

Informatics Technology for Cancer Research (ITCR)

2021 Evaluation Panel Report

June 2021

Li Ding, PhD, Panel Chair

Professor of Medicine and Genetics; Director of Computational Biology, Oncology; Assistant Director, McDonnell Genome Institute, Washington University School of Medicine

Tina Hernandez-Boussard, PhD

Associate Professor of Medicine (Biomedical Informatics), Biomedical Data Science, Surgery, and, by courtesy, Epidemiology and Population Health, Stanford University School of Medicine

Sandy Napel, PhD

Professor of Radiology, Division Chief Integrative Biomedical Imaging Informatics, and, by courtesy, Professor of Medicine (Medical Informatics) and Electrical Engineering, Stanford University

Kristin Swanson, PhD

Professor, Neurosurgery and Radiation Oncology; Vice Chair for Research, Neurosurgery; Co-Director, Precision Neurotherapeutics Innovation Program, Mayo Clinic

Sam Volchenboum MD, PhD, MS

Associate Professor of Pediatrics; Dean of Master's Education; Director, Pediatric Cancer Data Commons; Associate Chief Research Informatics Officer, The University of Chicago

Table of Contents

Introduction and Panel Charge	3
Summary of Panel Conclusions	6
Panel Response to Charge	7
Question 1: What impact is the program having on advancing the field of cancer informatics and disseminating the necessary informatics tools and platforms to cancer researchers?	7
Question 2: Should NCI continue to support a dedicated program for informatics technology development? Are the unique characteristics that drove its initiation still relevant?	9
Question 3: Is the current portfolio balanced and well distributed, and should some current program directions be modified?	10
Question 4: Are the current funding mechanisms (R21, U01, two U24s) appropriate to achieve the program goals?	11
Question 5: Are there additional activities or directions that should be undertaken by the program to support its goals?	13
Appendix A: Panelist Biographies	15

Introduction and Panel Charge

The Informatics Technology for Cancer Research (ITCR) program is a trans-NCI grant program initiated in 2012 by NCI to support investigator-initiated, research-driven informatics technology development using a wide variety of technologies and spanning all aspects of cancer research. The program was conceived in 2011 as a response to reports from the scientific community that noted a need to catalyze development of informatics tools for the community. The current ITCR portfolio includes tools supporting -omics, imaging, network biology, clinical research, and data standards with growing support for additional fields such as radiation therapy and immuno-oncology. The program emphasizes development of open source tools and interoperability among the tools, promotes broad dissemination of user-friendly resources, and is structured around supporting informatics across the development life cycle.

The goals of the ITCR program are as follows:

- 1. Promote integration of informatics technology development with hypothesis-driven cancer research and translational/clinical investigations.
- 2. Provide flexible, scalable, and sustainable support using multiple mechanisms matched to various needs and different stages of informatics technology development throughout the development life cycle.
- 3. Promote interdisciplinary collaboration and public-private partnerships in technology development and distribution.
- 4. Promote data sharing and development of informatics tools to enable data sharing.
- 5. Promote technology dissemination and software reuse.
- 6. Promote communication and interaction among development teams.
- 7. Leverage NCI program expertise and resources across the Institute and bridge gaps of existing NCI grant portfolios in informatics.

The first funding opportunities were published in September 2012 as Program Announcements (PARs). The first round of funding opportunities included a U01 for early stage development; a U24 mechanism to support the advanced stage development of technologies as well as maintenance and dissemination; and competing supplements to existing R01, P01, and U01 to incorporate tool development into ongoing NCI research projects.

The program was first renewed in 2015 and added 2 additional funding mechanisms: an R21 to support innovative algorithm and computational method development, and a second U24 to support sustainment of highly accessed resources. A requirement was added for the U01 and U24 recipients to set aside 10% of their budget for collaborative activities that would be proposed post-award. The competitive revisions were discontinued.

The program was renewed for a second time in 2018 and the Funding Opportunity Announcements (FOAs) converted from PARs to Requests for Applications (RFAs). Based on feedback from an evaluation

panel, the technology development FOAs were continued, and 2 additional mechanisms were added: a set of new competitive revisions to support adoption of ITCR technology into ongoing NCI-funded research, and an ITCR Education Resource to develop courses in informatics and tool development to better support the adoption and use of the ITCR technologies.

The program is currently supported through 4 funding opportunities in the following:

- Algorithm Development (RFA-CA-21-013): Development of innovative methods and algorithms in biomedical computing, informatics, and data science addressing priority needs (R21).
- Prototyping & Hardening (RFA-CA-21-014): Development of enabling informatics technologies to improve the acquisition, management, analysis, and dissemination of data (U01).
- Enhancement & Dissemination (RFA-CA-21-015): Advanced development and enhancement of emerging informatics technologies to improve the acquisition, management, analysis, and dissemination of data (U24).
- Sustainment (RFA-CA-21-016): Continued development and sustainment of high-value informatics research resources to serve current and emerging needs (U24).
- Revision Applications: Novel collaborations to support adoption, adaptation, and integration of ITCR tools and resources, R01 – RFA-CA-21-017, U01 – RFA-CA-21-018, and U24 – RFA-CA-21-019.

To date, 112 projects have been funded across all categories, with 78 currently active. The program is approaching 1000 applications received. Forty-eight ITCR collaborations across ITCR members have been supported as of January 2021, as well as collaborations across other NCI groups.

In support of a third renewal request, NCI requires an independent evaluation of the program. Thus, NCI convened an expert panel to evaluate the program and provide insights. The panel has 5 members with a mix of backgrounds in cancer biology, oncology, and informatics, and who are not funded through the program. (See Appendix A for biographies of the panelists.) The panel was charged to assist NCI in addressing 5 questions regarding the ITCR program, as listed below.

Question 1: What impact is the program having on advancing the field of cancer informatics and disseminating the necessary informatics tools and platforms to cancer researchers?

Question 2: Should NCI continue to support a dedicated program for informatics technology development? Are the unique characteristics that drove its initiation still relevant?

Question 3: Is the current portfolio balanced and well distributed, and should some current program directions be modified?

Question 4: Are the current funding mechanisms (R21, U01, two U24s) appropriate to achieve the program goals?

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

NCI provided information to the panel for review. The panelists did not review confidential materials such as grant applications and review documents. The panel met in 4 video teleconferences between February and May 2021 during which the Program Director, Dr. Juli Klemm, provided detailed descriptions of the program, answered questions, and facilitated discussion among the panel members. The panel members provided written responses to the charges following the May teleconference.

It is anticipated that the third request will be submitted to NCI Scientific Program Leadership in October 2021, with this program evaluation providing input for preparing and submitting the request. If approved to renew the program FOAs as RFAs, the renewal request will also require approval by the Board of Scientific Advisors in December 2021.

Summary of Panel Conclusions

The panel came to the following 5 summary conclusions:

- Impact: The ITCR program has a fairly broad range, with a portfolio of tools covering various experimental platforms and different areas of cancer basic biology and translational science. ITCR has been crucial to cancer research and should continue to remain so. The ITCR program demonstrated its synergy with other NCI programs and will continue to meet the needs of the research community by developing, maintaining, and hardening software tools supporting emerging technologies.
- **Continued support:** The ITCR program has facilitated much progress toward fostering the development of NCI-relevant approaches to informatics software development. The unique characteristics that drove the development of the ITCR program were the increasing need to integrate and analyze complex, multi-modal data, difficulty in large-scale data sharing, and the need for robust, user-friendly software tools for cancer research. By many measures, the ITCR program has been successful at developing tools with general cancer research applicability and making them useful and available to cancer researchers working on highly specific projects.
- Program portfolio: The program portfolio included ~17 categories such as data analysis platform, data visualization, education resource, epigenetics, genomics, histology, immuno-oncology, informatics infrastructure, and medical imaging. The panel noted that only 2 projects (~3%) support informatics infrastructure, which is crucial for the future development of cancer research. Overall, the portfolio represents a wide range of impactful informatics projects. Some minor tweaking of the emphasis, as described above, will help round out the project landscape and increase the overall impact across cancer informatics.
- Funding mechanisms: ITCR-supported projects encompass the broad range of cancer research needs, utilizing a wide variety of informatics technologies. To support these efforts, the program supported applications across mechanisms including R01 revision, R21, U01, U24 for Advanced Development of Informatics Technologies, U24 for Sustainment of technologies, and UE5 as an educational resource. On the early development end of the spectrum, it is notable that the overall funding rate for the R21 mechanism (7%) is lower than the other mechanisms while still accounting for 21.4% of the overall funded ITCR awards. This suggests that there is a large community interest in mechanisms that support earlier development of ITCR-like technologies that may benefit from a focus on advising applicants on laudable R21 proposals.
- Other directions for ITCR: The ITCR program has the opportunity to expand its outreach and impact in the field, which will further support its growing portfolio of tools across different areas of cancer basic biology and translational science. Additional activities that will further benefit the program include expanding resources to support skill and workforce development; developing standards for the development, evaluation, and dissemination of tools; and further developing academic-industry relationships. ITCR has been crucial to cancer research and should undertake opportunities to ensure the tools and science developed under this funding mechanism are fair, ethical, transparent, and standardized.

Panel Response to Charge

Question 1: What impact is the program having on advancing the field of cancer informatics and disseminating the necessary informatics tools and platforms to cancer researchers?

The ITCR program has a fairly broad range with a portfolio of tools covering various experimental platforms and different areas of cancer basic biology and translational science. The overall answer to the question of impact can be thought of in terms of how the investigator community would have had to address their bioinformatics needs in the absence of these tools. Algorithm development and software implementation are not typical areas of expertise for biologists and clinicians, and it is likely that the explosive progress in cancer research over roughly the last decade would have been less dramatic without these tools. ITCR has been crucial to cancer research and should continue to remain so. Specific comments follow on the relevant topics of metrics, synergy, and innovation.

Metrics: The utility of ITCR is impact through "usage," which can be reflected by downloads, citations, and/or sizes of user communities. The metrics for established tools are impressive and suggest that past ITCR funding has been well-targeted to projects deemed worthwhile and useful by the investigator community and, importantly, that these projects were actually brought to fruition and are now in use.

Synergy: Collaborations have been climbing: 9, 11, and 15 in the respective years from 2018–2020. This is an impressive trend and suggests that a larger synergistic network is taking shape to multiply the power of ITCR tools. Some are efforts to operationally bridge major software systems, like the Pratt-Mesirov-NDEx-MSigDB collaboration. The software engineering complexities of these sorts of efforts should not be underestimated. This aspect of ITCR should continue to be vigorously promoted. There are fruitful interactions among the more established tools and their developers/investigators, but interactions might be further stimulated for the newer/early stage tool developers. Some examples were also given on how ITCR tools are supporting various NCI programs. This aspect should also be vigorously promoted and extended to other NCI programs, such as Human Tumor Atlas Network (HTAN) and Genomic Data Commons (GDC). Synergy should continue to be a key aim of ITCR moving forward.

Innovation: This is perhaps the most crucial aspect related to vision and procedure that would further leverage ITCR funding in the future. First, while there are elements of high-performance computing and cloud computing with broad representation of established data types, the program should continue to be mindful of emphasizing emerging technologies and data types in order to "stay ahead of the curve." For example, spatial transcriptomics, which maps expression data to spatial locations, is a methodology that is now experiencing rapid growth. Analysis of the Clarivate Web of Science database shows that the number of papers having "spatial transcriptomics" in their titles increased from 26, to 34, to 42, to 68 over the last 4 years up to 2020. ITCR should keep a close eye on such emerging and/or rapidly growing technologies (e.g., integrated multi-omics and proteomics, single cell/nuclei methods, etc.). Similarly, the onslaught of machine learning driven radiomics technologies into the biomedical landscape has been dramatic over the recent past. Hardening of those tools for wide deployment and portability is a principal bottleneck to leveraging these tools to advance biomedicine. Because of the dramatic portability and interoperability challenge common to many of these radiomics approaches, and the particularly challenging environment to fund hardening of such tools, the ITCR program is an ideal place to herald forward such radiomics-like platforms. The ITCR portfolio is a mixture of 1) new algorithm and method development (2 years of funding), 2) intermediate projects (3–5 years of funding), and 3) mature projects with 5 years of development whose funding has also been renewed. There is a substantial U24 budgetary component devoted to refining, hardening, and maintaining fairly mature

members of the second and third categories. To maximize agility and innovation, ITCR could consider shifting monies somewhat more toward new project development by increasing the numbers of R21 and U01 grants awarded. This aspect would seem to be key to being able to cover investigators' evolving needs within the "bioinformatics software marketplace" with the finite funds that are available.

Question 2: Should NCI continue to support a dedicated program for informatics technology development? Are the unique characteristics that drove its initiation still relevant?

The ITCR program has facilitated much progress toward fostering the development of NCI-relevant approaches to informatics software development. The unique characteristics that drove the development of the ITCR program were: (a) modern multidisciplinary approaches to cancer research, diagnosis, and treatment demands informatics technology that facilitates integration of disparate data types for discovery, predictive modeling, and response assessment; (b) despite data-sharing requirements for grant funding, large data sets collected for individual projects had been difficult to access and reuse; and (c) despite the existence of bioinformatics software packages developed for specific projects and their potential to be reused in other applications, interested cancer researchers often had to devote significant resources for modification and adoption to a related but distinct investigation.

In recent years, informatics tool sharing among NCI investigators has become more common, most often among investigators within the same funded program. Examples of such programs are the following: <u>Cancer Systems Biology Consortium (CSBC)</u>, <u>Physical Sciences-Oncology Network (PS-ON)</u>, <u>The Cancer</u> <u>Genome Atlas (TCGA) Genomic Data Analysis Network</u>, <u>Quantitative Imaging Network</u>, <u>Clinical</u> <u>Proteomic Tumor Analysis Consortium (CPTAC)</u>, <u>HTAN</u>, and the <u>Early Detection Research Network</u> (<u>EDRN</u>). Adoption of informatics tools outside of the originating program was limited until more recently, when some have been "pushed" to ITCR for further development, hardening, and dissemination (e.g., cBioPortal for Cancer Genomics, originally developed through TCGA and now sustained through ITCR; and 3D Slicer, originally developed under several mechanisms [National Center for Research Resources, National Institute of Biomedical Imaging and Bioengineering, NIH Roadmap, NCI, National Science Foundation, and the US Department of Defense] and now under ITCR). Tool development within other awards such as investigator-initiated R01s is limited, and where it does exist, it is highly tailored to the aims of the award, not toward general use.

In addition to the "push" mechanism described above, tools may be developed de novo within ITCR and "pulled" into other programs. By many measures, the ITCR program has been successful at developing tools with general cancer research applicability and making them useful and available to cancer researchers working on highly specific projects. For example, 6 NCI programs (Consortium for Molecular and Cellular Characterization of Screen-Detected Lesions, EDRN, Translational Liver Cancer, HTAN, CSBC, and CPTAC) have incorporated and employed 24 different ITCR tools, with 1 tool (cBioPortal) represented in 5 programs, 2 tools (Bioconductor and Integrative Genomics Viewer) each represented in 4 programs, and 4 tools (3D Slicer, Gene Set Enrichment Analysis, Galaxy, and GenePattern) each represented in 3 programs. While this summary only looks over NCI programs, which are the main focus of ITCR's genesis, overall impact is actually much stronger, as can be seen by the numbers of downloads and citations for each ITCR tool. For example, Bioconductor is downloaded thousands of times per month, and while GenePattern and 3D Slicer are each used in only 3 NCI programs, they have been downloaded and installed many tens of thousands of times each.

Nonetheless, as the tools developed within specific NCI programs get validated within the program under which they were developed, the need for generalization and successful sharing has grown. As the number of applications to ITCR for support has shown, the unique characteristics that called for its original development still exist. Even when tools are shared successfully and used to good effect, ongoing support is critical. Therefore, mechanisms recently added to the ITCR program, such as those aimed at tool sustainment, are important and should be continued.

Question 3: Is the current portfolio balanced and well distributed, and should some current program directions be modified?

The program portfolio was reviewed by the panel, and select projects were presented to the panel in more detail. The active grants were grouped by categories, which included data analysis platform (7), data visualization (5), education resource (1), epigenetics (2), genomics (6), histology (9), immuno-oncology (2), informatics infrastructure (2), medical imaging (11), medical informatics (7), network biology (2), proteomics (3), radiation therapy (3), transcriptomics (7), and variant interpretation (3). Of the 70 projects listed here, 18 (~25%) are genomic focused, while only 7 (~10%) are focused on medical informatics, and 2 (~3%) are based on informatics infrastructure. Informatics projects have historically been very difficult to fund, especially from NCI/NIH funding mechanisms. ITCR represents a unique opportunity to focus funding on this critically important area. In particular, funding for data standards and interoperability could be increased, as this would facilitate better data sharing.

The emergence of the Cancer Research Data Commons (CRDC) ecosystem, along with the Center for Cancer Data Harmonization (CCDH) and the Cancer Data Aggregator (CDA), represents a unique opportunity to develop and leverage tools for cancer research. The tools being developed by the CCDH and CDA are focused on data interoperability between CRDC nodes. A major gap is in how data are collected, harmonized, and prepared for submission to the CRDC. Funding programs to develop tools and infrastructure to support data collection and submission to the CRDC and other NIH/NCI programs would greatly benefit the cancer informatics landscape and help lower barriers to research.

Other areas of potential focus are data governance and provenance. A major shortcoming of many tools and platforms is the lack of robust data governance and data provenance, and programs addressing these important issues should be supported. In addition to potentially funding applications that specifically address issues of data governance and provenance, the RFPs for the R21, U01, and U24 mechanisms should ask applicants to specifically address these issues in their application or data sharing plans.

While imaging projects have been robustly supported (~15% of total active projects), much of the work has focused on normalizing and aggregating data from CT scans. There is an opportunity to expand this focus to include other imaging modalities, especially MRI, to support projects that offer ways to design analysis algorithms that are portable and generalizable, as this is a major impediment to the long-term impact of imaging informatics techniques developed within and beyond ITCR.

Finally, the application process should work to incorporate issues of addressing sex as a biological variable. Not only are multi-omics databases mostly populated with data from male subjects, the sex of the research subject is often not even collected (PMID: 34099934). In addition, lack of gender (as distinct from chromosomal sex), race, and ethnicity data can also prohibit research that takes these differences into account. In both the RFAs as well as the review process, special attention should be paid to these inequities, particularly in the propagation of biases as a result of such imbalances in software that become widely used through the ITCR program.

Overall, the portfolio represents a wide range of impactful informatics projects. Some minor tweaking of the emphasis, as described above, will help round out the project landscape and increase the overall impact across cancer informatics.

Question 4: Are the current funding mechanisms (R21, U01, two U24s) appropriate to achieve the program goals?

The ITCR program is a trans-NCI program supporting investigator-initiated informatics technology development that is driven by critical needs in cancer research. The ITCR program emphasizes the development of open source tools and the interoperability among the tools, as well as promotes broad dissemination of user-friendly resources. ITCR-supported projects encompass the broad range of cancer research needs, utilizing a wide variety of informatics technologies. To support these efforts, the program has received nearly 1000 applications resulting in 112 awards (overall 12% funding rate) across mechanisms. Each funding mechanism serves distinct but complementary roles:

- **Competing Revisions (3/11 = 2.7% of all ITCR awards):** This revision mechanism provides an opportunity for supplemental incorporation of ITCR tools into other funded projects (R01s, P01s, and U01s). This program is an excellent means to expand the exposure, accessibility, and impact of ITCR-developed technologies; however, there has been only limited response to this RFA so far. The program does not provide for revision applications to other large-scale funding mechanisms, such as U54s, which could expand the adoption of ITCR technologies. There have been 13 applications with 3 funded awards for a funding rate of 23%.
- **R21 (25/117 = 21.4% of all ITCR awards):** The R21 mechanism supports high-risk/high-reward applications to help launch new ITCR technologies. There have been 358 applicants with 25 awards for a funding rate of 7%.
- **U01 (35/117 = 29.9% of all ITCR awards):** The U01 mechanism supports developing and establishing ITCR technology that needs significant development. There have been 346 applications with 35 awards for a funding rate of 10%.
- **U24 for Advanced Development (43/117 = 36.7% of all ITCR awards):** This U24 mechanism provides for the hardening and deployment of technologies developed under the U01 mechanism or in other programs. There have been 147 applications with 43 awards for a funding rate of 29%.
- **U24 for Sustainment (6/117 = 5.1% of all ITCR awards):** This U24 mechanism is paramount in providing sustained maintenance for central ITCR technologies. There have been 27 applications with 6 awards for a funding rate of 22%.
- **UE5 (1/117 = 0.8% of all ITCR awards):** The UE5 mechanism provides for increased visibility and adoption of ITCR technologies through educational opportunities in which ITCR technologies are highlighted. There have been 6 applications with 1 award for a funding rate of 17%.

The ITCR program has also served to develop projects within the progressive funding mechanisms provided within the program. There has been 1 proposal that developed from the R21 level to a U01, 3 U01s that progressed to U24 Advanced Development projects, 6 U24 Advanced Development renewals, and 1 U24 that progressed from Advanced Development to Sustainment. Each of these mechanisms provides essential synergistic opportunities to develop, innovate, and sustain ITCR technologies that have a critical impact on cancer research.

There are many challenges facing the community of individuals developing ITCR-type tools, including how to support infrastructure around informatics tools in order to develop, deploy, and sustain such tools, and how to sustain such informatics tools in the long term, not to mention educational initiatives thereof.

On the early development end of the spectrum, it is notable that the overall funding rate for the R21 mechanism (7%) is lower than the other mechanisms, while the number of applications remains quite high. This suggests the opportunity to help facilitate earlier identification of potential ITCR-viable technologies. Further, it is possible the R21 mechanism applied to ITCR-like projects creates a mismatch between review expectations, making it more difficult to build fundable R21 applications. In that case, there may be an opportunity to consider short-term early U01 mechanisms that provide for a similar initiation of new ITCR tools within a more limited temporal framework that could later compete for longer-scale U01 or U24 mechanisms.

On the other end of the development spectrum, it is clear that success of the overall ITCR program's impact on the cancer community relies on the sustainment of multiple tools/software. The relatively modest portfolio for sustaining technologies (6 funded in the last 5 years) could limit the long-term impact of laudable technologies developed within the ITCR portfolio. Thus, there is strong reason to support the ongoing progressive portfolio of U01 to the 2 types of U24 mechanisms as part of the portfolio.

The Competing Revision mechanism is a laudable opportunity to expand the adoption of ITCR technologies across the scientific community. It is noteworthy that only 13 Revision Applications have been received over 15 funding cycles, and only 3 funded. This funding opportunity is notable for its potential impact on defining success of the ITCR program in the form of broader sustained adoption of ITCR-developed technologies that could be meaningfully measured as the program grows. That said, the low response to the funding call suggests the potential need to 1) eliminate the mechanism, instead focusing on R21, U01, and U24 proposals, or 2) more broadly advertise the potential revision application mechanism (which is admittedly fairly uncommon across NCI). To this end, a common place in which significant and meaningful ITCR-like tool development happens is in U54 or similar center grants (e.g., CSBC and PS-ON), yet the current Competing Revision funding call is only for R01, U01, and P01 mechanisms. Allowing the U54 mechanism to participate in this Competing Revision call would not only expand the visibility of the program, but also provide a unique opportunity to transition burgeoning tools being actively developed within the community around U54s into meaningful broader impacts for those NCI programs that include U54s, including several notable networks such as CSBC and PS-ON.

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

The ITCR program has the opportunity to expand its outreach and impact in the field, which will further support its growing portfolio of tools across different areas of cancer basic biology and translational science. Additional activities that will further benefit the program include expanding resources to support skill and workforce development; developing standards for the development, evaluation, and dissemination of tools; and further developing academic-industry relationships. ITCR has been crucial to cancer research and should undertake opportunities to ensure the tools and science developed under this funding mechanism are fair, ethical, transparent, and standardized, as well as ensure these resources provide opportunities for educational and workforce development.

Minimize bias: The influx of tools in the community, including those developed under ITCR, presents a fundamental shift in the way we use, process, and disseminate information for cancer research and care. Recently, reports suggest that biases hidden in the data used to develop the tools could result in negative consequences for certain populations. ITCR has a responsibility to ensure that the tools and frameworks developed under the program have minimal bias and are ethical and trustworthy related to their effects and implications on users and society. Issues include the accuracy, reliability, and fairness of data and tools, as well as the transparency, accountability, and auditability of tools and tool development.

Develop standards: ITCR should support the development and implementation of guidelines and standards for its growing portfolio of tools across different areas of cancer basic biology and translational science. There is a need to develop standards for evaluation metrics—for example, what metrics should be evaluated (thinking beyond simple model performance) and what is the minimal level of performance a model should achieve. Additional research is needed to ensure tools do not exacerbate disparities and inequities in downstream health decisions and outcomes, integrating social determinants of health and psychosocial factors influencing biology, health, and disease, when appropriate.

Promote transparency: ITCR should support transparency across 3 main categories: data acquisition, model design and development (including training data), and model evaluation and validation. ITCR can promote transparency through reporting standards, such as MINIMAR (<u>PMID: 32594179</u>) and MI-CLAIM (<u>PMID: 32908275</u>). A lack of transparency directly affects the reproducibility, generalizability, and interpretability of the tools developed. Therefore, we need transparency in the reporting of the design, development, evaluation, and validation of ITCR-sponsored tools to achieve and retain confidence and trust for all the stakeholders.

Develop skills and workforce: The tools developed under the ITCR program are diverse and very crossdisciplinary. ITCR should support further cross-disciplinary collaborations across a broad array of expertise, including both technical and nontechnical backgrounds. ITCR can help bridge expertise across bioinformatics, biomedical, and team science. There are opportunities to support the integration of ethics, translational science, and other cross-disciplinary domains in order to enhance the generalizability of the tools, resource sharing, and skill development beyond the core investigators. Team diversity is especially critical for the development of unbiased tools that represent the backgrounds and needs of all groups. There is an opportunity for ITCR to expand its impact in the field through focused skill development activities. This could include integrated and coordinated curricula and educational activities to support use of the development and/or use of the tools developed through the program, as well as to support use of the products and cross-cutting best practices developed by all the grantees of the program. Furthermore, this would open opportunities to support career development and mentoring in the field. ITCR could consider supporting the education of the next generation through the support of graduate postdoctoral scholars, as well as internship programs associated with funded grants. The encouragement of a diverse team and the consideration of training awards and diversity supplements should be considered.

Further develop academic-industry relationships: The academic-industry relationship is important in the ITCR community, and this relationship should be further developed and supported. Industry has a long tradition of support for tool development, dissemination, and sustainability, and it has unique resources and expertise that can be leveraged to further support ITCR-funded initiatives. Companies contain technical expertise and business-savvy teams. Coupling with industry can provide opportunities to support the scaling of products based on profitable business plans. This relationship is also advantageous for industry, as it often lacks data, particularly real-world evidence. Therefore, it is also beneficial for industry to partner with academia, and the recommendation is that industry partners be part of scientific advisory boards and other areas of engagement. Fostering and supporting academic-industry relationships can help support the sustainment and dissemination of tools developed under ITCR.

Appendix A: Panelist Biographies

Li Ding

Dr. Ding received her BS in biology from Fudan University in 1991 and her PhD in biochemistry from the University of Utah School of Medicine in 1998. She was a postdoctoral fellow in the Department of Biochemistry, Stanford University School of Medicine, from 1998–2000. She then moved to Incyte Genomics from 2000–2002 and then to the McDonnell Genome Institute, Department of Genetics, Washington University School of Medicine. She has remained there, becoming the Assistant Director of the McDonnell Genome Institute in 2008, Professor in the Departments of Medicine and Genetics in 2015, and Director of Computational Biology, Oncology, in 2016.

Dr. Ding's research focuses on the discovery of genetic changes contributing to human diseases by integrating various data types, including DNA, RNA, and proteomics data. Her research team has developed a collection of widely used computational tools. Dr. Ding has successfully led many large-scale, multi-institute studies on the genomics of lung adenocarcinomas, AML, and breast cancer, and has produced a series of seminal publications in the fields of cancer genomics research and cancer biology.

Dr. Ding contributes to TCGA, the International Cancer Genome Consortium (ICGC), and CPTAC. She cochairs the TCGA PanCanAtlas Oncogenic Process Group, the TCGA Sarcoma Analysis Working Group, and the ICGC Mutation Calling Group. She also serves on the Steering Committees of the GDC, CPTAC, and TCGA. She holds a number of awards and honors including The Hottest Scientific Researchers of 2012 and The World's Most Influential Scientific Minds, 2014, Thomson Reuters, and was chair for the TCGA Fourth Annual Joint Scientific Symposium, NIH.

Tina Hernandez-Boussard

Dr. Hernandez-Boussard received her BS in biology and BA in psychology from the University of California, Irvine, in 1991. She obtained an MPH in epidemiology from Yale University in 1993 and a PhD from the Université Claude Bernard Lyon 1 in computational biology in 1999, as well as an MS in health services research from Stanford University in 2013. She holds a number of academic appointments including Associate Professor, Medicine–Biomedical Informatics Research; Associate Professor, Biomedical Data Science; Associate Professor, Surgery; Associate Professor (by courtesy), Epidemiology and Population Health; Member, Bio-X; Member, Maternal & Child Health Research Institute; Member, Stanford Cancer Institute; and Member, Wu Tsai Neurosciences Institute.

Dr. Hernandez-Boussard's expertise is in the field of clinical informatics and epidemiology, with a concentration in predictive analytics, population health, and health policy. A key focus of her research is the application of novel methods and tools to large clinical data sets for hypothesis generation, comparative effectiveness research, and the evaluation of quality healthcare delivery. The research involves managing and manipulating big data, which range from administrative claims data to electronic health records, and applying novel biostatistical techniques to innovatively assess clinical and policy-related research questions at the population level. This research enables the laboratory to create formal, statistically rigid evaluations of healthcare data using unique combinations of large data sets.

Dr. Hernandez-Boussard is on numerous boards, advisory committees, and professional organizations; is a Fellow, American College of Medical Informatics (2020); and won the Innovation Award in Population Science, Stanford University (2011 and 2012).

Sandy Napel

Dr. Napel received his BS in 1974 from SUNY Stony Brook University in engineering sciences, and both his MS in 1976 and PhD in 1981 from Stanford University in electrical engineering. He is currently Professor of Radiology, Division Chief Integrative Biomedical Imaging Informatics since 2009, and, by courtesy, Professor of Medicine (Medical Informatics) and of Electrical Engineering at Stanford University. Dr. Napel also has been co-director of the Radiology 3D and Quantitative Imaging Laboratory since 1996.

Dr. Napel's primary focus is on radiomics and radiogenomics, and he has been involved in developing diagnostic and therapy-planning applications and strategies for the acquisition, visualization, and quantitation of multidimensional medical imaging data. Some examples are creation of 3D images of blood vessels using CT, visualization of complex flow within blood vessels using MR, computer-aided detection and characterization of lesions from cross-sectional image data, visualization and automated assessment of 4D ultrasound data, and fusion of images acquired using different modalities (e.g., CT and MR). He has also been involved in developing and evaluating techniques for exploring cross-sectional imaging data from an internal perspective (i.e., virtual endoscopy) and in the quantitation of structure parameters. Dr. Napel is also interested in creating workable solutions to the problem of "data explosion," i.e., how to look at the thousands of images generated per examination using modern CT and MR scanners.

Dr. Napel is a member of Stanford's Bio-X program, the Stanford Cardiovascular Institute, and the Stanford Cancer Institute. He is a member of the College of Fellows and the American Institute for Medical and Biological Engineering (November 2009), and he received the Distinguished Investigator Award, Academy for Radiology and Biomedical Imaging Research (2012).

Kristin Swanson

Dr. Swanson received her BS in mathematics with a minor in physics in 1996 from Tulane University. She then earned her MS in 1998 and PhD in 1999 in mathematical biology from the University of Washington. Dr. Swanson went on to a postdoctoral fellowship in mathematical and computational medicine at the University of California, San Francisco. She joined the faculty at the University of Washington in 2000, with appointments in both neuropathology and applied mathematics. In 2015, she joined Mayo Clinic in Arizona as Professor and Vice Chair of the department of neurological surgery. She is currently the Vasek and Anna Maria Polak Professor in Cancer Research and also holds appointments as Professor of Radiation Oncology, Director of the Mathematical Neuro-Oncology Lab, and Co-Director of the Precision Neurotherapeutics Innovation Program at Mayo Clinic. She also holds an appointment as Professor of Mathematical and Statistical Sciences at Arizona State University.

Her research lab is driven by the motto that "every patient deserves their own equation." As a mathematical oncologist, Dr. Swanson's research interests are in clinical trial design and predictive mathematical modeling for the treatment of patients with brain cancer. Her laboratory group works to generate patient-specific predictive models to effectively and accurately predict tumor growth and response to therapy in individual patients. The group works with clinical and research teams at Mayo Clinic to bring these innovations to the clinic while identifying new predictive models. This work can also be used to inform novel therapy design, resulting in better treatment and outcomes for patients.

Dr. Swanson is recipient of the 2017 Mayo Clinic Service Award for Diversity and Inclusion and the 2008 University of Washington Award for Undergraduate Research Mentor of the Year.

Sam Volchenboum

Dr. Volchenboum received his BS from the University of Illinois in biochemistry with honors in 1991. He attended the Mayo Clinic College of Medicine and Science, obtaining his MD and PhD in molecular biology in 1998. He followed with a residency in pediatrics at the Cincinnati Children's Hospital Medical Center from 1998–2001 and a fellowship at Dana-Farber Cancer Institute/Boston Children's Hospital in Pediatric Hematology/Oncology from 2001–2004. He completed a fellowship in informatics and received his MS in biomedical informatics from the Massachusetts Institute of Technology in 2007. Dr. Volchenboum has been on The University of Chicago faculty since 2007.

Dr. Volchenboum is currently Associate Professor of Pediatrics; Dean of Master's Education; Associate Chief Research Informatics Officer; and Associate Director, Institute for Translational Medicine, The University of Chicago. He directs a program in health sciences informatics. His clinical specialty is pediatric hematology/oncology. As an expert in pediatric cancers and blood disorders, he has a special interest in treating children with neuroblastoma, a tumor of the sympathetic nervous system. His research methodologies include using proteomics to study pediatric solid tumors and building tools for high-throughput mass spectrometry data analysis. His laboratory has a number of outside collaborations, including an international multi-institutional effort to establish a database for neuroblastoma patient data. He also works with the Children's Hospital of Philadelphia to study the effects of TrkA and TrkB signaling in neuroblastoma cell lines.

In addition to caring for patients, Dr. Volchenboum studies ways to harness computers to enable research and foster innovation using large data sets. He directs the development of the International Neuroblastoma Risk Group database project, which connects international patient data with external information such as genomic data and tissue availability. The center he runs provides computational support for the Biological Sciences Division at The University of Chicago, including high-performance computing, applications development, bioinformatics, and access to the clinical research data warehouse.

Dr. Volchenboum also directs The University of Chicago's Pediatric Cancer Data Commons, and until 2019, Dr. Volchenboum directed the Center for Research Informatics, a 40-person group that supports biological research throughout the division. He participates in and leads various data governance initiatives throughout the University and medical center. He is the director of the Informatics Core for the Clinical and Translational Science Award. Since 2015, he has been the faculty director for the Master's in Biomedical Informatics at The University of Chicago.

Dr. Volchenboum was named a St. Baldrick's Foundation Scholar in 2009, was awarded Castle Connolly's Regional Top Doctor in 2014, and won The University of Chicago Innovation Fund Award in 2012.