June 2012 COGR Meeting Thursday Afternoon NCATS Presentation - Insel

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Catalyzing Innovation
NIH National Center for Advancing Translational Sciences

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COGR Presentation
June 7, 2012
Creation of the National Center for Advancing Translational Sciences (NCATS)

- Established on December 23, 2011
- Part of Consolidated Appropriations Act 2012 (PL 112-74)
Pursuing Opportunities for Disruptive Innovation

“To 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.”

National Institutes of Health
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES
The Need for NCATS

Biomarkers – Precision Medicine

More efficient treatment development (incl. rare diseases)

More effective translation (T1 – T4)

Training for translational science (T1 – T4)
Disorders with Known Molecular Basis

Source: Online Mendelian Inheritance in Man, Morbid Anatomy of the Human Genome
NCATS: The Need

New Molecular Entities Entering Marketplace

Source: FDA
Development of New Therapeutics Is Slow, Expensive and Failure-Prone

- Drug Discovery: 10,000 Compounds
  - Preclinical Testing: 250 Compounds
  - Clinical Trials: 5 Compounds
- FDA Review: 1 Approved Drug
- Clinic: 1.5 Years
- 6.5 Years
- 6 Years

National Institutes of Health
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES
RESULTS
We found that during the past 40 years, 153 new FDA-approved drugs, vaccines, or new indications for existing drugs were discovered through research carried out in PSRIs.

PSRI-discovered drugs are expected to have a disproportionately large therapeutic effect.
Challenges & Opportunities

- Deluge of new discoveries of potential targets
- Unmet therapeutic needs for many conditions, especially rare and neglected diseases
- Need to view drug development pipeline as a scientific problem – ripe for experimentation and process engineering
Programs and Initiatives

Clinical and Translational Science Activities

- Clinical and Translational Science Awards

Rare Diseases Research and Therapeutics

- Therapeutics for Rare and Neglected Diseases
- Office of Rare Diseases Research

Re-engineering Translational Sciences

- Tox-21 and Tissue Chip Programs
- Repurposing
- New Therapeutic Uses for Existing Drugs
FY12 Research Budget ($576M)
Clinical and Translational Science Activities

Clinical and Translational Science Awards (CTSAs)

- Support a national consortium of medical research institutions
- Work together to improve the way clinical and translational research is conducted nationwide
- Aim to accelerate the research translation process
CTSAs: 60 CTSA sites in 30 states + DC

National Institutes of Health
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES
CTSAs: Accelerating Translation

Research Electronic Data Capture (REDCap)

- Easy-to-use, freely available tool for clinical study management and data capture
- Secure Web application that enables investigators to:
  - Create standardized surveys
  - Easily transfer data
  - Export data into a variety of statistical programs
- Makes it faster and easier to securely build and manage online surveys and databases
- Visit redcap.org
CTSAs: Accelerating Translation

ResearchMatch:

*Enabling New Opportunities for Research Participation (Researchmatch.org)*

- A free, secure, Web-based registry to improve clinical research
- Enables investigators and volunteers to find the right “match”
- Database of more than 20,000 registrants includes:
  - Rare diseases, common diseases, no disease
- Reduces recruitment costs
- Increases study enrollment
- Speeds research progress
Therapeutics for Rare and Neglected Diseased (TRND) Program

- Designed to re-engineer the development of new drugs for rare and neglected diseases
- Specifically intended to stimulate research collaborations for drug discovery and development between NIH and:
  - Academic scientists
  - Nonprofit organizations
  - Pharmaceutical and biotechnology companies
Why the low success rate in R&D?

High Rate of Phase 2 Failures – Efficacy, Toxicity, Commercial

Development Success Rates

NME Success Rates By Phase And Overall
2006-2010 Industry

Success rate for each phase

- Preclinical: 63%
- Phase 1: 47%
- Phase 2: 20.5
- Phase 3: 23%
- Registration: 32.4

Percent that will achieve 1 Approval

- 3%
- 5%
- 10%
- 46%
- 79%

Success Rate = (number of successes) / ((number of terminations) + (number of successes))
Why the low success rate? Toxicity

Preclinical (21%) + Clinical (12%) Tox = 33% of all failures

- Skin
- Cardiovascular
- Endocrine
- GI
- Hematopoietic
- Hepatic
- Neurological
- Urinary
- Other

% of compounds judged safe in animals that are non-toxic in humans

Source: Nature Reviews Drug Discovery 3, 227-236, 2004
Predictive toxicology

Tissue Chip for Drug Screening

Aims to develop a tissue chip that mimics human physiology to screen for safe, effective drugs

- Liver, heart, lung, other cell types
- Designed for multiple types of readouts

- NIH and Defense Advanced Research Projects Agency (DARPA) contribute $70M over 5 years; FDA provides guidance

- Seeking best ideas in engineering, biology, toxicology
Predictive toxicology

Tox21: Toxicology in the 21st Century

- A collaboration with:
  - NIH’s National Institute of Environmental Health Sciences
  - U.S. Environmental Protection Agency
  - U.S. Food and Drug Administration
- Designed to screen a collection of 10,000 compounds composed of environmental chemicals and drugs approved for use
- Looks for compounds’ potential to disrupt biological pathways that may be toxic
Improving Efficacy: Target Validation

- Many, many potential drug targets
- Genotype to Phenotype (G2P); Phenotype to Genotype (P2G)
- Opportunity to work collaboratively across sectors in precompetitive way to speed drug development
- Early stage of development
Drug Rescue and Repurposing

NIH – INDUSTRY ROUNDTABLE
April 21-22, 2011

Exploring New Uses for Abandoned and Approved Therapeutics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial Indication</th>
<th>Subsequent Indication</th>
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<tbody>
<tr>
<td>AZT</td>
<td>Antineoplastic</td>
<td>HIV/AIDS</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Bacterial infection</td>
<td>Amyotrophic lateral sclerosis</td>
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<tr>
<td>Hydroxyurea</td>
<td>Cancers</td>
<td>Sickle cell anemia</td>
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<tr>
<td>Metformin</td>
<td>Type 2 diabetes</td>
<td>Breast cancer</td>
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<tr>
<td>Pioglitazone</td>
<td>Type 2 diabetes</td>
<td>Hepatic steatosis</td>
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<tr>
<td>Raloxifene</td>
<td>Osteoporosis</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>Breast cancer</td>
<td>Bipolar disorder</td>
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Although the U.S. National Institutes of Health (NIH) has made a post-Biomedical Research and Development Act (BRD) and a new center for research on existing pharmacological compounds, so far the main effort to persuade drug companies to disclose their treasures of abandoned projects was made by Francis Collins, who revealed the ambitious plan to repurpose drugs for new uses.

NIH’s Secr...
Drug Rescue and Repurposing

- Match abandoned compounds from pharma with innovative ideas for new indications from NIH scientists
- NIH provides: RFA, review, funding
- Pharma provides: compounds and pertinent data
- Grantees provide: Great ideas and access to patients
- Program to launch this year, awards early in FY13
- Can this new model for collaboration deliver new medicines faster?
Drug Rescue and Repurposing

NIH

Grant review; funding; template agreements

New ideas for applications

Patients

Grant

MOU

Compounds; pertinent data

Researchers

Industry Partners

CRA
Cures Acceleration Network

- Created to advance development of “high need cures”
- Reduces barriers to translation in areas the private sector is less likely to pursue
- Funded via:
  - Grant awards with or without partnership
  - Flexible Research Awards: DARPA-like authority
    - Not to exceed 20 percent of total appropriated funds per fiscal year
- FY 2012 budget: $10 million
Catalyzing Collaborations With External Partners

NIH Translational Sciences

- Biotech
- Academia
- Advocacy Groups
- Pharma
- Non-Profits
- FDA
Learn More About NCATS

ncats.nih.gov

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