Translational Medicine and Therapeutics

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Outline

- New Charge to the SMRB: Translational Medicine and Therapeutics
- Impetus for Translational Medicine and Therapeutics Deliberations: A Changing Landscape
- Advancing Translational Medicine and Therapeutics Discovery: A Role for NIH
- TMAT Working Group: Next Steps

New Charge to the SMRB – Translational Medicine and Therapeutics

TMAT Membership

Non- Federal

Arthur Rubenstein, MBBCh *(Chair)*

William Brody, MD, PhD

Gail Cassell, PhD

William Roper MD, MPH

Solomon Snyder, MD

Huda Zoghbi, MD

Norman Augustine *(ad hoc)*

Federal

Josephine Briggs, MD

Anthony Fauci, MD

Stephen Katz, MD, PhD

Griffin Rodgers, MD MACP

Susan B. Shurin, MD

Harold Varmus, MD

Francis Collins, MD, PhD *(ex officio)*

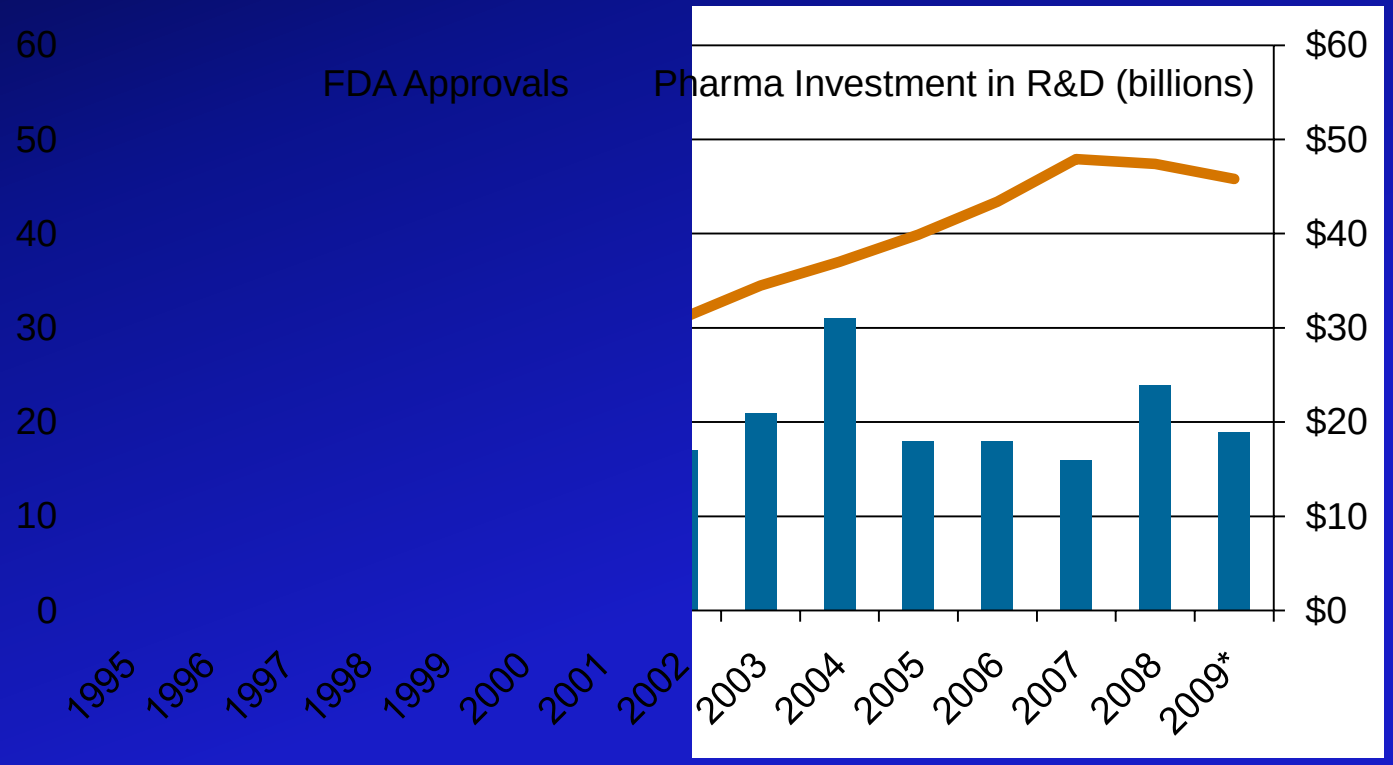
TMAT Charge

- Identify the attributes, activities, and functional capabilities of an effective translational medicine program for advancing therapeutics development; and
- Broadly assess, from a high- level view, the NIH landscape for extant programs, networks, and centers for inclusion in this network and recommend their optimal organization.

Impetus for Translational Medicine and Therapeutics Deliberations: A Changing Landscape

A Changing Landscape: Decline in Approved NMEs

- Despite greater investments in R&D by Pharma, FDA approvals of new medical entities have declined

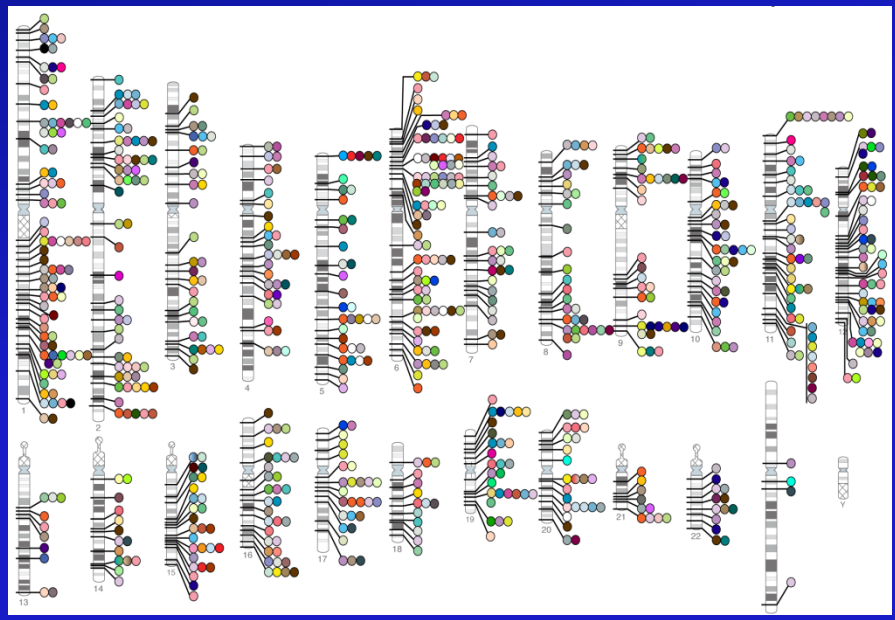


Pharmaceutical Research and Manufacturers of America; FDA

A Changing Landscape: Increases in Potential Molecular Targets

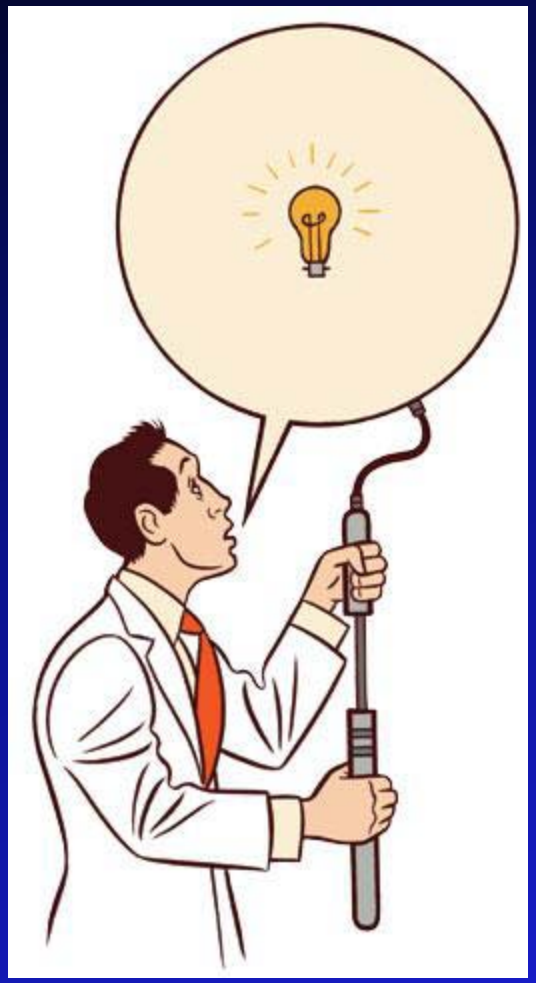
- Most recently, due to lack of available venture capital and shrinking resources for R&D, efforts have been reduced by biotech and pharmaceutical companies to develop new entities
- Paradoxically, new molecular targets for therapeutics are being discovered in unprecedented numbers as a result of advances in genomics and molecular biology

Validated GWAS hits 2010 1st Quarter



www.genome.gov/gwastudies/

A Changing Landscape: Need for A Paradigm Shift



If the process of therapeutics discovery and translational medicine is to be accelerated, improved, and streamlined, a new paradigm of discovery will be needed

A Changing Landscape: Shifting the Paradigm for Therapeutics Discovery


ANALYSIS

How to improve R&D productivity: the pharmaceutical industry's grand challenge

Steven M. Paul, Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg and Aaron L. Schacht

Abstract | The pharmaceutical industry is under growing pressure from a range of environmental issues, including major losses of revenue owing to patent expirations, increasingly cost-constrained healthcare systems and more demanding regulatory requirements. In our view, the key to tackling the challenges such issues pose to both the future viability of the pharmaceutical industry and advances in healthcare is to substantially increase the number and quality of innovative, cost-effective new medicines, without incurring unsustainable R&D costs. However, it is widely acknowledged that trends in industry R&D productivity have been moving in the opposite direction for a number of years. Here, we present a detailed analysis based on comprehensive, recent, industry-wide data to identify the relative contributions of each of the steps in the drug discovery and development process to overall R&D productivity. We then propose specific strategies that could have the most substantial impact in improving R&D productivity.

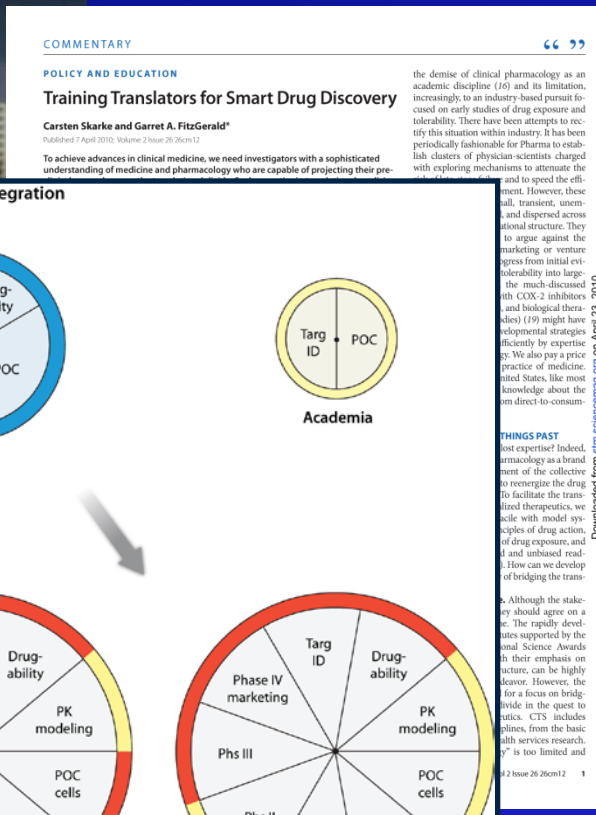
Growing "environmental" pressures on pharmaceutical industry

- Search for ways to increase # and quality of cost effective new medicines w/o unsustainable R&D risks and costs
- Traditional drug development paradigm → proposed alternative paradigm "quick win- fast fail"

Steven M. Paul, et al. *Nature Reviews Drug Discovery* 2010

A Changing Landscape: Shifting the Paradigm for Therapeutics Discovery *(cont.)*

- Shift from silo approach to highly collaborative model that distributes risk
- Need innovative models for R&D partnerships that transcend sectors and international boundaries
- Need for training and incentives for investigators who pursue careers in clinical and translational research


COMMENTARY

POLICY AND EDUCATION

Training Translators for Smart Drug Discovery

Carsten Skarke and Garret A. FitzGerald*

Published 7 April 2010; Volume 2 Issue 26 26cm12

To achieve advances in clinical medicine, we need investigators with a sophisticated understanding of medicine and pharmacology who are capable of projecting their pre-

the demise of clinical pharmacology as an academic discipline (16) and its limitation, increasingly, to an industry-based pursuit focused on early studies of drug exposure and tolerability. There have been attempts to rectify this situation within industry. It has been periodically fashionable for Pharma to establish clusters of physician-scientists charged with exploring mechanisms to attenuate the

Skarke and FitzGerald, *Science Translational Medicine* 2010

Advancing Translational Medicine and Accelerating Therapeutics Discovery:

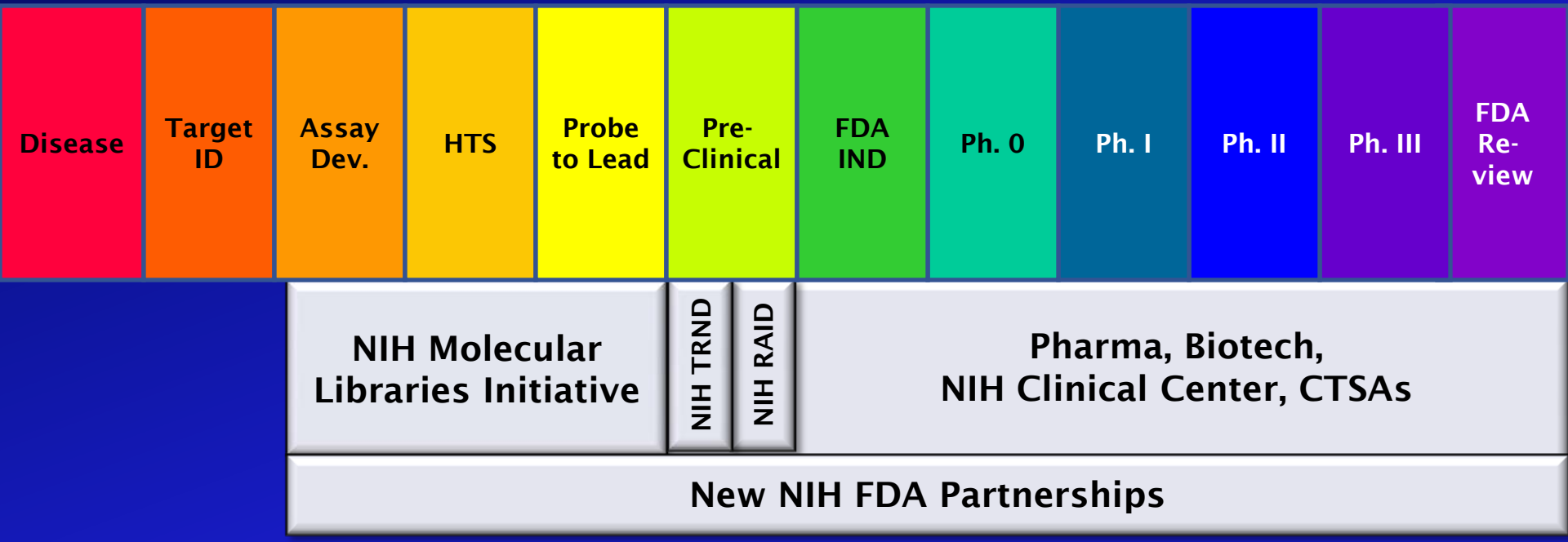
A Role for NIH

A Role for NIH: Areas of Opportunity

- Applying high throughput technologies to understand fundamental biology, and to uncover the causes of specific diseases
- Translating basic science discoveries into new and better treatments
- Putting science to work for the benefit of health care reform
- Encouraging a greater focus on global health
- Reinvigorating and empowering the biomedical research community

A Role for NIH: Areas of Expertise

- NIH possess scientific and technological resources to assist in the creation of this new paradigm, and extant and emerging programs at NIH are expertly equipped to catalyze its progress.



A Role for NIH: Health Care Reform

An Act

Entitled The Patient Protection and Affordable Care Act.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "Patient Protection and Affordable Care Act".

(b) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

A Role for NIH: Health Care Reform *(cont.)*

- The Patient Protection and Affordability Act authorizes the NIH to establish a Cures Acceleration Network. **Functions include:**

  1. Conduct and support revolutionary advances in basic research, translating scientific discoveries from bench to bedside;

  2. Award grants and contracts to eligible entities to accelerate the development of high need cures;

A Role for NIH: Health Care Reform *(cont.)*

- **Functions include:** *(cont.)*

  3. Provide the resources necessary for government agencies, independent investigators, research organizations, biotechnology companies, academic research institutions, and other entities to develop **"high need cures"**;

  4. Reduce the barriers between laboratory discoveries and clinical trials for new therapies; and

  5. Facilitate review in the FDA for the high need cures funded by the CAN

A Role for NIH: Health Care Reform *(cont.)*

- A **"High Need Cure"** is defined as a drug, biological product, or device that, in the determination of the Director of NIH:

  A. is a priority to diagnose, mitigate, prevent, or treat harm from any disease or condition; and

  B. for which the incentives of the commercial market are unlikely to result in its adequate or timely development.

TMAT Working Group:

Next Steps

Next Steps: Deliverables

- The TMAT Working Group will present to the full SMRB:
  - Attributes, activities, and associated functional capabilities of a translational medicine program optimized to enhance therapeutics development;
  - Recommendations for organizing the Agency's existing components to optimize a translational medicine and therapeutics program; and
  - Metrics for evaluating successes and any untoward consequences of organizational and/or management change, in particular, consequences for the progress of research in the areas affected by the proposed changes.

Next Steps: Process for Deliberations

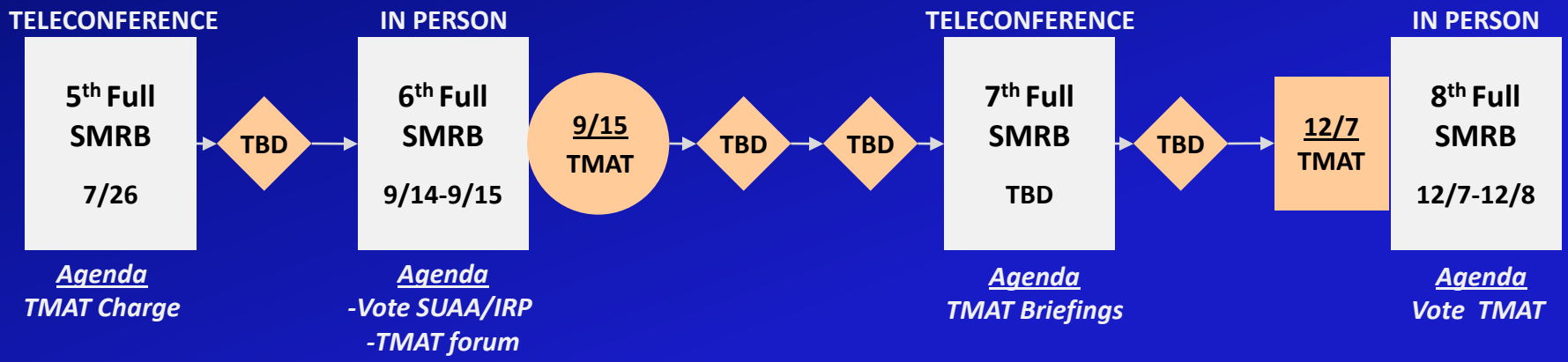
In addressing its charge, the Working Group will consider how the Agency could leverage and organize a wide range of existing NIH resources and effectively implement the CAN (assuming appropriation of funds)

Next Steps: Process for Deliberations

- Additionally, in executing its charge, the **Working Group should consider** the following:
  - Infrastructure, initiatives, and resources with direct relevance to the therapeutic pipeline currently supported by the Agency;
  - Methods to synergize, and avoid competition with, resources in the private sector;
  - Prior recommendations for strengthening the clinical and translational research enterprise at NIH, including recommendations of the IOM in its report *Enhancing the Vitality of the National Institutes of Health*, and relevant lessons learned from industry, academia, non- profit organizations, etc.; and
  - Metrics and methodologies that could be used for evaluating the impact of changes in the organization and management of the therapeutic development program.

Next Steps: Time Frame for Deliberations

The TMAT Working Group will present its findings and recommendations to the full SMRB in a timeframe that positions the full Board to complete its deliberations on this matter by December 2010



Discussion

What questions and issues should the working group consider as it undertakes this task?