Request to Reissue RFAs for the Innovative Molecular Analysis Technologies (IMAT) Program

June 2017

Motivation for Request for Reissuance

1. IMAT program continues to account for the majority of support for exclusively *early-stage technology development* research reviewed by NCI, *addressing an area unmet by other FOAs*

2. IMAT solicitations continue to receive a *significant number of high-scoring applications* that offer potential to address unmet research needs
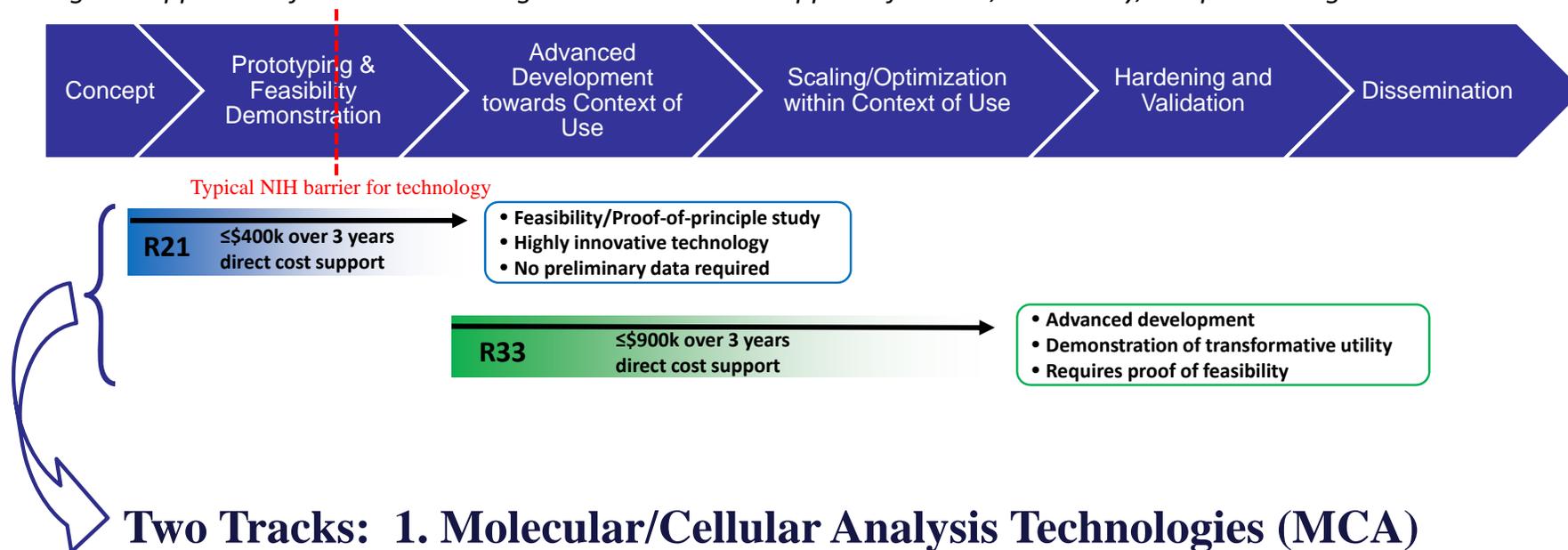
3. Strong *record of success*, as documented by multiple external program outcome evaluations.

Presentation Overview

1. Overview of the program

2. Portfolio Evaluation Summary

3. RFA Reissuance request details

IMAT Program Structure

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.

| Concept | Prototyping & Feasibility Demonstration | Advanced Development towards Context of Use | Scaling/Optimization within Context of Use | Hardening and Validation | Dissemination |

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
- Demonstration of transformative utility
- Requires proof of feasibility

Two Tracks:
1. **Molecular/Cellular Analysis Technologies (MCA)**
2. **Biospecimen Science Technologies (BST)**

Distinguishing Features of IMAT

- Emphasis on supporting development, testing, and validation of **high-risk/high-impact**, multidisciplinary, **cancer-relevant technologies** for improved analysis and/or targeting at the molecular and cellular level.

- **100% Investigator-initiated technology** research project grants.

- **Trans-divisional**, cooperative initiative focused on technological innovation with specific exclusions to minimize overlap or duplication with other programs and initiatives; feeding into both downstream technology development and hypothesis-driven research programs.

Trans-divisional IMAT Program Team

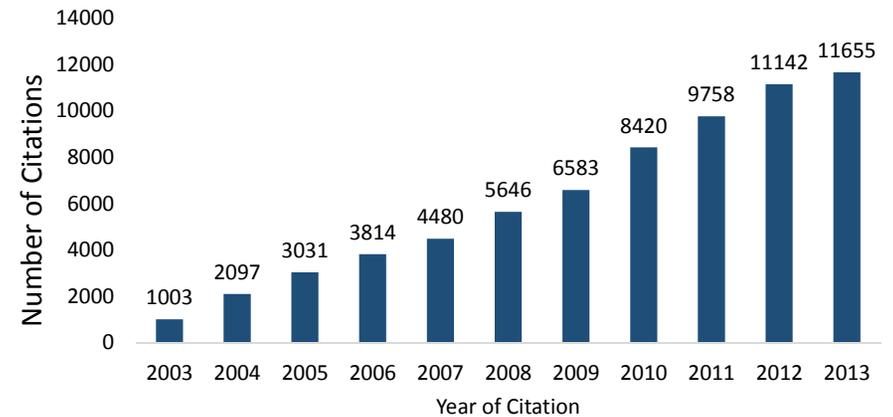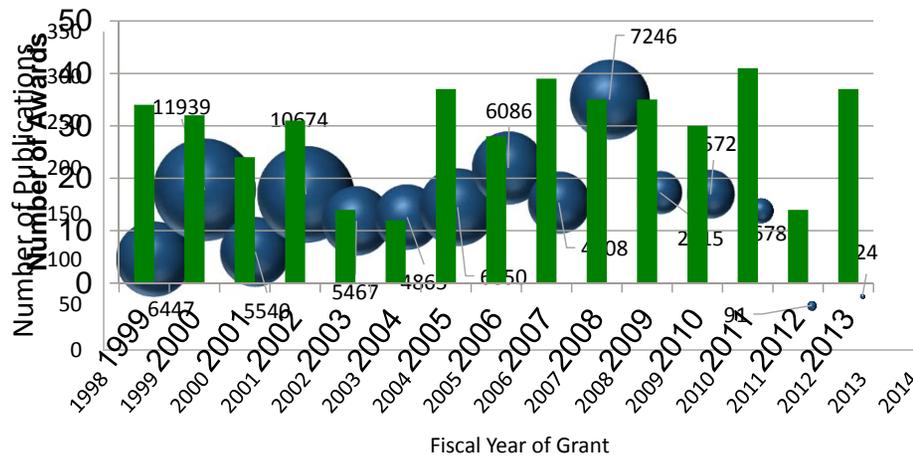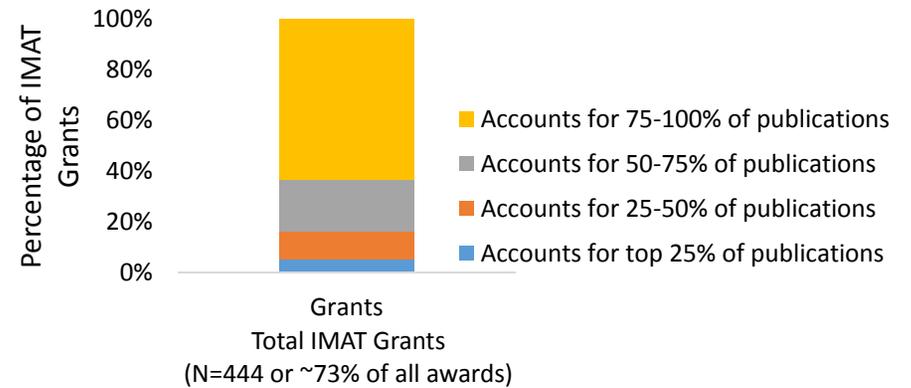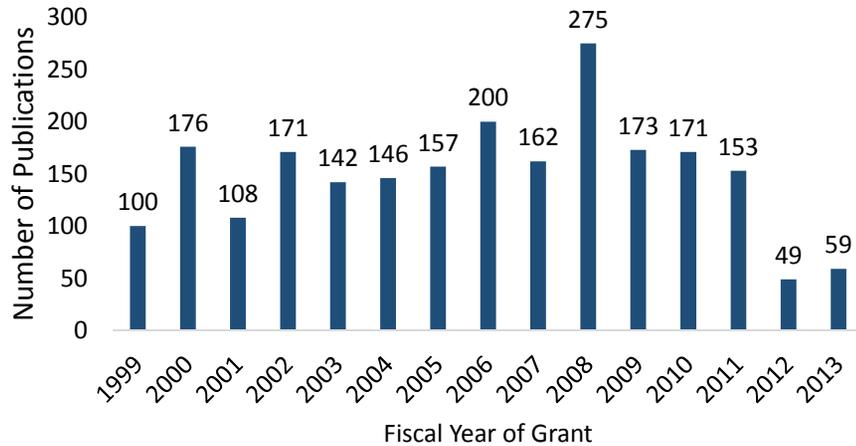| DOC	Program Officer	Contact
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IMAT Award Distribution
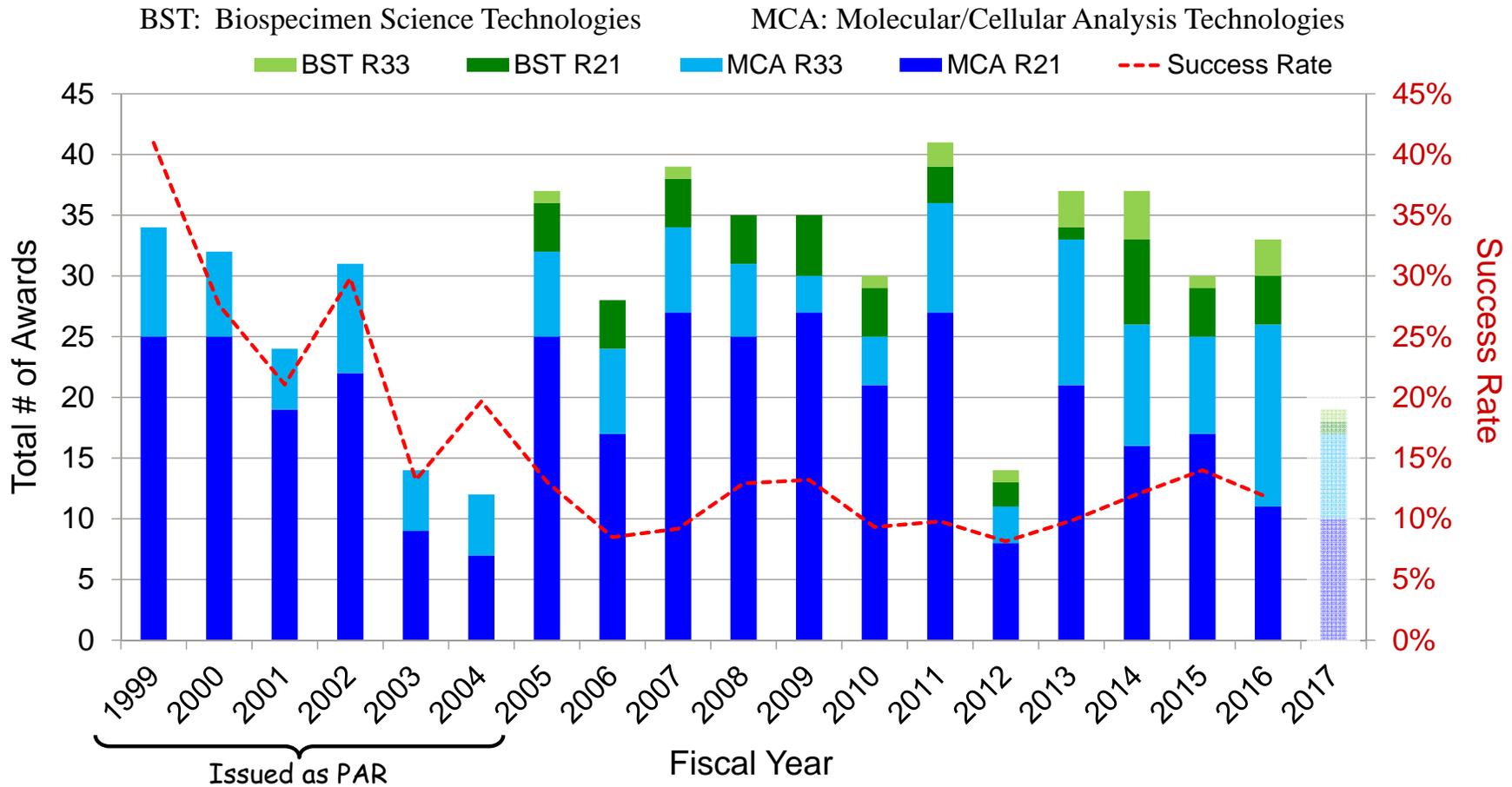
Presentation Overview

1. *Overview of the program*

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3. *RFA Reissuance request details*

IMAT FOA & Evaluation History

IMAT PAR Released
- 1 R21/R33
- 1 STTR/SBIR

IMAT PAR Renewed
- 2 R21/R33
- 1 STTR/SBIR

IMAT PAR Renewed
- 2 R21/R33
- 2 STTR/SBIR

IMAT RFAs Approved for 3 years
- 3 R21/R33
- 2 STTR/SBIR

RFAs Renewed for 5 years
- 3 R21 (1 is a 3-yr award)
- 2 R33
- 2 STTR
- 2 SBIR

RFAs Renewed for 2 years
- 2 R21 (both 3-yr awards)
- 2 R33

RFAs Renewed for 1 year
- 2 R21 (3 yr awards)
- 2 R33

RFAs Renewed for 3 years
- 2 R21 (3 yr awards)
- 2 R33

Renewal Request
- 2 R21(3 yr awards)
- 2 R33
- Comp Revisions

Timeline: 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017

Ongoing Evaluation

MACRO INTERNATIONAL INC.
Evaluation Feasibility Study

SAIC
Full Program Evaluation

IDA SCIENCE AND TECHNOLOGY POLICY INSTITUTE
Evaluative Update

THOMSON REUTERS
Targeted Evaluation

Ripple Effect
Full Program Evaluation (until FY2016)

Number of Publications by Fiscal Year of Grant (1999–2013): 1999: 100, 2000: 176, 2001: 108, 2002: 171, 2003: 142, 2004: 146, 2005: 157, 2006: 200, 2007: 162, 2008: 275, 2009: 173, 2010: 171, 2011: 153, 2012: 49, 2013: 59

Percentage of IMAT Grants — Total IMAT Grants (N=444 or ~73% of all awards)
- Accounts for 75-100% of publications
- Accounts for 50-75% of publications
- Accounts for 25-50% of publications
- Accounts for top 25% of publications

Number of Publications / Number of Awards by Fiscal Year of Grant

Number of Citations by Year of Citation: 2003: 1003, 2004: 2097, 2005: 3031, 2006: 3814, 2007: 4480, 2008: 5646, 2009: 6583, 2010: 8420, 2011: 9758, 2012: 11142, 2013: 11655

- Web surveys of IMAT group (N=540) vs Comparison Group (N=473)
  - Selection guided by a trans-NIH Evaluation Advisory Committee

- Key Findings
  - More published manuscripts with higher impact factor per $ invested compared to Comparison Group.
  - More patent applications and awards per $ invested compared to Comparison Group
  - *"IMAT grantees achieved marketability with their technology more than the Comparison Group" –Ripple Effect*
    - ~1/3 establish spin-off companies
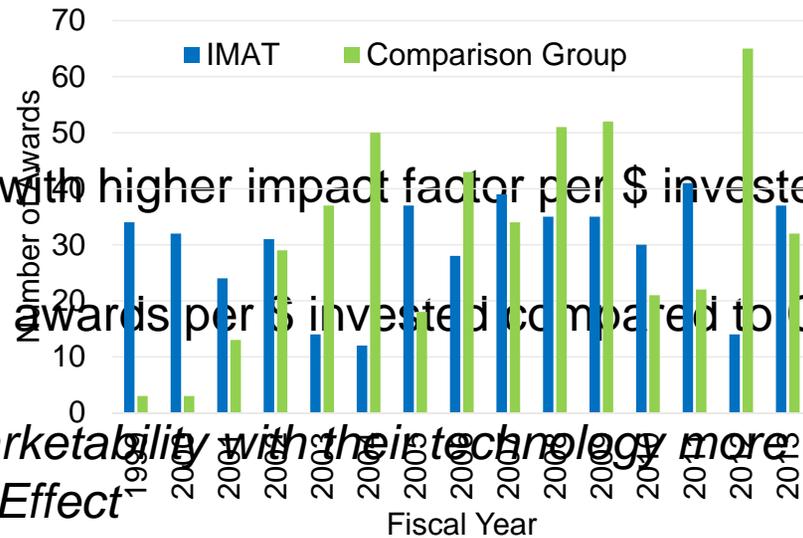
1. *Overview of the program*

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Request Summary

FOA	Mechanism	Est. # Awards	Est. 1st Year Total Costs
Early-Stage Innovative Molecular/Cellular Analysis Technologies for Cancer Research (MCA R21)	R21	16-19	$4-$4.5M
Advanced Development and Validation of Emerging Molecular/Cellular Analysis Technologies for Cancer Research (MCA R33)	R33	10-12	$4-$4.5M
Early-Stage Innovative Technologies for Cancer-Relevant Biospecimen Science (BST R21)	R21	2-4	$0.5-$1M
Advanced Development and Validation of Emerging Technologies for Cancer Biospecimen Sciences (BST R33)	R33	1-2	$0.4-$0.8M
Competitive Revisions	R01, U01, U54, P01, P50	2-3	$0.6M
		Total	$11M

Need for the RFA Mechanism

- Assurance of NCI interest in technology development
  - Designed to address a specific need that other initiatives are not currently meeting.
  - Investigators at every stage of their career, but especially young investigators, do not consider the NIH and NCI as interested in supporting technology development research.

- Control over responsiveness and review
  - Administrative responsiveness determination, controlling the locus of review, and ability to work with DEA Scientific Review Officers seen as critical to managing the program.

BSA Subcommittee Questions

- Consider making more clear the distinction between IMAT BST RFAs and other biospecimen science-focused solicitations supported by the NCI Biorepositories and Biospecimens Research Branch (e.g. PAR-16-166)

- Consider developing a strategy or mechanism that might allow reintegration of the MCA and BST RFAs

- Consider the competitive revisions solicitations be focused on IMAT-supported technologies for a pilot period to be more broadly inclusive if successful in subsequent years.

IMAT Reissuance Request Summary

Technology Development Pipeline:

Concept → Prototyping & Feasibility Demonstration → Advanced Development towards Context of Use → Scaling/Optimization within Context of Use → Product Development and Validation → Dissemination

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**
- **Demonstration of transformative utility**
- **Requires proof of feasibility**

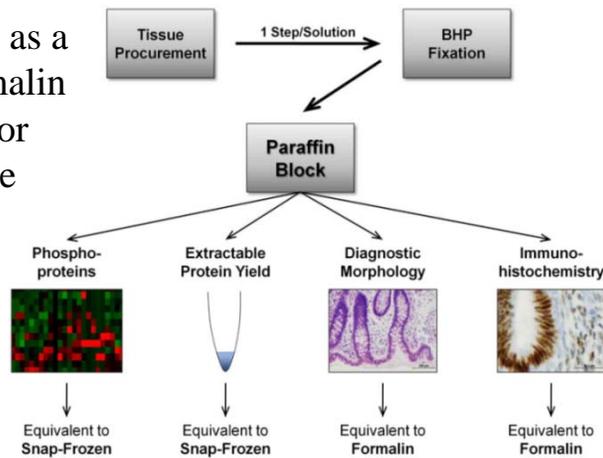**Competitive Revisions** (R01, U01, U54, P01, P50) ≤$300k over 2 years direct cost support
- **Validation within the context of a compelling hypothesis**
- **Pursued in collaboration with end-users**

RFA	1st Year Total Cost
MCA R21	$4-$4.5M
MCA R33	$4-$4.5M
BST R21	$0.5-$1M
BST R33	$0.4-$0.8M
Competitive Revisions	$0.6M
Total	$11M

Extra Slides

Theralin®: A novel biomarker and histology preservative

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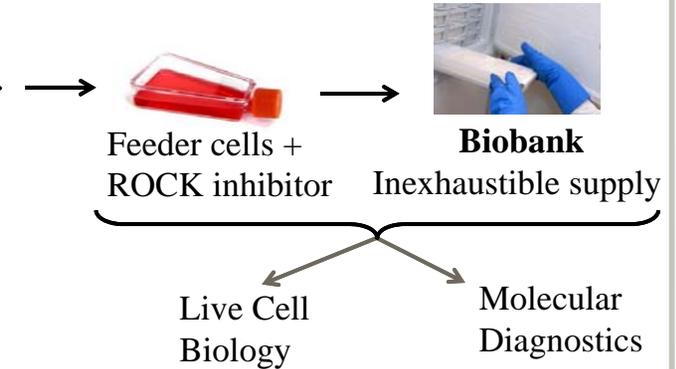

Tissue Procurement → 1 Step/Solution → BHP Fixation → Paraffin Block

Phospho-proteins → Equivalent to Snap-Frozen

Extractable Protein Yield → Equivalent to Snap-Frozen

Diagnostic Morphology → Equivalent to Formalin

Immuno-histochemistry → Equivalent to Formalin

Mueller *et al*, PloS One, 2011

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

GEORGE MASON UNIVERSITY

Conditionally Reprogrammed Cells (CRC)

Surgical specimens
Core biopsies
FNA
Blood/Urine

→ Feeder cells + ROCK inhibitor → **Biobank** Inexhaustible supply

Live Cell Biology   Molecular Diagnostics

Suprynowicz *et al*, PNAS, 2012

Richard Schlegel, MD, PhD
Center for Cell Reprogramming

Anton Wellstein, MD, PhD
Center for Cell Reprogramming

GEORGETOWN UNIVERSITY

BST Successes

| 1st Year BST Award	PI	Institution	Project Title
2009	LIOTTA, LANCE ALLEN	George Mason University	Nanotechnology for One Step Concentration and Preservation of Labile Biomarkers
2012	AKSAN, ALPTEKIN	University of Minnesota	Development of Room-Temperature Storage Technique for Plasma/Serum Biospecimens
2011	LIOTTA, LANCE ALLEN	George Mason University	Implementation of phosphoprotein preservation technology for cancer biospecimens
2012	DAYTON, PAUL	University of North Carolina at Chapel Hill	Cavitation Enhancement of Biospecimen processing for Improved DNA Fragmentation
2013	SCHLEGEL, RICHARD	Georgetown University	Conditionally reprogrammed cells as a novel tool for biobanking

Awards Comparison

RFA Series	MCA R21			MCA R33			BST R21			BST R33		
	Apps	Awards	Ave Score	Apps	Awards	Ave Score	Apps	Awards	Ave Score	Apps	Awards	Ave Score
CA05-X	102	17	155	36	5	153	33	4	152	6	1	165
CA06-X	144	9	157	27	3	137	32	4	175	2	0	N/A
CA07-X	248	29	151	57	6	139	65	8	160	13	1	157
CA08-X	125	16	158	42	3	158	24	5	154	7	0	N/A
CA09-X	174	14	23.5	34	4	22.3	33	4	27.5	8	1	32
CA10-X	223	16	21.9	51	9	22.8	30	3	28	10	2	25.5
CA12-X	276	19	21.7	100	11	18.5	44	3	23.3	12	3	17.3
CA13-X	177	21	21.0	80	10	22.5	28	5	22.8	14	4	21.5
CA14-X	177	21	24	87	12	22.6	41	6	22.7	17	2	20.5
CA15-X	187	11	24	71	15	21.7	29	4	23.8	16	3	19.7
Total	1833	173		585	78		359	46		105	17	

Early Stage Investigator Trends as a % of All vs Scored Applications

3-year R21 introduced
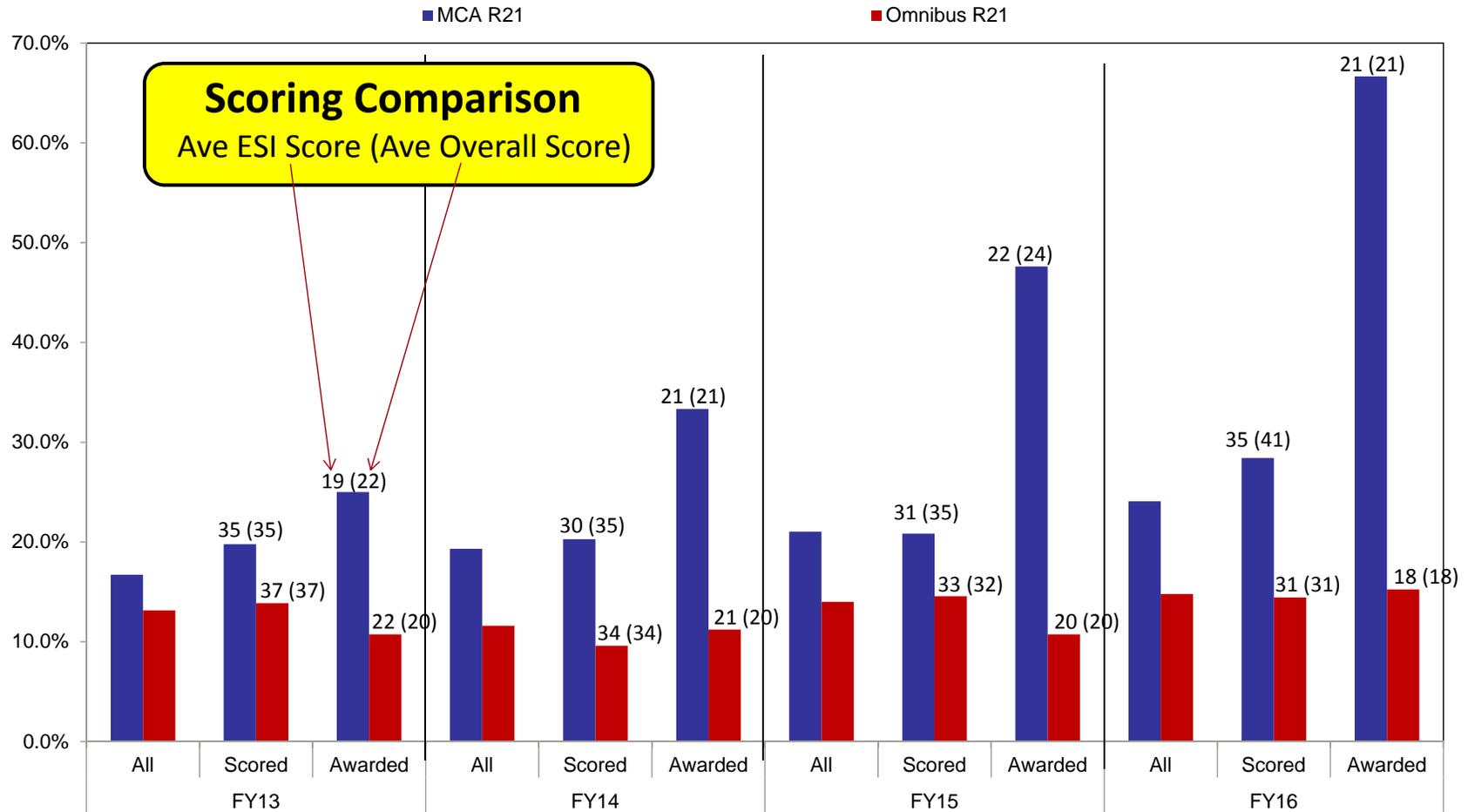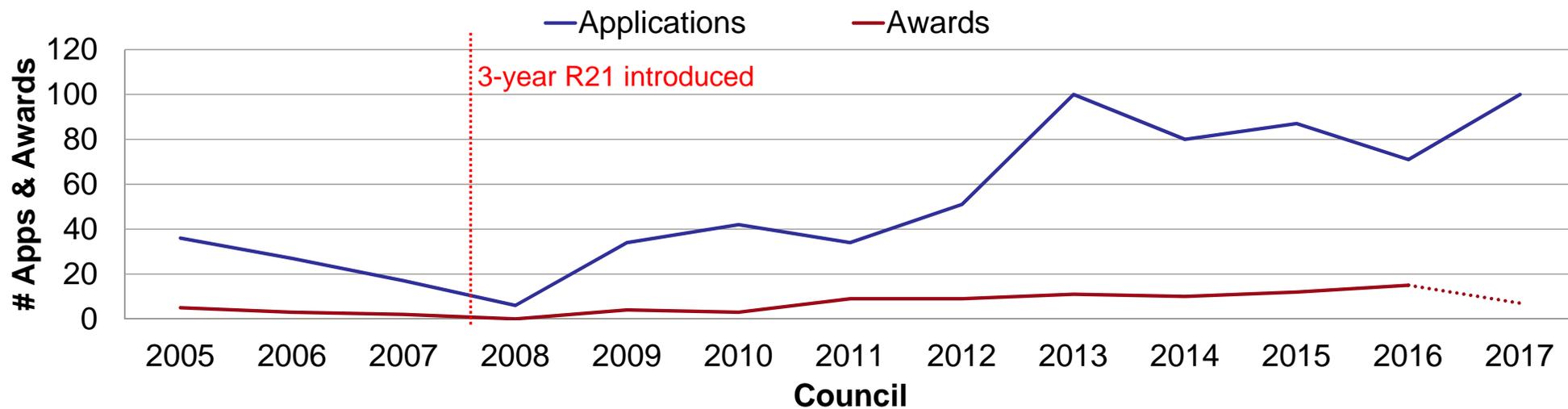
RFA	# Applications	# Awards	1st Year Total Costs
RFA-CA-08-008	34	3	$1,127,645
RFA-CA-09-007	42	4	$1,557,932
RFA-CA-10-004	34	9	$2,636,412
RFA-CA-12-003	51	11	$3,540,841
RFA-CA-13-002	100	10	$3,711,401
RFA-CA-14-004	80	12	$4,576,942
RFA-CA-15-003	87	15	$5,666,971

IMAT R21-R33 Transition Trends

Chart legend (top): # of R21s seeking transition per FOA — % of all R21s seeking transition per FOA

Chart legend (bottom): # Successful Transitions — % of all R21s successfully transitioning

Left axis (top): Attempts — 0, 3, 6, 9, 12, 15, 18
Right axis (top): 0%, 25%, 50%, 75%, 100%

Left axis (bottom): Successes — 0, 2, 4, 6, 8, 10
Right axis (bottom): 0%, 5%, 10%, 15%, 20%, 25%

X-axis categories: PAR98, PAR99, PAR01, CA05, CA06, CA07, CA08, CA09, CA10, CA12, CA13

X-axis label: **Base R21 Awarding FOA**

~18% of all R33 applications based on prior IMAT R21

~25% of all R33 awards based on prior IMAT R21

Chart does not indicate the number of transitions based on "phased innovation awards", which allowed for automatic transition for meeting milestones

IMT R21 Applications Submitted/Awarded per round of receipt

2017
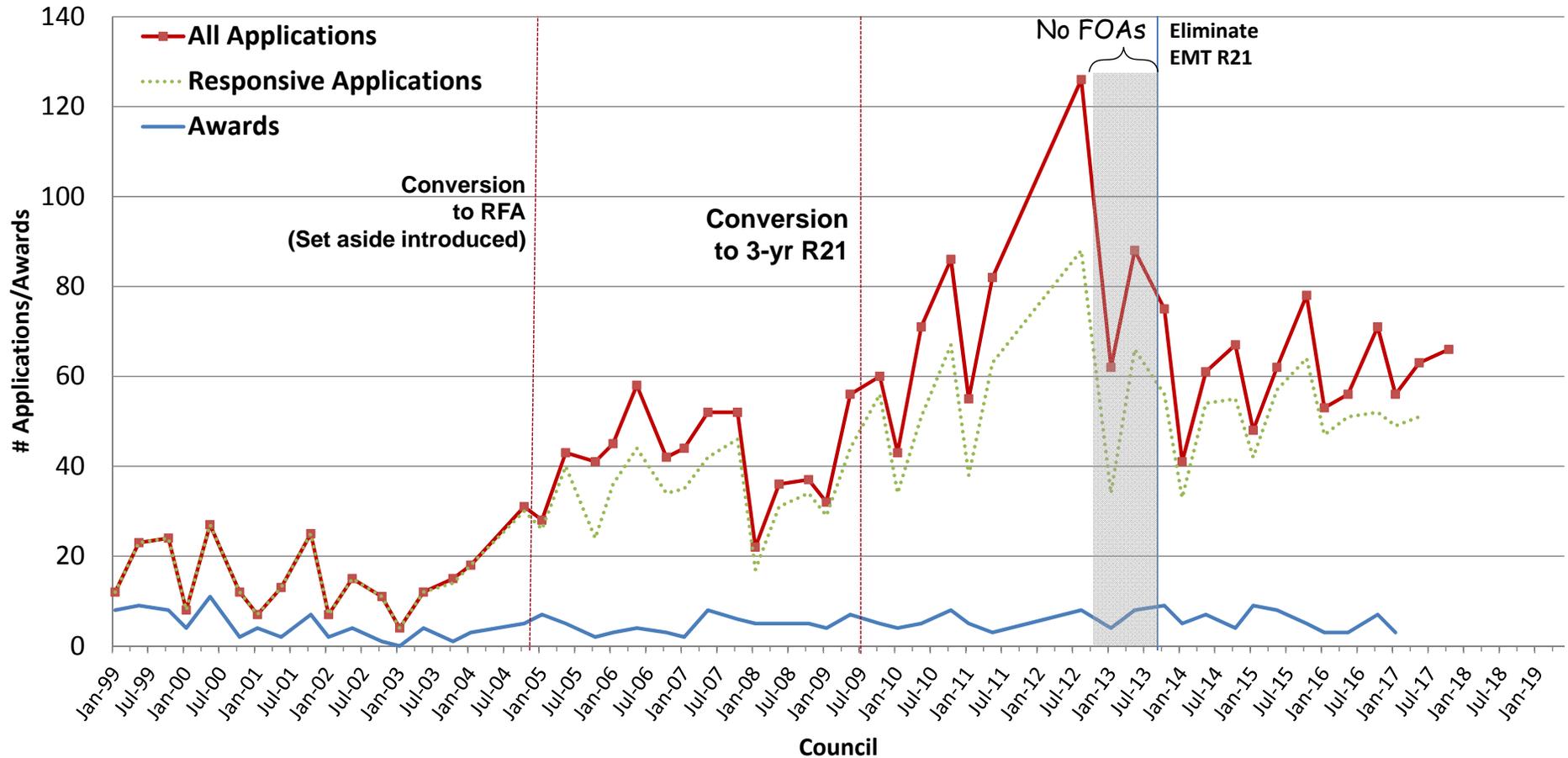
IMAT Evaluation Criteria

- number of publications that cite a specific IMAT award number;

- number of patent applications submitted to the US Patent & Trademark Office (USPTO);

- number of patent applications granted or approved by the USPTO based on patent applications that cite a specific IMAT award number in one of four government interest fields;

- number of IMAT-funded technologies now used in other NCI and NIH strategic initiatives; and

- follow-up case studies on previously funded technology development projects and platforms, including their current use by and utility to the extramural scientific and clinical communities.

- Conducted by Ripple Effect Communications with support from the NIH Evaluation Set-Aside program

- Assessed outcomes for all IMAT project prior to 2014 (705 unique awards)
  - archival data records, web-surveys, and phone interviews
  - Included web-survey of and archival data analysis for a comparison group and phone interviews with IMAT technology end-users

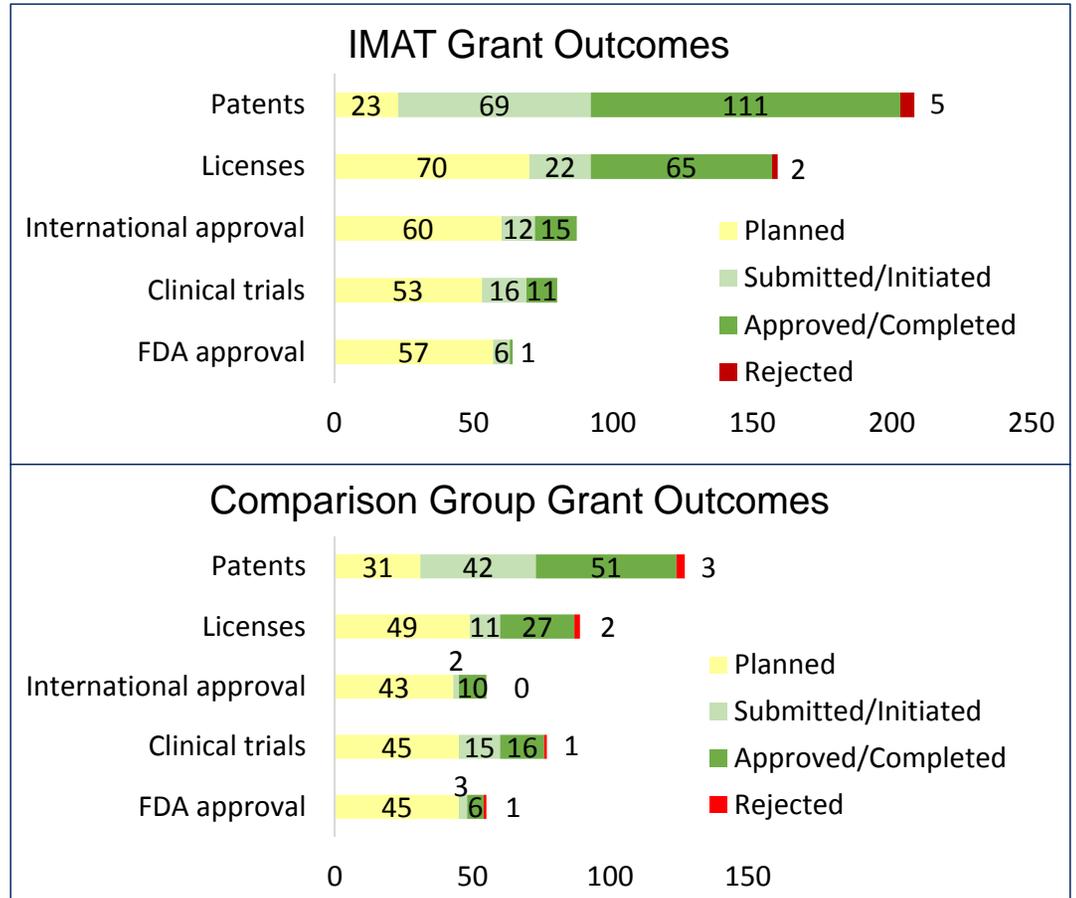- Based on an evaluation study design produced by Macro International during a prior Evaluation Feasibility Study for the IMAT program
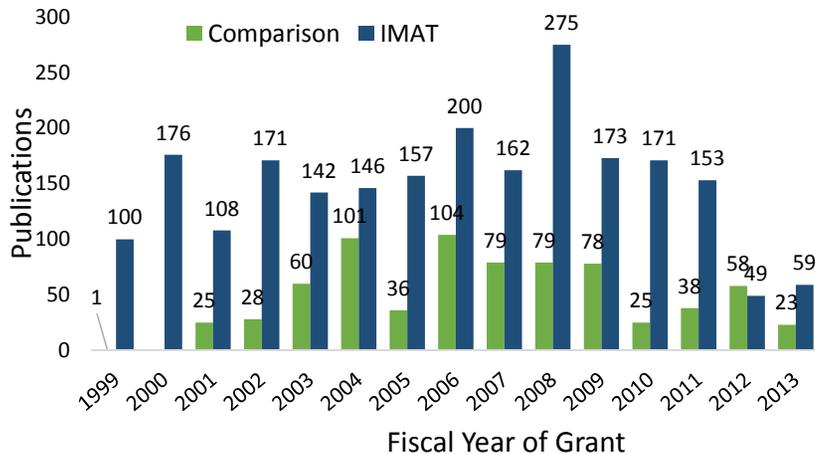
IMAT Program Award Breakdown (540 Total)

- R21: 334 awards
- R33: 206 awards
- SBIR/STTR
  - Phase 1: 123
  - Phase 2: 42

Comparison Group Breakdown (473 Total)

- R21: 331 awards
- R33: 9 awards
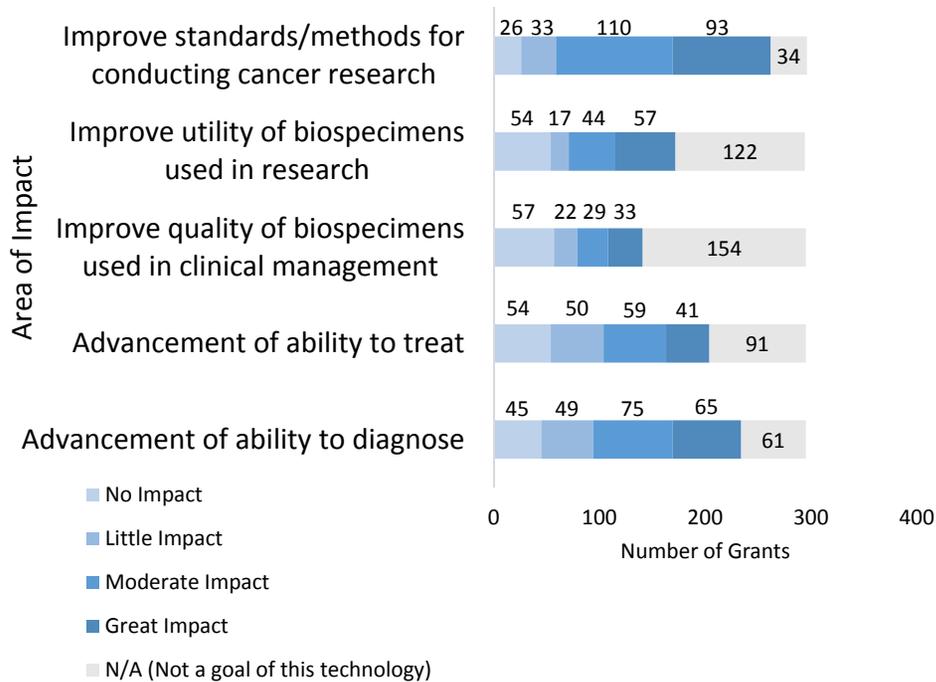- SBIR/STTR
  - Phase 1: 98
  - Phase 2: 35

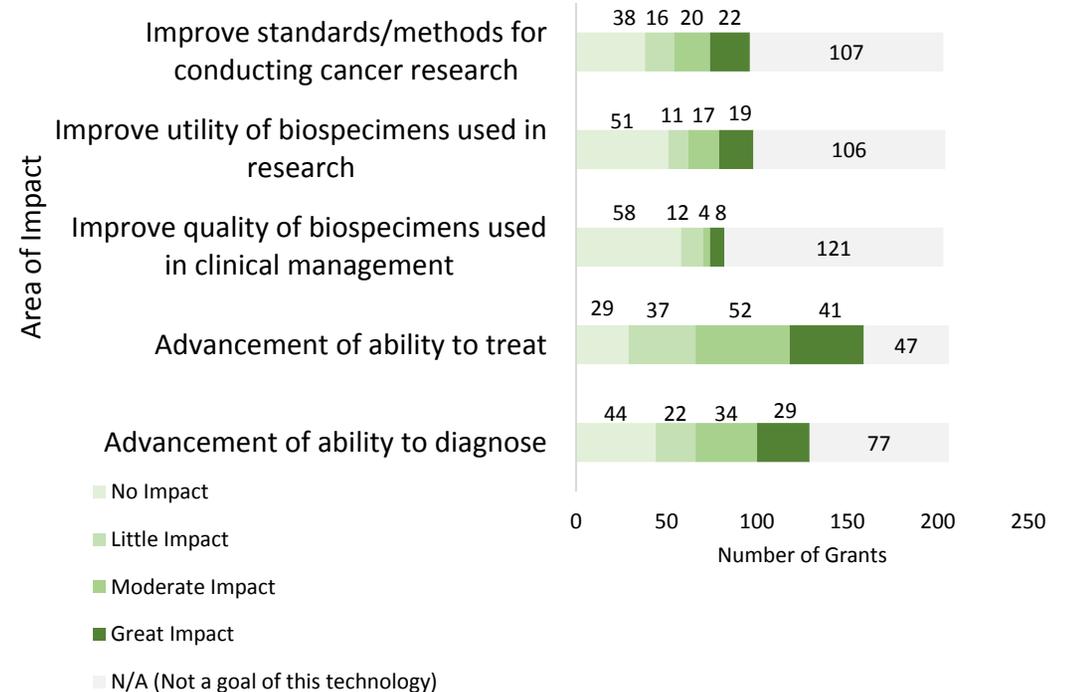**IMAT Grant Outcomes**

Outcome	Planned	Submitted/Initiated	Approved/Completed	Rejected
Patents	23	69	111	5
Licenses	70	22	65	2
International approval	60	12	15	
Clinical trials	53	16	11	
FDA approval	57	6	1	

Comparison Group Grant Outcomes

Outcome	Planned	Submitted/Initiated	Approved/Completed	Rejected
Patents	31	42	51	3
Licenses	49	11	27	2
International approval	43	2	10	0
Clinical trials	45	15	16	1
FDA approval	45	3	6	1

Diversity of the IMAT Portfolio

**Innovative Technologies for Cancer Research (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 R21 Portfolio (75 Active Projects)

Current R33 Portfolio (49 Active Projects)
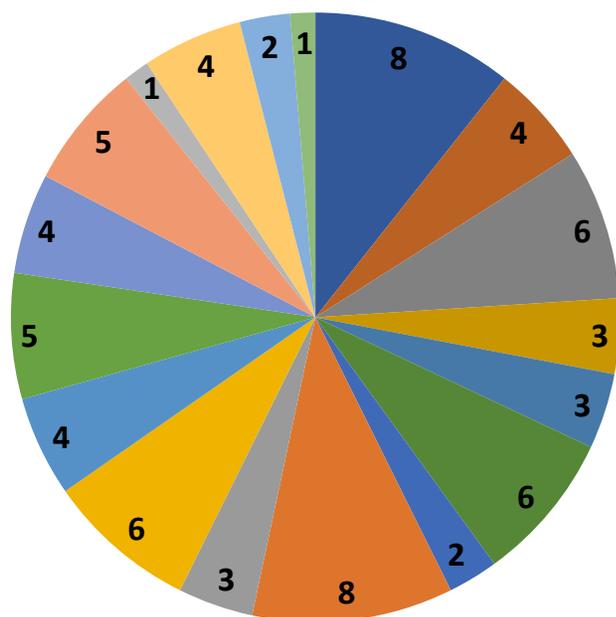
- clinical diagnostics
- drug screening
- epigenomics
- genomics
- glycomics
- imaging
- immunotherapy
- liquid biopsy
- metabolomics
- modeling
- novel biosensor
- pathway tools
- proteomics
- sample prep
- sample QA
- single cell
- transcriptomics
- treatment