



Promoting Innovation in Translational Science

Creating Efficient Knowledge Flows To Benefit Health

Syril D Pettit, MEM
HESI Executive Director

**COLLABORATIVE
CONSORTIA**



**'SUPPORT
INNOVATION'**



Big Ideas

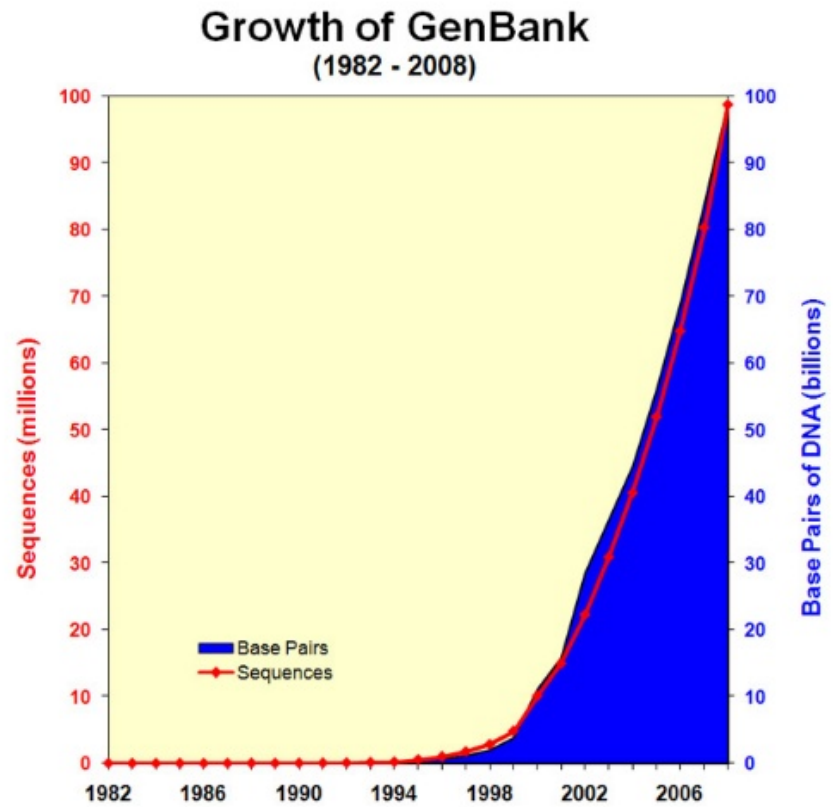
**CALLS FOR
CROSS-DISCIPLINE
PARTNERSHIP**



**CALLS FOR GOVT FUNDED
PUBLIC-PRIVATE EFFORTS**



Massive Growth of Biological Data



<http://www.ncbi.nlm.nih.gov/genbank/genbankstats-2008/>



— EXECUTIVE PERSPECTIVE —

Using “Big Data” to Predict – and Improve – Your Health

By Dr. Greg Steinberg | JUN 26 2014

<http://news.aetna.com/big-data-can-predict-and-improve-health/>

PRESS RELEASES

Japan Big Data Market is Expected to Reach \$1.72 Billion by 2019 - A Report by MicroMarket Monitor

Thursday, 5 Feb 2015 | 8:00 PM ET



FORT WORTH, Texas, February 6, 2015 /PRNewswire/ --

This report on Japan Big Data Analytics market defines the market on the basis of its major components and key driving factors. it provides details about the growth forecasts and challenges for the key players in this region. As per the report, the market in this region is expected grow at an impressive CAGR of 34.1% to reach \$1.72 billion in 2019.

<http://www.cnbc.com/id/102403005#>.

Google Earth Engine Brings Big Data to Environmental Activism

A new forest-mapping tool relies on unprecedented data crunching

By Eliza Strickland
Posted 16 Apr 2014 | 19:53 GMT

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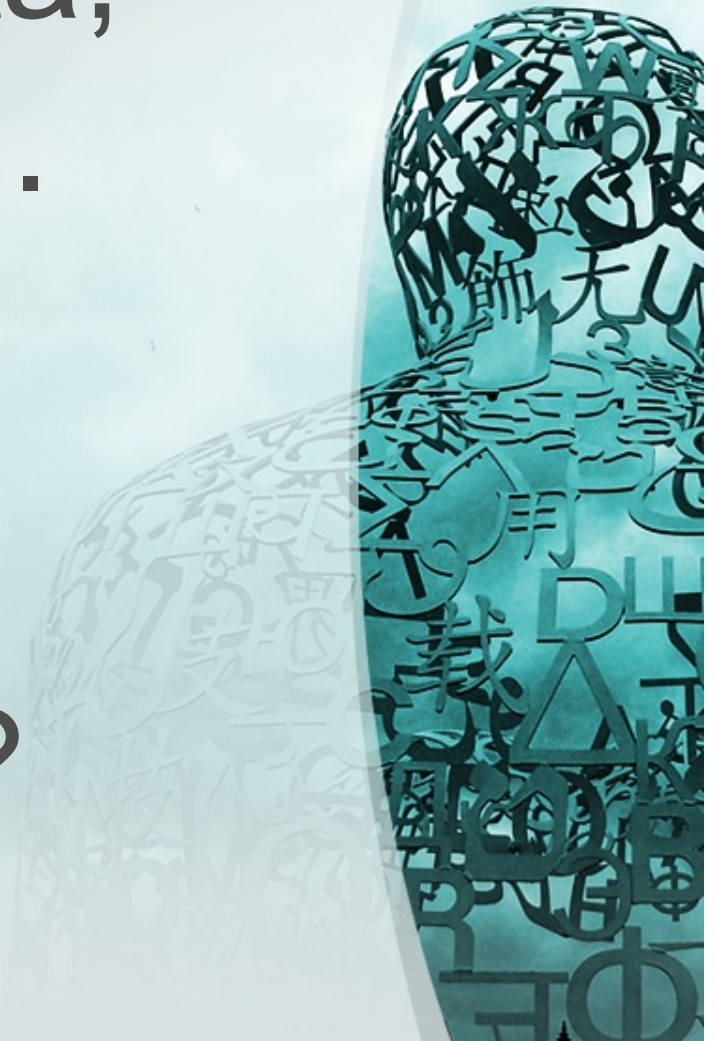
<http://spectrum.ieee.org/>

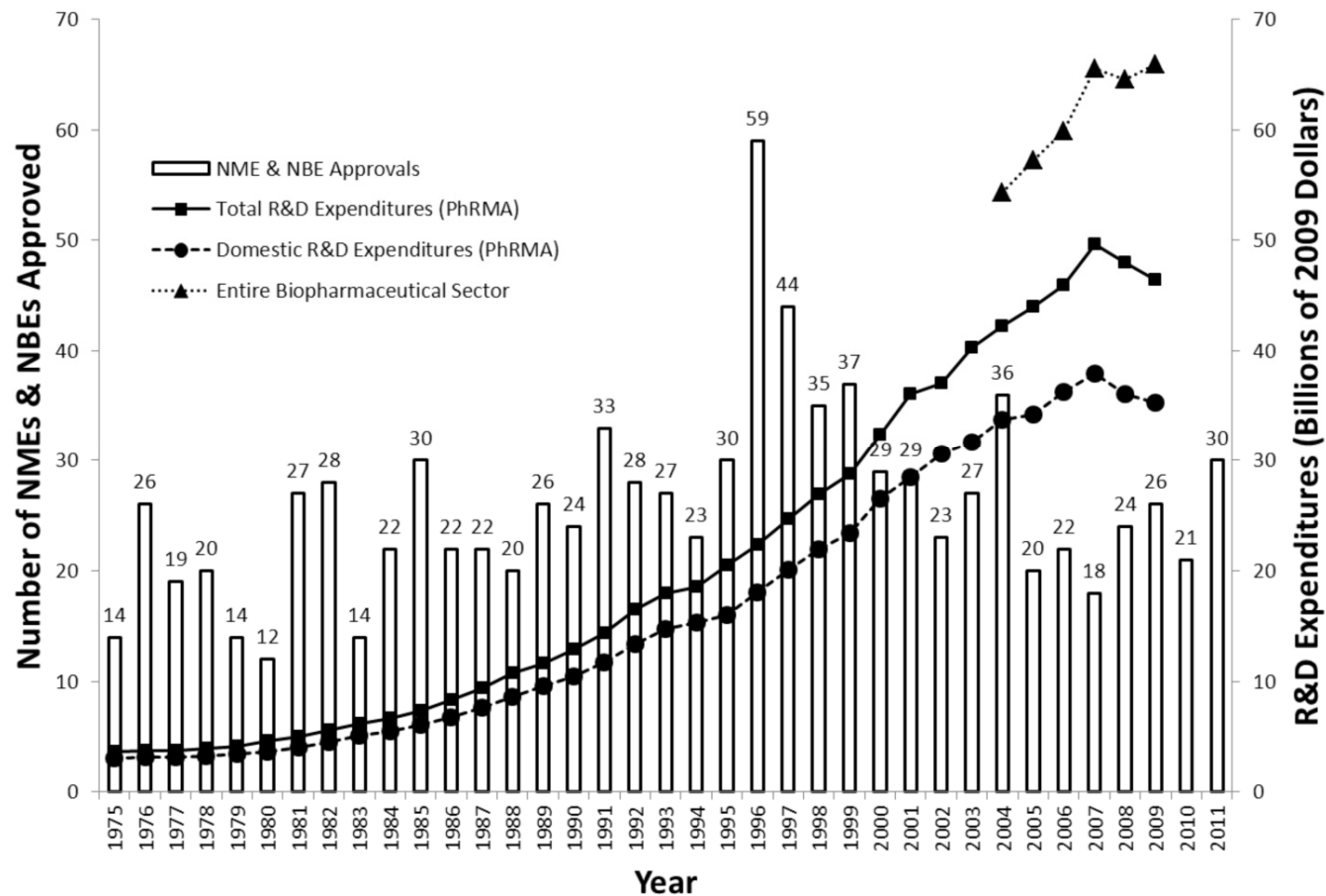




Big Ideas, Big Data, Good Intentions.....

What is the issue?





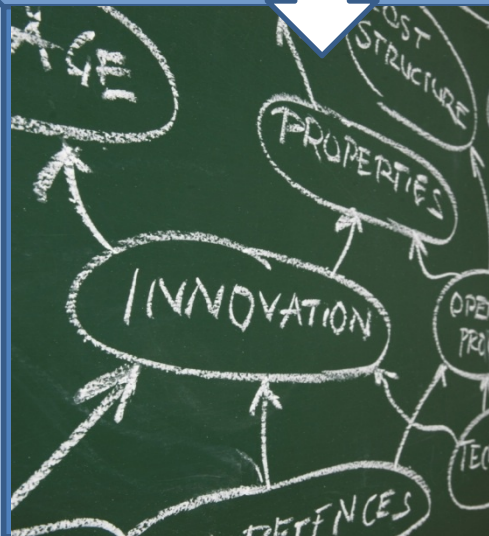
Report to the US president on “*propelling innovation in drug discovery, development and evaluation*”.
US President’s Council of Advisors on Science and Technology. September 2012

TRANSLATION



HUMAN & ENVIRONMENTAL HEALTH NEEDS

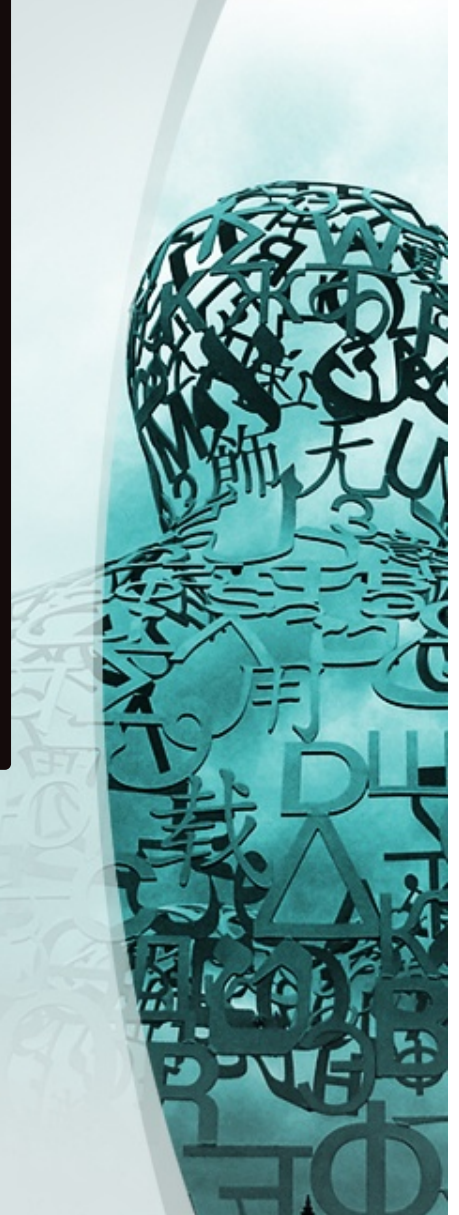
HUMAN & ENVIRONMENTAL HEALTH BENEFIT





CITE

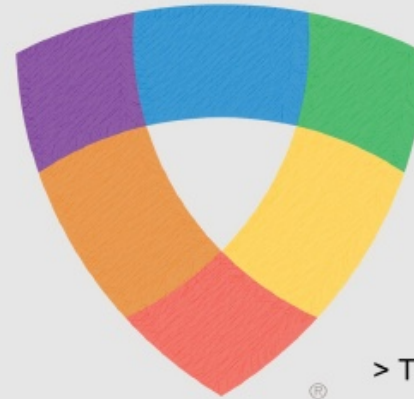
COMBINING INTERDISCIPLINARY & TRANSLATIONAL EXPERTISE





TECHNICAL COMMITTEES

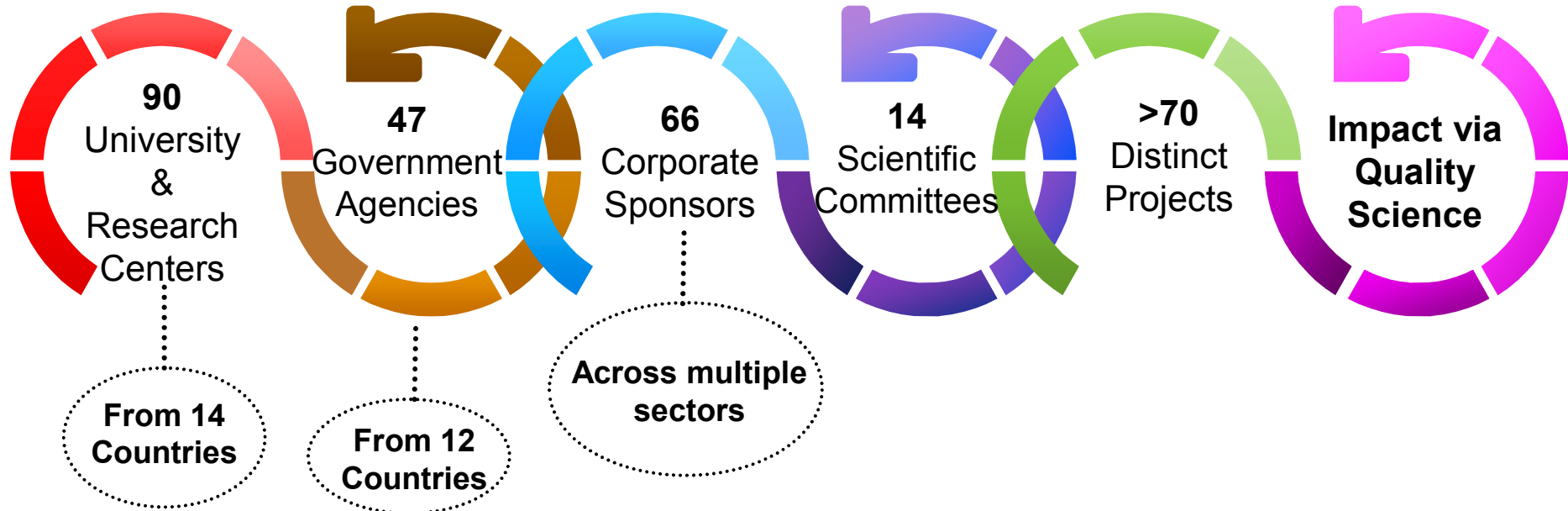
- > Animal alternatives in environmental risk assessment
- > Application of genomics to mechanism-based risk assessment
- > Biomarkers of nephrotoxicity
- > Cardiac safety
- > Developmental and reproductive toxicology (DART)
- > Development of methods for a tiered approach to assess bioaccumulation of chemicals



- > Genetic toxicology
- > Immunotoxicology
- > Protein allergenicity
- > Risk assessment in the 21st century (RISK21)
- > Sustainable chemical alternatives
- > Translational biomarkers of neurotoxicity
- > Use of imaging for translational safety assessment

Emerging Issues Subcommittee

- > Framework for intelligent non-animal methods for risk assessment





HESI Mission

Create science-based solutions for a sustainable, healthier world.

**Accurate
and Efficient
Chemical
Risk
Assessment**

**Safe and
Effective
Medicines**

**Environmental
Quality and
Sustainability**

Food Safety



Protecting sensitive populations

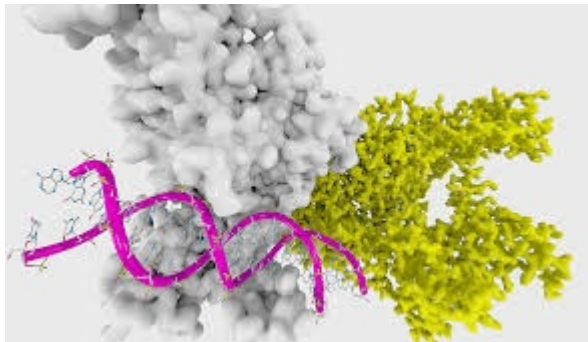


Supporting ecological and human safety of essential food resources

Sustaining critical environments



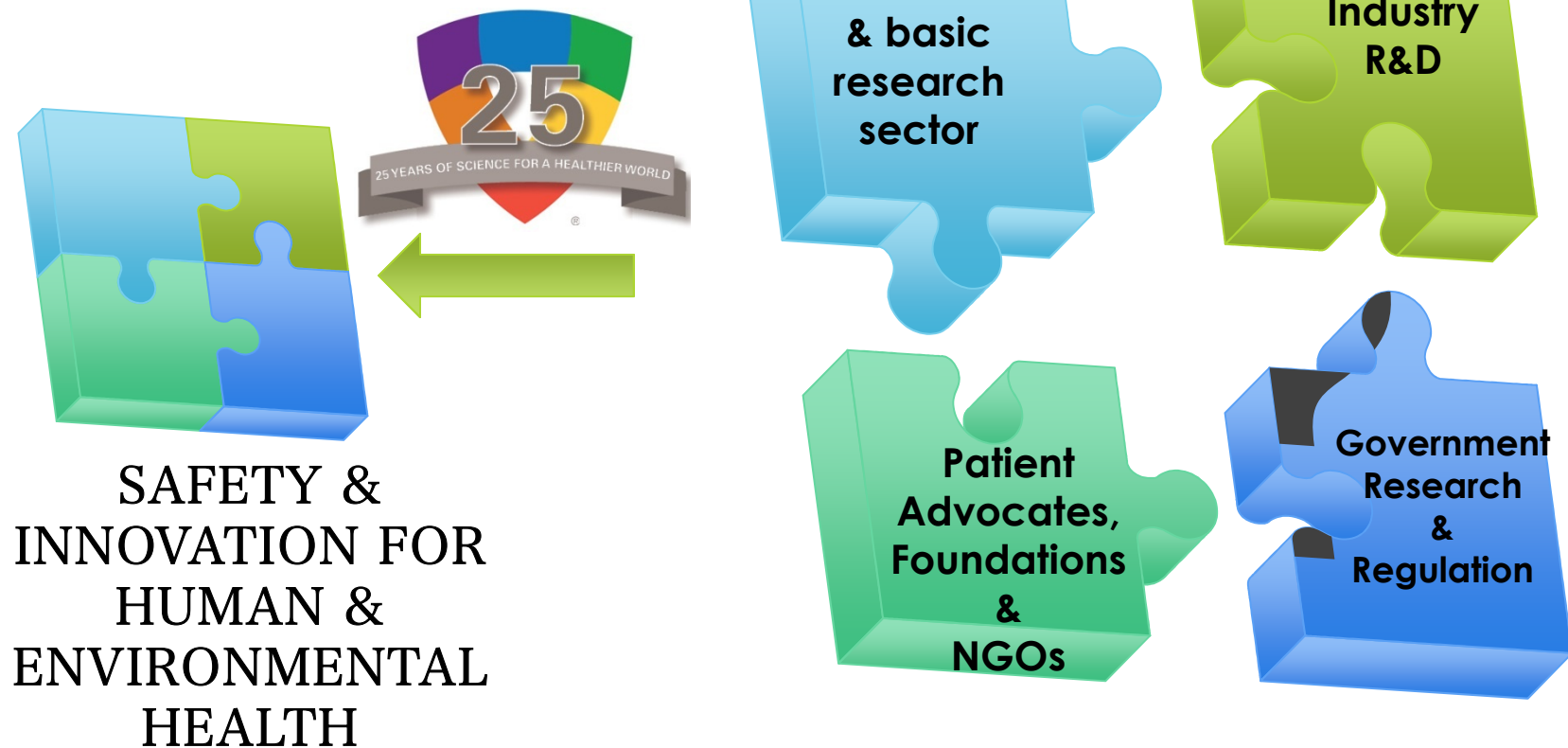
Predicting and Protecting Against Adverse Effects from Chronic Exposures



Promoting Discovery

The HESI Model:

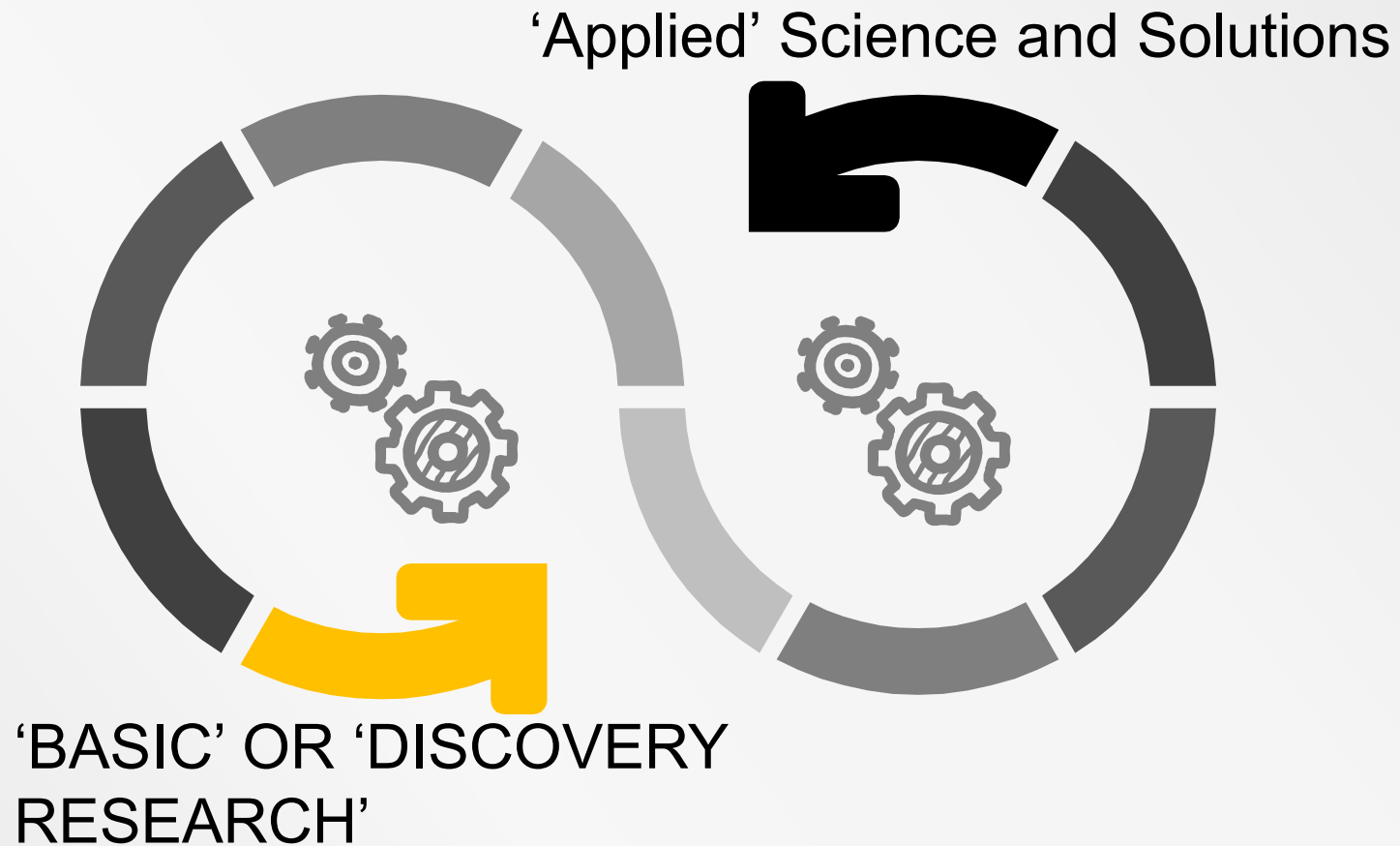
Bridging Research to Application



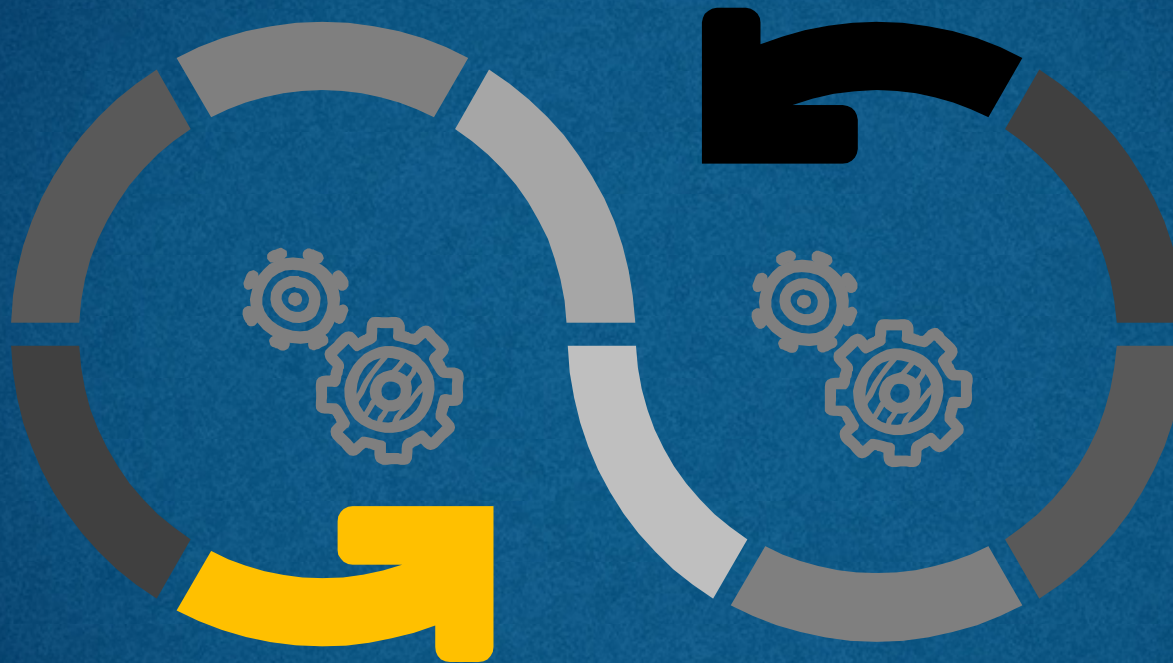
What have we
observed at
HESI
as a
cross-section of
scientific
community?



NOT A CONTINUUM: WHY NOT? HOW TO FIX?

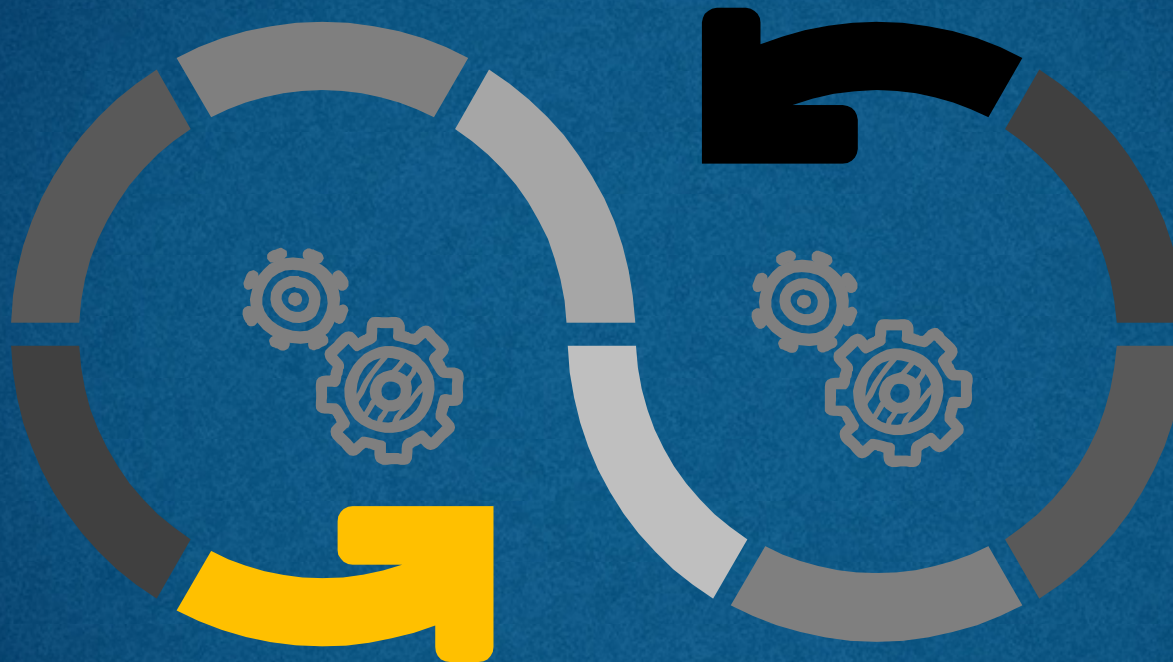


Drug Safety & Discover: Bench to Bedside



Chemical, Consumer, Ag Products: 'Cradle to Grave'

How do we extend this thinking to make it more of a
CONTINUUM WITH MULTIPLE EXCHANGES?



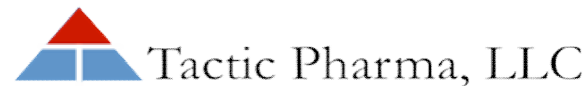
A NEW Translational PARADIGM?

Design, Execution, Knowledge-Sharing

To Increase Health Benefit & Efficiency



Workshop participants
December 6-7, 2012
Arlington, VIRGINIA



**As a Scientific Community: How do we do a better job at moving
research to application:**

Efficient Resources, Effective Solutions

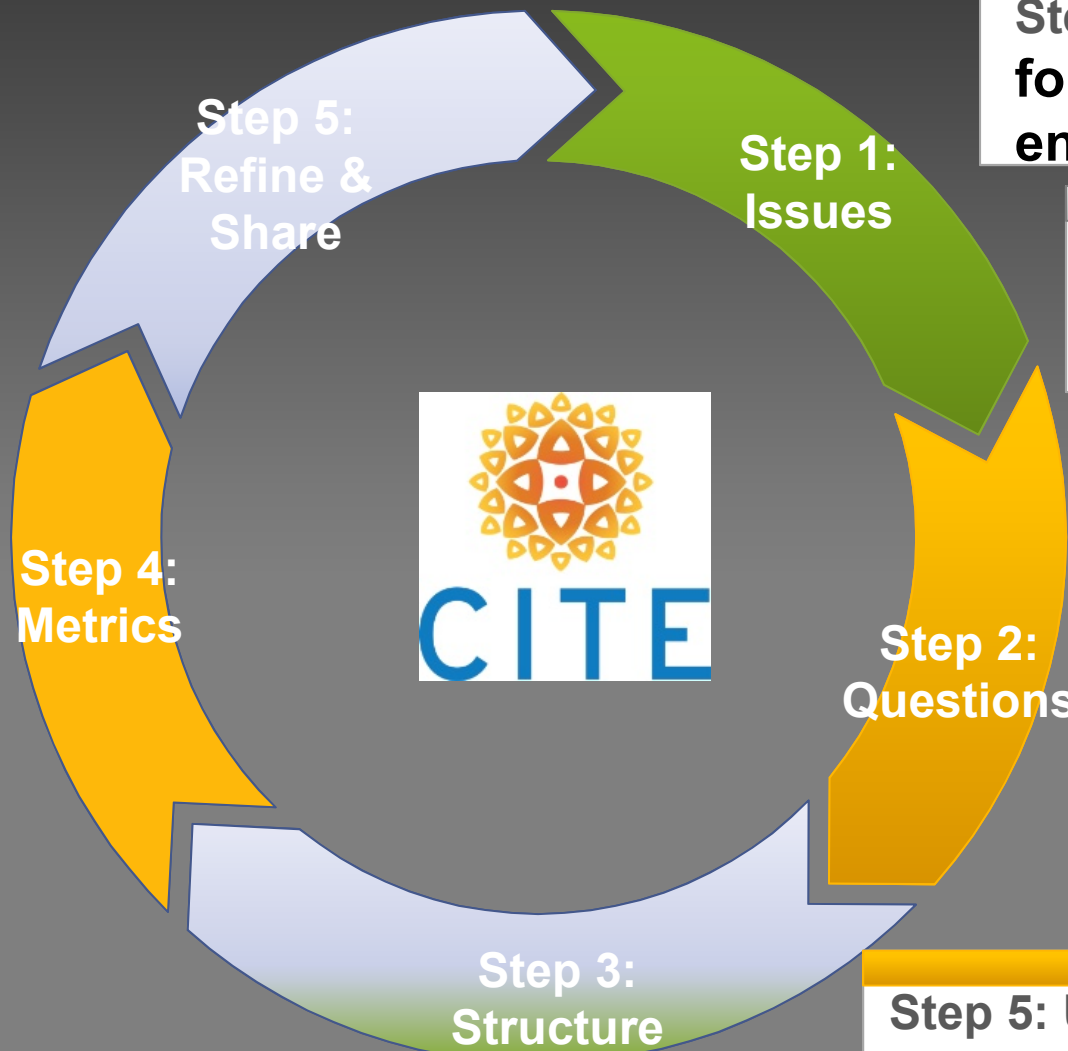


CITE

- **Multi-sector**
 - Academe, industry, government, foundations, global NGO
- **Multi-Discipline**
 - Drug, Chemical, AgChem Research
 - Business
 - Grants and Financial Capital
 - University Management
 - Regulatory
 - Legal
 - Economic
 - Program Management
 - Entrepreneurship
 - Publishing

**Common Challenges
Across Disciplines
and Sectors
Formed basis for
Recommendations**

TRANSLATIONAL SCIENCE KNOWLEDGE-CYCLE



Step One: Identify the foundational human or environmental health issue

Step Two: Define Researchable Question that is Fit for Purpose

Step 3: Structure the Right Environment for Success

Step 4: Establish Metrics to Drive & Assess Progress

Step 5: Use Outcomes to Inform Priority Issue and/or Refine Process Moving Forward

Challenge

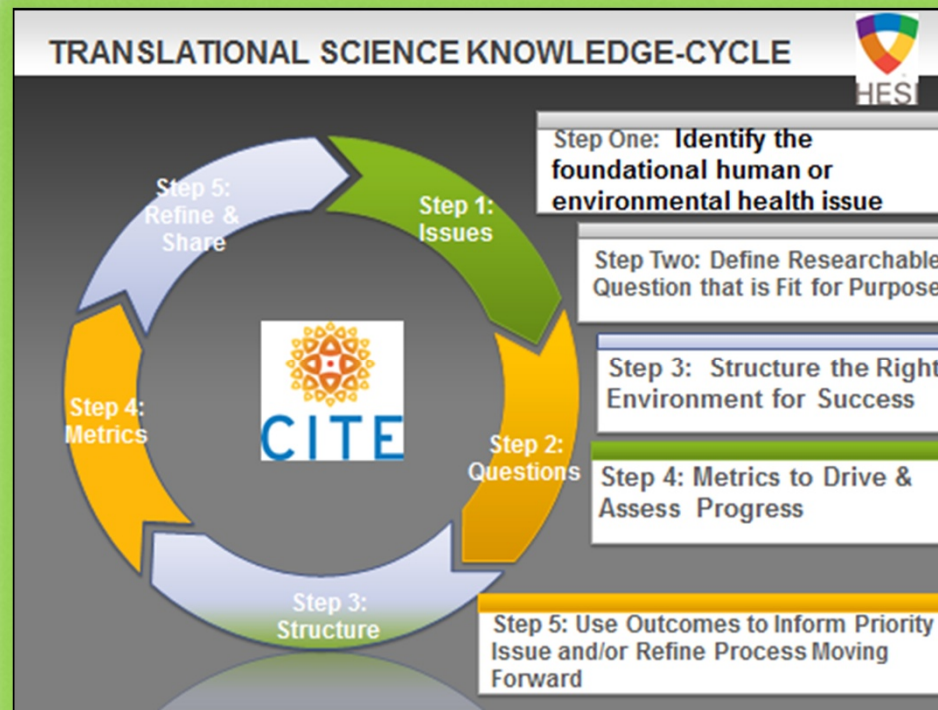
How to maintain clear 'lines of sight'
from research focus to critical health
and environmental issues

(TSK Step 1 & 2)

*Are we doing the
right stuff?!*

Opportunity

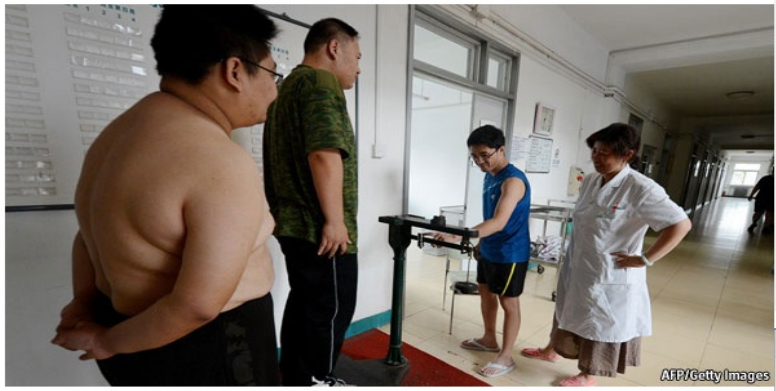
Increase relevance
and efficiency of
meeting health
challenges.



Resources for Defining Central Health Issues...

Global health
Lifting the burden
 People are living longer than ever before. But what they are dying of is changing in ways doctors have few answers to
 Dec 15th 2012 | From the print edition

Like 334 | Tweet 79



www.thelancet.com Vol 380 December 15/22/29, 2012

- Supported by Gates Foundation
- 50 countries
- 7 partners including U of Tokyo

Human Health: One Example.... ‘Global Burden of Disease Report’

Data Rich

- Measured DALYs – (disability adjusted life year) re: ill health, disability or early death
- #1 is ischemic heart disease - just 20 years ago this was #4.
- Significant increase in stroke risk (#5 to #3)

GBD 2010: understanding disease, injury, and risk

Publication of the Global Burden of Disease Study 2010 (GBD 2010) is a landmark event for this journal and, we hope, for health. The collaboration of 486 scientists from 302 institutions in 50 countries has produced an important contribution to our understanding of present and future health priorities for countries and men, are dying in far higher numbers than previously appreciated. But the most afflicted continent remains Africa. Here, maternal, newborn, and child mortality, along with a broad array of vaccine-preventable and other communicable diseases, remain urgent concerns. GBD 2010 also puts an important spotlight on

See Comment pages 2054, 2055, 2058, 2060, 2062, and 2063
 See Special Report page 2067
 See Articles pages 2071, 2095, 2129, 2144, 2163, 2197, and 2224



Ecosystem Services

Volume 12, April 2015, Pages 1–15



Exploring connections among nature, biodiversity, ecosystem services, and human health and well-being: Opportunities to enhance health and biodiversity conservation *

Paul A. Sandifer^{a,1}, Ariana E. Sutton-Grier^{a,1}, Bethney P. Ward^c

Show more

doi:10.1016/j.ecoser.2014.12.007

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The Fourth Basic Environment Plan

Cabinet Decision on April 27, 2012

Ministry of the Environment, Japan

UNEP perspectives for GEF-6 Programming priorities

By Maryam Niamir-Fuller



In the preparation of its own Medium Term Strategy for 2014-2017, the United Nations Environment Programme has undertaken a comprehensive consultative process to determine priorities for action on global environmental issues, and to identify emerging issues. The results can be of significant importance to helping to better define the programming priorities for the GEF-6 funding replenishment period, which runs from 2014 to 2018.

‘Effects of individual activities can combine and interact with each other to cause aggregate effects...’

Defining
Environmental
Health &
Quality
Priorities

Once we have the 'Big Issues' How to move to 'Researchable Questions'

DRIVERS

- *Resources*
- *Grant Opportunities*
- *Geography*
- *Commercial Interests*
- *Expertise and Interests...*

Define the Issue
Define the Question...

What is new about
that?



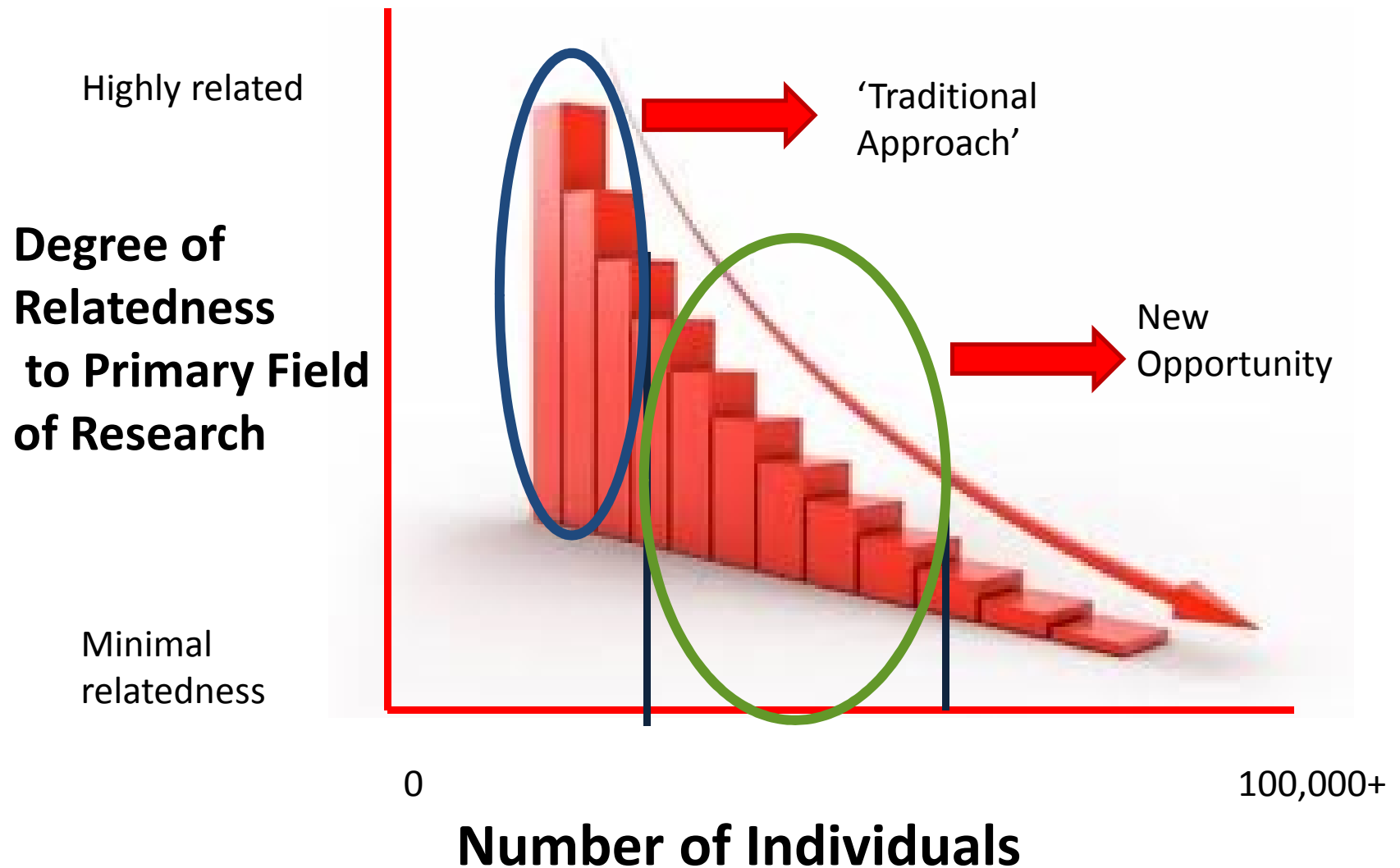
Have we asked the
right question...

...in the right way
and to the right
people?

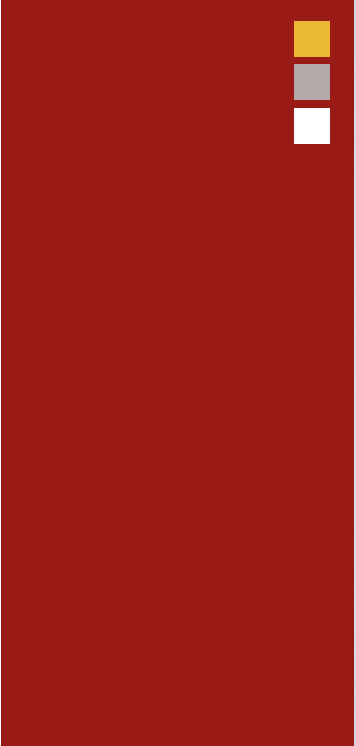
Can we use multi-
disciplinary input in
approaching the
question ...

To innovate the way
we get to an answer.

The tail of innovation: Untapped 'Solvers' and Expertise



First step in building a toolbox

- 
- Provide example to academic community
 - Address feasibility of sourcing and framing a problem
 - Demonstrate ability, creativity and speed of an external solver community
 - Produce a practical, concrete deliverable
 - Wide, active broadcast to *untraditional* solvers

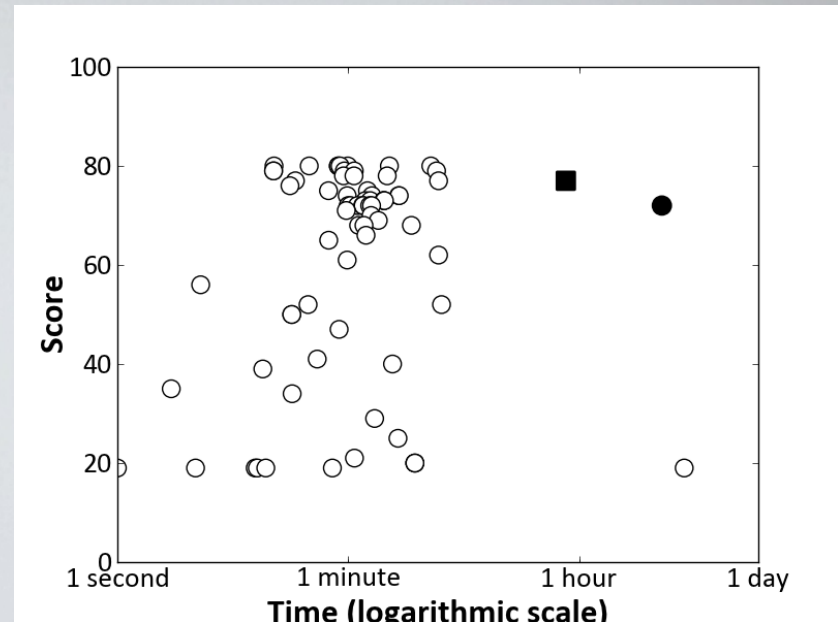
Provided by Eva Guinan, MD, Dana-Farber Harvard Cancer Center



Algorithm development contest

- ❖ Objective: Improve on NIH MegaBlast algorithm for nucleotide sequence alignment
 - ❖ Experiment: Generate and evaluate external solver participation in development of sequence annotation tools applied to immunoglobulin and antibody genomics
 - ❖ Two week long competition - \$2000 prize pot x 3
-
- ❖ TopCoder – “a place to create. The world’s largest competitive community for software development and digital creation. The TopCoder Community is 202,124 strong.”

- 122 coders submitted 654 submissions
- speed exceeded state of the art by $10^2 - 10^5$
- accuracy improved
- 89 different approaches identified
- winners from Russia, France, Egypt, Belgium & US
- annotate 10 million sequences in < 3 mins; quarter billion sequences in ~ 1 hr on laptop



Results show the long-tail and discovery of extreme value outcomes relatively quickly

Innovative
approaches to
defining questions &
'solver communities'
can bring new value



Challenge

How to create the right structure to support research success?

(TSK Step 3)

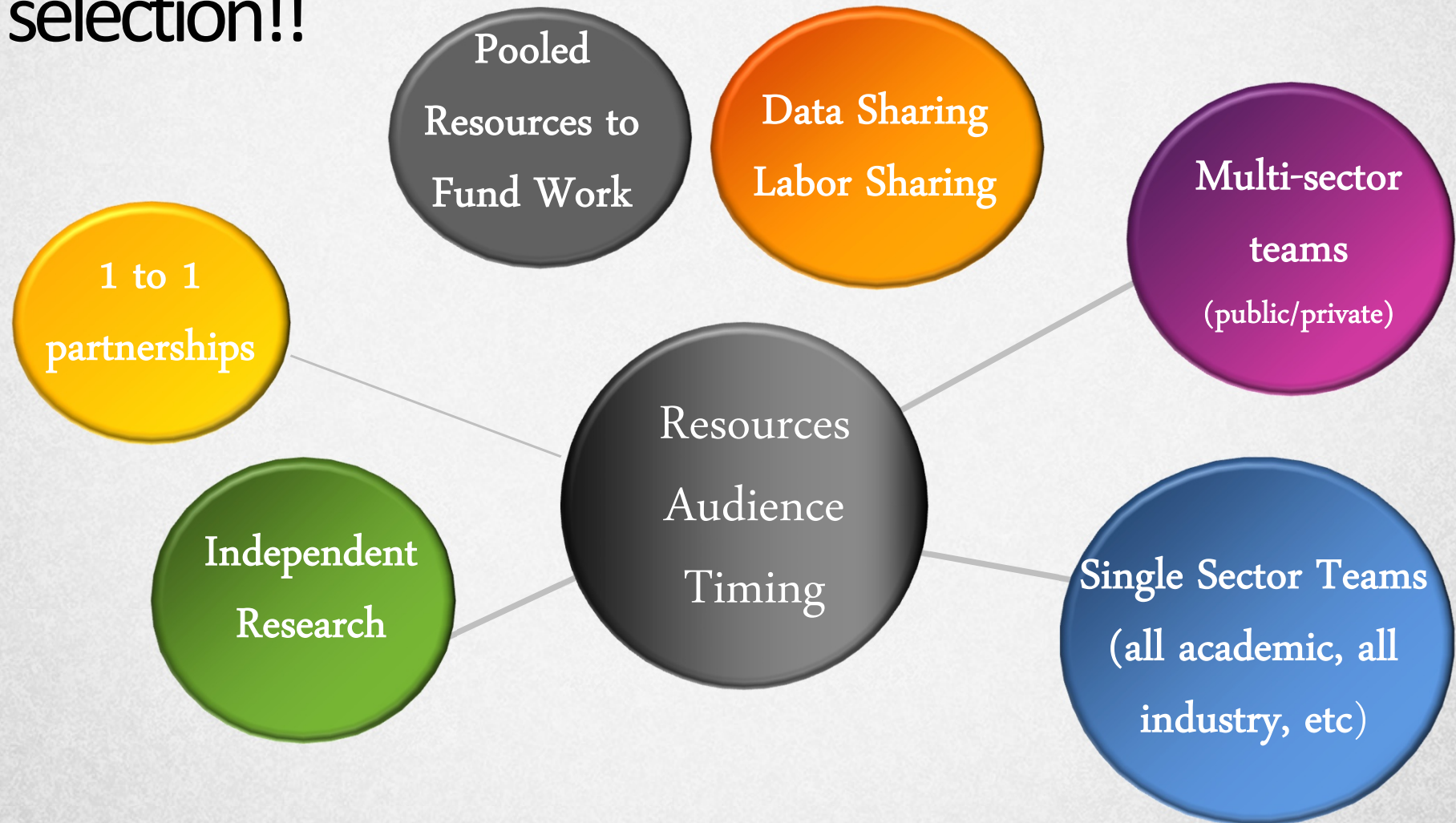
How do we get this done?!

Opportunity:

Learn from & share experience on the right design model for the right challenge

Collaboration Models

Share experiences to help inform future selection!!





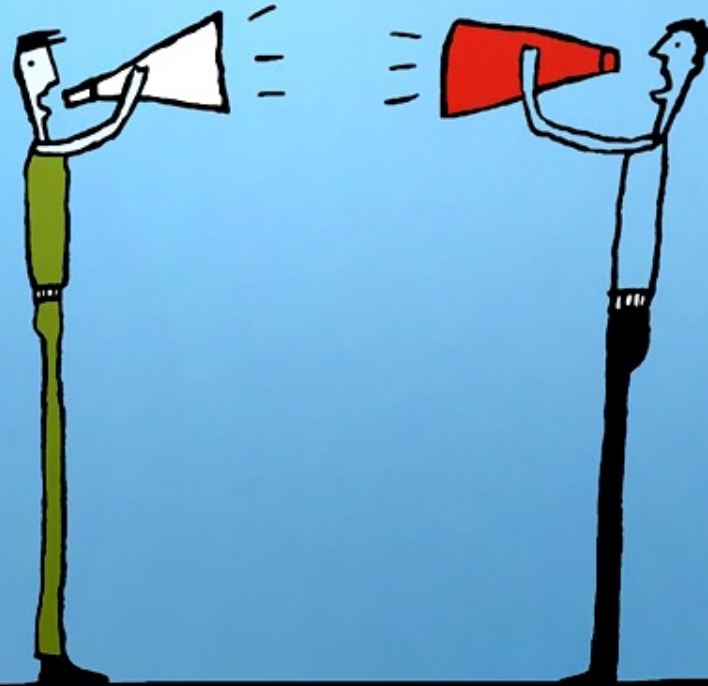
Model Selection Considerations...



WHO IS THE AUDIENCE?

**WHAT ARE THEIR INTERESTS AND
BIASES?**

*trust, credibility, need to 'speak the
same language'*



Faster Outputs

Broad Consensus

Which is more critical?



Centralized vs. de-centralized study leadership




Do you need to access 'long tail of innovation?'

Resources...

Journal of Pharmacological and Toxicological Methods xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect




Journal of Pharmacological and Toxicological Methods

journal homepage: www.elsevier.com/locate/jpharmtox

Original article

A public-private consortium advances cardiac safety evaluation: Achievements of the HESI Cardiac Safety Technical Committee

Jennifer B. Pierson ^{a,*}, Brian R. Berridge ^b, Marjory B. Brooks ^c, Kevin Dreher ^d, John Koerner ^e, A. Eric Schultze ^f, R. Dustan Sarazan ^g, Jean-Pierre Valentin ^h, Hugo M. Vargas ⁱ, Syril D. Pettit ^j



Journal of Pharmacological and Toxicological Methods

journal homepage: www.elsevier.com/locate/jpharmtox

Original article

A HESI consortium approach to assess the human predictive value of non-clinical repolarization assays

Elena S. Trepakova ^{a,*}, John Koerner ^{b,1}, Syril D. Pettit ^{c,2}, and Jean-Pierre Valentin ^{d,3} on behalf of the HESI Pro-Arrhythmia Committee members



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THE MAGAZINE


December 2008

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Which Kind of Collaboration Is Right for You?

by [Gary P. Pisano](#) and [Roberto Verganti](#)

Comments (0)      



consortia-pedia

An In-Depth Look at the Research-by-Consortium Trend in Medical Research and Development

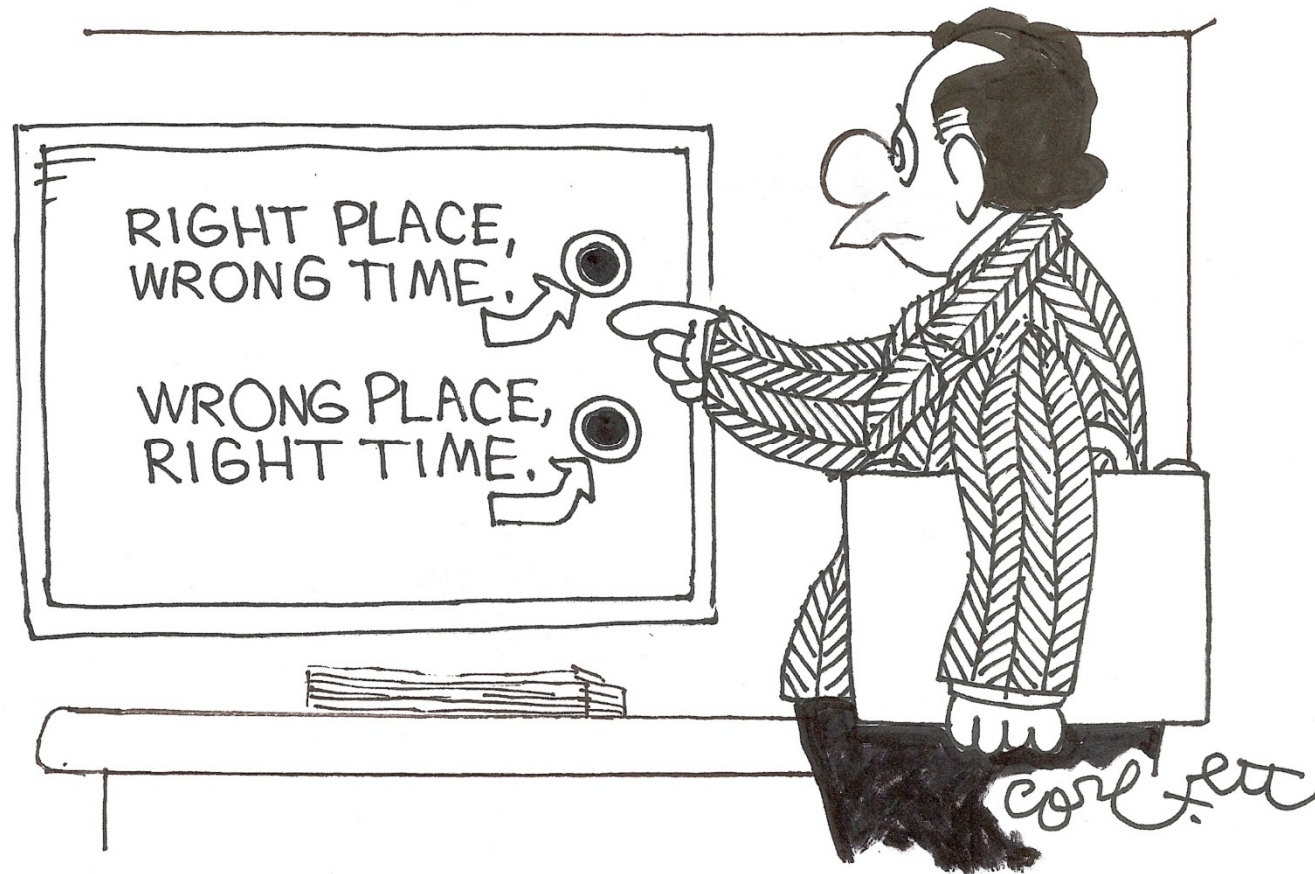
www.hesiglobal.org



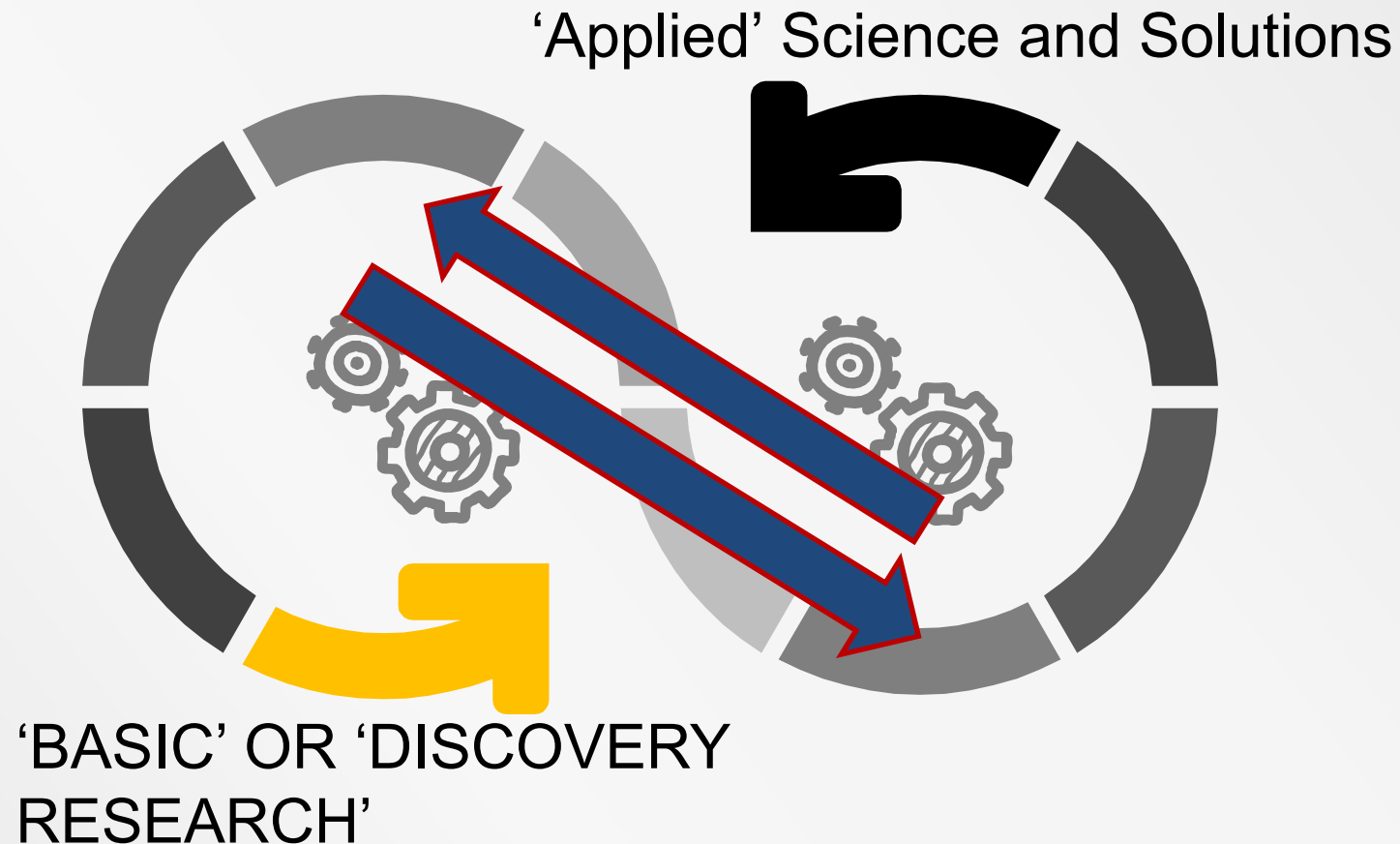
FasterCures
A CENTER OF THE MILKEN INSTITUTE

Collaboration:

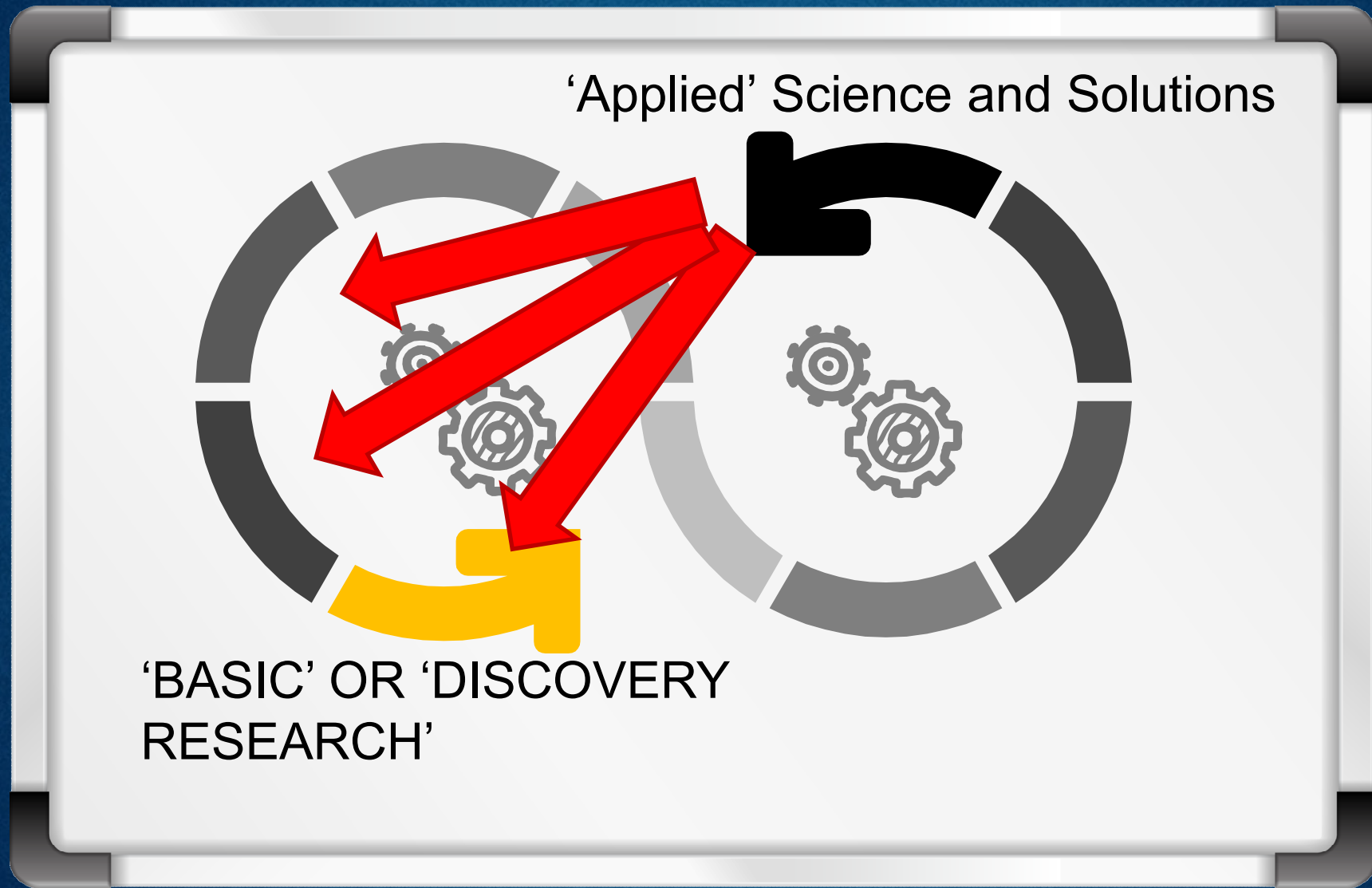
Not only how, but when



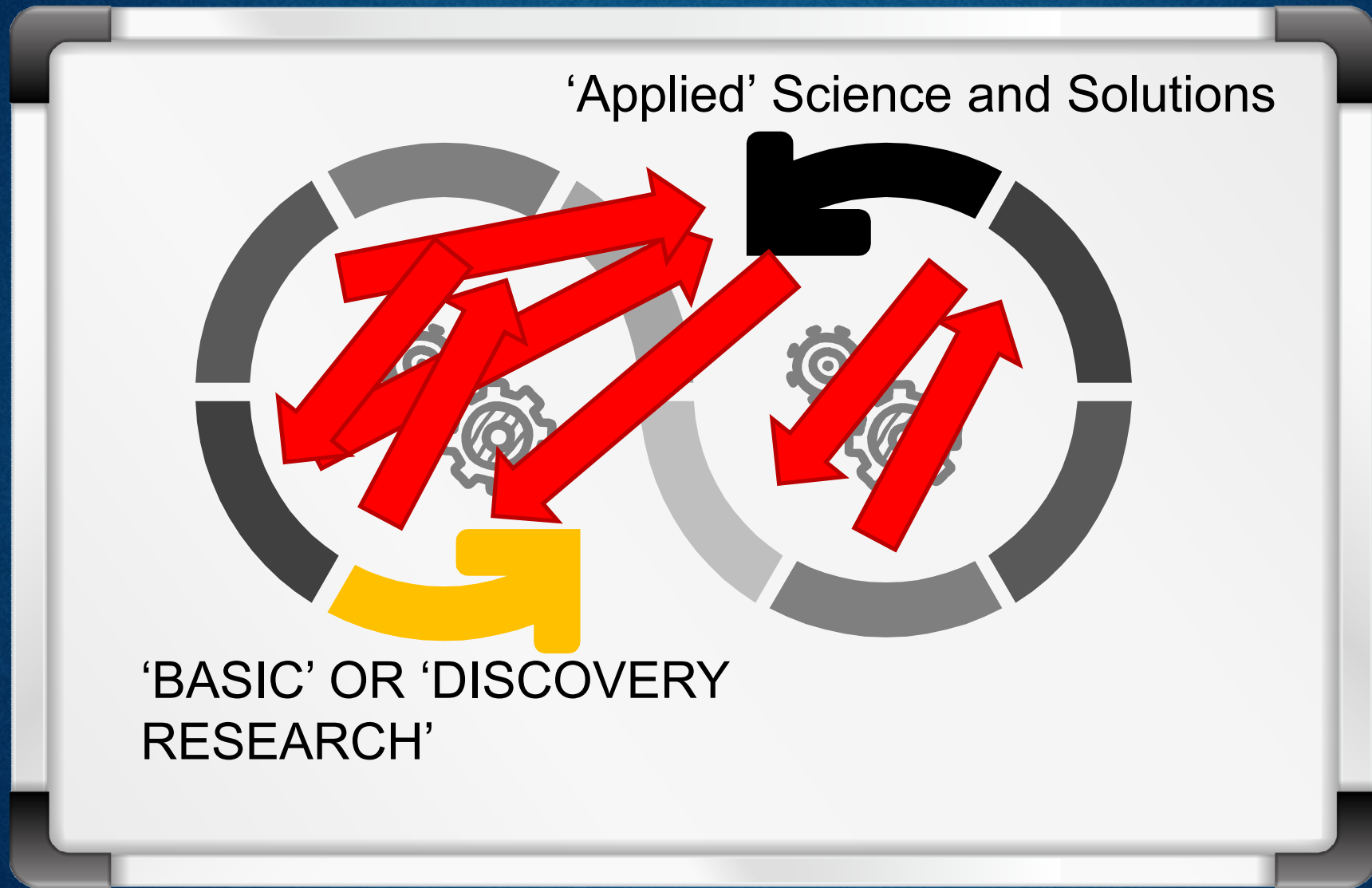
The current standard...



Recommendation: Create NEW opportunities for interactions at the ‘tails’ of the spectrum as well as along the way.



Recommendation: Create more opportunities for interactions at the 'tails' of the spectrum as well as along the way. **BOTH DIRECTIONS**



WHY IS THIS SO IMPORTANT?

- Readies applied community to engage new approaches
- Allows basic research community to benefit from early discussions on context of use, 'real world' needs

Recommendation:

Model is not yet widely engaged – let's support new platforms to promote it.

Challenge

Create metrics & incentives that support
efficient & impactful new science
(multi-sector, multi disciplinary)

(TSK Step 4)

Why doesn't this happen
more readily already?

DOES SCIENCE
COMMUNITY VALUE
OUTPUTS OR
OUTCOMES?

*CONSIDER THIS
EXAMPLE...*

1990s: Public health AEs from anti-arrhythmic drugs + 'non-cardiac' drugs such as anti-fungals, antibiotics, antihistamines, etc.



The Seattle Times
Winner of Nine Pulitzer Prizes

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Wednesday, July 8, 1992 - Page updated at 12:00 AM

[E-mail article](#) [Print](#)

Seldane Risk Reported -- Fda Warns About Popular Antihistamine

By Rita Rubin

Times News Services: Dallas Morning News

The U.S. Food and Drug Administration warned yesterday that Seldane, the most widely prescribed antihistamine, can cause life-threatening heartbeat irregularities in a small number of patients.

The irregularities occur when excessive levels of Seldane build up in patients' blood, according to the FDA. Patients at risk include those who take more than the recommended two tablets a day or those who use Seldane with certain other drugs.

Those drugs are Nizoral - an anti-fungal medication commonly used by AIDS patients - and the antibiotic erythromycin. Nizoral and erythromycin appear to interfere with the body's ability to utilize Seldane, the FDA said.

"Use of Seldane together with ketoconazole (the generic name for Nizoral) and erythromycin must be



**COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
(CPMP)**

**POINTS TO CONSIDER:
THE ASSESSMENT OF THE POTENTIAL FOR QT INTERVAL
PROLONGATION BY
NON-CARDIOVASCULAR MEDICINAL PRODUCTS**

“There is no scientific consensus on the preferred approach to, or internationally recognized guidance on, addressing the risk for repolarization-associated ventricular tachyarrhythmia (e.g., TdP).....submission of data to regulatory agencies to support use of these methods is encouraged.” EMA 2000.



The Approach

- Public-private sector, international team.
- 12 drugs (+/- controls) with clinical data.
- Evaluated leading nonclinical models in study.

Hanson et al. 2006. JPTM. 54:116-129.

Table 1

Drug	Dose (mg/kg)	Vehicle	
<i>a. Dose limiting effects in vivo of compounds not associated with Torsades de Pointes</i>			
Amoxicillin	0, 10, 100, 1000	Capsule	1
Aspirin	0, 10, 30, 100	Capsule	1
Captopril	0, 3, 30, 100	Capsule	1
Diphenhydramine	0, 1, 3, 10	Capsule	1
Propranolol	0, 3, 10, 20	Capsule	1
Verapamil	0, 1, 5, 15	Capsule	1
<i>b. Dose limiting effects in vivo of compounds associated with Torsades de Pointes</i>			
Bepriidil	0, 1, 10, 30	Capsule	1
Cisapride	0, 1, 2, 4	Solution	1
Haloperidol	0, 0.1, 0.3, 1.0	Solution	1
Pimozide	0, 1, 5, 10	Capsule	1
Terfenadine	0, 10, 30, 100	Capsule	1
Thioridazine	0, 5, 10, 15	Capsule	1



Available online at www.sciencedirect.com



Journal of Pharmacological and Toxicological Methods 54 (2006) 116–129

**Journal of
Pharmacological
and
Toxicological
Methods**

www.elsevier.com/locate/jpharmtox

Original article

ILSI-HESI cardiovascular safety subcommittee initiative: Evaluation of three non-clinical models of QT prolongation

Laurie A. Hanson^a, Alan S. Bass^b, Gary Gintant^c, Scott Mittelstadt^d,
David Rampe^e, Karluss Thomas^{f,*}

^a *Worldwide Safety Sciences, Pfizer Inc., 7000 Portage Road, Kalamazoo, MI 49001, USA*

^b *Investigational and Regulatory Safety Pharmacology, Schering-Plough Research Institute, 2015 Galloping Hill Road, K15-2-2770, Kenilworth, NJ 07033-0539, USA*

^c *Department of Integrative Pharmacology, Global Pharmaceutical Research and Development, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-3500, USA*

^d *Procter and Gamble Pharmaceuticals, Miami Valley Laboratories, 11810 East Miami River Road, Cincinnati, OH 45252, USA*

^e *Sanofi-Aventis, P.O. Box 6800, Route 202-206, Bridgewater, NJ 08807-0800, USA*

^f *International Life Sciences Institute Health and Environmental Sciences Institute, One Thomas Circle NW, Ninth Floor, Washington, DC 20005, USA*

Received 7 April 2006; accepted 14 April 2006

**Journal
impact factor
= 2.1**

(Nature is 42)

Only yielded ONE publication, however...



New Global Standard for Safety Evaluation = Largely Eliminated Risk to Patients

Translation to Practice

- HESI studies directly informed the ICH S7B Guideline, 2004
- FIRST guideline to use nonclinical safety pharmacology data to inform clinical safety.

Unanticipated TdP largely eliminated in marketed drugs

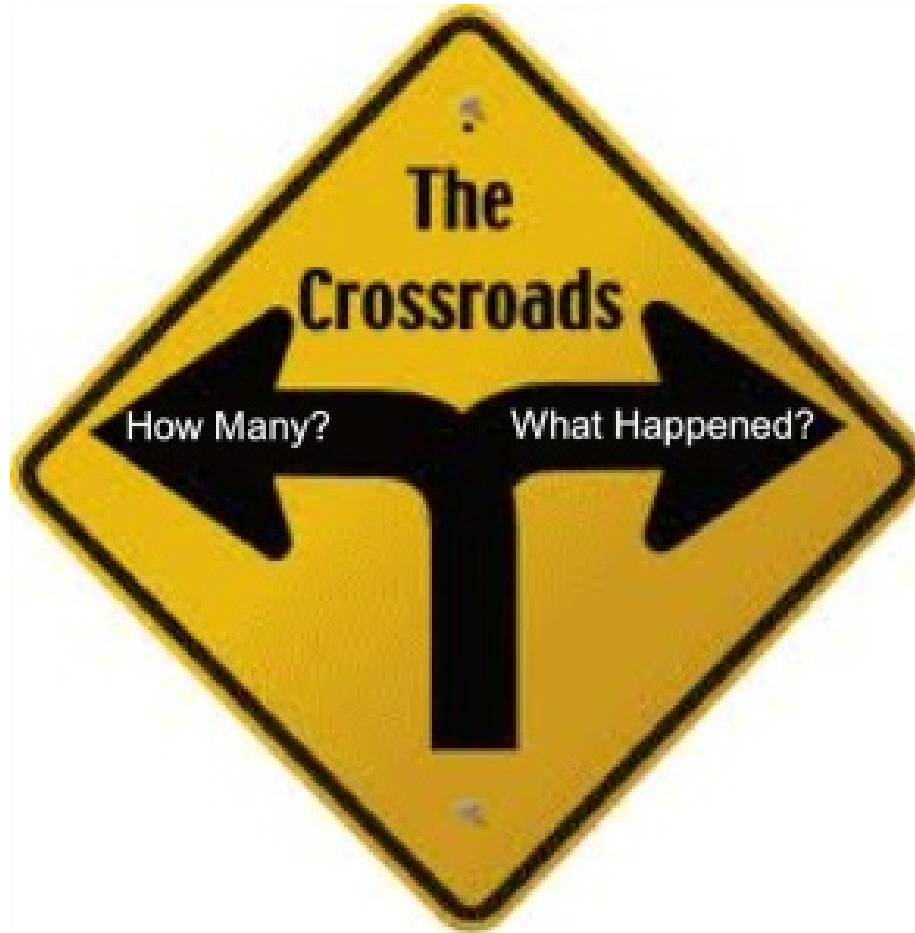


New Global Standard for Safety Evaluation = Largely Eliminated Risk to Patients

Would this have met traditional criteria for project funding and impact assessment?

How do we help ensure that future critical work gets resourced to meet health needs?

DO WE HAVE THE RIGHT VALUES?



Science 17 May 2013:
Vol. 340 no. 6134 p. 787
DOI: 10.1126/science.1240319

EDITORIAL

Impact Factor Distortions

Bruce Alberts

Bruce Alberts is Editor-in-Chief of *Science*.

But perhaps the most destructive result of any automated scoring of a researcher's quality is the "me-too science" that it encourages. Any evaluation system in which the mere number of a researcher's publications increases his or her score creates a strong disincentive to pursue risky and potentially groundbreaking work, because it takes years to create a new approach in a new experimental context, during which no publications should be expected. Such metrics further block innovation because they encourage scientists to work in areas of science that are already highly populated, as it is only in these fields that large numbers of scientists can be expected to reference one's work, no matter how outstanding. Thus, for example, in my own field of cell biology,

VALUE OF CITATION?



PLoS Biol. 2014 Nov; 12(11): e1002003.

Published online 2014 Nov 25. doi: [10.1371/journal.pbio.1002003](https://doi.org/10.1371/journal.pbio.1002003)

FORTY YEARS' WAR

Grant System Leads Cancer Researchers to Play It Safe



Bryce Vickmark for The New York Times

Dr. Ewa T. Sicinska turned to a private foundation to finance her research.

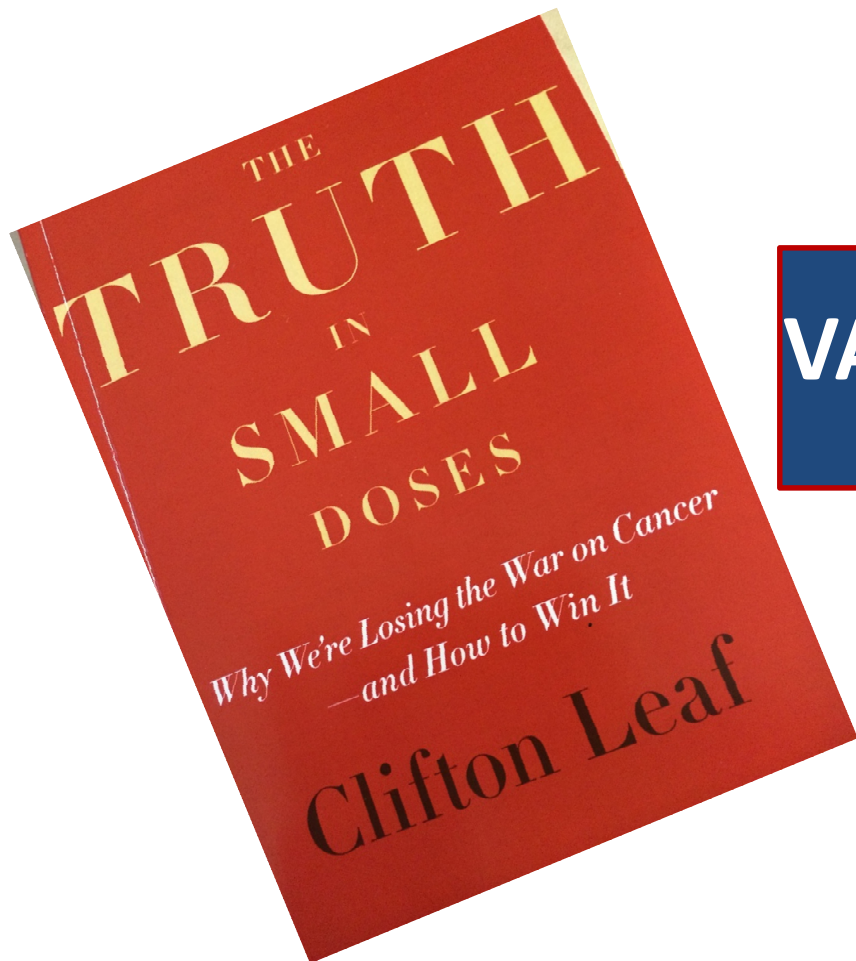
By GINA KOLATA

Published: June 27, 2009

**VALUE OF
HISTORY?**

- **“...we also recognize that the system probably provides disincentives to funding really transformative research.”**

Dr. Raynard S. Kington, former acting director of the [National Institutes of Health](#),




VALUE OF CERTAINTY?

“How did we get here?....(we must) align the funding system with the right goals. The R01 grants framework...encourages cautious incrementalism in cancer science investigations, when what we need, by most accounts, is bold thinking and innovation.”

OK....

SO WHAT DO
WE WANT TO
ENCOURAGE?

- 
- POSITIVE IMPACT ON PUBLIC HEALTH OR THE ENVIRONMENT
 - CREATION OF NEW SCIENTIFIC THOUGHT – SPUR INNOVATION
 - RESOURCE EFFICIENCY
 - REWARD PROGRESS, NOT JUST EASILY MEASURED OUTPUTS

An example of how...

Measuring & Supporting New Collaboration Networks

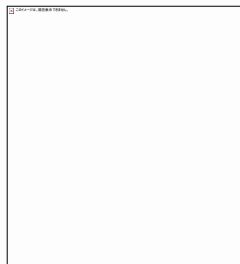


Unique Program **==** Unique Evaluation

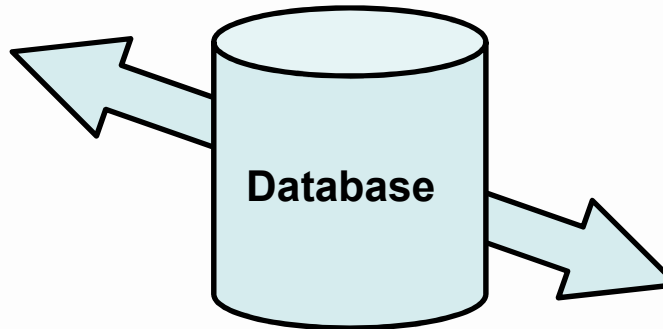
Semi-Annual
~70-80 pages
5 reports to date

Extended Scientific Report	
Report Date:	Course Name:
E-mail Address:	PI Name:
	Affiliation:
1. PS-OC Overall Progress Summary (since last report)	
2. Progress on Course Framework	

Investigators



Nicole Moore
nicole.moore@nih.gov



Program Staff

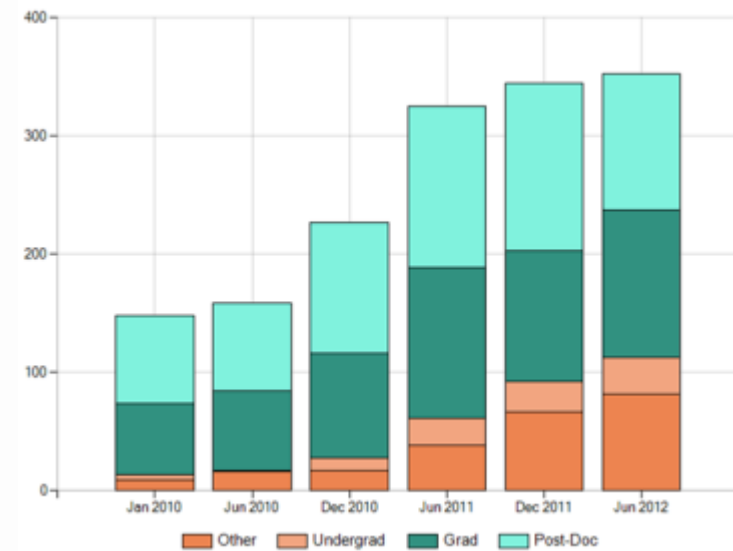
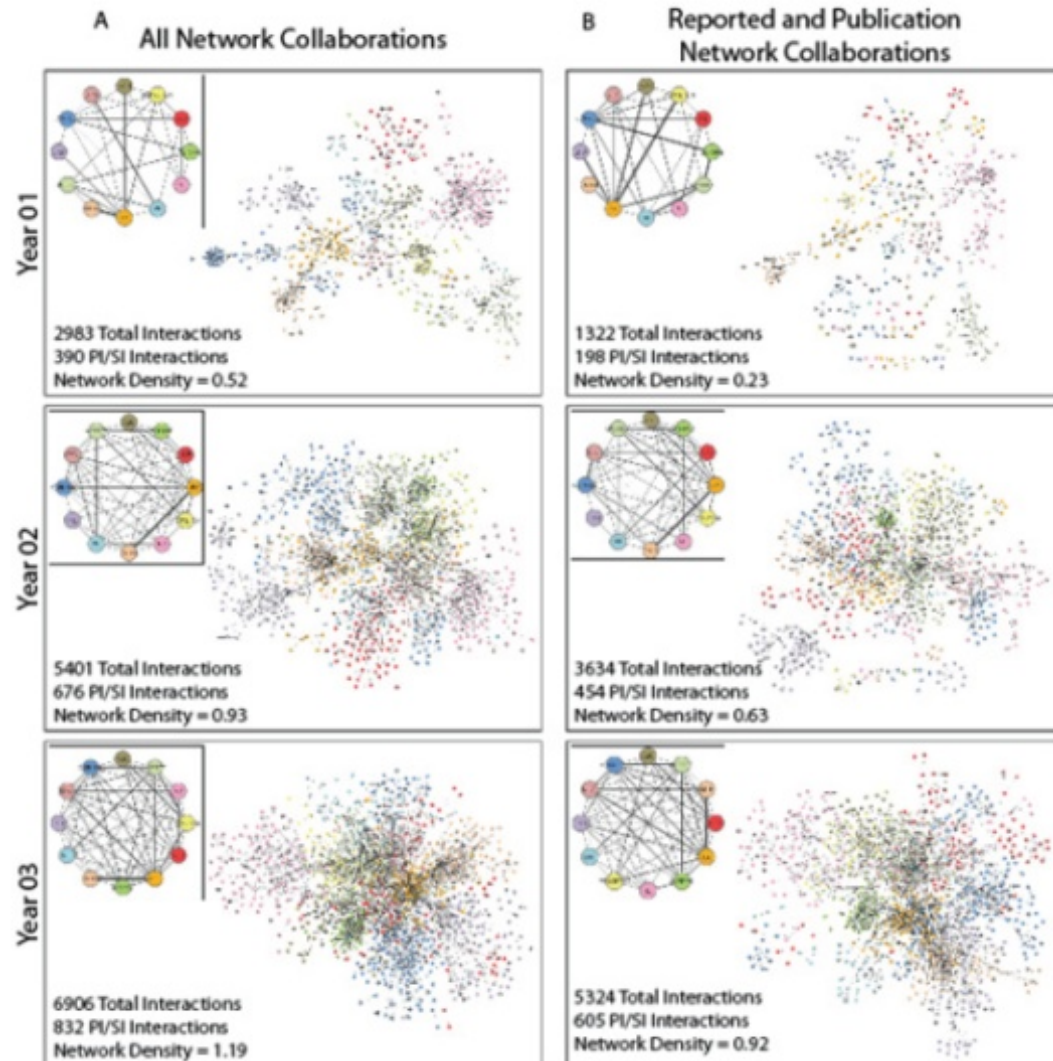


Interdisciplinary Team Reporting, Analysis, and Query Resource
(ITRAQR)

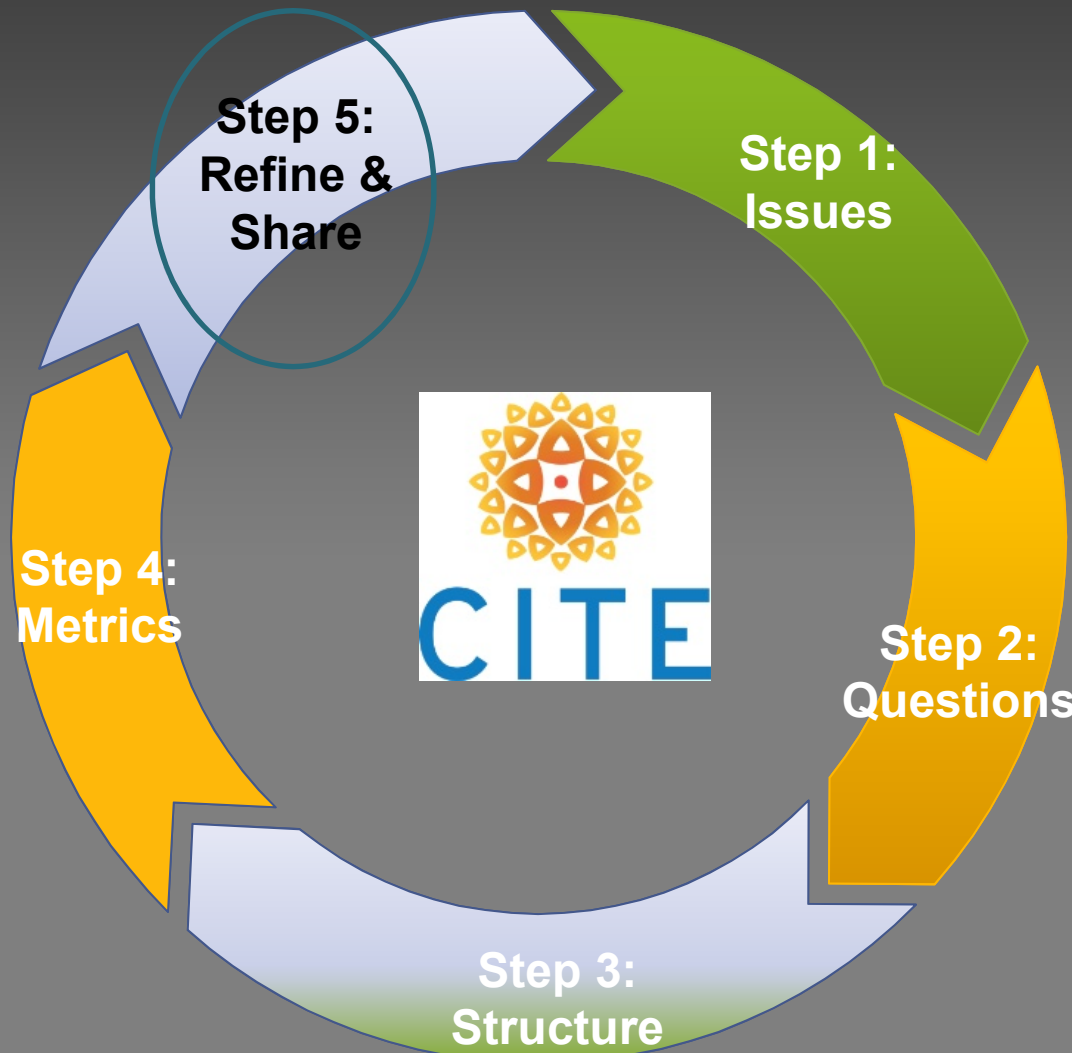


Slide Provided by J. Lee, NCI

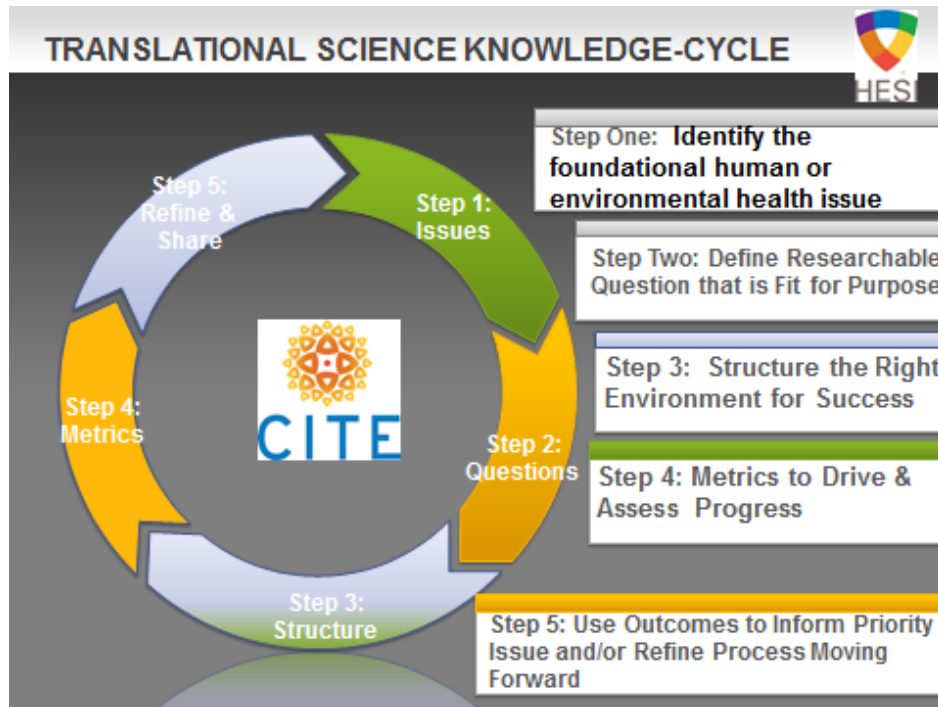
iTRAQR Output Snapshots (Nov 2012)



TRANSLATIONAL SCIENCE KNOWLEDGE-CYCLE



**BRINGING
IT BACK
TOGETHER**

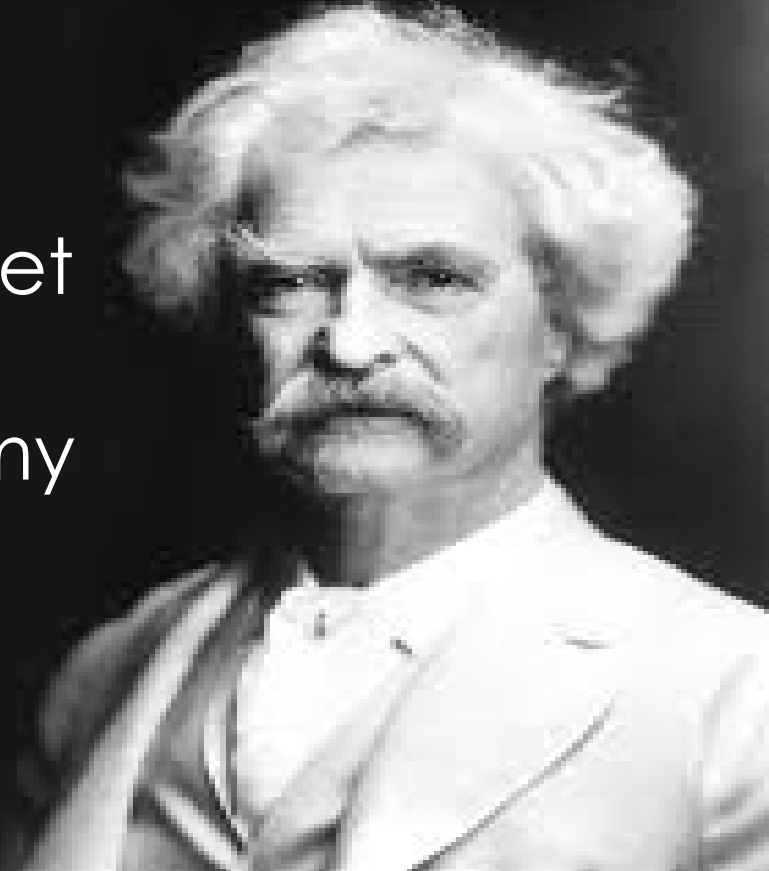


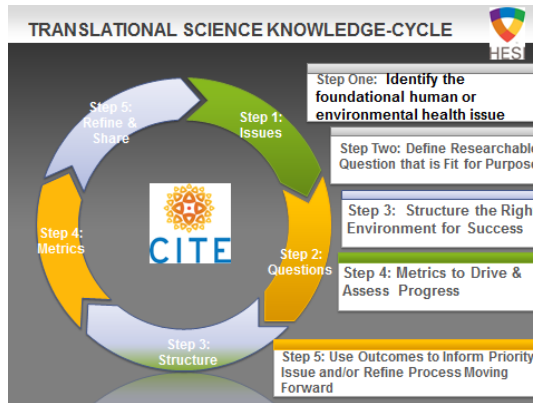
**HOW DO WE
LEARN TO DO
BETTER??**

- MORE BENEFITS TO HEALTH
- MORE EFFICIENCY
- RIGHT SCIENCE

“I have never let
my schooling
interfere with my
education.”

— Mark Twain





POLICY

From Silos to Multilingual Science



Syril D. Pettit is Executive Director of the International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute (HESI), a global nonprofit organization based in Washington, D.C., that facilitates public-private partnerships in the health and environmental sciences. E-mail: spettit@hesiglobal.org

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10.1126/scitranslmed.3008386

TRANSLATION—THE PROCESS OF MOVING SCIENCE FROM DISCOVERY TO application—has become a mantra of collaborative science initiatives worldwide. It extends from the drug and medical device development arena, to chemical safety, agricultural research, environmental sustainability, and beyond. These efforts are set against a backdrop of complex challenges in the prevention and treatment of emerging and chronic diseases and increasing environmental impacts associated with population growth and industrialization. Undoubtedly, there is a critical need for multidisciplinary scientific initiatives that move research from the pages of a journal to the promotion of public health (1, 2). Basic researchers, clinicians, regulators, industrial scientists, and entrepreneurs are all strongly invested in the “why” and “what” of translational science. But what about the “how”?

As the executive director of a nonprofit organization that facilitates public-private partnerships in the health and environmental sciences (3), I routinely hear and espouse the benefits of translational science initiatives that offer the opportunity to enhance the efficiency of the scientific process by breaking down siloes across sectors and disciplines. When optimized, these initiatives provide the interactive framework necessary to link those who define public health challenges with those who can generate solutions and, subsequently, those who can implement those solutions. However, I also often hear and experience frustration with this same process. Even with a team of well-intentioned scientists, many of us have faced the seemingly intrinsic challenge of moving to a model in which engagement across disciplines and sectors is fluid and ongoing. Too often, translational scientific programs are characterized by a stochastic series of cross-disciplinary interaction points.

What is the basis of this phenomenon? Are there opportunities to alter the kinetics of translational science teams away from a perpetual tendency to shift back to a more siloed state? I believe the answer is yes, but not without a change in the way we develop and support applied sciences.

www.ScienceTranslationalMedicine.org 12 February 2014 Vol 6 Issue 223 223ed3

cemag.org on February 12, 2014

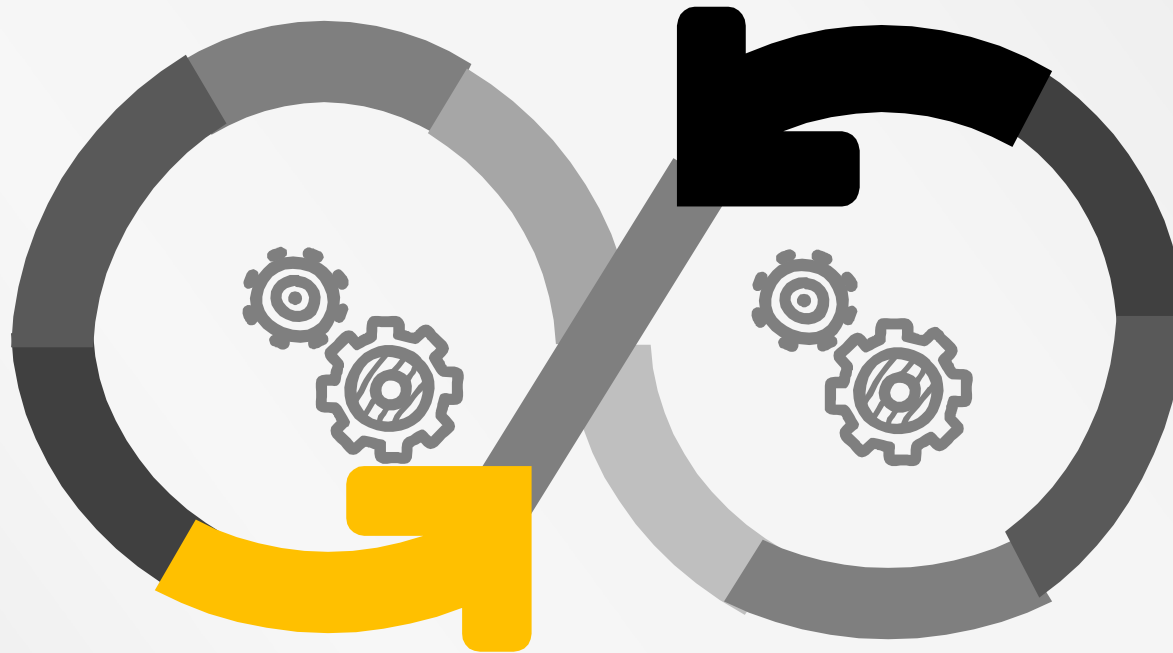
✓ **Train scientists**

✓ **Fund translational research**

X **Teach/Provide experience in ‘HOW to translate’**

IT IS OUR RESPONSIBILITY AS A PUBLIC HEALTH
COMMUNITY TO BRIDGE THESE EFFORTS

'Applied' Science and Solutions



'BASIC' OR 'DISCOVERY
RESEARCH'



CITE

COMBINING INTERDISCIPLINARY & TRANSLATIONAL EXPERTISE

OPPORTUNITY

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