NIH: Steward of Medical and Behavioral Research for the United States

“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 reduce illness and disability.”
NIH’s Impact on U.S. Health and Medicine

U.S. Life Expectancy

- Cardiovascular disease death rates have fallen more than 70% in the last 60 years
- Cancer death rates now falling more than 1% per year; each 1% drop saves ~$500 billion
- HIV therapies enable people in their 20s to live to age 70+
Shaping the Health Care Landscape

- Unraveling Life’s Mysteries through Basic Research
- Translating Discovery into Health
- Precision Medicine Initiative®
- The National Cancer “Moonshot”
- Supporting Research Essentials
Disorders with Known Molecular Basis

Source: Online Mendelian Inheritance in Man, Morbid Anatomy of the Human Genome
Undiagnosed Diseases Program (UDP)

- Patients with longstanding, undiagnosed medical conditions are seen at NIH Clinical Center
- UDP’s NIH-wide staff, led by Dr. William Gahl, has:
  - Evaluated ~3,300 medical records
  - Accepted ~900 cases
  - Determined some diagnosis in ~25%
- From UDP to “UDN”: expanding the model ...

HARD CASES: INVESTIGATING RARE & TOUGH DISEASES

*Dr. William Gahl is one of the last, best hopes for people suffering from rare.*
The NIH site will continue to enroll about 150 patients per year, each of the clinical sites will ultimately enroll about 50 patients per year.
NIH’s Rare Diseases Clinical Research Network (RDCRN)

Designed to advance medical research on rare diseases by facilitating collaboration, study enrollment, data sharing

- 22 consortia at 250 institutions worldwide; each:
  - Focuses on at least three rare diseases
  - Participates in multisite studies
  - Actively involves patient advocacy groups as partners

- Studying >200 diseases with 83 active protocols
  - More than 85 patient advocacy groups participating
Collaborative clinical research
Centralized data coordination and technology development
Public resources and education
Training

www.rarediseasesnetwork.org
Harnessing Data to Improve Health: BD2K (Big Data to Knowledge)

NIH’s 6-year initiative to use data science to foster an open digital ecosystem that will accelerate efficient, cost-effective biomedical research to enhance health, lengthen life, and reduce illness and disability.

Programs and activities:
- Advance discovery for biomedical research
- Facilitate use and re-use of biomedical data
- Develop analytical methods and software
- Enhance biomedical data science training
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~500 with therapy
National Center for Advancing Translational Sciences (NCATS)

Mission:
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.

http://ncats.nih.gov/
Human Tissue Chip Program

Goal: develop biochip to screen for safe, effective drugs

- NIH phase 1: create individual chips (18 awards)
- NIH phase 2: cell incorporation and organ integration
  - Awards support 11 institutions, to collaborate over three years
- Current focus:
  - Integration, compound testing, validation
  - Partnerships (MTA: GSK, Pfizer; MOU: IQ Consortium)
  - Adoptions of the tech to the community
Human Tissue Chip, Phase II: Toward an Integrated Microphysiological System

‘Organs-on-chips’ go mainstream
Therapeutics for Rare and Neglected Diseases (TRND) Program

To speed the development of new drugs for rare and neglected diseases

- Model: collaboration between NIH labs and extramural labs with appropriate expertise
- Projects:
  - May enter at various stages of development
  - Taken to stage needed to attract external organization to adopt for final clinical development
  - Serve to develop new generally applicable platform technologies and paradigms
- Encourages creative partnerships and novel approaches to intellectual property
TRND Development of Cyclodextrin
For the Treatment of Niemann-Pick Type C1 (NPC) Disease

- NPC: fatal autosomal recessive, neurodegenerative childhood disease characterized by failure to metabolize and dispose of cholesterol and lipids
  - Defects in NPC1, NPC2 proteins cause cholesterol accumulation in lysosomes
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  - Granted breakthrough therapy designation by FDA, Jan. 2016
Accelerating Medicines Partnerships (AMP)

NIH partnered with FDA, 10 biopharmaceutical firms, multiple non-profits (including patient advocacy groups), to:
- Increase the number of new diagnostics, therapies
- Reduce time, cost of developing them

Investing >$230M over five years on three pilot projects:
- Alzheimer’s disease
- Autoimmune disorders (rheumatoid arthritis and systemic lupus erythematosus)
- Type 2 diabetes
Zika Virus Research

- Discovered in Uganda in 1947; member of flavivirus family
  - NIH scientists, grantees, have long studied Zika’s relatives – such as dengue and West Nile Virus
  - Findings may aid current investigations of Zika

- NIH is accelerating Zika research – to understand its natural history; develop rapid, specific diagnostic tests; create effective vaccines, treatments

- New White House request to expand Zika research funding

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“Tonight, I’m launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes – and to give all of us access to the personalized information we need to keep ourselves and our families healthier.”

President Barack Obama
State of the Union Address, January 20, 2015
Engaged Participants

EHRs

Technologies

Genomics

Data Science
Precision Medicine Initiative® (PMI) Cohort
Enrolling One Million or More U.S. Volunteers

www.nih.gov/precisionmedicine
Scientific Opportunities in U.S. PMI Cohort Program

- Develop quantitative estimates of risk for a range of diseases by integrating environmental exposures and genetic factors
- Identify causes of individual variation in response to commonly used therapeutics (pharmacogenomics)
- Discover biological markers that signal increased or decreased risk of developing common diseases
- Understand and address causes of health disparities
- Use mobile health (mHealth) technologies to correlate activity, physiological measures, environmental exposures with health outcomes
- Develop new disease classifications and relationships
- Empower study participants with data and information to improve their own health
- Create platform to enable trials of targeted therapies
Assembling the PMI Research Cohort

- One million or more volunteers
  - Broadly reflect the diversity of the U.S. (including all ages, health statuses, areas)
  - Strong focus on underrepresented groups
- Longitudinal cohort with continuing interactions
  - Collect EHR data, provide biospecimen(s) and survey, complete baseline exam
- Two methods of recruitment
  - Direct volunteers
    • Anyone can sign up
  - Healthcare provider organizations (incl. FQHCs)
    • Consider diversity of HPO participants, robustness of EHR, patient follow-up
PMI Core Values

1. Participation is open to interested individuals
2. Representing the rich diversity of America is essential
3. Participants are partners (not patients, not subjects) in all phases of the cohort program
4. Participants have access to study information and data about themselves
5. Project adheres to the PMI privacy principles and forthcoming security framework
6. Data can be accessed broadly for legitimate research purposes
7. PMI is a catalyst for progressive research programs and policies
First PMI Cohort Program Funding Opportunities
Announced November, 2015

www.nih.gov/precision-medicine-initiative-cohort-program/funding-opportunities
First PMI Cohort Program Funding Opportunities

Announced November, 2015

- Two “Other Transactions” award announcements
  - Direct Volunteer Pilot
  - Communications and Engagement
  - Stay tuned for news …

- Four cooperative agreements announcements
  - Coordinating Center
  - Healthcare Provider Organization Enrollment Centers
  - Biobank
  - Participant Technologies Center

- PMI Cohort Program Advisory Panel formed
  - Will provide external oversight, expert advice on vision, goals, operations of Cohort Program
U.S. Precision Medicine Initiative® (PMI) for Oncology

*Goal: Apply tenets of precision medicine to cancer*

To reach this goal, PMI-Oncology (PMI-O) will enable research to:

- Create multi-drug, multi-arm trials driven by cancer genomics
  - Solid tumors, lymphomas
- Identify new cancer subtypes, therapeutic targets
- Partner with private sector to test multiple targeted drugs
  - >20 companies participating
- Test combination therapies – to go beyond remission to cure?
- Understand and combat drug resistance
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National Cancer “Moonshot”

“For the loved ones we’ve all lost, for the families that we can still save; let’s make America the country that cures cancer once and for all. What do you think? Let’s make it happen. And medical research is critical.”

~ President Barack Obama
State of the Union Address, January 12, 2016
National Cancer “Moonshot”

- Multi-year initiative, led by the Vice President, to:
  - Break down silos to unite “cancer fighting” community
  - Increase resources devoted to fighting cancer
- NIH’s role: with proposed additional $680M for FY 2017
  - Encourage cooperation, data sharing
  - Expand access to leading-edge treatments, clinical trials
    - Follow pioneering, participant-centric new models (PMI)
  - Accelerate research on new approaches for cancer prevention, screening, diagnosis, treatment
    - Including efforts to narrow or overcome health disparities
“Moonshot”: Accelerating Research

**Cancer Vaccines**

- **Scientific Rationale**
  - Cancers caused by viruses, or that produce unique or signature premalignant genetic changes, can be prevented by vaccines

- **Possible Activities**
  - Produce Epstein-Barr Virus (EBV) vaccine for human safety testing
  - Explore development of vaccines for high risk individuals
“Moonshot”: Accelerating Research

Early Cancer Detection

- Scientific Rationale
  - Tumors shed DNA, RNA, exosomes, other biological materials into circulation, where they can be detected

- Possible Activities
  - Develop tools and techniques to improve sensitivity, specificity of detection assays
“Moonshot”: Accelerating Research

**Single-cell Genomic Analysis**

- **Scientific Rationale**
  - Genomic mutations that occur in tumor cells and nearby cells (stromal, immune) can help inform design of targeted drugs, immunotherapy

- **Possible Activities**
  - Conduct single-cell analyses to uncover genomic heterogeneity of the cells in a tumor
“Moonshot”: Accelerating Research

Cancer Immunotherapy

- **Scientific Rationale**
  - Key molecules on cancer cells may make them more (or less) likely to attract tumor-killing immune cells

- **Possible Activities**
  - Support basic research to better understand cancer immunology and extend immunotherapy’s reach to all kinds of cancer
“Moonshot”: Accelerating Research

**Pediatric Cancer**

- **Scientific Rationale**
  - In contrast to adult cancers, many childhood tumors have transcription factors that are permanently switched on, which has made it more difficult to develop drugs

- **Possible Activities**
  - Prepare and screen new libraries of compounds chosen for their potential to interfere with these transcription factors
  - Intensify collection, analysis of very rare childhood cancers
“Moonshot”: Accelerating Research

Data Sharing

- **Scientific Rationale**
  - Sharing of data can break down barriers between institutions to maximize the knowledge gained, benefits for patients

- **Possible Activities**
  - Expand capacity of NCI Genomic Data Commons to handle genomic, clinical data from patients, health-care providers
“Moonshot”: Accelerating Research

Exceptional Opportunities in Cancer Research Fund

- Scientific Rationale
  - Providing a competitive opportunity for high-risk, high-reward ideas can stimulate innovation

- Possible Activities
  - Pursue previously unanticipated scientific opportunities to improve cancer outcomes
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National Institutes of Health Funding 1990-2017

Note: The 3.7% Real Annual Growth is based on real compound annual growth between 1971 and 2000. Dollar values are adjusted to 2012 dollars using the Biomedical Research and Development Price Index (BRDPI), http://officeofbudget.od.nih.gov/gbiPriceIndexes.html. Source: NIH Office of Extramural Research and Office of Budget source data (January 19, 2016)
21st Century Cures

- Bipartisan effort to:
  - Establish Innovation Fund
    - $8.75B over 5 years
  - Raise cap on loan repayment program
  - Reduce administrative burden for researchers
- Status: passed by the House (344-77) on July 10, 2015
  - Senate currently working on companion legislation
NIH’s New Strategic Plan

Overview
- Mission of NIH
- Unique moment of opportunity in biomedical research
- Current NIH-supported research landscape
- Constraints confronting the community in the face of lost purchasing power

Objective 1: Advance Opportunities in Biomedical Research

Fundamental Science
- Foundation for progress
- Consequences often unpredictable
- Technology leaps catalyze advances
- Data science increases impact/efficiency

Health Promotion/Disease Prevention
- Importance of studying healthy individuals
- Advances in early diagnosis/detection
- Evidence-based reduction of health disparities

Treatments/Cures
- Opportunities based on molecular knowledge
- Breakdown of traditional disease boundaries
- Breakthroughs need partnerships, often come from unexpected directions
- Advances in clinical methods stimulate progress

Objective 2: Set Priorities
- Incorporate disease burden as important, but not sole factor
- Foster scientific opportunity; need for nimbleness
- Advance research opportunities presented by rare diseases
- Consider value of permanently eradicating a pandemic risk

Objective 3: Enhance Stewardship
- Recruit/retain outstanding research workforce
- Enhance workforce diversity
- Encourage innovation
- Optimize approaches to inform funding decisions
- Enhance impact through partnerships
- Ensure rigor and reproducibility
- Reduce administrative burden

Objective 4:
Excel as a Federal Science Agency by Managing for Results
NIH... Turning Discovery Into Health

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