NCI Director’s Report
Norman E. Sharpless, M.D.

March 7, 2018
NCI Appropriations
FY 2013-2018 (in millions)

Source: NCI Office of Budget and Finance
Intergovernmental Affairs
Collaborating with FDA and CMS

Scott Gottlieb
Commissioner of FDA

• Oncology Center of Excellence
• Joint Training
• Data Sharing
• Compliance advice on cell manufacture

Seema Verma
Director, CMS

• Help with NGS coverage decision
• Data Sharing
• Discussions over enhanced coverage of clinical trials
Interactions with HHS

Alex M. Azar II
Secretary, HHS

Eric D. Hargan
Deputy Secretary, HHS
Congressional Outreach
Promoting Value, Affordability, and Innovation in Cancer Drug Treatment

A Report to the President of the United States from the President’s Cancer Panel
Early Stage Investigators

- NCI recognizes that Early Stage Investigators (ESI) face challenges.
- In addition to increased ESI payline, NCI is announcing its new use of the MERIT Award in 2018.
- The award gives eligible investigators applying for first R01 the opportunity to obtain up to seven years of grant funding (5+2)
- This will provide critical time for ESIs to launch their careers and become more established before attempting renewal.
Applied Proteogenomics Organizational Learning and Outcomes (APOLLO)

Veterans
Active Duty & DoD Beneficiaries
Civilians

Consents to APOLLO

VA Hospitals
Murtha CC

VA ORD & NCI-sponsored Clinical Trials

Adaptive Learning Healthcare System

Clinical Data
Research Data

American Genome Center
CTEP
CPTAC
Global Health Working Group

Sample questions

1. Balance of functions for CGH (representational vs. research)?
2. Portfolio analysis?
3. How to set priorities for NCI given the tremendous international burden of cancer?

Global Health

• Deborah Bruner, RN, PhD
  Emory University
• Satish Gopal, MD
  UNC Chapel Hill
Sample questions

1. Are award sizes for the different phases of funding for SBIR/STTR appropriate?
2. How to improve review?
3. What resources in addition to funding should SBIR provide?
4. How to speed delivery of funds to small companies?
Informatics Working Group

- Provide input into the role of the CBIIT director, focusing particularly on whether the duties of a chief information officer should be separate.
- Advise on expanding funding opportunities for data science and bioinformatics research across the NCI research portfolio and building a cancer-focused data science and bioinformatics workforce.
- Provide guidance for improving data sharing to maximize the impact of cancer research on patients.

Informatics

- Mia Levy, MD
  Vanderbilt University
- Charles Sawyers, MD
  Memorial Sloan Kettering Cancer Center
Cancer Moonshot

April 2017
- Cancer Moonshot Implementation Teams Developed Scientific Proposals

May 2017
- NCI Scientific Program Leaders reviewed and recommended

June 2017
- BSA reviewed and recommended

Oct 2017
- FY 2018 FOAs Released
Partnership for Accelerating Cancer Therapies (PACT)

National Cancer Institute - Division of Cancer Treatment & Diagnosis

Cancer Immune Monitoring Analysis Centers (CIMACs)
- Dana-Farber
- Stanford
- Mount Sinai
- MD Anderson

Cancer Immunologic Data Commons (CIDC)
- Dana-Farber Cancer Institute

Companies:
- AbbVie
- Amgen
- Boehringer Ingelheim
- BMS
- Celgene
- Genentech
- Gilead
- GSK
- Janssen
- Novartis
- Pfizer
- Sanofi
Two New Immunotherapy Networks

ADULT CANCERS

Immuno-Oncology Translational Network
(IOTN, U01)

PEDIATRIC CANCERS

Pediatric Immunotherapy Discovery and Development Network
(PIDDN, U54)
Projects enter the pipeline on a competitive basis at any stage of the pipeline. Since inception in 2009 NExT has received over 650 applications.
NExT Pipeline

**Discovery**
- Target Validation
- Exploratory Screen Development
- Screening/Hit-to-Lead
- Lead Development

**Preclinical Development**
- Candidate Selection

**Development**
- **MCL1 Inhibitor**
  - Mutant IDH1 inhibitor
- **DNMT1 Inhibitors (TdCyd)**
- **11-1F4 mAb Amyloidosis**
- **Endoxifen**
- **Mer Kinase Inhibitors**
- **NIR Fluorophore**
- **EGFR Panitumumab**
- **LUM15**

Artemis Endonuclease inhibitor
AAA ATPase p97 inhibitor
Taspase1 inhibitor
WDR5-MLL1 inhibitor
LDHA inhibitor
SHP2 inhibitor
PHGDH inhibitor

Endoxifen

DNMT1 Inhibitors (TdCyd)
11-1F4 mAb Amyloidosis
Endoxifen
Mer Kinase Inhibitors
NIR Fluorophore
EGFR Panitumumab
LUM15
Mcl-1 Inhibitor Discovery by Fragment-Based Methods & Structure-Based Design

**K_i = 131 μM**

**K_i = 60 μM**

**Fragment hits**

**Fragment-guided fragment merging**

**Binding interface Expansion**

**Structure-guided Tethering**

**Med. Chem. Optimization**

> 200,000x improvement in affinity for target

**Likely candidate profile**

- K_i < 0.3 nM to Mcl-1
- Cellular IC_{50} < 100 nM
- Oral bioavailability
- Robust pharmacodynamic response

**Leads feature**

- K_i < 0.3 nM to Mcl-1
- IC_{50} < 300 nM in multiple cancer cell-lines
- Target-based on-mechanism activity (Caspase activation, JC-1/BH3 profiling, co-IP, multiplex PD apoptosis assays)
- Good PK properties

Current work focused on identification of clinical candidate by profiling compounds for *in vivo* efficacy and therapeutic window.
Cigarette use in the United States

*Percent never, former, daily, non-daily.*

- Never: 25%
- Former: <10 cpd
- Daily: 25%
- Non-daily: 10%

Source: TOBACCO USE SUPPLEMENT, CURRENT POPULATION SURVEY
Lifelong consistent low-intensity smokers had increased risk of mortality vs. never-smokers

Inoue Choi et al, *JAMA Internal Medicine*, 2017
Rural Cancer Control Update

BACKGROUND

• 14-19% of the US population lives in non-metropolitan (rural) counties

• Notable challenges, compared to urban areas:
  • Higher poverty
  • Lower educational attainment
  • Higher proportion of elderly individuals
  • Lower access to health services
  • Higher rates of behavioral risk factors (tobacco use, obesity)
Rural Cancer Control Update
Planning & Engagement Efforts

- Rural Cancer Control Workshop, Memphis, May 4-5, 2017
- HRSA/NCI/CDC Webinar, Aug 30, 2017
- Understanding Definitions of Rural/Rurality, Oct 27, 2017
- National Academy Workshop on Small Populations, Jan 18-19, 2018
- Rural Health Policy Institute, Feb 6-8, 2018
- National Rural Health Assoc. Annual Meeting, May 8-11, 2018
Save the Date

Accelerating Research in Rural Cancer Control Conference

Natcher Conference Center
National Institutes of Health
Bethesda, Maryland
May 30-31, 2018

Program Committee Chair: Robin Vanderpool, University of Kentucky
NCI-MATCH
Molecular Analysis for Therapy Choice
NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

- Precision medicine trial to explore treating patients based on the molecular profiles of their tumors
- 1,089 sites in U.S. across NCTN and NCORP
NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

Rare Variant Initiative:

• Patients with low frequency mutations (< 2%) where well qualified drugs/targets available

• Foundation Medicine, Caris Life Sciences, MDACC, MSKCC will notify treating physician at any of the MATCH sites when results of their NGS panel would make patient eligible for a MATCH treatment arm

• Results verified centrally by NCI-MATCH Oncomine® assay

• RFP from other NGS providers posted August 2017 and received January 2018 to broaden the base of patients available to enroll in precision oncology studies
## NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

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<th>Time period</th>
<th># enrolled</th>
<th># first samples submitted</th>
<th># first sample fail</th>
<th># assay complete</th>
<th># assigned to Rx</th>
<th># enrolled on Rx</th>
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<tr>
<td>Total Pre Pause</td>
<td>794</td>
<td>739</td>
<td>116</td>
<td>645</td>
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<tr>
<td>Total Post Pause</td>
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<td>4,912</td>
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<td>Overall Total Screening Cohort</td>
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<td>5,962</td>
<td>544</td>
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<td>992</td>
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<td>Total Outside Assay</td>
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<td>36</td>
<td>2</td>
<td>68</td>
<td>59</td>
<td>45</td>
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</tbody>
</table>
First NCI-MATCH Efficacy Data: Nivolumab in MSI high cancers

- Median cycles 3.5 (range 1-13+ cycles)
- Median time to first response was 2.1 months (includes unconfirmed PRs)
- 6-Month PFS was 49% (95% CI: 32-67%)
- Median duration of response has not been reached (4-8+ months; 7/8 still under treatment at time of data cutoff)
- 11 patients remain on therapy at time of data cutoff
Vision – In progress

- ‘Listening Tour’ to conclude in March

- Clearly, there are 3 Bins:
  - Things We Have to Do
  - Things We Want to Do
  - Things We Are Already Doing (but need ongoing investment)