Outcome Evaluation Summary Report

for the

National Cancer Institute Innovative Molecular Analysis Technology Program

August 2013

Executive Summary

An evaluation of the NCI Innovative Molecular Analysis Technologies (IMAT) program was engaged by the NCI Office of Science Planning and Assessment (OSPA) at the request of the NCI IMAT program director. The request was made as program evaluations are required to accompany any request for reissuance of Request for Applications (RFA) funding opportunities. As requested by the NCI IMAT program director, the evaluation strategy focused on only the most recently available data, scaled to match the request for a single year of issuance, as is the restriction of current NCI policy for RFA solicitations. Further, the strategy was designed to eliminate overlapping findings from prior evaluations and avoid overlapping findings from possible future evaluations of the IMAT program.

A broad variety of data, including technical progress reports, publication records, patent filings, NIH application records, and qualitative interviews were used as a part of this effort to address the following questions:

1. *Are submissions to and awards from the IMAT program significantly unique within the NCI portfolio?*
2. *Does the program work to support technology development appropriately?*
3. *Does the program support technologies useful to the cancer research community?*

OSPA collected some of the data necessary for the evaluation, but the majority of the data collection and analysis was executed by the Thomson Reuters – Custom Analytics group along with some data collection from the NCI IMAT program team to support the assessment of the program. Given the short time lag associated with all of the projects assessed, there was no expectation that individual indicators could support conclusive findings for the merits of the program. Rather, the data considered collectively were meant to provide an amalgam of evidence that might indicate whether or not the program was making progress against its stated goals.

Question I - Uniqueness of applications and awards in NCI portfolio

When compared to study sections with a similar focus to the IMAT program, IMAT applications are clearly more unique. The minimum calibrated dissimilarity score of the IMAT applications as a whole are greater than any of the companion sub-cohorts. This demonstrates that the IMAT program does indeed attract relatively unique applications, suggesting that the IMAT work would be unlikely to be conducted under other programs. In addition, the IMAT program has been successful in attracting applications and providing awards to applicants with limited previous experience in receiving grants from the NCI or NIH, especially as relevant to cancer. These findings suggest that IMAT is breaking new ground in its scope and fulfilling a need that would otherwise not be fulfilled by existing NCI research programs.

Question II – Effectiveness of the program structure for developing technologies

For R21 grantees, a significant amount of success has been attained in attaining project milestones. For the FY2010 project cohort, out of 25 projects awarded, only 2 projects have reported that no progress has been made on proposed milestones. In the majority of cases (N=19), milestones have been completed, exceeded, or are mostly complete. Furthermore, a number of R21 awardees submit applications for R33 awards, suggesting that R21 milestones

have been reached and the R33 mechanism can then be approached to further develop the proposed technology. FY2010 awardees also submitted 37 distinct patent applications (and 3 distinct provisional applications. Four patent awards were obtained and 6 IMAT-developed technologies were licensed. These findings suggest IMAT projects are generally making sound progress and are leading to useful technologies that have a significant amount of potential for continued development.

Question III – Effectively supporting useful technologies

Although relatively little time has elapsed since the FY2010 IMAT projects were initiated, the awardees have already achieved a commendable publication record. Over, there have been 108 publications resulting from the projects, with an average count of 4 publications per project. The average number of citations per project is 29, suggesting that other scientists find usefulness in the IMAT project research. It is important to understand that more publications (thus more citations) will likely occur within the next few years, so these counts will increase. In addition, NIH grant applications that indicate significant use of the IMAT technology have been identified. Of a total of an identified 60 applications, 13 have been funded and 8 are pending review. Therefore, the IMAT projects have directly impacted the scientific community and the relevant technologies are likely to be expounded upon in future research endeavors.

Background

The NCI Innovative Molecular Analysis Technologies (IMAT) program was conceived on the notion that innovative technologies hold the potential to radically accelerate progress in any field for which they are developed. The program was launched in 1998 as a broad solicitation for the development of highly innovative cancer-relevant technologies. The IMAT program was evaluated formally by external professional evaluation firms in 2007 and 2010, both of which concluded that it was meeting all of its scientific objectives.

The NCI has periodically modified the structure of the IMAT program to meet the changing needs and the landscape of technology development. In order to properly monitor the effectiveness of the IMAT program, and maximize its utility for the continuum of cancer researchers, clinicians and ultimately patients, it is important to engage in on-going evaluation of the IMAT portfolio and assess progress on the intended mission and goals of the program.

Program Goals

Mission: *To support the development, maturation, and dissemination of novel and potentially transformative next-generation technologies in support of basic, clinical, and epidemiological cancer research.*

The intended purpose of the IMAT program is to empower basic and translational research through targeted (and potentially disruptive) technology innovation. While the structure of the program has evolved, the goals remain largely unchanged:

- To catalyze innovative technology development for cancer research;
- To focus efforts from the technology-development community on cancer-related issues; and
- To accelerate the maturation of meritorious technologies from feasibility through development and into the hands of researchers and clinicians.

This IMAT outcome evaluation assesses the extent to which the IMAT program has been successful in making progress on these goals and will hopefully facilitate decision-making about whether the program should continue, be revised, discontinued, or whether the objectives should be met through other means.

Program Details

The IMAT program currently utilizes an atypical R21 award mechanism and a standard R33 award mechanism to support highly innovation technology platforms and approaches. The IMAT Program was most recently authorized to grant up to $10.5M (total costs) for new awards per year (resulting in roughly 30-40 awards, annually), where both the R21 and R33 awards may support up to 3 years or research. The IMAT portfolio generally includes between 60 – 100 active grants, with total award outlays (including new and continuing awards) of ~$20M - $30M per year. To date, the program has issued nearly 500 R21 and R33 awards. A comprehensive summary of all R21 and R33 awards made from the program are listed in Appendix A of this report.

The program is organized into two thematic areas supporting technology development.

1. *Innovative and emerging molecular and cellular analysis technologies*. These awards are designed to support highly-innovative molecular and/or cellular analysis technologies with significant potential for having a transformative impact in cancer research and/or clinic application.
2. *Innovative and emerging cancer-relevant biospecimen science technologies*. These awards focus on the development and application of novel and potentially transformative technologies to improve the quality and utility of biospecimens used in cancer research. Applications should offer novel capabilities to procure, process, and/or preserve human biospecimens and derivatives, or offer means to assess the biological integrity or quality of analytes for cancer research.

Awards for either theme support establishment of feasibility (R21) through validation (R33) of the technology for application in a basic, clinical, and/or epidemiological research settings. The program is managed by a trans-divisional team of program officers from across the extramural divisions of the NCI, and centrally coordinated by a program director from the NCI Office of the Director in the Center for Strategic Scientific Initiatives (CSSI). A list of participating program officers is included in Appendix B of this report.

Program Evaluation

The last approval for reissuance of IMAT solicitations in Fall 2011 included the following list of evaluation criteria, approved by both the NCI Scientific Program Leaders (SPL) and the NCI Board of Scientific Advisors:

1. the number of publications that cite a specific IMAT award number;
2. the number of patent applications submitted to the USPTO that cite a specific IMAT award number in one of four government interest fields;
3. the 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;
4. the number of IMAT-funded technologies now used in other NCI and NIH strategic initiatives; and
5. a series of 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.

Evaluation Strategy

New NCI policy requirements have been implemented with respect to Request for Applications (RFA) solicitations that permit reissuance for only a single year with multiple receipt dates for any RFA. As such, and in response to areas of interest from NCI leadership with regards to RFA concept reissuance, the strategy pursued for this evaluation covers the criteria identified above

while answering the questions listed below in an effort to assess the overall effectiveness of the program.

I. Are submissions to and awards from the IMAT program significantly unique within the NCI portfolio?
II. Does the program work to support technology development appropriately?
III. Does the program support technologies useful to the cancer research community?

As the request can only be for a single year of issuance for each of the past IMAT RFAs, the evaluation involved collecting only the most recently available data appropriate for answering each of the questions above, scaled to represent a single year of issuance.

Question I - Uniqueness of applications and awards in NCI portfolio

In addressing Question I, text-mining based analytical approaches were pursued in assessing applications and awards associated with IMAT RFAs issued with 3 receipt dates during FY2012 (CA12-002, CA12-003, CA12-004, and CA12-005). 432 applications were submitted to all RFAs, with 316 deemed responsive. It is important to consider only responsive applications submitted to the program, as inclusion of non-responsive applications would diminish the characterization of what is unique to the IMAT RFAs. These solicitations often get a significant number of applications that do not meet the scope of the solicitations, and as such these non-responsive applications are administratively rejected from the collection of applications to be reviewed any given round. Beyond text-mining comparisons, the principle investigators (PIs) of these applications were assessed for their record of past cancer-relevant research, and evidence of support for cancer research.

The text-mining strategies for comparing ***responsive*** applications submitted to the IMAT solicitations versus applications submitted to a variety of other funding opportunity announcements (FOAs) for the NCI leveraged prior experience using a similar text-mining based comparisons for applications submitted to the NCI *Provocative Questions (PQ)* FOAs. The specific aims of responsive applications submitted to the IMAT RFAs were with the same text in applications submitted and reviewed at the same period to other solicitations. The comparison group selected were applications reviewed by study sections with similar focus to the IMAT program, including the following review groups: Instrumentation and Systems Development [ISD]; Nanotechnology [NANO]; Bioengineering, Technology and Surgical Sciences [BTSS]; Modeling and Analysis of Biological Systems [MABS]; Gene and Drug Delivery [GDD]; and Biomaterials and Biointerfaces [BMBI].

Question II – Effectiveness of the program structure for developing technologies

In addressing question II, various measures of individual project outcomes were collected for awards from IMAT RFAs issued during FY2010, which accounts for awards made to the following RFAs: RFA-CA-09-004, RFA-CA-09-005, RFA-CA-09-006, RFA-CA-09-007 and RFA-CA-09-008. 322 applications were submitted to these RFAs, with 30 awards made, accounted for by 25 R21 awards and 5 R33 awards. Technical progress reports, the NIH applications database (QVR) records, associated journal publications, and other written material associated with the projects will be searched for evidence of progress made on developing the

various technologies proposed. Elements of interest included progress against proposed milestones, indications of patent submission, publications and bibliometric indicators of impact, and evidence of follow-up applications for further support of technology development or to otherwise apply the newly developed technology towards pursuit of biological hypothesis testing.

Another element of interest will be to assess the impact of the IMAT R21 award, which awards more money (up to $500k in direct costs) over a longer period (up to 3 years support) than the traditional NIH R21 award. These "3-year R21 awards" began in FY2009 at the urging of the NCI Board of Scientific Advisors specifically for awards from the IMAT program. While it is the consensus of the NCI IMAT Program Team that this analysis is still premature for this aspect of the program, there was interest in searching for any early indicators supporting this change. Of the 25 R21 awards granted in FY2010, 10 received support beyond that allowed by the standard NIH R21 mechanism.

Question III – Effectively supporting useful technologies

In addressing question III, the same awards evaluated for question II will be targeted. Technical progress reports, the NIH applications database (QVR), journal publications, and other written material associated with the projects were searched for evidence that the technologies developed were being applied towards cancer research. Elements of interest included bibliometric indicators of publication impact, evidence of new collaborations, evidence of licensing or other commercialization activity, professional recognitions, and evidence of follow-up applications for support involving the technology developed (both by the principle investigators or others). In addition to the data provided above, 9 projects were randomly selected for case-study interviews, using an interview protocol developed for past evaluations by the IMAT program. The protocol used is included as Appendix D in this report.

Evaluation Findings

QI:Uniqueness of applications and awards

As described above, two approaches were taken to assess the uniqueness of IMAT applications and awards. The text-mining task (described below) was pursued by the Thomson Reuters evaluation team involved in a similar screening of the applications to the NCI Provocative Questions RFAs. The approach involved using a combination of subject matter expert review and an automated process based on measuring the *dissimilarity* of specific aims text from applications submitted to the IMAT funding opportunities to specific aims text in a companion cohort of applications from other program solicitations. The companion cohort was constructed to have temporal and topical overlap with IMAT, but also to be large enough to include cases of unanticipated similarity to IMAT so as reduce the chance of an overestimate.

The procedure to estimate *dissimilarity* involved seven steps[1]

1. A companion cohort was specifically selected after thoughtful consideration by NCI IMAT program officers, OSPA program evaluators, and the Thomson Reuters evaluation team. The specific aims text of the companion was utilized in the comparison.
   1.1. This cohort included ~4,932 applications reviewed by 134 standing study sections (90% accounted for by 40 study sections) and 3,234 applications reviewed by 334 special emphasis panels (72% accounted for by 40 panels).
2. A "gold-standard" was established by the NCI IMAT program team by estimating the dissimilarities between a sample of 101 IMAT-companion cohort application pairs using a fixed scale between 0 and 1 where 1 was most dissimilar.
3. A text similarity score for each IMAT-companion cohort pair was generated using automated text similarity methods. Each IMAT application was scored against each companion cohort application generating a set of scores for each IMAT application.
4. A model was constructed from the "gold-standard" dissimilarity ratings and their corresponding auto-generated similarity scores, giving a best-fit formula for converting similarity scores with variable ranges to dissimilarity ratings in a fixed range (0-1).
5. **The reported metric, termed minimum calibrated dissimilarity (MCD), for each IMAT application was the *smallest calibrated dissimilarity* of that IMAT application compared to any application in the companion cohort.** Higher values of MCD thus correspond to larger dissimilarities to even the most similar companion application (see Figure 1.1). Using the minimum dissimilarity rather than similarity allows the measurement to follow the more common "higher values are better" interpretation.

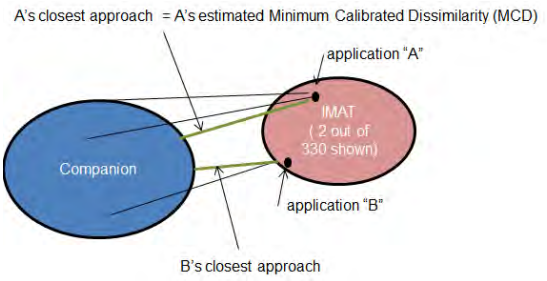


Figure 1: Minimum Calibrated Dissimilarity (MCD) is computed as the minimum dissimilarity of a given IMAT application to the companion cohort as a whole. Dissimilarity is represented here as analogous to a physical distance, making the MCD, the "closest approach" of an IMAT application to the companion. The lengths of the lines from IMAT to the companion correspond to the calibrated dissimilarity values (longer line=more dissimilar). In this example, A has a higher estimated dissimilarity from its closest companion application than B.

[1] See the Task 1 Appendix of the Thomson Reuters Summary Report for further details of each procedural step.

6. The accuracy of an MCD score to capture the *actual* dissimilarity of an IMAT application was assessed by a final quality review by NCI program scientists of MCD scores for a sample of 29 IMAT applications.
   6.1. This "final quality review" of MCD scores for IMAT->companion measurements resulted in a median error of +0.2 (estimate-true), indicating a slight overestimation by the algorithm of the MCD score, especially for higher dissimilarity scores.
7. In addition to measuring the distribution of IMAT MCDs for the IMAT->companion cohort pair, Thomson Reuters also examined 2 other pairs of cohorts, as an informal null hypothesis test. Since there is an assumed difference in the extent and character of the incentives in the IMAT program and programs that composed the companion cohort, DL examined two cohort pairs in which this difference could be assumed to be absent, namely IMAT compared internally to itself and the companion cohort compared to itself. Figure 2 summarizes the findings for these three comparisons.

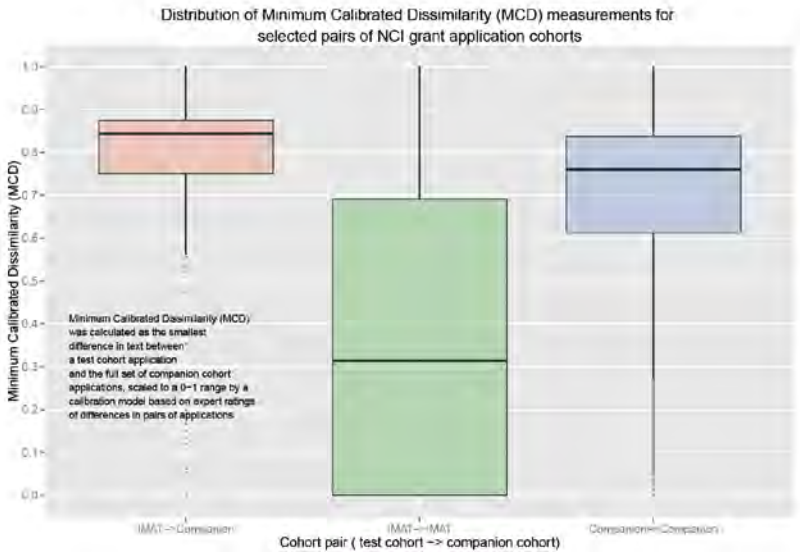
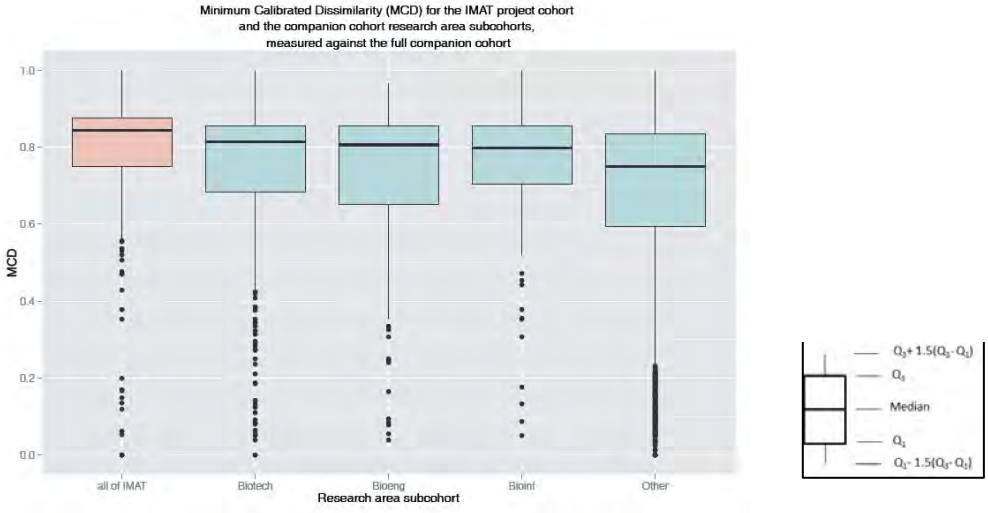


Figure 2: Distribution of the MCD scores for three groups: IMAT→companion cohort,; IMAT→IMAT; and companion→companion.

Several other pairs were formed using sub-cohorts of the companion based on their study section assignment. Sub-cohorts were selected based on study section assignment for each application. The categorization of study sections to either Biotech (predominantly technology development focused review), Bioeng (predominantly bioengineering focused review, with significant technology involved), or Bioinf (predominantly bioinformatics and statistical methods focused review) groups were executed by the NCI IMAT program officers familiar with these standing study sections. As shown in Figure 3 below, the median MCD for IMAT as a whole is greater than that of any of the companion sub-cohorts. Projects reviewed under the study sections and special emphasis panels focused on biotechnology, bioengineering, and bioinformatics appear to have a slightly higher median MCD than projects reviewed by other sections/panels. This is analogous to the higher MCD seen for IMAT vs. the entire companion than for the companion-to-companion measurement. An further breakdown of 20 cohort-pair comparisons were made, as well as breakdowns of MCD for selected cohort pairs by selected project characteristics (e.g. funded vs. not funded) are included in the appendix to the Thomson Reuters Evaluation Report Summary document.

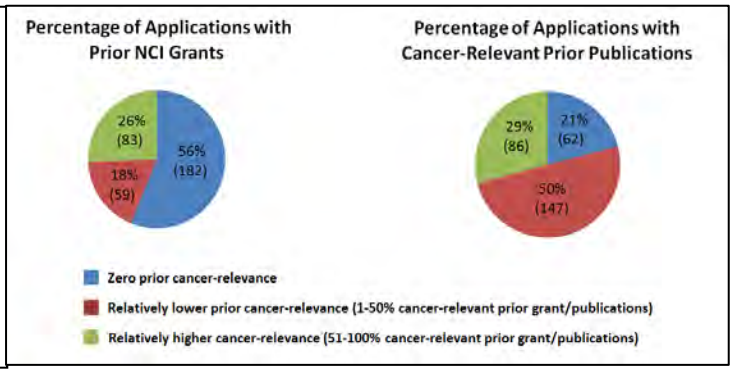
The first graph, Figure A1.4 below, shows how the distribution of minimum calibrated dissimilarities varies between the entire IMAT cohort and 4 research area subcohorts of the companion cohort, all measured against the full companion cohort.



The second task was also pursued by Thomson Reuters to investigate the degree to which the IMAT solicitations drew applications from investigators with a limited history of cancer-relevant research. The interest in understanding this element is that NIH is typically not known as a source for supporting technology development, specifically, so the IMAT solicitations are intended to focus the attention of technology developers on cancer-relevant research questions, where they might not have pursued such research otherwise.

Thomson Reuters assessed the same IMAT 2012 application portfolio used for the prior analysis from two perspectives: (1) whether the applicant was previously awarded a grant by the National Cancer Institute (NCI) and, (2) whether and the degree to which their prior publications (in the last 5 years) were relevant to cancer. The 2012 application portfolio for the IMAT program included 308 different project proposals.[2] As shown in Figure 4, they found that the IMAT solicitation was successful in attracting applications from (and, incidentally, providing awards to) investigators with a limited history of cancer-relevant research.

Figure 4.The breakdown of applications with zero, relatively lower and relatively higher prior cancer-relevant experience based on either having been previously awarded an NCI grant or having previously published cancer-relevant research. Fifty-six percent (N=182) of the 324 applications did not receive a previous grant from the NCI with 111 of these applicants not receiving any prior NIH grants and 71 having received prior NIH grants but no NCI grants.



[2] 432 total applications minus 116 non-responsive and 16 resubmitted applications.

Of the 62 applicants with no prior publication history (in the last 5 years) of cancer-relevant research, 3 of these won grant awards (out of 35 awards given that year). Of the 147 applicants with relatively less cancer-relevant research history, 20 of these won grant awards (out of 35 awards given that year).

QII: Supporting Innovative Technology Development

One unique element of the IMAT program is the requirement for investigators to propose quantitative milestones to serve as part of the technical review of applications. Progress against these milestones for supported projects was assessed by the assigned program officer through technical progress reports or otherwise through interactions with the investigator. NCI program staff made a thorough assessment of each of the R21 projects awarded during FY2010 (RFA-CA-09-00X awardees, N=25), which yielded the breakdown seen in Table 1.

Status of Progress	Number
Completed or exceeded all milestones	8
Mostly completed milestones	11
Limited progress on milestones	4
Unsuccessful altogether	2

Table 1. Breakdown of R21 progress on proposed milestones.

Another unique element of the NCI IMAT program is the phased structure of the IMAT program, offering a follow-up phase of support (via R33 awards) for projects in which the PI feels confident they have made sufficient progress on the R21 project. A requirement of the R33 application for those with prior R21 support is a discussion of progress against their originally-proposed milestones. Completing all milestones is only one of the review elements for the follow-up R33 application, so this element is necessary, though not on its own sufficient.

A comprehensive history of IMAT R33 applications and awards related to a previously held R21 award are shown in Table 2 on the following page. As the tables clearly show, a relatively steady percentage of all R21 awardees (including FY2010 awardees) submit R33 applications. Given that this evaluation was conducted in 2013, significantly more are expected from R21 awardees receiving grants since FY2010 in the coming years. 7 of the 11 FY2010 R21 awardees who submitted applications for R33 may still submit revised applications responding to the review critiques, and program officers have received indications from several more FY2010 R21-awarded investigators that they plan on submitting new R33 applications.

As indicated in the Evaluation Strategy section of this report, the structure of the R21 award fundamentally changed beginning with FY2009 awards. Before this period, the IMAT program R21 awards mirrored the standard NIH R21 award of no more than $275k in direct costs distributed over 2 years, with no more than $200k in direct costs in a single year. Since FY2009, the IMAT program began giving R21 awards with no more than $500k in direct costs distributed over 3 years, with no more than $200k in direct costs in a single year. In FY2010, there was a mix of 2-year R21 awards (N=15) and 3-year R21 awards (N=10).

Table 2. Comprehensive history of IMAT R33 applications and awards related to a previously held IMAT R21 award.

Applications Submitted		FOA Series for R21 Base Award										Total # Appl'ns	# of R33 Apps Received	% of all R33 Apps Received
	FOA series	PAR98	PAR99	PAR01	CA05	CA06	CA07	CA08	CA09	CA10	CA12			
# of R33 applications submitted based on a prior R21 award	PAR98	0										NA	24	NA
	PAR99		0									4	48	8%
	PAR01			1								11	79	14%
	CA05											8	68	12%
	CA06		0									5	60	8%
	CA07	1										21	105	20%
	CA08	0	0	0	0							8	49	16%
	CA09	0	0					0				9	42	21%
	CA10	0	0	1	0							15	61	25%
	CA12	0	0			0						22	112	20%
	CA13*	0				0					0	13	64	20%
	Total	**14**	**16**	**19**	**11**	**9**	**16**	**12**	**15**	**4**	**0**	**116**	**712**	16%
	# resubmitted	3	2	4	5	3	4	3	4	0	0			
	Total # R21 awards per FOA	25	44	38	29	21	60	32	25	30	22			
	% of R21 Awds from base FOA	**44%**	**32%**	**39%**	**21%**	**29%**	**20%**	**28%**	**44%**	**13%**	0%	*2 of 3 rounds of receipt accounted for		

Awards Granted		FOA Series for R21 Base Award											success rate per R33 FOA	Total # of R33 Awards Given	% of R33 Awards Given
	FOA series	PAR98	PAR99	PAR01	CA05	CA06	CA07	CA08	CA09	CA10	CA12	Total			
Successful R21 → R33 Transition	PAR98	0										0	NA	9	NA
	PAR99		0									1	25%	14	7%
	PAR01		0									2	18%	17	12%
	CA05	0		0								2	25%	8	25%
	CA06		0	0	0							1	20%	7	14%
	CA07		0			0						4	19%	14	29%
	CA08	0	0	0	0							2	25%	3	67%
	CA09	0	0	0		0	0	0				1	11%	5	20%
	CA10	0	0	0	0							6	40%	11	55%
	CA12	0	0	0		0	0			0		4	18%	14	29%
	CA13**	0				0					0				
	Total	**4**	**2**	**2**	**4**	**2**	**3**	**4**	**2**	**0**	**0**	**23**			
Success Rate per attempt for base R21 FOA		**29%**	**13%**	**11%**	**36%**	**22%**	**19%**	**33%**	**13%**	0%			**1 of 3 rounds accounted for		

NOTE: Table does not account for 102 successful phased innovation awards (R21/R33 combined) in which R33 awards were made by programmatic approval if PI met proposed milestones from R21 period (discontinued in FY2008).

Another way of assessing the appropriateness of the IMAT program for supporting innovative technology development useful to the research community is to monitor evidence of commercial activity involving the supported technology. The consideration is that resources and effort are required to pursue patent protection and generally commercialization activity is justified because a significant market need has been identified. The US Patent & Trademark Office certifies patent protection for legitimately new ideas with some utility for society. The Thomson Reuters evaluation team queried the USPTO database for evidence of patent applications and awards stemming from the same group of FY2010 awardees. This information is provided in Table 3, along with evidence derived from technical progress reports evaluated by NCI program officers.

Table 3. Patent activity associated with FY2010 IMAT-awarded projects.

Method to Identify Application/Award	Provisional Patent Application	Patent Application	Patent Award	Licensure
Acknowledgement of IMAT Grant Number in Patent Record	0	1	0	0
Match by Technology Short Name and Investigator Name	0	31	2	0
Technical Progress Reports	4	45	2	6
Distinct Total	**3**	**37**	**4**	**6**

One common metric for determining whether or not a new technology was successfully developed is to consider any publication record, focused on novel research publications in peer-reviewed journals (rather than reviews, conference abstract submissions, or letters, for example). An assessment of these publications often involves an assessment of the impact of each publication through a variety of bibliometric measures, which is handled more appropriately a consideration of the usefulness of this research. Therefore, analysis of the publication record associated with projects awarded initially in FY2010 is included in the next section.

QIII: Usefulness of Supported Technologies

Three approaches were taken to assess the utility of applications awarded in FY2010. The first involved an assessment of the bibliometric measures on qualified publications (as referenced in the last section). The second approach involved a screening of the NIH application database (using the Query View Report [QVR] database) for any applications to NIH for follow-up research, where the technology developed under IMAT support is a significant component of the new research project described in the application. The third approach involved interviews with nine randomly selected grantees to provide a more qualitative assessment of grantee experience, and also to provide continuity with prior evaluations of the program by using the same interview protocol.

Tracking publications generated by funded research projects, and various associated bibliometrics, are a standard means of assessing outcomes for any research program. Provided in Table 4 below is a summary of the bibliometric analysis for this task, also assembled by the

Thomson Reuters evaluation team. At the time of this evaluation, 8 of the 30 projects[3] awarded in FY2010 were either in no-cost extension or still active. It must further be noted that many research projects yield additional publications 2 years beyond the closeout, and an additional 6 months (at a minimum) should be allowed for the accumulation of citation activity to assess the potential impact of these. Therefore, the findings summarized below should be considered as preliminary, rather than as final, bibliometric finding for these projects. Information defining some of the metrics in Table 4 are included below, but are discussed more thoroughly in the Thomson Reuters Evaluation Report Summary document.

Table 4. Summary of bibliometrics based on citations

	2-yr R21 (15 projects)	3-yr R21 (10 projects)	R33 (5 projects)	Total (30 projects)
Total Publications[4]	53	43	12	108
Average Publications (Maximum)	4 (17)	4 (14)	2 (5)	4 (17)
Average Total Citations (Maximum)	28 (123)	40 (216)	9 (24)	29 (216)
Average Cancer-Relevant Citing Publications (Maximum)	4 (21)	3 (11)	1 (5)	3 (21)
Average Prestige Ratio (Maximum)	29% (69%)	40% (77%)	18% (50%)	31% (77%)
Median Impact Factor Quartile (Minimum)	1 (1)	1 (1)	2 (1)	1 (1)
Median Citation Benchmark Quartile (Minimum)	1 (1)	2 (1)	1 (1)	2 (1)

Bibliometric measures:

- Prestige Cites/Prestige Ratio: The Impact Factor ranking of a citing publication's journal for each of its assigned Journal Subject Categories is obtained as a percentile. If the minimum percentile is <=10%, which is to say that the citation is coming froma journal in the top 10% of journals in that subject category, then the citing publication is considered prestigious. Prestige ratio is the fraction of prestige citations over all citations times 100.
- Impact Factor Quartile: All journals in a Journal Subject Category (262 categories) are ranked and assigned a quartile according to their Journal Impact Factor within each journal subject category. Quartile 1 is the quartile with the higher journal impact factors.
- One-Year and Two-Year Citation Benchmark Quartile: The one-year (two-year) citation counts of all articles published within 6 months, in the same journal, and the same document type as the IMAT publication being analyzed are ranked and assigned a quartile within the appropriate journal subject category. The quartile position of the IMAT publication one-year (two-year) citation count is then determined where quartile 1 contains those with the higher citation counts.

[3] 2 projects still active and 6 projects under no-cost extension.

[4] These publications are indexed in Web of Science with citation data available.

The overall breakdown of these Publication records indicate useful contributions to the field across both R21 and R33 awards, smaller R21 (2-yr, $275k DC award cap) and larger R21 (3-yr, $500k DC award cap) awards, and by award solicitation series or theme (molecular & cellular analysis technologies [IMT/EMT] versus biospecimen science technologies [BSP]). These breakdowns are shown in Figure 5 & 6 below. Breaking down by solicitation theme is useful beyond the thematic distinctions because EMT R21 awards and BSP R21 awards were limited to standard NIH R21 time and budget caps. See Appendix A for a breakdown of these award types.

Table 5. Publication record broken down by award type

	Count	All Publications	Ave	Max
R21 Projects	25	114	4.56	18
R33 Projects	5	14	3.00	7
All Projects	30	128	4.27	18
Further R21 breakdown				
	Count	All Publications	Ave	Max
2yr R21	15	61	4.07	18
3yr R21	10	53	5.30	16

Table 6. Publication record broken down by solicitation theme

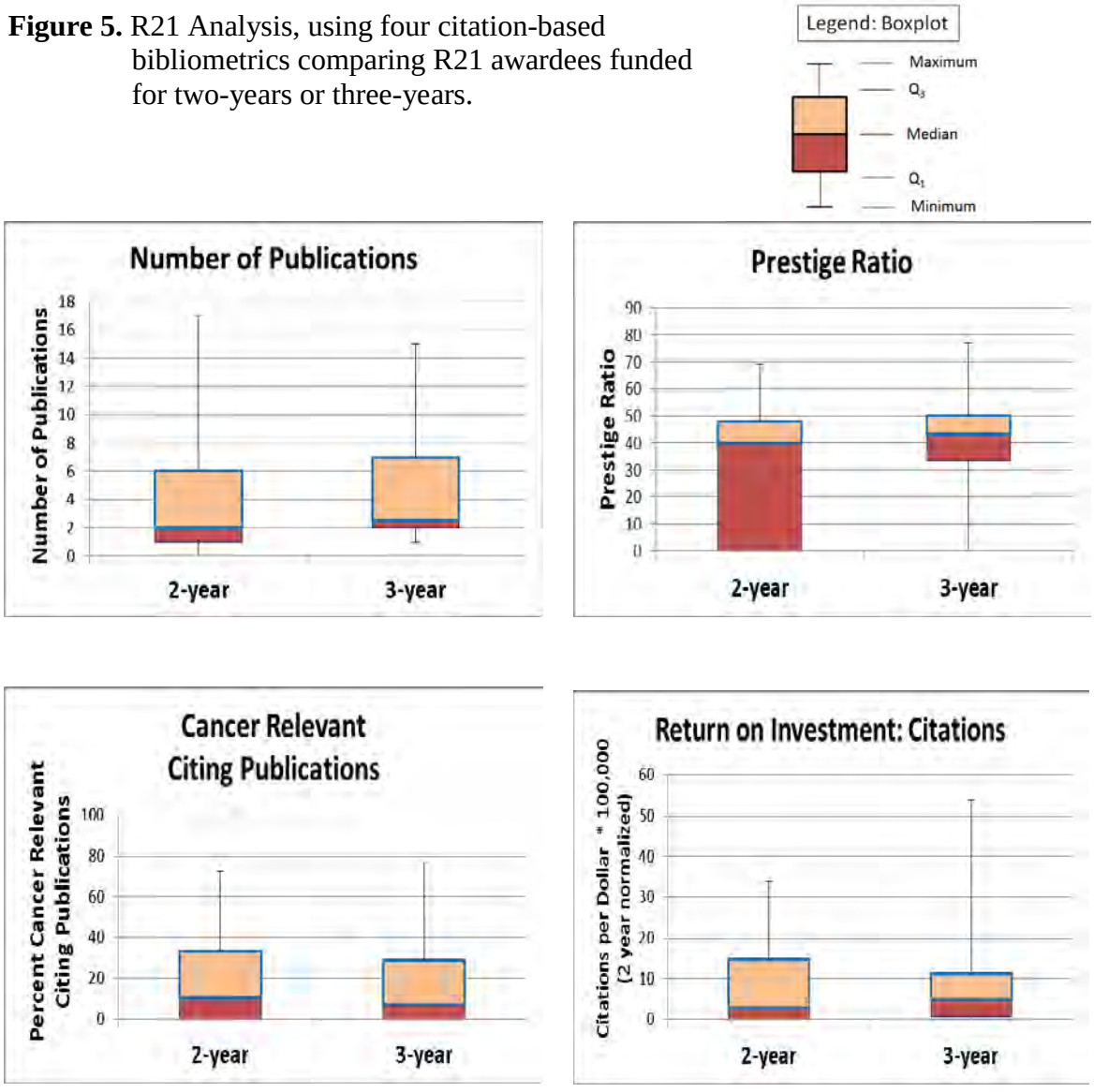
	Count	All Publications	Ave	Max
IMT [3-yr R21]	14	62	4.43	16
EMT [2-yr R21 & R33]	11	27	2.45	8
BSP [2-yr R21 & R33]	5	39	7.80	18
All Projects	30	128	4.27	18

The short-term assessment of outcomes suggested no significant difference in the median (examined with the Mann-Whitney U test[5] between the 2-year and 3-year level of R21 support

[5] The Mann-Whitney test is a nonparametric test (i.e. does not assume the data follow any particular distribution such as a normal distribution) and provides a more robust, conservative test for the statistical significance of an observed mean or median difference between two groups. The test uses a ranking of the intermixed values observed in two groups. Under the null hypothesis that the two groups do not have a location (e.g. median) difference, it computes the probability (p value) of the observed ranks. If this probability is below the significance threshold (a=0.05), then the null hypothesis is rejected and the group median difference is significant at the 0.05 level. The 2-year and 3-year groups do not show a significant difference by this test. However, the Mann-Whitney also assumes that the two groups have distributions of similar shape. Although the boxplots show obvious visual differences, plots of the estimated distributions are visually more similar. A sensitivity analysis using either alternative nonparametric tests or bootstrap methods would be needed to assess the risk in applying the test under these conditions, but note that with this low sample size (N=25 / 15 2-year and 10 3-year) there is little power with any test to detect anything except a large effect. The large visual difference in the first quartile (Q1)

groups, although there are visual differences in the interquartile ranges and in the first quartile for the number of publications and prestige ratio, with the 3-year level groups having a higher Q1 value. Figure 5 displays boxplots for some variables which suggested slight differences between the groups. Future analysis of these two groups is recommended, using outcomes data collected 2 years after the end date of the grant to provide a longer-range view of outcomes associated with the program.

Figure 5. R21 Analysis, using four citation-based bibliometrics comparing R21 awardees funded for two-years or three-years.



value for the prestige ratio is caused by having 7 applications in the 2-year group with 0 prestige cites and 2 such applications in the 3-year group and by the nature of the ratio -- the lowest non-zero value is 33.33 = 1 prestige cite out of 3 total cites.

As described above, the IMAT program team screened the NIH database using the QVR database tool, to find new applications submitted to the NIH that indicate significant use of the technology supported by one of the FY2010 IMAT awards. 60 new applications were identified in QVR, based on 18 (of 25) IMAT R21 projects and 3 (of 5) IMAT R33 projects. Of these 60 applications, 13 have been funded and 8 are pending review. Applications were submitted in roughly equal proportion in response to technology-focused solicitations (29 of 60) and non-technology focused solicitations (31 of 60). Nearly a quarter (13) of the new applications were R33 applications to the IMAT program for follow-up support on allegedly successful R21-supported projects, with the remainder of applications submitted to a broad variety of NIH FOAs. Regardless of the solicitation focus and the review panel, summary statements (SS) from reviewed applications included some expression of enthusiasm specifically for the IMAT-supported technology platform in a significant majority of all applications. The tables provided below provide further breakdown of this analysis. A list of successful awards, excluding the successful IMAT R33 applications, is included as Appendix C.

Table 7.Status of all submitted applications

Pending	8
Funded	13
Not funded	39
Total	60

Table 8. Follow-up Applications to IMAT Program

Pending R33	4
Funded R33	2
Not funded R33	7
Total	13

Table 9. Based on R21

Pending	6
Funded	12
Not funded	35
Total	53

Table 10. R01 applications?

Pending	1
Funded	7
Not funded	16
Total	24

Table 11. Based on R33

Pending	2
Funded	1
Not funded	4
Total	7

Table 12. R21 Applications?

Pending	4
Funded	2
Not funded	12
Total	16

Table 13. IRG enthusiasm for IMAT-supported technology in SS

Focus of FOA	Technology focused	Non-Tech focused
# Submitted Applications	29	31
Mentioned in SS	27	18

Table 14. Primary IC Referral for application

NCI	32
Other	28

NOTE: most applications with referral outside NCI are still focused on cancer

Finally, nine awardees from were interviewed regarding their experience with the IMAT program and assessing the impact of the awards on their research and the impact of their technology in the field.

IMAT Prinicipal Investigator Interview Summary

The 9 randomly selected interviews with principal investigators on projects awarded in FY2010 followed the protocol detailed in Appendix D. Below is a summary of what was learned through those conversations.

Background of the investigator and proposed IMAT technology

Several of the IMAT investigators had received NIH funding support for cancer-relevant research prior to receiving their IMAT awards, including R01, R21, R29, and K01 awards. In addition, several of the investigators had also received funding support from other sources, such as the U.S. Department of Defense (DOD), the National Science Foundation (NSF), various foundations, and universities. Since receiving the IMAT award, some of the investigators have applied for cancer-relevant R01 and other NIH grants and some of these have been awarded. Other investigators are in the process of applying for additional NIH funding and, in some cases, are working with IMAT staff to identify such opportunities. Some of the investigators have subsequently obtained funding from other government agencies, universities, and private foundations.

IMAT structure

Overall, the investigators stated that it was not very difficult to frame their ideas to fit within the context and themes of the IMAT program. Quite typical were comments such as "*I had specific novel ideas about technology development, and they fit well within the IMAT paradigm. As far as I know there are no other mechanisms to fund this type of work.*" The IMAT application process requires that quantitative milestones be developed. Overall, investigators indicated that milestone development was slightly challenging because of the lack of preliminary data and the need to predict findings, although this requirement was met without extreme difficulty. In most cases, investigators developed their milestones without direct IMAT staff assistance. Nearly all of the investigators reported that milestones have been met or exceeded, although in a few cases this was still in progress (one investigator indicated the need for a no-cost extension for this reason).

Application and dissemination of the research/technology

Typically, the IMAT investigators had worked on their area of technology interest before applying for the IMAT funding. Investigators are moving their technology toward widespread application and commercialization but, in some cases, this is a still a work in progress. Some of the investigators cited funding challenges in the private sector as a concern regarding application. In other cases, the technology is currently being used, especially in clinical trials and medical school environments. Many of the investigators are collaborating with researchers in the United States and abroad to refine their technology.

Specific feedback on awarded project

The IMAT investigators unanimously agreed that they would not have been able to pursue the technology development without the IMAT grant. Comments such as *"without this IMAT grant, funds [, I] would not have been available to hire the necessary personnel to move development of this technology forward. If [there were] no IMAT funding, [I] possibly would have internal start-up funds, but they are very meager"* were common. Some of the investigators are aware of NIH research that their IMAT work played a role and others have received related grants from other sources, such as DOD and NSF. The investigators were asked if they had any suggestions for improvement to the program. Some of the investigators suggested more opportunities for networking. Others mentioned more specific guidance regarding what program requirements are and accelerating the process by which grants are awarded. Overall, investigators were highly complementary of the program and emphasized its critical role.

Evaluation Summary

Question I - Uniqueness of applications and awards in NCI portfolio

When compared to study sections with a similar focus to the IMAT program, IMAT applications are clearly more unique. The minimum calibrated dissimilarity score of the IMAT applications as a whole are greater than any of the companion sub-cohorts. This demonstrates that the IMAT program does indeed attract relatively unique applications, suggesting that the IMAT work would be unlikely to be conducted under other programs. In addition, the IMAT program has been successful in attracting applications and providing awards to applicants with limited previous experience in receiving grants from the NCI or NIH, especially as relevant to cancer. These findings suggest that IMAT is breaking new ground in its scope and fulfilling a need that would otherwise not be fulfilled by existing NCI research programs.

Question II – Effectiveness of the program structure for developing technologies

For R21 grantees, a significant amount of success has been attained in attaining project milestones. For the FY2010 project cohort, out of 25 projects awarded, only 2 projects have reported that no progress has been made on proposed milestones. In the majority of cases (N=19), milestones have been completed, exceeded, or are mostly complete. Furthermore, a number of R21 awardees submit applications for R33 awards, suggesting that R21 milestones have been reached and the R33 mechanism can then be approached to further develop the proposed technology. FY2010 awardees also submitted 37 distinct patent applications (and 3 distinct provisional applications. Four patent awards were obtained and 6 IMAT-developed technologies were licensed. These findings suggest IMAT projects are generally making sound progress and are leading to useful technologies that have a significant amount of potential for continued development.

Question III – Effectively supporting useful technologies

Although relatively little time has elapsed since the FY2010 IMAT projects were initiated, the awardees have already achieved a commendable publication record. Over, there have been 108 publications resulting from the projects, with an average count of 4 publications per project. The average number of citations per project is 29, suggesting that other scientists find usefulness in the IMAT project research. It is important to understand that more publications (thus more citations) will likely occur within the next few years, so these counts will increase. In addition, NIH grant applications that indicate significant use of the IMAT technology have been identified. Of a total of an identified 60 applications, 13 have been funded and 8 are pending review. Therefore, the IMAT projects have directly impacted the scientific community and the relevant technologies are likely to be expounded upon in future research endeavors.

Appendix A. Comprehensive listing of all R21 and R33 awards granted through the IMAT program

IMT R21		IMT R33		EMT R21		EMT R33		BSP R21		BSP R33	
PAR98-067	25	PAR98-067	26								
PAR99-100	30	PAR99-100	28	PAR99-102	14	PAR99-102	20				
PAR01-104	15	PAR01-104	18	PAR01-106	23	PAR01-106	15				
CA05-002	17	CA05-002	2	CA05-003	8	CA05-003	5	CA05-004	4	CA05-004	1
CA06-002	9	CA06-002	4	CA06-003	8	CA06-003	3	CA06-004	4	CA06-004	1
CA07-001	5	CA07-001	4	CA07-002	9	CA07-002	2	CA07-003	3	CA07-003	0
CA07-015	8	CA07-016	1	CA07-017	1	CA07-018	0	CA07-022	1	CA07-023	0
				CA07-019	4			CA07-024	0		
CA07-033	16	CA07-034	2	CA07-035	9	CA07-036	4	CA07-037	4	CA07-038	0
CA08-006	16			CA08-007	11	CA08-008	3	CA08-009	5	CA08-010	0
CA09-008	14			CA09-006	7	CA09-007	4	CA09-004	4	CA09-005	1
CA10-005	16			CA10-003	11	CA10-004	9	CA10-001	3	CA10-002	2
CA12-002	19					CA12-003	11	CA12-004	3	CA12-005	3
Total	**190**		**85**		**105**		**76**		**31**		**8**

- 495 awards total since 1998. NOTE: Table includes 102 R33 awards granted programmatically from phased innovation awards (R21/R33 combined application)
- IMT = Innovative Molecular Analysis Technologies for cancer research
- EMT = Emerging Molecular Analysis Technologies for cancer research
- BSP = Innovative and emerging technologies for cancer relevant biospecimen science or sample preparation
- Grey shading indicates no FOA offered for this category at that time

Appendix B. NCI IMAT Program Team

	DOC	Contact
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NOTE: This list does not include the significant efforts contributed by the NCI Division of Extramural Activities, especially from Scientific Review Officers of the Special Review and Logistics Branch. Special mention of Dr. Jeffrey DeClue and Dr. Donald Coppock from that office is well warranted.

Appendix C. List of non-IMAT awards from NIH that indicate significant use of technology supported by an IMAT FY2010 award

Follow-up Award	Priority Score	Project Title
R01GM104047	24	Modeling human phosphorylation networks through kinome-wide signaling
R01CA159467	10	Cdk4/6 inhibitor therapy for GBM
R01CA169345	14	Analysis of STAG2 inactivation and aneuploidy in human cancer
R01HD070038	20	Physical and Chemical Cues that Guide Sperm Migration
R01HL108016	21	Inherited genetic risk factors common to COPD and lung cancer
R21AI100216 (PIA R21/33)	36	Multiplex nano-diagnostic array for detection of emerging pathogens
R01GM106027	29	Spatially-delineated system-level analyses and control of cytoskeletal regulation
R21GM103536	34	Development of nano-proteomic technologies
R43/44-GM090386	20	High-throughput cell migration assay amenable to HCI
R01CA170546 (PQ)	13	Methylation Suicide in Cancer
P01CA168585 (co-PI proj 4)	41	Microfluidic diagnostics for monitoring of BRAF-inhibitor resistance in melanoma

Appendix D. Interview protocol for IMAT principal investigators

Hello, is this is Dr. _____? My name is _____, and I'm a member of the project team working with NCI to evaluate the Innovative Molecular Analysis Technologies Program. I work for _____, charged with the task of conducting this evaluation. We greatly appreciate your willingness to answer a few questions about the IMAT Program and the technology funded by the IMAT award. You have been selected because you received IMAT funding for [provide grant numbers and names]. I want to assure you that your participation is voluntary and that your responses will be kept strictly confidential. We would like you to be totally candid. We will take careful precautions to ensure that your name cannot be associated with your responses. We expect our discussion to take about ____ minutes. Do you wish to proceed at this time?

If yes: Good. We realize that your time is valuable, so let's get started.
If no: Would you like to schedule another time for this discussion? (Try to schedule another time and thank the respondent for his or her willingness to participate.)

Our interview is divided into four sections, specifically:

- Your background as PI for the IMAT grant(s) and your proposed technology for your IMAT grant(s)
- The structure of the IMAT Program
- The application and dissemination of the proposed technology or research
- Specific information related to the IMAT grant

Background of PI (prepare by looking at the individual's summary statement)

1. Had you received support to pursue cancer-relevant research prior to your IMAT award?
2. Have you received support to pursue cancer-relevant research since your IMAT award?

IMAT Structure

1. Was it difficult to frame your idea within the context/themes of the IMAT Program?
   a. Can you describe (generally) what made it difficult?
   b. What would have made it easier to frame?
2. How did you develop your milestones? Did you get input from IMAT staff regarding your milestones? If there were issues associated with developing your milestones, do you have any recommendations on what the NCI could do to be more helpful?
3. Did you reach your milestones? If not, what happened when the milestones were not reached by the end of the grant?

Application and Dissemination of the Research/Technology

1. Did the technology that you developed under the IMAT Program have any relation to an earlier technology used by you or someone else?
2. Is this technology ready for widespread application or already being used in the research community?
   a. What do you see as the eventual outcome of this technology?
   b. How do you envision achieving this outcome?
3. Could you describe some ways in which you have been able to apply your research/technology?
4. Are you aware of others who are using your research/technology? Are you aware of any additional technologies that have been developed as a result/extension of the technology you developed from your IMAT grant?
   a. Are you aware of how this use began?
   b. Are you aware of an impact that your activities have had on other researchers in the field?
5. Can you report on any efforts to commercialize this technology, or do you otherwise have any plans to commercialize this technology? To the degree that you are able, please provide details on any patent or licensing activities that you are aware of, and which organizations are involved.

Our intention with the next few questions is to identify ways in which your technology is being applied or disseminated.

6. According to our research, you have published [xx] articles related to your IMAT grant. Would you agree with this list or are there more/fewer publications related to this research/technology?
7. Do you list the grant number on all publications associated with this grant?
8. Have others been involved with your grants, including any of your students/junior investigators who have taken the initial technology and moved forward with it?

PI's Specific Grant

1. Would you have pursued development of this particular technology without the IMAT funding?
   a. If so, what mechanisms would you have pursued/used?
2. Are you aware of any research supported by the NIH (e.g., R01), in which your IMAT-supported technology played a major role? If so, could you very briefly describe that work and who the primary investigators were? [Looking for enough information to find the award]
3. Are there other grants that you are currently receiving in which your IMAT-supported technology (e.g., NSF, DOD, NIST) plays a major role?
4. Were IMAT funds leveraged to increase research funding/support from other sources? (If yes, please explain.)

This concludes the structured interview/discussion. Do you have any questions regarding the interview? Thanks so much for your time and input to this study, and please don't hesitate to contact the IMAT program director, Tony Dickherber, with any additional questions or concerns.