

The NCI Informatics Technology for Cancer Research (ITCR) Program

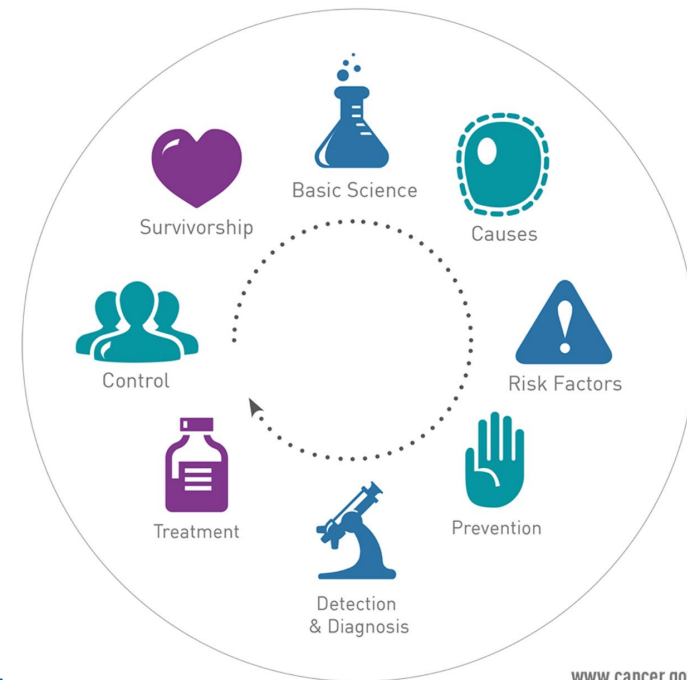
Juli Klemm, Ph.D.

NCI Center for Biomedical Informatics and Information Technology

The Informatics Technology for Cancer Research (ITCR) Program

ITCR is a trans-NCI program to support investigator-initiated informatics technology development driven by critical needs in cancer research.

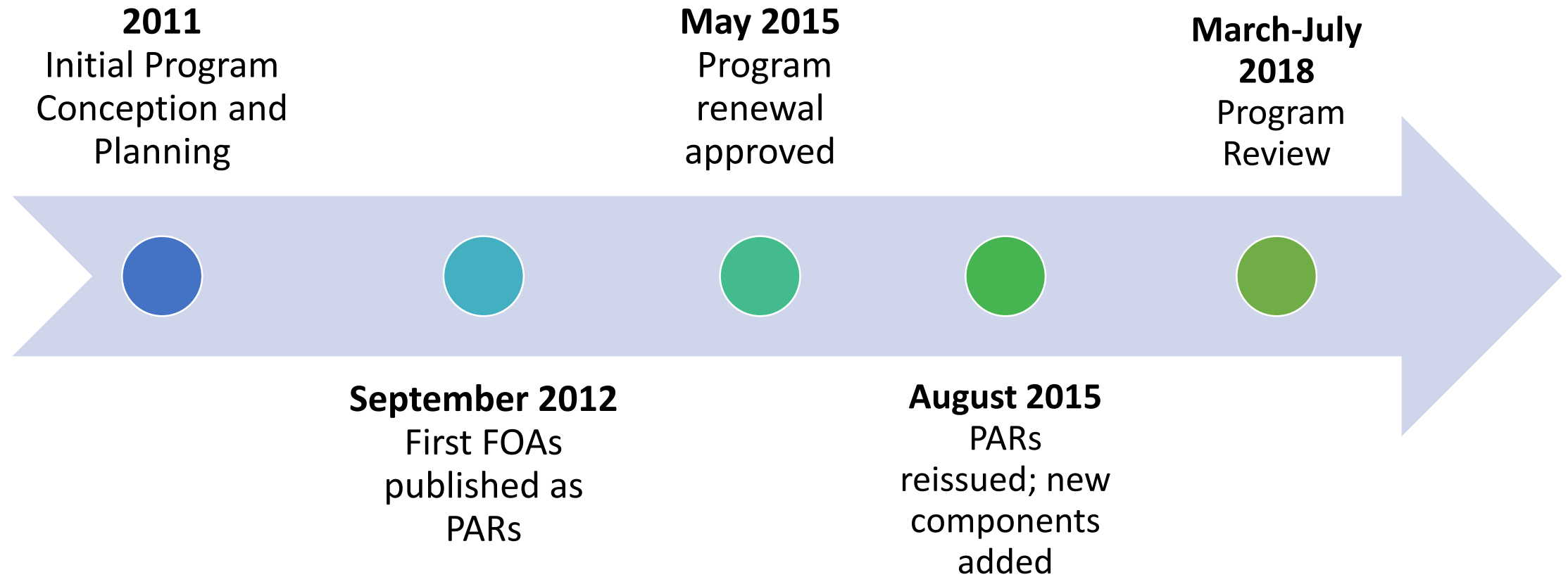
- Support informatics technology development driven by cancer research
- Develop open-source, interoperable software tools and resources
- Promote broad dissemination of user-friendly resources



<https://itcr.cancer.gov>

www.cancer.gov

ITCR History



ITCR Program Impact

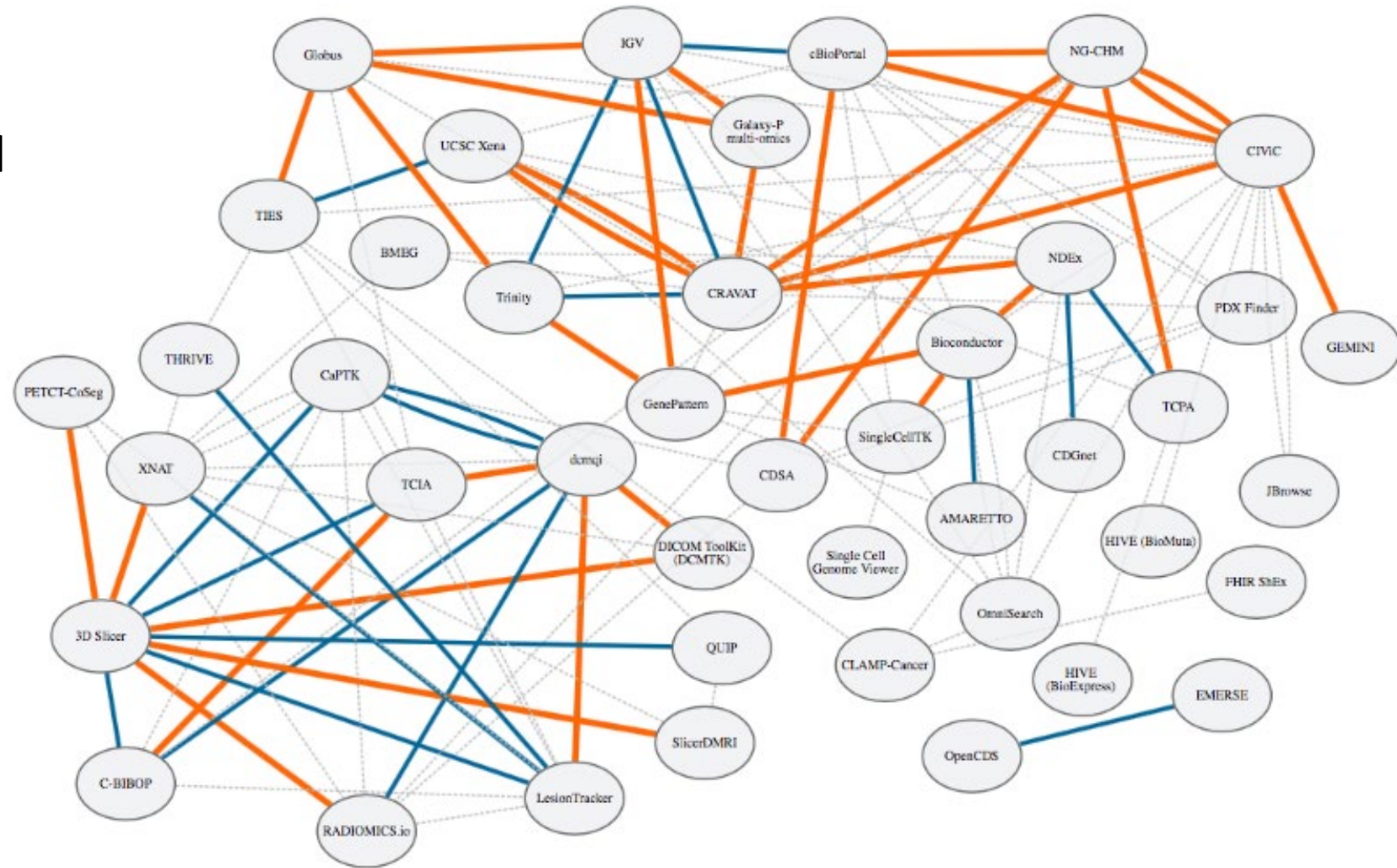
- Improved connection of informatics tool development with cancer research
- Emphasis on interoperable tool development
- Training for NCI intramural scientists
- Support for informatics technology needs across NCI programs
- Improved adoption and citation of ITCR tools
- Enhanced outreach and training

| Tool | Purpose | Usage |
|---|--|---|
| 3D Slicer | Platform for medical image visualization and analysis | 100,000 downloads/year |
| cBioPortal | Visualization, analysis, and download of large-scale cancer genomics datasets | 25,000 unique user/month >1600 citations |
| CIViC | Community-driven, curated knowledge resource for Clinical Interpretation of Variants in Cancer | 2500 web users/month >1M API calls/month |
| CRAVAT | Web-based tool for the analysis of cancer variants | 50,000 job submissions/year 1200 downloads >555 citations |
| GenePattern | Workflow platform for -omics data analysis and visualization | AWS-hosted instance: 47,000 registered users; 2000-5000 analyses/week |
| Globus | Provides secure transfer of large datasets | 15,000 users 8000 endpoints |
| GSEA/MSigDB | Identifies coordinated activation or repression of gene groups | 113,000 users >10,200 citations |
| Integrative Genomic Viewer (IGV) | High-performance visualization tool for interactive exploration of genomic datasets | 35,000 launches/week 9000 distinct IP addresses >3000 citations |
| Trinity | Supports de novo transcript assembly and focused analysis on cancer transcriptomes | 3000 users/month >4000 citations |
| UCSC Xena | Supports co-analysis and visualization of private and public genomic/phenotypic data | 7000 users/month |

Tools supported through ITCR are among the most widely-used informatics resources in cancer research

ITCR Promotes Collaboration and Outreach

- Collaborations supported through set-aside funds and administrative supplements
- Tool catalog and introductory videos available on itcr.cancer.gov
- Special Issue of *Cancer Research* focused on cancer informatics (Nov, 2017)

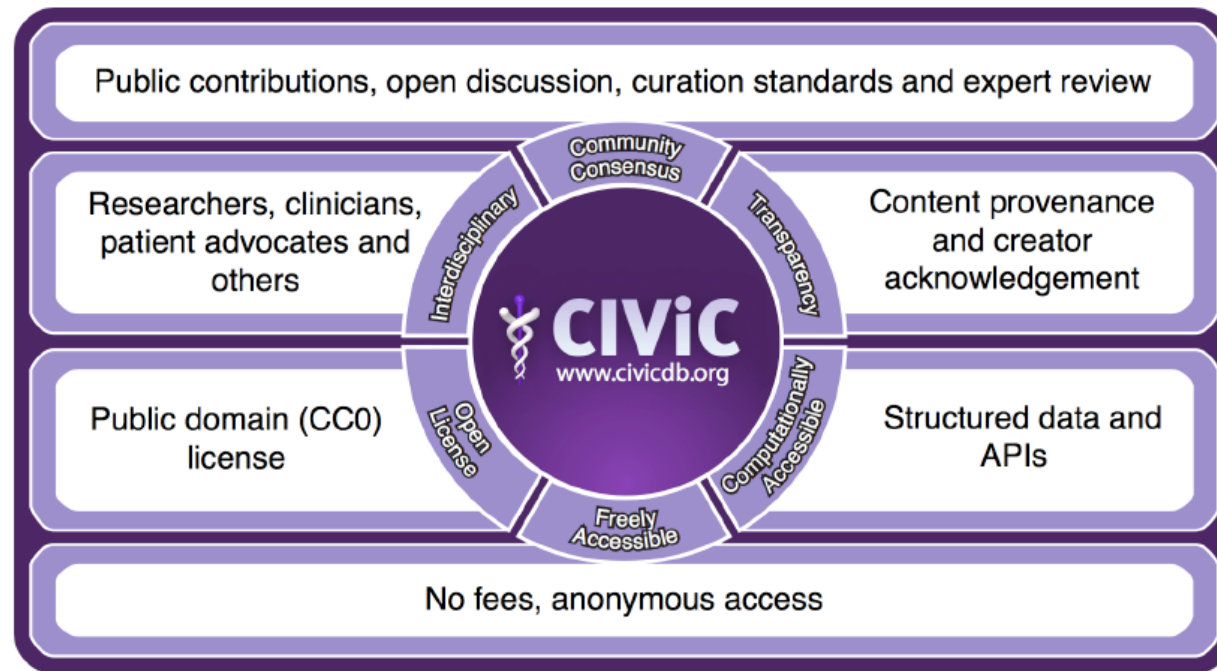


ITCR Connectivity Map on itcr.cancer.gov, hosted by NDEx

Clinical Interpretations of Variants in Cancer (CIViC)

Obi Griffith, Wash U

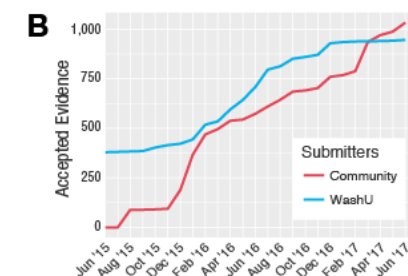
- Curated, web-based knowledgebase of the clinical significance of cancer genome alterations
- Many contributors including major data donations by Illumina and ASCO
- Adopted by the ClinGen Somatic Working Group as their curation platform
- Integrated into several tools including the UCSC Genome Browser, cBioPortal, and commercial applications



- Used by several molecular tumor boards to develop interpretations of variants for cancer patients
- Engaged in collaborations with ITCR and IMAT investigators

A Contribution Totals (2017-07-19)

| Category | Current |
|------------------|---------|
| Variants | 1,524 |
| Genes | 323 |
| Cancer types | 201 |
| Drugs | 372 |
| Evidence Records | 4,289 |
| Publications | 1,620 |
| Contributors | 84 |



Tools to Analyze Morphology and Spatially Mapped Molecular Data

Joel Saltz, Stony Brook

- Quantitative imaging pathology tools are being used to support several research collaborations
 - Led a TCGA Pan Cancer Atlas Immune group whole slide tissue image analysis effort
 - SEER pilot study on integrating whole slide tissue image data into cancer registries
- Collaborating with several ITCR groups
 - Pathology analysis extension added to 3D Slicer
 - MICCAI Digital Pathology challenges
 - Integrative analysis of pathology, radiology and – omics data in collaboration with several groups
- IMAT collaborative supplement
 - Spatially map tumor-associated collagen

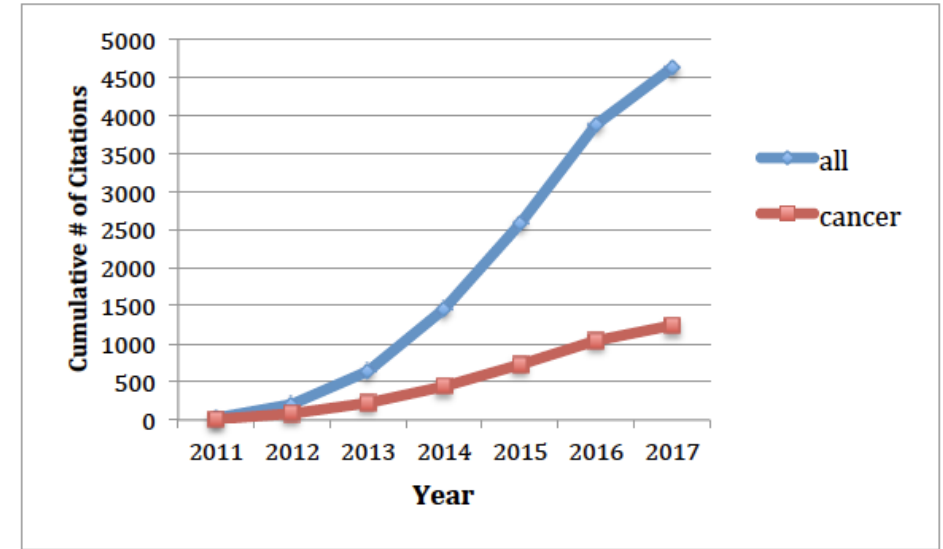


Spatial Organization and Molecular Correlation of Tumor-Infiltrating Lymphocytes Using Deep Learning on Pathology Images (Cell Rep., 2018)

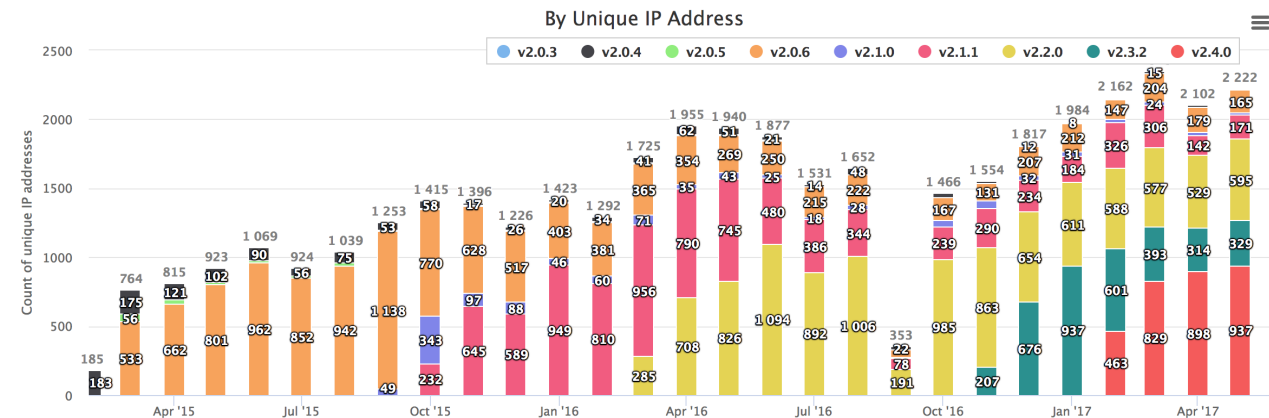
Trinity Cancer Transcriptome Analysis Toolkit (Trinity-CTAT)

Aviv Regev, Broad Institute

- Trinity supports de novo transcriptome assembly; Trinity CTAT applications are more specifically dedicated to cancer research.
- Examples of scientific studies using Trinity CTAT include:
 - *Decoupling genetics, lineages, and microenvironment in IDH-mutant gliomas by single-cell RNA-seq (Science, 2017)*
 - *Dissecting the multicellular ecosystem of metastatic melanoma by single-cell RNA-seq (Science, 2016)*
 - *A distinct gene module for dysfunction uncoupled from activation in tumor-infiltrating T cells (Cell, 2016)*
- Trinity CTAT is available through Galaxy hosted at the Indiana University national-scale cyber-resource
- Several informatics collaboration efforts within and beyond ITCR, including CRAVAT/MuPIT (Karchin), IGV (Mesirov), and CIViC (Griffith)



Cumulative literature citations for the Trinity 2011 Nature Biotechnology paper



Weekly usage of Trinity according to version

Expert Panel Review of ITCR: Summary of Conclusions

1. Informatics technology development remains a pressing need in cancer research
2. Enhancements are needed to further the program's impact and influence
3. Additional outreach is needed for ITCR-developed tools to be fully integrated into the cancer research community
4. New funding mechanisms are needed to foster collaboration between ITCR tool developers and cancer researchers
5. Successful tools will require sustainment to remain world-class

Proposed ITCR Program Structure

Training & Outreach

U24 Training and Outreach Coordination Center

Technology Development

R21: Algorithm Development

U01: Early-stage development

U24: Advanced development

U24: Sustainment

Adoption & Implementation

Competitive Revisions

Responsive to
Additional outreach is needed for ITCR-developed tools to be fully integrated into the cancer research community

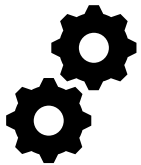
Responsive to
New funding mechanisms may be needed to foster collaboration between ITCR tool developers and cancer researchers

ITCR Training and Outreach Coordination Center

Mission: To conduct activities that engage the research and informatics community to use and extend the ITCR technologies



Provide **in depth courses and workshops** on topics in cancer informatics using the ITCR tools as exemplars



Organize **informatics challenges and hackathons** to evaluate or adapt ITCR technologies for specific research needs



Coordinate **program presence at conferences** and **online outreach** opportunities

Revisions to Support the Application of Informatics Technology to Cancer Research

- Address challenges in applying informatics technology developed through the ITCR program in support of NCI-sponsored research
- Example activities:
 - Adaptation of one or more existing tools to meet the unique needs of the research
 - Generation of data necessary to support the appropriate application of the informatics technology
 - Integration of informatics tools to support the research goals
 - System installation and configuration at a adopting institution

Justification for RFA Issuance

RFAs will support a set aside budget that is anticipated to:

- Promote continuity of the program and signify the ongoing commitment of the NCI
- Incentivize applications in cancer research domains not currently supported by the program
- Incentivize applications for the proposed Training and Outreach Coordination Center and Competitive Revisions

Additionally, RFAs will support:

- Continued peer review through NCI DEA and creation of appropriate Special Emphasis Panels
- Regular engagement and review by BSA

Evaluation Criteria

- The degree to which successfully developed tools and resources have been utilized by the research community and clinicians, as measured through citations in publications and tool usage metrics.
- The effectiveness of approaches to community engagement and dissemination, including number of training sessions and level of participation.
- The level of collaboration among teams funded through ITCR and/or participating in ITCR programmatic activities.
- The impact of ITCR products on promoting scientific discovery and enabling translational science and cancer management capabilities.

Proposed Budget for New Awards

| | Direct costs per project per year | Est. awards per year | Total costs per year |
|--|-----------------------------------|----------------------|----------------------|
| R21 Methods Development | \$137,500 | 6 | \$1.24M |
| U01 Early Stage Development | \$300,000 | 5 | \$2.25M |
| U24 Advanced Development | \$600,000 | 4 | \$3.60M |
| U24 Sustainment | \$750,000 | 2 | \$2.25M |
| TOTAL for Informatics Development | | | \$9.34M |
| Competitive Revisions | \$100,000 | 4 | \$0.60M |
| T&O Coordination Center | \$700,000 | 1 (only) | \$1.05M |
| 1st Issuance Total | | | \$11M |
| Reissuance Total | | | \$9.94M |

ITCR Program Team

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www.cancer.gov

www.cancer.gov/espanol

Extra Slides

ITCR Applications received and funded per round

↓ First renewal

| | 13-08 | 14-01 | 14-05 | 15-01 | 15-05 | 16-01 | 16-05 | 17-01 | 17-05 | 18-01 | 18-05 | 19-01 | TOTAL |
|-----------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Revision Rec'd | 3 | 4 | 2 | 2 | 1 | 1 | - | - | - | - | - | - | 13 |
| Revision Funded | 0 | 1 | 1 | 0 | 0 | 0 | - | - | - | - | - | - | 2 |
| U01 Rec'd | 25 | 8 | 23 | 13 | 12 | 19 | 12 | 27 | 17 | 21 | 27 | 22 | 226 |
| U01 Funded | 3 | 2 | 3 | 2 | 1 | 2 | 1 | 2 | 1 | 3 | 3 | - | 23 |
| U24 AD Rec'd | 16 | 11 | 8 | 8 | 8 | 20 | 15 | 15 | 5 | 20 | 8 | 13 | 147 |
| U24 AD Funded | 4 | 2 | 3 | 3 | 4 | 4 | 2 | 3 | 1 | 3 | 1 | - | 30 |
| U24 Sust Rec'd | - | - | - | - | - | - | 2 | 5 | 4 | 3 | 2 | 3 | 19 |
| U24 Sust Funded | - | - | - | - | - | - | 1 | 1 | 1 | 1 | 0 | - | 4 |
| R21 Rec'd | - | - | - | - | - | - | 32 | 26 | 38 | 29 | 39 | 36 | 200 |
| R21 Funded | - | - | - | - | - | - | 3 | 1 | 2 | 3 | 4 | - | 13 |
| | | | | | | | | | | | | | |
| Total Received | 44 | 23 | 33 | 23 | 21 | 40 | 61 | 73 | 64 | 73 | 76 | 74 | 605 |
| Total Funded | 7 | 5 | 7 | 5 | 5 | 6 | 7 | 7 | 5 | 10 | 8 | | 72 |

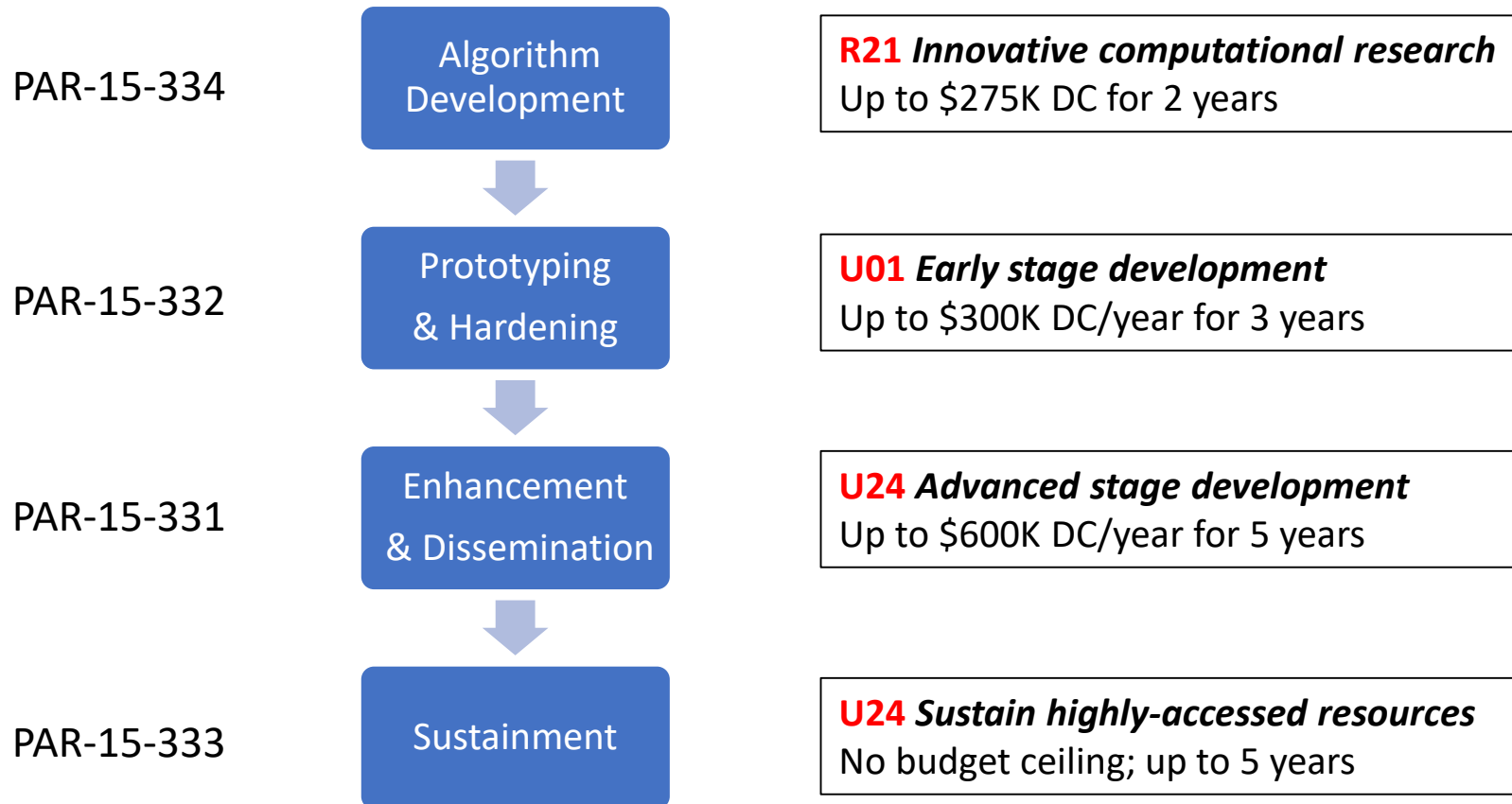
Revisions mechanisms were not issued in the first renewal of the program. The U24 Sustainment and R21 mechanisms were introduced in the first program renewal. 2018-5 round include grants anticipating funding.

Funded applications by mechanism and domain

| FOA -type | Applications Funded |
|------------------|---------------------|
| Revision | 2 |
| U01 Early Dev | 23 |
| U24 Advanced Dev | 30 |
| U24 Sustainment | 4 |
| R21 | 13 |
| TOTAL | 72 |

| Domain | Applications Funded |
|-------------------|---------------------|
| -omics | 31 |
| medical imaging | 11 |
| clinical data | 7 |
| pathology imaging | 6 |
| network biology | 5 |
| data standards | 2 |
| protein structure | 1 |
| radiation therapy | 1 |
| infrastructure | 1 |
| animal models | 1 |

Current ITCR FOAs



- Two receipt dates per year
- Reviewed by NCI DEA Special Emphasis Panel
- 10% of U01 and U24 award budget is set-aside for collaborative activities proposed post-award