

“Innovation to Impact: Beginning the Process”

ATVB/PVD, May 5, 2016

“Turning Discovery into Health: The NIH translation paradigm”

Zorina S. Galis, Ph.D.

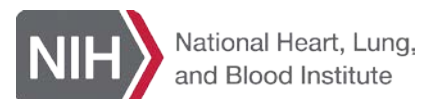
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National Heart, Lung, and Blood Institute

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National Institutes of Health

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Conflict disclosures

- No financial conflicts
- **Note:** The opinions presented do not necessarily represent the opinions of the National Heart, Lung, and Blood Institute (NHLBI).

“Turning Discovery into Health”

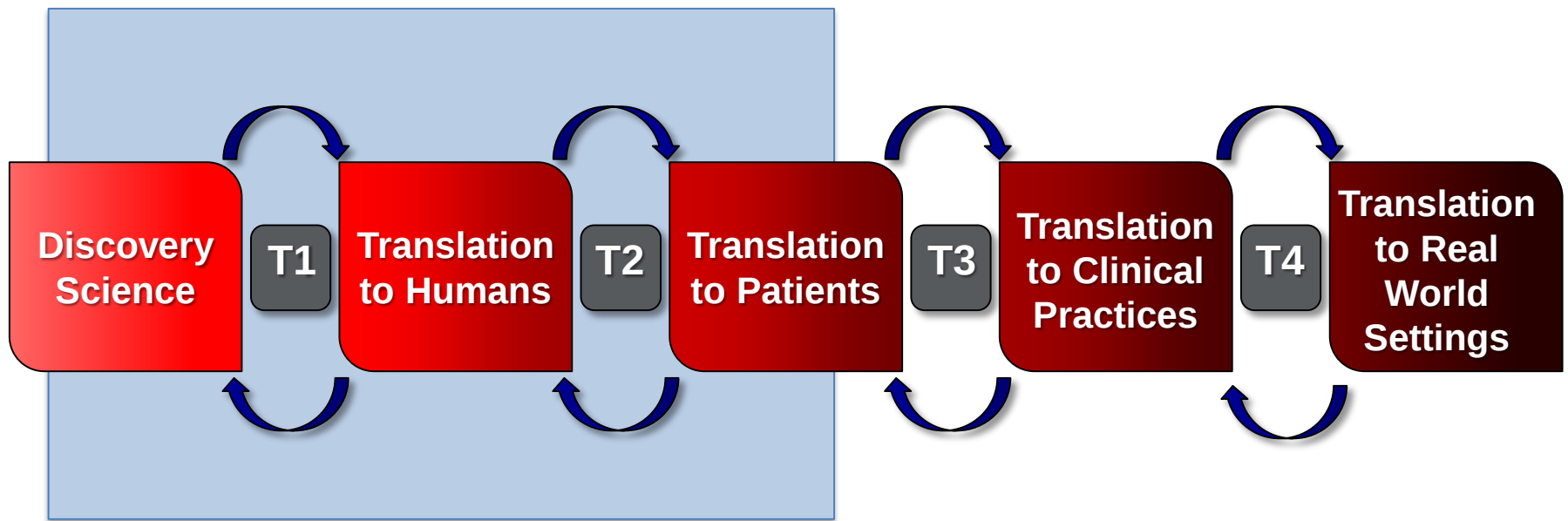


NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability

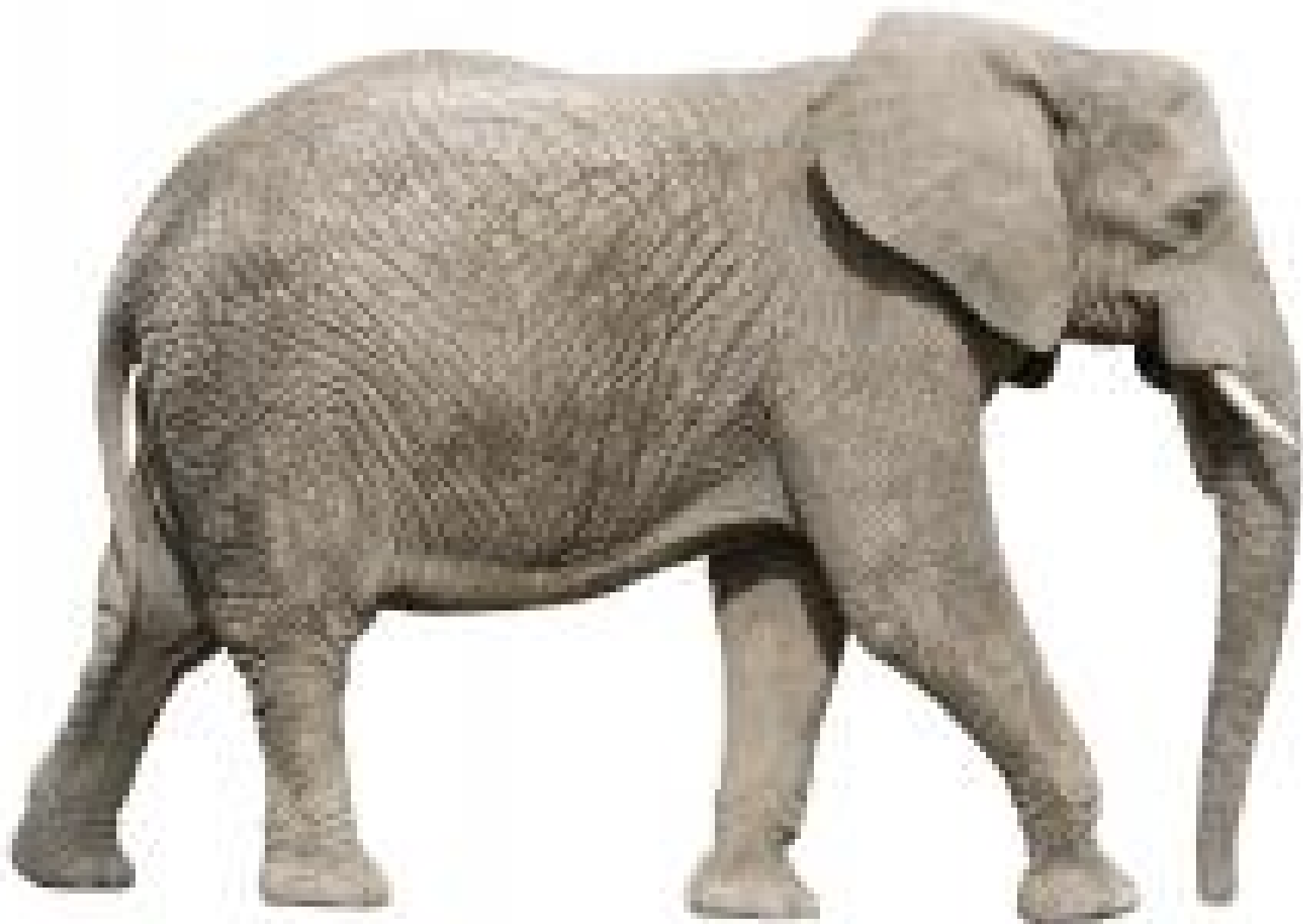
<http://www.nih.gov/about/mission.htm>

Defining “*Translational research*”

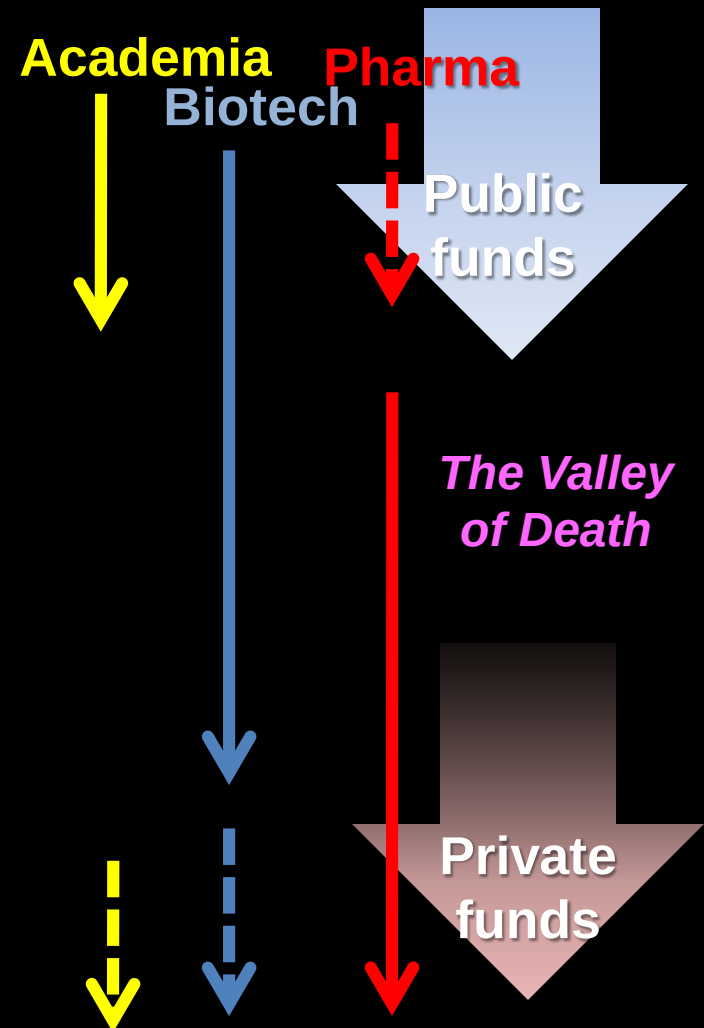
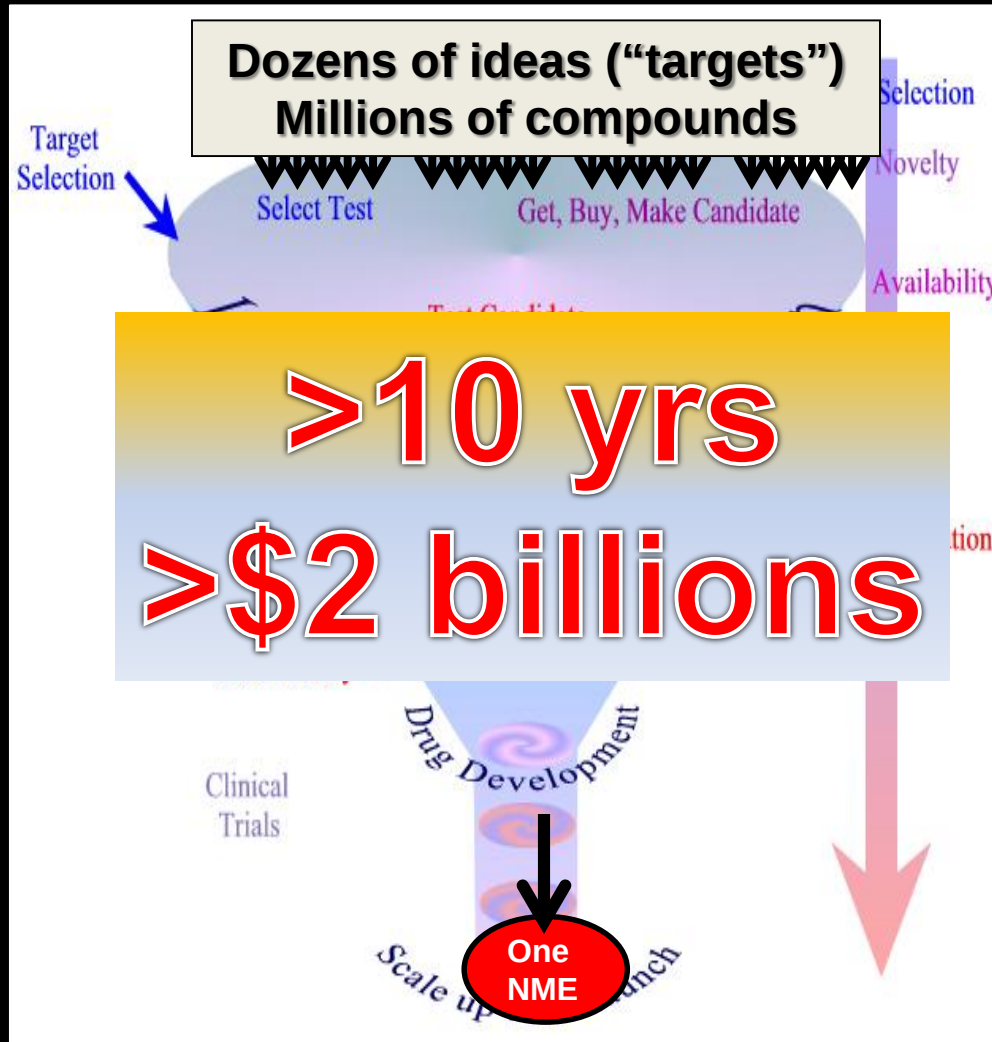
NHLBI FY2016



Who funds US biomedical research?



Main contributors to the current paradigm of finding a cure

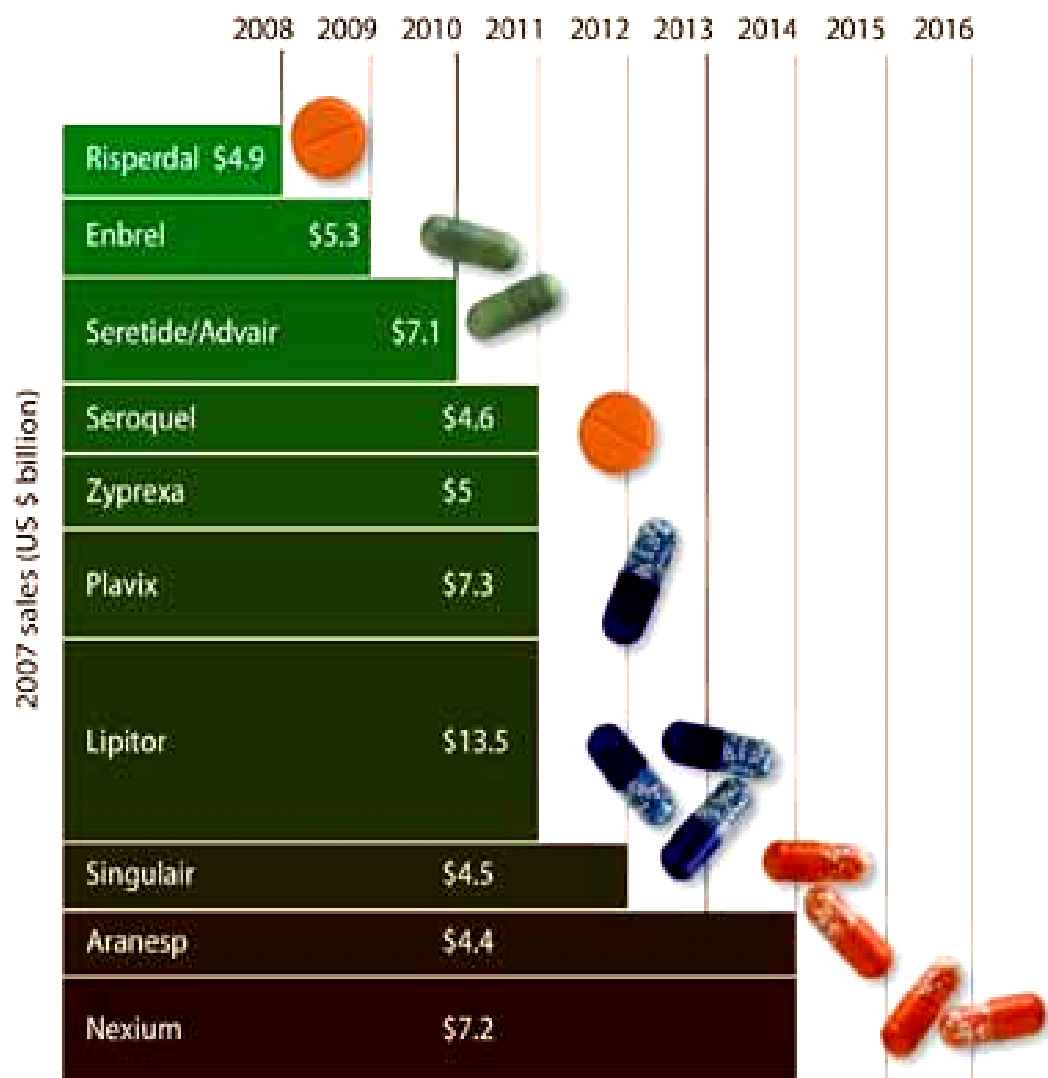


NIH-funded basic research is needed for development of (CV) therapies

Example...

- Robert J. Lefkowitz, M.D. and Brian K. Kobilka, M.D. 2012 Nobel Prize for Chemistry for important basic scientific contributions to the field of G-protein coupled receptors (GPCRs)
- NHLBI grantees: Lefkowitz since 1974, Kobilka since 1990
- GPCRs are the target of the majority of currently used therapeutic agents (> 40%)
- Their discoveries specifically led to the development of beta-adrenergic receptor blockers used to treat hypertension (HTN), angina, and coronary heart disease.

Pharma in the news: The “*patent cliff*”!



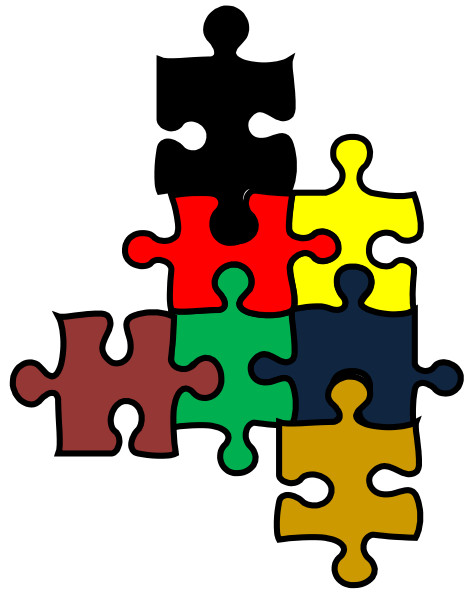
- “*Drug makers face \$140 billion patent ‘cliff’*”
Reuters
<http://bit.ly/clNXp8>
- “*Warning: Patent cliff approaching*”
FiercePharma
<http://bit.ly/16y64u>
- “*Pharma refocuses on the patent cliff*”,
Chemistry World
<http://bit.ly/drGns7>

How can we do more with less?



© Andy Freeberg

Cooperation and Efficient *transitions* among major stakeholders



- Academia
- Biotech/Small private
- Pharma/Large corporation
- Government
- Investment/Venture
- Consumer/patient
- Other

- ***Understanding and aligning goals***
- ***Understanding drivers, barriers, and strengths***
- ***Need for “champions”***
- ***Effectively managing transitions***

Key Questions

Should public funds be spent on drug development? What is the role of NIH?

- **What are the developmental/regulatory hurdles in NIH's view?**
- **What is NIH doing about it?**
- **Is the NIH approach working?**
- **What could NIH do to make it better?**

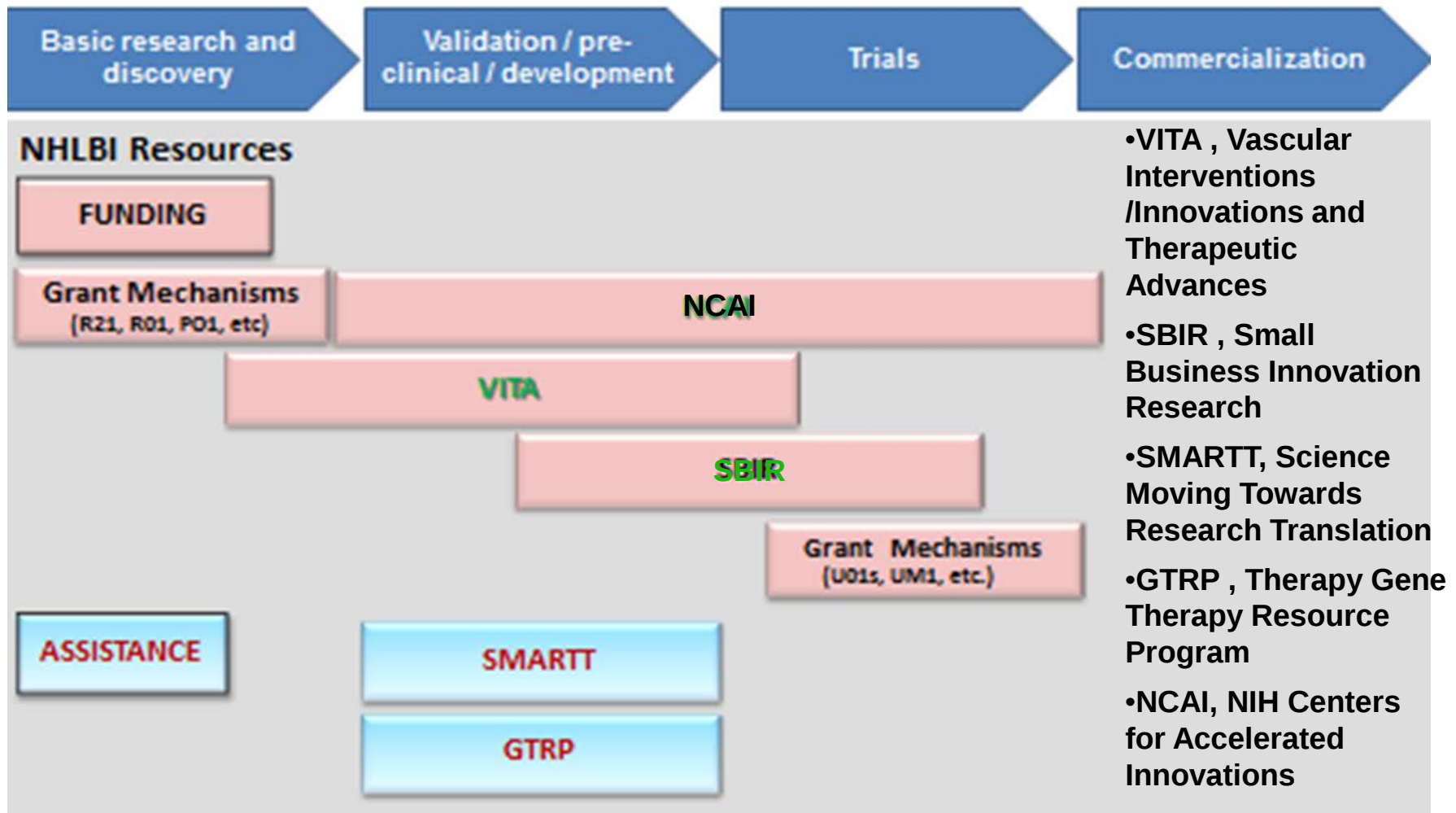
Role of NIH in early biomedical product development?

- Identify unmet medical needs
- Support fundamental knowledge
- Assess the best clinical evidence to inform health care decisions
- Work across the board to better serve the health needs of the patient (/tax-payer):
- Assume risk of early funding (“de-risking”)
 - Provide assistance to the extramural inventors community
 - Assess critical development/regulatory gaps and hurdles
 - Special funding programs for early product development efforts, including critical national or local resources, à-la carte assistance
 - Create a framework to help accelerate translation

“ROI” – seek commercial development, however therapeutic value may trump potential financial return

Discovery to Development Pipeline

NHLBI Funding and Resources



Galis, Black, Skarlatos, 2013 *Circulation Research* 112 (9), 1212-1218

“NHLBI is hearing you”: A biomedical product development sandbox



**Vascular Interventions/Innovations
and Therapeutic Advances**

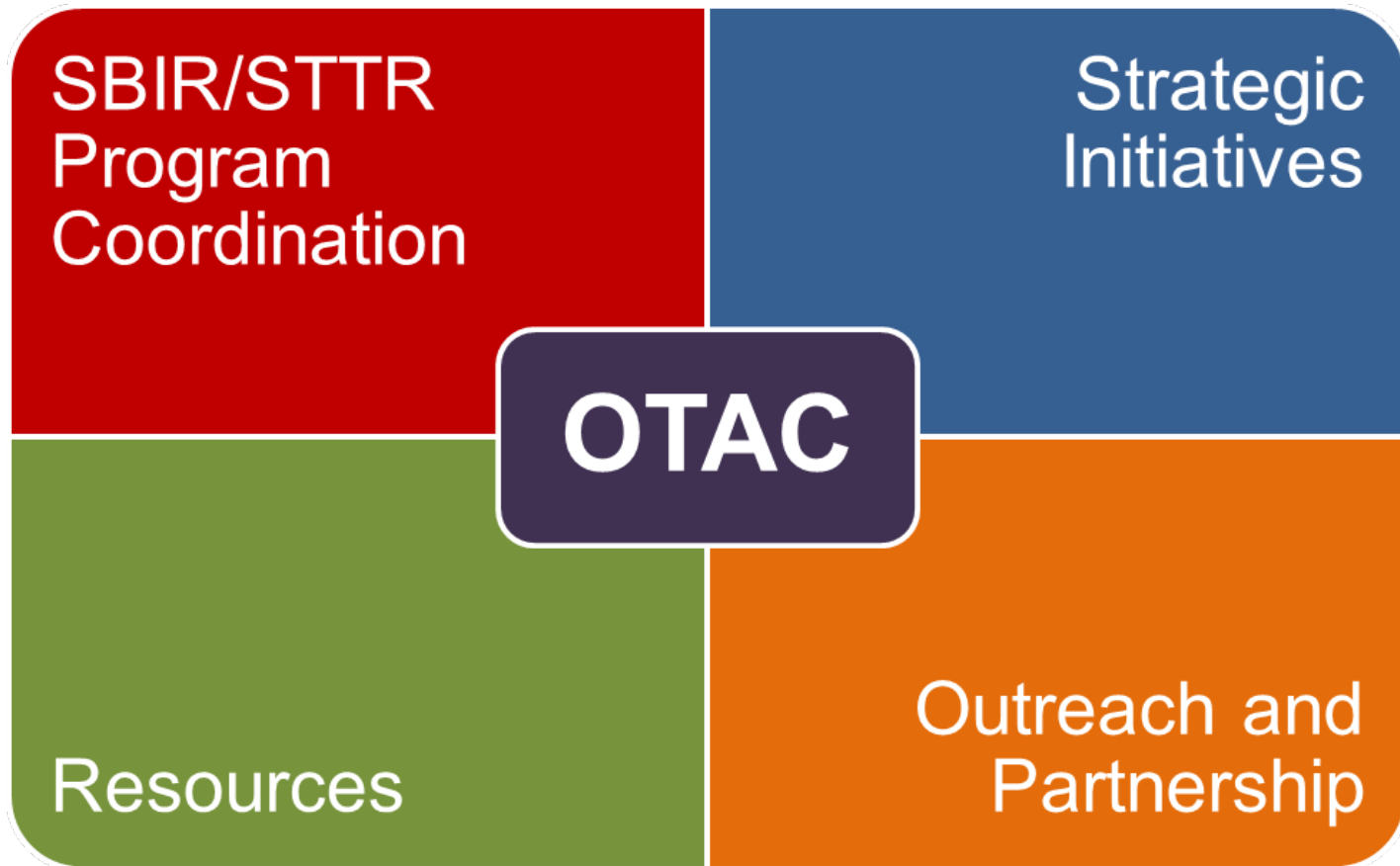


***Managing ideas *lightly...*
and the process *tightly****

- **NHLBI requirements:**
 - Focus on specific medical conditions (what is/not included)
 - Funding mechanism: BAA w/check points (milestones-driven, “go/no go” decisions)
 - Maximum time/amount of funding
- **Applicant-driven:**
 - Propose project: product type, goals and milestones, allocation of effort/resources (\$, time)
 - No restrictions on institutional affiliation
 - No required level of expertise/current access to resources

SBIRs: NHLBI Office of Translational Alliances and Coordination (OTAC)

Charge: Develop and implement initiatives to enhance translation of technologies from the bench to the market



Lab to Market for Health

NHLBI SBIR-supported Products

CoaguChek®
Because it's my life



MENSSANA
RESEARCH, INC.

Heartsbreath™ Heart
Transplant Rejection point-
of-care breath test

Life Recovery Systems

The FASTEST non-invasive cooling in the world of medicine.



ThermoSuit



THORATEC®
CORPORATION



THERMEDICAL

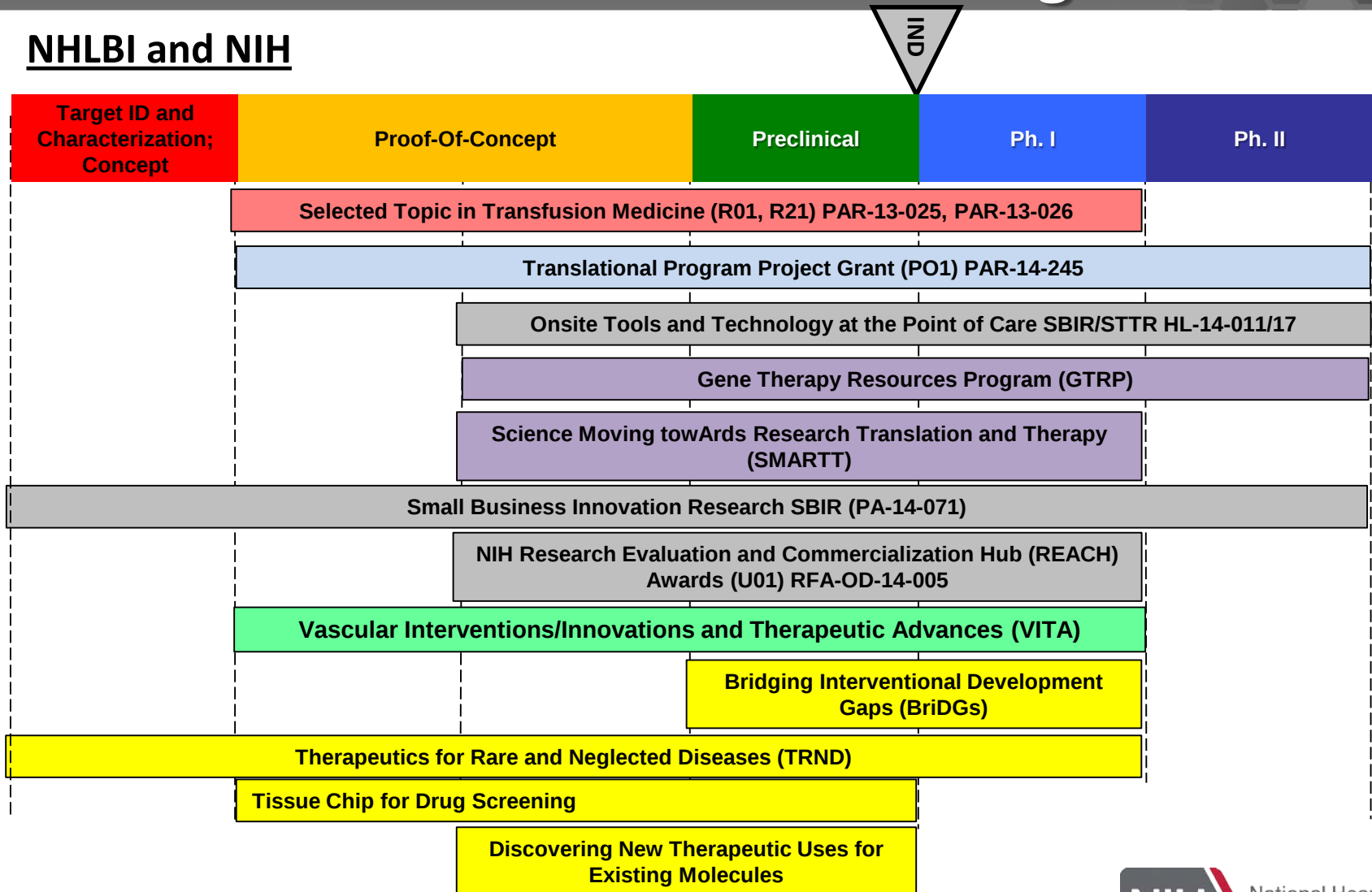
SERF Ablation System



alphacore
pharma

Examples of various translational resources for NHLBI investigators

NHLBI and NIH



Resources to help you get started with a translational research project: NHLBI repositories

The logo for BioLINCC, with "Bio" in red and "LINCC" in blue, set against a background of stylized red and blue mountain peaks.

BioLINCC

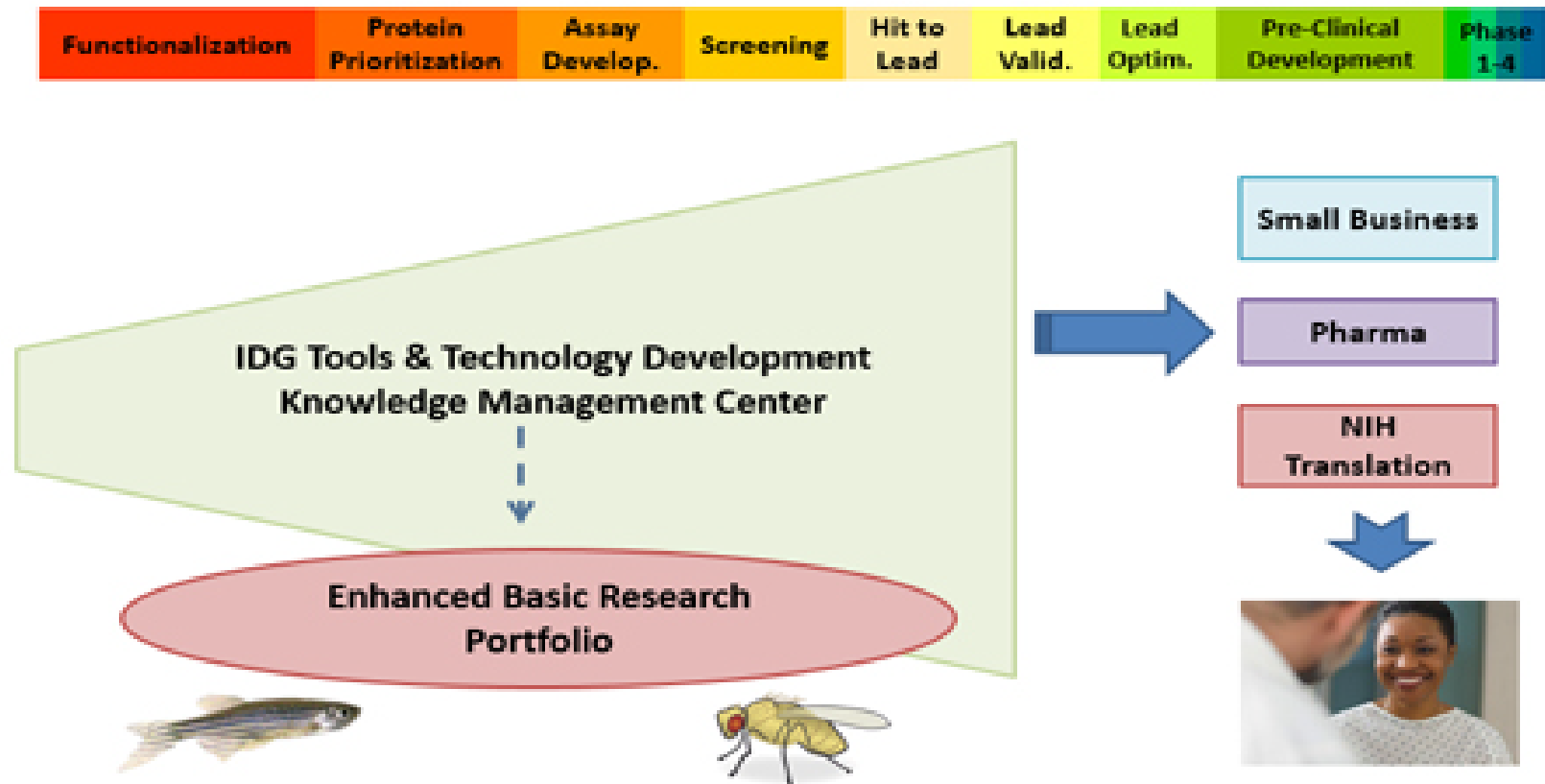
BioLogic Specimen & Data Repositories
INformation Coordinating Center

([BioLINCC](https://biolincc.nhlbi.nih.gov/home/)) <https://biolincc.nhlbi.nih.gov/home/>

- Clinical Trials (N > 80)
- Observational Epidemiology Studies (N >30)
- Searchable function for specimens/data of interest
- Apply directly on the website

Target discovery: “*Illuminating the Druggable Genome (IDG)*” NIH Common Fund

IDG Will Foster Basic Research to Enable Translation



NIH 2015 Precision Medicine Initiative

<http://www.nih.gov/precisionmedicine/who.htm>



***Precision medicine* is an emerging approach for disease prevention and treatment that takes into account people's individual variations in genes, environment, and lifestyle.**

The NIH Precision Medicine Initiative will generate the scientific evidence needed to move the concept of precision medicine into clinical practice.

[What are the near-term goals?](#)
[What are the longer-term goals?](#)
[How is it different?](#)
[Who will participate?](#)
[ACD Working Group on PMI](#)
[Events](#)

**[NIH Request for Information](#) (RFI)
Closes May 7th!!**

Find potential collaborators and resources available within the NIH Intramural program

NIH Clinical Center

Search the Collaborations Site

Welcome Funding Opportunities Resources Current Research Frequently Asked Questions Contact Us

Research Resources at the NIH Bethesda Campus

Equipment, Technology & Tools



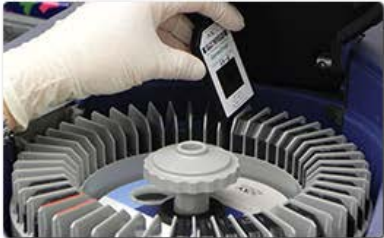
Biomedical Specimens



Rare Diseases



Protocol Support/Unique Data Sets



Healthy Volunteers



NOTE: PDF documents require the free [Adobe Reader](#).
This page was last updated: September 20, 2013

<http://www.cc.nih.gov/translational-research-resources/index.html>

“Got idea?” Find NIH funding opportunities!

Google: “*NIH funding opportunities*”



The image shows a screenshot of the NIH Grants & Funding website. A large red rotary phone is overlaid on the right side of the page. The website header includes the NIH logo and the text "National Institutes of Health Office of Extramural Research". The main navigation bar has links for HOME, ABOUT GRANTS, FUNDING (highlighted in green), FORMS & DEADLINES, and GRANTS. Below this is a blue banner with the text "Grants & Funding". The left sidebar contains several sections: "Funding Opportunities" (with links to RFAs, PAs, Notices, Unsolicited Applications, Research Training & Career Development, Small Business, and Contract Opportunities), "NIH-Wide Initiatives" (with links to New and Early Stage Investigators, Stem Cell Information, NIH Common Fund, and OppNet), and "Award Data" (with links to NIH Reports and Search NIH Awards). The main content area is titled "Funding Opportunities and Notices" and includes a search bar, a list of search criteria (Active RFAs, Active PAs, Notices), and a search button. A red oval highlights the search bar. Below the search bar is a link to "Advanced Search". The bottom section is titled "Browse Active Funding Opportunities" and lists "Requests for Applications (RFAs)", "Program Announcements (PAs)", and "Parent Announcements (unsolicited applications)". To the right of this section is a link to "Browse Recent Policies and Guidelines Notices". In the bottom right corner, there is a small graphic for the "HHS OIG Hotline REPORT FRAUD" with the URL "oig.hhs.gov".

NIH National Institutes of Health
Office of Extramural Research

HOME ABOUT GRANTS **FUNDING** FORMS & DEADLINES GRANTS

Grants & Funding

Funding Opportunities

- Funding Opportunities (RFAs, PAs) & Notices
- Unsolicited Applications (Parent Announcements)
- Research Training & Career Development
- Small Business (SBIR/STTR)
- Contract Opportunities

NIH-Wide Initiatives

- New and Early Stage Investigators
- Stem Cell Information
- NIH Common Fund
- OppNet (Behavioral & Social Sciences)

Award Data

- NIH Reports (RePORT)
- Search NIH Awards (RePORTER)

Funding Opportunities and Notices

The **NIH Guide for Grants and Contracts** is the official source for medical and behavioral research grant policies, guidelines, and opportunities. Definitions and More Information...

Search the NIH Guide for:

- ☒ **Active RFAs** (Requests for Applications)
- ☒ **Active PAs** (Program Announcements)
- ☐ **Notices**

With Announcement # or Keywords (Optional)

Advanced Search

Browse Active Funding Opportunities

- Requests for Applications (RFAs)
- Program Announcements (PAs)
- Parent Announcements (unsolicited applications)

Browse Recent Policies and Guidelines Notices

HHS OIG Hotline
REPORT FRAUD
oig.hhs.gov

Specific considerations for clinical research applications

 U.S. Department of Health & Human Services

 National Institutes of Health

Contact Us |  Get Email Alerts |  Font Size

 National Heart, Lung, and Blood Institute

[Accessible Search Form](#)

NHLBI Entire Site

SEARCH

Public

Health Professionals

Researchers

Clinical Trials

News & Resources

About NHLBI

[Home](#) » [Researchers](#) » [Funding Opportunities & Award Policies](#) » [Research Support Mechanisms](#) — [Guidelines and Descriptions](#) » [Clinical Research Guide](#)

[CRG Home](#)

Clinical Research Guide for NHLBI Investigators

Preparing, submitting and managing a clinical research award can be challenging. This site is designed to guide potential investigators in organizing a clinical research application and to provide information on conducting a study and maintaining an award. Here you will find:

- [An Overview of Human Subjects Research](#)
- [Pre-application Information](#)
- [Peer Review Details](#)
- [Funding Information](#)
- [Grants Oversight and Management Tips](#)
- [Closing a Study Specifics](#)
- [Toolkit Resources](#)

[ATTENTION: Specific Guidelines for Applications with Direct Costs of \\$500,000 or More in Any One Year](#)

NEW requirements for Multi-site Clinical Trials will apply as of Oct 16, 2016 (to be published in April 2016)

Heart, Lung,
Institute

NIH RePORT

U.S. Department of Health & Human Services

Printer Friendly  Text Size  A A A



Search

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[QUICK LINKS](#)

[RESEARCH](#)

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[FUNDING](#)

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The RePORT Expenditures and Results Tool (RePORTER)

Search a repository of NIH-funded research projects and access publications and patents resulting from that funding.



RePORTER

[CLICK TO VIEW](#)



AWARDS BY LOCATION



NIH DATA BOOK



FUNDING FACTS



CATEGORICAL SPENDING



REPORT CATALOG



SPECIAL REPORTS



ABOUT REPORT

Research Portfolio Online Reporting Tools (RePORT)

In addition to carrying out its scientific mission, the NIH exemplifies and promotes the highest level of public accountability. To that end, the Research Portfolio Online Reporting Tools provides access to reports, data, and analyses of NIH research activities, including information on NIH expenditures and the results of NIH



[ADVANCED SEARCH](#)

Institute/Center: Fiscal Year: Principal Investigator:
 (Last Name, First Name)

<http://report.nih.gov/>



Find collaborators, home for your applications. etc.

“NIH Re-PORTER”

Which NIH Institute might be interested in my research?

What type of mechanism (e.g., R01, R21, etc.)?

Which Study Section is likely to review my application?

What other similar research was funded by the NIH?

Who are the PIs?

Results

from the entered text. (100 maximum).

Click on chart labels to sort search results by the Institute/Center or Activity Code or Study Section

INSTITUTE/CENTER

Institute/Center	Count
NIDDK	28
NHLBI	22
NIAID	8
NCI	6
NIH	5

ACTIVITY CODE

Activity Code	Count
R01	45
R21	5

STUDY SECTION

Study Section	Count
AICS	9
SAT	9
ZDK1	5
BDPE	3
ODCS	3
HLBP	3

Click on the column header to sort the results

Click here to view detailed Charts

1 of 4 [Next](#) [Last](#) [▶](#) [▶▶](#)

T: Application Type; Act: Activity Code; Project: Ad

ar/Su

Match Score	T	Act	Project	Year	Sub #	Project Title	Contact PI	Project Lead	Organization	FY	Admin IC	Funding IC	FY Total Cost by IC	Similar Projects
☐ 900	5	K08	DK102357	02		EPIGENETIC CHANGES IN BONE MARROW PROGENITOR CELLS IMPAIR DIABETIC WOUND HEALING	GALLAGHER, KATHERINE ANN		UNIVERSITY OF MICHIGAN	2014	NIDDK	NIDDK	\$154,904	
☐ 645	5	R01	DK065073	12		INFLAMMATORY GENE REGULATION IN DIABETIC CONDITIONS	NATARAJAN, RAMA		CITY OF HOPE/BECKMAN RESEARCH INSTITUTE	2014	NIDDK	NIDDK	\$410,903	
☐ 553	5	R01	HL085119	10		ROLE OF CYTOKINE-INDUCED INFLAMMATION IN ENDOTHELIAL	HILL, MICHAEL A		UNIVERSITY OF MISSOURI-COLUMBIA	2015	NHLBI			

Turning discovery into health...



WE WANT YOU!



Links to Resources

The NHLBI webpage

www.nhlbi.nih.gov

FY 2016 NHLBI FUNDING AND OPERATING GUIDELINES

<http://www.nhlbi.nih.gov/funding/policies/operguid.htm>

NHLBI Strategic Visioning

<http://strategicvisioning.nhlbi.nih.gov>

Research Portfolio Online Reporting Tools ([Re-PORTER](http://projectreporter.nih.gov/reporter.cfm))

<http://projectreporter.nih.gov/reporter.cfm>

NIH-sponsored Clinical Trials

www.clinicaltrials.gov

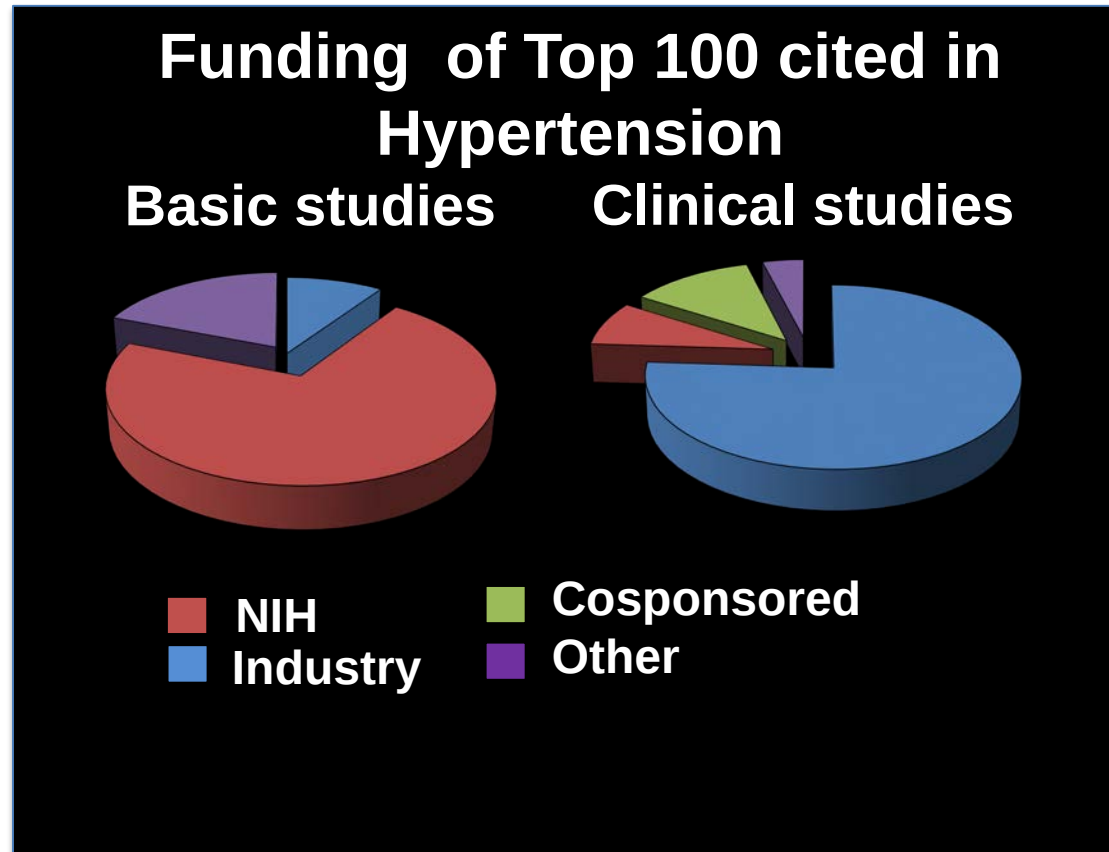


When in doubt.... Google it!



National Heart, Lung,
and Blood Institute

Basic research is essential for development of new therapeutics: Hypertension



Most cited by patents are ALL basic science studies

(n=165, Uehata *et al.*, 1997; n=154, Halushka *et al.*, 1999, n=113, Mullins *et al.*, 1990)

NIH sponsored development of essential building blocks: some NCATS translational programs

Clinical and Translational Science Awards (CTSAs) https://www.ctsacentral.org	National consortium of academic center-associated research bastions focused on the translation and the training of the next generation of academic medicine researchers
Molecular Libraries Program (MLP) http://www.ncats.nih.gov/research/reengineering/ncgc/mlp/mlppc.html	This program gives researchers access to the large-scale small molecule screening capacity, along with medicinal chemistry and informatics necessary to identify chemical probes to study the functions of genes, cells and biochemical pathways.
Bridging Interventional Development Gaps (BrIDGs) http://www.ncats.nih.gov/research/rare-diseases/bridgs/bridgs.html	Previously known as the NIH Rapid Access to Intervention Development (RAID) program, was launched under its new name in October 2011. BrIDGs makes available, on a competitive basis, certain critical resources (synthesis, formulation, pharmacokinetic and toxicology services) needed for the development of new therapeutic agents.
Therapeutics for Rare and Neglected Diseases (TRND) http://www.ncats.nih.gov/research/rare-diseases/trnd/trnd.html	Program to stimulate and speed the development of new drugs for rare and neglected diseases. Research collaborations between NIH and academic scientists, non-profit organizations, and pharmaceutical and biotechnology companies are highly encouraged.
Cures Acceleration Network (CAN) http://www.ncats.nih.gov/funding-and-notices/can/can.html	This program is to advance the development of high need cures and reduce significant barriers between research discovery and clinical trials.
Office of Rare Diseases Research (ORDR) http://www.ncats.nih.gov/research/rare-diseases/ordr/ordr.html	ORDR supports and coordinates rare disease research, responds to research opportunities for rare diseases and provides information on rare diseases.

Getting started with a translational research project: other specific opportunities

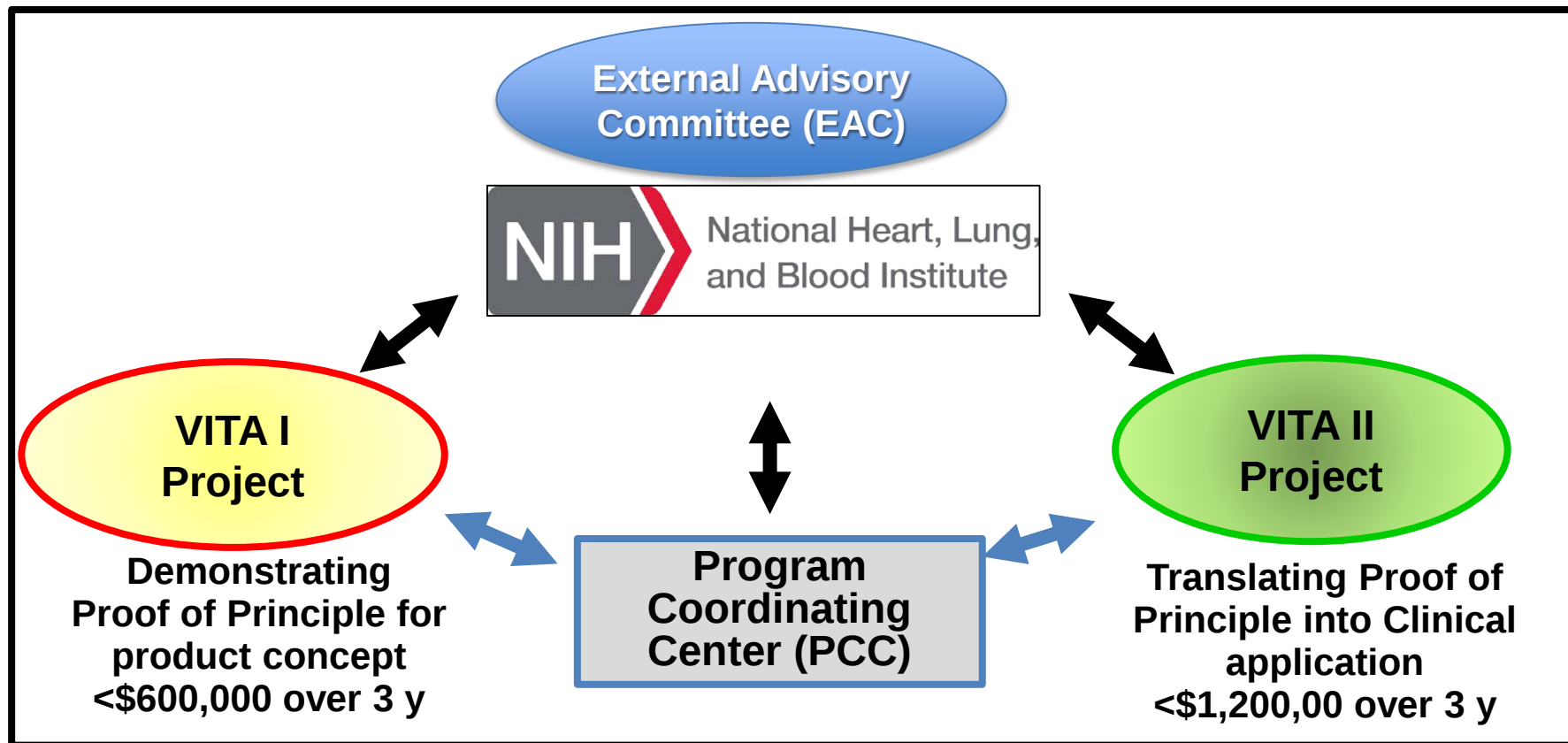
- [Secondary Dataset Analyses in Heart, Lung, and Blood Diseases and Sleep Disorders \(R21\)](#) funding to investigate existing human datasets to test innovative hypotheses relevant to the NHLBI mission. Up for renewal **Scientific contact: Ruth Kirby, RN at Ruth.Kirby@nih.gov**
- [Genetically-Triggered Thoracic and Aortic Aneurysms \(GenTAC\)](https://gentac.nhlbi.nih.gov/) <https://gentac.nhlbi.nih.gov/> **Active Registry** of clinical data and biological specimens. Apply for access directly on website or **contact: Dr. Eser Tolunay, (301) 435-0560, Eser.Tolunay@nih.gov**

How can we do more with less?



Understanding key barriers (and drivers) for major stakeholders

- Academia: tension between publishing and IP, resource fragmentation, lack of know-how
- Biotech/Small private: scarce resources
- Pharma: tension between mission and goals (profit), legacy business model, “The patent cliff”
- Government: multiple constituencies, “red tape,” limited reach
- Investment/Venture: risk adverse (!)
- Consumer/patient: unmet medical needs, wants personalized care, worries about cost of innovation



Offerors: academic, industry, partnership, +/- CRO

Product (offer) types: therapeutics, devices, diagnostics

Solutions for: Vascular disease, Pulmonary hypertension, Thrombotic disorders

Enablers: NHLBI, EAC, PCC

SBIR/STTR Funding Program



PHASE I – R41, R43

- Feasibility Study
- \$225K for 6-12 months



PHASE II – R42, R44

- Full Research/R&D
- \$1.5M for 2 years
- Commercialization plan required



PHASE III

- Commercialization Stage
- Use of non-SBIR/STTR Funds



Bridge and Small Market Awards

- \$1 million per year for 3 years
- Supports products requiring FDA clearance/approval
- Requires matching funds

Contact NHLBI Office of Translational Alliances and Coordination (OTAC)



301-496-2149

nhlbi_sbir@mail.nih.gov





New type of translational program designed to address community's concerns

Perceived need/barrier	Proposed VITA feature
Unmet medical need: widespread disease conditions “neglected” by the industry	Focused on: •vascular disorders •thrombotic diseases •pulmonary hypertension
Many untested early concepts/ideas for medical products	Consider new diagnostics, therapeutic agents, or devices; repurposing
Scarcity of funding for early product concepts	Provide support for very/early stage development

New type program designed to address community's concerns

Perceived need/barrier	Proposed VITA feature
Difficult career decision for academics to engage in early product development	Eliminate requirements regarding PI affiliation with a company
Lack of 'know-how' and/or local access to needed product development resources	Provide needed training and project support regardless of geographical localization (within US)
Diverting NIH money from funding basic research	Increased fiscal responsibility, Contract style (BAA): milestone-driven process, "go/no go" decisions points

Vascular Interventions/Innovations and Therapeutic Advances (VITA)

NHLBI VITA team:

- **Division of Cardiovascular Sciences (DCVS)**, Basic and Early Translational Research (BETR)
 - Vascular Biology and Hypertension Branch (VBHB) : Zorina Galis,* Eser Tolunay,* Yunling Gao,* Cheryl McDonald,* VITA Program Director, Marc Charette, * VITA Program Director
 - Advanced Technologies and Surgery Branch (ATSB): Simhan Danthi*
- **Division of Blood Diseases and Resources (DBDR)**, Thrombosis and Hemostasis Branch, Andrei Kindzelski
- **Division of Lung Diseases (DLD)**: Tim Moore
- **Division of Extramural Research Activities (DERA)**, Office of Acquisitions (OA): Keli Malkin, Janet Mattson, Jennifer Swift, Contracting Officers

(*previous industry experience)

With input from:

Community: “Translational Research in Vascular Diseases,” NHLBI WG, July 2010,
NHLBI Board of External Experts and Council
NHLBI colleagues and leadership