Beyond Inspiration and Invention to Innovation:
Translational Science at NIH

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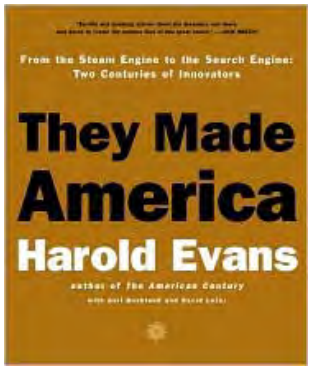
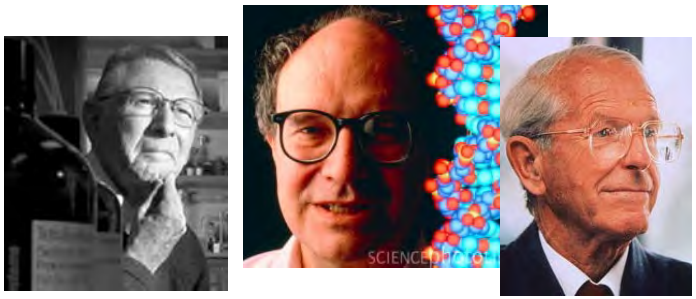
Largest Impact?

Paul Lauterbur and Peter Mansfield

Magnetic Resonance Imaging

Raymond Damadian





Paul Berg, Walter Gilbert, and Fred Sanger

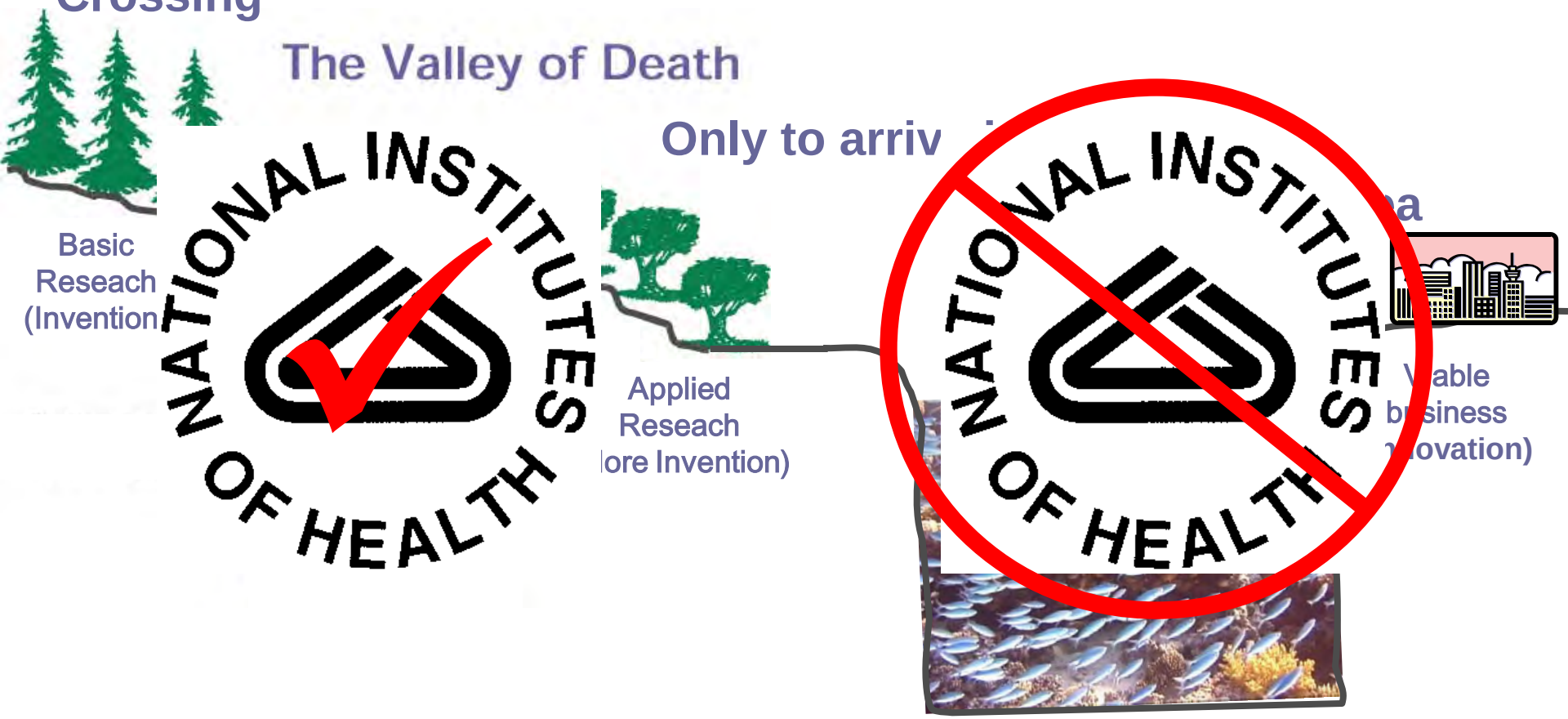
Recombinant DNA

Herb Boyer and Bob Swanson

Between Invention and Innovation:

Moving Technology from the Laboratory to the Marketplace

Branscumb and Auerswald (2002). NIST GCR 02-841



Death Valley suggests a barren territory. In reality, between the stable shores of the science and technology environment and the business and finance enterprise is a sea of business and technical ideas, of big fish and little fish contending, with survival going to the creative, the agile, the persistent.

Translational Medicine:
moving the development of new drugs, devices, and treatment options from bench to bedside; translating research into practice

The Broad Reach of the NIH

There are resources--
FY11 budget: $31B

NIH *is* an institution
(Intramural Research)

~ 6,000 scientists
~ 10% of NIH budget

NIH *supports* institutions & people
(Extramural Research)

> 4,000 institutions
> 300,000 scientists & research personnel
~ 85% of the NIH budget

NIH Grant Statistics

Fiscal Year 2010

- **62,000** applications reviewed
- **240** Review Officers organized **1,600** meetings with **18,000** reviewer
- **16,600+** n grants awa

We have lots of experience in evaluating science!

NIH is organized into:

- **…itutes & Centers (IC) each …rent:**
  - **…rities**
  - **budge…**
  - **ways of deciding grants to fund**

The culture is complex.

NIDCD National Institute of Deafness and Communications Disorders

NIMHD National Institute on Minority Health and Health Disparities

NIAAA National Institute on Alcoho Abuse and Alcoholism

National Heart Lung and Blood Institute

National Institute of Allergy and Infectious Diseases

NATIONAL CANCER INSTITUTE

FOGARTY International Center

Eunice Kennedy Shriver NICHD National Institute of Child Health & Human Development

NIDA NATIONAL INSTITUTE ON DRUG ABUSE

NIEHS National Institute of Environmental Health Sciences

National Eye Institute NATIONAL INSTITUTES OF HEALTH

National Institute of Dental and Craniofacial Research

National Institute of General Medical Sciences

NIDDK National Institute of Diabetes and Digestive and Kidney Diseases

NIMH National Institute of Mental Health

NATIONAL LIBRARY OF MEDICINE

National Human Genome Research Institute

NATIONAL INSTITUTE OF NURSING RESEARCH

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

center for scientific review

CIT Center for Information Technology

Clinical Center

NIAMS National Institute of Arthritis and Musculoskeletal and Skin Diseases

NIBIB National Institute of Biomedical Imaging and Bioengineering

NCCAM NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE

National Center for Research Resources

NATIONAL INSTITUTE ON AGING National Institutes of Health

"Family Tree" for Grants

Sorting out the locus for Translational Research…

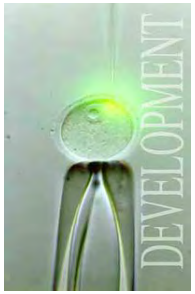
Find a Trusted Guide!

Some examples of translational research supported by NIH…

Small Business Innovation Research (SBIR)
Small Business Technology Transfer (STTR)
Programs

PHASE I – Feasibility Study

- **Average award: $170K**
- **Project period varies, most 6 – 12 months**



PHASE II – Full R&D

- **Average $850K, 2 years but some longer**
- **Commercialization plan required**

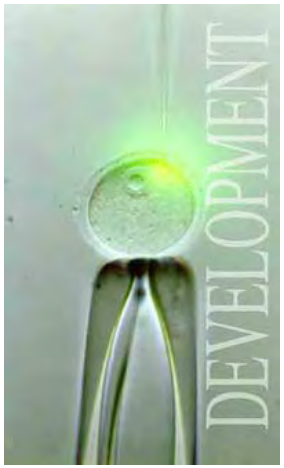
PHASE III – Commercialization

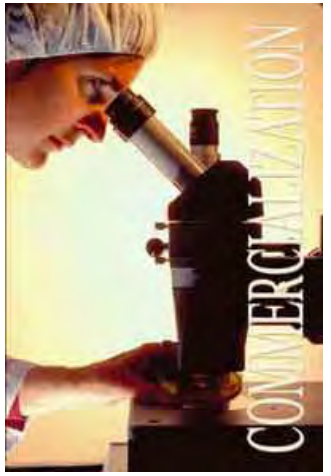
- **Use of non-SBIR/STTR Funds**
- **Consider exit strategy**

Issues

- Budgets inadequate for expectations
- Gap between Phases I and II can be almost two years
- Reviewers do not understand challenges of the “D” in “R&D”

NIH SBIR Gap Funding Programs





- **Phase II Competing Renewal Award**

Phase I → Phase II → Phase III

- **No-Cost Extension**
- **Phase I / Phase II Fast Track**
- **Administrative / Competitive Supplements**

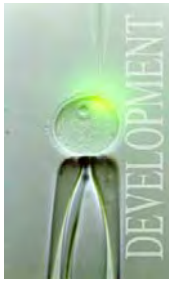
NIH Phase I / Phase II Fast-Track

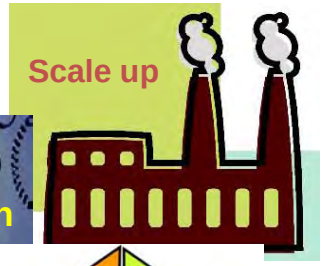
Are you ready to run with the big dogs?

Critical Considerations

- Review both Phases together
- Convincing preliminary data
- Clear, measurable, achievable milestones, especially for the Phase II transition after administrative review
- Well-conceived, compelling Commercialization Plan
- Letters of Phase III support/interest?
- Track record for commercializing?
- Discussed with NIH Program Staff?

SBIR Phase II+
Competing Renewal Awards





Phase I → Phase II → Phase III

"Valley of Death"

- Take existing, promising compounds or devices developed in Phase II through the next step of drug discovery/medical device refinement and development
- Support complex instumentation, clinical research tools, behavior interventions
- Not all ICs participate

CTSA Clinical & Translational Science Awards®

Translating Discoveries to Medical Practice

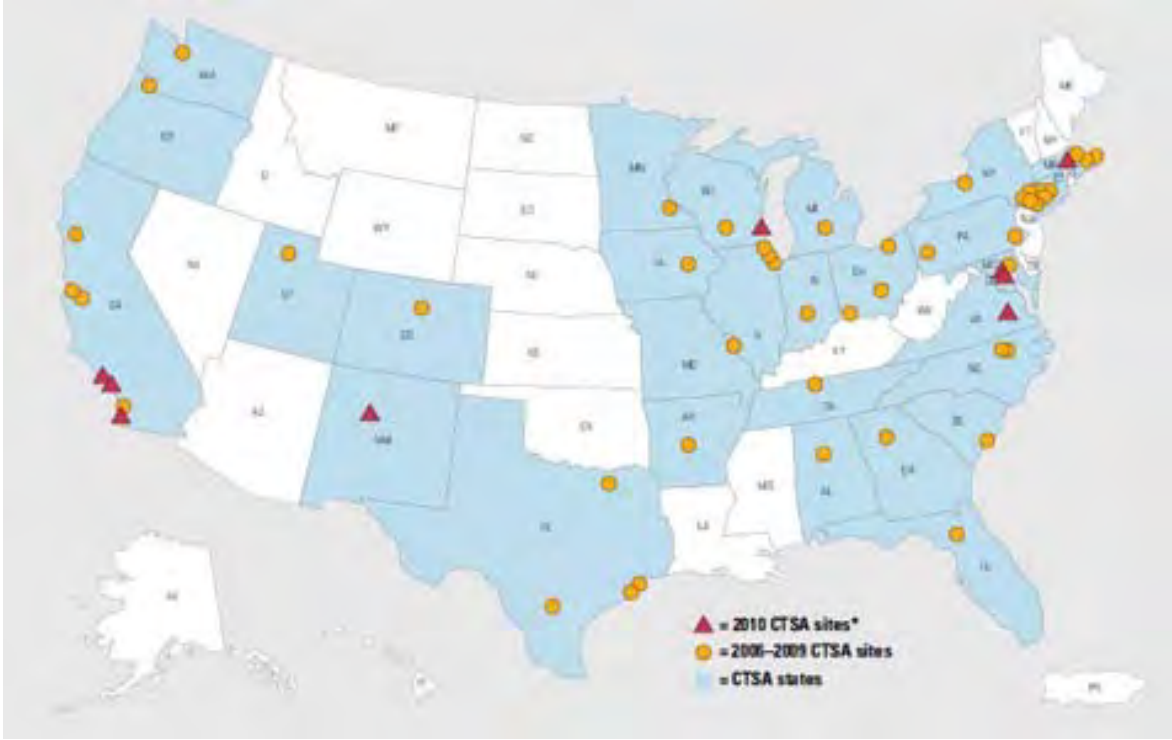
http://ctsaweb.org/

Goals:

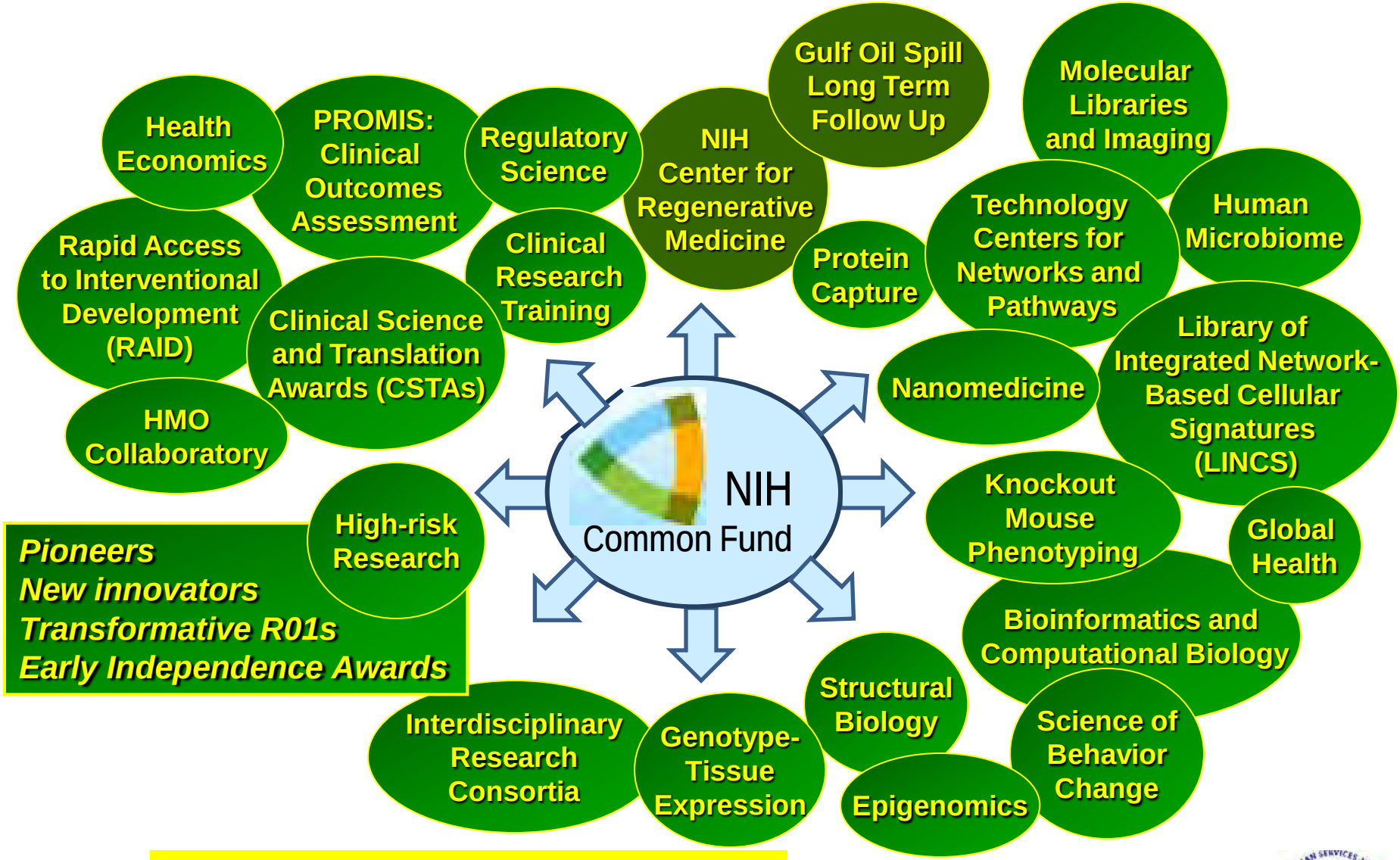
- create a definable academic home for clinical and translational research
- transform the local, regional, and national environment for clinical research and training

Features:

- Integrates diverse teams from across academia, university hospitals, industry
- 60 institutions in 30 states and DC
- Collaborations encouraged



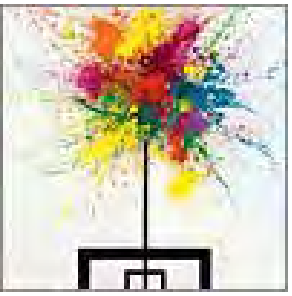
Cross-Cutting, trans-NIH Programs



http://commonfund.nih.gov/

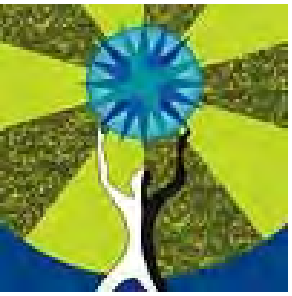
Ongoing Investments in Innovation

The NIH Common Fund invests millions of dollars to fund new high-risk research to explore ideas that have strong potential to improve health



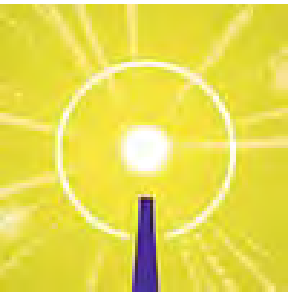
Transformative R01 Program places the emphasis on creative ideas—projects with the potential to overturn paradigms. Flexible budgets. (**79 awards since 2009**).

stresses projects



Pioneer Awards support individual scientists of exceptional creativity who propose pioneering approaches to major challenges in biomedical and behavioral research (**94 awards since 2004**).

stresses individuals



New Innovator Program address two important goals: stimulating highly innovative research and supporting promising new investigators (**164 awards since 2007**).

http://nihroadmap.nih.gov/

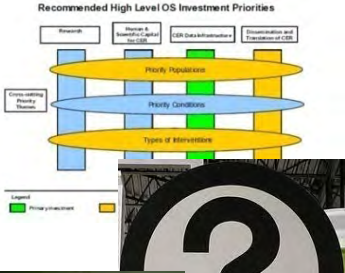
NIBIB

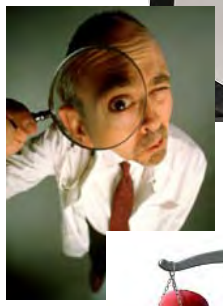
… improving health by leading the development and accelerating the application of biomedical technologies

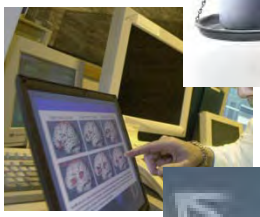
NATIONAL INSTITUTES OF HEALTH

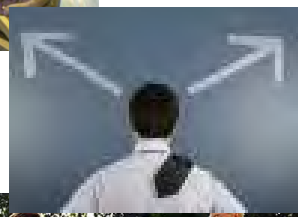
DEPARTMENT OF HEALTH & HUMAN SERVICES USA

NIH's Role in Comparative Effectiveness Research (CER)









Key NIH CER Activities

- Research to generate evidence enabling physicians and patients to optimize health care decisions.
- Research training to develop the CER workforce.
- Personalized Medicine probes impact of uniqueness of individuals and special populations.
- CER Centers support integration and dissemination of evidentiary knowledge.
- Behavioal Economics to increase "uptake" of CER findings by providers and payers.

Key Considerations

- Emerging Role of NIH in CER: differentiating from AHRQ?
- Early standards efforts can accelerate effective translation.

More at: http://www.nejm.org/doi/full/10.1056/NEJMp1109407

NIH and Non-Hypothesis Driven Research

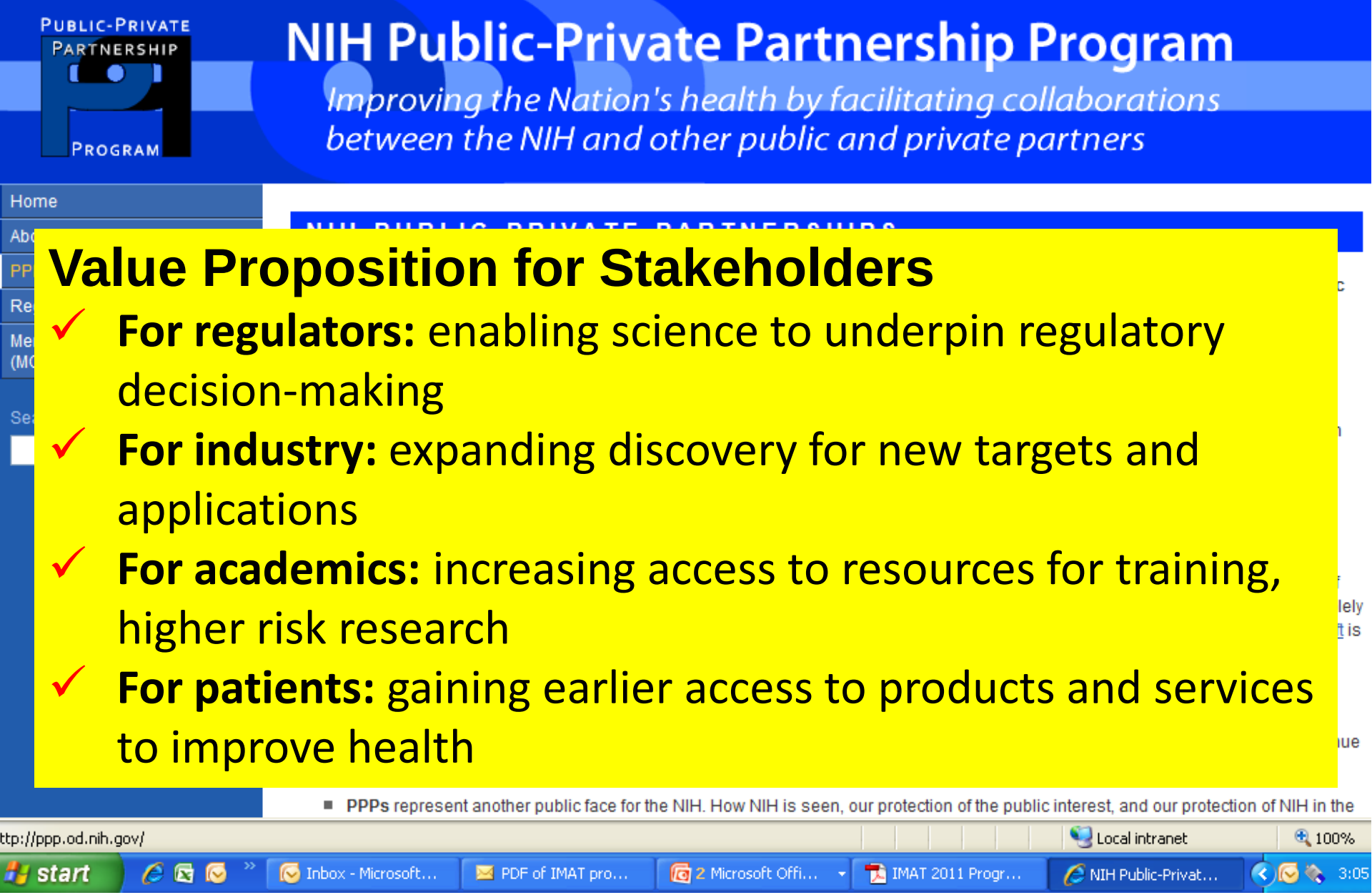
There are two kinds of scientific revolutions, those driven by new tools and those driven by new concepts… The effect of a concept-driven revolution is to explain old things in new ways. The effect of a tool-driven revolution is to discover new things that have to be explained.

-Freeman Dyson, 1997

Getting Funded in an Emerging Field

NIH funds high risk/high reward research if there is

- **Potential for high impact**
- **Novel approach, not necessarily a new idea (a fundamental publication builds credibility)**
- **Deep expertise in the general area on the team (confidence in capability is key)**
- **A compelling research plan—anticipate obstacles and propose alternatives**
- **BONUS POINTS: reviewer familiarity with the basics**



http://ppp.od.nih.gov/pppinfo/description.asp

Public-Private Partnership Program Examples

accelerate identification, development and regulatory qualification of biomarkers for: cancer, inflammation and immunity, metabolic disorders, and neuroscience

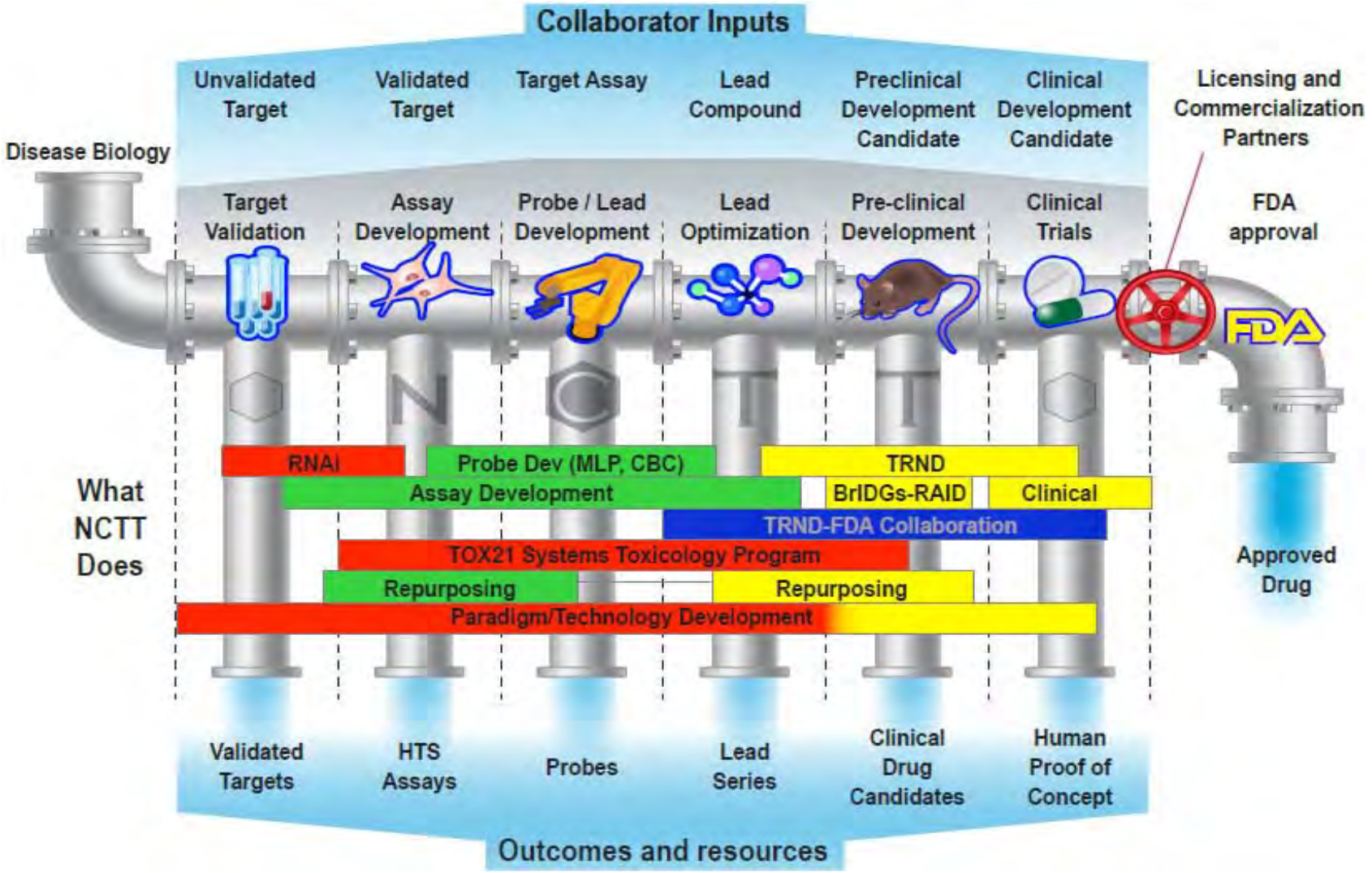
Alzheimer's Disease Neuroimaging Initiative
- NIA, NIBIB, FDA -

Federal partners: NIAMS, NIA, NIDCR, ORWH, NCCAM, NIMHD
Private partners: Merck, Novartis, Pfizer

Publically available database of gene-gene association studies
-NIH, Pfizer, Affeymetrix, Abbott -

– effective, inexpensive, simple health tools for low resource settings

Accelerating Drug Development



Bridging Interventional Development Gaps

(BrIDGs)

- formerly RAID

- Access to contract resources for formulation and GMP Manufacturing
- Assay Development for ADMET, PK/PD
- Drugs (small molecules, biologics) and delivery systems (no vaccines, devices or diagnostics)
- Product Development and Regulatory Advice

Therapeutics for Rare and Neglected Diseases

(TRND)

- New chemical entities and repurposed drugs
- Access broad scientific, translational, clinical expertise
- In-kind and collaborative research to accelerate development
- Spans spectrum from lead optimization to IND filing
- Integrated approach: underlying mechanisms thru technology platform development

Production Assistance for Cellular Therapies

National Heart Lung and Blood Program

- Manufacture a clinical grade product for PIs lacking cGMP facility
- Work closely with FDA to facilitate translation to clinical studies
- Processing Centers
  - Baylor College of Medicine Center for Cell and Gene Therapy
  - Center for Human Cell Therapy, Boston
  - City of Hope Center for Applied Technology Development
  - University of Minnesota Molecular and Cellular Therapeutics Facility
  - University of Wisconsin – Madison, Waisman Biomanufacturing
- Application and Information at: http://www.pactgroup.net/

NIH-FDA Regulatory Science Initiative

- a Common Fund Program

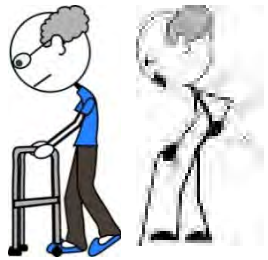
- development and use of the scientific knowledge, tools, standards, and approaches necessary for the assessment of medical product safety, efficacy, quality, potency, and performance

- **ACCELERATING DRUG AND DEVICE EVALUTATION THROUGH INNOVATIVE CLINICAL TRIAL DESIGN** (University of Michigan: William Barsan, Roger Lewis, Donald Berry)
- **REPLACEMENT OCCULAR BATTERY (ROBATT)** (MB Research Labs: Daniel Cevern, George DeGeorge)
- **CHARACTERIZATION/BIOINFORMATICS-MODELING OF NANOPARTICLE:COMPLEMENT INTERACTIONS** (University of Washington: Dennis Hourcade)
- **HEART-LUNG MICROMACHINE FOR SAFETY AND EFFICACY TESTING** (Harvard University: Donald Ingber)


Coming soon:
Regulatory Science, Part 2
HOGWARTS EXPRESS
59 2
Microphysiological Systems DARPA-BAA-11-73
Integrated Microphysiological Systems RFA-XX-12-xxx
Don't get left behind!

Common Themes in NIH's Translational Research

- **Outcomes/Milestone-driven**
- **Leveraging diverse resources** **(often both NIH intramural and extramural collaborations)**
- **Multi- and Interdisciplinary investigators**
- **Active FDA involvement**
- **Emphasis on training**
- **Trans-NIH in scope**
- **Early stage/pilot programs (evaluations?)**





National Center for Advancing Translational Science (NCATS)

Proposed Mission:

catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions

Possible Activities

- Catalyze translation by promoting innovative research that is too risky or too early for commercial investment
- Galvanize and support partnerships: leveraging funds and providing access to tools, technologies, and platforms
- Augment Regulatory Science, especially in conjunction with FDA
- Expand the pre-competitive space with open-access data repositories, and a special focus on promising compounds/devices that failed
- Harness the power of the CTSA program
- Transform through training across boundaries, both scientific and situational
- Steamline administrative processes

See Advisory Committee report at
http://www.nih.gov/about/director/ncats/acd-report.pdf

NCATS

Complement—not compete with—private sector by

- ✓ **studying the steps in diagnostics and therapeutics development, testing, and implementation into patient care**
- ✓ **identifying bottlenecks amenable to re-engineering**
- ✓ **experimenting with innovative methods to streamline the process**

CAN – Cures Acceleration Network (not appropriated)
CTSA – Clinical and Translational Science Awards
ORD – Office of Rare and Neglected Diseases
TRND – Therapeutics for Rare and Neglected Diseases
RAID – Rapid Access to Interventional Development
SBIR – Small Business Innovation Research
STTR – Small Business Technology Transfer Research


“Failure is not an option.”
- Gene Kranz