NCI Update

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NIH NATIONAL CANCER INSTITUTE

CTAC Meeting
November 4, 2015

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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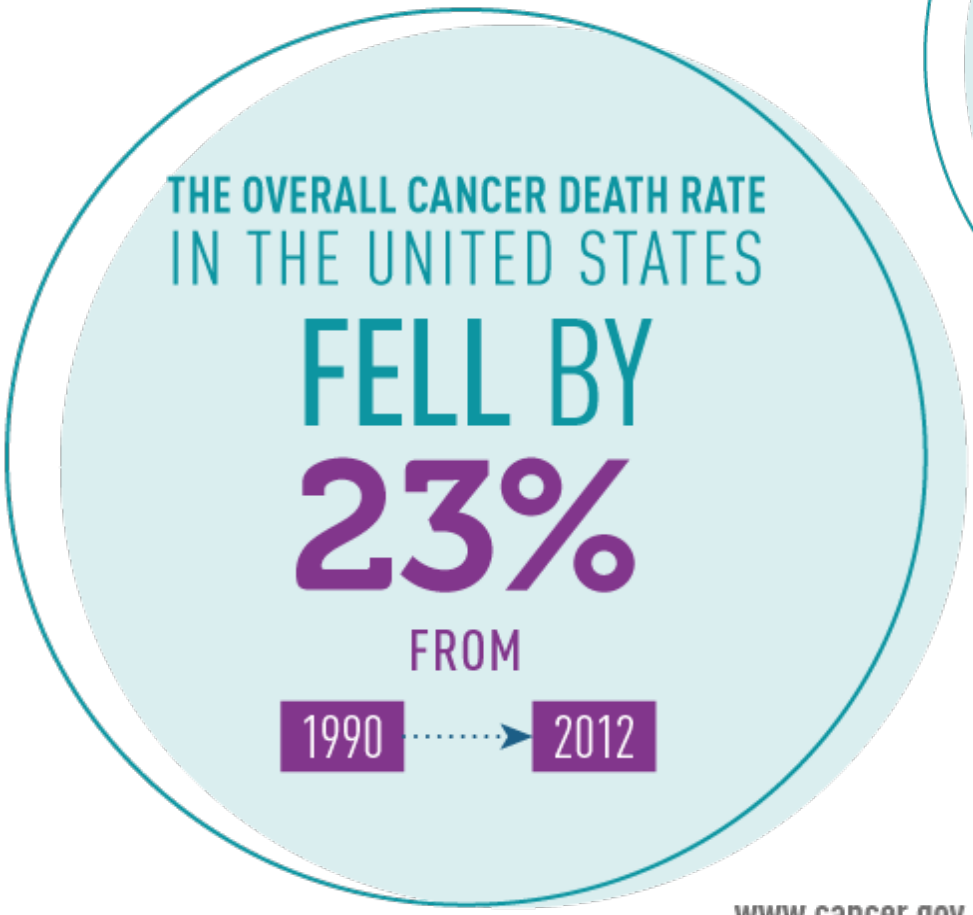
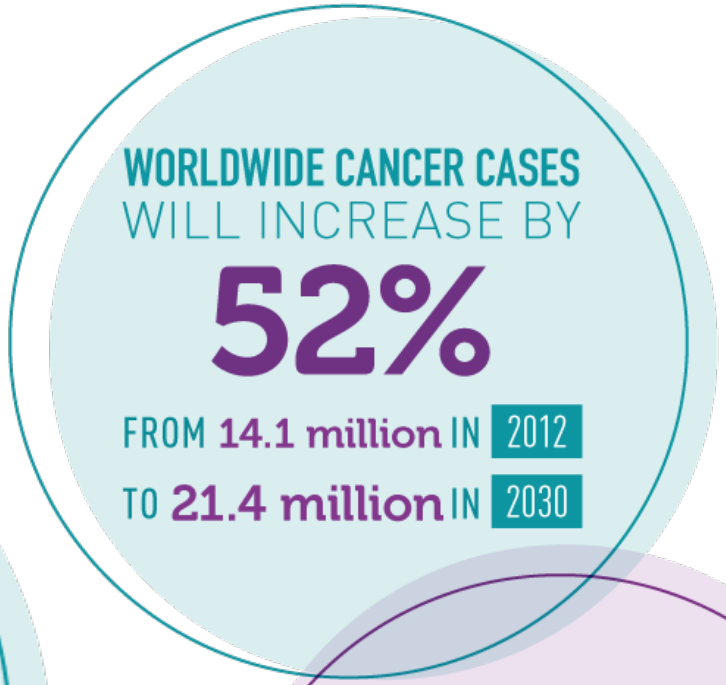
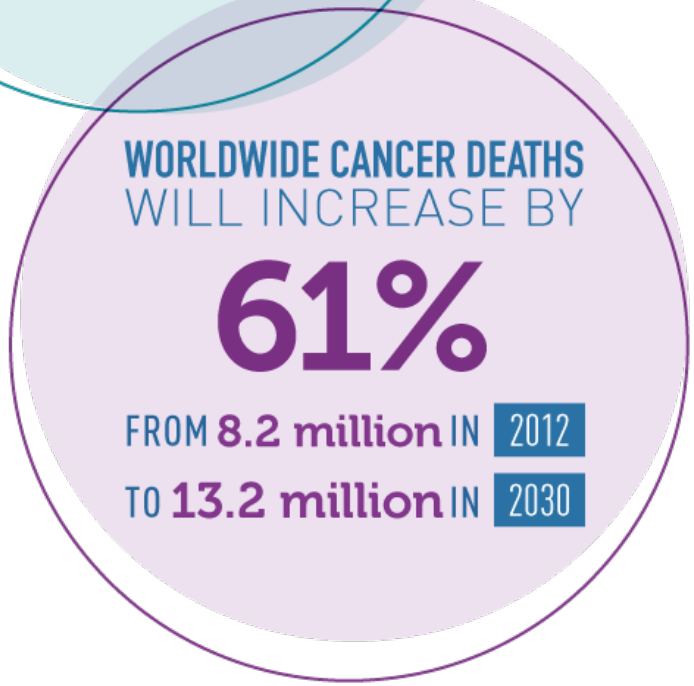
Cancer Trends



www.cancer.gov

Source: SEER Cancer Statistics Review 1975-2012

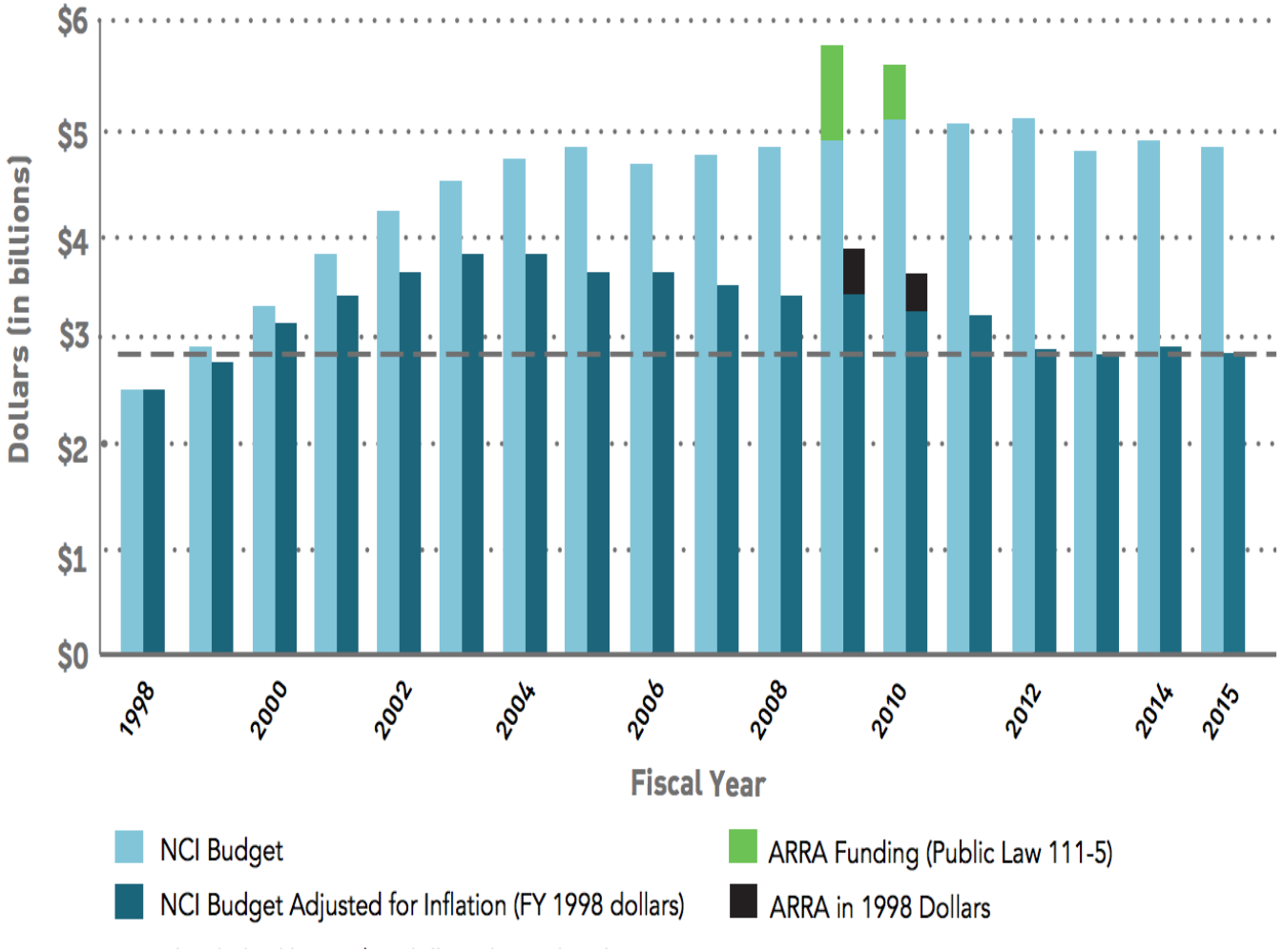




www.cancer.gov

Source: American Cancer Society: Global Cancer Facts & Figures, Second Edition

NCI Budget 2004-2014: A Decade of Level Budgets and Progressively Decreasing Purchasing Power



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

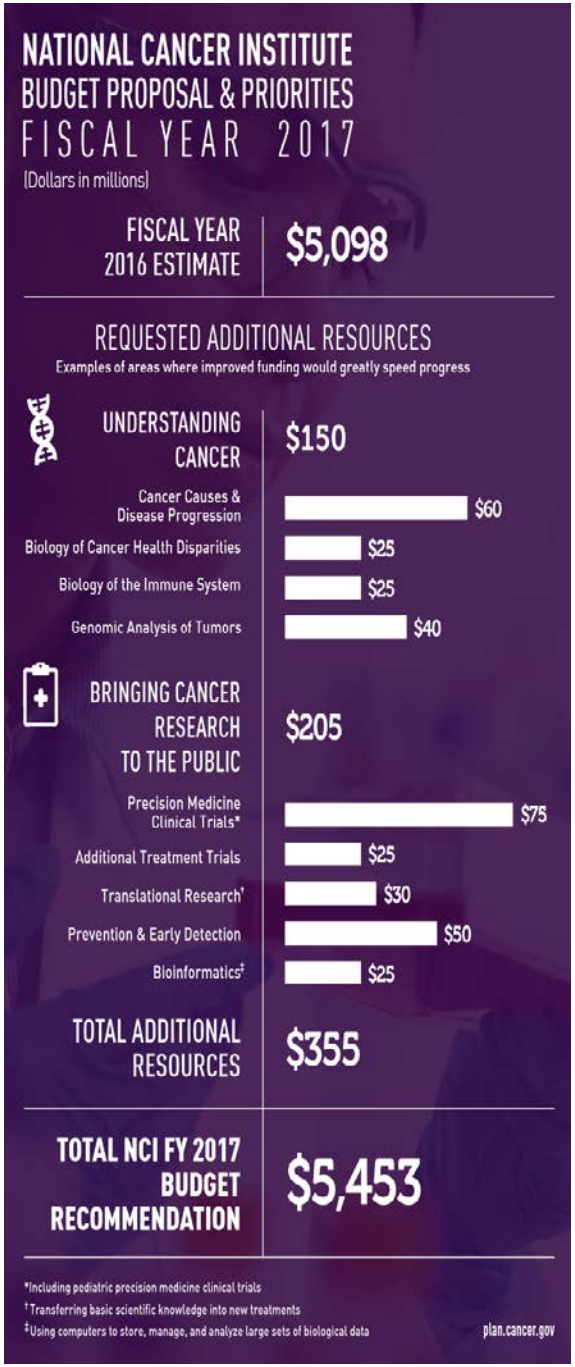
The FY17 NCI Budget Proposal

http://www.cancer.gov/about-nci/budget/plan; thanks to Richard Manrow, Julie Cheh, Peter Garrett, Anne Lubenow, and many others

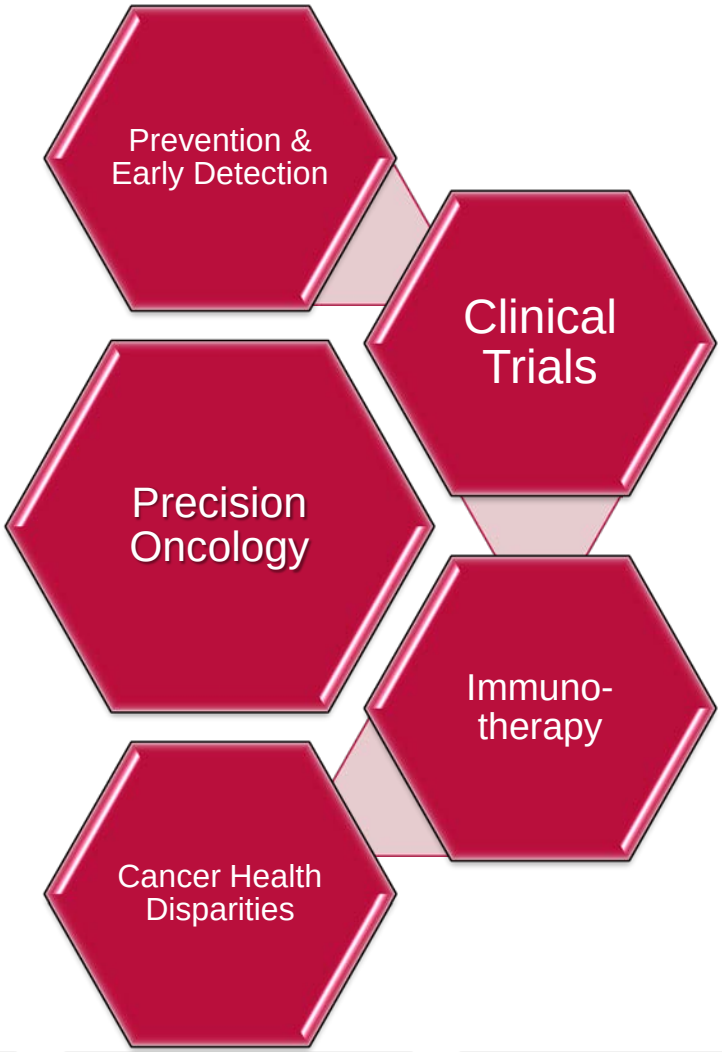
NCI Budget Proposal & Priorities for FY 2017

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.

Steady funding increases, sustained over time, are necessary to significantly reduce the burden for people with all types of cancer. **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



Basic | Translational | Clinical | Population

Cancer Research Spectrum

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

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The New York Times

Novel government cancer study will test precision medicine

By MARILYNN MARCHIONE Jun. 1, 2015 11:56 AM EDT

The Washington Post

To Your Health

A new way to study cancer and its treatments

THE WALL STREET JOURNAL.

U.S. Cancer Study to Match Existing Drugs to Genetic Mutations

Study marks ambitious effort to advance emerging field of precision medicine

The Washington Post

Health & Science

Cancer trials are changing. That could mean faster access to better drugs.

Precision Oncology Trials Launched

2014:

MPACT

Lung MAP

ALCHEMIST

Exceptional Responders

2015:

NCI-MATCH

ALK Inhibitor

MET Inhibitor

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NCI-MATCH:

Molecular **A**nalysis for **Th**erapy **Ch**oice

- 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

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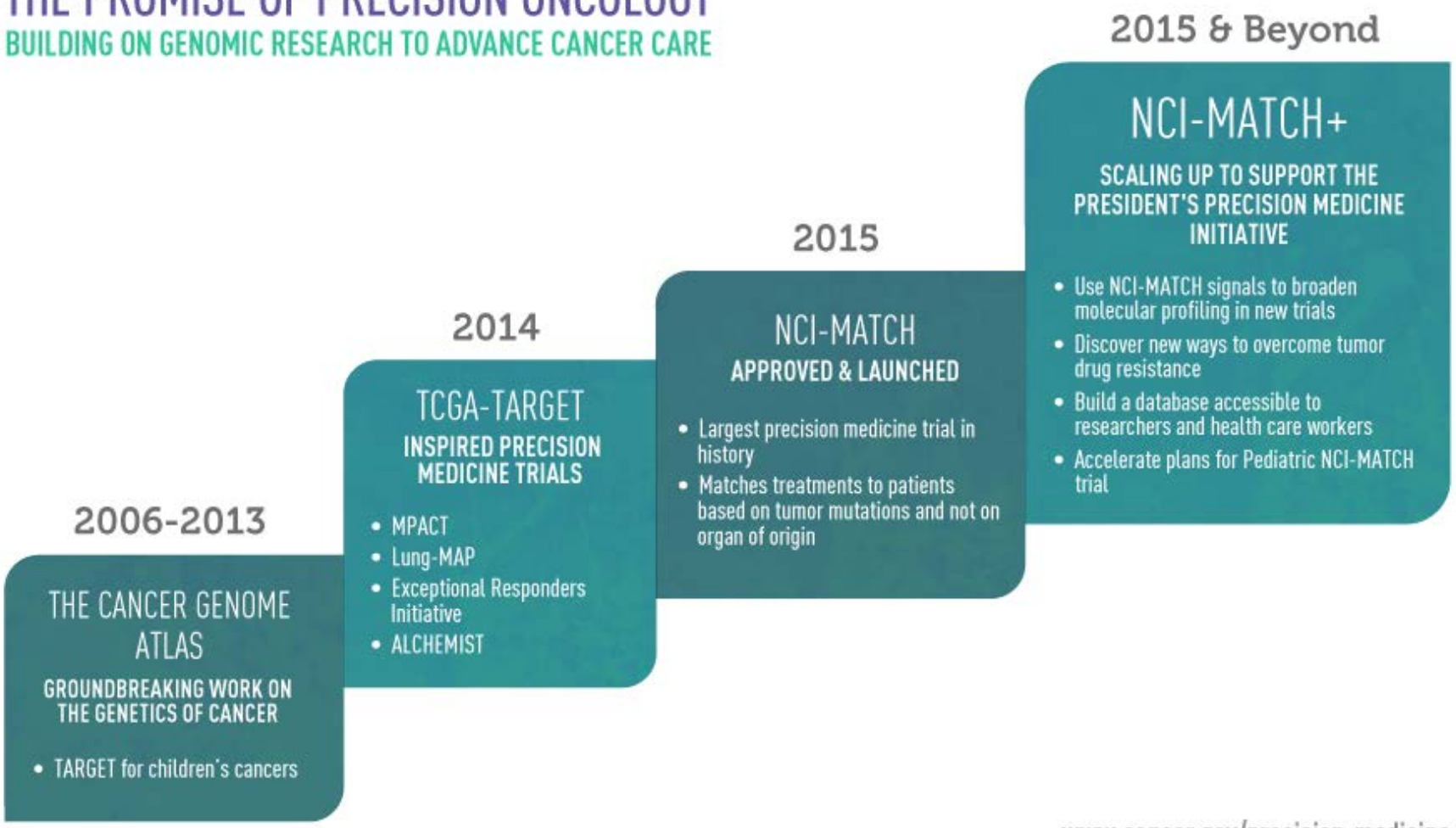
THE PROMISE OF PRECISION ONCOLOGY

BUILDING ON GENOMIC RESEARCH TO ADVANCE CANCER CARE



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

Novel recurrently mutated genes in African American colon cancers

Kishore Guda[a,b,c], Martina L. Veigl[b,c,1], Vinay Varadan[a,b,1], Arman Nosrati[d], Lakshmeswari Ravi[d], James Lutterbaugh[d], Lydia Beard[d], James K. V. Willson[e], W. David Sedwick[b,c,d], Zhenghe John Wang[b,f], Neil Molyneaux[f], Alexander Miron[f], Mark D. Adams[g], Robert C. Elston[b,h], Sanford D. Markowitz[b,c,d,i,2,3], and Joseph E. Willis[b,c,i,j,2]

[c]Department of Medicine, [f]Department of Genetics and Genome Sciences, [h]Department of Epidemiology and Biostatistics, [j]Department of Pathology, [a]Division of General Medical Sciences-Oncology, [d]Division of Hematology and Oncology, [b]Case Comprehensive Cancer Center, and [i]Case Medical Center, Case Western Reserve University, Cleveland, OH 44106; [e]Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX 75390; and [g]J. Craig Venter Institute, La Jolla, CA 92037

"…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."

Guda et al., 2015. Proc. Natl. Acad. Sci. 112:1149

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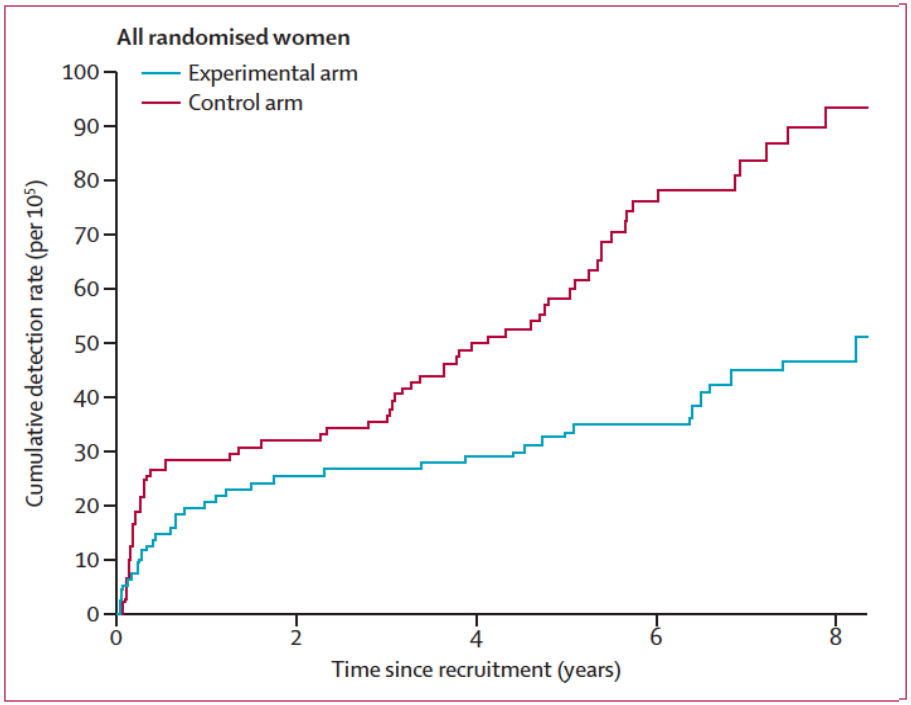
Precision Oncology in **Cancer Screening**

- 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



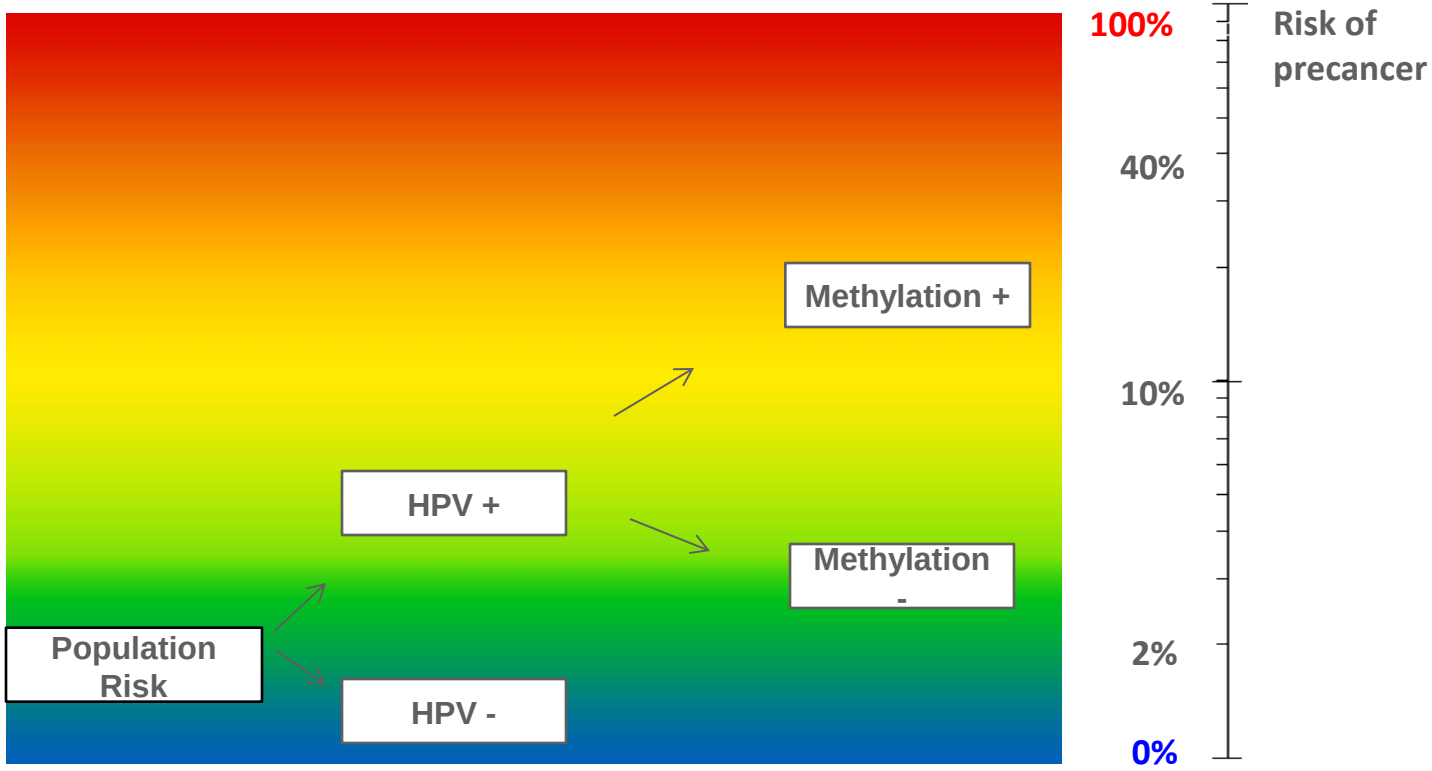
	Pooled rate ratio* (95% CI)
Morphology	
Squamous-cell carcinoma	0·78 (0·49–1·25)
Adenocarcinoma	0·31 (0·14–0·69)
Adenocarcinoma *vs* squamous-cell carcinoma	0·34 (0·12–0·90)

* Ratio of incidence with HPV testing vs. incidence with cytology

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

Ronco et al, Lancet 383: 524-33, 2014

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

	Non-Users	Regular aspirin users
All CRC	1.0	0.73 (0.62-0.86)
High 15-PGDH CRC	1.0	0.49 (0.34-0.71)
Low 15-PGDH CRC	1.0	0.90 (0.63-1.27)

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**

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www.cancer.gov

www.cancer.gov/espanol