"Innovation to Impact: Beginning the Process"

ATVB/PVD, May 5, 2016

"Turning Discovery into Health: The NIH translation paradigm"

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National Institutes of Health

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National Heart, Lung, and Blood Institute

Conflict disclosures

- No financial conflicts

- **Note**: The opinions presented do not necessarily represent the opinions of the National Heart, Lung, and Blood Institute (NHLBI).

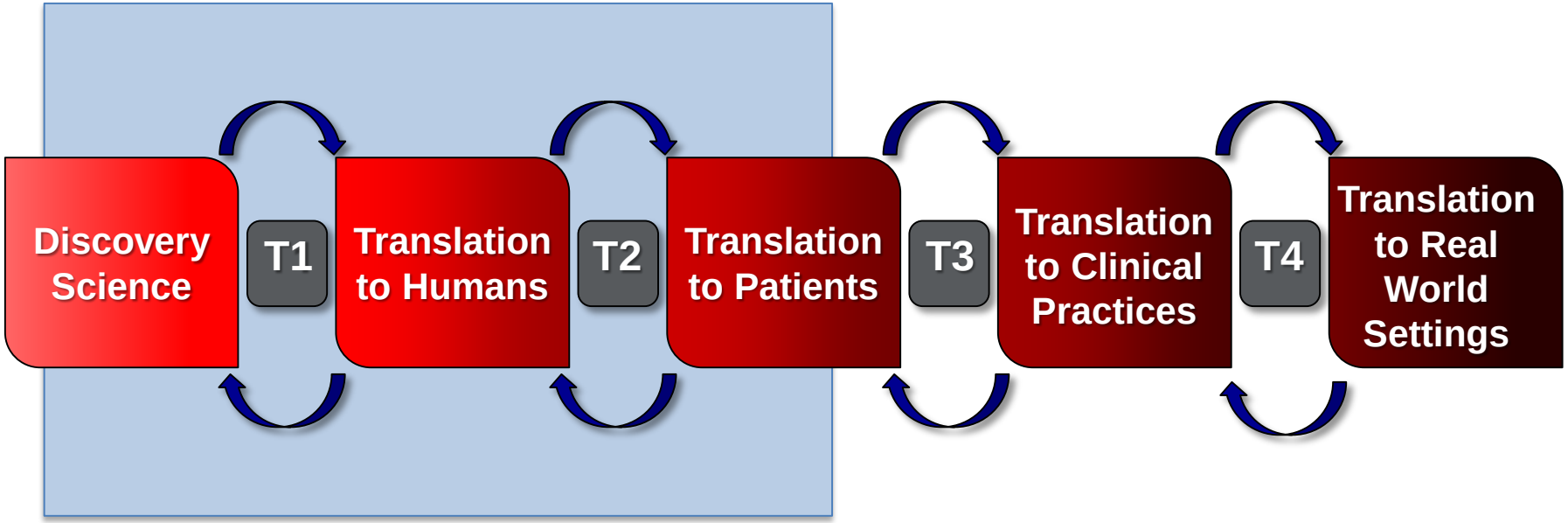
“Turning Discovery into Health”

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

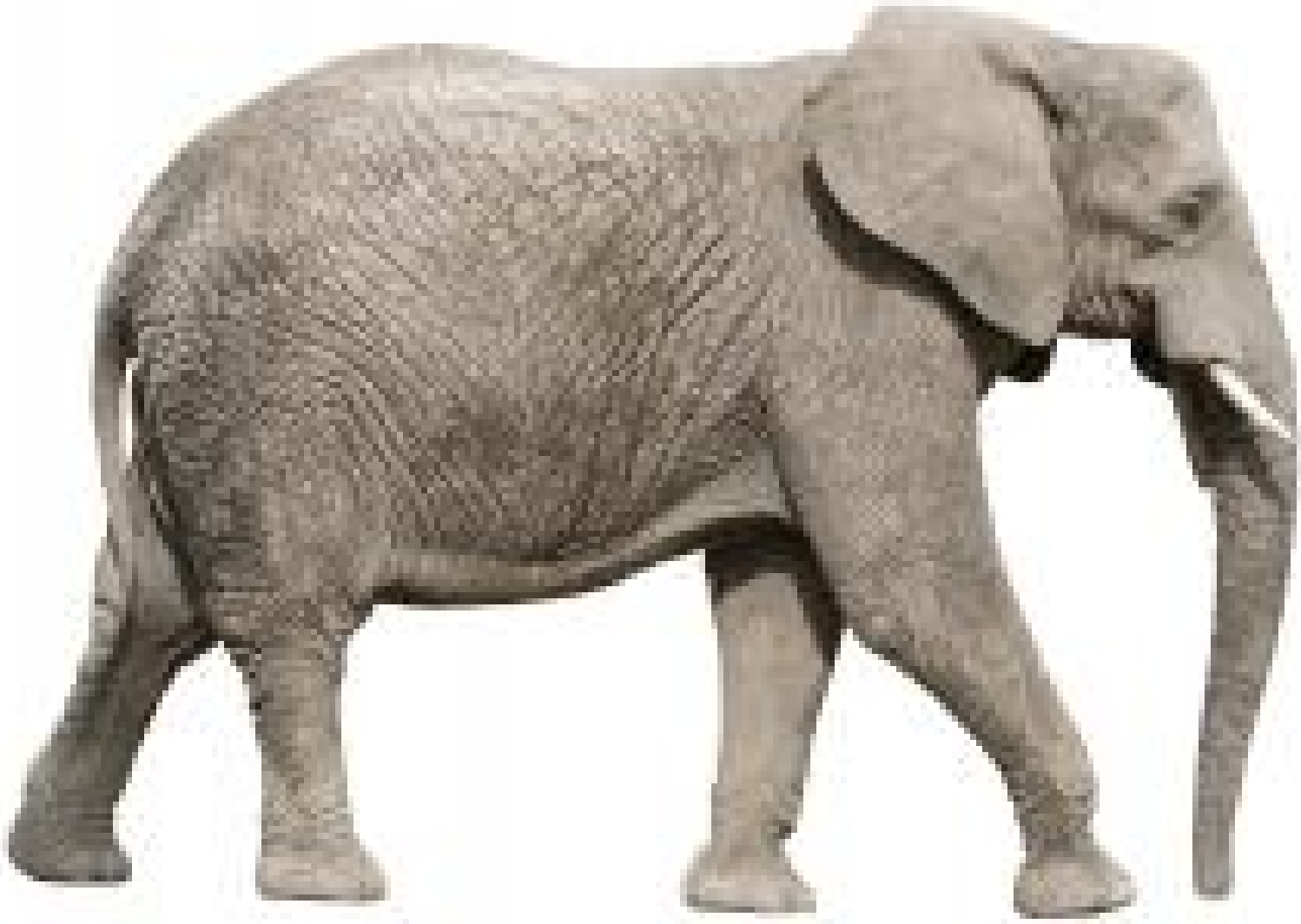
http://www.nih.gov/about/mission.htm

Defining "*Translational research*"

NHLBI FY2016



Who funds US biomedical research?



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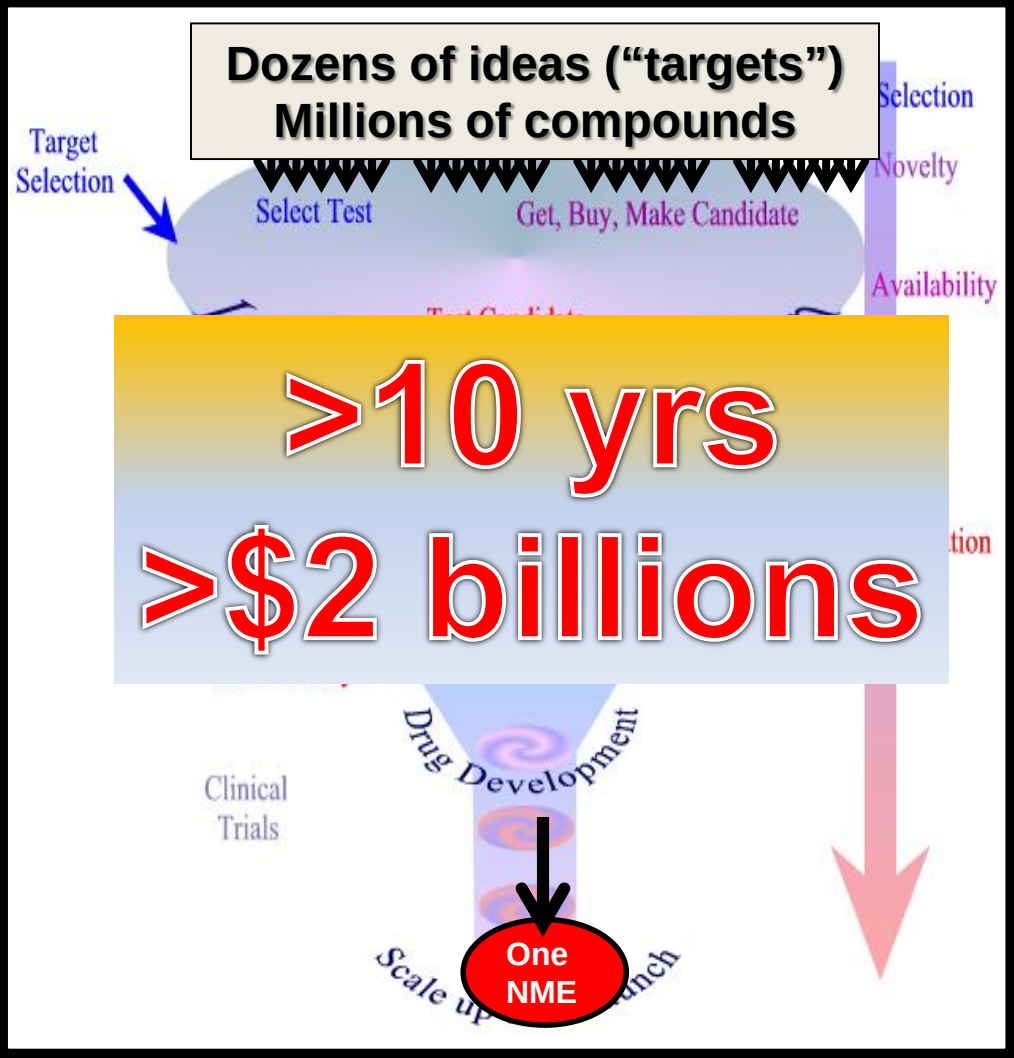
Main contributors to the current paradigm of finding a cure



http://www.w3.org/2004/Talks/0612-sb-wsswapps/slide33-0.html

Academia

Biotech

Pharma

Public funds

The Valley of Death

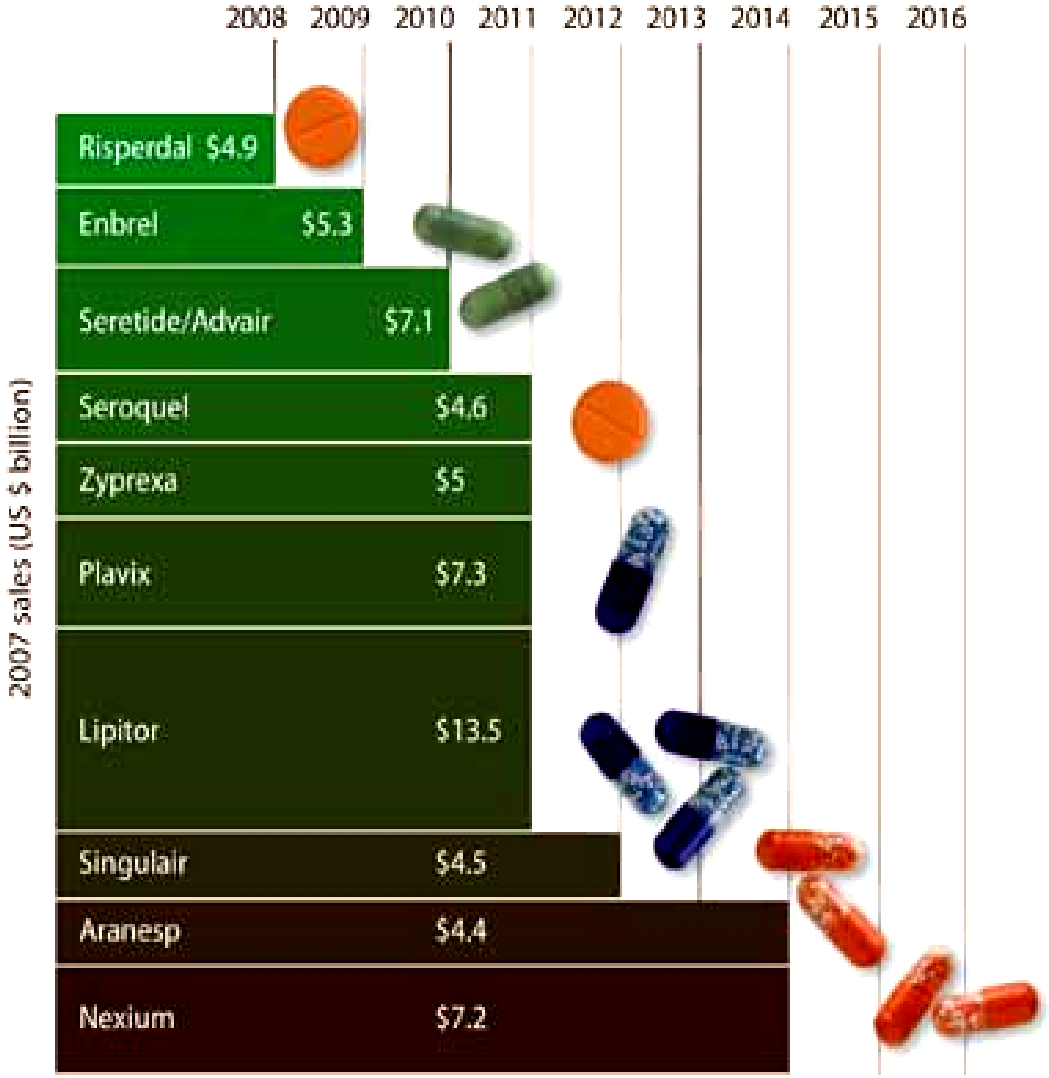
Private funds

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

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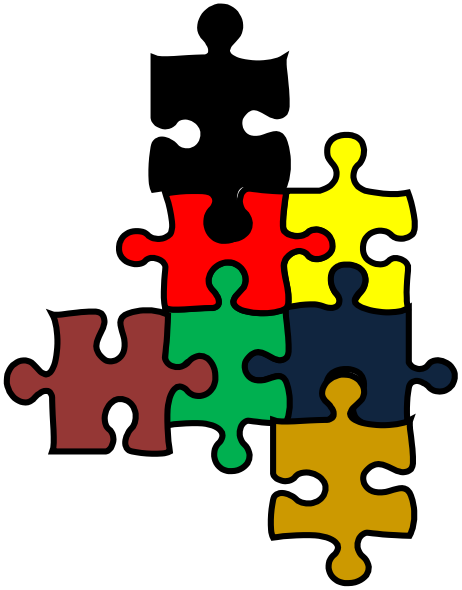
How can we do more with less?

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?

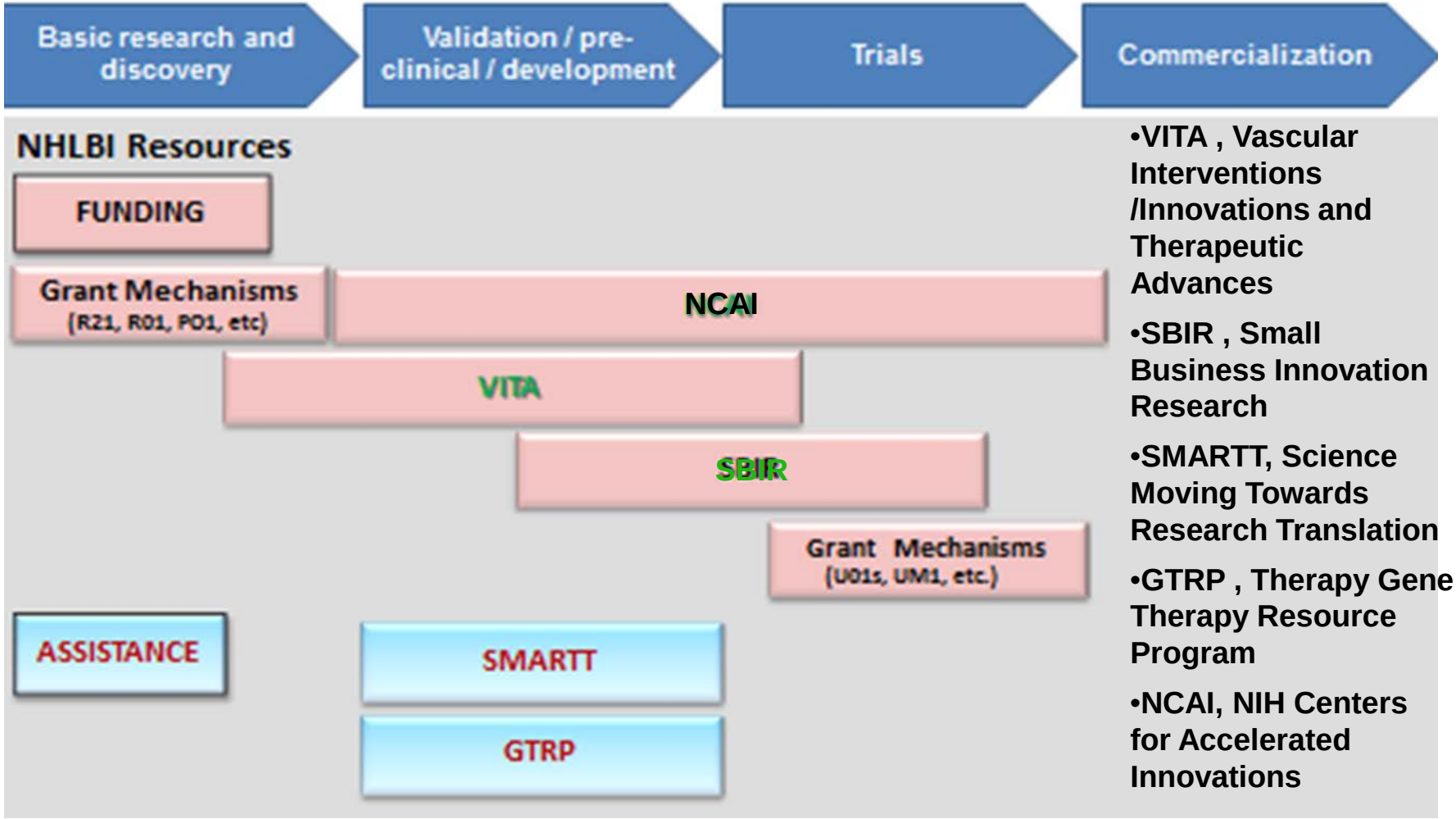
- **What are the developmental/regulatory hurdles in NIH's view?**
- **What is NIH doing about it?**
- **Is the NIH approach working?**
- **What could NIH do to make it better?**

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



- **VITA , Vascular Interventions /Innovations and Therapeutic Advances**
- **SBIR , Small Business Innovation Research**
- **SMARTT, Science Moving Towards Research Translation**
- **GTRP , Therapy Gene Therapy Resource Program**
- **NCAI, NIH Centers for Accelerated Innovations**

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

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"*NHLBI is hearing you*": A biomedical product development sandbox

Vascular Interventions/Innovations and Therapeutic Advances

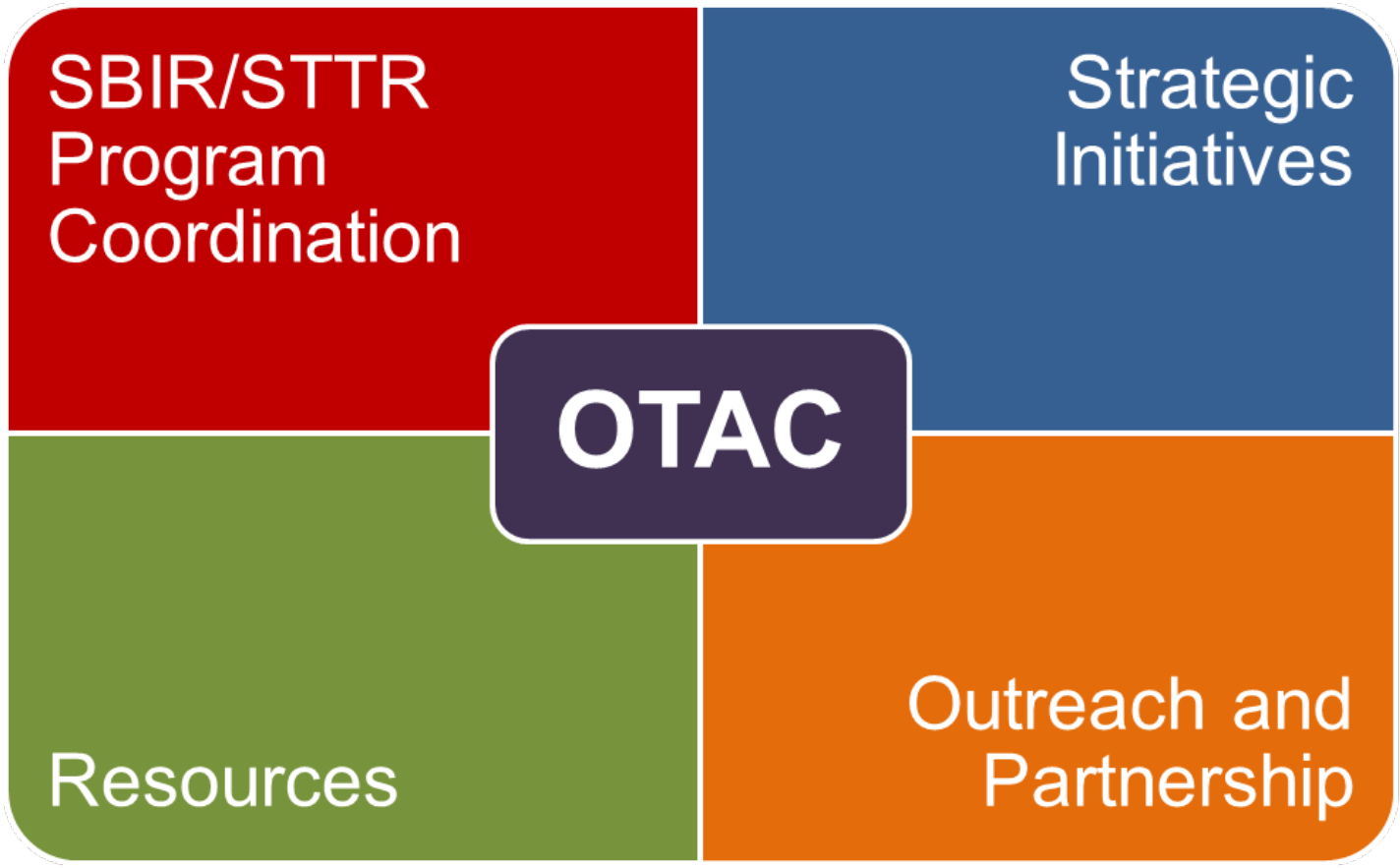
VITA

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

Contact NHLBI OTAC 301-496-2149

NHLBI SBIR-supported Products

CoaguChek®
Because it's my life

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

MENSSANA RESEARCH, INC.

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

ThermoSuit

THORATEC CORPORATION

THERMEDICAL

SERF Ablation System

alphacore pharma

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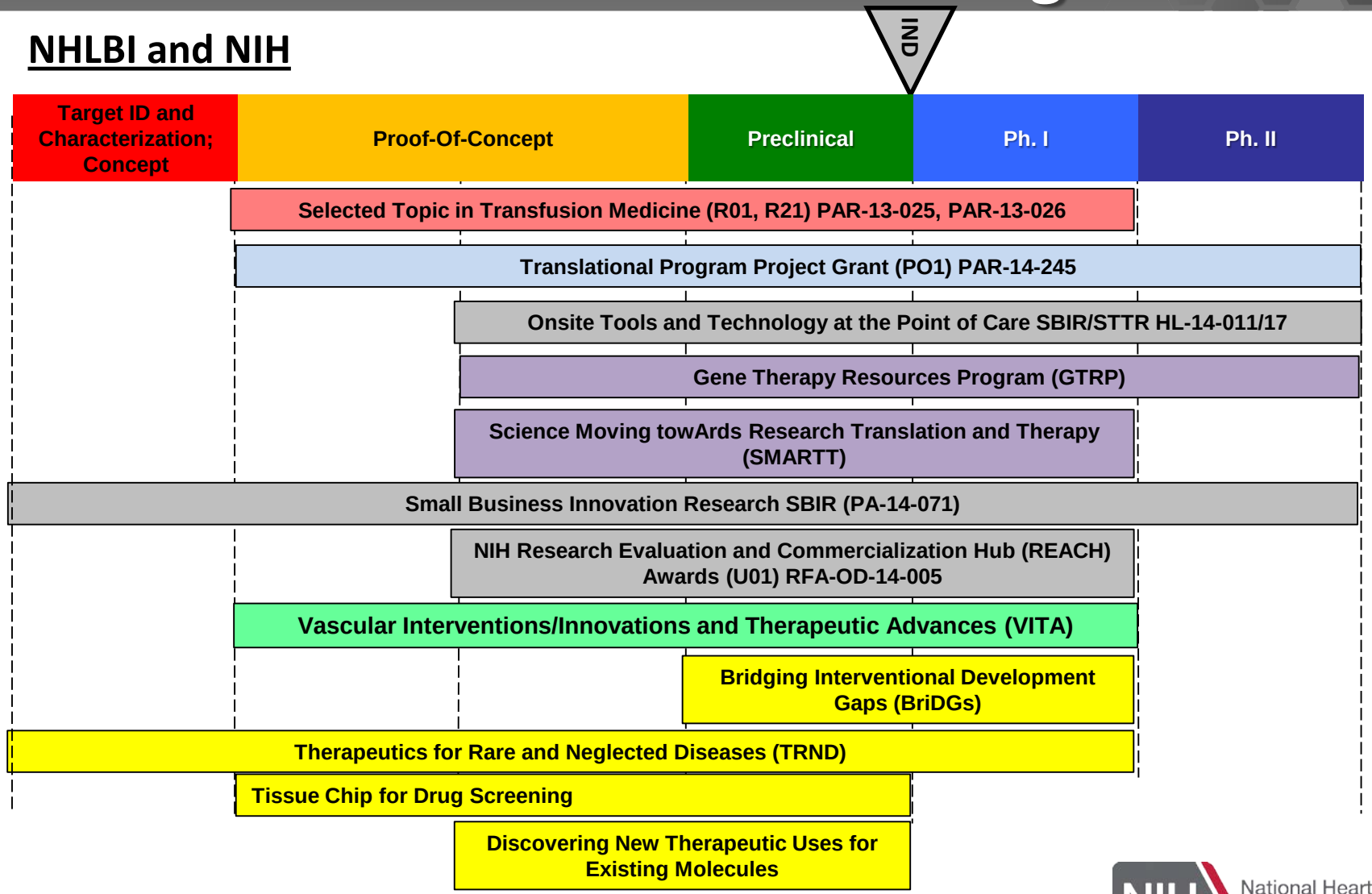
Examples of various translational resources for NHLBI investigators

NHLBI and NIH



c/o NHLBI Translational Research Working Group

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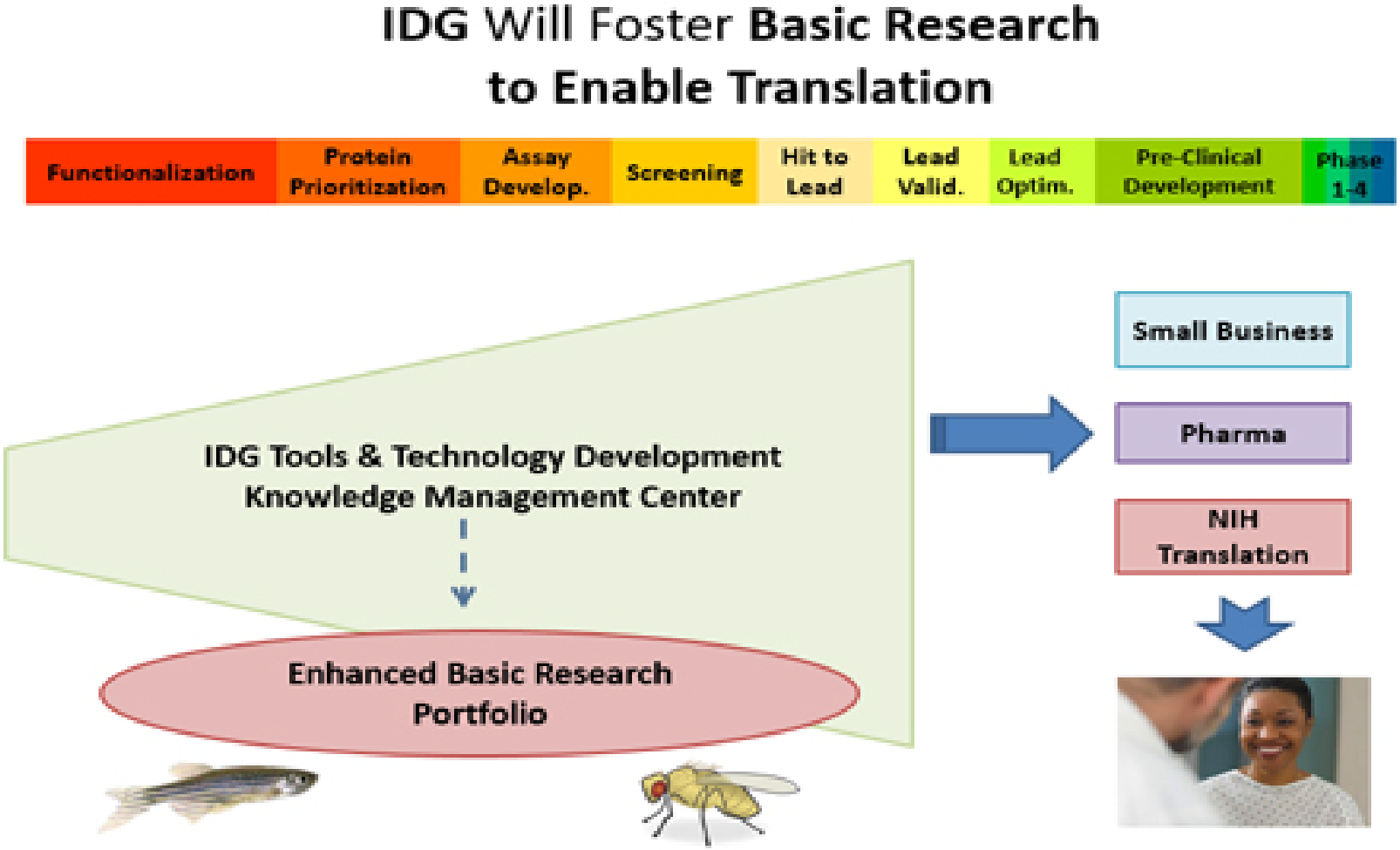
Resources to help you get started with a translational research project: NHLBI repositories

(BioLINCC) 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



http://commonfund.nih.gov/idg/index

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NIH 2015 Precision Medicine Initiative

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

[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

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.

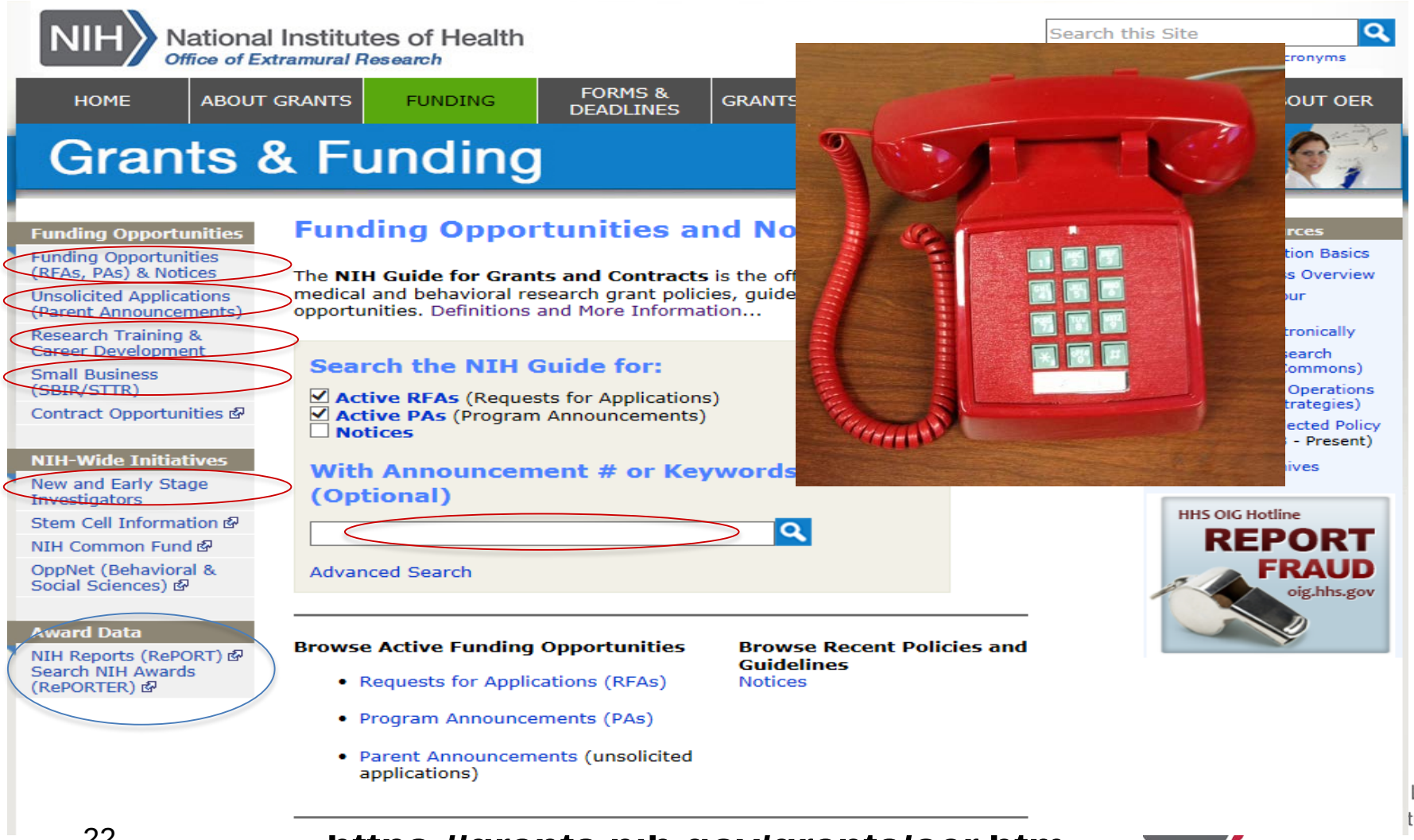
NIH Request for Information (RFI)
Closes May 7th!!

Find potential collaborators and resources available within the NIH Intramural program

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

“Got idea?” Find NIH funding opportunities!

Google: “*NIH funding opportunities*”



https://grants.nih.gov/grants/oer.htm

Specific considerations for clinical research applications

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)

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NIH RePORT

http://report.nih.gov/

National Heart, Lung, and Blood Institute

Find collaborators, home for your applications, etc.

"*NIH …er*"

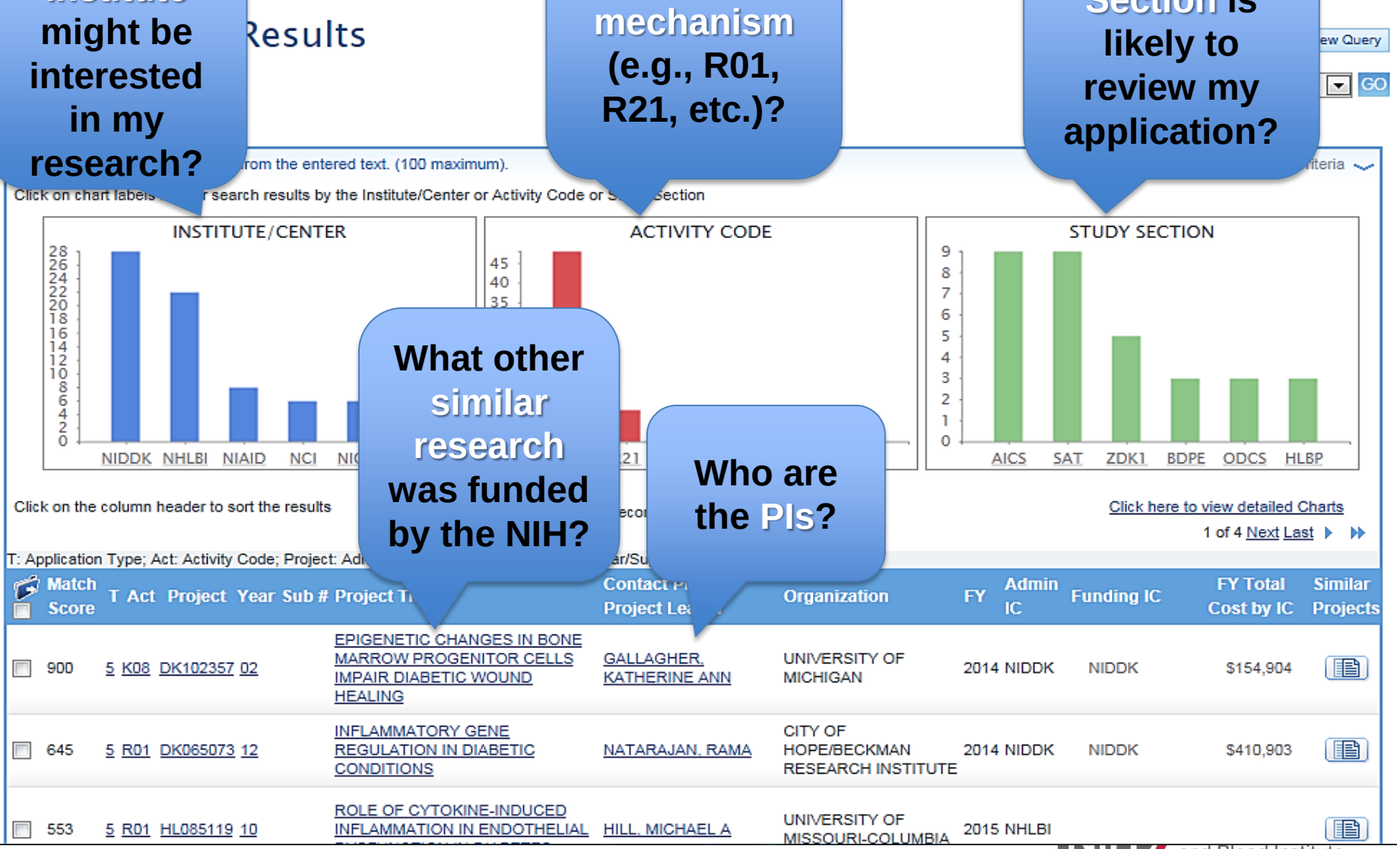
Which NIH Institute might be interested in my research?

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?



Active Awards FY2015 NIH [Re-PORTER]

and Blood Institute

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
NIH-sponsored Clinical Trials
www.clinicaltrials.gov

When in doubt…. Google it!

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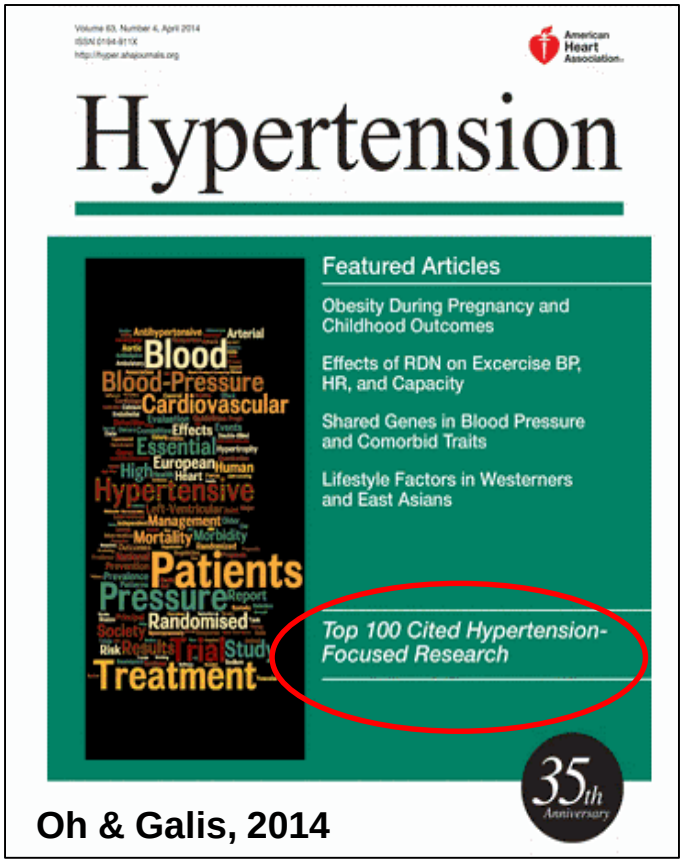
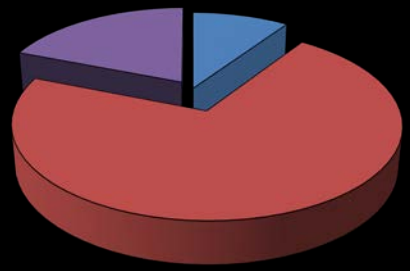
Basic research is essential for development of new therapeutics: Hypertension



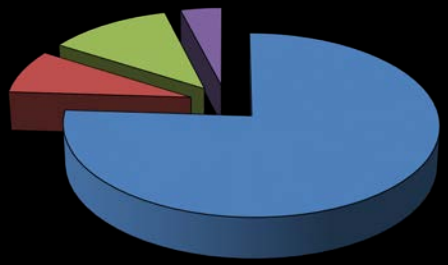
Oh & Galis, 2014

Funding of Top 100 cited in Hypertension

Basic studies



Clinical studies



NIH
Industry
Cosponsored
Other

Most cited by patents are <u>ALL basic science studies</u>

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

>> Presented at *CV Drug Development Think Tank*, July 2014

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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**

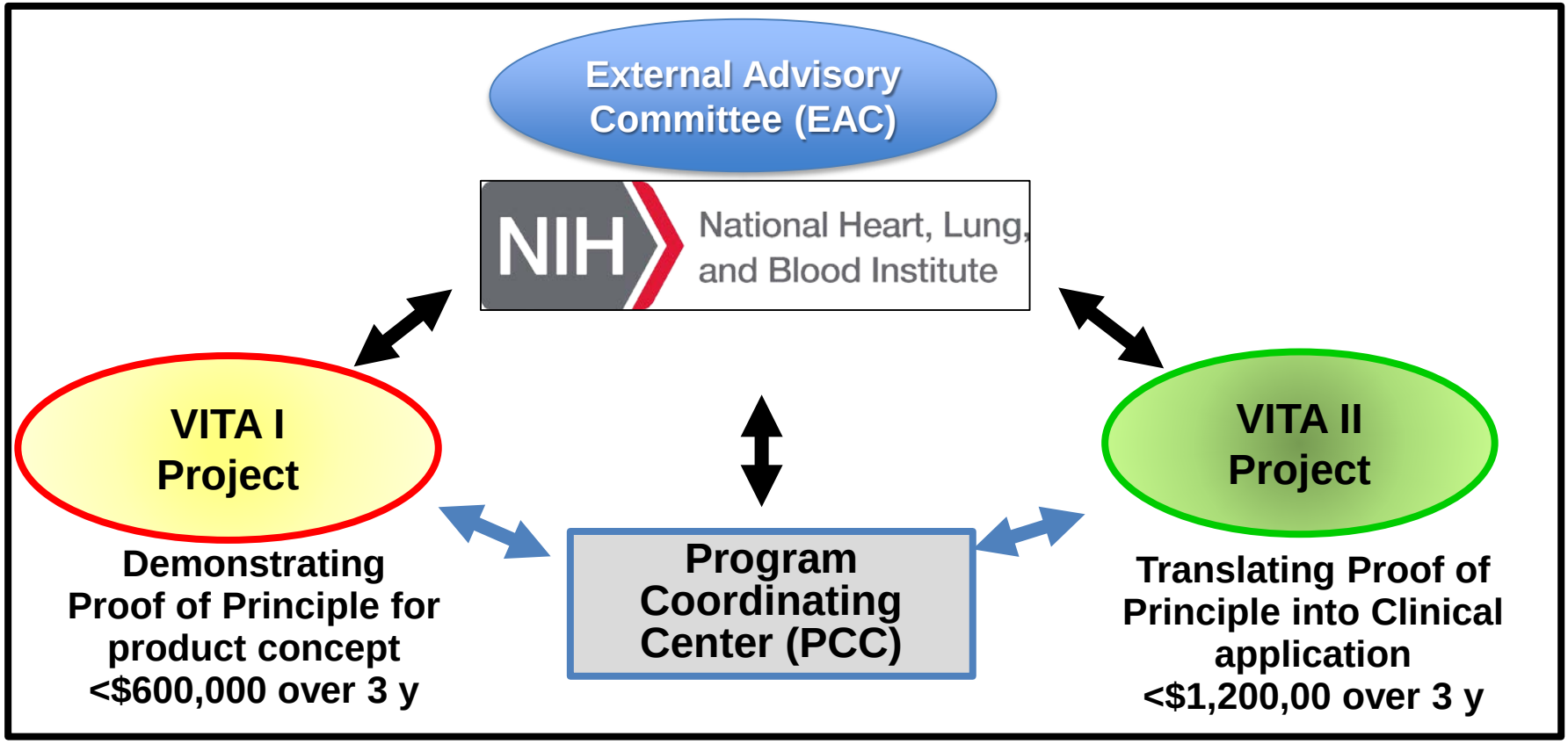
- ***Genetically-Triggered Thoracic and Aortic Aneurysms* (GenTAC) https://gentac.nhlbi.nih.gov/** **Active Registry** of clinical data and biological specimens**.** Apply for access directly on website or **contact: Dr. Eser Tolunay, (301) 435-0560, Eser.Tolunay@nih.gov**

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

Enabling innovation: biomedical product development "cloud"



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

http://www.nhlbi.nih.gov/research/funding/sbir/

VITA

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