Pre-application webinar for RFA-CA-15-014: U54 CSBC Research Centers

CANCER SYSTEMS BIOLOGY CONSORTIUM

Agenda:

1. *Begin presentation at 3:05 ET*
2. *RFA Presentation (Shannon Hughes)*
3. *Q&A*

Link to WebEx can be found on NOT-CA-16-055
Audio for webinar: 1-855-244-8681
Meeting access number: 734 805 901
Note: meeting audio is being recorded

Shannon Hughes
shannon.hughes@nih.gov

NIH NATIONAL CANCER INSTITUTE

August 4, 2016

Goal of the CSBC

The CSBC is a community of systems biologists who aim to integrate experimental biology and computational models across multiple temporal and spatial scales towards a better understanding of cancer.

From the FOA:
CSBC Research Centers will consist of **interdisciplinary teams** of scientists (e.g., engineers, chemists, computer scientists, mathematicians, physicists) and cancer researchers (e.g., cancer biologists, oncologists, pathologists) who collaborate to advance our understanding of cancer biology and oncology**.** CSBC Research Centers proposed in response to this FOA must demonstrate explicit integration of experimental biology and computational modeling to test and validate novel hypotheses or ideas of high importance in cancer research. In addition to the major research components, the Research Center will be required to develop an outreach effort in cancer systems biology aligned with the goals of the Research Center and the CSBC.

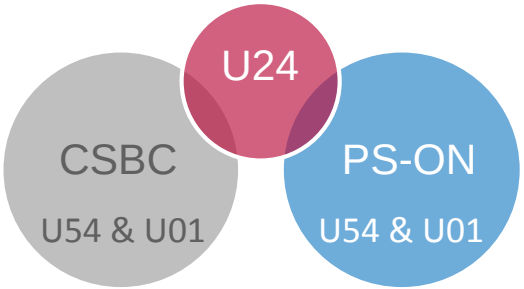
Systems Biology at NCI

- 10 years of the Integrative Cancer Biology Program (ICBP)
- 2014 – 2015 program evaluation
- New Initiative - Cancer Systems Biology Consortium (CSBC)
- Approved March 2015
- 2 New RFAs (U54 & U24) and 1 continuing PAR (U01)
- Sept 9, 2016 is the second receipt date of RFA-CA-15-014 (of three)

About the CSBC

CANCER SYSTEMS BIOLOGY CONSORTIUM

- U54 CSBC Research Centers (8-10) RFA-CA-15-014
- U24 CSBC/PS-ON Coordinating Center (1) RFA-CA-15-015
- U01 Research Projects
  - 10+ U01 Collaborative Research in Integrative Cancer Biology (PAR-13-184)
  - 5+ U01 Bridging the Gap Between Cancer Mechanism and Population Science (PAR-13-081)
  - U01 CSBC Research Projects (PAR-16-131)
- U54s and U01s from Physical Sciences in Oncology Network



Mechanism of Support & Funding: CSBC U54 Research Center

Mechanism of support: U54, Specialized Center-Cooperative Agreements

*The spectrum of activities comprises a **multidisciplinary attack** on a specific disease entity or biomedical problem area. These differ from a program project in that they are usually developed in response to an announcement of the programmatic needs of an Institute or Division and subsequently **receive continuous attention from its staff**. Centers may also serve as **regional or national resources** for special research purposes, with funding component staff helping to identify appropriate priority needs.*

Application Type: New applications and resubmissions are accepted

Budget: Not to exceed **$1.5M per year (direct costs)** per Center. *Cap is exclusive of 3rd part F&A costs.*

Project Period: Not to exceed **5 years**.

CSBC U54 Leadership Expertise

CANCER SYSTEMS BIOLOGY CONSORTIUM

From RFA-CA-15-014:

…this FOA encourages the use of the multi-PD/PI mechanism (but it is not required).

***The CSBC Research Center contact PD/PI … must be a scientist with formal training and/or expertise in cancer systems biology**, with contributions demonstrating substantial impact on the field.*

[If the contact PD/PI does not satisfy the above statement:] ***The leadership team must also include a PD/PI or other senior investigator with …. expertise and substantial contributions in the field of cancer research.***

Effort commitment requirement: **2.4 person-months per year for single PD/PI**
1.2 person-months per year for multiple PD/PI (2+)

Scientific Area of Interest

CANCER SYSTEMS BIOLOGY CONSORTIUM

Scientific questions should be of high importance and not readily addressable through other research mechanisms or initiatives due to their non-intuitive nature. Examples of such cancer-related issues that would require a systems biology effort might include, *but are not limited to*:

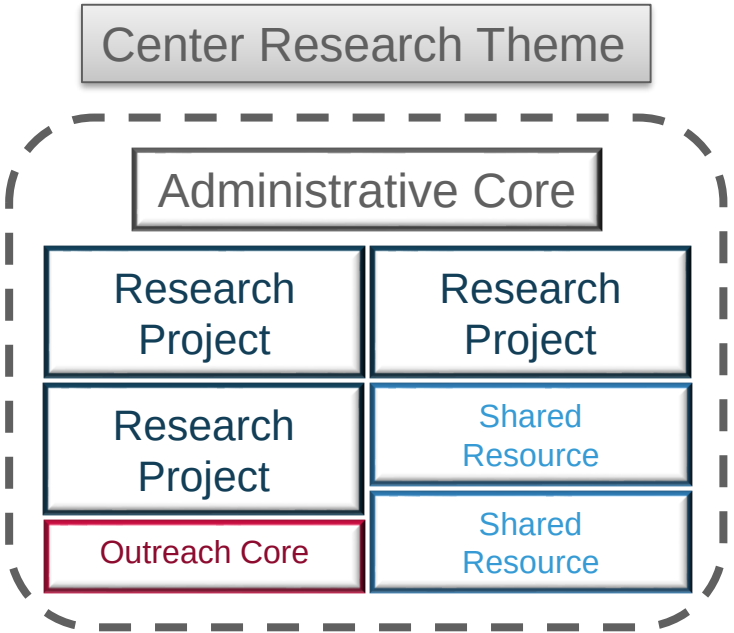
- Dynamic, predictive models that provide a robust and actionable understanding of the effect of multiple biological interactions and/or **incorporate multi-scale, spatial analysis over varying resolution scales** to describe cancer initiation, progression and metastasis.
- Models of networks and signal transduction pathways capable of **predicting phenotypes** in cancer, including but not limited to biochemical, statistical, graphical, logic, and relational modeling techniques. Phenotypes might be predicted at the molecular, cellular, tissue or organ level.
- Predicting and validating **critical genetic and epigenetic changes** in the initiation and progression of cancer.
- Modeling the **molecular and cellular communication** within and across cells of the tumor eco-system, including but not limited to the tumor micro-environment and the immune system.
- **Integration of data obtained through new imaging modalities**, such as super-resolution microscopy and cryo-electron microscopy (cryo-EM), into systems biology modeling frameworks to predict tumor phenotypes on multiple spatial scales.

Scientific Area of Interest (cont.)

Scientific questions should be of high importance and not readily addressable through other research mechanisms or initiatives due to their non-intuitive nature. Examples of such cancer-related issues that would require a systems biology effort might include, *but are not limited to*:

- Prediction and validation of **early disease indicators** through systematic modeling of genetic factors and other high-risk disease phenotypes.
- Development of modeling techniques that **span the scale between basic cellular mechanism and patient/population**-level response or phenotype.
- *In silico* modeling to **predict effective treatment**. This includes predicting tumors most likely to benefit from a given treatment; converting transient responses into durable responses; and identifying rational combinations to address the emergence of resistance in ***future*** clinical trials.
- **Systems analysis of cancer completed in endogenous settings** (*in vivo* or *ex vivo*), with consideration of the tumor microenvironment, tumor heterogeneity, and tumor plasticity.

Organization of Individual CSBC U54 Research Centers



Application & Submission Information

Component Types Available in ASSIST	Research Strategy / Program Plan Page Limits	Required number of Components
Overall	12	1
Admin Core (use for Administrative Core)	6	1
Project (use for Research Projects)	12 *per Research Project*	2-3
Core (use for Shared Resource Core and Outreach Core)	6 *per Core*	0-2 (Shared Resource*) 1 (Outreach)

*Proposed Shared Resource Cores must support two or more Research Projects

Overall Component –
Research Strategy (12 page limit, FOA Part 2 – Section IV)

- **Research Theme**: Define the overall research theme of the Research Center. Include brief background and rationale.
- **Research Center Organization**: Provide a concise description of Center structure and address how the whole is more than a sum of its parts. Include a description of Center expertise.
- **Research Projects**: Address the rationale for each project and its contribution to advancing the overall Research Theme.
- **Intra-Center Projects:** Briefly state how the intra-Center pilot projects will be incorporated into the efforts advancing the Research Theme.
- **Shared Resource Core(s)**, if applicable: Explain the need for the shared resource and state what Research Projects it will support.
- **Outreach Core**: Briefly state plans for outreach programs.
- **Research Center Scientific Integration**: Applications should demonstrate that the use of the U54 Center mechanism is essential to accomplishing the goals that would not occur without the climate, facilities, and research resources that a Research Center can uniquely provide.

Administrative Core – Research Strategy (FOA Part 2 – Section IV)

Describe the Admin Core structure using three sub-sections (6 page Research Plan limit):

- **Center logistics and communication**: Describe the strategies for communication across the Research Center leadership, between project teams of multidisciplinary investigators, and between the Research Center and the NCI. State who will be the lead for each level.
- **Intra-Center pilot projects**: State how one-year intra-Center pilot projects will be solicited, selected, and evaluated. Note: Admin Core budget includes $50K for intra-Center pilot projects.
- **External Advisory Committee**: Each Research Center will recruit external experts (outside the center) to serve as scientific advisors. Describe the general composition, range of expertise, and utilization. **DO NOT** state specific names in application or contact individuals.

Research Projects – Research Strategy (FOA Part 2 – Section IV)

Each application should consist of 2-3 Research Projects (12 page Research Plan limit *per* Research Project)

The Research Projects constitute the most important activities of the Research Center and should focus on *innovative approaches that integrate systems biology and cancer research* perspectives….

Additional aspects to address within the Research Plan:

- How does the Project contribute to the Research Center's overall research theme?
- State the multidisciplinary aspects of the Research Project and how it benefits from the unique scientific expertise of Research Center personnel.
- How will the project team take advantage of the Research Center infrastructure to allow for alternative approaches or perspectives?
- Highlight any innovative systems biology approaches utilized within the project.
- If the Research Project will utilize the Shared Resource Core(s), describe how the Core(s) capabilities impact the proposed project.

Shared Resource Cores – Research Strategy (FOA Part 2 – Section IV)

Each application should consist of 0-2 Shared Resource Cores (6 page Research Plan limit *per* Shared Resource Core)

- The Shared Resource Cores may be **physical or virtual infrastructures** (e.g. cloud-based computing or storage) providing a biological, computational or engineering resource.
- Each Shared Resource Core is **expected to support two or more Research Projects**.
- Issues to be addressed include, but are not limited to: value of the Core services to the Research Center and Research Projects, integration between the Core and Research Projects, quality control, procedures for selecting Research Projects to use the Core and allocating resources, cost effectiveness, and increased efficiency.

These proposed new shared resources **must not duplicate analogous resources** already established in the applicant institutions (although supplemental funding to such existing resources may be requested).

Outreach Core – Research Strategy (FOA Part 2 – Section IV)

Each application should consist of one Outreach Core (6 page Research Plan limit)

- A minimum of **$100K *direct costs* per year** must be allocated to the Outreach Core
- The Outreach Core will serve to promote cancer systems biology **at all career stages** and to disseminate advances and capabilities of cancer systems biology to the cancer research and broader communities.

Potential activities include, but are not limited to:

Seminar Series: Hosting of speakers that compliment the capabilities and advances of the CSBC.

Workshops: Small focused meetings that bring together critical researchers in areas of cancer systems biology.

Personnel Exchanges: Exchange of graduate students, postdoctoral fellows, or investigators within a Research Center or across the Consortium

Cross-training: early stage and established investigators in the various areas of systems biology to cross train within the CSBC or at NCI-funded programs

Center Website

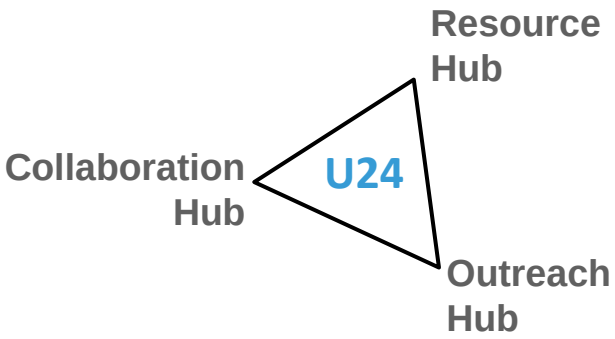
Research Center Annual Meeting

Think Tanks: Small meetings of investigators at all stages of career development to identify gaps in knowledge

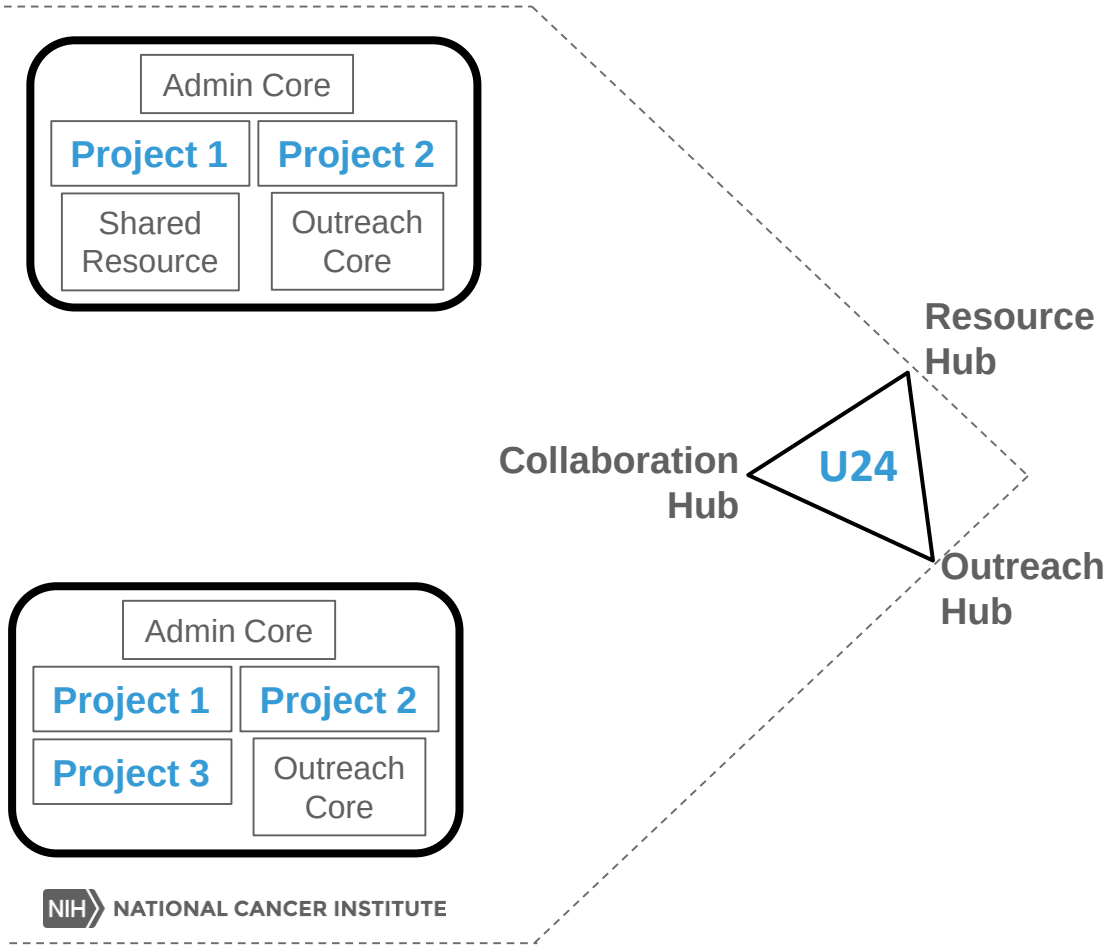
Research Center Newsletter

Consortium Structure

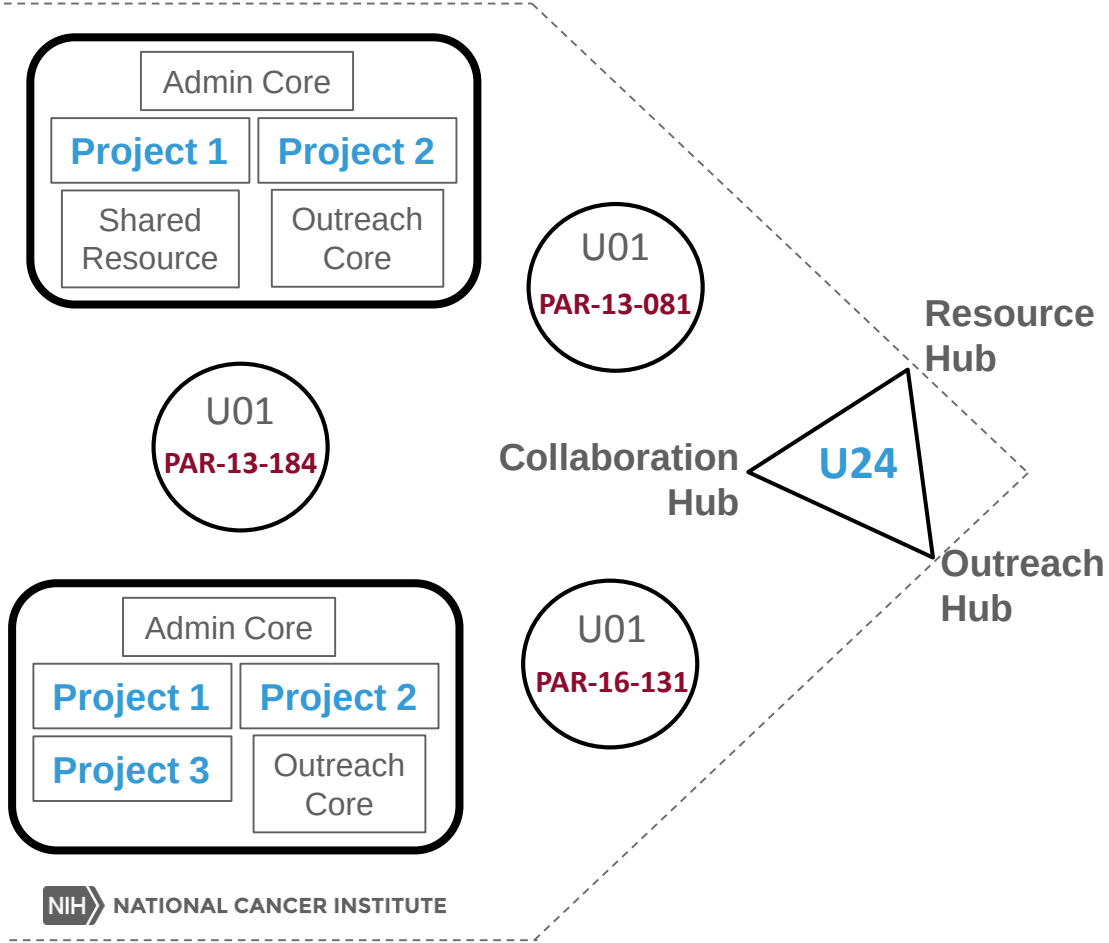
CSBC/PS-ON U24 Coordinating Center



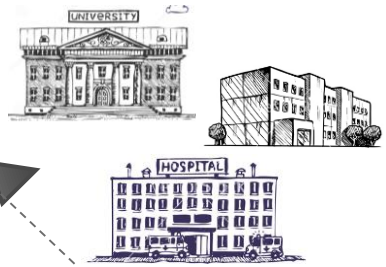
CSBC


Admin Core
Project 1
Project 2
Shared Resource
Outreach Core
Resource Hub
Collaboration Hub
U24
Outreach Hub
Admin Core
Project 1
Project 2
Project 3
Outreach Core

CSBC


Admin Core
Project 1
Project 2
Shared Resource
Outreach Core
U01
PAR-13-081
U01
PAR-13-184
Collaboration Hub
U24
Resource Hub
Outreach Hub
Admin Core
Project 1
Project 2
Project 3
Outreach Core
U01
PAR-16-131

CSBC



Admin Core

Project 1 **Project 2**

Shared Resource

Outreach Core

U01
PAR-13-081

U01
PAR-13-184

Resource Hub

Collaboration Hub

U24

Outreach Hub

Admin Core

Project 1 **Project 2**

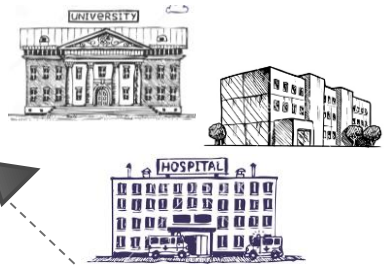
Project 3

Outreach Core

U01
PAR-16-131

Arrow indicates CSBC U54 Pilot Project

CSBC



Admin Core

Project 1 | Project 2

Shared Resource | Outreach Core

U01 PAR-13-081

U01 PAR-13-184

Resource Hub

Collaboration Hub

U24

Outreach Hub

U01 PAR-16-131

Admin Core

Project 1 | Project 2

Project 3 | Outreach Core

CSBC U54 Pilot Project

CSBC U24 Pilot Project

CSBC

PS-ON

Admin Core

Project 1 | Project 2

Shared Resource | Outreach Core

U01 PAR-13-081

U01 PAR-13-184

Collaboration Hub

U24

Resource Hub

U54 PS-OC (PAR-14-169)

U01 PAR-15-021

U01 PAR-15-021

Outreach Hub

U01 PAR-16-131

Admin Core

Project 1 | Project 2

Project 3 | Outreach Core

U54 PS-OC (PAR-14-169)

CSBC U54 Pilot Project

CSBC U24 Pilot Project

CSBC

PS-ON

Admin Core

Project 1

Project 2

Shared Resource

Outreach Core

U01 PAR-13-081

U01 PAR-13-184

Collaboration Hub

U24

Resource Hub

U01 PAR-15-021

U01 PAR-15-021

Outreach Hub

U01 PAR-16-131

Admin Core

Project 1

Project 2

Project 3

Outreach Core

U54 PS-OC (PAR-14-169)

U54 PS-OC (PAR-14-169)

CSBC U54 Pilot Project

CSBC U24 Pilot Project

Information about CSBC/PS-ON U24 Coordinating Center

Several aspects of the CSBC will be coordinated through the U24 Center, which has three main “hubs”:

- The Resource Coordinating Hub: A curated source of CSBC and PS-ON research output.
  - CSBC U54 Research Centers will be expected to share data and models through the Resource Coordinating Hub. Hub structure will be determined by U24 Awardee and NCI Program Officials.
- The Collaboration and Pilot Project Hub: Funds for CSBC-led research projects.
  - *Starting Year 2 of the U24 Award*, restricted funds are allocated to support CSBC-led research projects (“CSBC Pilot Project Fund”). Final approval of projects by CSBC Steering Committee & NCI. Budget details: $100K DC (Yr 2) and $300K DC (Yr 3-5).
- The Outreach Hub: Centralized resource for Outreach activities across the CSBC and PS-ON.
  - The Outreach Hub will coordinate activities that may span CSBC members (for example, summer research programs) and serve as a central information source.

Key Dates

	Pre-Application Webinar	Letters of Intent Due Dates	Application Due Dates	Review Dates	Earliest Anticipated Start Dates
Round 1	~~September 28, 2015~~	~~Oct 20, 2015~~	~~Nov 20, 2015~~	~~Feb-Mar, 2016~~	~~July 2016~~
Round 2	July 2016	Aug 9, 2016	Sept 9, 2016	Oct-Nov, 2016	April 2017
Round 3	TBD, estimated Jan 2017	Mar 20, 2017	April 20, 2017	June-July, 2017	Nov 2017 (?)

Letter of Intent (LOI)

CANCER SYSTEMS BIOLOGY CONSORTIUM

Due date: **August 9, 2016**; March 20, 2017

Highly encouraged, but not required

Standard elements:

- Descriptive title of CSBC Research Center
- Name(s), address(es), telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating Institution(s)
- Number and title of funding opportunity

Additional recommended information:

- **Provide a brief (3-5 sentence) description of the overall research theme**
- **Include relevant expertise and Keywords**

Application & Submission Information

CANCER SYSTEMS BIOLOGY CONSORTIUM

Electronic submission is required for RFA-CA-15-014

NIH's **Application Submission System & Interface for Submission Tracking (ASSIST)** is available for the electronic preparation and submission of multi-project applications through Grants.gov to NIH. Applications to this FOA must be submitted electronically; paper applications will not be accepted. ***ASSIST replaces the Grants.gov downloadable forms*** currently used with most NIH opportunities and provides many features to enable electronic multi-project application submission and improve data quality, including: pre-population of organization and PD/PI data, pre-submission validation of many agency business rules and the generation of data summaries in the application image used for review.

ASSIST Website: https://public.era.nih.gov/assist/public/login.do
ASSIST Webinar: http://grants.nih.gov/grants/webinar_docs/webinar_20130813.htm
Problems accessing or using ASSIST?
Contact the eRA Commons Help Desk: http://grants.nih.gov/support/index.html

Application & Submission Information

CANCER SYSTEMS BIOLOGY CONSORTIUM

Electronic submission is required for RFA-CA-15-014

You are strongly encouraged to upload and test your application in ASSIST at least five days prior to the application deadline. This will allow time to correct any formatting or technical errors. Once the deadline passes (5:00 PM local time on November 20th) you will *no longer be able to access your application to correct errors*.

ASSIST Website: https://public.era.nih.gov/assist/public/login.do

- Familiarize yourself with ASSIST early.
- Pay attention to the order of the application components to save time and reduce errors.

Problems accessing or using ASSIST?

Contact the eRA Commons Help Desk: http://grants.nih.gov/support/index.html

Updated NIH Application Forms

See NOT-OD-16-004 for details on new application forms (FORMS-D) that are required for applications with due dates of May 25, 2016 and beyond.

Link to FORMS-D annotated form set:

http://grants.nih.gov/grants/ElectronicReceipt/files/Annotated_Forms_General_FORMS-D.pdf

A list of significant changes can be found at:

http://grants.nih.gov/grants/how-to-apply-application-guide/forms-d/general/g.120-significant-changes.htm

PHS 398 Research Plan: *New Rigor & Reproducibility Standards*

All applications submitted after January 25, 2016 must address **Scientific Rigor and Reproducibility.** http://grants.nih.gov/reproducibility/index.htm#guidance

The "Resources" section includes examples and two videos about what to include in your application and how the new criteria will be reviewed.

Scientific Premise, Scientific Rigor and Inclusion of Relevant Biological Variables must be addressed **within the 12 page** Research Plan.

Use the new attachment for Authentication of Key Biological and/or Chemical Resources to address plans for authentication.

NEW GRANT GUIDELINES

what you need to know

WHY UPDATE THE GUIDELINES?

The updates focus on four areas deemed important for enhancing rigor and transparency:

1. **PREMISE** — The scientific premise forming the basis of the proposed research
2. **DESIGN** — Rigorous experimental design for robust and unbiased results
3. **VARIABLES** — Consideration of relevant biological variables
4. **AUTHENTICATION** — Authentication of key biological and/or chemical resources

Send inquiries to reproducibility@nih.gov

See also NIH Notice NOT-OD-16-011
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-011.html

WHAT ARE THE UPDATES?

1 UPDATES TO RESEARCH STRATEGY GUIDANCE

The research strategy is where you discuss the significance, innovation, and approach of your research plan. Let's look at an R01, for example:

The new **research strategy** guidelines require that you:

- State the strengths and weakness of published research or preliminary data crucial to the support of your application
- Describe how your experimental design and methods will achieve robust and unbiased results
- Explain how biological variables, such as sex, are factored into research design and provide justification if only one sex is used

2 NEW ATTACHMENT FOR AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES

From now on, you must briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies.

These include, but are not limited to:

CELL LINES · ANTIBODIES · SPECIALTY CHEMICALS · OTHER BIOLOGICS

Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common biologicals or chemicals.

- **DO NOT** put experimental methods or preliminary data in this section
- **DO** focus on authentication and validation of key resources

3 NEW REVIEWER GUIDELINES

Here are the additional criteria the reviewers will be asked to use:

- Is there a **strong scientific premise** for the project?
- Have the investigators presented adequate plans to address **relevant biological variables**, such as sex, for studies in vertebrate animals or human subjects?
- Have the investigators presented strategies to ensure a **robust and unbiased approach**, as appropriate for the work proposed?

Reviewers will also be asked to comment on that new attachment (see **Update 2**)!

NIH Genomic Data Sharing Policy

NIH GDS Policy : NOT-OD-15-027

- Applies to applications submitted after January 25, 2015
- Covers wide range of genomic analyses across various experimental platforms and sample types (human and non-human)
- NCI specific guidelines for the number of samples that qualify as ‘large-scale’ data collection. Minimum threshold is met quickly given different combinations of patient samples, cell lines, time points, and chemical/therapeutic perturbations.
- Documentation to satisfy GDS policy is part of the standard Just-in-Time information so now is the correct time to determine if your work will fall under the policy.
- If applicable, generate a Genomic Data Sharing Plan and apply for Institutional Certification.
- **Include a cover letter stating the GDS Policy applies to your application**

New NIH Biosketch Required

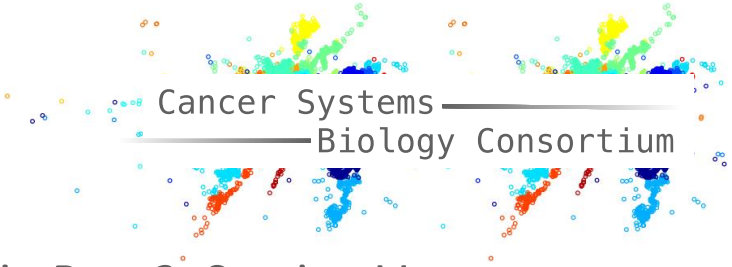
All research applications are required to utilize the new NIH Biosketch format:

See NOT-OD-15-032 for general information and tools -- including instructions and a sample.

**Further updates have been made to the NIH Biosketch instructions and are required for submission after May 25th, 2016. Please see NOT-OD-16-080 for more information.

Frequently asked questions are addressed at:
http://grants.nih.gov/grants/policy/faq_biosketches.htm

Application Review Information



- Consider the **FOA-specific review criteria** defined in Part 2, Section V
- Overall impact scores provided for Overall Component, Administrative Core, Research Projects, Outreach Core & Shared Resource Core(s).
- Individual Criterion Scores for Overall Component and Research Projects include:
  - Significance
  - Investigator(s)
  - Innovation
  - Approach
  - Environment
  - Integration
- Scores for Cores (Administrative, Outreach, Shared Resource) will be based on bulleted lists defined in Part 2, Section V.

Review Information

Applications will compete for available funds with all other recommended applications submitted in response to this FOA. Following initial peer review, recommended applications will receive a second level of review by the National Cancer Advisory Board.

The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

Review Information

(NEW) Applicants are encouraged to include a PHS Assignment Request Form with their application that includes information about:

- Potential conflicts of interest
- Areas of scientific expertise needed for a fair and knowledgeable review of the application
- https://grants.nih.gov/grants/how-to-apply-application-guide/forms-d/general/g.600-phs-assignment-request-form.htm

The review panel roster will be available in eRA Commons 30 days prior to review. Applicants may contact the Scientific Review Officer with concerns prior to review.

Contact Information

CANCER SYSTEMS BIOLOGY CONSORTIUM

Scientific/Research Contact(s):

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Financial/Grants Management Contact:

Sean Hine
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hines@mail.nih.gov

Slides from this webinar will be available on the Division of Cancer Biology website:
dcb.nci.nih.gov/News

Or email Shannon: Shannon.Hughes@nih.gov