

Report from the Acting Director

*Douglas R. Lowy
Acting Director, National Cancer Institute,
National Institutes of Health*

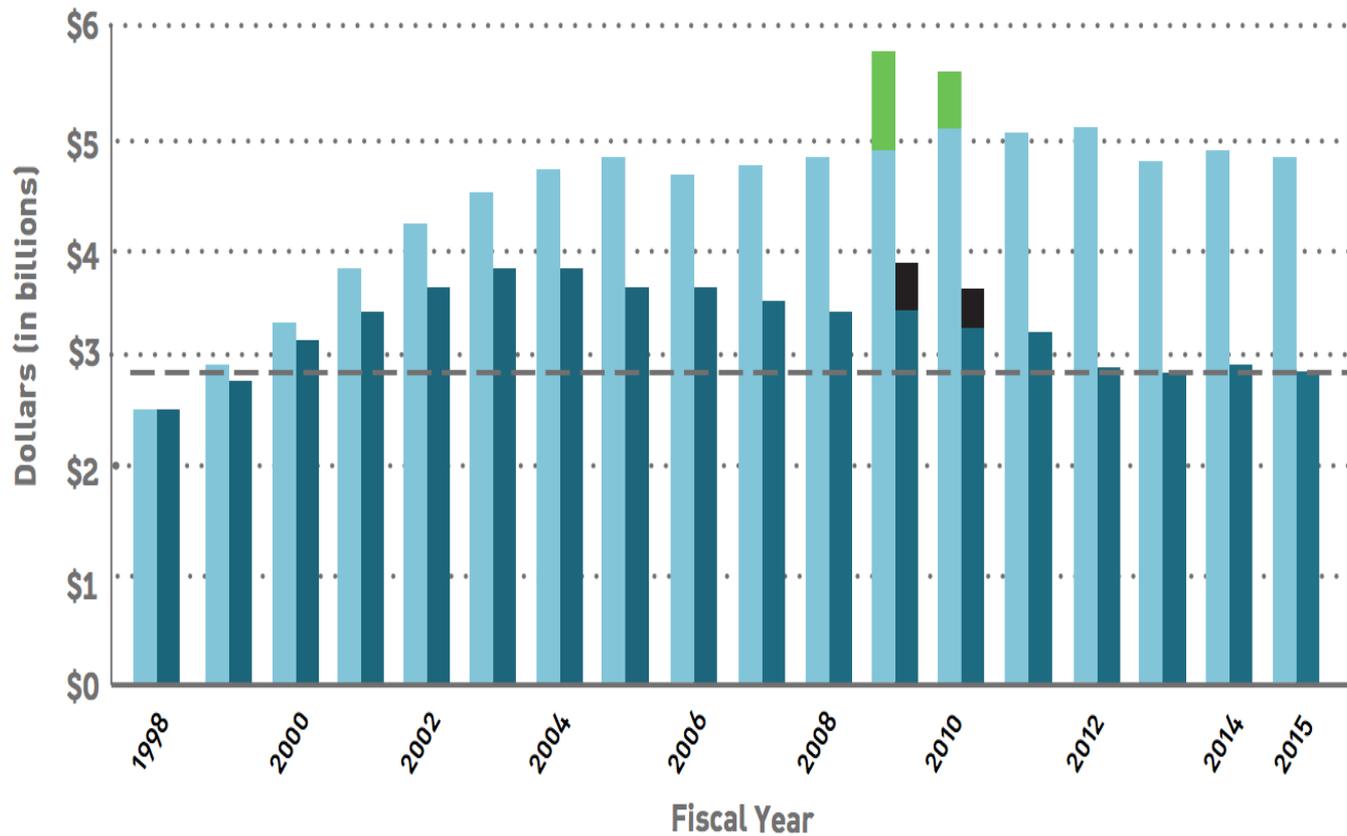
Outline of Presentation

- NCI FY16 budget and beyond
- Frederick National Laboratory & FNLAC
- Some current NCI priorities

Outline of Presentation

- NCI FY16 budget and beyond
- Frederick National Laboratory & FNLAC
- Some current NCI priorities

The Declining Purchasing Power of the NCI Budget



■ NCI Budget
 ■ NCI Budget Adjusted for Inflation (FY 1998 dollars)
 ■ ARRA Funding (Public Law 111-5)
 ■ ARRA in 1998 Dollars

-- The dashed line at \$2.9 billion shows that the current NCI budget, adjusted for inflation, is essentially the same as the NCI budget in FY 1999.

Source: NCI Office of Budget and Finance



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



The Current Status of FY16 Funding

- A continuing resolution that keeps the government funded, at FY15 levels, October 1-December 11 is very likely
- The possibility of a government shutdown in mid-December. Another issue: raising the debt ceiling during this period
- NCI will participate 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

NCI is the nation's leader in cancer research



Annual Plan and Budget Proposal for FY2017

NCI's Annual Plan describes research that warrants increased funding. Read about these opportunities and comment on our Cancer Currents blog.



Outstanding Investigator Award: Apply Now

The award supports investigators with outstanding records of productivity in cancer research. Letter of intent due Oct. 23; application due Nov. 23.



NCI Resources in Spanish

NCI provides Spanish-language resources online and in print for patients, their loved ones, and health care providers.



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

Outline of Presentation

- NCI FY16 budget and beyond
- Frederick National Laboratory & FNLAC
- Some current NCI priorities

The Frederick National Laboratory for Cancer Research

- A Federally Funded Research and Development Center (FFRDC) sponsored by the NIH
- To provide a unique biomedical resource for development of new technologies and translation of basic science discoveries into novel agents for prevention, diagnosis, and treatment of cancer and AIDS
- Provides exceptional acquisition and response capabilities: e.g., flexibility, rapid response, efficiency

Some Activities at the Frederick National Laboratory

- Ras initiative
- Nanotechnology characterization laboratory
- Antibody characterization laboratory
- NEXT (NCI Experimental Therapeutics) Program
- Clinical trials reporting program
- Molecular diagnostics
- Biopharmaceutical development program

Recent CRADAs at FNLCR

FNL Lead	Partner	Subject	Duration	Signed
C RTP Nissley	University of California, San Francisco	RAS biology, reagent, cell line development and validation	5 yrs	January 2015
C RTP Holderfield	Daiichi-Sankyo	K-RAS/C-RAF inhibitor screen	2 yrs	March 2015
C RTP Stern	Onyx Pharmaceuticals	Novel polymeric micelles of a regulatory inhibitor	1.5 yrs	July 2015
C RTP Stephen	University of Maryland	NMR studies of KRAS 4b hypervariable region and targeted small molecules	2 yrs	May 2015
ACVP Estes	University of California, San Francisco	Effect of ART and CD4 depletion treatment on SIV reservoirs	1 yr	May 2015
BSP Carrington	Oxford University	Newton Abraham Visiting Professorship	1 yr	May 2015
C RTP Stephen	University of California, San Francisco	Identification of small molecules that bind to KRAS4b-GDP with an extended Switch 1 domain	1 yr	September 2015

Laboratory Directed Exploratory Research (LDER)

- Modeled after DOE FFRDC Lab-directed R&D funds; up to \$1 million for pilot projects
- Enhance innovation, creativity, originality, and quality of research activities
- Facilitate collaborations within FNLCR
- Engage academic institutions to encourage collaboration and strategic interactions
- Enable demonstration of exploratory “proof of concept” projects which will lead to durable funding through contract or grant mechanisms
- The Laboratory Director of FNLCR is responsible for overall execution and performance of the program

Initial Strategic Focus Areas of LDER

- Improving Therapeutic Efficacy
- AIDS and Cancer Associated Viruses: Immune Responses/ Immunogenetics, Pathogenesis, Treatment, and Prevention
- Tumor Microenvironment and Heterogeneity
- Immunotherapy

First Year of LDER Proposals

- 18 Proposals Submitted
- 12 Selected for Oral Presentations
- Five approved for funding
 - M. Carrington – “Influence of KIR/HLA Interactions on Risk of Nasopharyngeal Carcinoma in China”
 - L. Pinto – “Oral Immune Profiles in HPV-related Oral Cancers”
 - X. Wu – “Genomic Analysis of NCF1 and Pseudogenes in p47phox CGD”
 - S. Lockett – “Modeling Cell Heterogeneity Dynamics in Tumors in Response to drugs”
 - Z. Weaver Ohler – “Identification of EGFR tyrosine Kinase Inhibitor drug Resistance and Development of Models to Improve Therapeutic Efficacy”

The Frederick National Laboratory Advisory Committee (FNLAC)

- Provides advice on the optimal use of the FNLCR to meet the most urgent needs of the NCI
- Reviews the state of research at the FNLCR and makes recommendations for the best use of its capabilities and infrastructure
- Reviews major new projects proposed to be performed, the existing portfolio of projects, and evaluation of their productivity
- helps to determine which projects should be transitioned to more conventional mechanisms of support and which should be considered for termination

The Re compete for the FFRDC

- Likely timeline: RFP Oct-Dec 2015; anticipated deadline for proposal submissions Jan-March 2016
- RFP will be posted on <http://www.fbo.gov> and at the FNLCR acquisition portal <http://ncioa.cancer.gov/oa-internet/fnlcr/index.html#/home>.
- Pre-proposal conference October 1-2 at NIH
- FFRDC's are operated, managed, and/or administered by either a university or consortium of universities, other not-for-profit or nonprofit organization, or an industrial firm
- Anticipated that the contract will be awarded as a single IDIQ (Indefinite Deliverable, Indefinite Quantity) award

Outline of Presentation

- NCI FY16 budget and beyond
- Frederick National Laboratory & FNLAC
- Some current NCI priorities

R35:Outstanding Investigator Award

- To provide long-term support to experienced investigators with outstanding records of cancer research productivity who propose to conduct exceptional research.
- To allow investigators the opportunity to take greater risks, be more adventurous in their lines of inquiry, or take the time to develop new techniques

OIA & other potential new awards

- Outstanding investigator award
 - Initial awards from first round: 40 with FY15 funds; another 24 anticipated with FY16 funds
 - Reissuance has been published: minor changes (e.g., page length for research strategy reduced from 12 pages to 6 pages)
- Some other types of award under consideration: Research Specialist; Graduate Student to Post-doc

Towards Increased funding for NCI Cancer Center P30 Core Grants

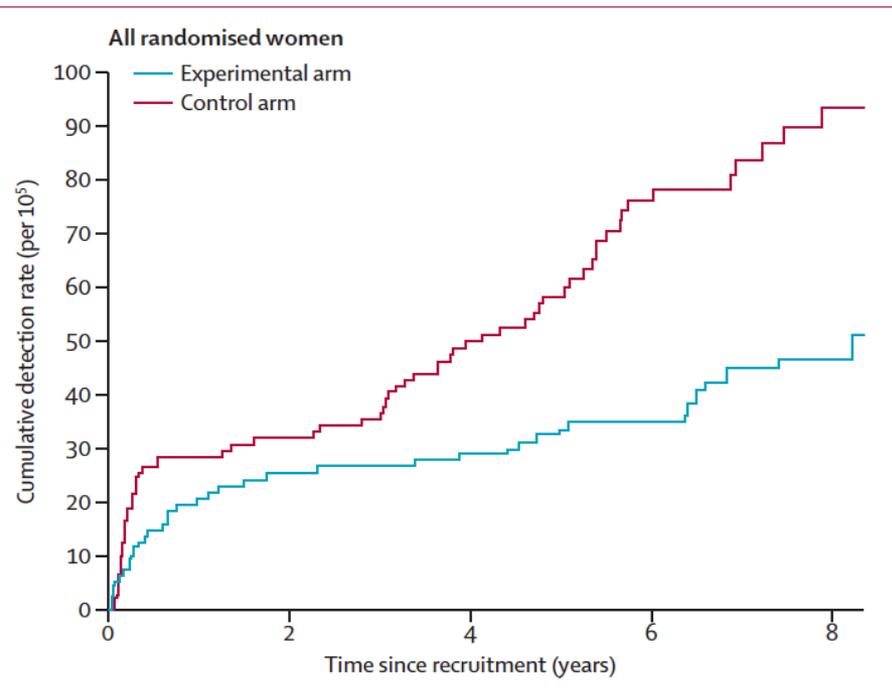
- Working group meeting of cancer center directors: October 9
- Goal: To develop a plan that can be presented at joint NCAB/BSA meeting in December
- Full funding would be contingent on an increased NCI appropriation for FY16



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

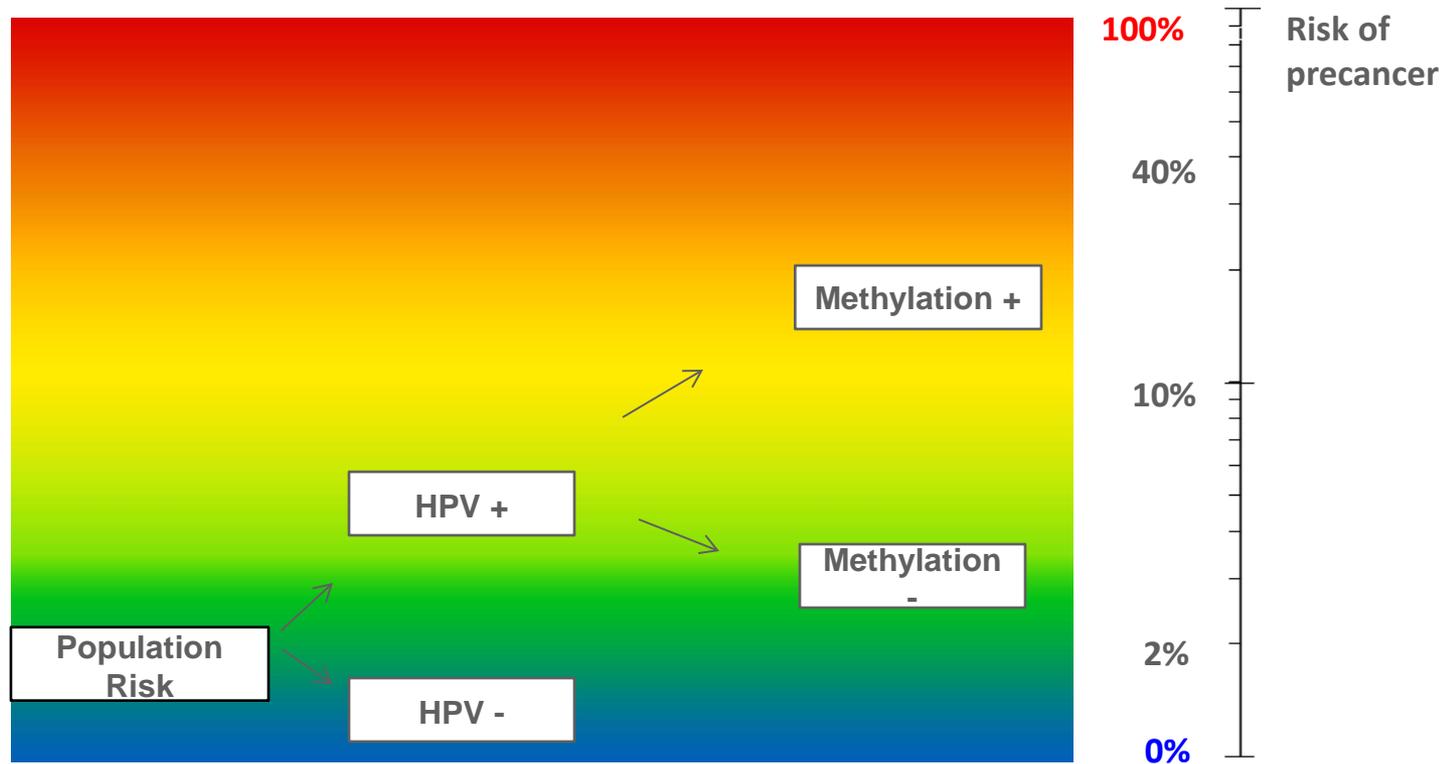


	Pooled rate ratio* (95% CI)
Morphology	
Squamous-cell carcinoma	0.78 (0.49–1.25)
Adenocarcinoma	0.31 (0.14–0.69)
Adenocarcinoma vs squamous-cell carcinoma	0.34 (0.12–0.90)

* 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)**

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

HPV testing: Next-Gen sequencing

- Next-Gen HPV sequencing can potentially become highly cost-effective for cervical cancer screening
 - Major implications for screening in Low and middle income countries (LMICs)
- Next-Gen HPV sequencing can also provide new insights into molecular pathogenesis of HPV-induced cancer

Precision Oncology in **Cancer Prevention**

- The example of **aspirin**
- Aspirin can reduce the risk of several cancers, especially colorectal cancer
- Concern about side effects from aspirin (especially an increased risk of bleeding) has prevented aspirin from being 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

Focus on specific cancers with health disparities (high-risk populations)

- Identify the specific cancers
- Some possible examples: colorectal cancer, liver cancer, breast cancer, prostate cancer, multiple myeloma
- Identify the risk factors and their relative contribution to the disparities: biologic factors, life-style factors, health care access/utilization
- Explore efforts to mitigate the risk factors

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}

^cDepartment of Medicine, ^fDepartment of Genetics and Genome Sciences, ^hDepartment of Epidemiology and Biostatistics, ^jDepartment of Pathology, ^aDivision of General Medical Sciences-Oncology, ^dDivision of Hematology and Oncology, ^bCase Comprehensive Cancer Center, and ⁱCase Medical Center, Case Western Reserve University, Cleveland, OH 44106; ^eHarold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX 75390; and ^gJ. Craig Venter Institute, La Jolla, CA 92037

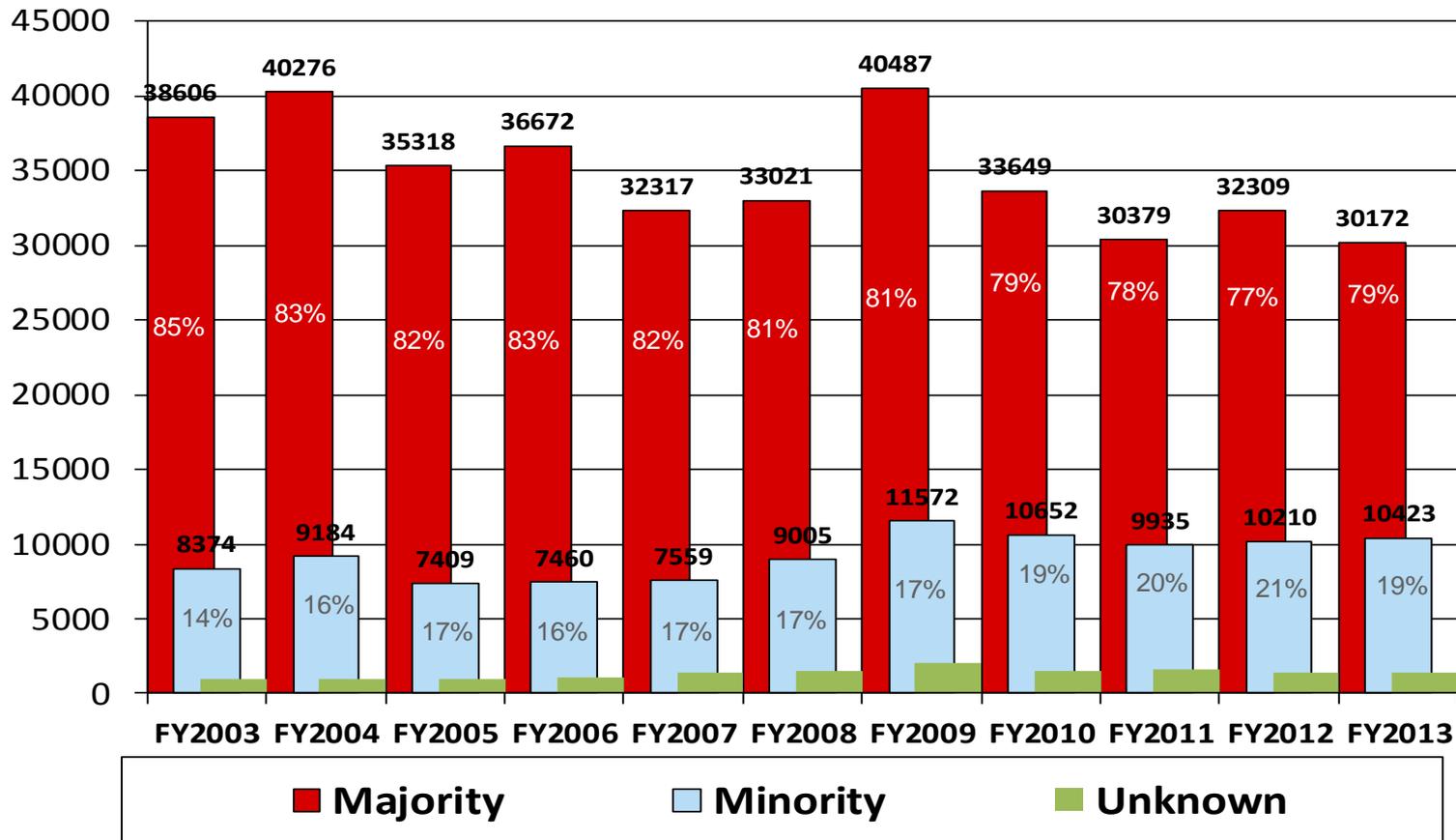
“...Mutations in a set of 15...genes appear to be strongly preferentially associated with CRCs arising in AA versus Caucasian individuals, suggesting an important difference in the mutational landscapes of CRCs arising in different ethnic groups. “

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

NCI Workshop on Cancer Health Disparities

- November 11-13, in Atlanta, just prior to AACR conference on cancer health disparities
- Co-chairs: Edith Mitchell (Thomas Jefferson University), Lisa Richardson (CDC), Sandy Markowitz (Case-Western Reserve)
- New NCI Center for Research Strategy; Michelle Bennett, director; coordination of NCI research in cancer health disparities & more

Minority Enrollment to NCI Cooperative Group Clinical Trials

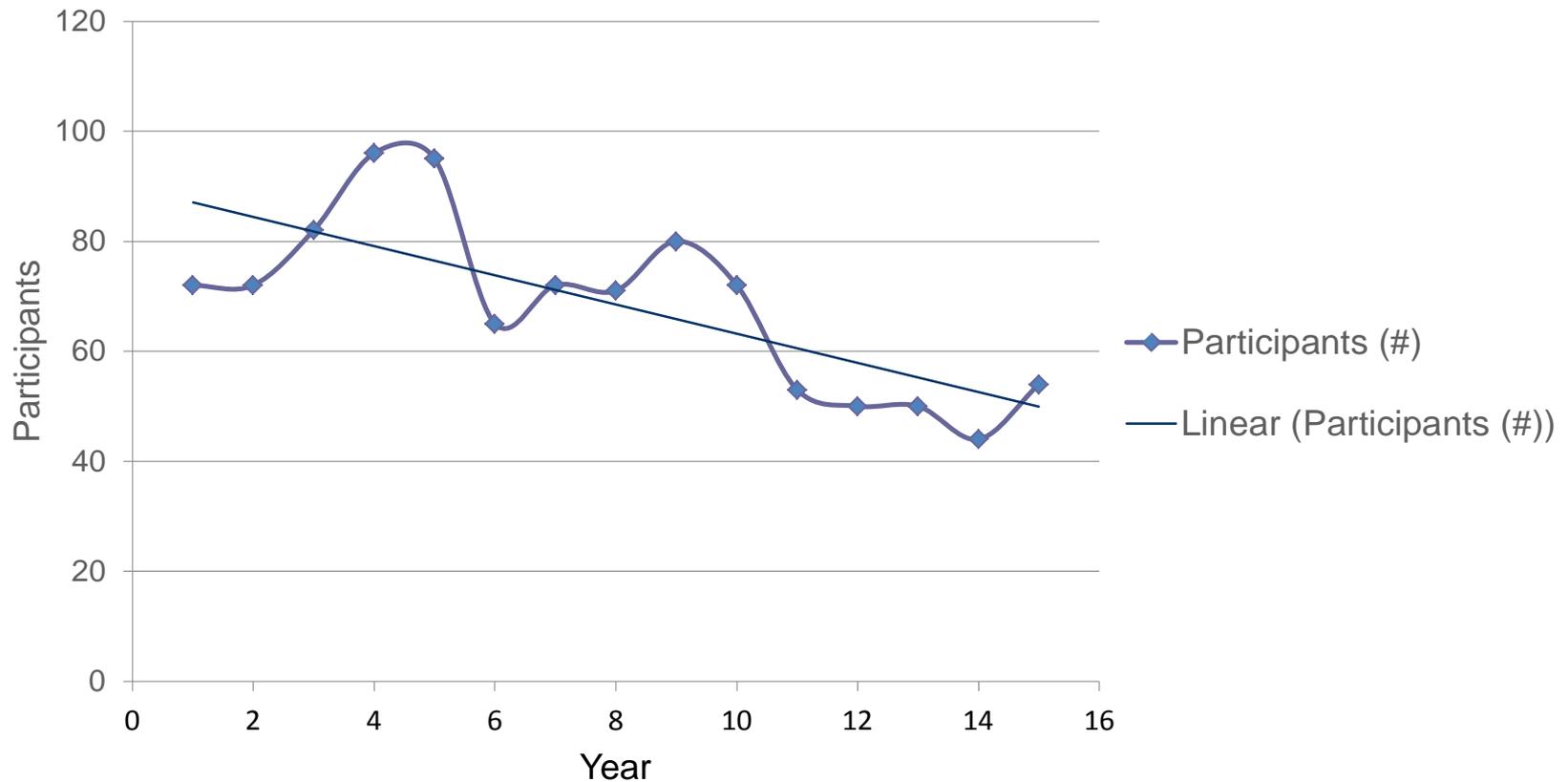


Worta McKaskill-Stevens et al, NCI Community Oncology Research Program, unpublished data

Strong Support for Basic Research

Fewer Early Stage Investigators may be Engaging in Basic Research

Attendance trends at the NCI Division of Cancer Biology new grants workshop





**NATIONAL
CANCER
INSTITUTE**

www.cancer.gov

www.cancer.gov/espanol