The Innovative Molecular Analysis Technologies

(IMAT) 2020 Program Evaluation Report

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Introduction and Panel Charge

The Innovative Molecular Analysis Technologies (IMAT) program was established by the National Cancer Institute (NCI) to spur highly innovative technology development efforts addressing critical needs in cancer research. The program was initiated in 1998 and has been renewed roughly every 3 years; it was last renewed in 2017.

The IMAT program supports the development, technical maturation, and dissemination of novel and potentially transformative next-generation technologies through an approach of balanced but targeted innovation relevant to the full breadth of the cancer research spectrum. The IMAT program is housed in NCI's Center for Strategic Scientific Initiatives (CSSI) and its management team is comprised of representatives from all of the extramural divisions of NCI and members of the Office of the Director. The trans-divisional, multidisciplinary nature of the management team is a unique feature and strength of the IMAT program and promotes a consolidated yet balanced representation of technology interests and needs across NCI. In support of its mission, the IMAT program utilizes a variety of investigator-initiated research-project grant mechanisms while retaining a strong commitment to diversity and to the training of scientists and clinicians across disciplines.

The IMAT program has adjusted its structure and budget over time to match institutional and environmental conditions. In 2003, the program terminated the use of Program Announcements (PAs) to solicit applications and started using Request for Application (RFA) solicitations, which allowed for unique application and review arrangements. It also published a set-aside budget, guaranteeing a minimum investment by NCI in these awards to the community. During that same period, it was decided that the IMAT program would no longer offer support for proposals to develop informatics technologies or to advance in vivo or whole-body imaging tools. However, the IMAT program also started a new series of funding opportunities for proposals focused on improved sample-preparation technologies. In 2008, the program changed the R21 mechanism to allow larger awards for a 3-year award period and discontinued use of the "phased award" mechanism that allowed for a linked R21 and R33 award to applicants. In 2017, the program launched a series of Competitive Revision funding opportunities that seek to encourage the incorporation of IMAT-supported technologies into ongoing hypothesis-driven research efforts (e.g., active R01, U01, and P50 grants). The program is currently supported through 10 funding opportunities (2 R21s, 2 R33s, and 6 competitive revision RFAs), where the R21 and R33 awards cover 2 tracks: Molecular/Cellular Analysis Technologies (MCA) and Biospecimen Science Technologies (BST). In the MCA category, 2,385 R21 and 879 R33 applications were submitted, resulting in 221 R21 and 111 R33 awards. For the BST grants, 427 R21 and 151 R33 applications were submitted, with 53 R21 and 23 R33 awards.

Authority for issuance of IMAT funding opportunities extends only until September 2020. In support of a new renewal request to continue offering the IMAT funding opportunities, NCI requires an independent evaluation of the program. It is anticipated that the renewal request will be submitted in spring 2020 to NCI leadership, and the program evaluation will provide important input for preparing and submitting this request. To this end, CSSI has convened a panel of esteemed scientists to engage in an evaluation of the IMAT program during the first quarter of 2020. The panel includes the following individuals: Joe Gray (Oregon Health & Science University, Panel Chair), Jennifer Elisseeff (Johns Hopkins University), Steven Chu (Stanford University), David Beebe (University of Wisconsin-Madison), James Lacey (City of Hope), and Susan Margulies (Georgia Institute of Technology and Emory University). See Appendix 1 for bibliographies of the panelists. The main objectives of the evaluation panel are to assess the merits of

the IMAT program and to recommend whether and/or how the IMAT program should continue. These recommendations are intended to assist NCI's leadership in making a final determination about the path forward for the IMAT program.

The panel evaluated the program by addressing 6 questions:

1. What impact is the program having on advancing cancer research and providing necessary tools for cancer researchers?
2. Is the emphasis balance between the 4 I's of technology development appropriate?
    a. **I**nnovative new technology
    b. **I**mprovement of an existing technology
    c. **I**ntegration of previously separate/siloed technologies
    d. **I**mplementation of new discoveries to the community
3. What are the most important characteristics for a future IMAT program?
4. Are the current funding mechanisms appropriate to achieve the program goals?
5. Are there additional activities that should be undertaken by the program to support its goals?
6. Should NCI continue to support a dedicated program with this scope and approach for cancer technology development?

The panelists, led by Dr. Gray, participated in 3 virtual meetings between January and March 2020. They reviewed and discussed information on the IMAT program, particularly information relevant to the questions. Drs. Tony Dickherber (Program Director, IMAT) and Kelly Crotty (Program Analyst) provided information to the panel drawn from analysis of IMAT funding from 1999–2019. The information spanned diverse measures, including bibliometric measures (publications and citations from IMAT-funded projects), examples of "blockbuster" technologies with significant impact developed out of IMAT-funded projects, IMAT-funded projects leading to meaningful cross-expertise collaboration, projects with clinical impact, and those leading to commercialization. Dr. Dickherber also provided information on the current funding structure, assessments of the sources of applications, award trends, success and failure analysis, and comments from grantees. Panelists did not review confidential materials such as applications and review documents.

Panel Response to Charge

Question 1: What impact is the program having on advancing cancer research and providing necessary tools for cancer researchers?

The IMAT program is producing a positive impact on cancer research through its support of tool development and tool translation. The ultimate goal of the program technology is to enable new discoveries in basic cancer research and to improve outcomes of patients with cancer. Here, we describe the impact of the IMAT program using both standard (academic) metrics and less conventional metrics that are relevant for technology-based and translational research.

Standard impact metrics for the IMAT program
Publications and their citations are a standard academic metric that can be considered a form of impact resulting from IMAT funding. Citation of research from the IMAT program can be tracked in both the technological discipline and in the cancer field. Over the 20-year period between 1999–2019, there were 3324 publications that resulted from 943 awards. On average, there were between 150 and 250

publications per year from IMAT funding, and citations to these publications ranged from 3000–11,000 during the period of 1999–2011. This standard metric of the IMAT program clearly demonstrates the productive academic impact of the grant awards.

Impactful outcomes of research can also be measured in follow-up funding, particularly that connecting the technology developer with cancer researchers and the end-user clinicians. Formation of new collaborations between technology developers and cancer researchers and clinicians is a catalyst for success and a metric of program impact. As discussed in more detail in response to a later question, suggestions are presented to further enhance introductions and interactions between technology developers and cancer researchers. However, IMAT has already achieved some success in supporting technology development that leads to new cancer biology and clinical collaborations.

Technology and translational-related impact
The technological nature of the IMAT support presents the opportunity to consider additional metrics of research impact, specifically translational impact. The ultimate impact, which can take many years to emerge, is improving treatment and outcomes for cancer patients. In the short term, translational impact can be measured in the form of widespread community adoption of technological advances, technology licensing to companies, starting new companies, and product development. Multiple IMAT-supported technologies have been the platform for start-ups including Transgenomic, RainDance Technologies, Viewpoint Medical, Triangle Biotechnology, Meditope Biosciences, and TwinStrand Biosciences. An example of an IMAT blockbuster is the BeadChip and BeadArray from Mark Chee and Sentrix, which became a foundation of Illumina's next-generation sequencing platform.

Question 2: Is the emphasis balance between the 4 I's of technology development (listed below) appropriate?

Technology development can be placed operationally into 4 Innovation categories or 4 I's as follows:

1. Development of an innovative new technology
2. Improvement of an existing technology
3. Integration of previously separate/siloed technologies
4. Implementation of new discoveries to the community

In terms of the category of projects most appropriate for IMAT to fund, the panel members unanimously agreed that the first 2 represent important sources of new innovations and should be the core of IMAT-funded technologies. The third category represents either a rapid repurposing of technology for cancer or a potential integration of different technologies that were previously disconnected. This category also represents a different type of innovation and should be part of IMAT's portfolio. The fourth category—implementation of new discoveries to the community—falls outside of IMAT's scope and is supported through other mechanisms in the public and private sector. For example, by coupling IMAT innovations to the NIH Innovation Corps (I-Corps™) program and the Foundation for the NIH (FNIH) Biomarkers Consortium (BC) for final development and deployment.

The NIH I-Corps™ program is focused on educating researchers and technologists on how to translate technologies from the lab into the marketplace. The program is an 8-week "intensive entrepreneurship" experience that provides 3-member project teams with access to instruction and mentoring in order to accelerate the translation of technologies currently being developed with NIH and Centers for Disease Control Small Business Innovative Research and Small Business Technology Transfer funding. To date,

3 IMAT-supported teams have participated, with 2 of them well on their way to making their technologies commercially available.

The BC is a public-private partnership involving NCI; FDA; multiple pharmaceutical, diagnostic, and technology companies; and nonprofit and patient advocate organizations. This specific working group focuses on developing pilot projects that use emerging technology platforms to overcome the limitations of established methodologies in the application of multidimensional biomarkers. The working group guides the project teams to generate fundable projects that enable rational clinical decisions, which may then attract funding from industry members of the consortium. The working group has already worked with 2 IMAT-supported grantees to develop projects that have received clinical trial funding since 2013.

The recent IMAT emphasis placed on the four "I" categories was assessed through a detailed analysis of awards (between 2015–2019) and applications (funded and non-funded between 2018 and 2019); see Appendix 2. All applications were placed into 1 of the 4 categories, and success rates per category were calculated for both the R21 and R33 funding mechanisms. Results showed that 44% of funded R21s and 0% of funded R33s were assigned to the first category. In the last 5 years, there has been a steady drop in the percentage of R21s in the first category, from 60% to less than 35% currently. Furthermore, only 10% of R21 applications in the first category are being funded at all, indicating that these applications are simply not getting through the gauntlet of the review process. Forty-seven percent of funded R21s and 95% of funded R33s were assigned to the second category (Appendix 2). The success rate for both R21s and R33s in this category was between 12% and 13%. Not every R33 application was originally funded as an R21 award, indicating that going through the R21 process does not give an application a bigger advantage and success in being funded as an R33 award. Five percent of R21s and 6% of R33s came under category 3. The success rate for R21s in this category is very low at 4%, and at 17% for R33s. Neither R21s nor R33s are presently part of funding category 4, although there are unfunded applications that fall under this category.

Looking at award distribution, funded awards predominantly fall under the second category. Although the panel would have expected R21s to be heavier in category 1 than in category 2, it is in fact evenly distributed. Despite representing a source of innovation, category 3 applications have a low success rate, particularly with regard to the R21 funding mechanism. These observations suggest that reviewers are not being risk tolerant, particularly when evaluating R21 applications addressing innovative new technologies. This is evident in the relatively high success rate now achieved by IMAT grantees. For example, over 2013–2014, the R21 failure rate ranged from 19–40% and the R33 from 9–20% (Appendix 2). A higher failure rate is expected for projects that are truly high risk. The panelists had a number of suggestions to improve risk tolerance and to increase the fundability of R21s in the first category.

1. The review process should weigh novel but potentially risky areas against the track record of the investigator. Institutions such as Stanford University and Bell Labs that give out seed grants adopt this strategy.

2. Extending the above recommendation, the IMAT R21 application could be restructured to potentially allow applicants an opportunity to demonstrate their innovation track record in the biosketch section. This approach has been adopted by NIH's Pioneer Award Program, which demands thinking outside of the norm. Applicants need to provide information on how they have successfully tackled problems outside the norm.

3. Ensure that mature projects that are most suited for R33 don't come in as R21 applications, as this would result in the bar being set too high for the R21s. To this end, the FOA should include some language to guide applicants to self-select the R33 vs. R21 mechanism and help risky R21s survive compared with the other more developed R33 applications.

In summary, with regard to the 4 I's of innovation, the panel has the following overall recommendations:

1. Fund more R21s in categories 1 and 3.
2. Maintain current level of funding for R33s in category 2.
3. Category 4 applications fall outside of IMAT's scope and need not be funded by IMAT.
4. Adopt strategies to improve overall risk tolerance for R21 projects falling under categories 1 and 3.

Question 3: What are the most important characteristics of the future IMAT program?

The future IMAT program might look for areas that are ripe for innovation but have difficulty in obtaining funding. The program might also facilitate bringing expertise from different areas of science together to solve problems that arise in developing and robustly deploying innovative technologies. The IMAT program could sponsor workshops, modeled loosely on the NCI-sponsored Provocative Questions workshops, to identify potential areas for innovation and facilitate collaboration across not only the IMAT community but also additional scientific disciplines.

For example, if a group developing a technology, such as nanoparticle delivery of a therapeutic antibody, finds problems with in vivo aggregation and targeting, it may be that promoting collaboration across disciplines such as analytical, pharmacological, and physical sciences will promote a formulation solution for successful particle delivery and pharmacokinetics in vivo. Bringing multiple scientific disciplines together to discuss an issue can provide insight into solving seemingly mundane but intractable problems that hamper robust translation of a breakout technology.

The IMAT program provides the mechanism to support development of truly innovative solutions, but to ensure the initial discovery moves forward from an initial publication to one of long-term impact, the technology needs to be robust and transferable to other groups. Thus, the program can support research bridging from the initial innovative discoveries to the fine-tuning and long-term success of technologies through providing a forum for scientists to discuss troublesome problems with others working in different scientific disciplines or disease areas who have relevant expertise, and it could promote collaboration and translation of new technology into additional areas (e.g., cancer clinical innovations into cardiology practice).

In the future, the IMAT program could work with investigators to identify problematic and weak areas in their work and then set up workshops with investigators and potential problem solvers to identify and discuss problems, and to connect the appropriate groups. In addition to increasing the potential for long-term success of some of the technologies and collaborations, this will enable the project managers and investigators to have "autopsies" that will inform future technology development and funding. The incentive for investigators to engage in these workshops and potential collaborations could be additional funding if they are able to solve an unanticipated problem by bringing in a completely peripheral technology solution.

Question 4: Are the current funding mechanisms appropriate to achieve the program goals?

The panelists approached the question by asking about ***Alignment of the funding mechanisms with the program goals: Which aspects of the current IMAT funding mechanism specifically help to advance the IMAT program goals, and which aspects of the funding mechanism present challenges, either to IMAT awardees or to the NCI program staff, in meeting program goals?***

The IMAT funding mechanism includes 2 tracks: 1 for MCA and 1 for BST. The IMAT RFAs invite R21 and R33 applications; each have 3-year project periods with up to $400,000 and $900,000, respectively, of total direct cost support.

Multiple features of the IMAT RFA contribute to this funding mechanism, helping to advance the goals of IMAT within NCI's overall portfolio for supporting technology development for cancer.

The use of the RFA mechanism sends a clear and strong signal to the research community that this type of innovation-driven technology development is important to the cancer ecosystem. The use of Special Emphasis Panels to review IMAT applications reinforces a message that these types of research questions warrant a particular commitment to ensure high-quality peer review in what are likely to be highly specialized, and at times, rapidly evolving, scientific areas.

In addition to the positive framework the funding mechanism provides, specific components of IMAT awards also help advance progress toward the program's goals. The annual meetings of IMAT awardees help both to foster tangible collaborations and to anchor a positive norm about the importance of collaboration among IMAT awardees and stakeholders.

As noted in previous reviews of the IMAT program, the output generated by IMAT awards—publications, technologies, methodologies, widespread community adoption and commercialized products based on those discoveries—has been substantial and significant. The high level of that output, compared with other funding opportunities, indicates that the IMAT program is successfully enabling promising ideas to be articulated in the form of applications; allowing the peer-review processes to identify ideas worthy of support; and managing those awards in ways that generate actual and productive output.

Especially in a "high-risk/high reward" environment, such as the type of technology development IMAT is designed to encourage, projects can encounter challenges and do not always succeed as planned.

Previous reviews of the IMAT program identified some characteristics of IMAT projects that encountered challenges. Among the themes that emerged were a) a desire/need for additional funding and b) the important role that additional institutional support, in the form of additional funding, infrastructure, or personnel, played in enabling IMAT awards to achieve success.

With a strong and growing network of current and former IMAT awardees and a community of researchers positively affected by IMAT successes, any additional steps to further increase the chances that IMAT awardees succeed could further bolster the program's overall success. The panel identified several situations in which potential additional flexibility in the program might help stimulate success:

1. Staged awards, partial funding, or early milestones may be needed for highly uncertain, especially high-risk, or borderline-funding projects. Increasing competition for finite NCI funds

leaves more good ideas potentially unfunded. The distribution of R21 vs. R33 awards in the areas of invention/creation vs. improvement/adaptation (see above) raises questions about whether higher-risk R21 applications focused on new inventions or creations might have particular difficulty meeting all of the review thresholds required for funding. Stages or milestones for awards might offer a low-risk route to provide partial funding for selected projects.

2. Dedicated funding for post-award modifications or troubleshooting may be needed for promising projects that run into unforeseen problems that could be overcome with additional help and expertise from others across the IMAT community. Identifying, evaluating, and obtaining that help, even within a like-minded community, requires resources. A program that made specific funds available to help support new or additional collaborations could help increase the chances that all awards achieve success. This tactic might be modeled on the U01 mechanism now used to being new investigators into established NCI U54 consortia.

3. Flexible funding and support from IMAT staff might also help IMAT grantees to succeed in high risk, high payoff project. Milestones or partial funding could enable a project that encounters a challenge to potentially end, when in fact persevering through that challenge would be possible and beneficial. Providing the IMAT program with the ability to flexibly fund new directions of development to address problems that arise through the course of IMAT research could achieve a good balance of "terminate vs. persevere." This type of flexibility could be especially helpful when awardees encounter challenges that were not identified or expected during the peer-review or pre-award stages. An environment in which program staff had additional flexibility and could work very closely with awardees could position itself for success. Overcoming those barriers might require assurances that problems or challenges were being addressed in new or creative ways, rather than just continuation of previous or existing paths of inquiry. Overcoming those barriers might require IMAT staff reaching outside the existing network to find the best and most appropriate new input, regardless of its origin. This could both help those projects and help expand the IMAT community in positive ways. Managing those new directions for awards in ways that gave IMAT staff both the requisite flexibility and appropriate oversight could help both the program and the awardees.

Question 5: Are there additional activities that should be undertaken by the program to support its goals?

Overall the IMAT program has served its mission well and has contributed significantly to the development of technologies that are having an impact on cancer research and patient outcomes. However, there are, of course, always potential areas to improve upon. In this section, we describe a number of additional or expanded activities that the IMAT program might consider to further the mission and impact of the program. The committee discussed a number of areas of potential additional activities. Each area is summarized below.

Identification of technology needs/gaps for priority research areas
An ongoing challenge is to find a balance between investigator-initiated ideas/topics (the dominant mode of operation of IMAT thus far) and a more targeted approach to focus technology development on the most important challenges in cancer at any given time. The committee felt there would be benefit from exploring ways to include some focus while maintaining the advantage of the current IMAT model. To enable this activity, the technology needs must first be identified and prioritized. This might be

efficiently accomplished through better coordination between IMAT and relevant workshops throughout NCI. These workshops typically focus on emerging challenges in cancer, but they often do not focus on technology solutions. The strategic attendance by IMAT personnel at these workshops would be an efficient method of identifying and defining (from a technology-need perspective) high-value questions that IMAT investigators could then be encouraged and/or incentivized to focus their proposals on. A recent example would be the workshop Tumor Heterogeneity: The Stromal Perspective organized by cochairs Dr. Simon Hayward and Dr. Sheila Stewart, and the NCI Division of Cancer Biology Tumor Biology and Microenvironment Branch. Increased coordination and sharing of outcomes between these types of workshops and IMAT would identify and define technology needs. Other examples of programs that could be better coordinated with IMAT include the Provocative Questions and Cancer Grand Challenges initiatives. These interactions would lead to improved identification of key technology gaps, and subsequently, these could be used to define focused IMAT RFAs or at least list priority areas for the existing IMAT RFAs.

Facilitating connections and collaborations with end users
Another area discussed was the potential for IMAT to better facilitate connections between technology developers and end users. This is a significant challenge, as the best interactions are typically grown organically and not through a matchmaking process. Still, there may be ways that IMAT could help initiate connections. One way is a natural extension of the suggested increased communication between IMAT and relevant NCI workshops discussed above. One could imagine taking this a step further and bringing IMAT-funded investigators to the workshops or even taking a small step of making workshop summaries and addenda lists more accessible to potential IMAT technology developers. Even just providing links from the IMAT website to the relevant workshop summaries could have some impact. At a local level, some universities have dedicated activities to facilitate these interactions (e.g., speed-dating sessions between engineering and medical school faculty). One could imagine extending such activities more globally, perhaps via IMAT-sponsored speed-dating events at cancer-focused conferences that draw both technology developers and end users.

IMAT should also encourage the dissemination of effective practices for institutions that have actively encouraged organic matchmaking across research boundaries. For example, Johns Hopkins holds a thematic annual retreat between the Department of Medicine and the School of Engineering to facilitate communications in a particular theme. In 2020, the theme of the retreat was Nanomedicine: Treating Diseases at the Molecular level.

Learning from past successes
It may be worthwhile to examine the case histories of how successful collaborations across nominally nonintersecting research disciplines began. It would be especially important to examine in detail the formation that leads investigators to reach out well beyond their own expertise and be the *first* to apply a novel technology from a completely different field. Also, there may be lessons to be learned of how particularly interactive institutions and their intellectual leaders were able to establish the cultural environments that increase the probability of spontaneous discussions and “chance encounters.”

Reviewer orientation
An acknowledged ongoing challenge across NIH is the orientation of reviewers for specific programs and their mission and reviewer criteria. IMAT should continue to emphasize this reviewer orientation to ensure that high risk/high reward projects are prioritized. Reviewers might be specifically charged to recognize that a high failure rate is expected in high-risk projects so that the possibility of failure should be discounted during review. Reviewers also might be instructed to play close attention to the

risk-reward balance and the innovative track record of applicants. Reviewers might be asked to give additional leeway to projects with high risk and high reward and to applicants with a strong record of successful innovation in molecular analysis technology.

Better support for technology dissemination and providing technology transfer resources
Two other areas with potential benefit from additional activities were discussed—namely, technology dissemination and providing technology transfer resources. These are both areas in which IMAT is currently actively engaged, but where it has been challenging to have significant impact (e.g., only a small number of IMAT-funded investigators take advantage of the available resources for technology transfer/commercialization efforts). One suggestion for improving technology dissemination would be the creation of a standards/technology coordinating center.

Question 6: Should NCI continue to support a dedicated program with this scope and approach for cancer technology development?

Continuation of the IMAT program is strongly recommended. Innovative molecular analysis technologies reveal new and important aspects of biology and physiology that enable advances in cancer detection, classification, and treatment throughout the approximately $5 billion per year NCI program. It is noteworthy that the $10.5 million per year IMAT program remains the main funding mechanism that drives 3 of the 4 I's of molecular analysis technology innovation (innovative new technology, improvement of an existing technology, and integration of previously separate/siloed technologies). IMAT staff have enabled the fourth I (implementation of new discoveries to the community) by coupling IMAT innovations to the NIH I-Corps™ program and the FNIH BC for final development and deployment.

Overall, the nature of the program and its importance to NCI have not changed substantially since the detailed review of the program in 2016 (2015-2016 Comprehensive Evaluation of the IMAT Program). The program is well run, and numerous metrics including publication citations (p35-37), patents, adoption of IMAT innovations by the community, and commercialization (p52-53) indicate its continuing high impact (Appendix 3). That said, in recent years, most IMAT grantees have focused on development of technologies to assess the -omic components of cancer and normal tissues and on the development of tissue-preparation technologies. Opportunities for innovative molecular-analysis technologies in these areas remain, and many new opportunities related to innovative approaches for single cell analysis and for the analysis of inter- and intracellular interactions and architectures are arising. Thus, renewal is strongly recommended either at the current level, or preferably at an increased level of support.

However, some modification and expansion of emphasis is recommended. In recent years, the program has focused heavily on improvements to existing technologies (Appendix 2). It has become increasingly risk adverse and has not adequately supported the sustained work needed to achieve sufficient analytical robustness needed for widespread technology dissemination. The renewed program should develop mechanisms that address these problems—for example, by developing better reviewer guidance language and by employing stronger portfolio management tools that enable IMAT program staff (with external oversight and guidance) to correct for inherent reviewer bias against high- risk projects and/or against highly important work needed to increase the robustness of innovative technologies. The IMAT program should also develop an idea intake program that regularly polls the broad cancer research community for technological needs and opportunities that might be addressed via focused requests for proposals, much as the NCI Provocative Questions program "stimulates research in perplexing and underexplored areas identified by the cancer research community."

Summary of Panel Conclusions

The panel came to the 7 summary conclusions listed below. The subsections that follow present the panel's response to the charge, in the order NCI asked the questions.

1. **Continuation of the IMAT program is strongly recommended.** The program and its importance to NCI have not changed. It remains well run, and numerous metrics including publication citations, patents, adoption of IMAT innovations by the community, and commercialization demonstrate its continuing high impact. The IMAT program remains the main funding mechanism that drives 3 of the 4 I's of molecular analysis technology innovation (innovative new technology, improvement of an existing technology, and integration of previously separate/ siloed technologies). The program has successfully enabled the 4th I (implementation of new discoveries to the community) by coupling IMAT innovations to the NIH Innovation Corps (I-Corps™) program and the Foundation for the NIH (FNIH) Biomarkers Consortium (BC) for final development and deployment.

2. **Renewal of the program at an increased level of support.** IMAT-funded technologies have addressed the -omic components of cancer and normal tissues and methodologies for tissue preparation. While opportunities for innovative molecular analysis technologies in all these areas remain, many new opportunities related to single cell analysis and the analysis of inter- and intracellular interactions and architectures are arising.

3. **Modification of the emphasis balance between the 4 I's of technology development is strongly recommended.** In recent years, the program has focused heavily on improvements to existing technologies at the cost of becoming increasingly risk adverse. The renewed program should develop mechanisms that address these problems, including strategies to improve overall risk tolerance for R21 projects falling under categories 1 and 3 and making sure that mature projects that are most suited for R33 don't come in as an R21 applications. Examples of modifications are developing better reviewer guidance language and employing stronger portfolio-management tools that enable IMAT program staff to correct for inherent reviewer bias against high-risk projects or against sustained work needed to increase the robustness of innovative technologies.

4. **Engage with the broader cancer research community to identify and prioritize technology needs.** The IMAT program might look for areas that are ripe for innovation but have difficulty in obtaining funding. The program should consider an idea-intake program that regularly polls the broad cancer research community for technological needs and opportunities that might be addressed via focused requests for proposals, as well as workshops to further enhance introductions and interactions between technology developers and cancer researchers, much like the NCI Provocative Questions program.

5. **Build in flexibility in the program to stimulate success.** For funding potentially high-risk projects, consider staged awards, partial funding, or building in early milestones. Providing the IMAT program the ability to flexibly fund new directions of development to address problems that arise through the course of IMAT research could achieve a good balance of "terminate vs.

persevere." This type of flexibility could be especially helpful when awardees encounter challenges that were not identified or expected during the peer-review or pre-award stages.

6. **Provide resources for post-award modifications or troubleshooting.** For projects that can run into unforeseen problems, additional help and expertise from others across the IMAT community could serve as an important resource. A program that made specific funds available to help support new or additional collaborations could help increase the chances that all awards achieve success. Through workshops or other mechanisms, the program might facilitate bringing expertise from different areas of science together to solve problems that arise in developing and robustly deploying innovative technologies.

7. **Facilitate connections between technology developers and end users and provide better support for technology dissemination.** Provide technology transfer resources, including creation of a standards/technology coordinating center.

Appendix 1: Panelist Biographies

Joe W. Gray

Dr. Joe W. Gray, a physicist and an engineer by training, holds positions at Oregon Health & Science University (OHSU) as Professor and Gordon Moore Endowed Chair, Biomedical Engineering; Director, OHSU Center for Spatial Systems Biomedicine; and Associate Director for Biophysical Oncology, Knight Cancer Institute. He is also Professor Emeritus, University of California, San Francisco (UCSF). He received a Professional Engineering degree from the Colorado School of Mines and a PhD in Physics from the Kansas State University. Prior to joining OHSU, he was a Staff Scientist in the Biomedical Sciences Division of the Lawrence Livermore National Laboratory (LBNL; 1972–1991), Professor of Laboratory Medicine at UCSF (1991–2011), and Associate Laboratory Director for Biosciences and Life Sciences Division at Lawrence Berkeley National Laboratory (2003–2011). He joined OHSU in 2011. He is the Principal Investigator (PI) of an NCI Cancer Systems Biology Consortium U54 Research Center that is aimed at developing a systems level understanding of how intrinsic and extrinsic factors work together to enable triple-negative breast cancer to escape therapeutic control; the PI of an NIH U54 Center in the Library of Integrated Network-based Cellular Signatures program; the PI of an NCI U2C Human Tumor Atlas Network Research Center aimed at developing a clinical, -omic, and multiscale atlas of metastatic breast cancer; and Co-director of a philanthropically funded study, Serial Measurement of Molecular and Architectural Responses to Therapy (SMMART) program, to develop more durable and tolerable therapies for cancers of the breast, prostate, pancreas, and leukemia; and the PI of a Susan G. Komen project to identify the mechanisms by which breast cancers escape therapeutic control. Dr. Gray's work is described in over 500 publications (scopus h-index 111) and in 80 US patents. He is a Fellow of the American Association for the Advancement of Science and the American Institute for Medical and Biological Engineering; an elected member of the National Academy of Medicine; a Fellow of the American Association for Cancer Research Academy; and the US Councilor to the Radiation Effects Research Foundation, Hiroshima, Japan.

David J. Beebe

Dr. David J. Beebe is a John D. MacArthur Professor and Claude Bernard Professor of Biomedical Engineering at University of Wisconsin-Madison (UW-Madison). He has appointments in the Department of Pathology and Laboratory Medicine and the Department of Biomedical Engineering. Between 2012–2017, he co-led the Tumor Microenvironment Program at the UW Carbone Cancer Center. Dr. Beebe's research has focused on the novel and simple use of microscale physics and phenomena to create tools and methods to further biological and medical goals ranging from basic science to research tools to diagnostics to drug delivery. He pioneered several areas including passive microfluidic mixing, embryo culture and manipulation in microchannels, autonomous microfluidic systems using stimuli-responsive hydrogels, and passive pumping in microfluidics. His current research interest is focused on the application of microscale physical phenomena to understand cancer biology (e.g., stromal-epithelial), improve cancer diagnosis and monitoring, and advance global disease diagnostics. The goal of his research is to create simple but enabling technologies that can be translated rapidly into clinical practice. He has published more than 250 archived journal articles (h-index of 81). He has cofounded several biotechnology companies and has received over $30 million in funding (as PI).

Steven Chu

Dr. Steven Chu is the William R. Kenan, Jr., Professor of Physics and Professor of Molecular and Cellular Physiology at Stanford University School of Medicine. Dr. Chu was the 12th US Secretary of Energy from January 2009 to April 2013. He received a BA degree in Mathematics and a BS degree in Physics from the University of Rochester, and a PhD in Physics from the University of California, Berkeley, as well as 32 honorary degrees. As the first scientist to hold a Cabinet position and the longest serving Energy Secretary, he recruited outstanding scientists and engineers into the Department of Energy. He began several initiatives including Advanced Research Projects Agency–Energy and Energy Innovation Hubs, and he was personally tasked by President Obama to assist BP in stopping the Deepwater Horizon oil leak. Prior to his Cabinet post, he was the Director of the Lawrence Berkeley National Laboratory, where he was active in pursuit of alternative and renewable energy technologies, and Professor of Physics and Applied Physics at Stanford University, where he helped launch Bio-X, a multidisciplinary institute combining the physical and biological sciences with medicine and engineering. Previously he was head of the Quantum Electronics Research Department at AT&T Bell Laboratories. Dr. Chu is the corecipient of the 1997 Nobel Prize in Physics for his contributions to laser cooling and atom trapping and has received numerous other awards. He is a member of the National Academy of Sciences, the American Philosophical Society, the American Academy of Arts and Sciences, and the Academia Sinica, and a foreign member of The Royal Society, Royal Academy of Engineering, Chinese Academy of Sciences, Korean Academy of Sciences and Technology, the National Academy of Sciences of Belarus, and an Academician of the Pontifical Academy of Sciences. He was president of the American Association for the Advancement of Science from 2019–2020 and currently the Chair of the American Association for the Advancement of Science Board. He has published over 280 papers in atomic and polymer physics, biophysics, biology, bio-imaging, nanoparticle synthesis, batteries, and other energy technologies. He holds 15 patents and an additional 14 patents or fillings since 2015.

Jennifer H. Elisseeff

Dr. Elisseeff is the Morton Goldberg Professor and Director of the Translational Tissue Engineering Center at Johns Hopkins Department of Biomedical Engineering and the Wilmer Eye Institute with appointments in Chemical and Biological Engineering, Materials Science and Orthopedic Surgery. She received a bachelor's degree in chemistry from Carnegie Mellon University and a PhD in Medical Engineering from the Harvard–MIT Division of Health Sciences and Technology. She was a Fellow at the National Institute of General Medical Sciences, Pharmacology Research Associate Program, where she worked in the National Institute of Dental and Craniofacial Research. Dr. Elisseeff is committed to the translation of regenerative biomaterials and has founded several companies and participates in several industry advisory boards including the State of Maryland's Technology Development Corporation (TEDCO). She was elected a Fellow of the American Institute of Medical and Biological Engineering, the National Academy of Inventors, and a Young Global Leader by World Economic Forum. In 2018, she was elected to the National Academy of Engineering and National Academy of Medicine. In 2019, she received the NIH Director's Pioneer Award.

James Lacey

Dr. James Lacey is Professor and the Director of the Division of Health Analytics, Department of Computational and Quantitative Medicine, Beckman Research Institute, City of Hope. Dr. Lacey received his PhD in epidemiologic sciences from the University of Michigan, Ann Arbor. He completed a postdoctoral fellowship at the NCI and spent 8 years as an Investigator in the NCI's Division of Cancer Epidemiology and Genetics. His research helped establish progression risks for uterine cancer precursors and increased risks of ovarian and uterine cancers associated with use of menopausal estrogens and

progestins. He joined the faculty at City of Hope in 2009, and he serves as a PI for the California Teachers Study, a prospective observational cohort study of over 133,000 volunteers who have been followed since the mid-1990s. Since 2013, he has led innovative and successful implementations of cloud computing, customer-engagement principles, and industrial-scale logistics to modernize biobanking, data collection, and informatics in large-scale population health research.

Susan Margulies

Dr. Susan Margulies is the Wallace H. Coulter Chair of the Coulter Department of Biomedical Engineering at Georgia Institute of Technology and Emory University, and a Georgia Research Alliance Eminent Scholar in Injury Biomechanics. She earned an undergraduate degree in Mechanical and Aerospace Engineering at Princeton University and a PhD in Bioengineering from the University of Pennsylvania. After a postdoctoral fellowship and faculty appointment at Mayo Clinic College of Medicine and Science, she joined the faculty at the University of Pennsylvania in 1993. Dr. Margulies focuses on prevention, intervention, and treatments. She has pioneered new methods for measuring functional effects of large or repeated tissue distortions; identified injury tolerances and response cascades; and translated these basic research discoveries to preclinical therapeutic trials to mitigate and prevent brain and lung injuries in children and adults. She has over 140 peer-reviewed papers, 11 book chapters, and numerous media features. Dr. Margulies has been nationally recognized for her scholarship by her election as a Member of the National Academy of Engineering, as a Fellow of the American Society of Mechanical Engineers, the Biomedical Engineering Society (BMES), and the American Institute for Medical and Biological Engineering. She has served as Chair of NIH study sections and on strategic planning advisory panels for NIH and several academic institutions. She was or is a member of the executive committees of AIMBE, BMES, and the World Congress of Biomechanics. She coauthored the Institute of Medicine's 300-page report on sports-related concussions in youth, highlighted by President Obama at a White House Summit in 2014. She has been honored for her excellence in mentoring, teaching, and advising with the S. Reid Warren, Jr. Award for Distinguished Teaching, the Ford Motor Company Award for Faculty Advising, and the Association of Women in Science's Elizabeth Bingham Award for the Advancement of Women in Science.

Appendix 2: Material Evaluated by the Panel

2020 Evaluation Findings of the NCI IMAT Program

Tony Dickherber & Kelly Crotty

Materials presented during Feb/Mar 2020

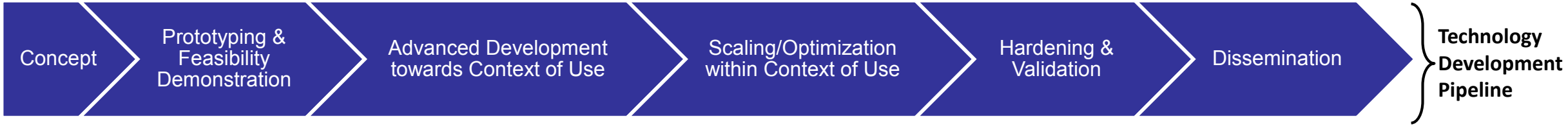
NIH NATIONAL CANCER INSTITUTE

Aggregated Slide Deck Organization

1. *Introduction Slides*
   - *IMAT Overview (4-15)*
2. *Evaluation Questions (16)*
   - *Question 1: Impact (17-41)*
   - *Question 2: 4 I's (42-49)*
   - *Question 3: Future Features (50-51)*
   - *Question 4: Mechanisms (52-66)*
   - *Question 5: Missing Opps (67-68)*
   - *Question 6: To Continue? (69-72)*

- **Evaluation Panel Members**
  - Joe Gray (Chair) Oregon Health Sciences University
  - David Beebe, University of Wisconsin
  - Steve Chu, AAAS/Stanford University
  - Jennifer Elisseeff, Johns Hopkins University
  - James Lacey, City of Hope
  - Susan Margulies, Georgia Institute of Technology
- **NCI** – Tony Dickherber & Kelly Crotty, Center for Strategic Scientific Initiatives
- **CCSA** (Evaluation Support Team)

Ongoing NCI Support for Technology Development



SBIR & STTR

NIH NATIONAL CANCER INSTITUTE Informatics Technology for Cancer Research

NCI CANCER MOONSHOT
A program of the National Cancer Institute of the National Institutes of Health

IMAT INNOVATIVE MOLECULAR ANALYSIS TECHNOLOGIES

CANCER TISSUE ENGINEERING COLLABORATIVE

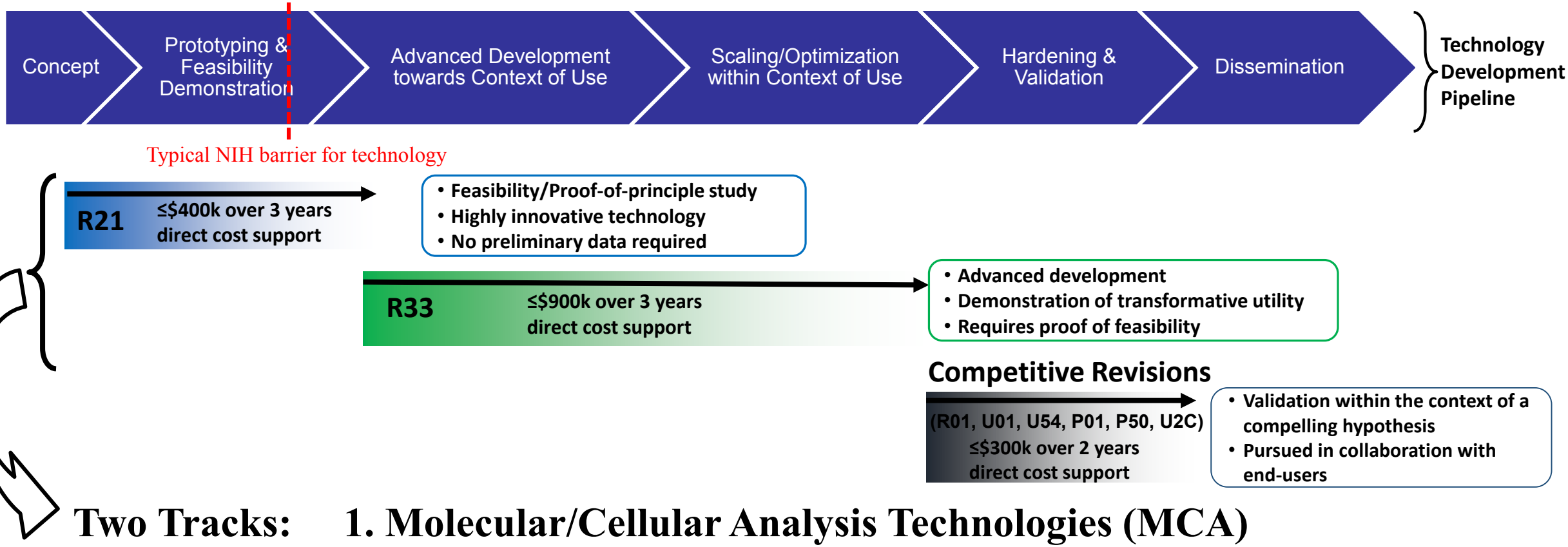
NIH NATIONAL CANCER INSTITUTE Academic Industrial Partnerships

PHYSICAL SCIENCES in ONCOLOGY

IMAT RFA Funding Opportunity Overview

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.



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

What is “Biospecimen Science”?

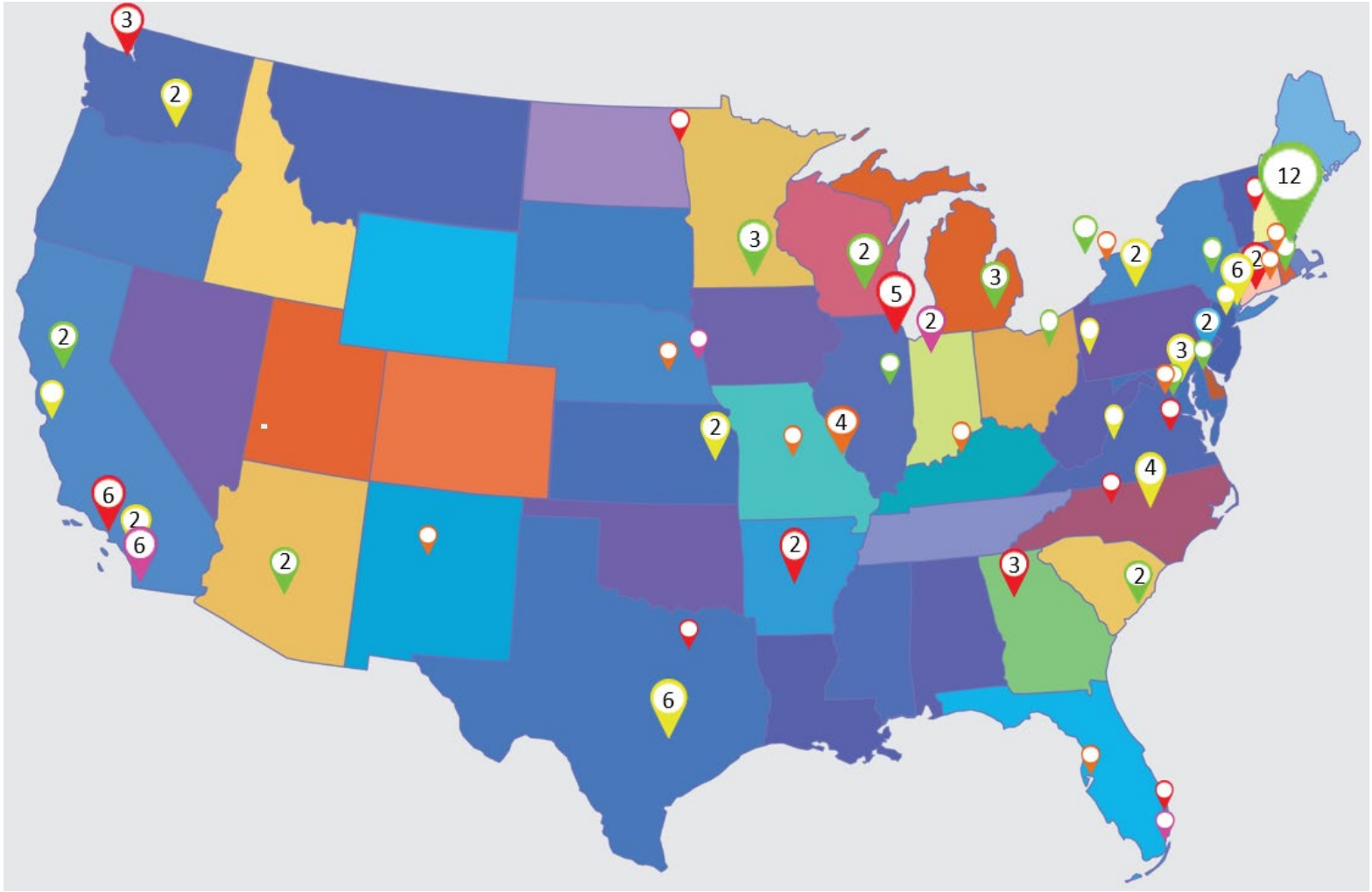
- **Sample Quality Control** (*e.g.,* RNALater)
  - Focus on preserving the biological integrity of the molecular and cellular targets to be assessed
  - Spans the preanalytical time period from patient management variables, through sample procurement, immediate handling and preservation, and processing prior to analysis
- **Sample Quality Assessment** (*e.g.,* RIN)
  - Focus on verifying the biological integrity of the molecular and cellular targets to be assessed

- **Solicitation:**
  - ***RFA-based*** to maintain control over responsiveness and impose additional review criteria
  - Emphasis on ***innovative technology with transformative potential*** (*i.e.* high-risk, high-impact)
  - Focus exclusively on ***technology development*** (*NOT biological/clinical hypothesis-driven research*)
  - ***Investigator-initiated*** research grants
- **Review:**
  - ***Special emphasis panels*** recruited based on focus of submissions, drawing heavily from former IMAT grantees
  - ***Quantitative performance measures*** required for all applications to assess the *feasibility* and *utility* of the proposed capabilities (*e.g.*, specificity, sensitivity, and speed) and characterize the improvement over state-of-the-art

2019 PI Meeting Agenda

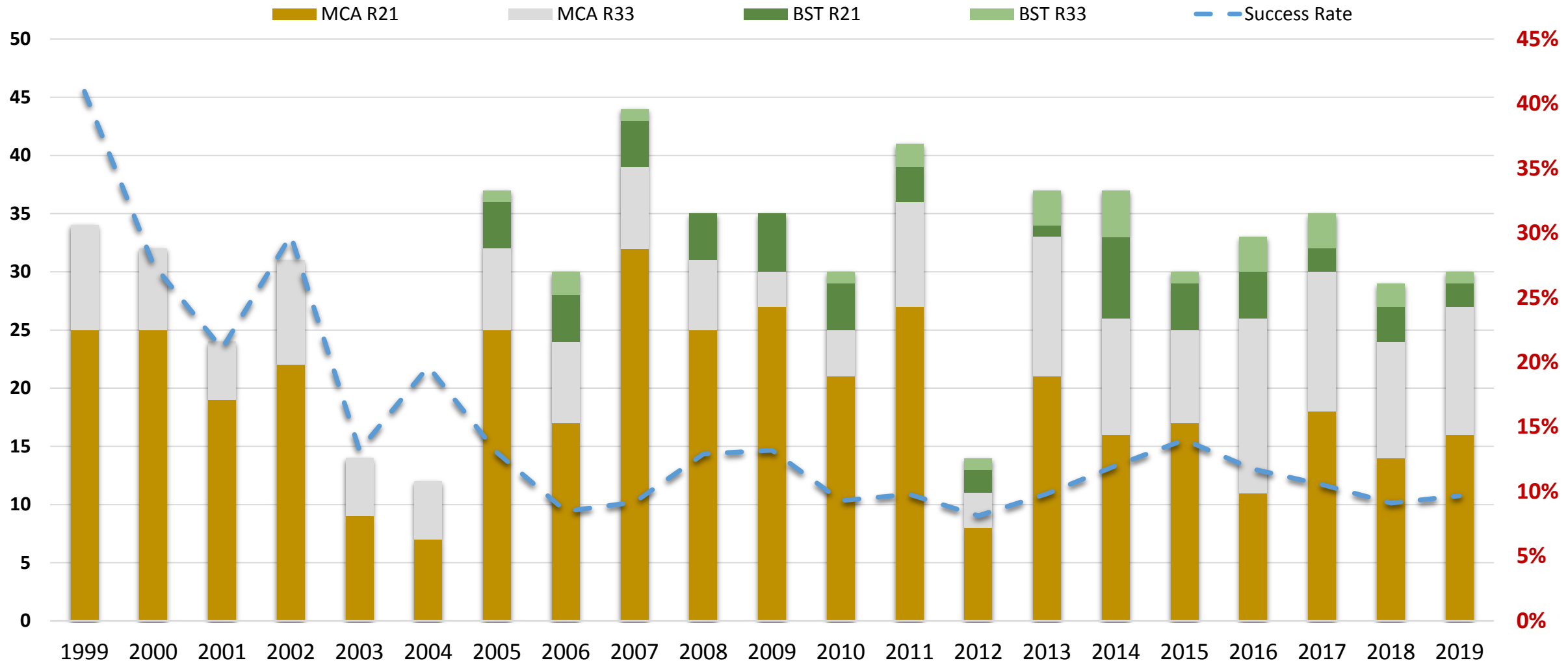
1. Next Gen Nucleic Acid-Targeting Technologies
2. Advancing Liquid Biopsy Technologies
3. Molecular Pathway Tools
4. Synthetic Biology-Driven Technologies
5. Biospecimen Science Technologies
6. Cancer Modeling Approaches
7. Novel Imaging Approaches
8. Advanced Imaging Probes

116 Active Projects (63 R21 & 53 R33)

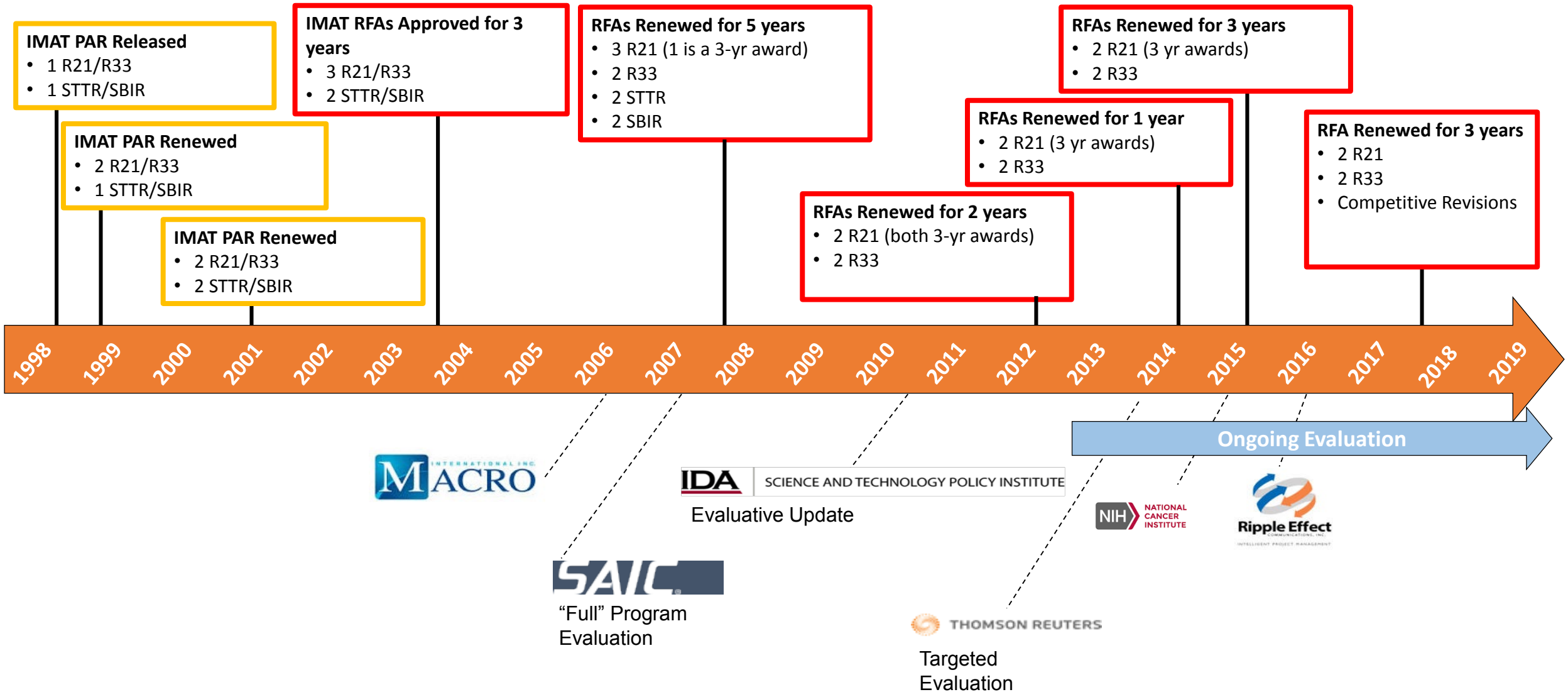


IMAT Application and Award History

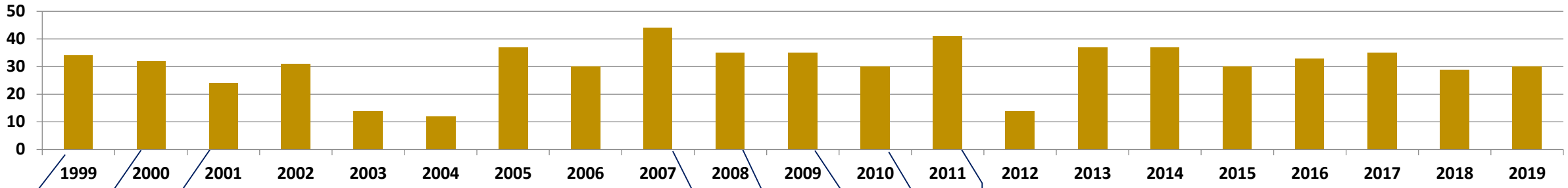
MCA: Molecular & Cellular Analysis Technologies BST: Biospecimen Science Technologies



IMAT FOA & Evaluation History



IMAT Success Stories



Multi-photon Intravital Imaging (**MPIVI**); *J Condeelis*
MicroSOL IEF (**Zoom IEF**); *D Speicher*
Syncrotron Protein Footprinting; *M Chance*
DEP-FFF **(ApoCell)**; *P Gascoyne*
Imaging Mass Spectrometry (IMS); *R Caprioli*

One-Bead One-Compound (**OBOC**); *K Lam*
Isotope-Coded Affinity Tags (**ICAT**); *R Aebersold*
DNA methylation hybridization (**DMH**); *T Huang*
Protease-activatable NIR probes; *CH Tung*
Methylated CpG-island Amplification (**MCA**); *JP Issa*

Dynamic Range Enhancement Applied to Mass Spec (**DREAMS**); *R Smith*
Multidimensional protein ID technology (**MuDPIT**); *J Yates*
Fluorophore-Assisted Light Inactivation (**FALI**); *D Jay*
Rolling Circle Amplification (RCA); *P Lizardi*
Interactome Mapping (**Gateway ORF**); PI: *M Vidal*
Representational Oligonucleotide Microarray Analysis (**ROMA**); *M Wigler*

BRET-FRET Probes; *J Rao*
Single Molecule Molecular Inversion Probes (**smMIP**); *J Shendure*
3D BrCa modeling scaffold;*C Fischbach*

Semiconducting polymer dots (**pDots**); *D Chiu*
Oligo-selective Sequencing (**OsSeq**); *H Ji*
NanoVelcro; *HR Tseng*
Crosslinked amino acid analysis (**xAAA**); *K Hansen*

COLD PCR; *M Makrigiorgos*
Exclusion-based Sample Prep (**VERIFAST**); *D Beebe*
Micro-Metastasis Assay 3D modeling system; *R Kamm*
NanoTrap; *L Liotta*
Suspended Microchannel Resonators; *S Manalis*

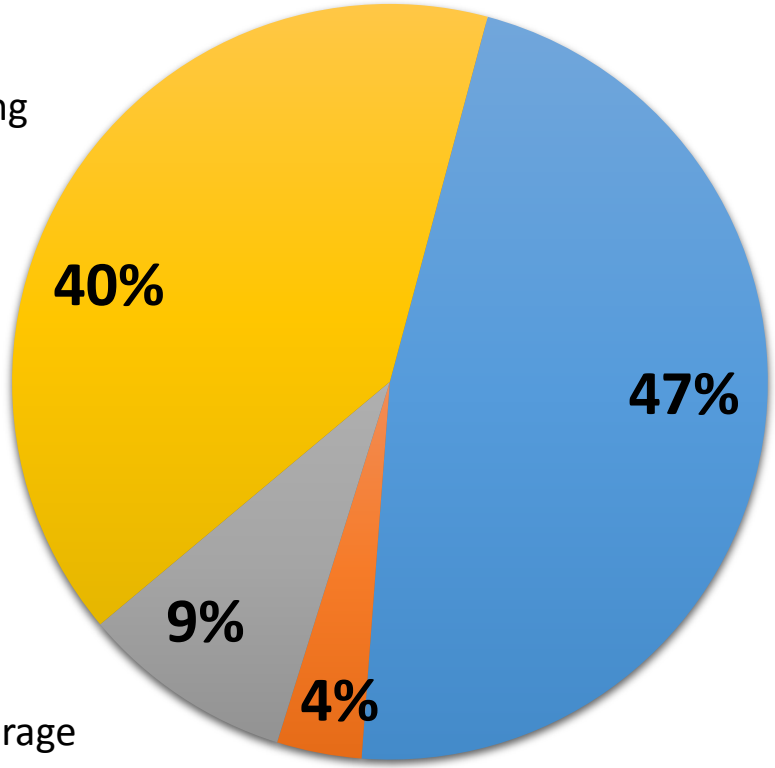
Cysteine oxidation probes (from KeraFast & Millipore); *L Poole & C Furdui*
Salivary protein+RNA collection device (**RNAPro-SAL**); *D Wong*
RNAi gene enrichment ranking (**RIGER**) Y Integrated Genomics Viewer (**IGV**); *W Hahn*
Isotopic labeling of metabolites for flux analysis; *J Rabinowitz*
Exclusion Combinatorial Refinement (**ExCoR**) for structural analysis; *K Nettles*

Oncomap (**OncoPanel);** *L Garraway*
Digital Transcriptome Subtraction; *P Moore*
Oil Droplet Microfluidics (**Raindance**); *D Link*
Genetically modified T-cells for ALL treatment; *L Cooper*
readDepth; *A Milosavljevic*

General Breakdown of the IMAT Portfolio

Technologies for Clinical Treatment and Diagnosis

- Drug screening platforms
- Patient-derived tumor modeling
- Diagnostic imaging agents
- Cancer-targeting
- Drug delivery vehicles
- Point-of-care diagnostics
- *et cetera…*



Cancer Biology Technologies

- Molecular fingerprinting (‘omic discovery)
- Molecular interactions
- Cancer modeling
- Imaging/spectroscopy probes
- Sample preparation
- Mechanobiololgy/microrheology
- *et cetera…*

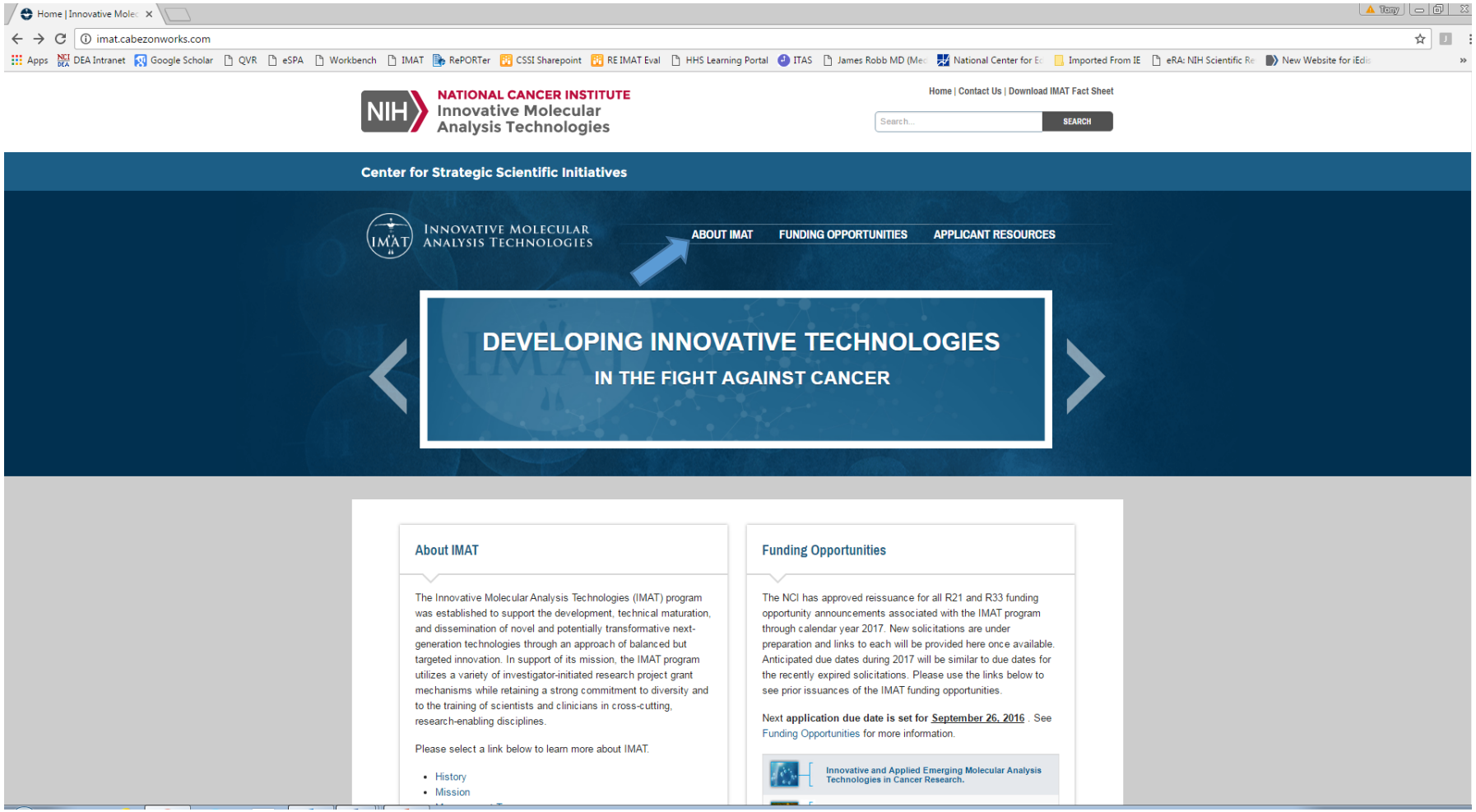
Early Detection Screening

- Point-of-care detection
- Field sample collection and storage
- Liquid biopsy platforms
- *et cetera…*

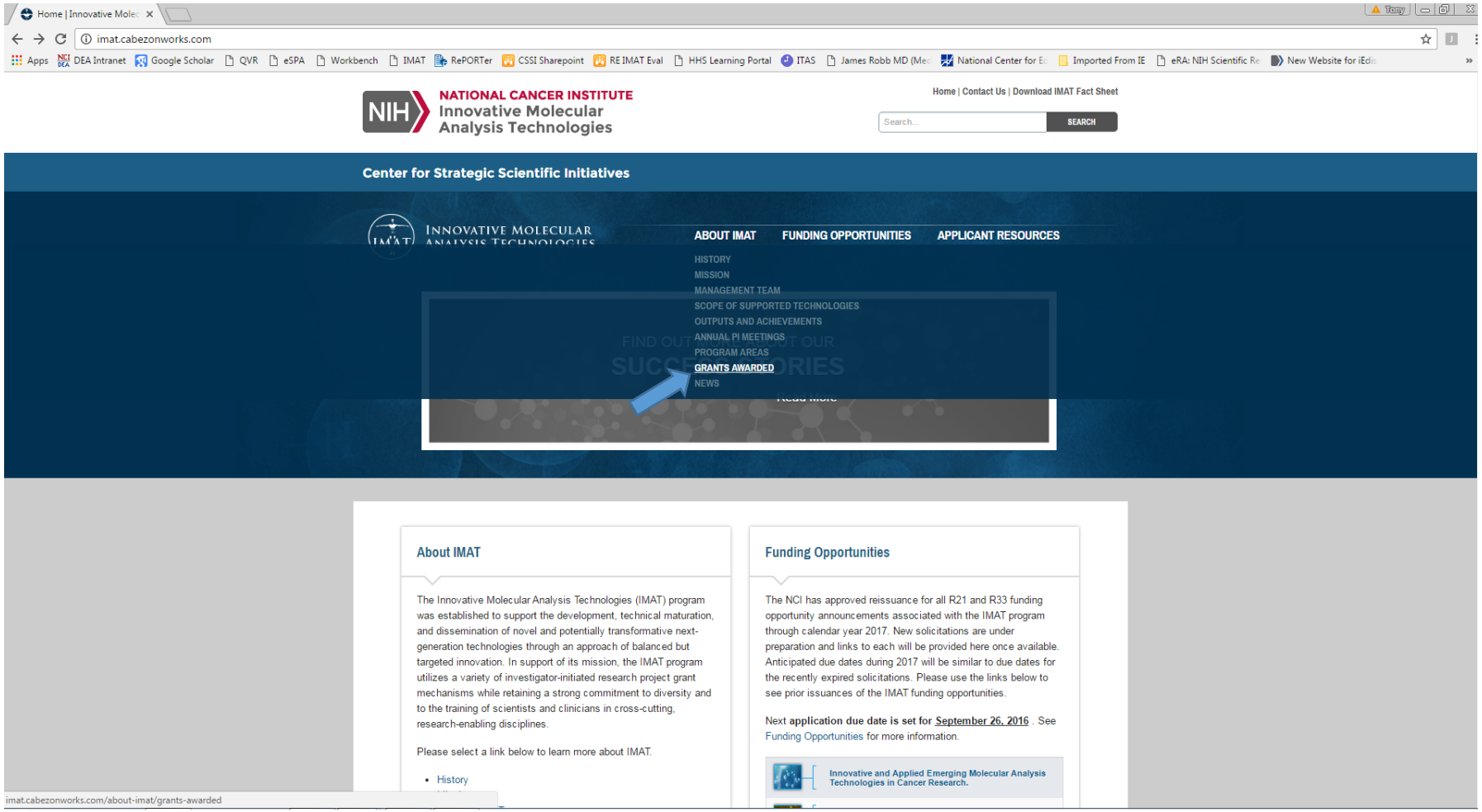
Molecular Epidemiology Tools

- Population-scale analysis
- Low-resource setting point-of-care technologies
- *et cetera…*

https://innovation.cancer.gov



https://innovation.cancer.gov



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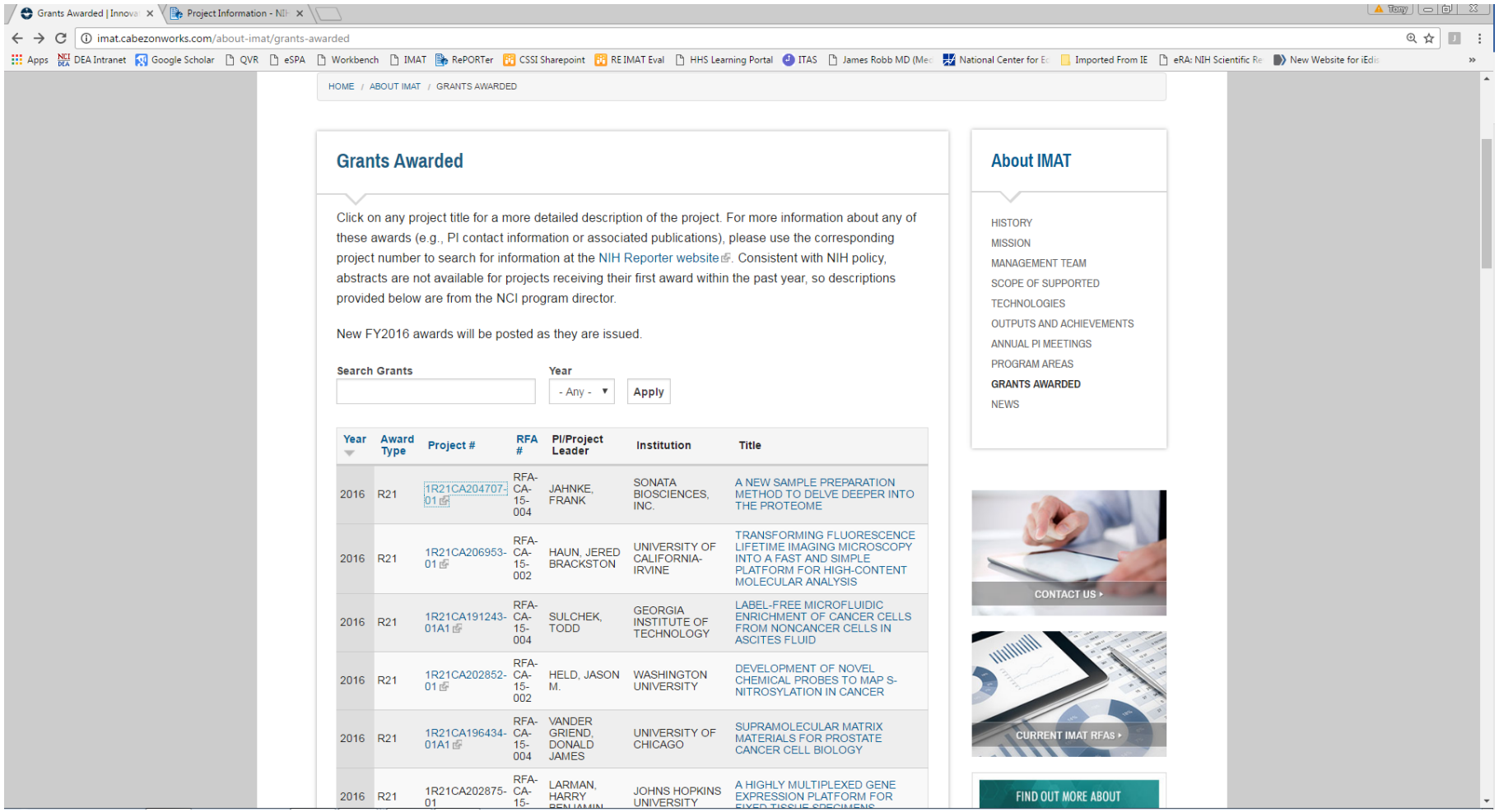


2020 IMAT Evaluation Objectives

1. *What impact is the program having on advancing cancer research and providing necessary tools for cancer researchers?*
   - *Slides 3-27*
2. *Is the emphasis balance between the four I's appropriate?*
   - *Slides 28-35*
3. *Should NCI continue to support a dedicated program with this scope and approach for cancer technology development?*
4. *What are the most important characteristics of the future IMAT program?*
   - *Slides 36-38*
5. *Are the current funding mechanisms appropriate to achieve the program goals?*
6. *Are there additional activities that should be undertaken by the program to support its goal?*

Question 1:
What is the impact of the program on cancer research?

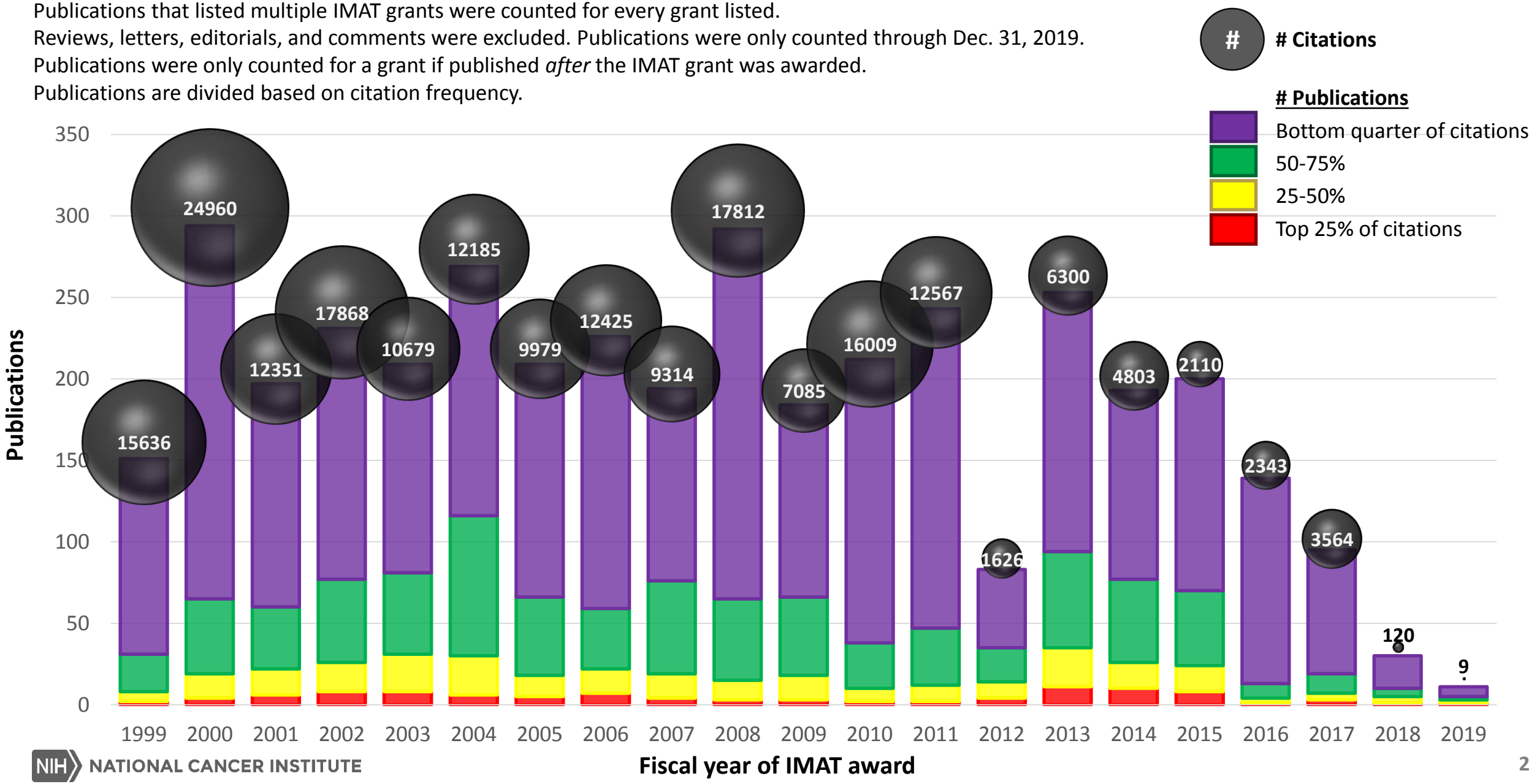
Lead: Jennifer Elisseef

Question 1 Summary

- Last meeting – assessed bibliometric measures (pubs/citations), sources of applications and discussion of success/failure stories
- Joe asked for *5 "blockbuster" examples* [slide 5-6]
- Jennifer suggested more recent examples from the following categories of impact
  - *Clinical Impact* [slides 7-12]
  - *Collaboration Impact* [slide 13-14]
  - *Commercialization Impact* [slides 15-16]
- NCI OIA awards to IMAT grantees [slide 17-18]

Publications and Citations by fiscal year

3324 publications from 943 awards from 1999-2019. R21, R33, R41, R42, R43, R44.
Publications that listed multiple IMAT grants were counted for every grant listed.
Reviews, letters, editorials, and comments were excluded. Publications were only counted through Dec. 31, 2019.
Publications were only counted for a grant if published *after* the IMAT grant was awarded.
Publications are divided based on citation frequency.



Awarded projects sorted by number of publications

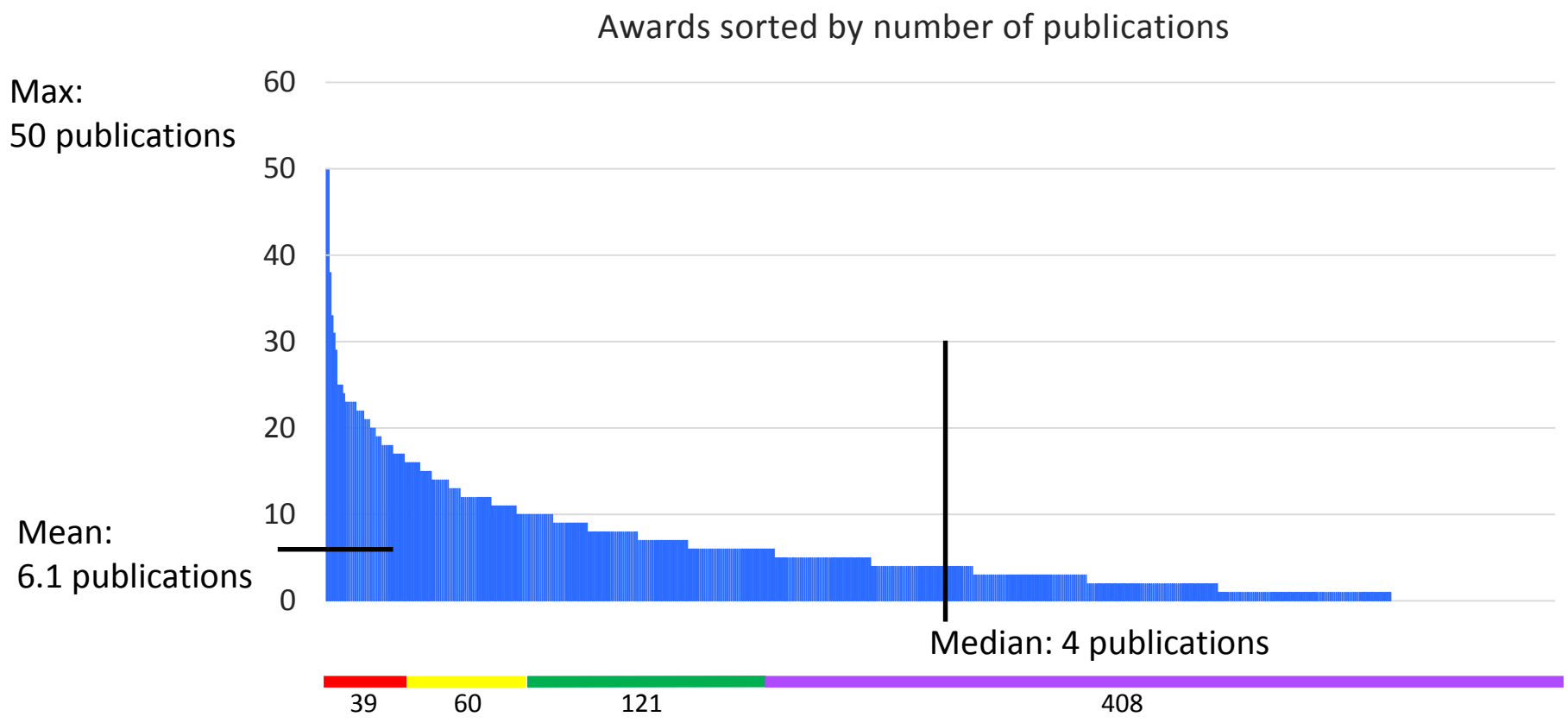
638 grants from 1999-2016. R21 and R33.

Number of publications associated with each award was calculated.

Reviews, letters, editorials, and comments were excluded. Publications were only counted through Dec. 31, 2019.

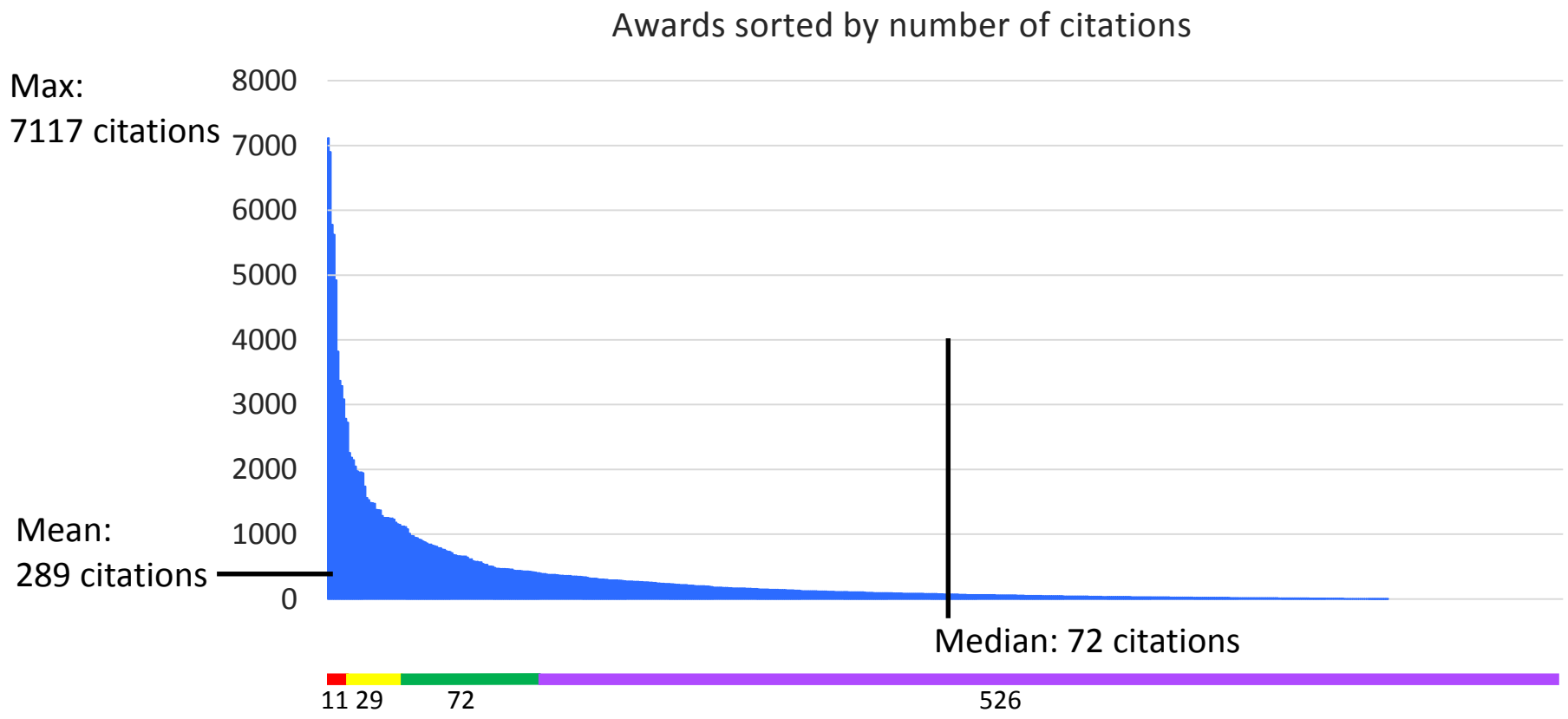
Publications were only counted for a grant if published *after* the IMAT grant was awarded.

Awards are divided by number of projects that make up a quarter of all publications.



Awarded projects sorted by number of citations

638 grants from 1999-2016. R21 and R33.
Citations from all publications associated with each project were added together.
Reviews, letters, editorials, and comments were excluded. Publications were only counted through Dec. 31, 2019.
Publications were only counted for a grant if published *after* the IMAT grant was awarded.
Awards are divided by number of projects that make up a quarter of all citations.



Assessing Success

Evaluating Awards from 2013 and 2014 awards (most recent complete records):

RFA	Mechanism	# of Awards	# of Successes	Success Rate	# of Failures	Failure Rate
CA12-002	R21	20	8	40%	6	30%
CA12-003	R33	11	7	64%	1	9%
CA12-004	R21	3	2	67%	0	0%
CA12-005	R33	3	2	67%	0	0%
CA13-001	R21	21	9	43%	4	19%
CA13-002	R33	10	4	40%	2	20%
CA13-003	R21	5	2	40%	2	40%
CA13-004	R33	4	2	50%	0	0%

- Success
  - Met and/or exceeded original goals and aims. Technology working.

  or
  - Project evolved towards different goals or even partial success offered sufficiently useful capabilities that overall was considered a success.

- Failure
  - Productivity failure – poor progress on aims and no new capabilities emerging
  - Unsuccessful attempt, but productivity satisfying in spite of no new technology available

- Partial – everything in between

FY2013 Success Stories

PI Name(s) All	Institution	Title	Mechanism
KAMM, ROGER D.	MASSACHUSETTS INSTITUTE OF TECHNOLOGY	Microfluidic 3D Assays for Metastatic Cancer	MCA R33
EWING, ROBERT & WANG, ZHENG	CASE WESTERN RESERVE UNIVERSITY	Developing novel technology for mapping dynamic oncoprotein interaction networks	MCA R21
CARON, MARC G.	DUKE UNIVERSITY	A Cancer Rainbow Mouse for the Simultaneous Assessment of Multiple Oncogenes	MCA R21
LIOTTA, LANCE ALLEN	GEORGE MASON UNIVERSITY	Protein Painting reveals hidden protein-protein interaction domains	MCA R21

FY2014 Success Stories

PI Name(s) All	Institution	Title	Mechanism
ZILBERBERG, JENNY & LEE, WOO YOUNG	HACKENSACK UNIVERSITY MEDICAL CENTER	Microfluidic approach for the development of a three-dimensional bone marrow micr	BST R21
NOLAN, GARRY P	STANFORD UNIVERSITY	Highly multiplexed ion-beam tissue molecular imaging with sub-micron resolution	BST R33
HANSEN, KIRK C & WEAVER, VALERIE MARIE	UNIVERSITY OF COLORADO DENVER	Advanced Methods to Evaluate Extracellular Matrix and Crosslinking in the Tumor M	BST R33
WANG, TZA-HUEI	JOHNS HOPKINS UNIVERSITY	Digital Detection of Tumor-Derived Circulating Methylated DNA	MCA R21

IMAT Blockbusters

BeadChip & BeadArray [Mark Chee, Sentrix (aka Illumina)]

- Foundation of Illumina's NGS platforms. Award made in 1999 as Illumina was launching. (1999 IMAT)

Rolling Circle Amplification [Paul Lizardi, Yale]

- Received an R33 after having just published the first paper on RCA, Dr. Lizardi further developed the method to rapidly amplify an entire genome (isothermal whole-genome amplification). (1999 IMAT)

Protein Footprinting [Mark Chance, Case Western]

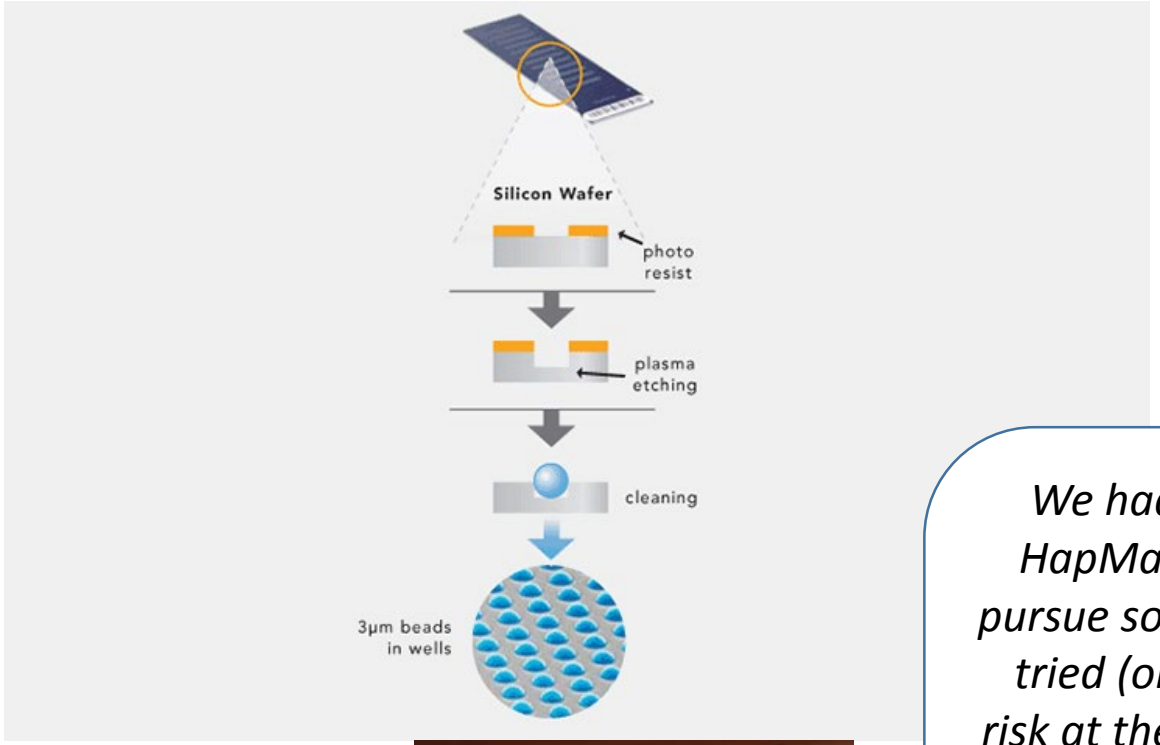
- Spectrometry-based method of biochemical analysis enabling visualization of protein folding and dynamics on millisecond timescales with high resolution. (2000 IMAT)

•**PROTACS** [Craig Crews, Yale]

- Chemical knockdown approach of targeted proteins in a novel, fast and effective way to generate protein depletion models, and has emerged as the basis for a new promising treatment approach. (2006 IMAT)

Shotgun proteomics [Dick Smith (**DREAMS**), PNNL; Ruedi Aebersold (**ICAT**), ISB; John Yates (**MuDPIT**), U Wash]

- Fundamental reagents, analytical tools and protocols for identifying proteins in complex mixtures using a combination of high-performance liquid chromatography combined with mass spectrometry. (RS 2000 IMAT; RA 2000 IMAT; JY 1999 IMAT)



illumina®

We had equity funding, and other SBIR and other grants (esp. HapMap) that also helped, but the IMAT funding allowed us to pursue some important avenues that we might not otherwise have tried (or would have tried much later) because of the perceived risk at the time. ***The IMAT funding helped us to develop the gene expression assay and advance the array matrix platform, both of which were successfully commercialized. I believe that the development of the BeadChip platform was also accelerated significantly as a result of the IMAT-funded effort****, and as you know this platform was a major advance for the company.*

Mark Chee, PhD
IMAT PI
Co-founder, Illumina

Evidence of Clinical Impact

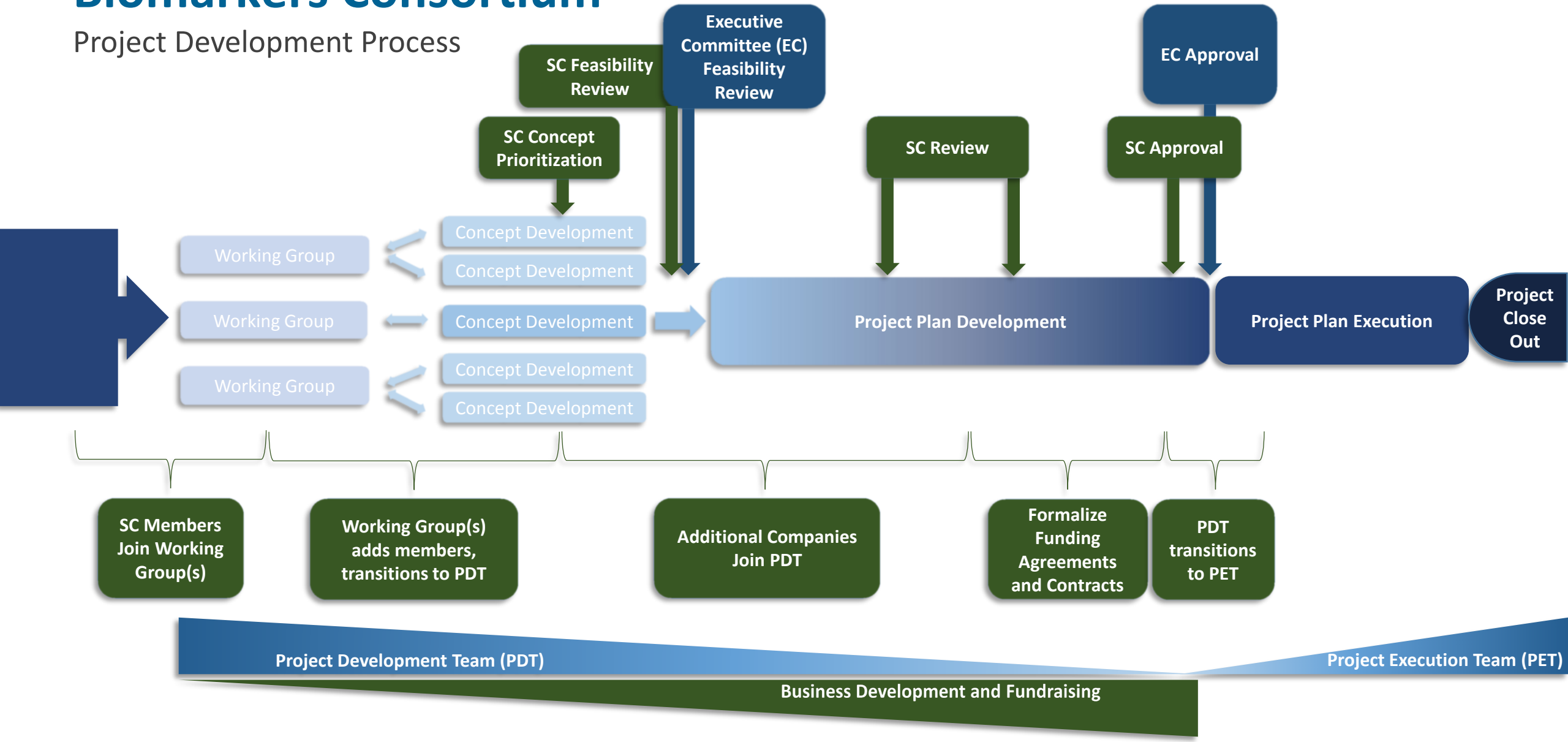
- FNIH Biomarkers Consortium
  - Brings together the expertise and resources of partners to rapidly identify, develop and qualify potential high-impact biomarkers.

For Profit Members

Non-profit Members

Biomarkers Consortium

Project Development Process



Steering Committee (SC)

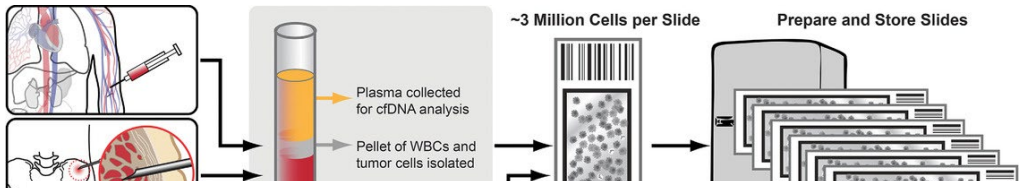
Working Group ⟷ Concept Development → Project Plan Development → Project Plan Execution → Project Close Out

Project Development Team (PDT) → Project Execution Team (PET)

Business Development and Fundraising

2016-2019

Peter Kuhn, PhD
USC
IMAT R33 2013-2016



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Research

Published June 4, 2016

JAMA Oncology | Original Investigation

Association of AR-V7 on Circulating Tumor Cells as a Treatment-Specific Biomarker With Outcomes and Survival in Castration-Resistant Prostate Cancer

Howard I. Scher, MD; David Lu, PhD; Nicole A. Schreiber, BA; Jessica Louw, BS; Ryon P. Graf, PhD; Hebert A. Vargas, MD; Ann Johnson, MS; Adam Jendrisak, MBA; Richard Bambury, MB, BCh, BAO; Daniel Danila, MD; Brigit McLaughlin, BS; Justin Wahl, BS; Stephanie B. Greene, PhD; Glenn Heller, PhD; Dena Marrinucci, PhD; Martin Fleisher, PhD; Ryan Dittamore, MBA

S
Clin

Steering Committee (SC) → Working Group ⟷ Concept Development → Project Plan Development → Project Plan Execution → Project Close Out

Project Development Team (PDT) → Project Execution Team (PET)

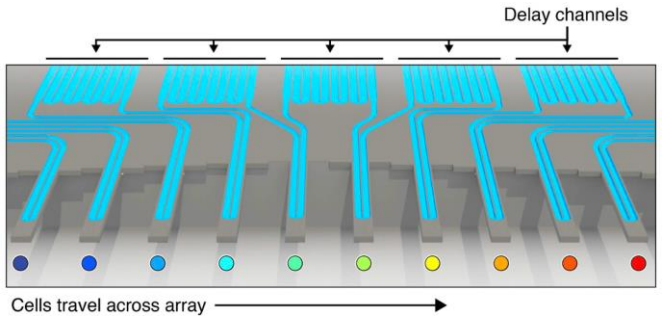
Business Development and Fundraising

Peter Kuhn, PhD
USC
IMAT R33 2014-2016

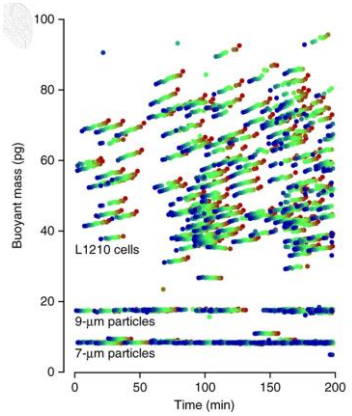
2016-2019

Scott Manalis, PhD
MIT
IMAT R21-33 2009-2018

2018-Present

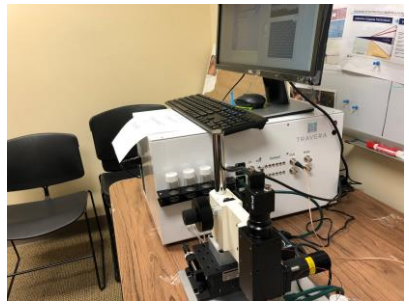


N Cermak *et al*,
Nat Biotech 2016



Measuring Mass Accumulation Rate (MAR) for primary cells isolated from patients for drug response

TRAVERA



Project goal: *Qualifying an entirely new biomarker (MAR) in the context of monitoring for minimally residual disease in patients treated for acute myeloid leukemia.*

Steering Committee (SC)

Working Group ⟷ Concept Development → Project Plan Development → Project Plan Execution → Project Close Out

Project Development Team (PDT) → Project Execution Team (PET)

Business Development and Fundraising

Peter Kuhn, PhD
USC
IMAT R33 2014-2016

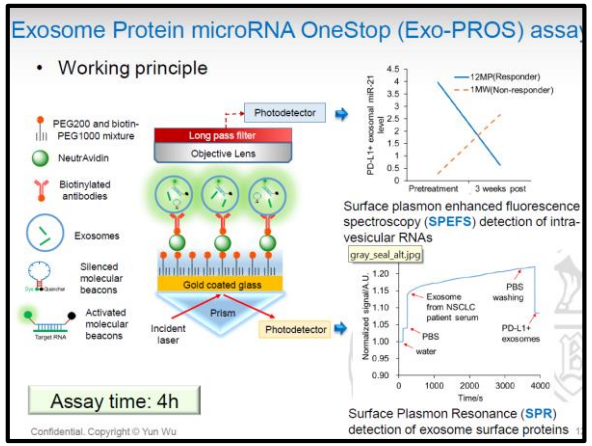
2016-2019

Scott Manalis, PhD
MIT
IMAT R21-33 2009-2018

2018-Present

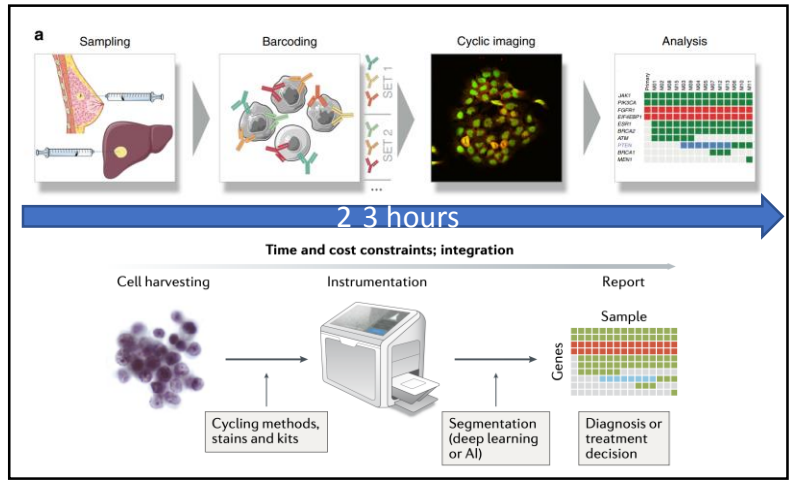
2020 - ?

Sunny Wu, PhD
SUNY Buffalo
IMAT R33 2015-2019



2020 - ?

Ralph Weissleder, PhD
Harvard
IMAT R33 2016-2019



Evidence of Clinical Impact

Protein Paint - small-molecule dyes that bind promiscuously and with high affinity to proteins, and can be used to sequence the interaction regions between proteins in a complex, informing design of inhibitor strategies.

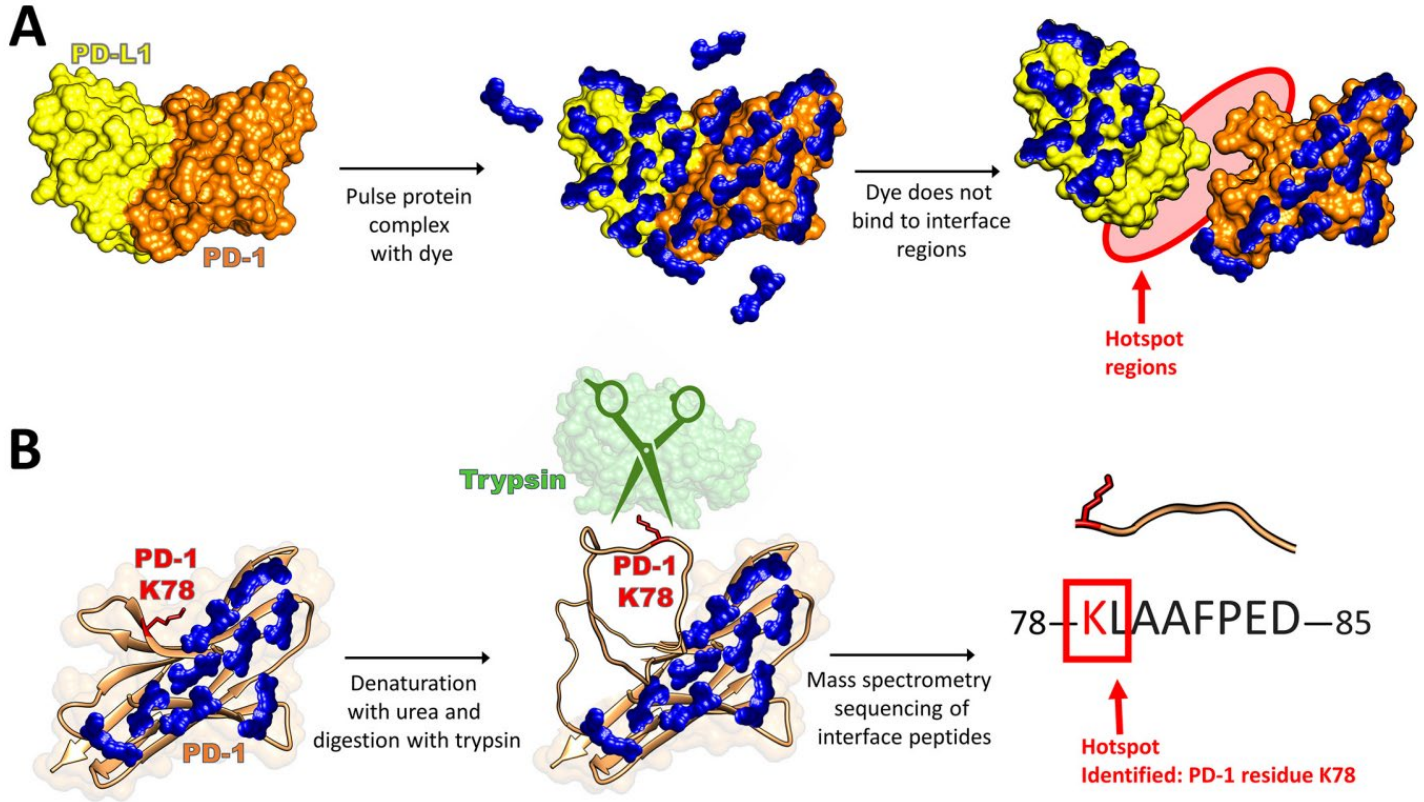
Virginia Espina, PhD

Lance Liotta, MD, PhD

Amanda Haymond, PhD

Alessandra Luchini, PhD

Interfaces of PD-1/PD-L1 and YAP2/ZO-1 revealed



Haymond *et al*, J Biol Chem 2019

IMAT R21-R33 from 2013-2019

Evidence of Collaboration Impact

Josh Rabinowitz & Eilleen White

- [2008 IMAT] Developed **MS-based tracers for profiling metabolic fluxes in cells,** which allowed for discovery of upregulation of 2-hydroxglutarate due to mutated IDH-1 in GBM.
- New metabolic methods became the cornerstone of a new partnership with Eilleen White (Cancer biologist, Rutgers) to explore the role of metabolism in cancer (multiple RO1s).

Hsian-Rong Tseng & Edwin Posadas

- [2010 IMAT] Developed **NanoVelcro**, which is a microfluidic platform to capturing CTCs by adhering capture agents to nano-fibers with clever release mechanisms for isolating viable target cells from complex samples.
- The Nano Velcro platform became the basis for a collaboration with Ed Posadas (Clinical oncologist, Cedars Sinai) to develop various screening and monitoring assays for his prostate cancer patients through numerous R01 and U01U01 awards, and for commercial development of the platform through a jjoint venture (Cytolumina, LLC).

Claudia Fischbach & Cliff Huddis

- [2012 IMAT] Developed mineralized 3D culture substrates for modeling breast cancer in vitro, to test the role of hydroxyapatite in breast microcalcifications and in bone tissue.
- The successfully developed platform led to a series of successful awards (multiple R01s and other awards) with Cliff Hudis (chief of BrCa medicine at MSK) to make substantial contributions to understand breast cancer metastasis.

Evidence of Collaboration Impact

Roger Kamm & Tyler Jacks, Bob Weinberg, Richard Hines, David Barbie…

- [2012 IMAT] Developed a microfluidic platform for 3D tissue culturing essential components of the in vivo tumor microenvironment. Very successful R21-R33 leading to commercialization of the platform through AIM Biotech (that holds non-exclusive licensing agreements with Biogen and Amgen).
- Led to several big collaborations with both basic and clinical research scientists looking at a broad variety of cancer phenomena and several critical advances in immuno-oncology.

Richard Schlegel & many

- [2013 IMAT] Created the **Conditionally Reprogrammed Cells** method (or "Georgetown Method") which allows short term culturing of nearly any type of cancer cell and to development of a substantial biobank at Georgetown for a broad array of expanded primary cancer cells across many different cancer types.
- The method has been adopted by a great many labs across the world, including the NCI (in several of their cancer modeling development centers) and according to the PI more collaboration opportunities than he can keep up with. An independent office at NCI was sufficiently excited about the technology they wrote up a summary of its impact here.

Evidence of Commercialization Impact

- **Mike Makrigiorgos** – **COLD-PCR** (2005 IMAT), exclusively licensed by Transgenomics in 2009 and novel formulations of the original method still commercially used.
- **Darren Link** – **RainDance** (2007 IMAT) one of the first droplet microfluidic platforms credited their IMAT award with allowing them to launch their first platform which focused on digital PCR (effectively becoming the first droplet-based digital PCR platform).
- **Lance Liotta** – **Nanotrap** (2009 IMAT) porous nano-scale hydrogel cages with chemical affinity bait loaded within the cage to capture and protect rare target analytes in complex solutions, commercialized through Ceres Nano.
- **Sarah Blair** – **SignalMark** (2011 IMAT) implantable markers to mark tumor margins for resection to ensure negative margins, being commercialized by View Point Medical.
- **Samantha Pattenden/Paul Dayton** – (2012 IMAT) nanodroplets that serve as cavitation agents for more efficient and uniform fragmentation of DNA. Being commercialized by Triangle Biotechnology.
- **John Williams** – **Meditopes** (2013 IMAT) are based cyclic peptides that bind a site within the Fab arm of an IgG antibody, allowing for full binding performance to the target antigen while allowing broad manipulation of the antibodies, in a manner that the firm commercializing them (Meditope Biosciences) calls a "LEGO-like conjugation system."
- **Larry Loeb** – developed **Duplex Sequencing** with a 2014 IMAT award, now being commercialized by TwinStrand Biosciences.

Evidence of Commercialization Impact

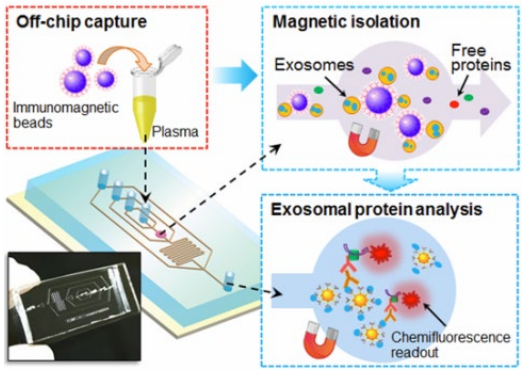
I-CORPS at NIH

2018

ExoSearch

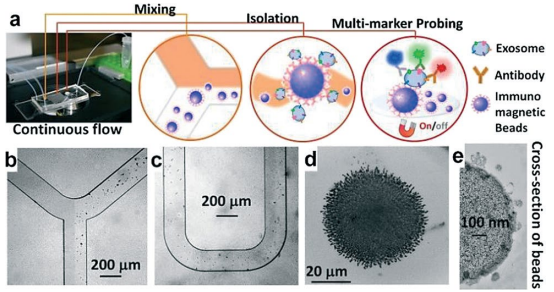
Integrated microfluidic exosome profiling assay for molecular analysis of circulating exosomes in microliter volumes of plasma.

CLARA BIOTECH



Zhao *et al*, Lab Chip, Jan 2016

Mei He, PhD
CSO, Clara Diagnostics



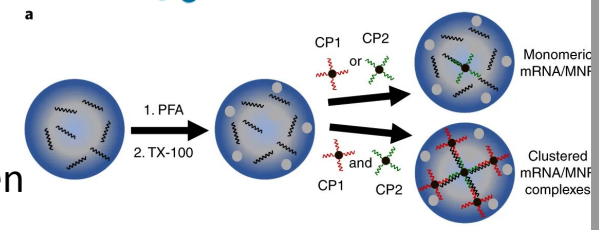
Launched with 2014 IMAT award

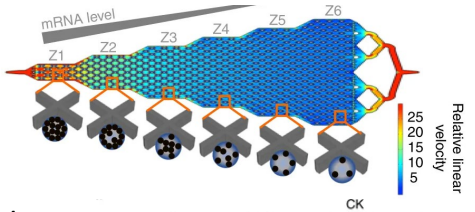
2019

CytoFind

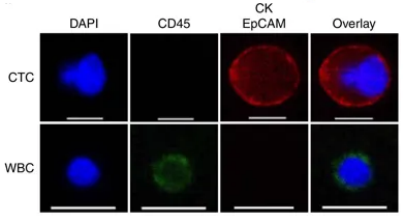
CELLULAR ANALYTICS

Purifies circulating tumor cells (CTCs) from whole blood samples by selectively marking the CTCs with magnetic particles and then isolating the cells using a magnetic microfluidic device





M Labib *et al*, Nat Chem, Apr 2018



Shana Kelley, PhD
CSO, Cellular Analytics

Launched with 2017 IMAT award

Other Evidence of Impact – NCI Outstanding Investigator Award

Ben Cravatt – Activity-based Protein Profiling

- 2006 IMAT (R33)

Craig Crews – PROTACs

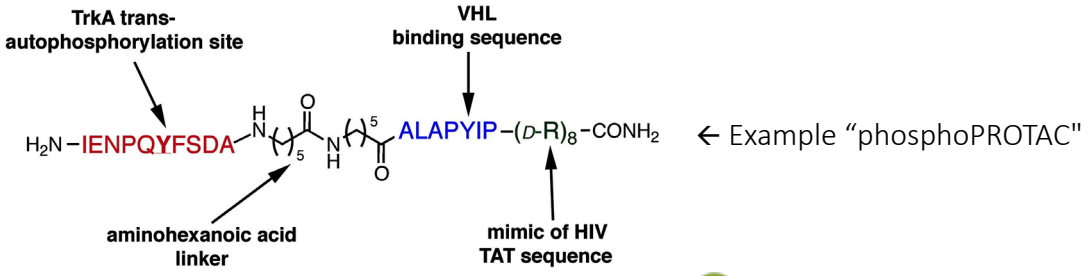
- 2006 IMAT (R21-R33)

Levi Garraway – OncoMap

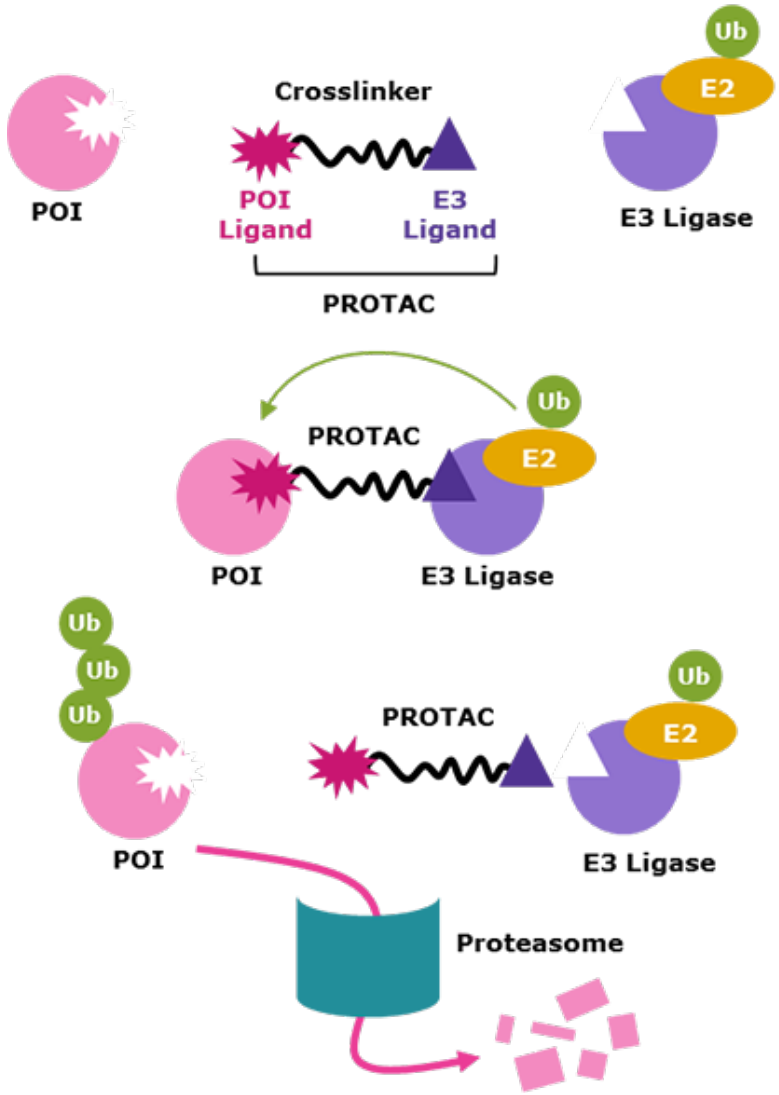
- 2007-2017 IMAT (R21-R33, R33); to

Patrick Moore – Digital Transcriptome Subtraction

- 2007 IMAT (R21-R33)



← Example "phosphoPROTAC"



1 **PROTAC design**
Constructed to bind both protein of interest (POI) and E3 ligase through a crosslinker

2 **Ternary complex**
PROTAC recruits POI to E3 ligase

3 **Polyubiquitination**
Ubiquitin (Ub) added to POI Lys residues

4 **Target degradation**
Ub-marked POI is degraded by the proteasome

Craig Crews, Ph.D., Yale University

2006—R21
2008—R33
"Analysis of Tumorigenic Signaling Pathways with PROTACs"

2013—Arvinas, Inc

2015—R35
"Inducing Protein Degradation: A New Pharmaceutical Paradigm"

Question 2:
Is the balance between the 4 Is appropriate?

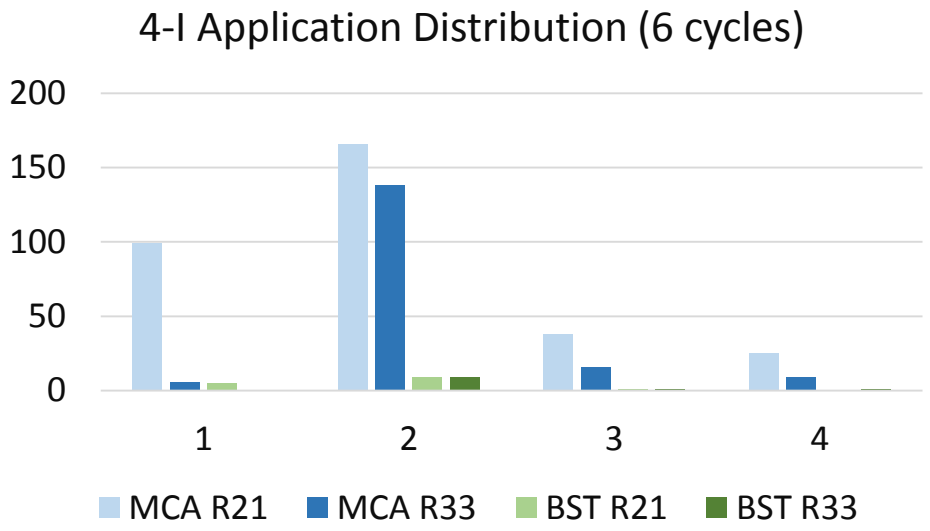
Lead: Susan Margulies

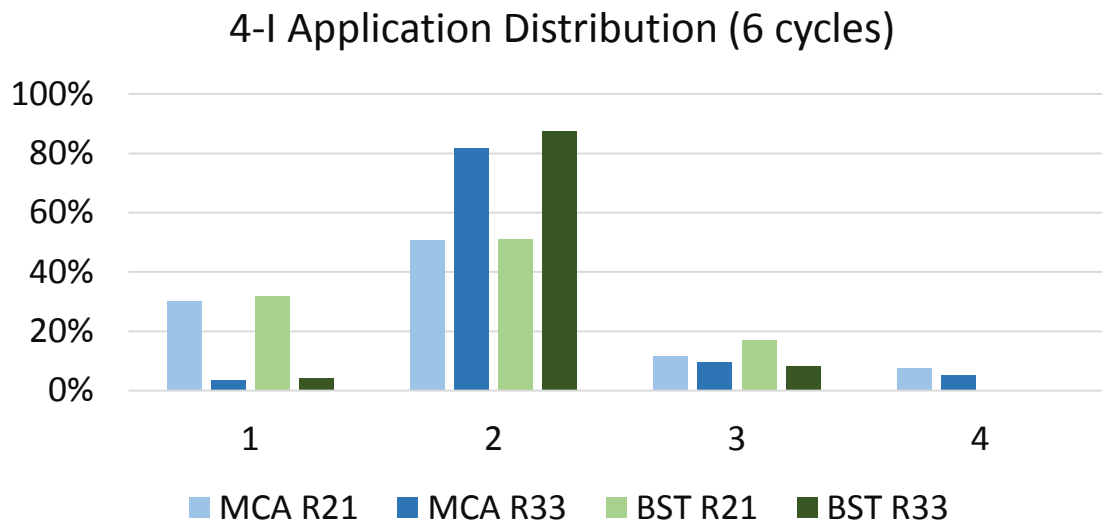
4-Is of Innovation

1. Innovative new technology
2. Improvement of an existing technology
3. Integration of previously separate/siloed technologies
4. Implementation of new discoveries to the community

4-Is of Innovation - Applications

All applications received during 2018 and 2019 (3 cycles per year) were assigned to the 4 I categories



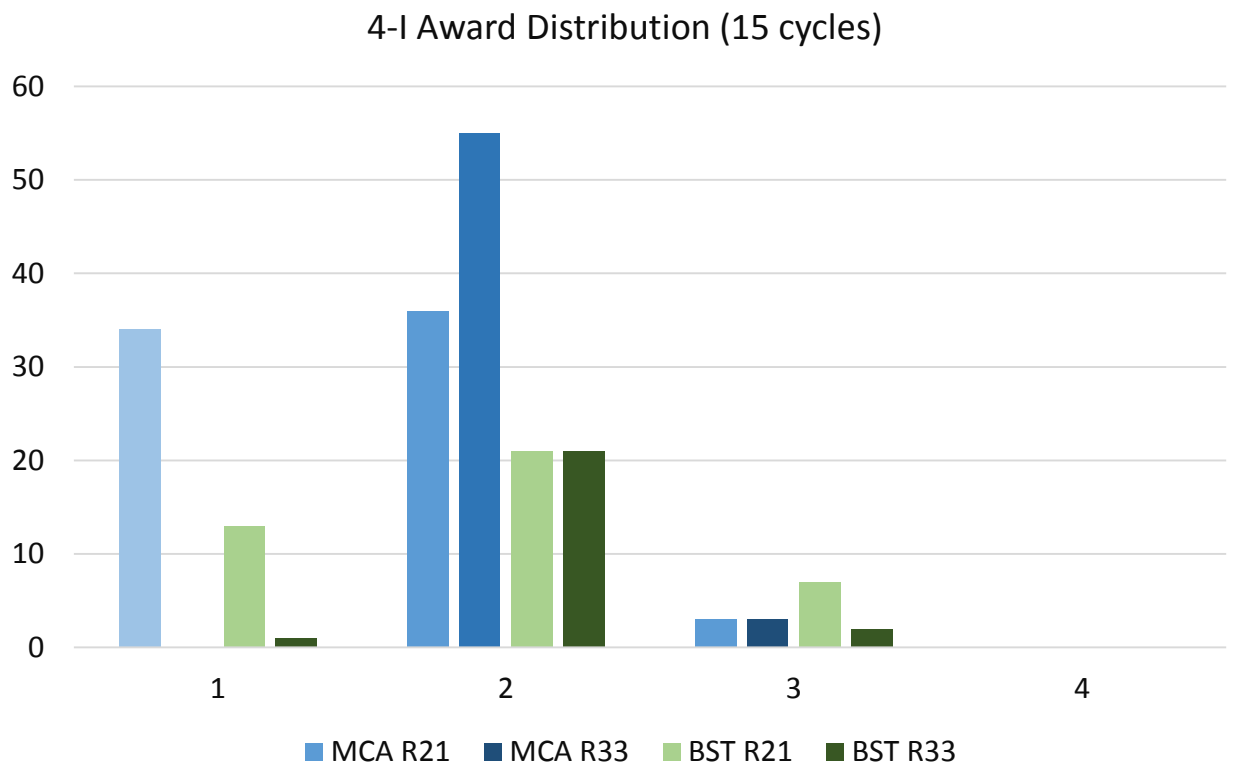


Applications			Category			
RFA #	Series	Activity	1	2	3	4
CA18 002	MCA	R21	61	83	24	16
CA18 003	MCA	R33	3	74	8	7
CA18 004	BST	R21	6	8	6	0
CA18 005	BST	R33	1	11	1	0
CA19 019	MCA	R21	38	83	14	9
CA19 020	MCA	R33	3	64	8	2
CA19 021	BST	R21	7	13	1	0
CA19 022	BST	R33	0	10	1	0
		Overall	119	336	62	34

4-Is of Innovation - Awards

All awards given between 2015 and 2019 (15 cycles) were assigned to the 4 I categories

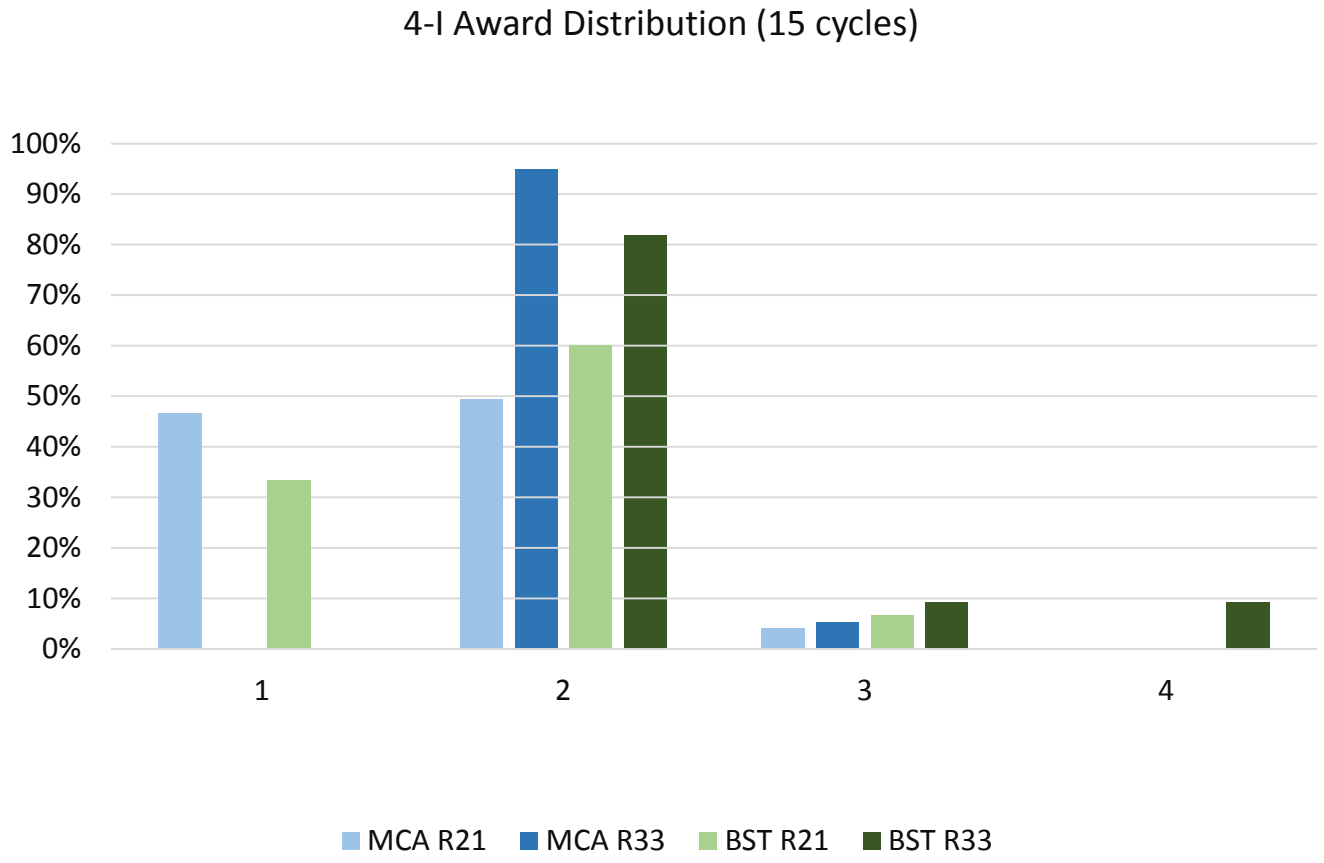
Awards			Category			
RFA	Series	Act	1	2	3	4
CA19 019	MCA	R21	6	8	0	0
CA18 002	MCA	R21	4	11	1	0
CA17 010	MCA	R21	6	8	0	0
CA16 001	MCA	R21	11	5	2	0
CA15 002	MCA	R21	7	4	0	0
	Overall		34	36	3	0
CA19 020	MCA	R33	0	9	1	0
CA18 003	MCA	R33	0	10	1	0
CA17 011	MCA	R33	0	10	0	0
CA16 002	MCA	R33	0	12	0	0
CA15 003	MCA	R33	0	14	1	0
	Overall		0	55	3	0
CA19 021	BST	R21	0	2	1	0
CA18 004	BST	R21	1	1	0	0
CA17 012	BST	R21	1	2	0	0
CA16 003	BST	R21	1	1	0	0
CA15 004	BST	R21	2	3	0	0
	Overall		5	9	1	0
CA19 022	BST	R33	0	1	1	0
CA18 005	BST	R33	0	1	0	0
CA17 013	BST	R33	0	1	0	1
CA16 004	BST	R33	0	3	0	0
CA15 005	BST	R33	0	3	0	0
	Overall		0	9	1	1



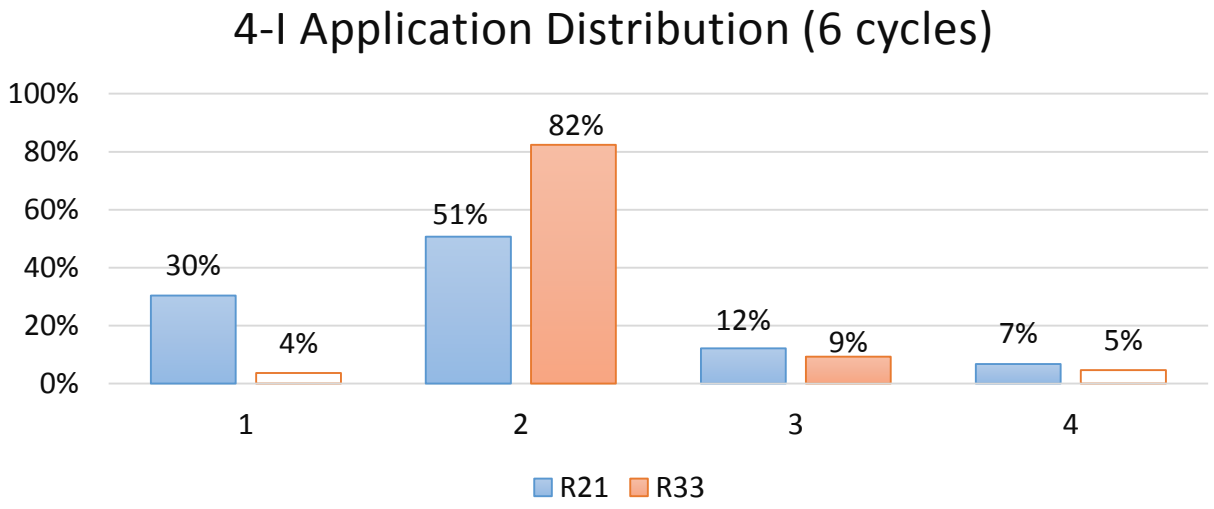
4-Is of Innovation - Awards

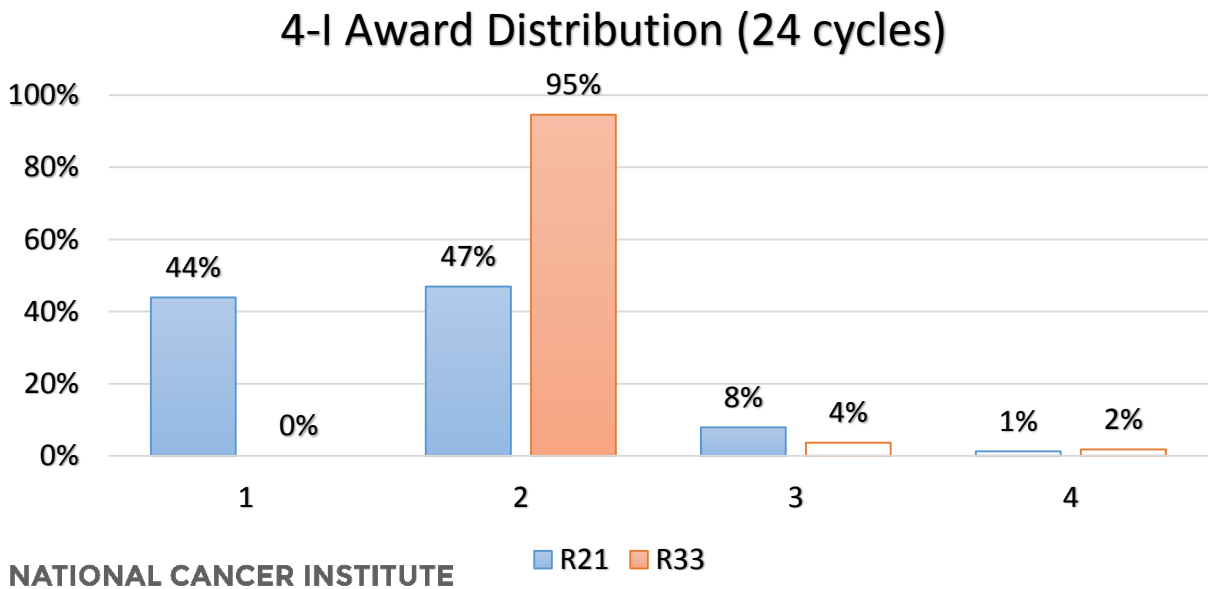
All awards given between 2015 and 2019 (15 cycles) were assigned to the 4 I categories

Awards		Category		
RFA			57%	0%
CA19 019	R21	25%	69%	6%
CA18 002	R21	43%	57%	0%
CA17 010	R21	61%	28%	11%
CA16 001	R21	64%	36%	0%
CA15 002		34	47%	49%
	Overall	0%	90%	10%
CA19 020	R33	0%	82%	9%
CA18 003	R33	0%	100%	0%
CA17 011	R33	0%	100%	0%
CA16 002	R33	0%	93%	7%
CA15 003		0	0%	93%
	Overall	0%	67%	33%
CA19 021	R21	50%	50%	0%
CA18 004	R21	33%	67%	0%
CA17 012	R21	50%	50%	0%
CA16 003	R21	40%	60%	0%
CA15 004		5	33%	60%
	Overall	0%	50%	50%
CA19 022	R33	0%	100%	0%
CA18 005	R33	0%	50%	0%
CA17 013	R33	0%	100%	0%
CA16 004	R33	0%	100%	0%
CA15 005		0	0%	82%



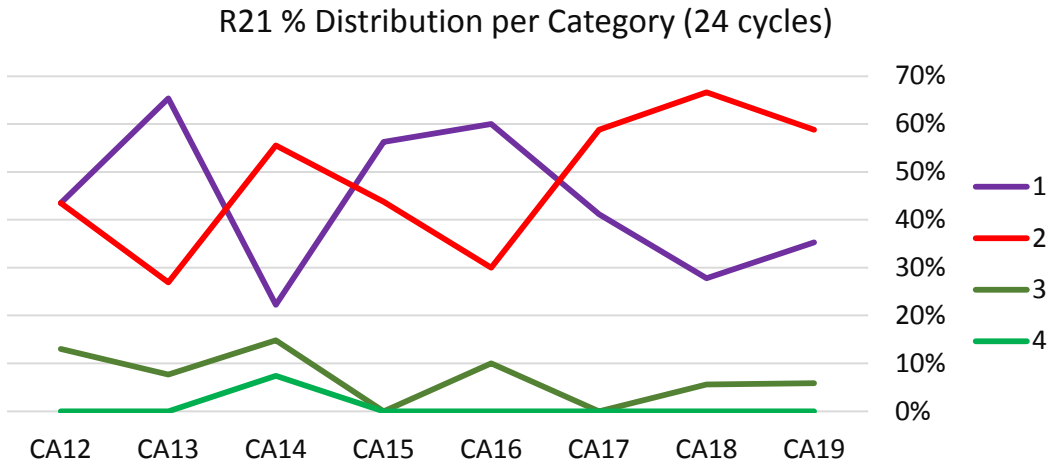
4-Is of Innovation - Comparison

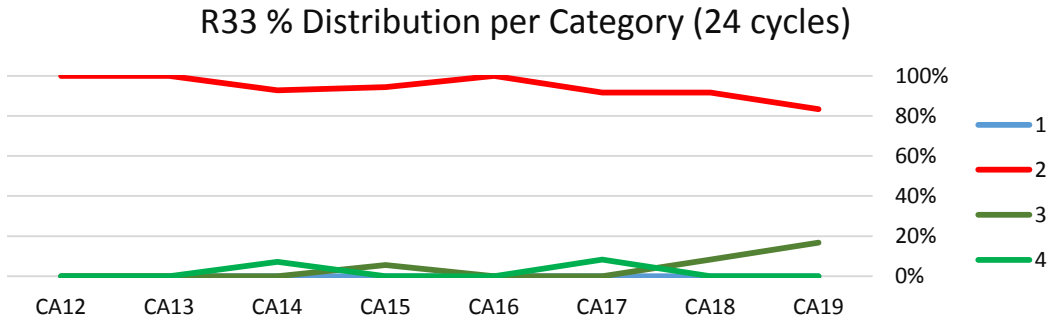




Success Rates per Category (2018-2019)

	1	2	3	4	Overall
R21	10%	12%	4%	0%	9%
R33	0%	13%	17%	0%	12%

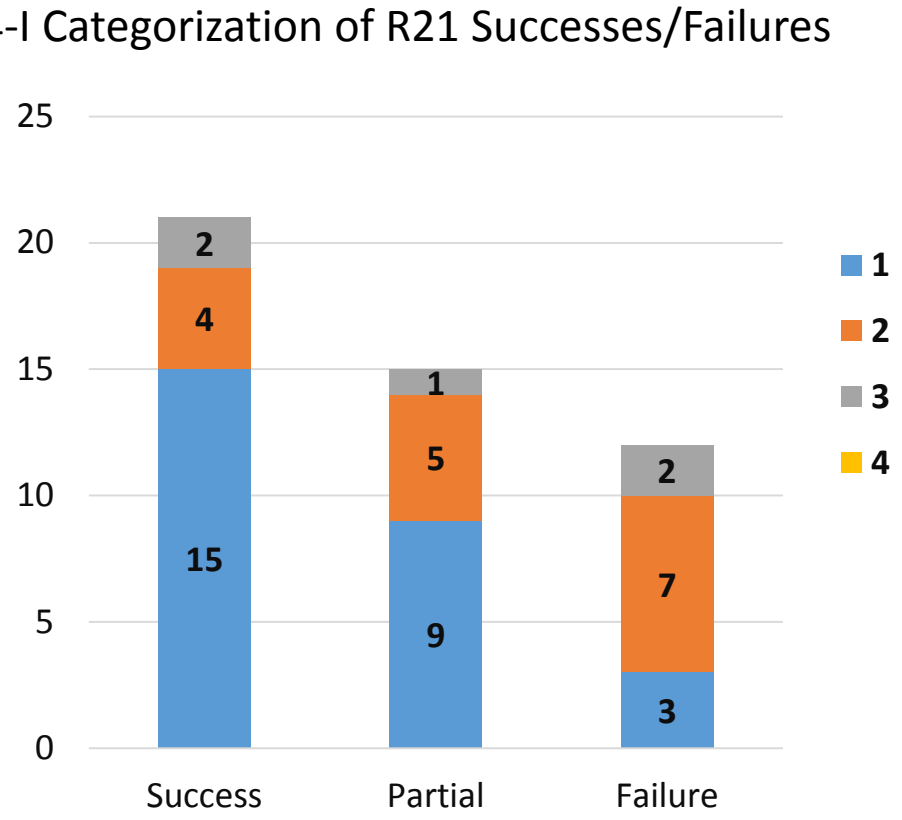




Categorizing Success/Failures with 4-Is

Evaluating Awards from 2013 and 2014 awards (most recent complete records):

Overall	Success	Partial	Failure	Total
R21		15	12	
R33				



Discussion items for Question 2

- Is this the portfolio balance the panel wants?
- How do we get to the right balance?

Question 3:
What are the most important characteristics of the future IMAT program?

Lead: Steven Chu

Question 4 Summary: Recent Efforts to Improve IMAT

- Incentivizing applicants and appropriate review
  - Constantly reviewing how to better orient reviewers
  - Is there sufficient appreciation for “simple” technology concepts
- During the award
  - Collaboration Supplements with ITCR
  - Participation in NIH ICorps Program
  - Targeted outreach for new funding opportunities
  - Holding the PI meeting outside of DC-area
  - NTRAP activities (PI meeting participation and clinical trials guidance)
- Beyond IMAT
  - Global Center for Medical Innovation Incubator
  - Competitive Revision RFAs
  - Telling success stories

Question 4:
Are the current funding mechanisms appropriate to achieve the program goals?

Lead: James Lacey

Appropriateness of Program Structure:

- Current structure:
  - R21 – Direct costs up to $400k for up to 3 years (no more than $200k in any given year); 6-page research strategy
  - R33 – Direct costs up to $300k/year for up to 3 years; 12-page research strategy
  - Competitive Revisions – Direct costs up to $150k/year for up to 2 years; recommend 5-page research strategy.
    - Eligibility: Active R01, U01, U54, P01, P50 and U2C awards from NCI
  - Program team includes program directors from across extramural funding divisions of NCI engaged in a broad diversity of funding mechanisms.

- Possible Measures to assess
  - Source of applications
  - R21/R33 application and award trends
  - Exit interviews & success/failure analysis
  - Transition success rates

Review Orientation

- *Exclusively* focused on supporting highly-innovative technology development research

- Key review points of interest to NCI
  - Potential to overcome persistent barriers or open new areas of research or approaches to clinical care
  - Offer SIGNIFICANT advantages over currently available technologies/approaches

- IMAT is NCI's only high-risk/high-impact technology development funding opportunity …

- Performance Measures must be quantitative (*required for all R21 and R33 applications*)
  - Objectively assessable target of performance for the new capability
  - Reaching each milestone demonstrates successful progress against the aims and captures superiority of technology over conventional approaches
  - Should involve a clear description of how this will be measured, if not inherently obvious

IMAT Program Management

Kelly Crotty, PhD

Amir Rahbar, PhD

National Cancer Institute

- Office of the Director
- SBIR DC
- Center for Cancer Research
- Division of Cancer Epidemiology and Genetics
- Division of Cancer Biology
- Division of Cancer Control and Population Sciences
- Division of Cancer Prevention
- Division of Cancer Treatment & Diagnosis
- Division of Extramural Activities

Jennifer Couch, PhD

Nas Zahir, PhD

Danielle Mercatante Carrick, PhD

Karl Krueger, PhD

Guillermo Márquez, PhD

Diagnostic Biomarkers & Technology Branch

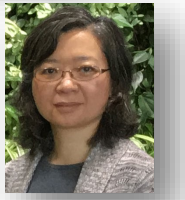
Tawnya McKee, PhD

Brian Sorg, PhD

Miguel Ossandon, PhD

Biorepositories & Biospecimen Research Branch

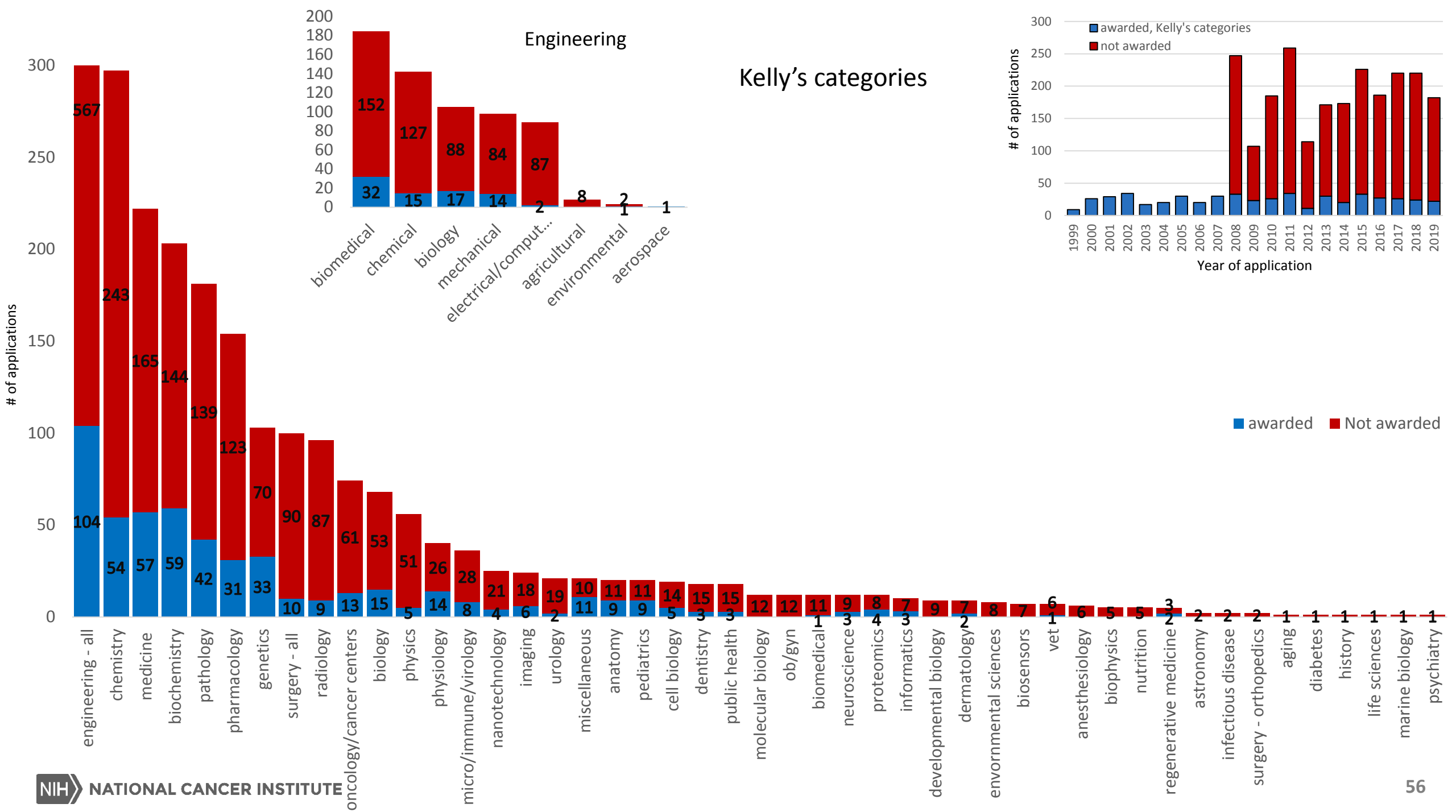
Lokesh Agrawal, PhD



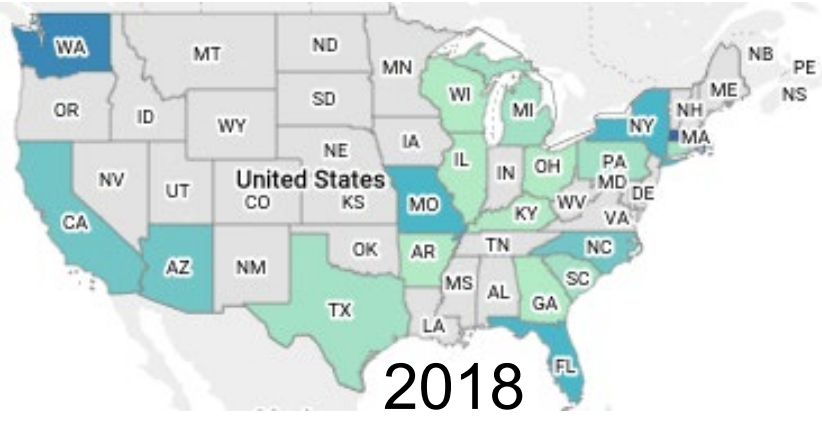
Ping Guan, PhD

Pathology Investigations & Resources Branch

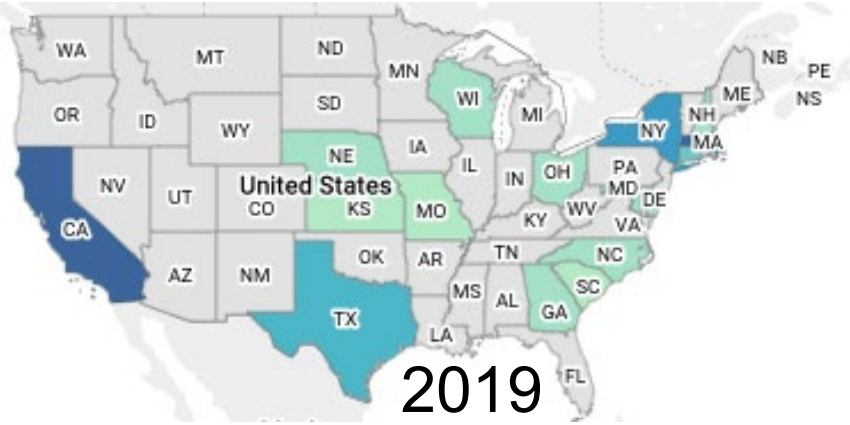
Rodrigo Chuaqui, MD


Kelly's categories
awarded
Not awarded
# of applications
engineering - all 104 567
chemistry 54 243
medicine 57 165
biochemistry 59 144
pathology 42 139
pharmacology 31 123
genetics 33 70
surgery - all 10 90
radiology 9 87
oncology/cancer centers 13 61
biology 15 53
physics 5 51
physiology 14 26
micro/immune/virology 8 28
nanotechnology 4 21
imaging 6 18
urology 2 19
miscellaneous 11 10
anatomy 9 11
pediatrics 9 11
cell biology 5 14
dentistry 3 15
public health 3 15
molecular biology 12
ob/gyn 12
biomedical 1 11
neuroscience 3 9
proteomics 4 8
informatics 3 7
developmental biology 9
dermatology 2 7
envornmental sciences 8
biosensors 7
vet 1 6
anesthesiology 6
biophysics 5
nutrition 5
regenerative medicine 2 3
astronomy 2
infectious disease 2
surgery - orthopedics 2
aging 1
diabetes 1
history 1
life sciences 1
marine biology 1
psychiatry 1
Engineering
biomedical 32 152
chemical 15 127
biology 17 88
mechanical 14 84
electrical/comput... 2 87
agricultural 8
environmental 1 2
aerospace 1
awarded, Kelly's categories
not awarded
# of applications
Year of application
1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019

2017



2018



2019


WASHINGTON
MONTANA
NORTH DAKOTA
MINNESOTA
OREGON
IDAHO
SOUTH DAKOTA
WISCONSIN
MICHIGAN
WYOMING
NEBRASKA
IOWA
ILLINOIS
NEVADA
UTAH
COLORADO
KANSAS
MISSOURI
INDIANA
OHIO
PENN
San Francisco
CALIFORNIA
Las Vegas
Los Angeles
ARIZONA
San Diego
NEW MEXICO
OKLAHOMA
ARKANSAS
MISSISSIPPI
TENNESSEE
KENTUCKY
WEST VIRGINIA
VIRGINIA
NORTH CAROLINA
SOUTH CAROLINA
ALABAMA
GEORGIA
TEXAS
Dallas
LOUISIANA
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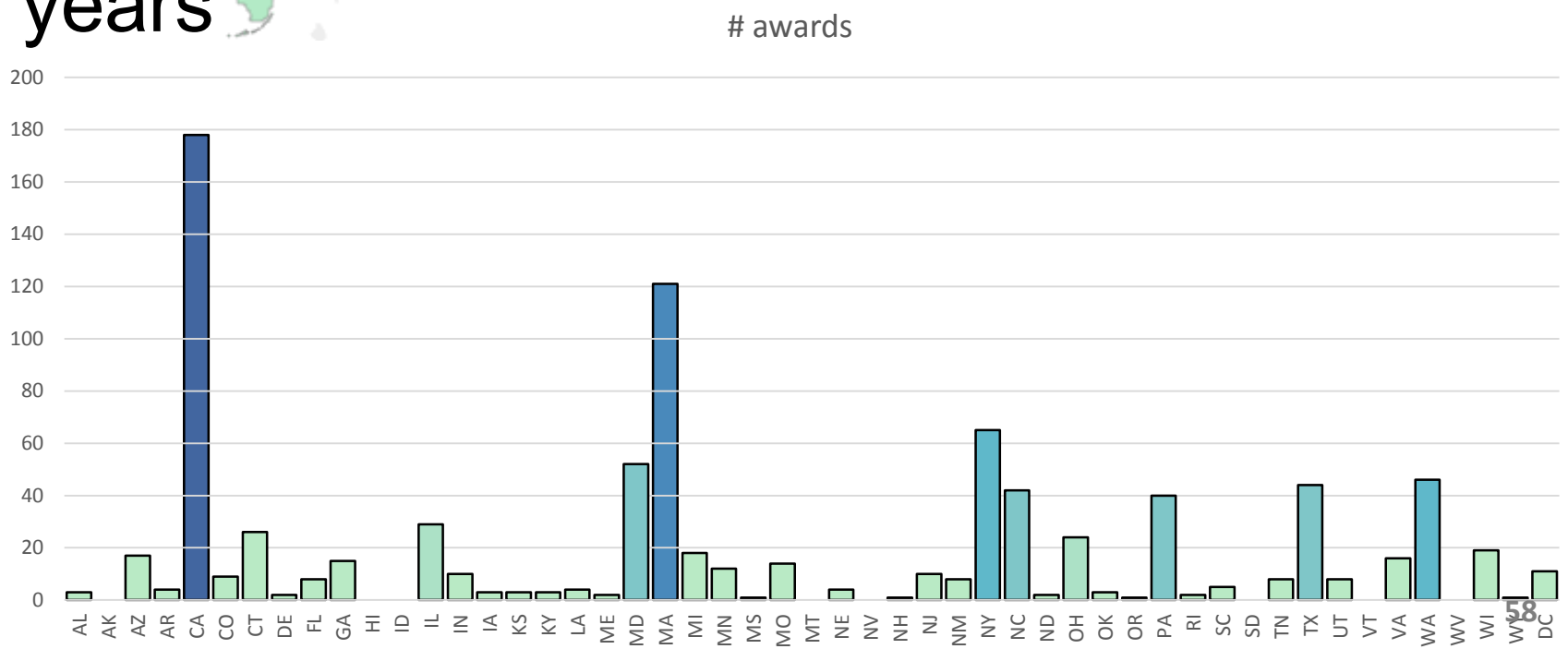
Ottawa
Montreal
NB
PE
NOVA SCOTIA
MAINE
Toronto
VT
NH
NEW YORK
MA
CT RI
Chicago
Philadelphia
MD
DE
NJ
United States

All years


awards
200
180
160
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120
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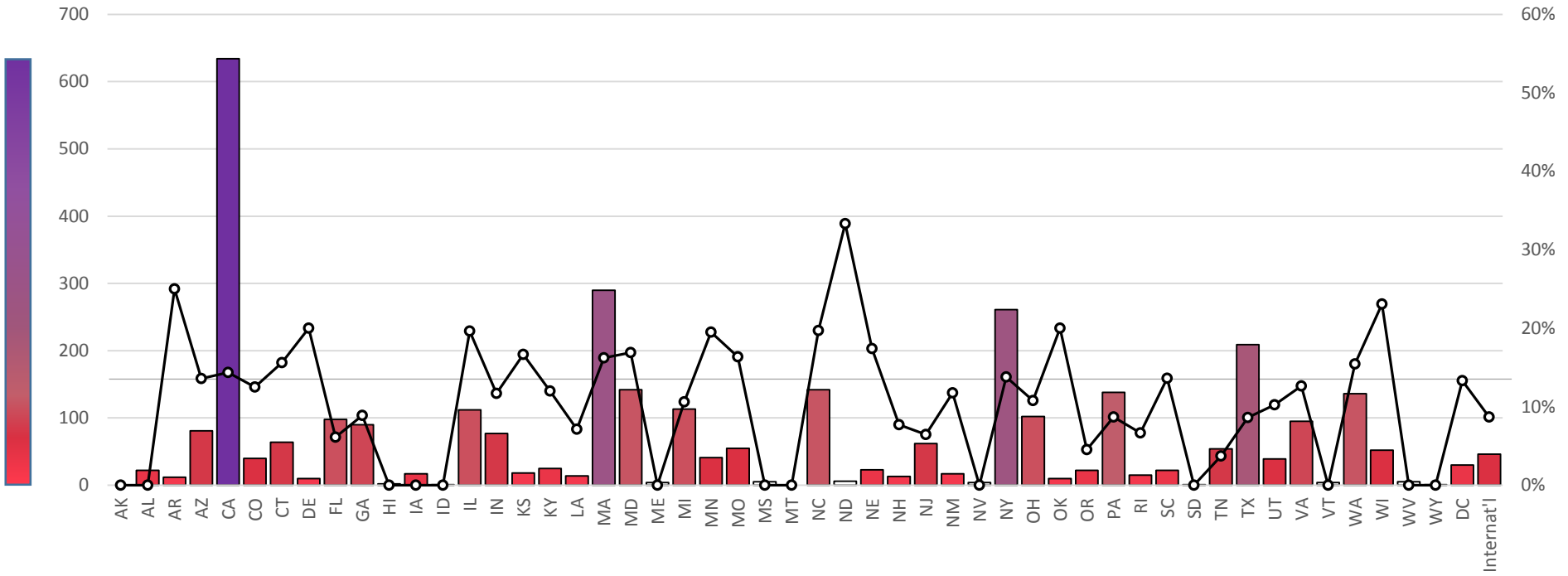
AL AK AZ AR CA CO CT DE FL GA HI ID IL IN IA KS KY LA ME MD MA MI MN MS MO MT NE NV NH NJ NM NY NC ND OH OK OR PA RI SC SD TN TX UT VT VA WA WV WI WY DC

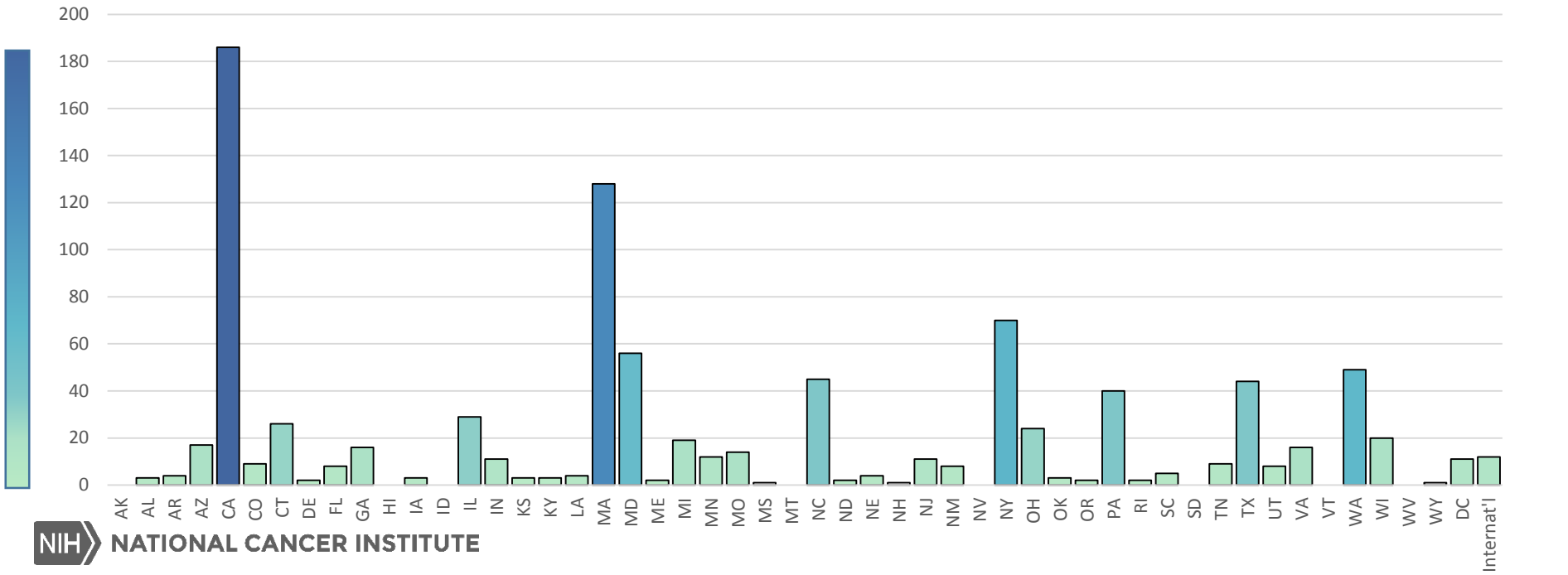


Applications

3477 applications (458 awards)
2008-2019
R21, R33, R41, R42, R43, R44

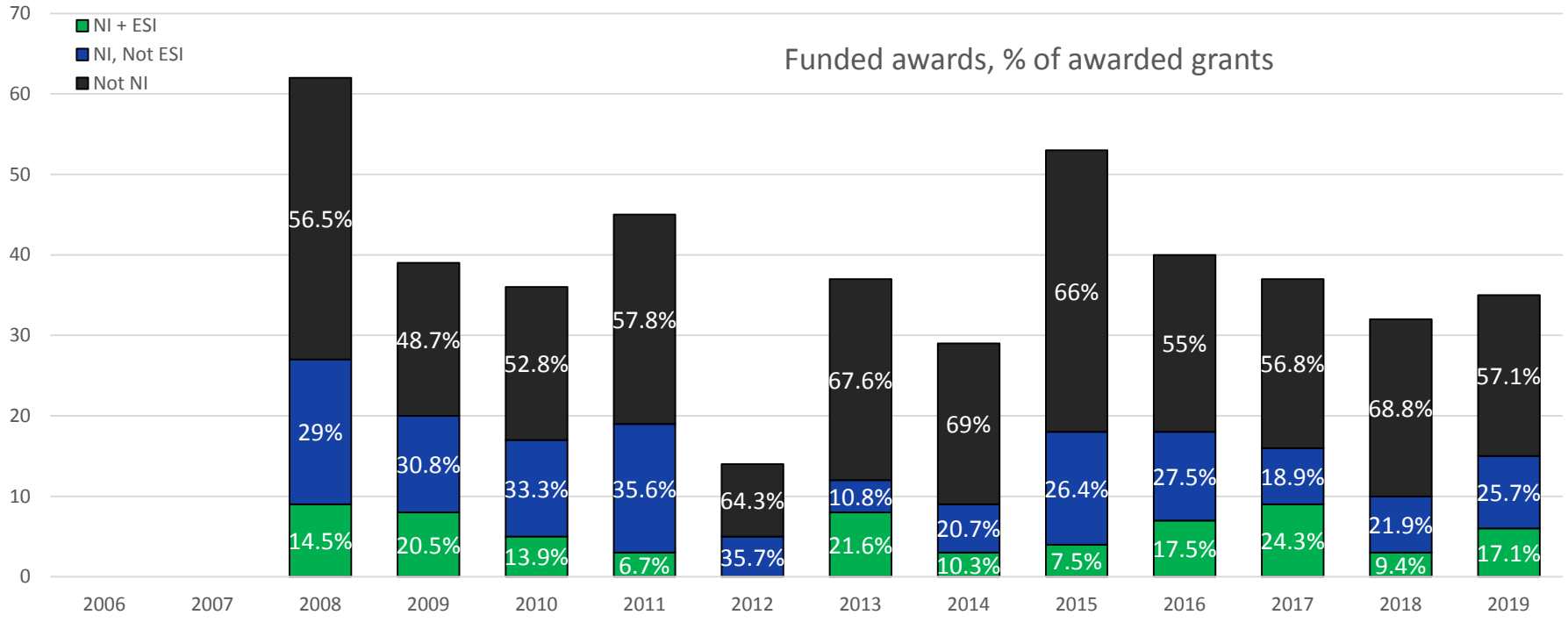
% funded by state
applications vs awards
2008-2019

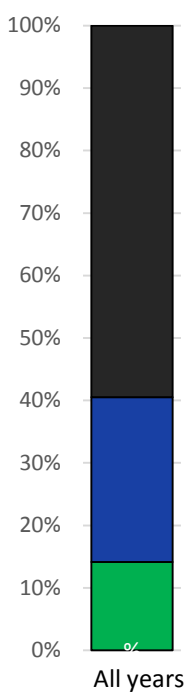
Total % funded
(13.1%)



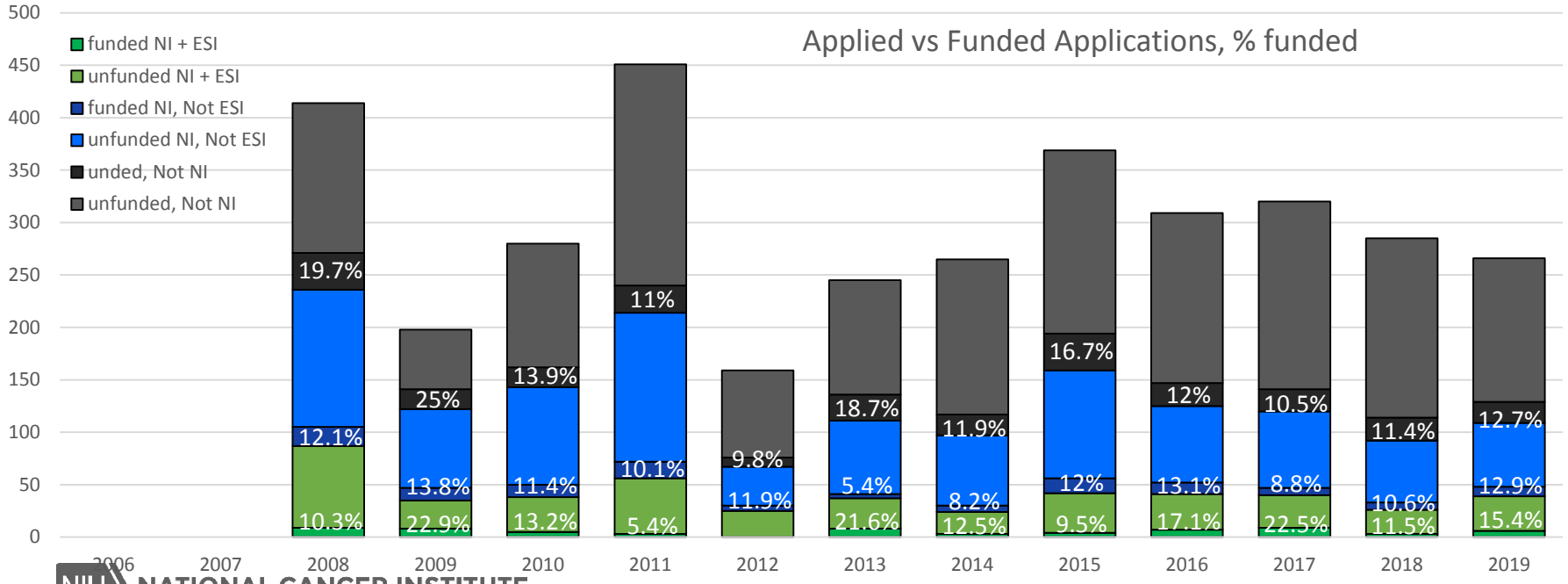
All awards

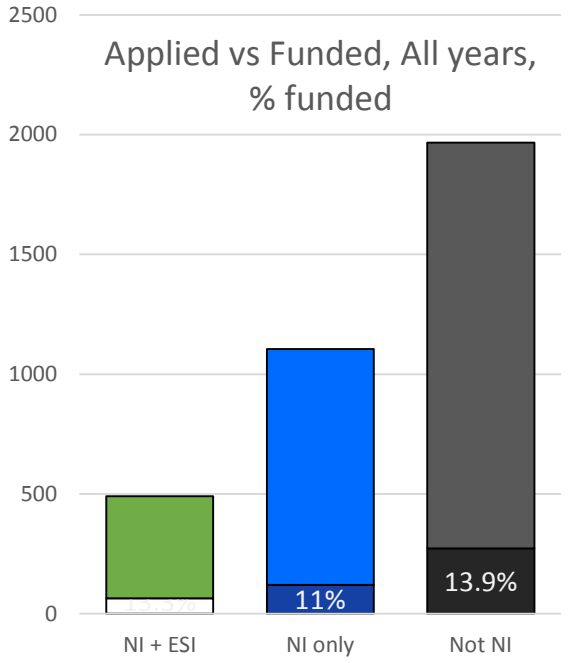
943 grants
1999-2019
R21, R33, R41, R42, R43, R44



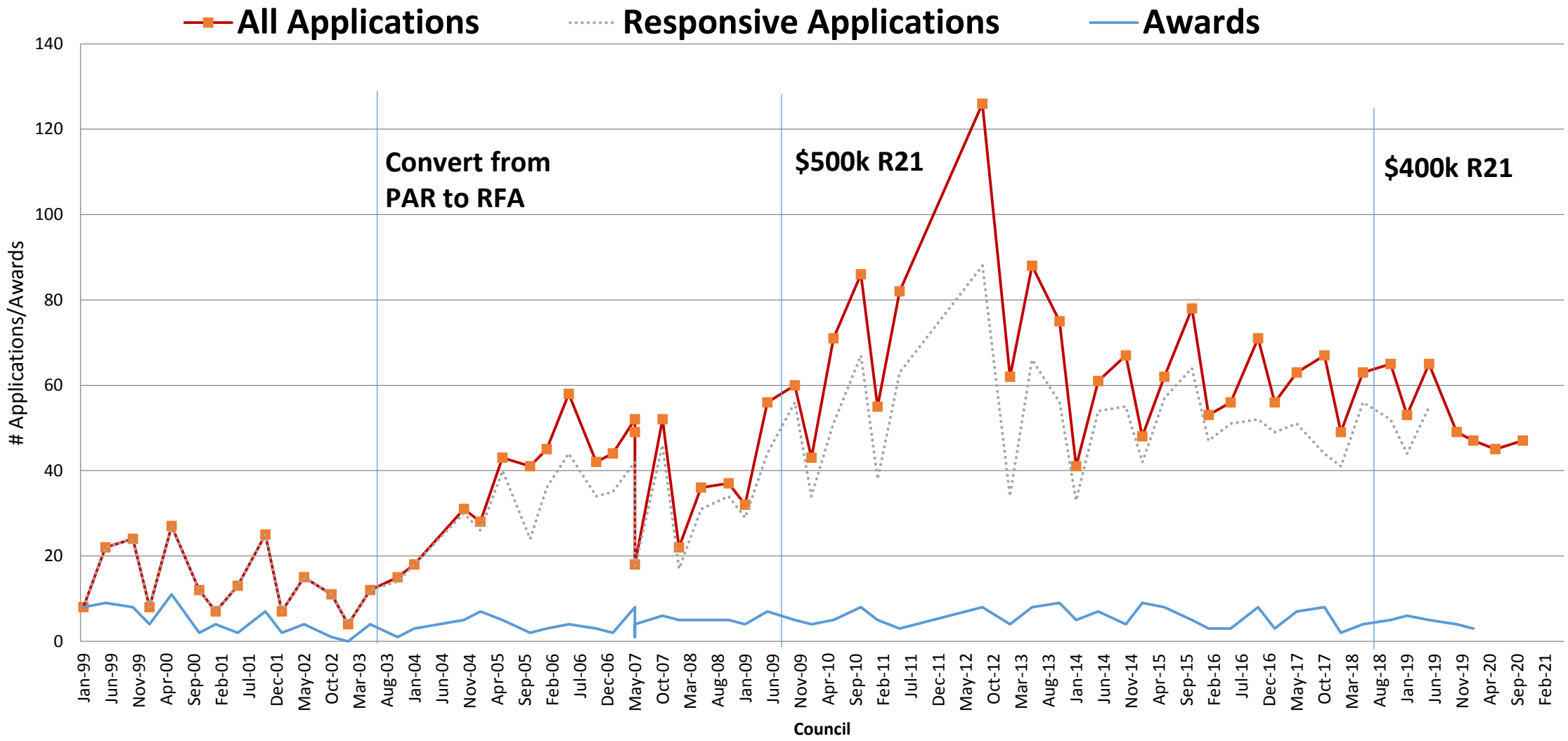


NI and ESI information is only available through QVR, so data only goes back to 2008. NI was determined based on year of first RPG versus year of IMAT award. ESI was determined based on year of most recent degree versus year of IMAT award plus NI status (all ESI's are also NI's).

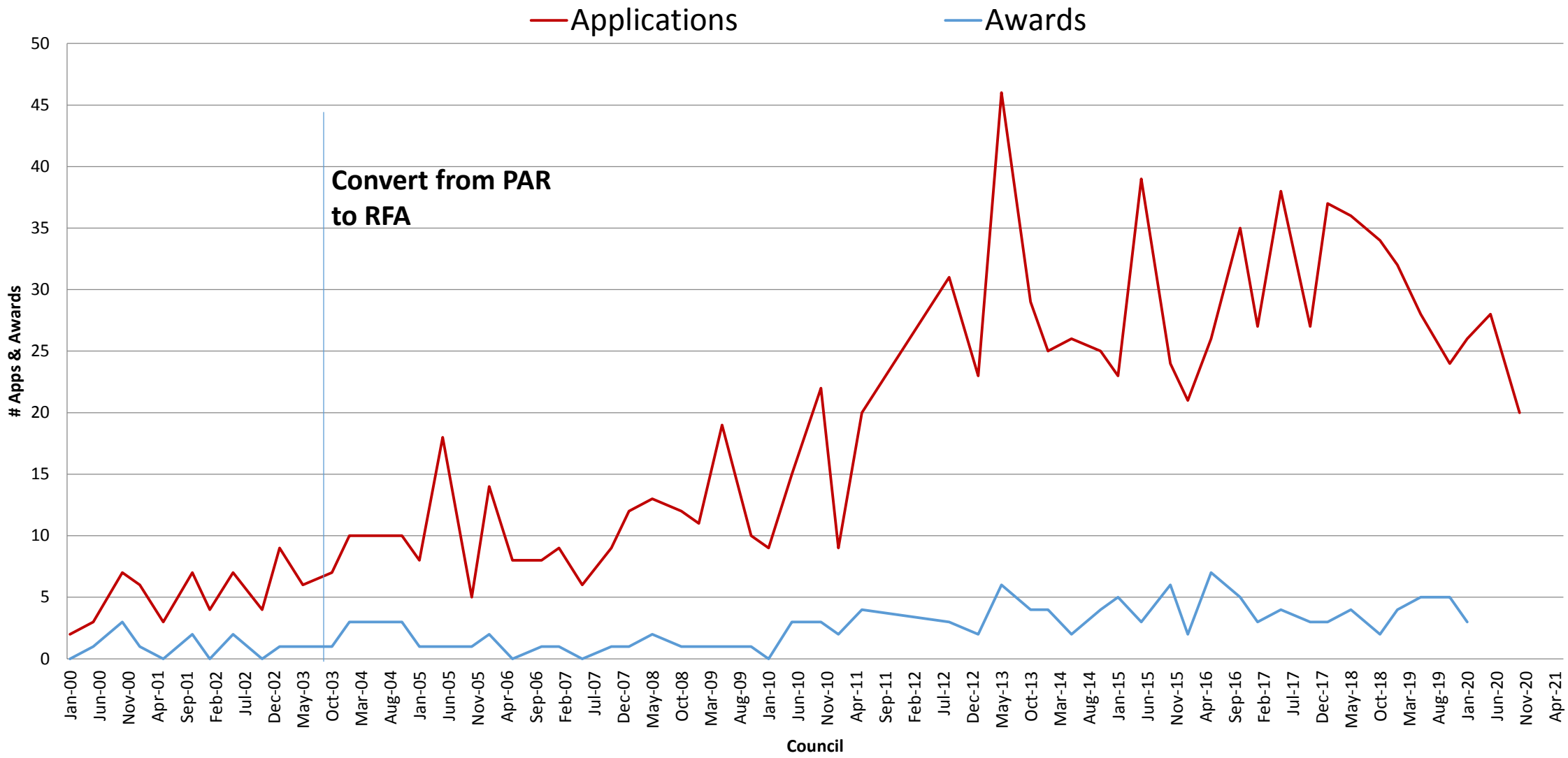




MCA R21 Applications Submitted/Awarded per round of receipt



MCA R33 Applications Submitted/Awarded per round



Defining Terms

- Success
  - Met and/or exceeded original goals and aims. Technology working.

  or
  - Project evolved towards different goals or even partial success offered sufficiently useful capabilities that overall was considered a success.

- Failure
  - Productivity failure – poor progress on aims and no new capabilities emerging
  - Unsuccessful attempt, but productivity satisfying in spite of no new technology available

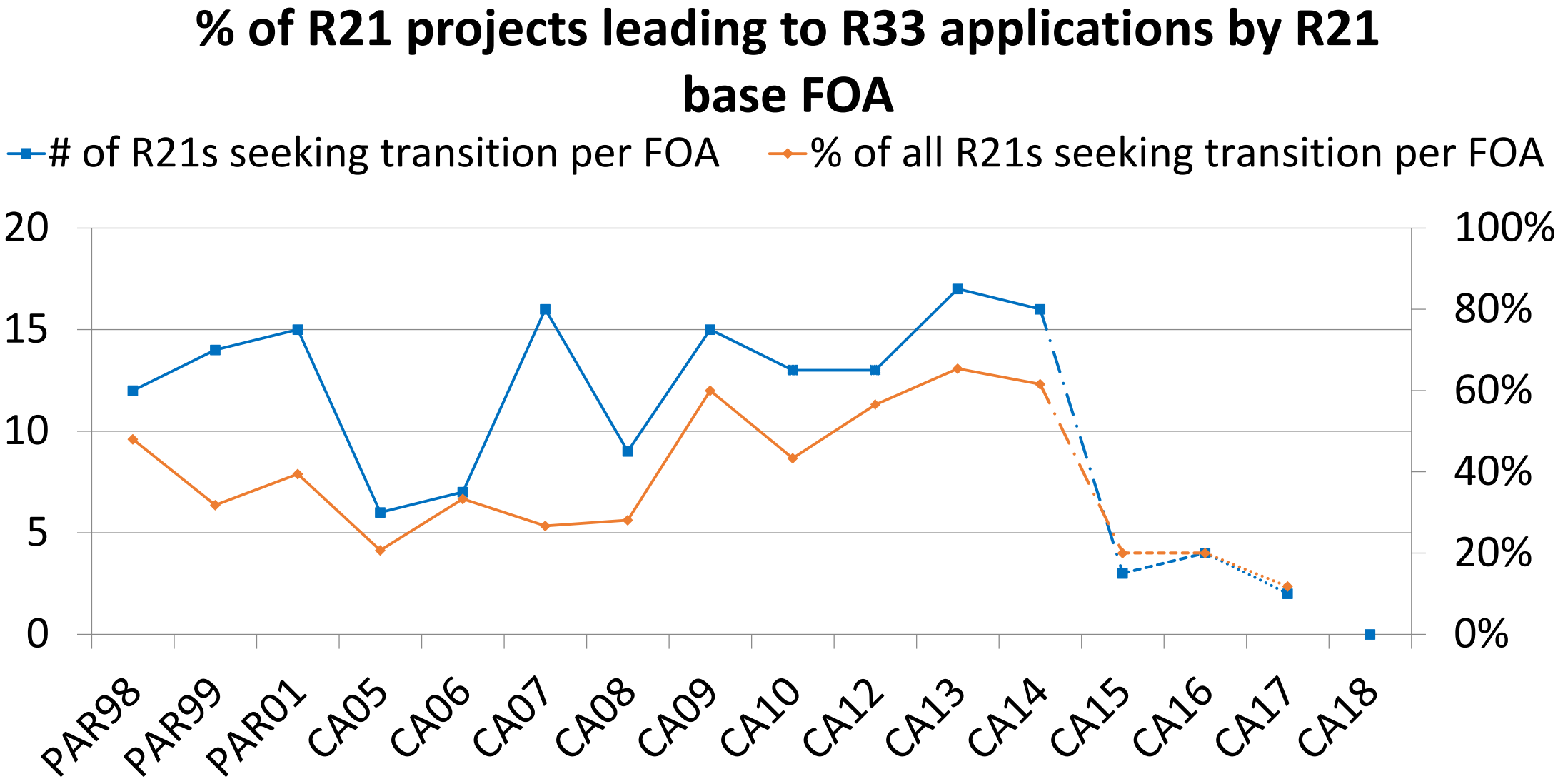
- Partial – everything in between

Assessing Success – Exit Interviews

Evaluating Awards from 2013 and 2014 awards (most recent complete records):

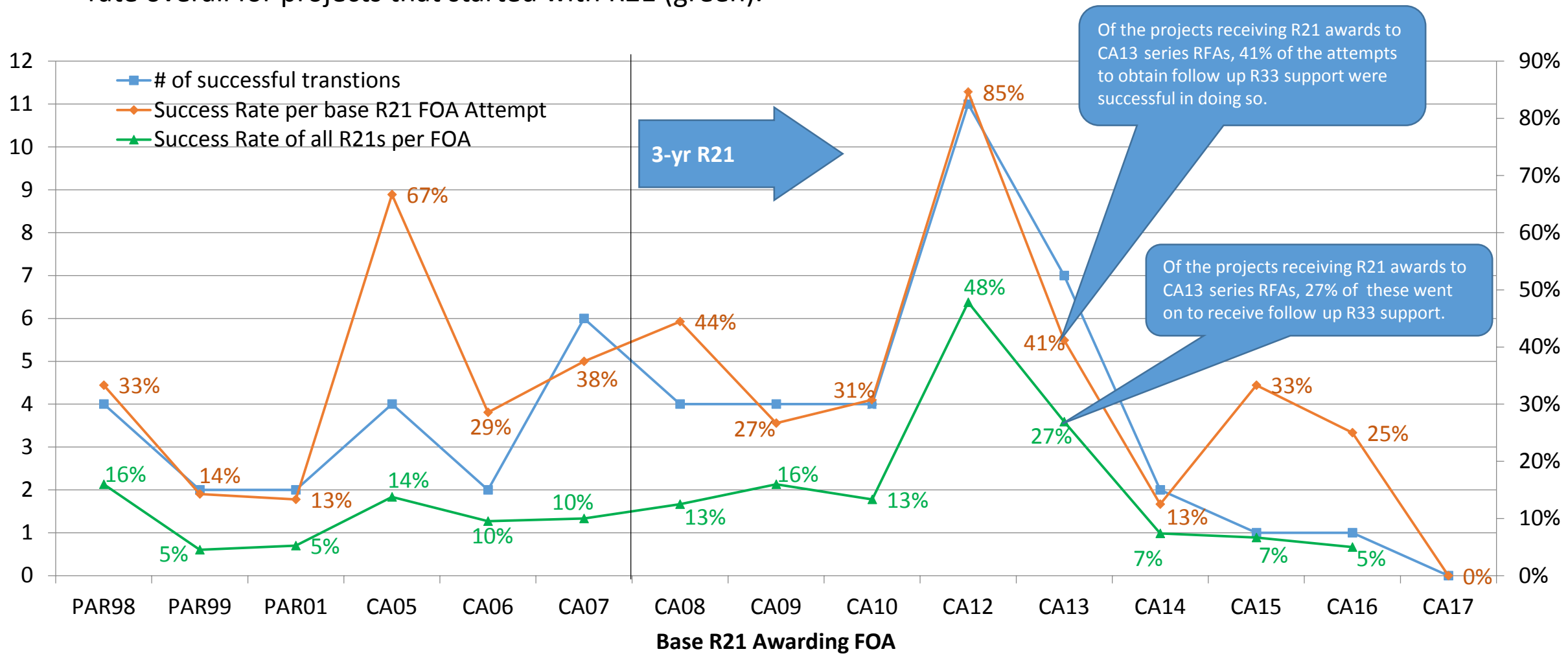
RFA	Mechanism	# of Awards	# of Successes	Success Rate	# of Failures	Failure Rate
CA12-002	R21	20	8	40%	6	30%
CA12-003	R33	11	7	64%	1	9%
CA12-004	R21	3	2	67%	0	0%
CA12-005	R33	3	2	67%	0	0%
CA13-001	R21	21	9	43%	4	19%
CA13-002	R33	10	4	40%	2	20%
CA13-003	R21	5	2	40%	2	40%
CA13-004	R33	4	2	50%	0	0%

Assessing Success – Transition Attempts (from IMAT R21 to R33)



Assessing Success – Transition Success (from IMAT R21 to R33)

Assessing the success in obtaining follow-up R33 support based on each attempt (orange) versus the success rate overall for projects that started with R21 (green).



Question 5:
Are there additional activities that should be undertaken by the program to support its goal?

Lead: David Beebe

Question 6 Summary

- “Wish-list” workshops to identify technology needs/gaps for priority research areas
  - Create a publicly accessible catalog of technology needs?
  - Connection to the Provocative Questions initiative or pending Cancer Grand Challenges initiatives (both run out of NCI\CSSI alongside IMAT) to gather input on landscape of pressing challenges in cancer?
- Review orientation
- Better support for technology dissemination
  - Facilitating connections and collaborations with end-users
  - Providing technology transfer resources

Question 6:
Should NCI continue to support a dedicated program with this scope and approach for cancer technology development?

Lead: Joe Gray

Question 3 Discussion topics

- Interesting to discuss: Narrow funding portfolio…too much in the “2’s”
  - Need to be more risk accepting
- What strategy allows us to take risks?
  - Create a safe haven for risk
  - Review panel needs to internalize this somehow
- Useful to know where else in the NCI that technology is being funded and how does that compare on 4I’s. talk about the EBRG (Exploratory Bioengineering Research rants) and SBIR pipelines, and Ripple Effect & STPI reports
  - Should IMAT be all-inclusive of 1-4?
  - Or should the program carve out a pipeline for higher-risk technology projects, relying on existing mechanisms for category 2 and 4 innovation projects?

Ongoing NCI Support for Technology Development

>300 active SBIR awards

SBIR & STTR

NCI CANCER MOONSHOT
A program of the National Cancer Institute of the National Institutes of Health

10 R33 awards (~$1.4M ea)

~70 active awards across multiple phases (R21, U01, U24)

NIH NATIONAL CANCER INSTITUTE Informatics Technology for Cancer Research

NCI Alliance for Nanotechnology in Cancer

NIH NATIONAL CANCER INSTITUTE Affordable Cancer Technologies Program

12 UG3 awards (~$2.6M ea)

IMAT INNOVATIVE MOLECULAR ANALYSIS TECHNOLOGIES

~65 R21 awards and ~45 R33 awards

NIH NATIONAL CANCER INSTITUTE Academic Industrial Partnerships

51 R01 awards spanning diagnosis and treatment technologies and for *in vivo* imaging systems

10 U54 centers & 10 U01 project awards

PHYSICAL SCIENCES in ONCOLOGY

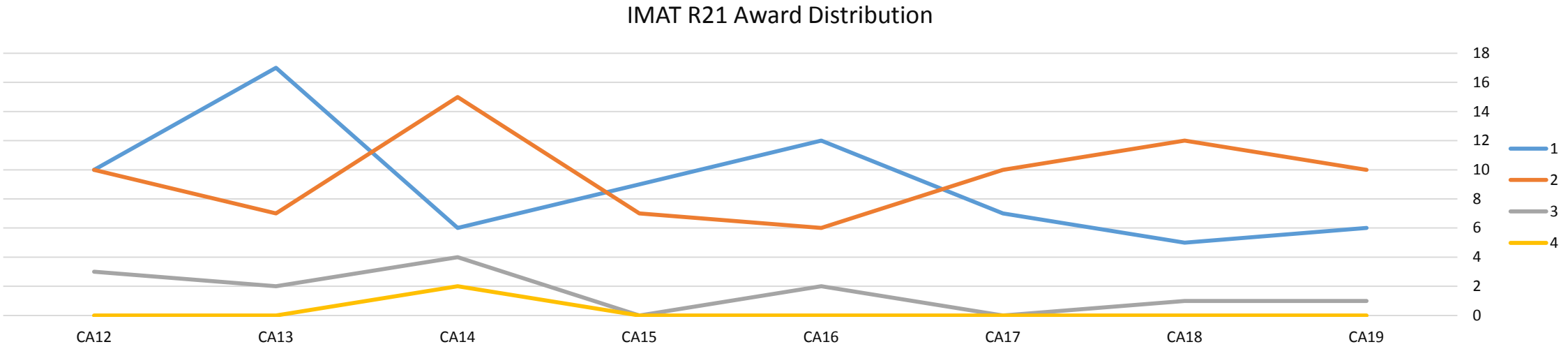
NIH NIBIB Bioengineering Research Grants Program

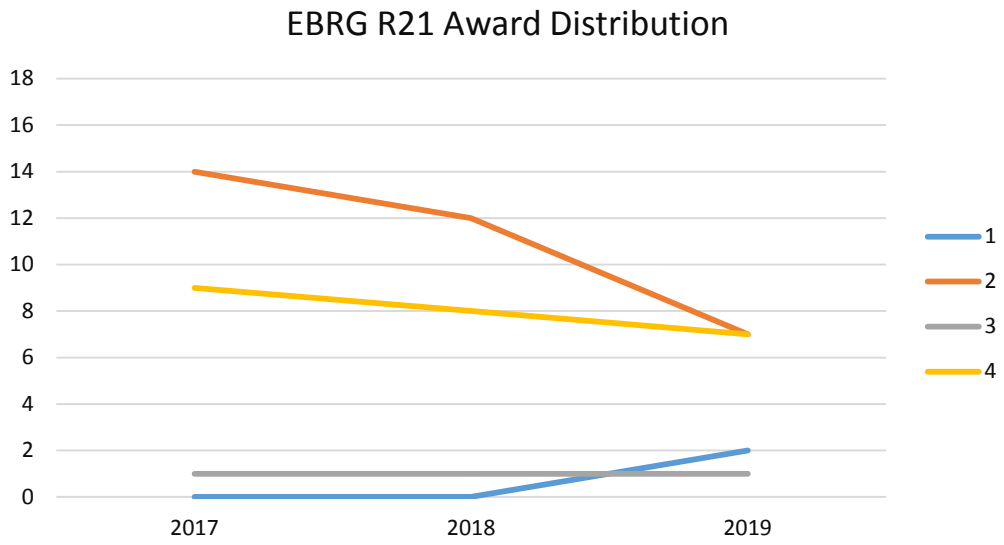
48 R21 and 63 R01 awards

CANCER TISSUE ENGINEERING COLLABORATIVE

8 U01 and R01 awards (~$2.5M ea)

4-I Distribution Comparison: IMAT vs EBRG





Appendix 3 : Portfolio Analyses Provided by NCI Program Staff

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The Innovative Molecular Analysis Technologies Program

The evaluation team began its analysis by gathering all IMAT-related RFAs and PARs from 1999-2019 and using them to find all awarded grants going back to 1999 using QVR and NIH RePORTER, all applications going back to 2008 using QVR, and all IMAT-funded publications using iSearch (which uses Web of Science-previously Thomson Reuters-for citation data). NCI staff first used this data to address the expert panelists' questions about who is applying to/aware of the IMAT program and where the awards are going. Links to the NIH Reporter file are provided in the electronic form of this document for all IMAT awards referenced in this Appendix.

Department of Applicants

Using data from QVR going back to 2008, NCI staff analyzed where applications and awards were coming from and going to by department. QVR assigns a department to each application based on reported department and NIH categories. **Figure 1** shows the number of applications received and awards made broken down by department category. The inlay shows different engineering departments that make up the "Engineering" category from the larger bar graph.

As expected, more applications came from engineering departments than any other department (655 applications) and awards were also more likely to go to these departments than any other category (86 awards [24% success rate]). Applicants from departments falling in the "Biochemistry" or "Pharmacology" categories were the next most likely to receive an IMAT award (34 awards/182 total applications [19%] and 25/144 [17%], respectively). Applicants from departments falling in the "Radiation-Diagnostic/Oncology" and "urology" categories were least likely to receive an IMAT award (7/98 [7%] and 1/19 [6%], respectively).

Geographical Location of Applicants

Using QVR data for applications going back to 2008 and using RePORTER data for awards going back to 1999, NCI staff analyzed applications and awards by the state the contact PI's institution was located. **Figure 2** shows that the most applications and awards came from/went to California, Massachusetts, and New York.

Early Stage Investigator Status

Using QVR data going back to 2008, NCI staff categorized applications and awards as Early Stage Investigator (ESI), New Investigator (NI), or Established Investigator.

Early Stage Investigator Application: All PIs on the application were within 10 years of their most recent degree and had not received an R01 award or equivalent at the time of the IMAT award.

New Investigator Application: None of the PIs on the application had received an R01 award or equivalent, but it did not qualify as ESI.

Established Investigator Application: The application did not qualify as ESI or NI.

Figure 3 shows that 16.2% of IMAT awards from 2008-2019 were ESI and 22.3% of awards were NI. The high percentage of NIs is likely due to many investigators that have typically received funding from agencies other than NIH and applicants from small businesses. **Figure 4** sorts all applications by review score and is color-coded by investigator type. It shows that the NI and ESI applications had a similar score distribution as established investigator applications.

Question 1: Evaluating the Impact of the IMAT Program

2016 Ripple Effect Evaluation

The panel was supplied with the report from the last IMAT program evaluation, performed in 2016 by Ripple Effect. To help answer the question of impact, NCI staff drew their attention to conclusions from the previous evaluation regarding impact:

> The program has a significant impact on scientific advancement within cancer research through manuscript publications and commercialization of IMAT funded technologies and methodologies. IMAT-funded PD/PIs published more manuscripts with higher impact factors and more manuscripts, applied for more patents and received more patent awards per $100,000,000 compared to the Comparison Group. *Summary of Findings, paragraph 1 Page i and viii*.

> PD/PIs and End Users were extremely positive about the importance of the IMAT program in regard to advancing cancer research…... They described IMAT funding as "unique," "crucial," and "essential" for moving cancer research forward because it allows for the exploration of risky, but potentially innovative and important, cancer research technologies and methodologies. End Users were similarly enthusiastic about the program, and they stated that the technologies and methodologies produced by IMAT-funded grants were critical and/or extremely important. End Users indicated that such technologies and methodologies maximized resources, increased knowledge, and furthered understanding of disease progression, thereby catalyzing cancer research. *Page ii: 1-3 and End User Use of Technology page 74.*

Award Outputs: Publications and Citations

To provide an update on the Ripple Effect team's assessment of publications (as a measure of productivity) and citations (as a measure of impact), NCI staff used the NIH iSearch tool to gather and analyze publications and associated citation data from IMAT awards. The bar graph in **Figure 5** shows the number of publications, and the bubble plot overlaying each bar indicates the associated number of citations from that pool of publications.

As expected, older awards that have had more time to accumulate publications and citations have higher numbers. Publications were further sorted by quartiles of most through least cited

publications from each group of publications, indicated in the colors making up the bar graph. For each year of new awards, fewer than 20 publications account for over 25% of citations and fewer than 50 accounted for 50% of citations for publications .

Looking at only R21s and R33s from before 2016, NCI staff analyzed IMAT awards using number of publications and citations as metrics for success. The top of **Figure 6** shows that the 39 most productive projects published 25% of research papers. The two most productive projects were R21/R33 phased projects that cited both grants on 50 papers (CA099835: Enhanced Crystallography of Cancer-Implicated Proteins, Dr. Virgil Woods). The bottom of **Figure 6** shows that 11 projects generated 25% of citations. The most highly cited project was R33CA126674: High-throughput Oncogene Mutation Detection in Human Cancer, PI: Levi Garraway.

Project Outputs Versus Review Score

NCI staff analyzed the number of publications and citations for each project versus the project's review score going back to 2010, shown in **Figure 7**.

NCI staff binned projects by review score and found no difference in the average number of publications or citations across the groupings. Fitting a trendline to the scatterplots of publications or citations versus review score found a slight negative correlation, but it was not significant based on the R^2. This indicates that that review scores are not a significant indicator for research productivity or impact among these projects, at least by these measures.

5 Blockbuster Success Stories

The evaluation team requested 5 examples of blockbuster success from the IMAT portfolio. The following examples were offered:

- **BeadChip & BeadArray** [Mark Chee, Sentrix (aka Illumina)]
  Foundation of Illumina's NGS platforms. Award made in 1999 as Illumina was launching. (1999 IMAT)
- **Rolling Circle Amplification** [Paul Lizardi, Yale]
  Received an R33 after having just published the first paper on RCA, Dr. Lizardi further developed the method to rapidly amplify an entire genome (isothermal whole-genome amplification). (1999 IMAT)
- **Protein Footprinting** [Mark Chance, Case Western]
  Spectrometry-based method of biochemical analysis enabling visualization of protein folding and dynamics on millisecond timescales with high resolution. (2000 IMAT)
- **PROTACS** [Craig Crews, Yale]
  Chemical knockdown approach of targeted proteins in a novel, fast and effective way to generate protein depletion models, and has emerged as the basis for a new promising treatment approach. (2006 IMAT)
- Shotgun proteomics [Dick Smith (**DREAMS**), PNNL; Ruedi Aebersold (**ICAT**), ISB; John Yates (**MuDPIT**), U Wash]

IMAT Portfolio Analyses

> Fundamental reagents, analytical tools and protocols for identifying proteins in complex mixtures using a combination of high-performance liquid chromatography combined with mass spectrometry. (RS 2000 IMAT; RA 2000 IMAT; JY 1999 IMAT)

The panel asked whether the IMAT program could legitimately claim credit for launching these technology platforms, and program staff referred to the review criteria for submitted applications, that in order to be competitive they must offer a high degree of technical innovation. Furthermore, the following statement was taken from a direct correspondence with the Mark Chee co-founder of Illumina and the PI for the BeadChip and BeadArray projects: .

> *We had equity funding, and other SBIR and other grants (esp. HapMap) that also helped, but the IMAT funding allowed us to pursue some important avenues that we might not otherwise have tried (or would have tried much later) because of the perceived risk at the time.* ***The IMAT funding helped us to develop the gene expression assay and advance the array matrix platform, both of which were successfully commercialized. I believe that the development of the BeadChip platform was also accelerated significantly as a result of the IMAT-funded effort****, and as you know this platform was a major advance for the company.*
>
> - Mark Chee

Evidence of Clinical Impact

To encourage clinical impact through development of IMAT-supported technology, NCI staff has worked with the Foundation for the National Institutes of Health (FNIH), Biomarkers Consortium (BC), Cancer Steering Committee (CSC), High Content Data Integration Working Group (HCDI WG) to identify novel technology platforms ready for clinical development projects funded by the FNIH. The BC is a division of the a non-profit, 501(c) (3) charitable organization, that is a public-private partnership involving the National Cancer Institute (NCI), the U.S. Food and Drug Administration (FDA), multiple pharmaceutical, diagnostic and technology companies, non-profit and patient advocate organizations. The mission of the HCDI WG is to develop and support pilot projects that use emerging technology platforms with the potential to overcome limitations of established methodologies in the application of multi-dimensional biomarkers. The working group provides project teams development and implementation guidance to generate fundable projects that fit the intended use of a technology and potentially enable rational clinical decisions. Starting in 2013 the HCDI WG worked to help develop the *High-Definition Single-Cell Analysis of Blood and Tissue Biopsies in Patients with Colorectal Cancer undergoing Hepatic Metastasectomy* project with Peter Kuhn (formally Scripps, now USC) that was funded and completed in 2019. The group also worked with Scott Manalis (MIT) starting in 2015 to develop a project for *Measurement of the Biomarker, Single Cell Mass Accumulation Rate (MAR)*, that has led to a clinical trial funded in part by working group member organizations. More recently in 2019 the HCDI WG also reviewed several IMAT funded technologies in light of two clinical challenges defined by the working group industry members. The group focused on the *Exo-PROS* platform Yun Wu (Buffalo), a liquid biopsy assay of exosomal protein and microRNA combined biomarkers to detect response to immunotherapy in non-small cell lung cancer, and Ralph Weissleder's

(Harvard) *Single Cell Analysis for Tumor phenotyping (SCANT)* technology for rapid measurement of multiple protein signaling in a small number of cells from fine needle aspirates in pancreatic ductal adenocarcinoma with possible inclusion of immune cell profiling. The working group ultimately decided to promote FNIH funding of the SCANT platform and FNIH is moving forward in developing a clinical trial with Dr. Weissleder's group. The working group decided that the ExoPros platform was too early in the development pipeline, but provided feedback from the industry perspective for additional development steps to Dr. Wu noting interest in working with her technology in the future.

NCI program staff also drew the panel's attention to a recently-developed platform from George Mason University with IMAT support called *Protein Paint* (R21/R33), which has recently offered new capabilities for discovering new inhibitors advancing immunotherapy approaches.

Evidence of Collaboration Impact

In response to the evaluation panel's request for evidence that the IMAT program supported projects that served to catalyze new collaborations, NCI staff offered the following examples:

Josh Rabinowitz and Eilleen White

- [2008 IMAT] Developed **MS-based tracers for profiling metabolic fluxes in cells,** which allowed for discovery of upregulation of 2-hydroxglutarate due to mutated IDH-1 in GBM.
- New metabolic methods became the cornerstone of a new partnership with Eilleen White (Cancer biologist, Rutgers) to explore the role of metabolism in cancer (multiple R01s).

Roger Kamm and Tyler Jacks, Bob Weinberg, Richard Hines, David Barbie…

- [2009 IMAT] Developed a microfluidic platform for 3D tissue culturing essential components of the in vivo tumor microenvironment. Very successful R21-R33 leading to commercialization of the platform through AIM Biotech (that holds non-exclusive licensing agreements with Biogen and Amgen).
- Led to several big collaborations with both basic and clinical research scientists looking at a broad variety of cancer phenomena and several critical advances in immuno-oncology.

Hsian-Rong Tseng and Edwin Posadas

- [2010 IMAT] Developed **NanoVelcro**, which is a microfluidic platform to capturing CTCs by adhering capture agents to nano-fibers with clever release mechanisms for isolating viable target cells from complex samples.
- The NanoVelcro platform became the basis for a collaboration with Ed Posadas (Clinical oncologist, Cedars Sinai) to develop various screening and monitoring assays for his prostate cancer patients through numerous R01 and U01 awards, and for commercial development of the platform through a joint venture (Cytolumina, LLC).

Claudia Fischbach and Cliff Huddis

- [2012 IMAT] Developed mineralized 3D culture substrates for modeling breast cancer in vitro, to test the role of hydroxyapatite in breast microcalcifications and in bone tissue.
- The successfully developed platform led to a series of successful awards (multiple R01s and other awards) with Cliff Hudis (Chief of Breast Cancer medicine at MSK) to make substantial contributions to understand breast cancer metastasis.

Richard Schlegel and many

IMAT Portfolio Analyses

- [2013 IMAT] Created the **Conditionally Reprogrammed Cells** method (or "Georgetown Method") which allows short term culturing of nearly any type of cancer cell and to development of a substantial biobank at Georgetown for a broad array of expanded primary cancer cells across many different cancer types.
- The method has been adopted by a great many labs across the world, including the NCI (in several of their cancer modeling development centers) and according to the PI more collaboration opportunities than he can keep up with. An independent office at NCI was sufficiently excited about the technology they wrote up a summary of its impact here.

Evidence of Commercialization Impact

In response to the evaluation panel's request for evidence that the IMAT program supported projects that became commercially available, NCI staff offered the following examples:

- **Mike Makrigiorgos** – **COLD-PCR** (2005 IMAT), exclusively licensed by Transgenomics in 2009 and novel formulations of the original method still commercially used.
- **Darren Link** – **RainDance** (2007 IMAT) one of the first droplet microfluidic platforms credited their IMAT award with allowing them to launch their first platform which focused on digital PCR (effectively becoming the first droplet-based digital PCR platform).
- **Lance Liotta** – **Nanotrap** (2009 IMAT) porous nano-scale hydrogel cages with chemical affinity bait loaded within the cage to capture and protect rare target analytes in complex solutions, commercialized through Ceres Nano.
- **Sarah Blair** – **SignalMark** (2011 IMAT) implantable markers to mark tumor margins for resection to ensure negative margins, being commercialized by View Point Medical.
- **Samantha Pattenden/Paul Dayton** – (2012 IMAT) nanodroplets that serve as cavitation agents for more efficient and uniform fragmentation of DNA. Being commercialized by Triangle Biotechnology.
- **John Williams** – **Meditopes** (2013 IMAT) are based cyclic peptides that bind a site within the Fab arm of an IgG antibody, allowing for full binding performance to the target antigen while allowing broad manipulation of the antibodies, in a manner that the firm commercializing them (Meditope Biosciences) calls a "LEGO-like conjugation system."
- **Larry Loeb** – developed **Duplex Sequencing** with a 2013 IMAT award, now being commercialized by TwinStrand Biosciences.

Innovation Corps (I-Corps™):

Also worth noting is that NCI arranged to allow IMAT investigators to participate in the NIH I-Corps™ program, normally restricted only to small businesses supported by an active SBIR or STTR award. I-Corps™ is an intensive entrepreneurial immersion course conducted over an 8-week period that requires the technology development team to take an empirical approach to developing a robust business plan for their technology.

Mei He—Clara Biotech

> **ExoSearch:** Integrated microfluidic exosome profiling assay for molecular analysis of circulating exosomes in microliter volumes of plasma.

Shana Kelley—Cellular Analytics

CytoFind: Purifies circulating tumor cells (CTCs) from whole blood samples by selectively marking the CTCs with magnetic particles and then isolating the cells using a magnetic microfluidic device.

Sergei Nechaev – Nodak Diagnostics

RNA-sequencing does not work well with patient specimens because their quality is variable and often cannot be controlled or predicted. To improve suitability of patient specimens for transcriptome profiling, Nodak Diagnostics is pioneering an approach for global analysis of RNA polymerase II derived short RNAs that, unlike existing methods, relies on RNA degradation and works better for low-quality RNA.

Other Evidence of Impact

NCI program staff also elected to draw attention to four Outstanding Investigator Awards, noting reviewer enthusiasm for the technologies pioneered by these investigators as a substantial contribution to meriting the award. The investigators are:

- **Ben Cravatt**: Activity-based Protein Profiling - 2006 IMAT (R21/R33)
- **Craig Crews**: PROTACs - 2006 IMAT (R21/R33)
- **Levi Garraway**: OncoMap - 2007 IMAT (R21/R33), 2016 IMAT (R33)
- **Patrick Moore**: Digital Transcriptome Subtraction - 2007 IMAT (R21/R33)

Question 2: The Balance of the 4 I's

Four I's of Technology Development

Panel members introduced the following categorical breakdown for considering technology innovation, which they called "The Four I's of Technology Development":

1. Innovative new technology
2. Improvement of an existing technology
3. Integration of previously separate/siloed technologies
4. Implementation of new discoveries to the community

NCI staff categorized all applications as one of the four I's going back 6 rounds of receipt and all awards going back 24 rounds of receipt. As shown in **Figure 8**, R21 applications and awards are mostly distributed between type 1 and type 2's while R33 applications and awards are almost all type 2's.

Question 3: Considerations for the future of IMAT

2016 Ripple Effect Evaluation

NCI staff pointed the panelists towards data gathered from the previous evaluation:

PD/PIs identified challenges toward developing and advancing technology during the funding period include taking an iterative approach to advance the technology, a strategy

of approaching the technology development from multiple angles until they could arrive at a successful model or optimum results, time constraints, slow and laborious methods, and funding restrictions.

Synopsis page iii, mid v, bottom. How were the technologies developed during the funding period for IMAT grantees.

- A few PD/PI mentioned several specific difficulties in the application and submission (grant writing) process, such as trouble framing how the research applied to IMAT, transitioning from hypothesis-driven to technology-driven grantsmanship. *middle page 19 and top page 78.*
- Feedback on the review process included suggestions from PIs that review panels did not have a good understanding of "high risk," "high impact," or "innovative" research or that the review process involved a certain level of luck." *mid page 19*
- NCI could help increase awareness through dissemination, including facilitating connections with companies to help commercialize new technologies, and increasing publicity of the IMAT program, creating networking opportunities for IMAT awardees to increase awareness of the IMAT program and its resultant technologies. ….. Suggestions that NCI could connect PD/PIs with programs and companies to achieve commercialization, such as helping with technology transfer, early education on commercialization, helping to start companies or connect with companies, and establishing linkages with SBIR/STTR*. page 26 Dissemination*

Recent Efforts to Improve IMAT

NCI program staff informed the panel of the following activities engaged over the last several years to improve the outcomes and impact of ongoing projects:

- During the award
  - Collaboration supplements with the NCI Informatics Technology for Cancer Research (ITCR) program. One of the funding opportunities supporting this are linked here.
  - Participation in NIH I-Corps™ Program (See *Evidence of Commercialization Impact*)
  - Holding PI meetings outside the DC area to improve variety of collaboration possibilities.
  - Recruited a panel of patient research advocates to work directly with NCI program staff to oversee activities and continuously search for opportunities for improved clinical impact. The team named themselves the NCI Technology Research Advocacy Partnership (NTRAP).
- Beyond IMAT R21 and R33 awards
  - Competitive Revision RFAs: support collaborations between IMAT investigators and PIS that hold active NCI grants to pursue hypothesis-based research. Offers 2

years of support to incentivize adaptation and independent validation of IMAT-supported technologies.
- Encouraged participation in the Global Center for Medical Innovation (GCMI) Accelerator program; a partnership opportunity made available through the White House Cancer Moonshot initiative.
- Telling success stories on the IMAT website

Question 4: Current funding mechanisms

Gauging Success Project-by-Project

Determining whether an IMAT award was a "success" or not is difficult to do objectively. Since 2012, the IMAT program has arranged calls with funded investigators within 1 year of closing out their award to ask a standard series of questions to understand how the project went, what outcomes could reasonably be attributed to the IMAT award, and to determine what next steps are planned. Based on this assessment, the IMAT program director offers a judgement on whether the project was "successful", "partially successful", or a "failure." The terms are considered as follows:

Success:
- Met and/or exceeded original goals and aims. The technology is working.
- Project evolved towards different goals or even partial success offered sufficiently useful capabilities that overall was considered a success.

Failure:
- Productivity failure – poor progress on aims and no new capabilities emerging.
- Unsuccessful attempt, but productivity may be considered satisfying in spite of no new technology becoming available.

Partially successful:
- Everything in between

Only two years of IMAT awards offer complete records of assessment by the time of the evaluation in early 2020. The outcomes for these are described in **Table 1**.

The original funding opportunities were for a phased R21/R33 project, though the program always allowed applications directly for R33 support. In 2008, these mechanisms were separated and investigators were no longer able to receive an R33 award without going through the application process again. Investigators with funded R21 projects could choose to apply for an R33, but these projects would not be linked systemically. Figure 9 summarizes PI efforts to transition from R21 support to an R33 award. The upper graph shows the ***attempts*** to transition from R21 to R33 support, and the lower graph shows the ***success rate*** of the transitions.

Question 5: Additional activities to support IMAT's goals

No data was requested for review of this question.

Question 6: Should there continue to be a dedicated program

2016 Ripple Effect Evaluation

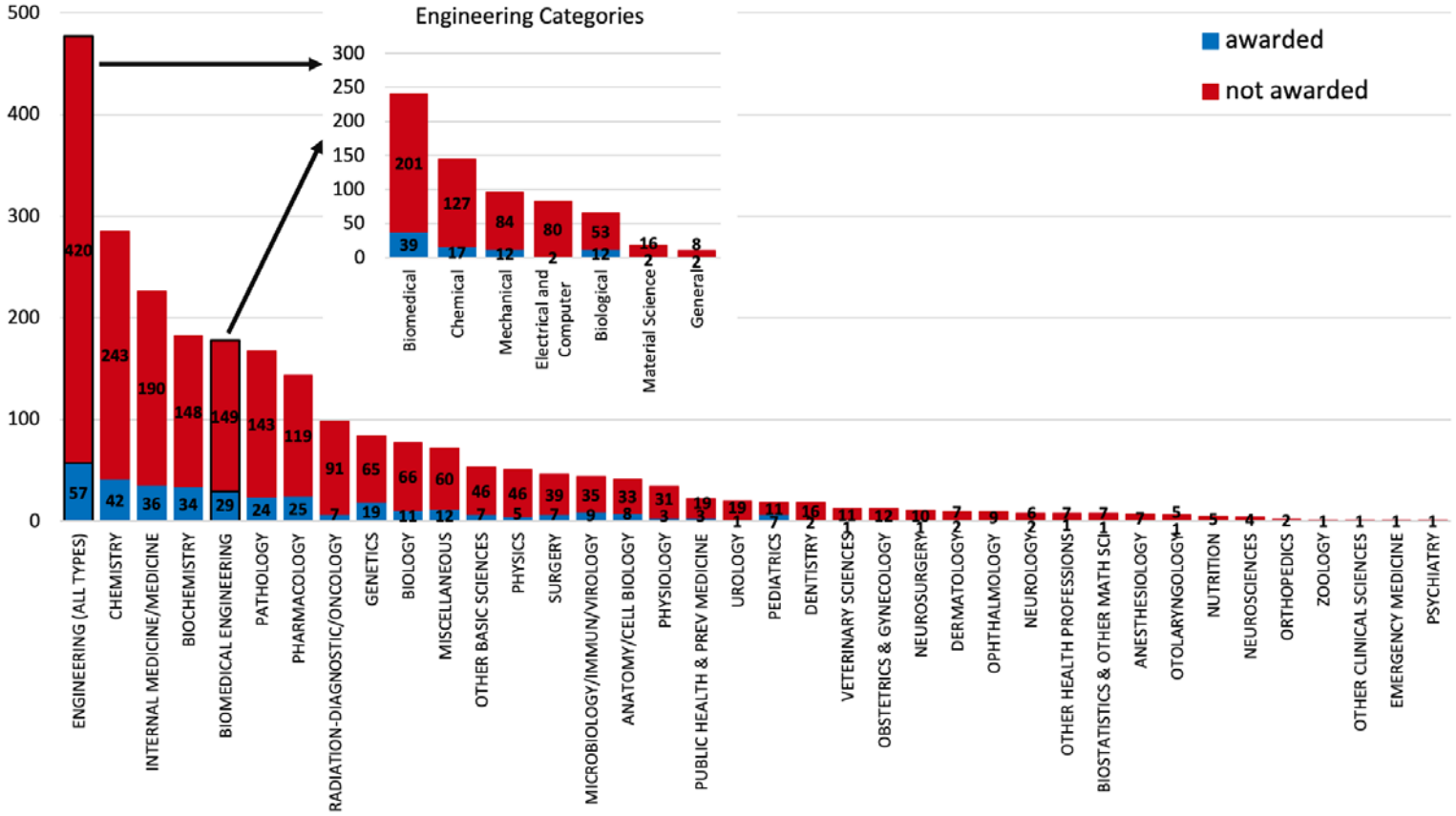
NCI staff pointed the panelists towards data gathered from the previous evaluation:

> Overall, the results of the 2016 evaluation suggest that IMAT is an essential and productive program within NCI. Maintenance of the IMAT program will ensure that cutting-edge, state-of-the-art research will continue to advance cancer research to the ultimate benefit of technology End Users, which includes clinicians, researchers, and patients. Mechanisms adopted by other institutions at NIH to promote technology development:
> - 2015 IDA Report on trans-NIH Technology Development efforts
> - National Human Genome Research Institute (NHGRI) and National Institute of General Medical Sciences (NIGMS) have both launched programs similar to IMAT
> - National Institute of Biomedical Imaging and Bioengineering (NIBIB) and National Heart Blood and Lung Institute (NHLBI) had both asked for assistance in launching new programs like IMAT
>
> *Summary of conclusions, page viii*

IMAT Portfolio Analyses

Figures

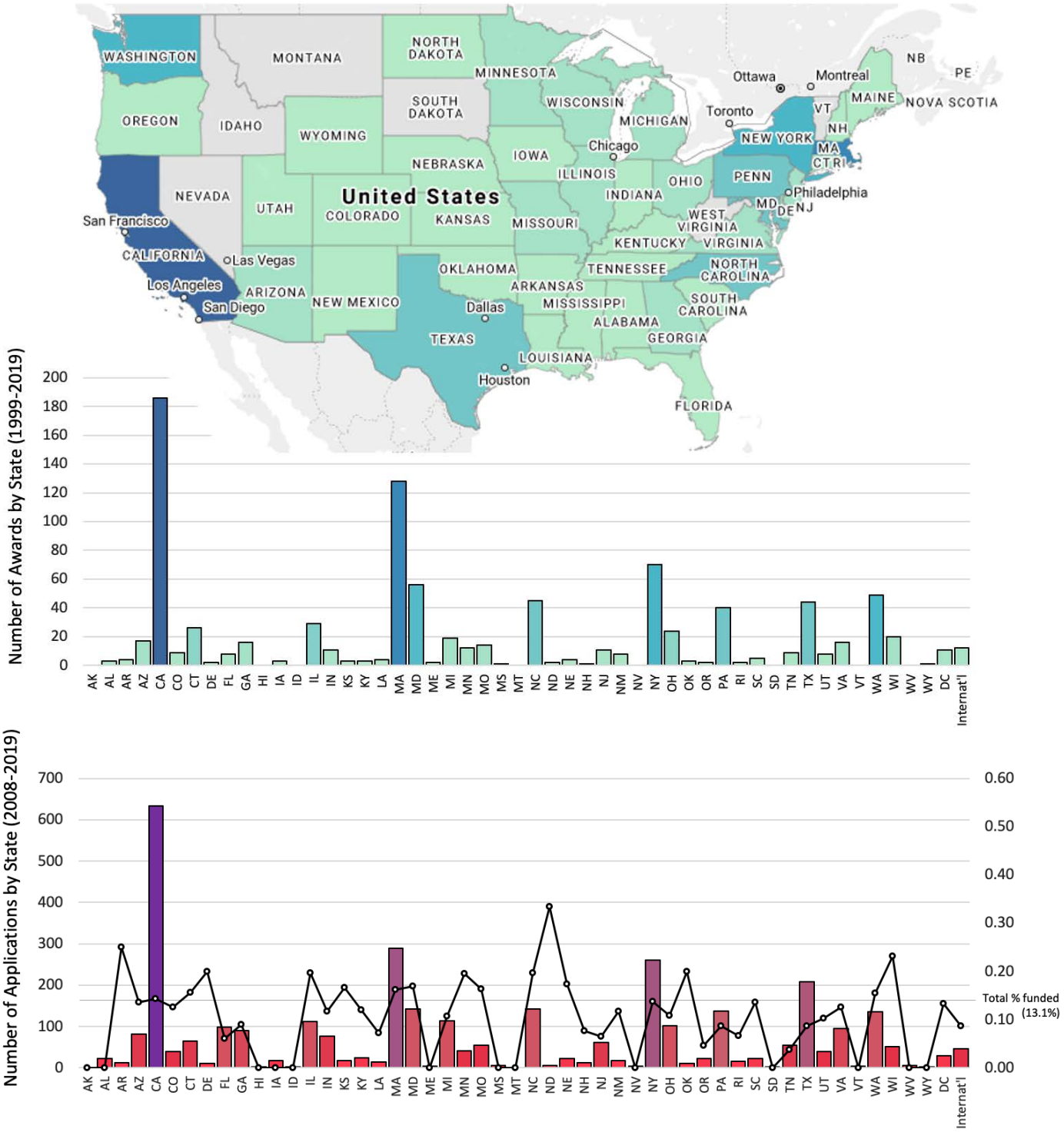
Figure 1. Applications and Awards by Department of Contact PI.



IMAT applications from 2008-2019 by NIH-designated department category of grantee. Depends on applicant reporting; mostly R21 and R33s reported a department. Inlay: break down of Engineering departments. Includes “Engineering (All Types)” and “Biomedical Engineering” categories.

IMAT Portfolio Analyses

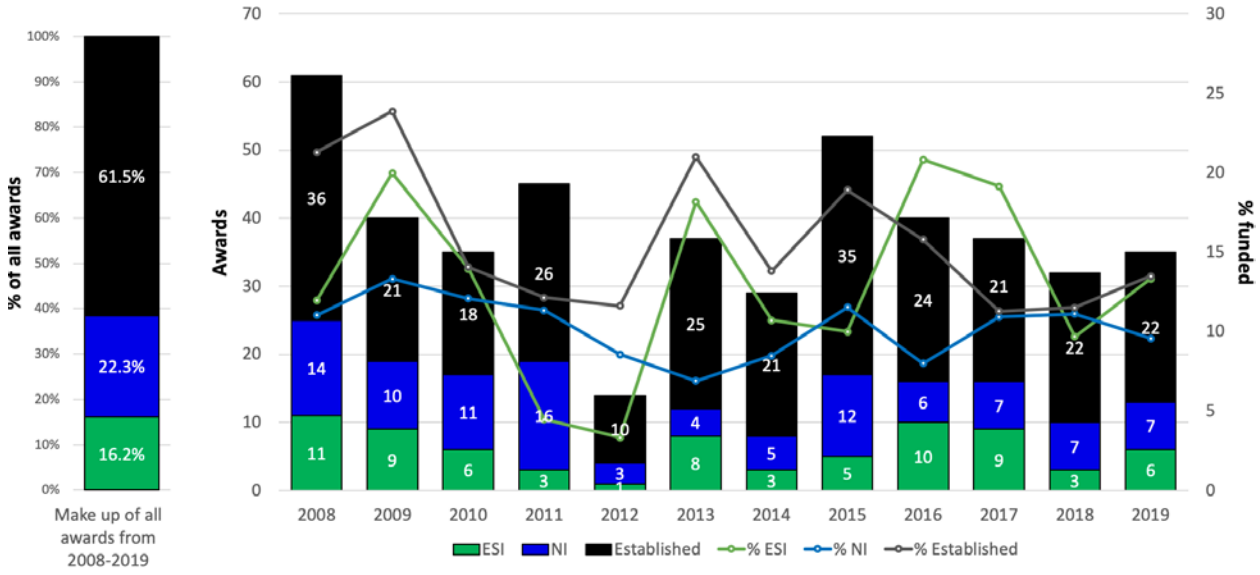
Figure 2. Applications and Awards by State of Contact PI's Institution



Top: IMAT awards from 1999-2019 by state of grantee.
Bottom: IMAT applications from 2008-2019 by state. Line graph: success rate by state.

IMAT Portfolio Analyses

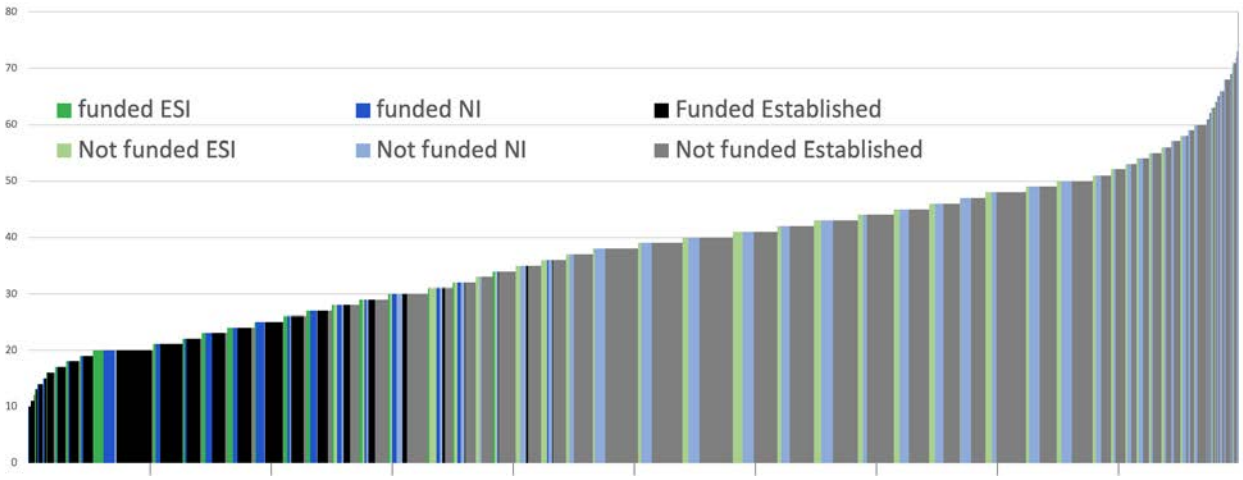
Figure 3. Distribution of Awards by ESI, NI, and Established Investigators by Year of Award.



Left: All awards from 2008-2019 classified by investigator type (includes R21, R33, R41, R42, R43, and R44 mechanisms).
Right: Awards classified by investigator type by fiscal year of IMAT award. Line graph shows % funded for each investigator type over the years.

IMAT Portfolio Analyses

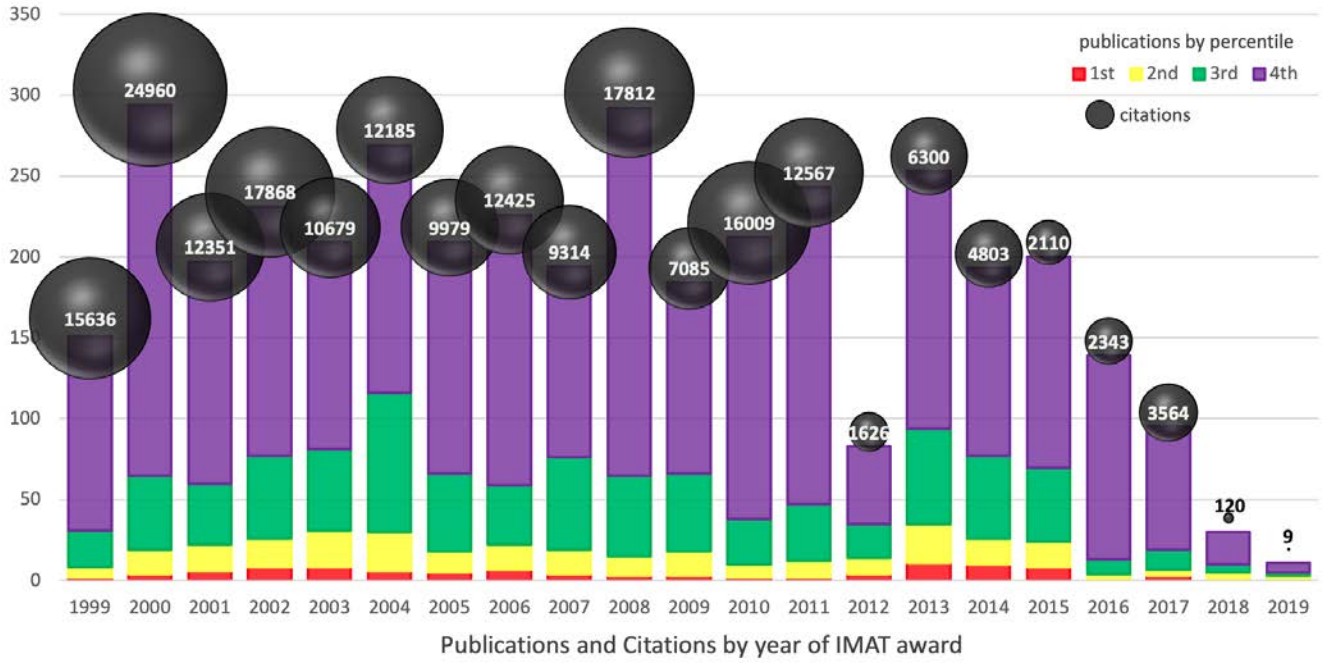
Figure 4. IMAT Applications Sorted by Review Score, Color-Coded by Investigator Type.



Applications and awards from 2010-2019 sorted by review score (includes R21, R33, R41, R42, R43, and R44 mechanisms). Applications color-coded by investigator type and funded or not funded.

IMAT Portfolio Analyses

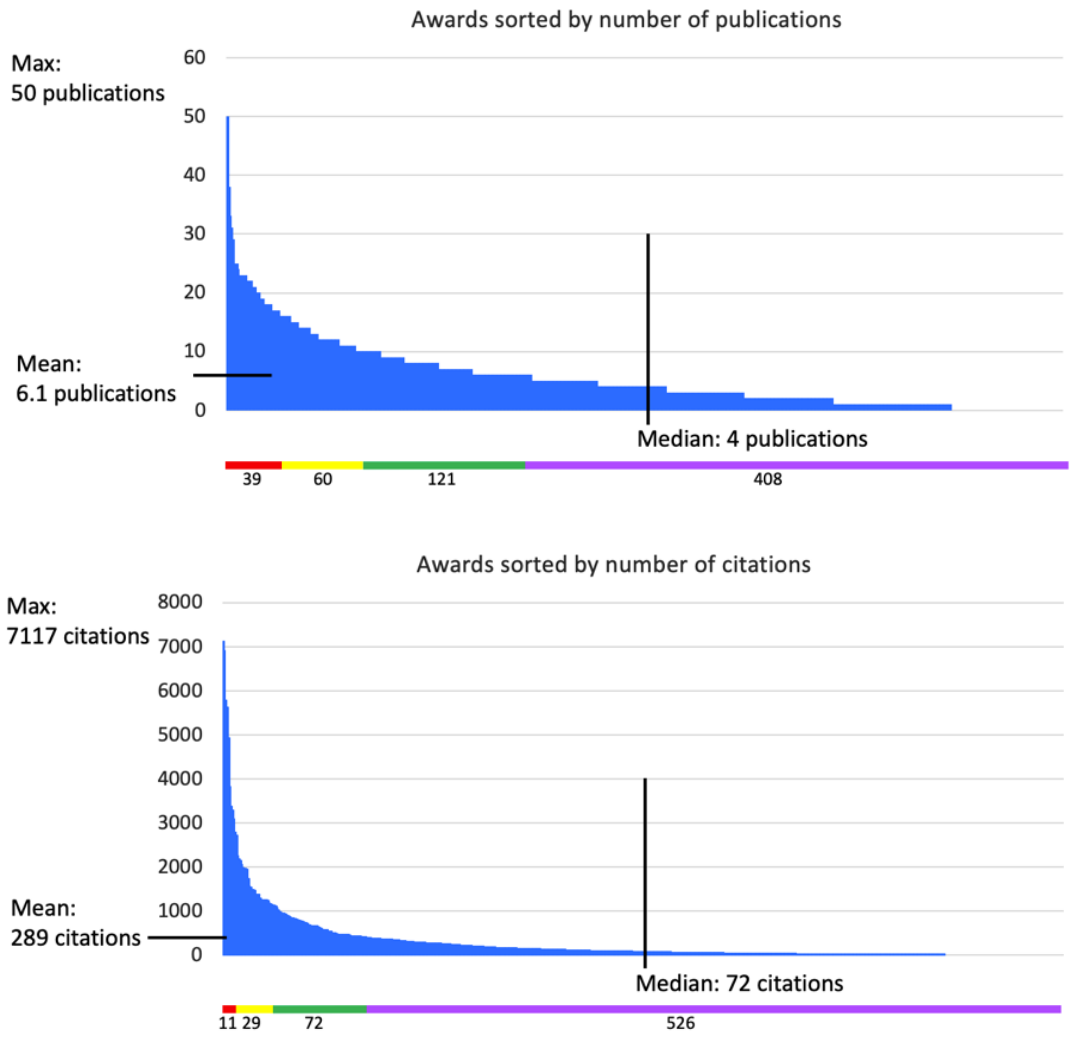
Figure 5. Publications and Citations by Year of IMAT Award



Bar graph of publications based on fiscal year of IMAT award (includes R21, R33, R41, R42, R43, and R44 from 1999-2019). Reviews, letters, editorials, and comments are excluded. Publications were included through December 31, 2019, were only counted if published after IMAT grant was awarded and are counted for every IMAT grant listed. Publications for every year of IMAT award are color-coded by citation frequency (most cited publications that account for first 25% of citations are red; publications for next 25-50% are yellow; 50-75% are green; last quarter are purple). Bubbles represent number of citations associated with publications from each year of IMAT awards.

IMAT Portfolio Analyses

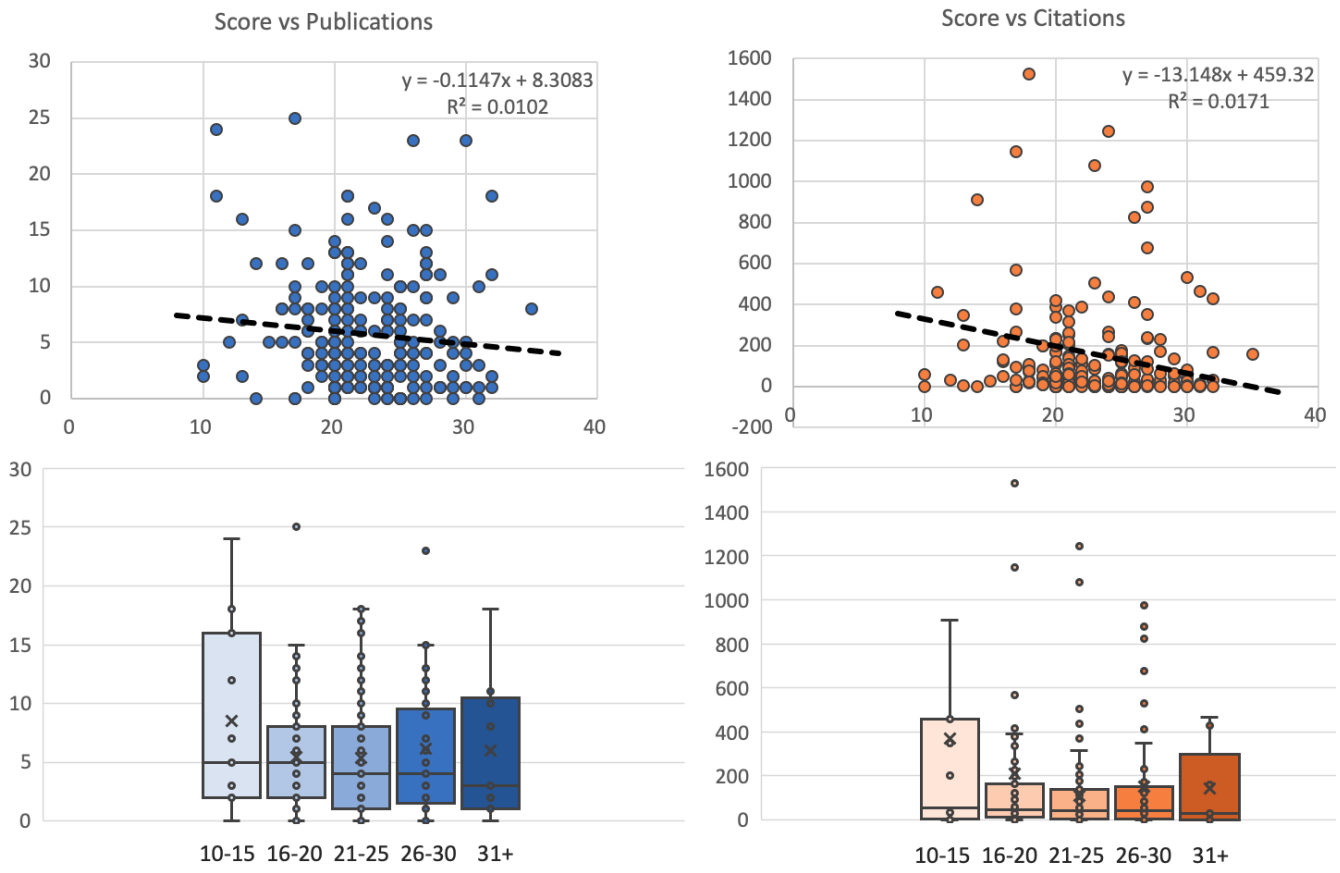
Figure 6. IMAT Awards Sorted by Number of Publications and Number of Citations



Top: IMAT grants awarded between 2010 and 2016 for R21 and R33 mechanisms sorted by number of associated publications. Below waterfall plot is number of grants that account for the first 25% of publications (red; 39 projects), 25-50% of publications (yellow; 60), 50-75% of publications (green; 121) and the last quarter of publications (purple; 408). The most productive projects were associated with 50 publications. The average project published 6.1 publications. 50% of projects published 4 or more publications.
Bottom: IMAT grants sorted by total citations (sum of citations for all associated publications). Below waterfall plot is number of grants that account for the first 25% of citations (red; 11 projects), 25-50% of citations (yellow; 29), 50-75% of citations (green; 72) and the last quarter of citations (purple; 526). The most cited project had 7117 citations. The average project had 289 citations. 50% of projects had 72 or more citations.

IMAT Portfolio Analyses

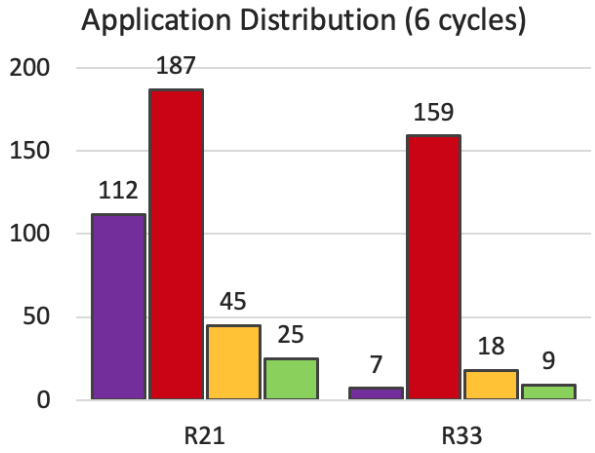
Figure 7. Publications and Citations Versus Review Score

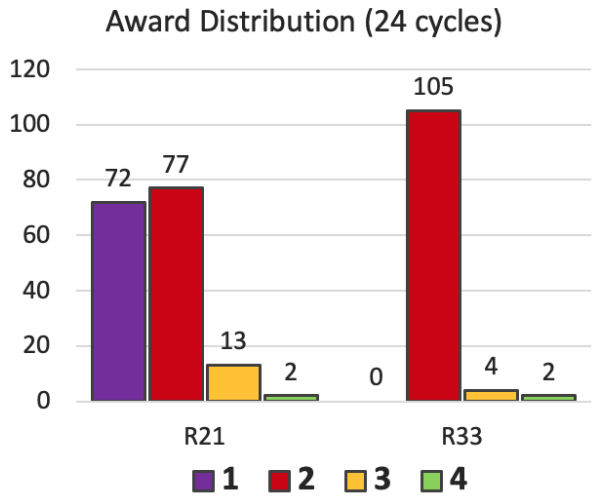


Top: Publications and total citations versus review score for IMAT grants awarded between 2010 and 2016 (R21 and R33 mechanisms only). Best fit line and equation shown.
Bottom: Box-and-whisker plots of publications and citations for IMAT awards binned by review score.

IMAT Portfolio Analyses

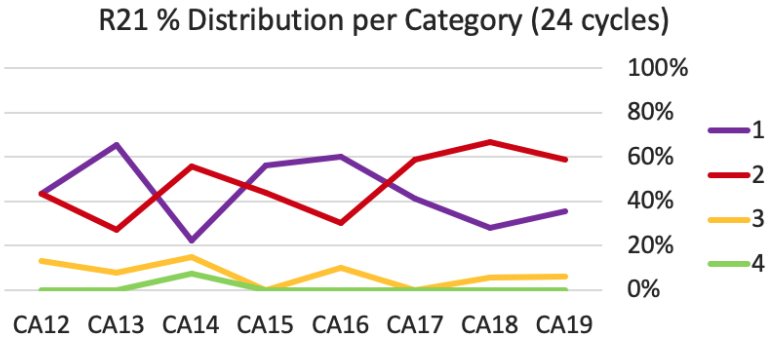
Figure 8. Distribution of Applications and Awards by the Four I's of Technology Development

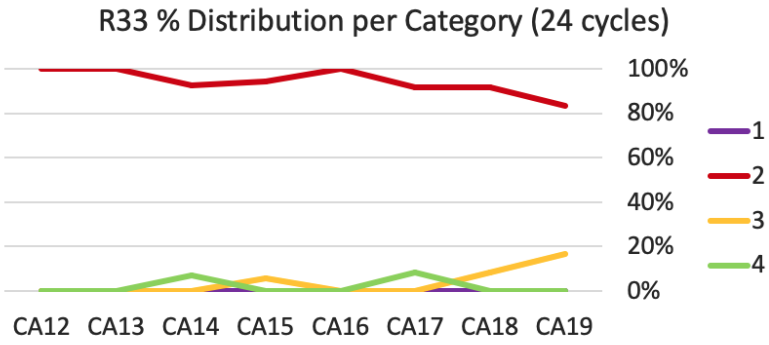




Success Rates per Category (2018-2019)

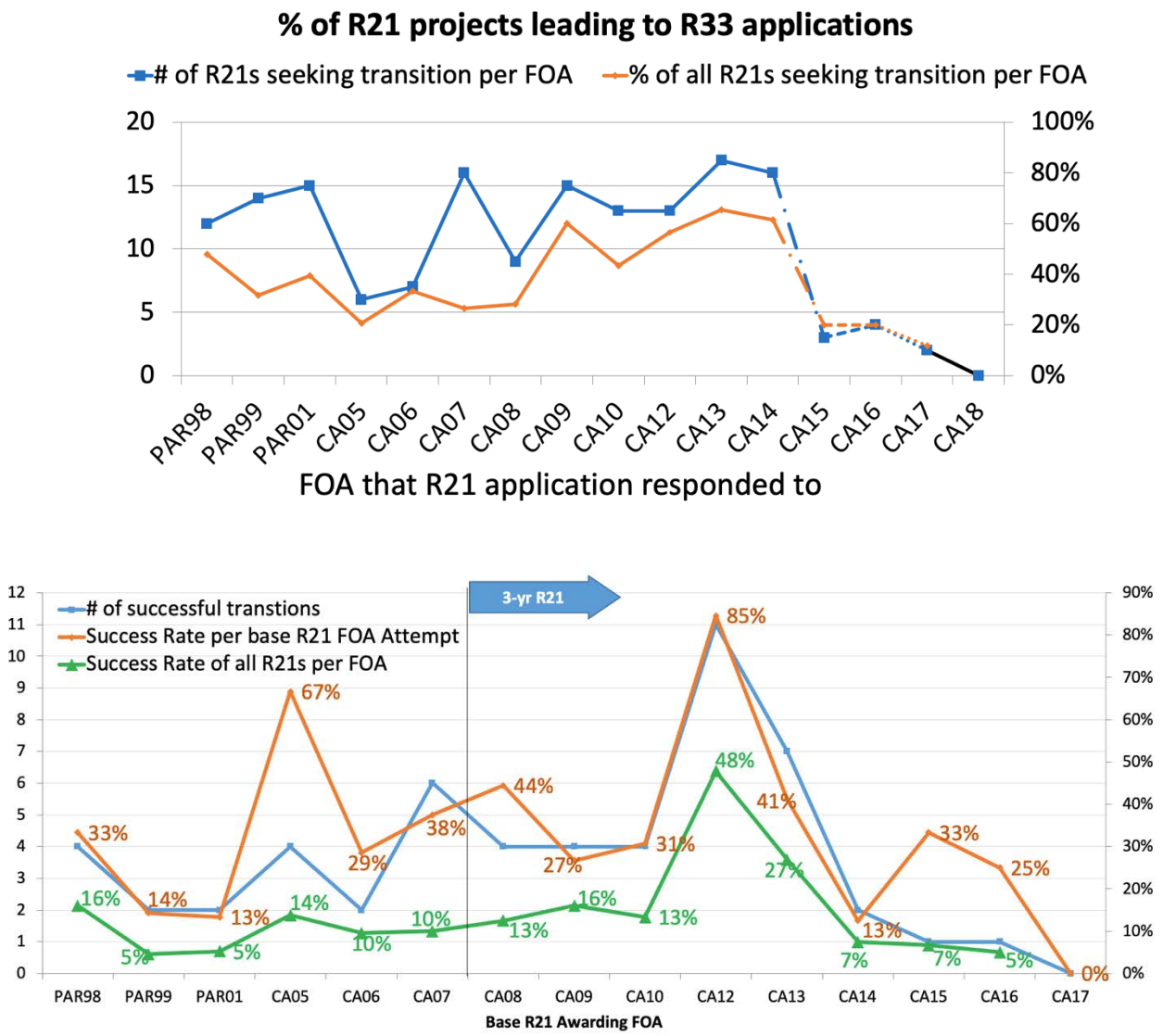
	1	2	3	4	Overall
R21	10%	12%	4%	0%	9%
R33	0%	13%	17%	0%	12%





Top left: Distribution of IMAT applications by 4-I's over 6 cycles of receipt dates (about 2 years)
Bottom left: Distribution of IMAT awards by 4-I's over 24 cycles of receipt dates (about 8 years)
Top right: Success rate per 4-I category by grant mechanism
Bottom right: 4-I distribution by FOA for R21s and R33s per FOA series.

Figure 9. Transition Attempts of Funded R21 Projects to R33s



Top graph: R21s that apply for an R33 by R21 FOA in number of applications (*blue line*) and percent of R21 awards (*orange line*).
Bottom graph: Total number of transitioned R33s awarded by base R21 FOA (*blue line*), success rate of R21 to R33 transition attempts (*orange line*), and percentage of all R21s that transitioned to R33 awards (*green line*).

Tables

Table 1. Evaluating Awards from 2013 and 2014 awards (most recent complete records)

RFA	Mechanism	# of Awards	# of Successes	Success Rate	# of Failures	Failure Rate
CA12-002	R21	20	8	40%	6	30%
CA12-003	R33	11	7	64%	1	9%
CA12-004	R21	3	2	67%	0	0%
CA12-005	R33	3	2	67%	0	0%
CA13-001	R21	21	9	43%	4	19%
CA13-002	R33	10	4	40%	2	20%
CA13-003	R21	5	2	40%	2	40%
CA13-004	R33	4	2	50%	0	0%