Opportunities for Research and NIH

Francis S. Collins

The mission of the National Institutes of Health (NIH) is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and to reduce the burdens of illness and disability. The power of the molecular approach to health and disease has steadily gained momentum over the past several decades and is now poised to catalyze a revolution in medicine. The foundation of success in biomedical research has always been, and no doubt will continue to be, the creative insights of individual investigators. But increasingly those investigators are working in teams, accelerated by interdisciplinary approaches and empowered by open access to tools, databases, and technologies, so a careful balance is needed between investigator-initiated projects and large-scale community resource programs. For both individual and large-scale efforts, it is appropriate to identify areas of particular promise. Here are five such areas that are ripe for major advances that could reap substantial downstream benefits.

High-Throughput Technologies

In the past, most biomedical basic science projects required investigators to limit their scope to a single aspect of cell biology or physiology. The revolution now sweeping the field is the ability to be comprehensive—for example, to define all of the genes of the human or a model organism, all of the human proteins and their structures, all of the extensive information about the genetic underpinnings of 20 major tumor types. This information will likely force a complete revision of diagnostic categories in cancer and will usher in an era where abnormal pathways in specific tumors will be matched with the known targets of existing therapeutics. Another example is the opportunity to understand how interactions between ourselves and the microbes that live on us and in us (the “microbiome”) can influence health and disease (2).

Translational Medicine

Critics have complained in the past that NIH is too slow to translate basic discoveries into new diagnostic and treatment advances in the bring them to clinical trials and U.S. Food and Drug Administration (FDA) approval.

As one example, the NIH Therapeutics for Rare and Neglected Diseases (TRND) (3) program will allow certain promising compounds to be taken through the preclinical phase by NIH, in an open environment where the world’s experts on the disease can be involved. Furthermore, as information about common diseases increases, many are being resolved into distinct molecular subsets, and so the TRND model will be even more widely applicable.

The first human protocol (for spinal cord injury) involving human embryonic stem cells (hESCs) was approved by the FDA in 2009, and the opening up of federal support for hESC research will bring many
Disorders with Known Molecular Basis

Source: Online Mendelian Inheritance in Man
GWAS hits for common disease
The Cancer Genome Atlas (TCGA)

- A comprehensive, collaborative effort led by NIH
  - To map genomic changes in major types, subtypes of cancer …
  - To help chart a new course in cancer research
- Pilot project
  - Established scientific infrastructure; demonstrated “proof of concept”
  - Focused on 3 types of cancer: glioblastoma multiforme; ovarian; lung
- Current goal: to identify recurrent genomic and epigenomic drivers for at least 20 cancers over next 3 years
Application of Fundamental Knowledge
Application of Fundamental Knowledge
A 2010 trans-NIH inventory of activities relevant to therapeutics development found:
- Substantial investments in therapeutics development research
- Approximately 65% preclinical research; 35% clinical research
- 550 activities reported of varying sizes and areas of emphasis
May 2010
- NIH Director asks SMRB to determine how NIH could better support translational and therapeutic sciences

December 2010
- SMRB recommends (12 to 1) that a new translational medicine and therapeutics center be created
- SMRB also recommends NIH undertake a more extensive and detailed analysis through a transparent process to evaluate the new center’s impact
SMRB Members

- Norman Augustine (Chairman) Lockheed Martin
- Jeremy Berg, NIGMS
- Josephine Briggs, NCCAM
- William Brody, Salk Institute for Biological Studies
- Gail Cassell, Eli Lilly and Company
- Francis Collins, NIH (ex officio)
- Anthony Fauci, NIAID
- Dan Goldin, Intellisis Corporation
- Eric Green, NHGRI
- Richard Hodes, NIA
- Stephen Katz, NIAMS
- Thomas Kelly, Sloan-Kettering Institute
- Deborah Powell, University of Minnesota Medical School
- Griffin Rodgers, NIDDK
- William Roper, University of North Carolina
- Arthur Rubenstein, University of Pennsylvania School of Medicine
- Susan Shurin, NHLBI
- Solomon Snyder, Johns Hopkins University
- Huda Zoghbi, Baylor College of Medicine
- Harold Varmus, NCI
Creation of the National Center for Advancing Translational Sciences (NCATS)

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.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Target ID</th>
<th>Assay Dev.</th>
<th>HTS</th>
<th>Probe to Lead</th>
<th>Pre-Clinical</th>
<th>FDA IND</th>
<th>Ph. I</th>
<th>Ph. II</th>
<th>Ph. III</th>
<th>FDA Review</th>
<th>Clinic</th>
</tr>
</thead>
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The diagram illustrates the stages of drug development from Disease to Clinic, including Target ID, Assay Dev., HTS, Probe to Lead, Pre-Clinical, FDA IND, Ph. I, Ph. II, Ph. III, FDA Review, and Clinic.
NCATS will:

- Facilitate – not duplicate – the translational research activities supported and conducted by the ICs
- Complement – not compete with – the private sector
- Reinforce – not reduce – NIH’s commitment to basic science research
New Paradigms: Rescuing and Repurposing

NIH – INDUSTRY ROUNDTABLE
April 21–22, 2011

Exploring New Uses for Abandoned and Approved Therapeutics
Cures Acceleration Network (CAN)

- Authorized in Affordable Care Act, awaits appropriation
- CAN will:
  - Advance development of “high need cures”
  - Reduce barriers to translation in areas the private sector is unlikely to pursue actively
- Funding mechanisms:
  - Grant Awards – with or without partnership:
    • Up to $15 million per award per fiscal year
  - Flexible Research Awards:
    • DARPA-like authority
    • Not to exceed 20% of total appropriated funds /fiscal year
SMRB Recommendations

Recommendation made, November 16, 2010:

- Create a new Institute focusing on substance use, abuse, and addition (“SUAA”) research and related public health initiatives
- Integrate relevant research portfolios from NIDA, NIAAA, other ICs
Substance Use, Abuse, and Addiction
Action Timeline

- January to March 2011: SUAA Task Force conducted internal discussions with NIH scientific staff in the ICs that could potentially be affected by the proposed changes
- April 2011: based on those discussions, Task Force developed draft guiding principles
Task Force Considerations and Guiding Principles

- **Science**: the nature of the science being conducted is the primary factor driving recommendations

- **Populations with Co-Morbid Addictive Behaviors**: addictive behavior frequently co-exists with other medical disorders, including mental disorders, e.g., post-traumatic stress, borderline personality, and schizophrenia
  - When the pathophysiology of the underlying disorder is distinct from the addictive behavior, the primary disorder requires separate consideration

- **Special Expertise**: the expertise of staff needed to manage and foster a research area is critical in recommending placement of programs
Substance Use, Abuse, and Addiction Action Timeline

- January to March 2011: SUAA Task Force conducted internal discussions with NIH scientific staff in the ICs that could potentially be affected by the proposed changes
- April 2011: based on those discussions, Task Force developed draft guiding principles
- June 2011 to Fall 2012: Task Force, NIDA/NIAAA Intramural, IC Leadership
  - Complete portfolio analysis of all relevant grants, cooperative agreements, contracts, and intramural research projects; develop final portfolio integration plan
  - Develop Scientific Strategic Plan including input from stakeholders
Substance Use, Abuse, and Addiction Action Timeline

- Tobacco Research at NCI
  - The Task Force is currently analyzing the NCI portfolio and has determined that portions of the nicotine and tobacco portfolios related to addiction and control could be candidates for inclusion in the proposed Institute. However, this portfolio is complex and more time needs to be taken to determine what would make the most sense to be included in the proposed Institute.
Substance Use, Abuse, and Addiction Action Timeline

- **Fall 2012:**
  - Release of Portfolio Integration Plan and public comment period
  - Release of Scientific Strategic Plan and public comment period
- **December 2012:** Final Recommendations to NIH Director
- **January/February 2013:** Include in President’s FY 2014 Budget
  - Start implementing parts of Scientific Strategic Plan not involved in reorganization
- **October 2013 (FY 2014):** National Institute of Substance Use and Addiction Disorders
Challenges to Biomedical Research

Appropriation History vs. Actual Purchasing Power

FY 1998 appropriation – FY 2012 Presidential Budget ($ in billions)

(Bar chart showing appropriations for each fiscal year from 1998 to 2012, with ARRA and ARRA in 1998 Dollars highlighted.)
NCATS: Functions

Improve the processes of diagnostics and therapeutics development, testing, and implementation by:

▪ Experimenting with innovative approaches in an open-access model
▪ Choosing therapeutic projects to evaluate these innovative approaches
▪ Promoting interactions to advance the field of regulatory science

Catalyze the development and implementation of new diagnostics and therapeutics by:

▪ Encouraging collaborations across all sectors
▪ Providing resources to enable diagnostics and therapeutic development and implementation
▪ Enhancing training in relevant disciplines
NIH-FDA Collaborations

- NIH-FDA Regulatory Science Initiative: cooperative research grant awards to advance translational and regulatory science
- NIH-FDA Joint Leadership Council (est. 2010)
  - Goal: advance translational sciences by ensuring that:
    - Regulatory considerations are integral to biomedical research planning
    - The latest science informs the regulatory review process
  - Six working groups currently reviewing proposals for collaboration:
    - To better define regulatory pathways for coordinated approval of co-developed diagnostics and therapeutics
    - To develop risk-based approaches for best review of diagnostics
Catalyzing Collaborations With External Partners

NIH Translational Sciences

- International Efforts
- Biotech
- Non-Profits
- FDA
- Advocacy Groups
- Academia
FY 2010 Percent Distribution of Basic and Clinical Research

- Basic Research: 52.0%
- Applied Research (Clinical): 34.6%
- Applied Research (Other): 10.5%
- Training & Overhead: 2.6%
- R&D Facilities: 0.3%
A Definitive List of Approved Drugs

- NIH Chemical Genomics Center (NCGC): national resource for translating genomic information into biological insights and new therapeutics.
- NCGC Pharmaceutical Collection:
  - Definitive list of all small-molecule drugs approved for human or veterinary use (U.S. and worldwide).
  - All data publicly available.
- Purpose: facilitate understanding of drug mechanisms; drug repurposing, especially for rare and neglected diseases.
Tell us what you think...

Feedback NIH

Provide input on important issues that affect NIH, the biomedical research community, and human health in general.