CANCER SYSTEMS BIOLOGY CONSORTIUM

Systems Biology and Mathematical Oncology at the National Cancer Institute

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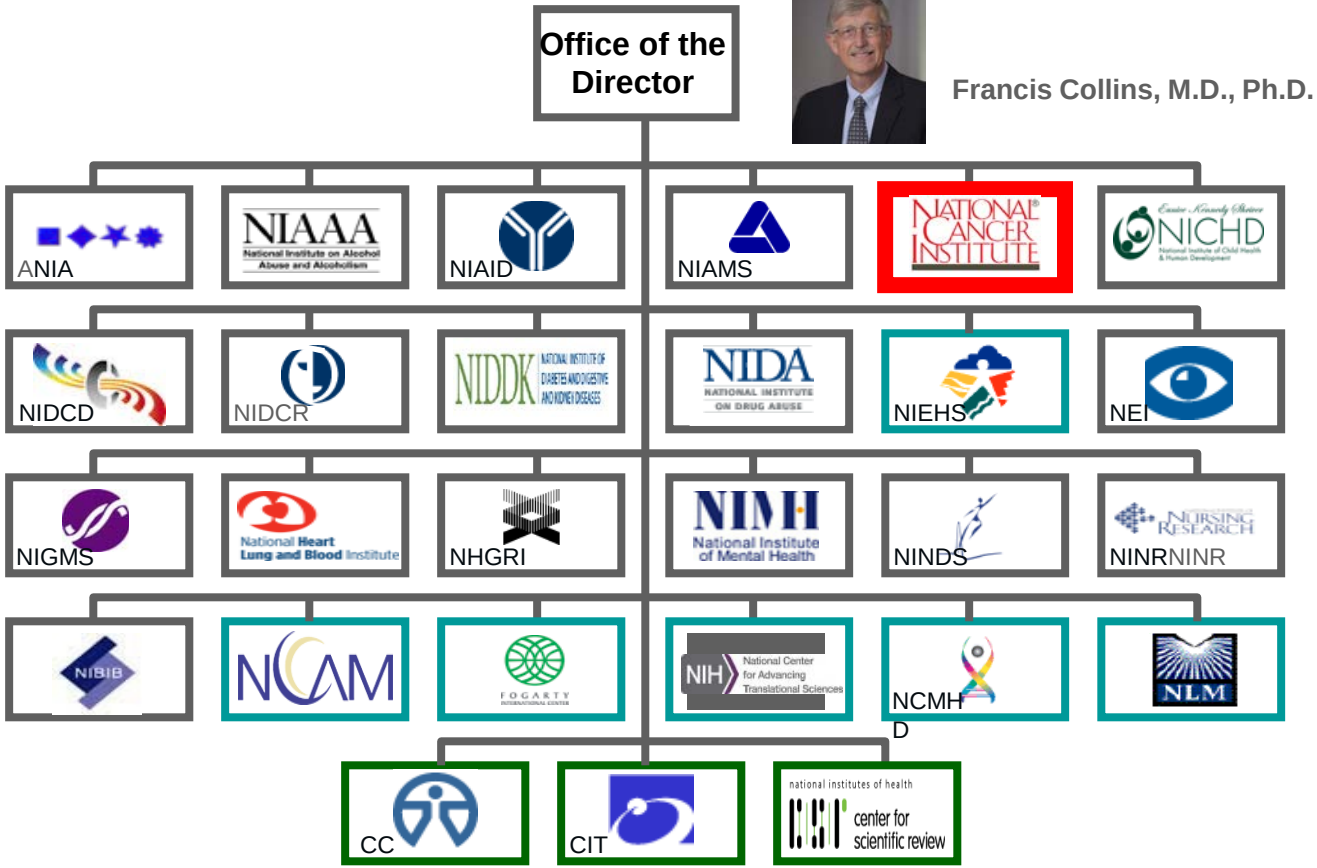
NIH NATIONAL CANCER INSTITUTE

April 28, 2017

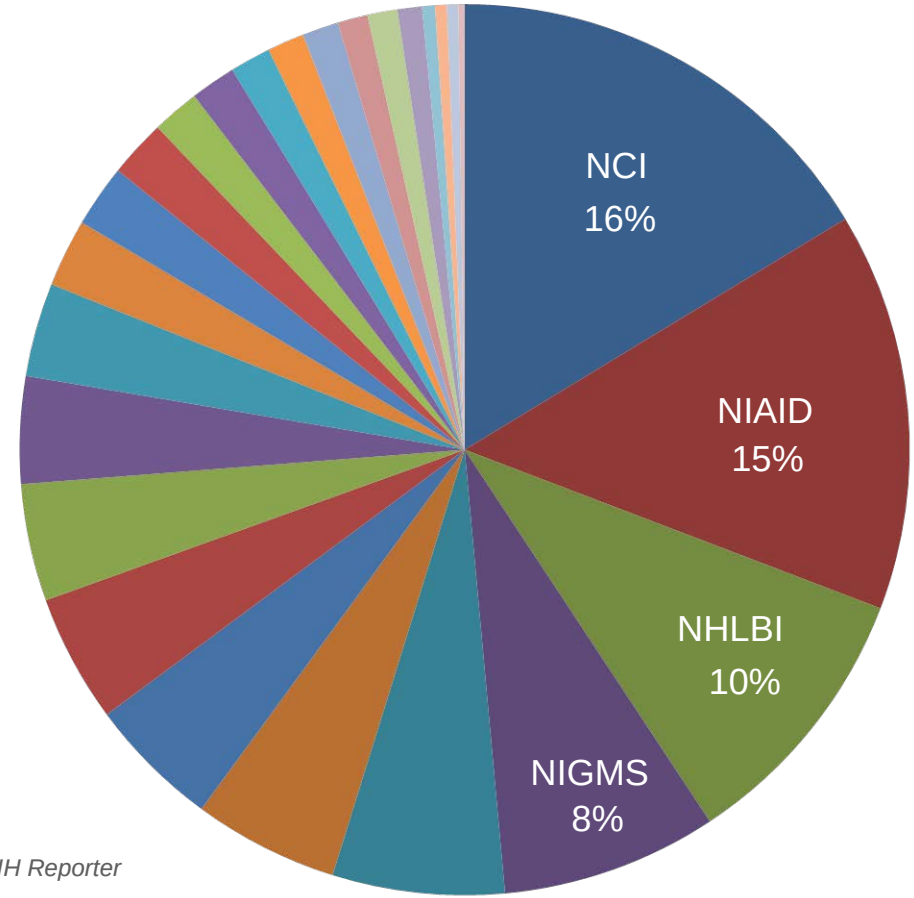
The National Institutes of Health

Francis Collins, M.D., Ph.D.



Source: *http://www.nih.gov*

NIH Budget Allocation by Institute/Center



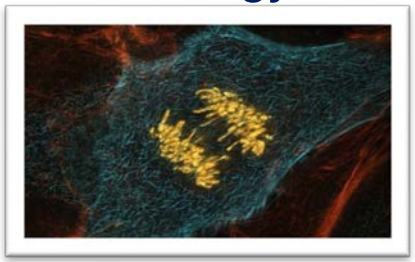
FY2016

$31 Billion

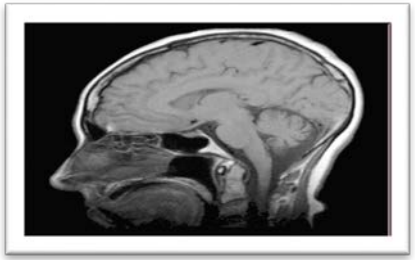
Source- NIH Reporter

The NCI supports a full spectrum of cancer research

Biology

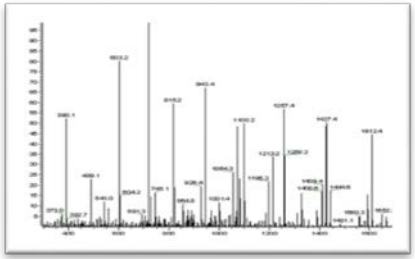


Diagnosis



Outreach

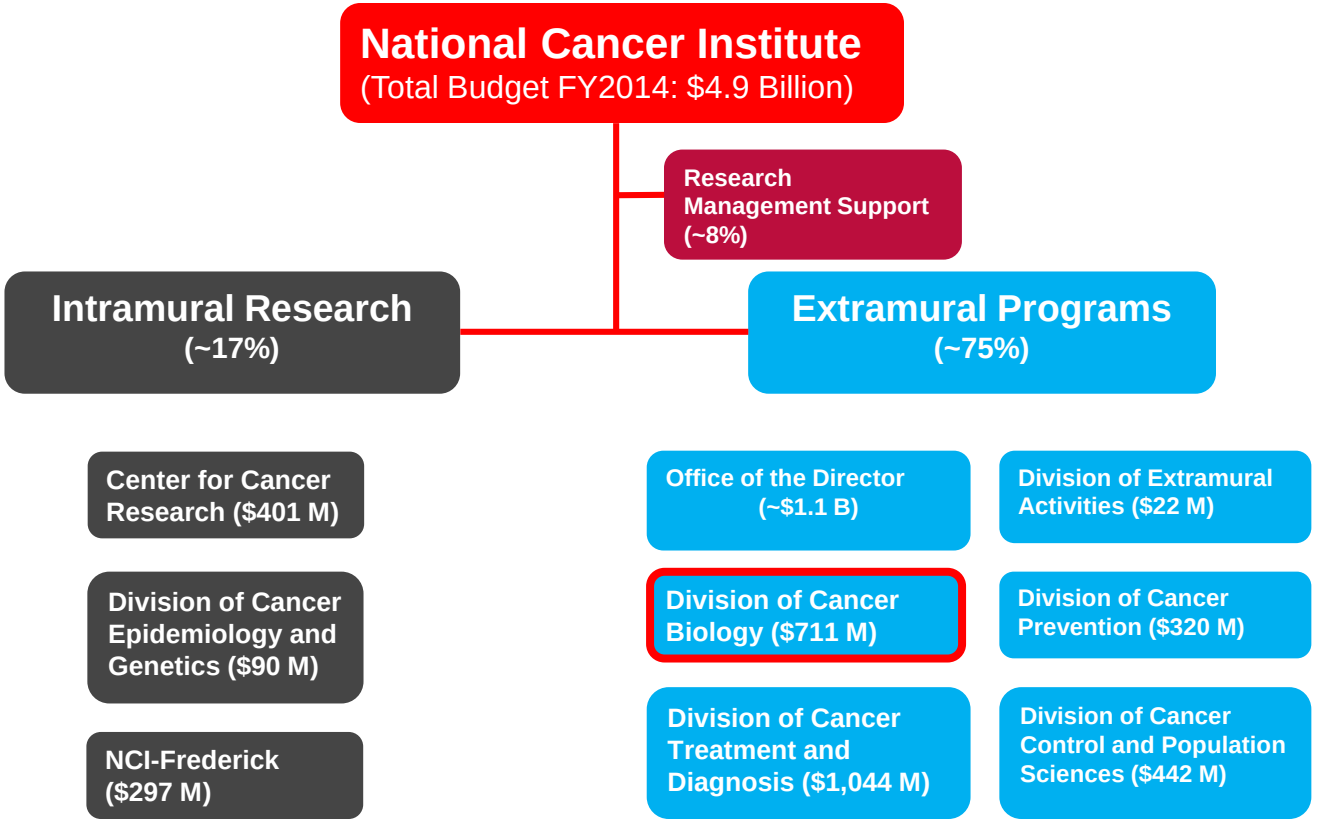
Prevention



Treatment

Population Science

Organization of the National Cancer Institute

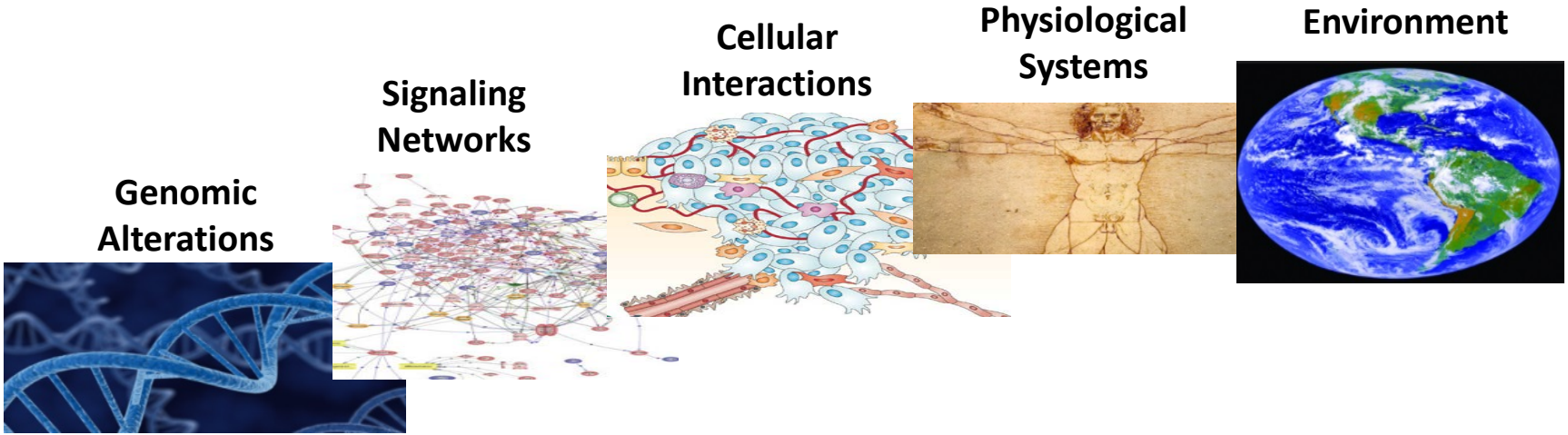


Source: http://fundedresearch.cancer.gov/nciportfolio/

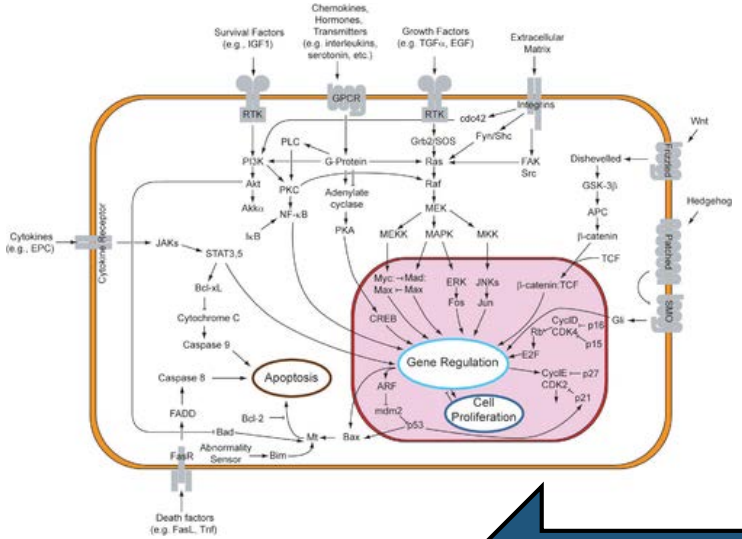
NCI, Division of Cancer Biology

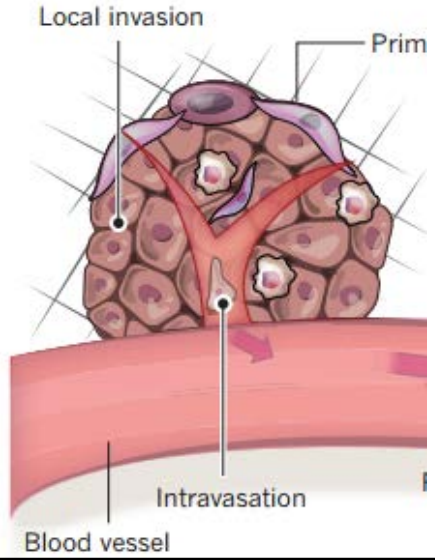
Our Mission:

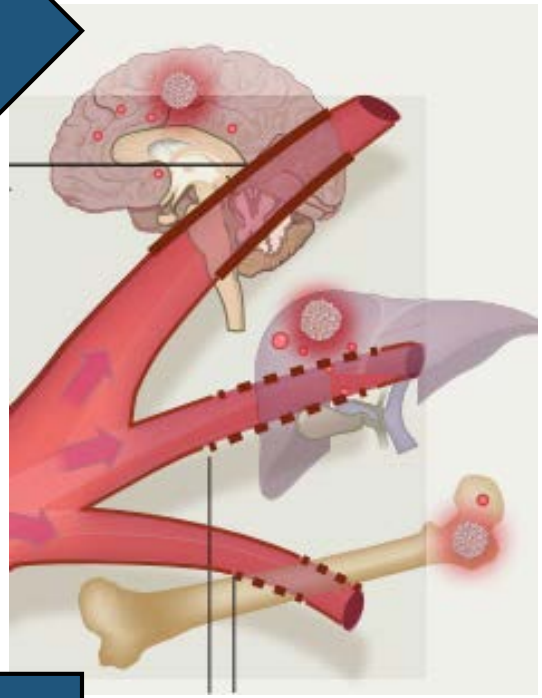
- *To ensure continuity and stability in basic cancer research while encouraging and facilitating the emergence of new ideas, concepts, technologies and possibilities through a broad portfolio of Investigator initiated research and specialized NCI programs.*



Cancer as a disease system







Graphics adapted from Wikipedia; Massague & Obenauf *Nature* 2016

Cancer systems biology and mathematical oncology provide an integrative approach

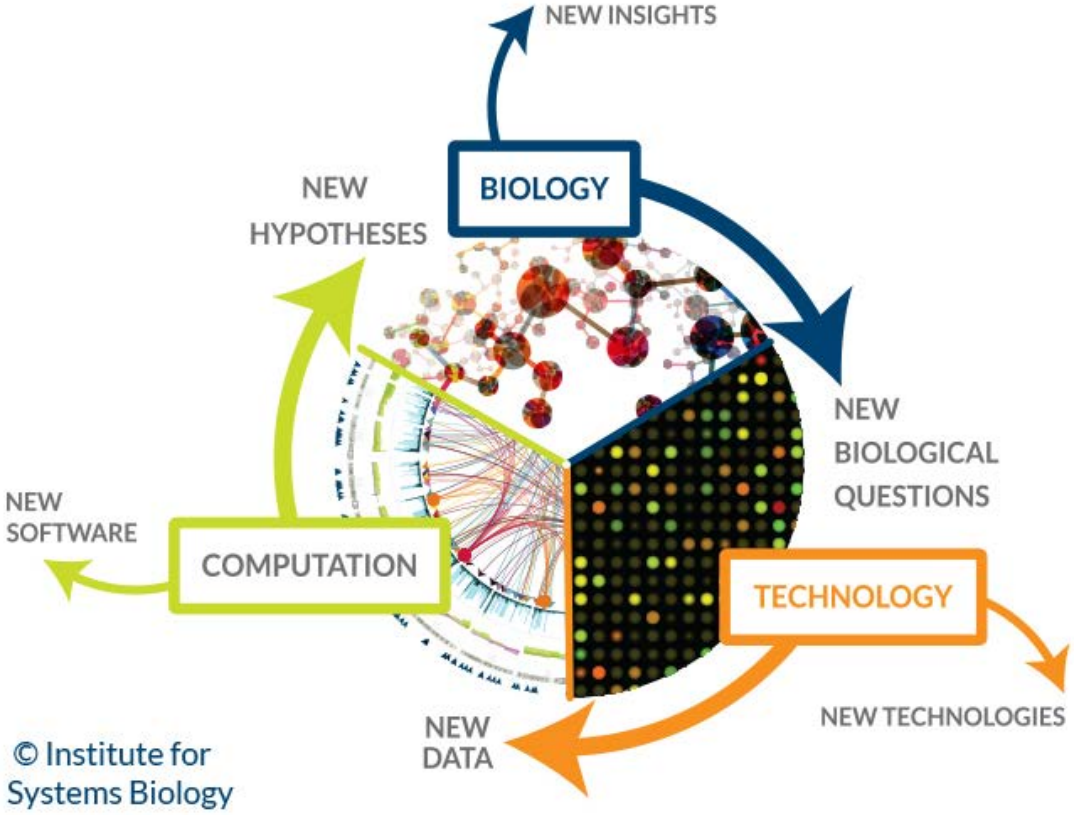


Figure from systemsbiology.org

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.

In the CSBC we define systems biology as the **explicit integration of experimental biology and computational or mathematical modeling** to build, test and/or validate hypotheses or ideas.

CSBC Scientific Areas of Interest

- 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.

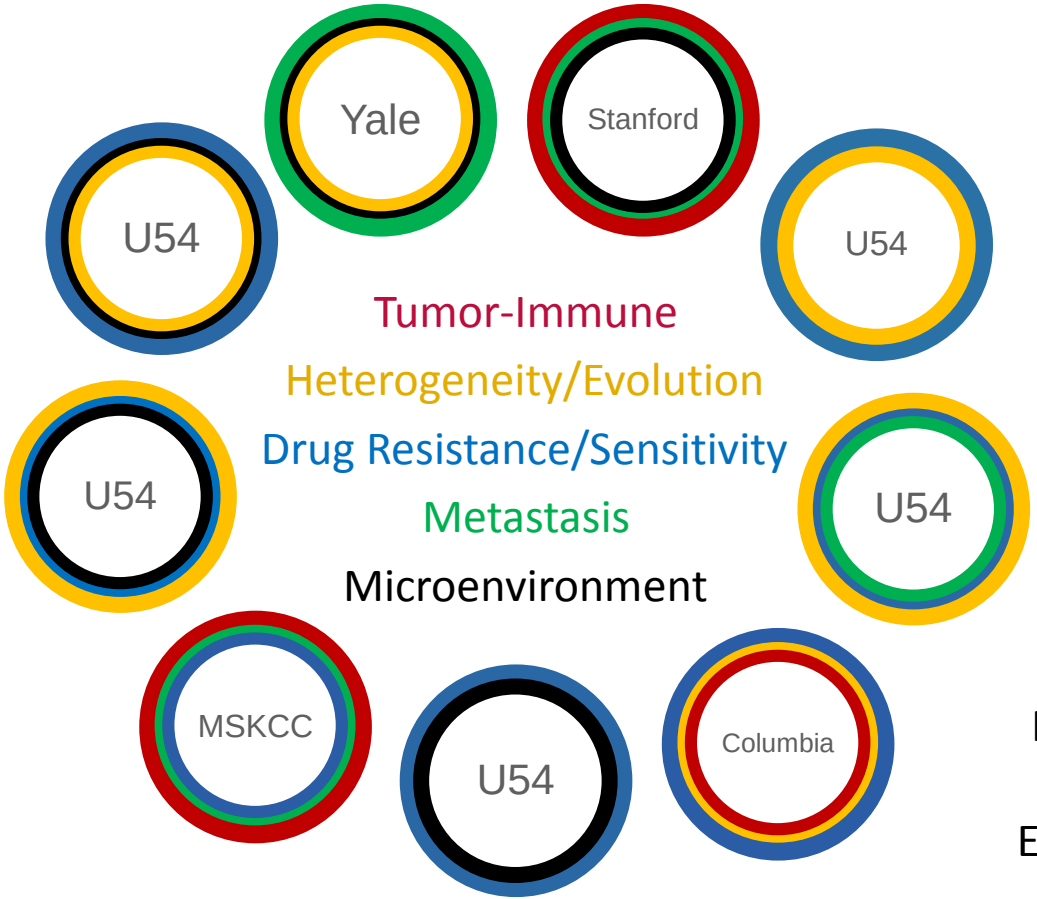
CSBC Scientific Areas of Interest (cont.)

- 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.

Research Themes and Systems Biology Approaches – CSBC U54s

Lung
Prostate
Breast
Colon

Head and Neck
Melanoma
Glioblastoma
ALL



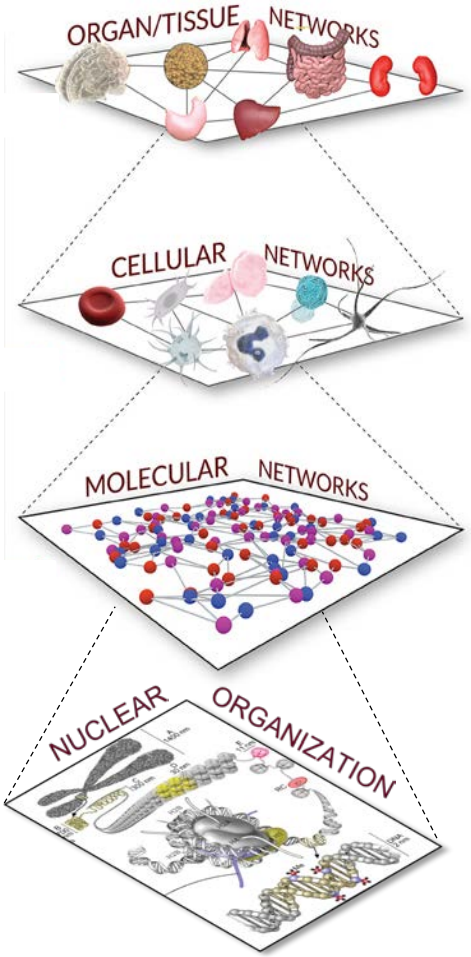
Clinical sample collection

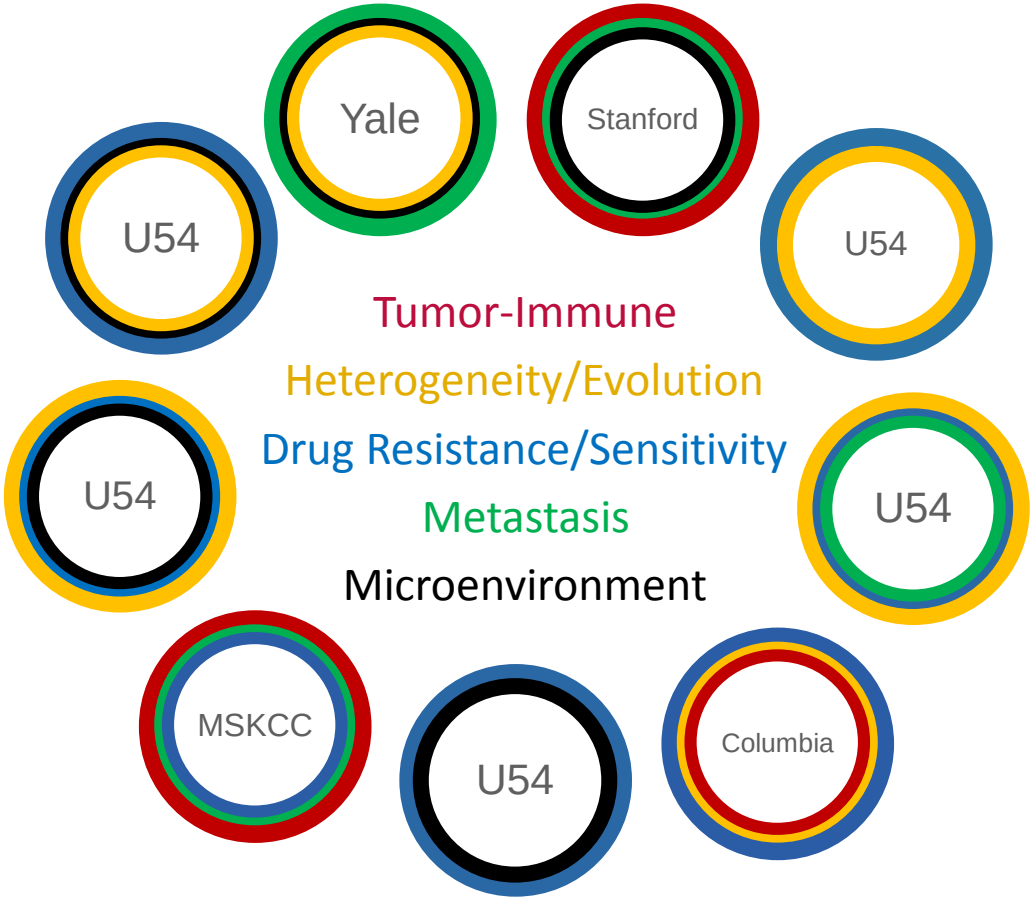
Novel single-cell measurement

Ecological Models
Machine Learning
ODE/PDE Models

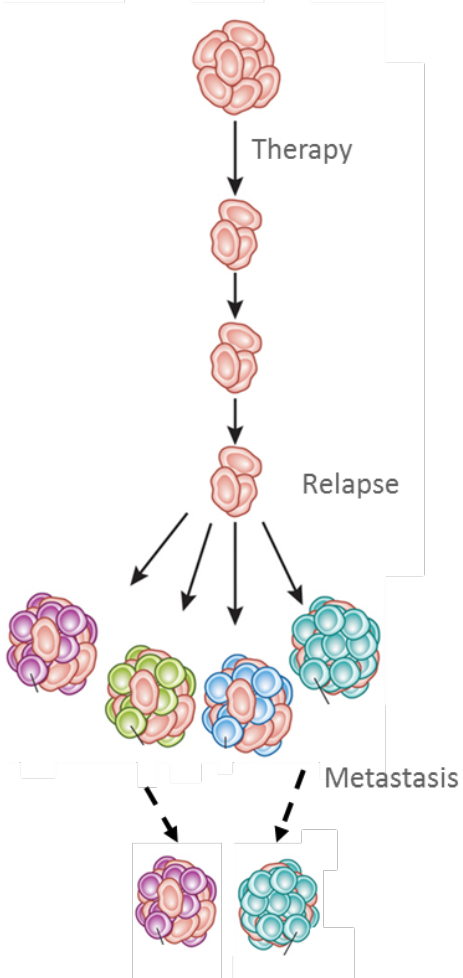
Network Inference
Image Analysis
Evolutionary Theory

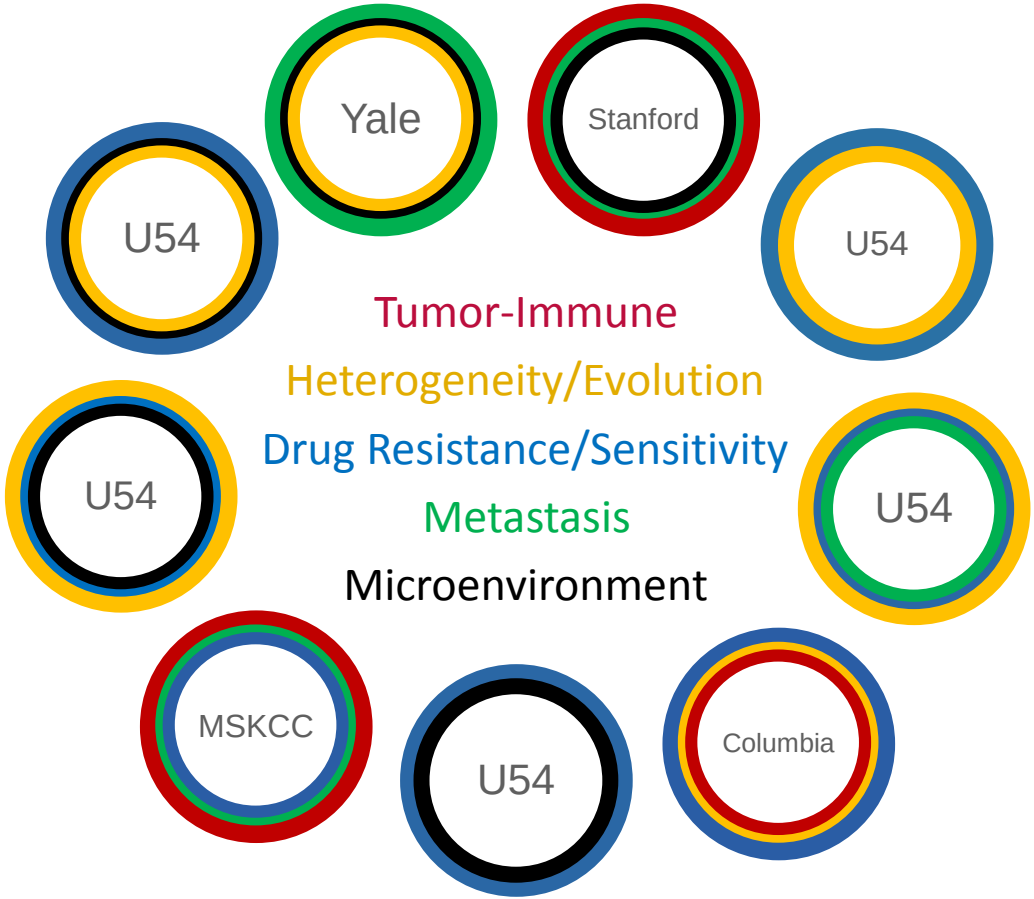
Summary of Research Themes and Systems Biology Approaches





Summary of Research Themes and Systems Biology Approaches





Physical Sciences-Oncology Network (PS-ON)
Overarching Goals

PHYSICAL SCIENCES— in ONCOLOGY

GOALS: support and nurture transdisciplinary environments and research ***integrating the perspectives*** of ***physical scientists*** (e.g., engineers, chemists, computer scientists, mathematicians, physicists) and ***cancer researchers*** to address fundamental questions in cancer biology using ***approaches and theories from the physical sciences***.

Research

- Originate and test novel, non-traditional physical sciences-based approaches to understanding and controlling cancer
- Generate orthogonal sets of physical measurements and integrate them with existing knowledge of cancer
- Develop and evaluate theoretical physics approaches to provide a comprehensive, dynamic picture of cancer

Education & Outreach

- Coordinate education, training, career development and scientific outreach to support and promote Physical Sciences in Oncology via patient advocates and academic educators

PS-ON Research Crosses Multiple Length - and Time-Scales

PHYSICAL SCIENCES in ONCOLOGY

Suggested PS-ON Scientific Themes

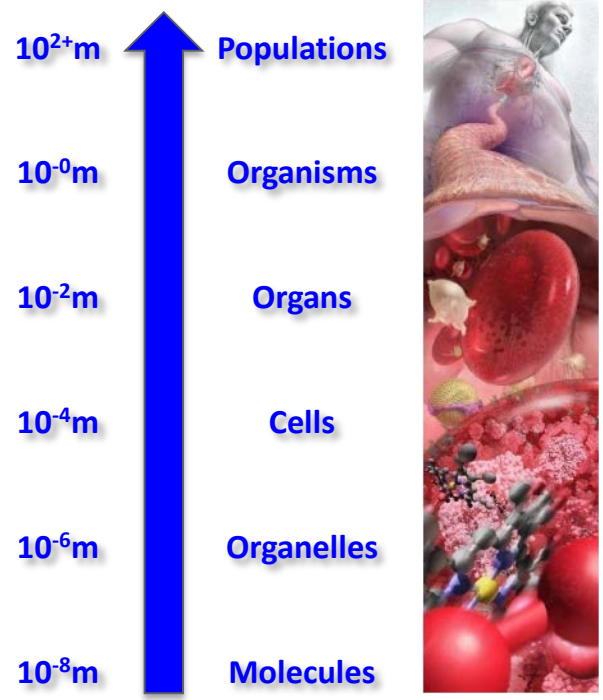
- ***The Physical Dynamics of Cancer***

Physical properties such as mechanical cues, transport phenomena, bioelectric signals, and thermal fluctuations can modulate the behavior of cancer cells, the microenvironment, tumors, and the host and may regulate the initiation and progression of cancer.

- ***Spatio-Temporal Organization in Cancer***

Appropriate spatial and temporal ***organization of structures across many biological and physical length-scales (e.g., subcellular, cell, tissue, organ, whole organism) and time scales*** is required for managing the transfer of information that is critical for regulated growth.

Across Length Scales



Multi-scale computational models

Novel technologies

Opportunities for Collaboration with the NCI PS-ON:
U54 Centers Annual Pilot Project Solicitations

U54 Centers (PS-OC; hyperlink to Center website and 2017 application receipt window)

Columbia (April-June)
Cornell (June-July)
Dana Farber (April-May)
Hopkins (April-May)
Methodist (April)
Minnesota (Feb)
MIT (July-Aug)
Moffitt (March-April)
Northwestern (Feb-March)
Upenn (Jan-Feb)

PS-ON Phase II

10 U54 Centers
7 U01 Projects

- ~50 institutions
- ~200 investigators
- ~30 trainees

and growing . . .

U24 Coordinating Center

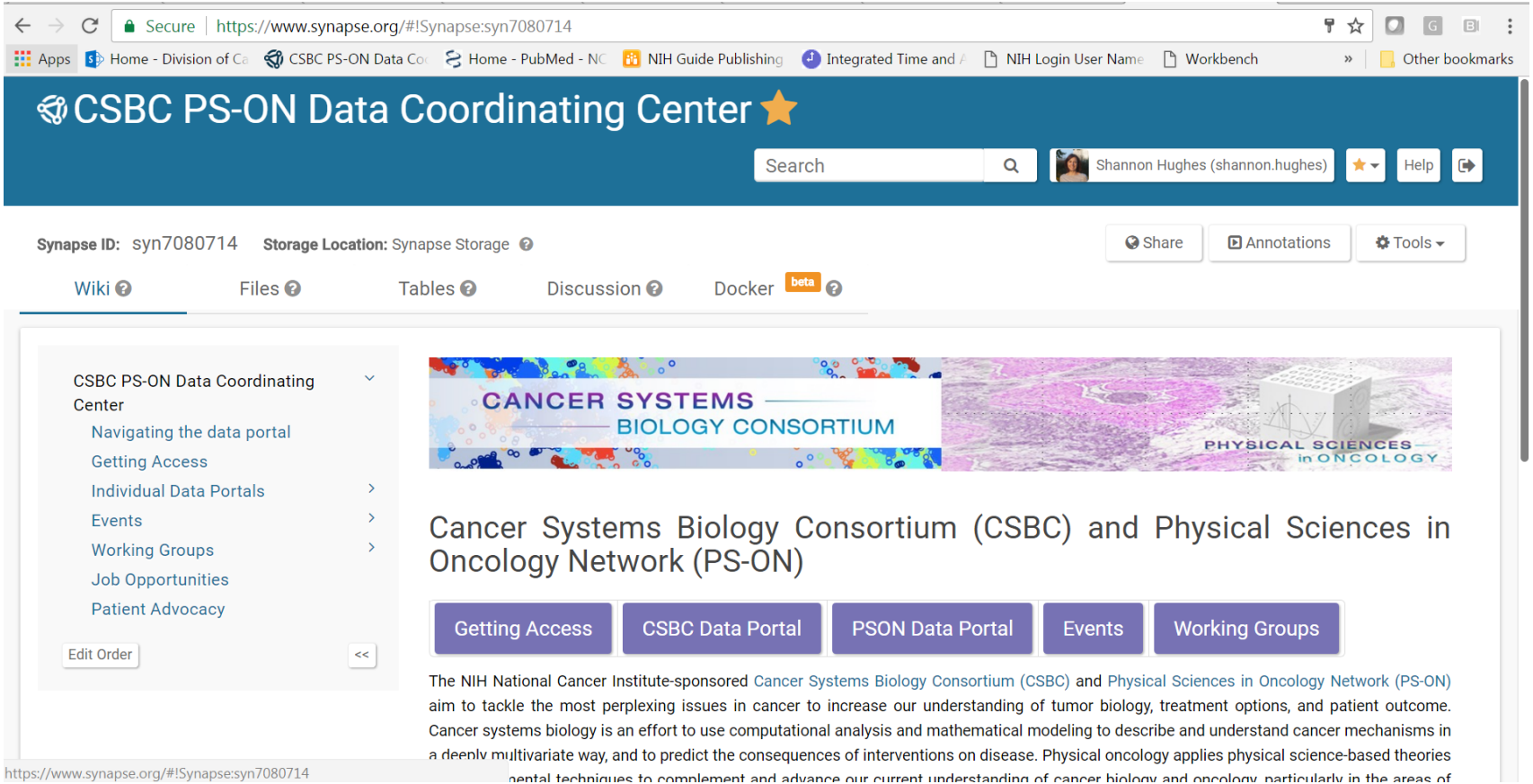
Sage Bionetworks

U01 Projects (PS-OP)

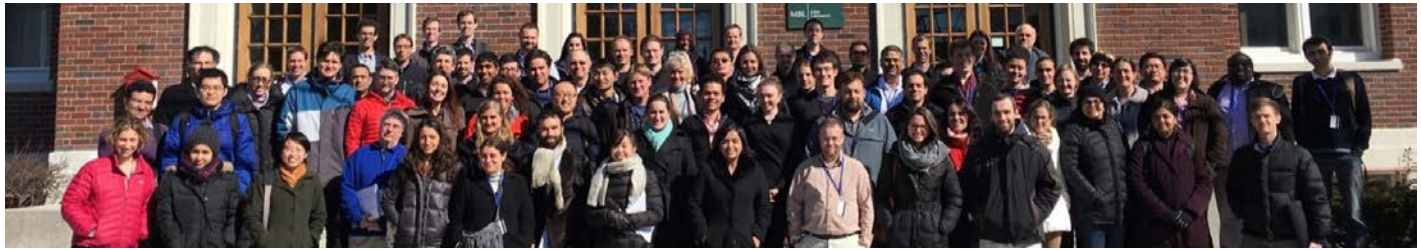
Berkeley
Georgia Tech
Harvard
Michigan
MIT
Utah
Vanderbilt

U01 FOA: PAR-15-021

www.synapse.org/CSBCPSON



Association of Early Career Cancer Systems Biologists (AECCSB)



Systems Approaches to Cancer Biology
Co-sponsored by the AECCSB & NCI: April 3-6 2016
www.SACBmeeting.org
NEXT MEETING: NOVEMBER 7-10, 2018

twitter.com/cancersysbio
@CancerSysBio

facebook.com/CancerSysBio

Contact: Aaron Meyer
(aameyer@mit.edu)
Or Stephen Piccolo
(stephen.piccolo.byu@gmail.com)

Goal: Tackle challenges in cancer metastasis by employing technologies and approaches across NCI-supported programs

Format: Open call for applications

25 participants chosen by scientific Mentors and workshop staff

Virtual pre-workshop activities

Investigator-initiated projects

Small pilot project funds available at the conclusion of the workshop

June 12-14, 2017: Seattle, WA

Goals of the Funding Opportunity Announcement (FOA)
Emerging Questions in Cancer Systems Biology (U01)

There are several highlighted areas of interest within the FOA. *Note that the list is non-inclusive and is not meant to restrict the scope of investigator-initiated research topics.*

- Dynamics of cell-cell interactions
- Integration of information across temporal and spatial scales
- Tumor behaviors reflecting single cell characteristics
- Systems-level analyses of the role of the microbiome in cancer
- The combination of systems and synthetic biology for understanding disease mechanisms
- Hierarchical models of cancer
- Systems biology aided clinical trial design

Please see Part 2, Section I Funding Opportunity Description for further details.

Goals of the Funding Opportunity Announcement (FOA)
Emerging Questions in Cancer Systems Biology

In addition to addressing specific biological hypotheses, the continued success of cancer systems biology depends on the development of new methodologies to address complex and multivariate questions, including new theoretical, mathematical and computational techniques, multi-scale modeling approaches capable of integrating across scales from the molecular to the population level, and new biological tools and systems for informing and testing cancer systems biology generated hypotheses.

Key Dates for PAR-16-131

	Pre-Application Webinar	Letter of Intent Due Dates	Application Due Dates	Review Dates	Earliest Anticipated Start Dates
Round 1	~~Apr 27, 2016~~	~~May 24, 2016~~	~~June 24,2016~~	~~Oct/Nov 2016~~	~~Apr 2017~~
Round 2	~~Sep, 2016~~	~~Oct 18, 2016~~	~~Nov 18, 2016~~	~~Mar/Apr 2017~~	~~Aug 2017~~
Round 3	May 8, 2017	May 23, 2017	June 23,2017	Oct/Nov 2017	Apr 2018
Round 4	TBD, est Aug 2017	Oct 24, 2017	Nov 24, 2017	Mar/Apr 2018	Aug 2018
Round 5	TBD, est Feb 2017	May 22, 2018	June 22,2018	Oct/Nov 2018	Apr 2019
Round 6	TBD, est Aug 2017	Oct 23, 2018	Nov 23, 2018	Mar/Apr 2019	Aug 2019

F30 and F31: NRSA for Predoctoral Fellows

Objective: To provide support for trainees' research training component in a MD/PhD program (F30) or PhD program (F31)

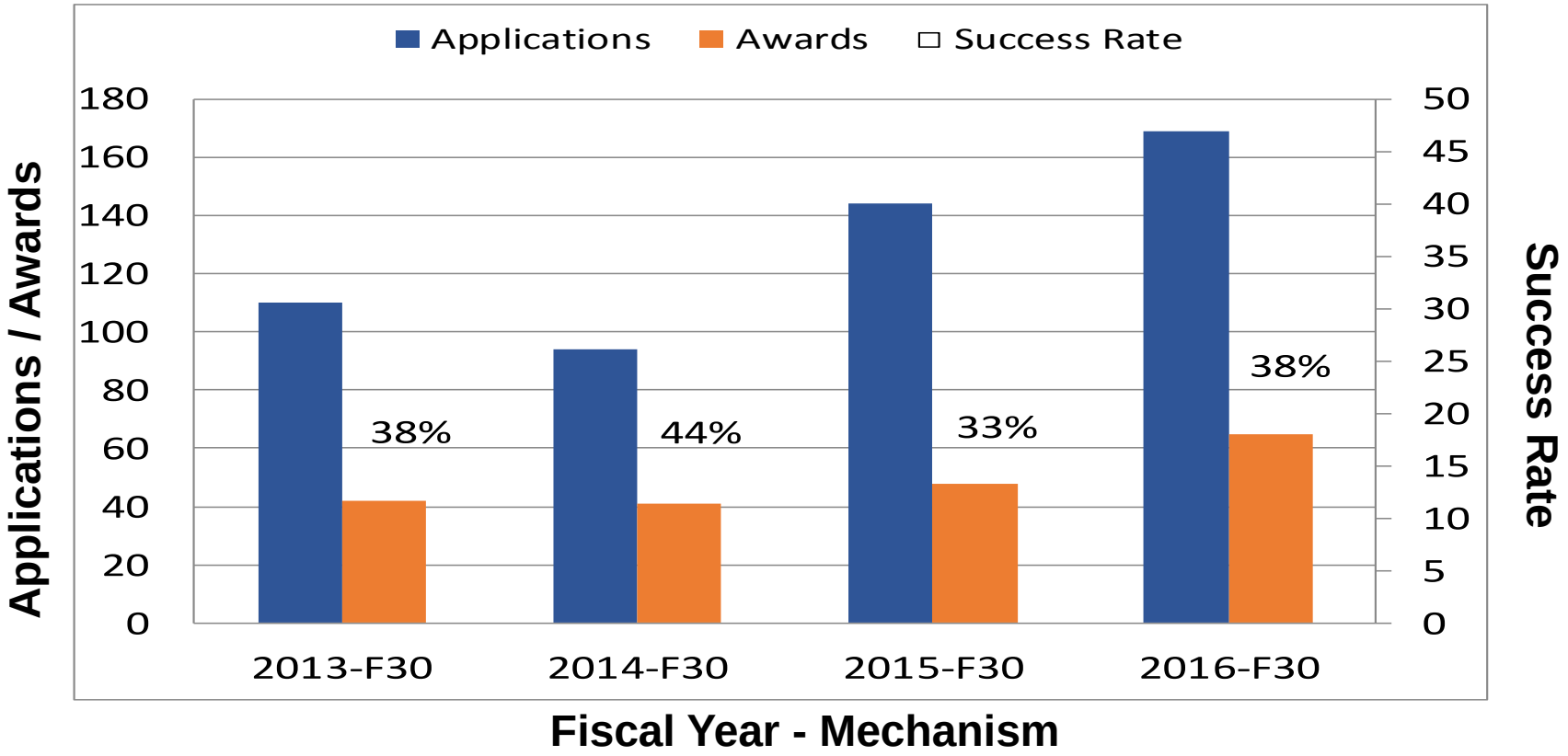
Candidate: Applicants must be enrolled in a MD/PhD program within the first 48 months of enrollment (F30), or a PhD program (F31). US citizenship or green card

Mentor: Principal investigator(s) with R01 or R01-like funding who can provide mentorship in both research and career development.

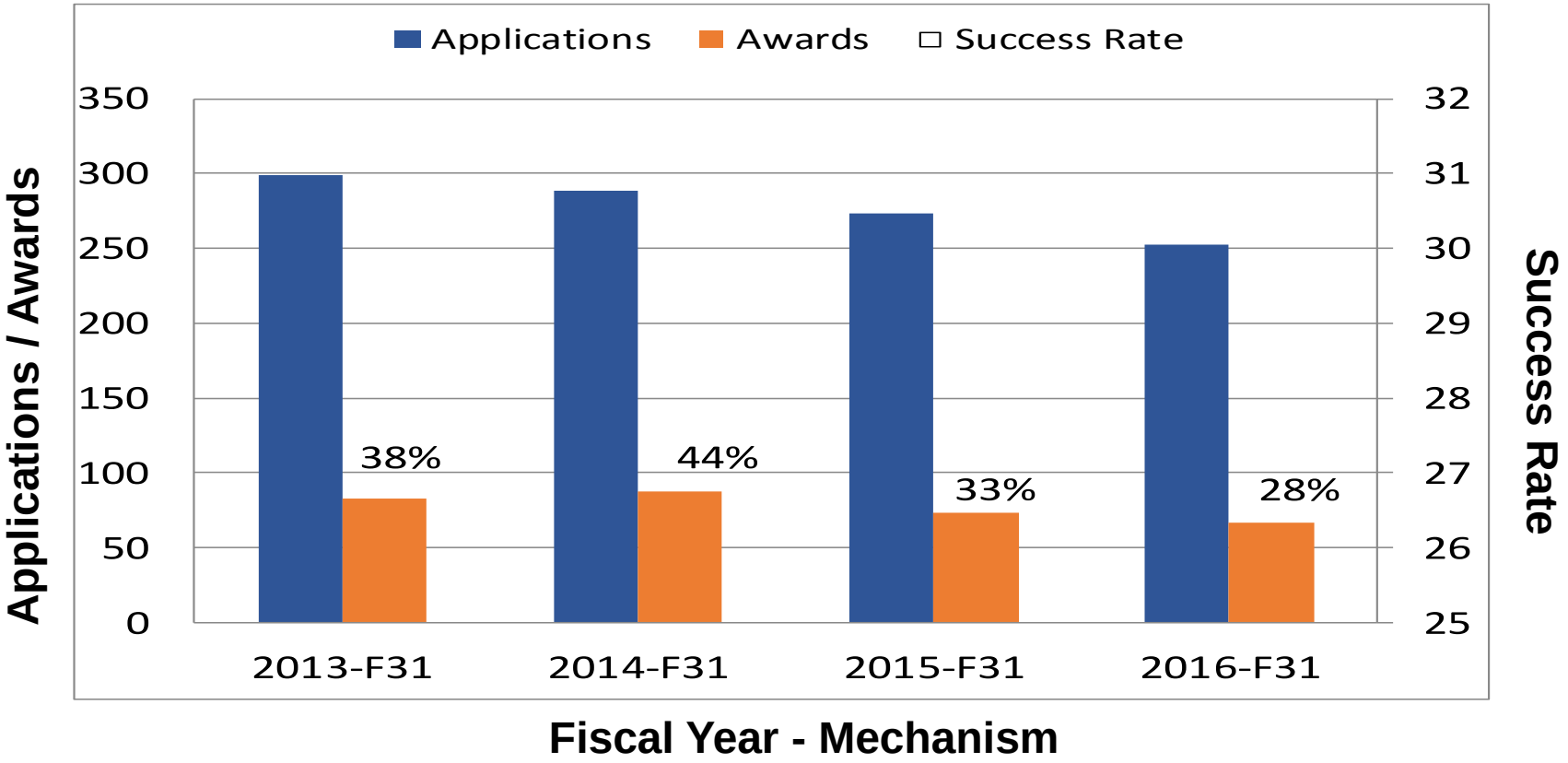
Award: For F30: $22,920 /yr; Tuition and fees: up to $21,000 /yr: Training Related Expenses: $4,200/yr; Up to 6 years.

For F31: $22,920 /yr; Tuition and fees: up to $16,000 /yr; Training Related Expenses: $4,200/yr; Up to 5 years

F30 Applications, Awards and Success Rates



F31 Applications, Awards and Success Rates



A Pilot Program: the F99/K00 Predoc-to-Postdoc Transition Award

- **There is a need to attract the very best graduate students to commit to a research career as independent researchers**
- **Highlighting a pathway to success may be an effective approach in trying to address this need**
- **The experiment: developing a new funding mechanism that would:**

  (1) empower the selected students in securing the most desirable postdoc positions

  (2) place them at strong positions to compete for the K99/R00 award for transitioning to independent positions

https://grants.nih.gov/grants/guide/pa-files/PA-16-193.html

Unique Features of the F99/K00 Award

- **Dual phase funding: support for up to 2 years for 3rd/4th-year students to complete graduate study, and 4 years for postdoctoral training in cancer research preferably at a different institution**

- **Institutional Nomination of Applicants: one nomination per institution each year to strengthen institutional input in the selection process**
- **Open to the best international students, removing one NRSA restriction considered outdated by the research community**
- **The K00 fellows, from the first day as postdocs, will be employees with family and retirement benefits etc.**

https://grants.nih.gov/grants/guide/pa-files/PA-16-193.html

F99/K00 Year 1 Portfolio Analysis

	Applications	Awards	Success Rate (%)
Total	**76**	**36**	**47**
Women	**40**	**17**	**43**
International Students	**20**	**7**	**35**
F31 Awardees	**6**	**6**	**100**
F31 Applicants	**15**	**7**	**47**
Cancer Centers	**55**	**31**	**55**
Top 150 NCI $ Institutions	**62**	**33**	**53**

F32: NRSA for Postdoctoral Fellows

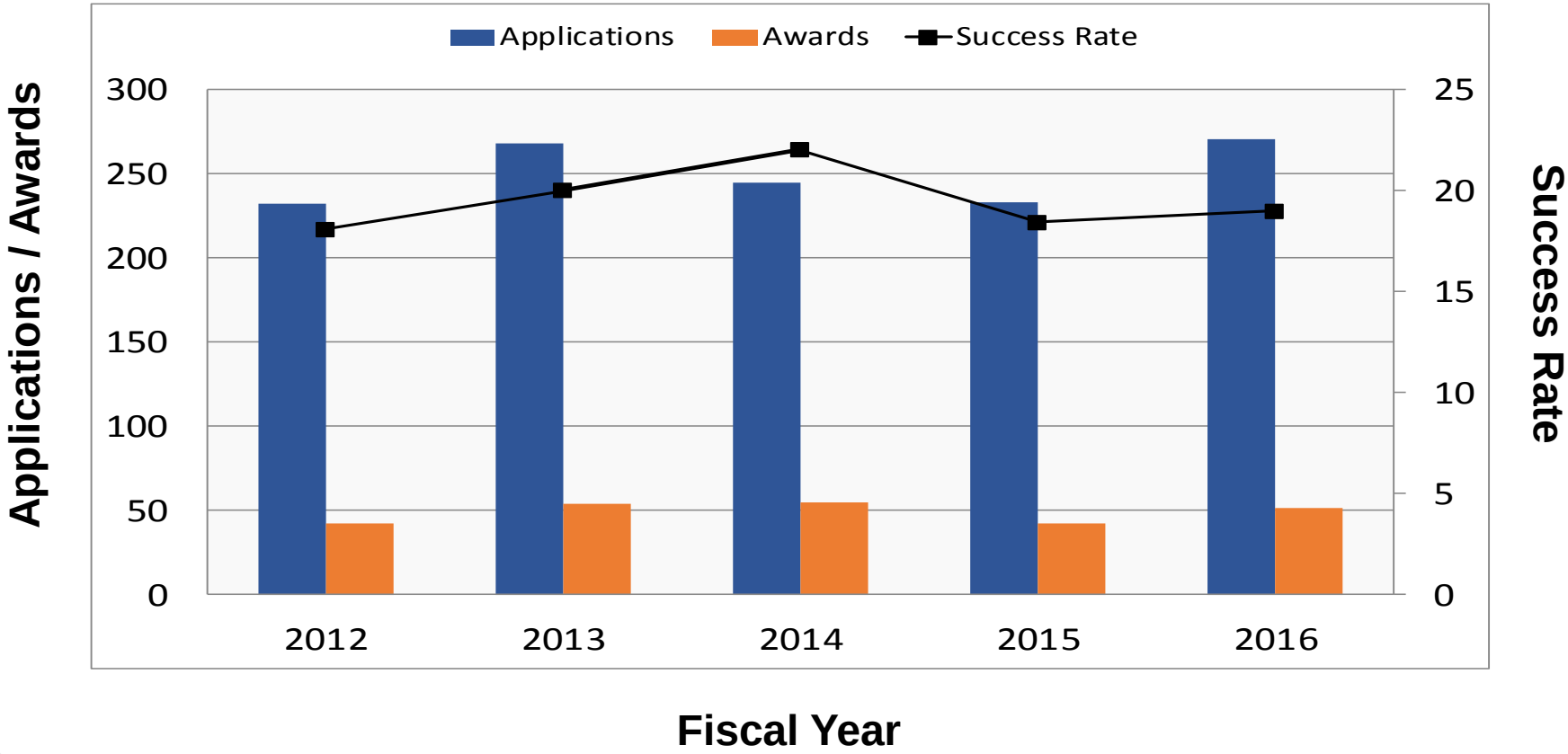
Objective: To support research training for postdoctoral applicants who have the potential to become productive independent research investigators

Candidate: Postdoctoral Fellows (Finishing PhD/Early post-doc, yrs1-3). US citizenship or green card

Mentor: Principal investigator(s) with R01 or R01-like funding who can provide mentorship in both research and career development.

Award: Up to three years' stipend at $42,840 - $56,375/yr; Tuition and fees: up to $16,000 /yr; Training Related Expenses: up to $8,850/yr; Full-time effort

F32 Applications, Awards and Success Rates



Take Home Message

- **NCI Cancer Training Branch Offers Fellowships, K awards and Institutional training grants for young cancer researchers at predoctoral, postdoctoral, and junior faculty stages, in all cancer research fields.**
- **The success rates of these funding mechanisms for training are usually 20-30%.**
- **Mentors should encourage and work with students to submit applications.**

Good Places to Go for Detailed Information

NCI CTB home page:
http://www.cancer.gov/grants-training/training/funding

NIH grant policy:
http://grants.nih.gov/grants/policy/nihgps/HTML5/section_11/11.3_institutional_research_training_grants.htm

NRSA F&Q: http://grants.nih.gov/training/faq_training.htm#1259

Thank you!

Please contact me with any questions:

shannon.hughes@nih.gov