TrIP-Chip)</i> Jingfang Ju, Ph.D. Stony Brook University	
10:20 a.m 10:40 a.m.	<i>Scanning Correlation Microscopy Methods for Quantifying DNA Repair Kinetics</i> 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.	<i>Genome-Scale DNA Methylation Profiling in the Developing Colon and Impact of Diet</i> Lanlan Shen, M.D., Ph.D. Baylor College of Medicine	the
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 Clinical Trial Samples</i> Lance A. Liotta, M.D., Ph.D. George Mason University
12:10 p.m 12:30 p.m.	<i>Sentinel RNAs as a Measure of mRNA Integrity in Clinical Biospecimens</i> 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 Subtelomere DNA in Cancer</i> Harold C. Riethman, Ph.D. The Wistar Institute
2:20 p.m 2:40 p.m.	<i>Application of Next-Generation Sequencing to Cancer Epigenomics</i> 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 Cells</i> Raoul Kopelman, Ph.D. University of Michigan
3:30 p.m 3:50 p.m.	<i>Scaffolds for Delivering Deoxycytidine Kinase to HER2 Positive Cancer Cells</i> Brian K. Kay, Ph.D. University of Illinois at Chicago
3:50 p.m 4:10 p.m.	<i>384-Well Cell Migration Assay Suitable for High-Throughput Screening</i> <i>(HTS) of Chemical Libraries for Cancer Therapeutics</i> 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 Cancer</i> Conor L. Evans, Ph.D. Harvard University
4:30 p.m 4:50 p.m.	<i>Ultra-Throughput Multiple Reaction Monitoring Mass Spectrometry for Large-Scale Cancer Biomarker Validation</i> 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	
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	
Henryk Szmacinski*	Method for Detection of Secreted Proteins in Single-Cell Assays	32
Deyu Li*	VEC <sup>3</sup> -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*	aoul Kopelman* Magnetorotation: A Rapid Assay for Single-Cell Drug Sensitivity of Cancer Cells	
Conor L. Evans	vans Hyperspectral and Structural Microscopy Platform for Therapy of Resistant Cancer	
Xudong Yao*	Ultra-Throughput Multiple Reaction Monitoring Mass Spectrometry for Large-Scale Cancer Biomarker Validation	
Brian K. Kay	Scaffolds for Delivering Deoxycytidine Kinase to HER2 Positive Cancer Cells	49

## Poster Abstracts

Poster Number	Presenter	Abstract Title	Page Number
1	Daniel Gowetski	2D-PCR for Spatially Mapping Gene Changes in Tumor Sections	54
2	J. Paul Robinson	A Flow-Based Selection Procedure for Analysis of Cytopathology for Cervical Cancer	55
3	Jonathan R. Lai	A Strategy for Phage Display Selection of Functional Domain-Exchanged Immunoglobulin Scaffolds With High Affinity for Glycan Targets	56
4	Jianghong Rao	Activatable BRET Probes for MMP Enzymatic Activity Detection	57
5	Hsian-Rong Tseng	Advanced Development of an Integrated CTC Enrichment Technology	58
6	Huidong Shi	Application of Next-Generation Sequencing to Cancer Epigenomics	60
7	Xiang Li	Application of an Innovative Technology to Develop Low- Toxicity Kinase Inhibitors	61
8	Kimberly Siegmund	Applying Molecular Phylogeny to Predict Patient Survival	62
9	Cheng Lee	CITP-Based Selective Tissue Proteome Enrichment	63
10	Michael Barrett	Deep Clonal Profiling of Formalin Fixed Paraffin Embedded Clinical Samples	64
11	Olivier Harismendy	Detection of Low-Prevalence Mutations in Solid Tumors via Ultra-Deep Targeted Sequencing	65
12	David Muddiman	Development and Application of Novel Glycan-Specific Reagents to Facilitate Early Detection of Epithelial Ovarian Cancer	66
13	Kathleen Conway-Dorsey	Development of a Methylation-Based Diagnostic Assay for Malignant Melanoma: Defining the Factors Affecting Marker Selection and Assay Performance	68
14	Steven Zeichner	Development of an In Vivo Screening Technology for Cancer Vaccine Immunogens	69
15	Rob Mitra	Digital Analysis of Proteins Through End Sequencing (DAPES)	70
16	Kevin Claffey	Discovery Platform for Cancer Antigens	71
17	Vladimir Kolossov	FRET-Based Biosensors to Monitor Redox in Cell Cycle Regulation	72
18	Lanlan Shen	Genome-Scale DNA Methylation Profiling in the Developing Colon and the Impact of Diet	73
19	Michael Diehl	Highly Multiplexed, Spatially Delineated Molecular Imaging in Cancer	74

Poster Number	Presenter	Abstract Title	Page Number
20	Sarah Blair	Hollow Perfluoropentane Filled Silica Nano and Microparticles for Breast Conservation Therapy	75
21	Eugene Kandel	Improved Insertional Mutagenesis for Molecular Analysis of Cancer	76
22	Daniel Chiu	Isolation and Analysis of Circulating Tumor Cells	77
23	Raoul Kopelman	Magnetorotation: A Rapid Assay for Single-Cell Drug Sensitivity of Cancer Cells	78
24	Henryk Szmacinski	Method for Detection of Secreted Proteins in Single-Cell Assays	79
25	Yin-Yuan Mo	Methods of Systematic microRNA Target Validation and Identification	80
26	Nathaniel Cady	Microfluidic Sorting of Blood Cells for SPR and Fluorescence Analysis	81
27	James Willey	Molecular Diagnostic Tests to Augment Cytomorphologic Diagnosis of Lung Cancer	82
28	Shan X. Wang	Multiplex Cancer Cell Purification With Magnetic Sifters	83
29	Laurie Parker	Multiple Reaction Monitoring to Profile Biosensor Phosphorylation in Leukemia	84
30	Jason Held	OxMRM: Quantifying Oxidation of Endogenous Redox- Sensitive Cysteines In Targeted Proteins Using Multiple Reaction Monitoring	86
31	Anthony DeCaprio	Platform for High-Throughput Analysis of Protein Adducts for Carcinogen Exposure Assessment	87
32	Mingming Wu	Probing Cancer Cell Chemoinvasion Strategies using 3D Microfluidic Models	89
33	Brian Hrudka	ProCure System	90
34	Songping Huang	Prussian Blue Nanoparticles as Cellular T1 MRI Contrast Agents	91
35	Keqi Tang	Pushing the Limit of Sensitivity for LC-MRM MS Quantification of Low-Abundance Protein Biomarkers	92
36	Margaret Gulley	Screening of Novel Small Molecule Candidates to Augment Formalin Fixation	93
37	Curt Hagedorn	Sentinel RNAs as a Measure of mRNA Integrity in Clinical Biospecimens	94
38	Bradley Messmer	Specific and Reversible Binding of DNA Nanoparticles to Cancer Cells	95
39	Thomas M. Blomquist	Standardized Mixtures of Internal Standards in Quantitative Sequencing Enables Inter-laboratory and Inter-platform Concordance and Reduces Costs by Log- Order Magnitudes	96

Poster Number	Presenter	Abstract Title	Page Number
40	Rui Sousa	Successful Construction and Validation of Fluorescent Sensors for Monitoring GTP Levels in Living Cells	97
41	Matthew Levy	Targeting Cancer Cells With Functionalized Nanoparticle Libraries	98
42	G. Mike Makrigiorgos	Temperature-Tolerant COLD-PCR Enables Mutation Enrichment Using a Single Cycling Protocol for Diverse DNA Sequences	99
43	Lance Liotta	Tissue Is Alive: Preserving Biomolecules and Tissue Morphology in Clinical Trial Samples	100
44	Xudong Yao	Ultra-Throughput Multiple Reaction Monitoring Mass Spectrometry for Large-Scale Cancer Biomarker Validation	101
45	David Beebe	Understanding Stromal-Cancer Cell Interactions via a Microscale 3D Model of DCIS	102
46	John McDonald	Use of Nanogels to Target Delivery of siRNA to Cancer Cells in Mice	104
47	Kenneth Greis	Validation of MALDI-MS-Based Inhibitor Screening Technologies for Cancer Targets	105
48	Deyu Li	VEC <sup>3</sup> -Valve Enabled Cell Co-Culture Platforms for Cancer Biology Study	107
49	Dale Larson	Development of a Nanoscale Calorimeter	108

### 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

