The Innovative Molecular Analysis Technologies (IMAT) Program:

A *resource* for catalyzing new directions in biospecimen science research

Tony Dickherber, NCI Office of Biorepositories & Biospecimen Research

Background

In 1998 the NCI established the groundwork for a highly successful program focused on innovative technology development to meet the specific needs of the cancer community by stimulating the next generation of cross-cutting technologies capable of catalyzing progress in the understanding of the molecular and cellular basis of cancer. Unlike other initiatives of the time, IMAT solicited *only* the most cutting-edge ideas despite their potential risk, thus restricting its application pool to those projects that were risky but that also had the potential to be truly transformative, if successful.

In 2005, the NCI expanded this program into the field of biospecimen science to solicit similarly innovative technology development initiatives. The IMAT Biospecimen Science solicitations focused on the development of innovative tools capable of assessing the effects of various preanalytical variables on biospecimens and technologies capable of appropriate preservation and/or assessment of the integrity (i.e. fitness-for-purpose) of molecular analytes in human biospecimens. The NCI has recently reissued solicitations for this research through 2013 and enthusiastically seeks the development of potentially transformative new tools from the biospecimen science community.

Examples of the needs*

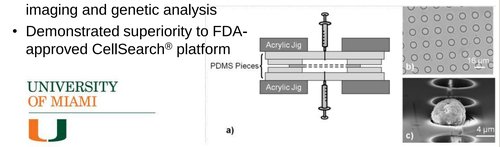
1. Long term (*i.e.* days) blood storage for circulating tumor cell (CTC) and biomarker analysis. Needs include technology, standard operating protocols (SOPs) and standards.
2. Methods to obtain clinical live cancer cells for research. Technologies should enable small scale collection and address sterility and capacity for transport.
3. Tools to minimize and document the time from surgical excision to storage. These should be accompanied with a determination as to whether collection and storage approaches affects specific analysis (protein, RNA, DNA, live cell and CTC isolation).
4. "Thresholds for Quality" - Surrogates or indicators to keep/discard sample or data. Analysis specific! A related need is standard samples across platforms.
5. Ability to assess metastatic lesions (biopsy or CTCs) to compare phenotype and heterogeneity with the primary tumor.
6. Enable access to early lesions to define progression steps with new technologies.
7. Other important issues: consent/collection challenges, underserved population samples, human tissues for technology prototype development.

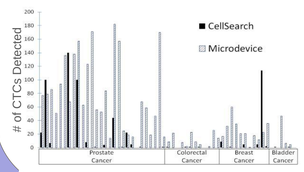
* Summary of biospecimen science gap analysis discussion points from 12th Annual IMAT Principle Investigator's Meeting. See full report at http://innovation.cancer.gov

Examples of Supported Research

Microdevice for CTC Capture

- Integrated capture and analysis filter-based device, capable of multiplex imaging and genetic analysis
- Demonstrated superiority to FDA-approved CellSearch® platform





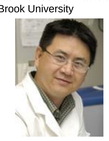
PI: Richard Cote, MD
Chair of Pathology
University of Miami

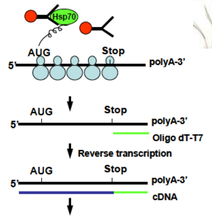
Lin *et al*, Clin Cancer Res, 16:5011-18, 2010

TrIP-Chip Technology

- Affinity capture beads that bind translationally-active mRNA only for high-throughput expression profiling
  - Enables investigation of translational control with limited sample quantities
- Licensed by OceanRidge Biosciences [2010]

PI: Jingfang Ju, PhD
Associate Professor of Pathology
Stony Brook University





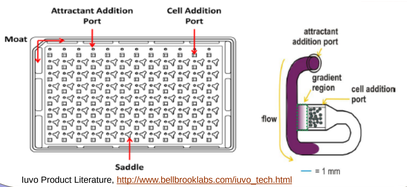
Gene Expression analysis (Microarray, qPCR and Sequencing)

Kudo *et al*, Nucleic Acids Res, Vol 38, Iss 9, e104, 2010

Iuvo™ Microconduit Cell Assay

- Microchannel cell-based assay for chemotaxis-based isolation and culturing of tumor cells for high-content analysis
- Commercialized by by Bellbrook Labs and exclusively licensed to Thermo Fisher Scientific[2012]

PI: David Beebe, PhD
Professor of Biomedical Engineering
University of Wisconsin, Madison

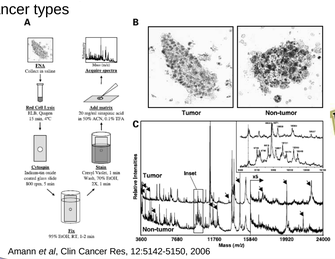


Iuvo Product Literature, http://www.bellbrooklabs.com/iuvo_tech.html

Preparation of Cancer Tissues for MS Imaging

- Developed standardized process for preparation of frozen and FFPE tissue for MS-based protein screening
- Novel lung cancer screening profile for fine-needle aspirates as model for other cancer types

PI: Pierre Chaurand, PhD
Associate Professor of Chemistry
Vanderbilt University (now @ U Montreal)

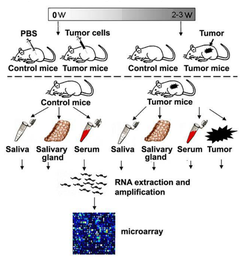


Amann *et al*, Clin Cancer Res, 12:5142-5150, 2006

Salivary Markers for Cancer Dx

- Established extraction and preservation methods for salivary mRNA, DNA and some proteins
- Developed a Direct Salivary Transcriptome Assay (DSTA)

PI: David Wong, DMD, DMSc
Professor of Oral Biology
University of Wisconsin, Madison



Gao *et al*, PLoS One, Vol.4, Iss.6, e5875, 2009

Biomarker & Histology Preservative

- Preservation of phosphorylated proteins in paraffin while maintaining full histomorphological detail and IHC diagnostics
  - Equivalent to snap-frozen quality marker preservation
- Utilized in 6 different national and international clinical trials
- Licensed by Theranostics Health, Inc [2010]

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

Mueller *et al*, PLoS One, Vol 6, Iss 8, e23780, 2011

Application Information

Funding Instrument	R21 & R33 Grants
Application Types Allowed	New Resubmission
Award Budget	**R21:** 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 **R33**: Direct costs are limited to $300,000 per year, and $900,000 in all direct costs over a 3-year period. *Application budgets must reflect actual needs of the proposed project*
Award Project Period	The total project period is allowed for up to, but may not exceed, 3 years for all awards
Letter of Intent Due Date	January 23, 2012; April 21, 2012; August 18, 2012
Application Due Date(s)	February 23, 2012; May 21, 2012; September 18, 2012, by 5:00 PM local time of applicant organization.
Scientific Merit Review	May/June 2012; August/September 2012; January/February 2013
Advisory Council Review	August 2012 ; January 2013; May 2013
Earliest Start Date(s)	December 2012; April 2013; July 2013

GENERAL REQUIREMENTS

Projects proposed in response to this FOA must meet the following general requirements:

- **Innovative, Biospecimen science-relevant technology.** The application must address the development of technologies and methodologies that improve the quality and utility of biospecimens and/or samples derived from biospecimens for cancer research and clinical control. The proposed technology may be targeted for the biospecimen/sample preparation needs of basic, preventative, diagnostic, translational, epidemiological, health disparities and/or clinical cancer research or for broad potential use in cancer research.
- **Substantial Improvement and/or New Capabilities.** All proposed applications, must offer the potential for substantial improvements over conventional approaches and/or add qualitatively new research capabilities not provided by current technologies.
- **Transformative Potential.** The application must clearly define the novelty of the proposed technology and describe its anticipated use in laboratory research and/or clinical settings. **A short narrative on the innovation and potentially transformative nature of the proposed technology must be included in the Specific Aims (under the heading "Statement of Impact").** Claimed potential impact is expected to be in line with the specific quantitative milestones (next bullet).
- **Quantitative Milestones.** Quantitative milestones are required as part of the application. Quantitative Milestones should be carefully selected and precisely defined, relative to existing technologies. Projects that do not include milestones will be rejected as non-responsive.

Note on Non-Responsive Applications

The following aspects/characteristics remain outside the scope of the IMAT Program and this FOA. Applications proposing any of the following will not be reviewed.

- Projects focused on a biological or clinical hypothesis (i.e. traditional biological-hypothesis driven research);
- Projects that propose to use existing (off-the-shelf) technologies without substantial new development and projects which propose only incremental technical advances to existing technologies;
- 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 embedded in new devices or small amounts of computational assessment as 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.

For more information, visit us at http://innovation.cancer.gov