Disclosures

- The National Institutes of Health (NIH) has 20 US patents on which I am a named inventor.

- The patents cover various technologies:
  - For producing virus-like particle vaccines
  - For producing papillomavirus pseudoviruses for tumor detection and treatment
  - For efficiently inducing therapeutic auto-antibodies
  - For measuring immune responses to papillomavirus infection or vaccination

- Parts of the technologies have been licensed to Merck, GlaxoSmithKline, Sanofi, Shanta Biotech, Cytos Biotech, Aura Biosciences, Etna Biotech, Acambis, PanVax
Outline of Presentation

- NCI’s FY17 Professional Judgment Budget
- PMI for Oncology
- Some current NCI priorities
- Advice from CTAC
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Cancer Trends

The overall cancer death rate in the United States fell by 23% from 1990 to 2012.

Worldwide cancer cases will increase by 52% from 14.1 million in 2012 to 21.4 million in 2030.

Worldwide cancer deaths will increase by 61% from 8.2 million in 2012 to 13.2 million in 2030.


Source: American Cancer Society: Global Cancer Facts & Figures, Second Edition
The horizontal dotted line at $2.9 billion indicates the inflation-adjusted 2015 budget was similar to the 1999 budget, the first year of the “NIH doubling”
The President’s FY16 Budget Appropriation Proposal for NCI/NIH

- A $1 billion increase for NIH (from $30.084 billion to $31.084 billion)
- A $145 million increase for NCI (from $4.953 billion to $5.098 billion)
  - $70 million of the increase for NCI is for the oncology portion of the Precision Medicine Initiative
- Each house of Congress has passed somewhat different bills that support at least these proposed increases for NCI & NIH
Current Status of FY16 Budget Proposal for NCI/NIH

- The current continuing resolution keeps the government funded at FY15 levels; it expires December 11, 2015
- Overall budget parameters for FY16 have been passed (10 AM presentation by MK Holohan)
- NCI participated in Senate Appropriation Committee hearing for NIH on October 7
- We plan to provide a legislative update at the joint NCAB/BSA meeting, December 1 – please join via webcast
The FY17 NCI Budget Proposal

A Transformational Moment in Cancer Research

http://www.cancer.gov/about-nci/budget/plan; thanks to Richard Manrow, Julie Cheh, Peter Garrett, Anne Lubenow, and many others
NCI recommends a funding increase of 7 percent over the fiscal year 2016 level to pursue promising research opportunities that improve our understanding of cancer and reduce the burden of the disease. An annual increase of 7 percent for the next 10 years is necessary to achieve these goals. These steady increases will result in a fiscal year 2026 budget for NCI that is twice what it is today.
Some Priorities and Opportunities Highlighted in NCI Annual Plan and Budget Proposal for FY 2017
FY 2017 Bypass Budget Blog Series

- Sept 24  NCI’s Research Response to Changing Cancer Trends
- Oct 8    Progress Against Cancer: The Role of Basic Science
- Oct 22   Bringing Cancer Research to the Public: NCI’s Networks and Programs
- Nov 5    A Holistic Approach to Reducing Cancer Health Disparities
- Nov 19   Precision Medicine Part I: Understanding Precision Medicine
- Dec 10   Precision Medicine Part II: Clinical Trials for Adults and Children
- Jan 13   Cancer Prevention: The Best Defense
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Components of PMI-Oncology

- Developing and expanding clinical therapy trials in precision oncology
- Improving predictive oncology: by overcoming drug resistance, determining effective combination targeted therapy, and advancing immunotherapy
- Creating a new array of laboratory models, to increase understanding of cancer biology and achieve the goals of predictive oncology
- Building a national cancer knowledge system that integrates cancer genomic information, clinical information, and laboratory model information
June 1, 2015
NCI MATCH* Trial
Announced:
Now Starting to Accrue Patients

*Molecular Analysis for Therapy CHoice
Precision Oncology Trials Launched
2014:
- MPACT
- Lung MAP
- ALCHEMIST
- Exceptional Responders

2015:
- NCI-MATCH
- ALK Inhibitor
- MET Inhibitor

NCI-MATCH: Molecular Analysis for Therapy Choice

- Foundational treatment/discovery trial that forms the basis for PMI
- Assigns therapy based on molecular abnormalities, not site of tumor origin for patients without available standard therapy
- Regulatory umbrella for phase II drugs/studies from > 20 companies; single agents or combinations
- Available nationwide (2400 sites)
- Accrual began mid-August 2015
THE PROMISE OF PRECISION ONCOLOGY
BUILDING ON GENOMIC RESEARCH TO ADVANCE CANCER CARE

2006-2013
THE CANCER GENOME ATLAS
GROUNDBREAKING WORK ON THE GENETICS OF CANCER
- TARGET for children’s cancers

2014
TCGA-TARGET
INSPIRED PRECISION MEDICINE TRIALS
- MPACT
- Lung-MAP
- Exceptional Responders Initiative
- ALCHEMIST

2015
NCI-MATCH
APPROVED & LAUNCHED
- Largest precision medicine trial in history
- Matches treatments to patients based on tumor mutations and not on organ of origin

2015 & Beyond
NCI-MATCH+
SCALING UP TO SUPPORT THE PRESIDENT’S PRECISION MEDICINE INITIATIVE
- Use NCI-MATCH signals to broaden molecular profiling in new trials
- Discover new ways to overcome tumor drug resistance
- Build a database accessible to researchers and health care workers
- Accelerate plans for Pediatric NCI-MATCH trial

www.cancer.gov/precision-medicine
PMI-O: Some Anticipated Deliverables

• Increase the number of drugs and indications for the targeted treatment of cancer in adults & children
• Expand our understanding of drug resistance and how to overcome it, and the rules of targeted combination treatment, including immunotherapy
• Sharpen our ability to diagnose cancer at its earliest stages, when it is usually most treatable
• Improve predictive oncology: the accurate prediction of the right treatment for the right patient
• Establish a sustainable infrastructure to accommodate a progressively increasing cancer genomic database
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Some Current NCI Priorities

- Investigator-initiated research
  - New Outstanding Investigator Award (R35): 7 years, up to $600,000/year in direct costs
  - Strong support for fundamental basic research
- Understanding and overcoming cancer health disparities: biology, lifestyle, access/utilization
- Support for research infrastructure
  - Increasing core grants for NCI-Designated cancer centers
- Precision oncology in cancer prevention & screening
“…Mutations in a set of 15…genes appear to be strongly preferentially associated with CRCs arising in AA versus Caucasian individuals, suggesting an important difference in the mutational landscapes of CRCs arising in different ethnic groups.”

Some Current NCI Priorities

- Investigator-initiated research
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Precision Oncology in Cancer Screening

- Moving from screening based mainly on “pattern recognition” towards screening based mainly on molecular understanding of disease and its application to molecular diagnostics

- The example of cervical cancer screening

- Cytologic (Pap) screening is more sensitive for detecting squamous cell cancer precursors than adenocarcinoma precursors; squamous cell cancer incidence has decreased, but not adenocarcinoma
HPV testing can prevent more cervical cancers, especially adenocarcinomas, than cytology.

Pooled cervical cancer incidence from 4 randomized controlled trials of cytology (control arm) vs. HPV testing (experimental arm)

HPV Methylation for Triage of HPV-positive women

- HPV methylation can achieve risk stratification that alters clinical management
- Methylation testing can be done from the HPV DNA sample, is applicable for self-sampling

Mirabello et al. JNCI 2012; Wentzensen et al. JNCI 2012; Clarke, Wentzensen et al. CEBP 2012
Precision Oncology in Cancer Prevention

- The example of aspirin
- Aspirin can reduce the risk of several cancers, especially colorectal cancer (CRC)
  - USPSTF draft recommendation (Sept 2015) for some patients to prevent cardiovascular disease & colorectal cancer
- Concern about side effects (especially an increased risk of bleeding) has prevented aspirin from being more widely recommended for reducing cancer risk
- To increase the benefit/harm ratio, use molecular understanding to risk-stratify those patients who will derive the most benefit
High 15-Hydroxyprostaglandin (15-HPGD) in normal colon is associated with reduced risk of CRC in regular aspirin users

<table>
<thead>
<tr>
<th></th>
<th>Non-Users</th>
<th>Regular aspirin users</th>
</tr>
</thead>
<tbody>
<tr>
<td>All CRC</td>
<td>1.0</td>
<td>0.73 (0.62-0.86)</td>
</tr>
<tr>
<td>High 15-PGDH CRC</td>
<td>1.0</td>
<td>0.49 (0.34-0.71)</td>
</tr>
<tr>
<td>Low 15-PGDH CRC</td>
<td>1.0</td>
<td>0.90 (0.63-1.27)</td>
</tr>
</tbody>
</table>

**Background information:** 15-HPGD is down-regulated in CRC; 15-HPGD knock-out mice have increased colon tumors that are resistant to COX-2 inhibitors

*Fink et al, Sci Transl Med, 2014*

**Potential for Genomic analysis to predict those who will benefit most from aspirin:** Nan et al, JAMA, 2015
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CTAC – Advice Resulting in Change

- Optimizing scientific opportunities by restructuring NCI’s Clinical Trials Infrastructure (NCTN, NCORP, and ETCTN) - 2014

- Integrating biomarkers, imaging and quality of life studies into clinical trials in a timely manner through the development of a funding mechanism (BIQSFP – 2008; $50 million as of April 2015)

- Reducing the timeline for clinical trial activation to bring new therapies to patients faster (CTAC - Operational Efficiency Working Group – 2010)

- Enhancing the quality of NCTN clinical trials through portfolio assessment and strategic recommendations (CTAC - NCTN Strategic Planning Working Group – 2014)

- Incentivizing clinical trial collaboration among SPORE, Cancer Centers, and NCTN investigators by harmonizing program guidelines (Guidelines Harmonization Working Group – 2009)
CTAC – Ongoing and Future Advice

• Oversight of the Recalcitrant Cancer Research Act
  – Identified scientific opportunities for advancing research progress in pancreas ductal adenocarcinoma (PDAC) and small cell lung cancer (SCLC)
  – Ongoing oversight of research progress on initiatives outlined in the scientific frameworks for PDAC and SCLC submitted to Congress in 2014

• Periodic assessment of NCI’s clinical trials portfolio and recommendations for improvement

• Providing a vision and recommended actions to guide the NCI clinical trials enterprise over the next decade