

National Cancer Institute Priorities

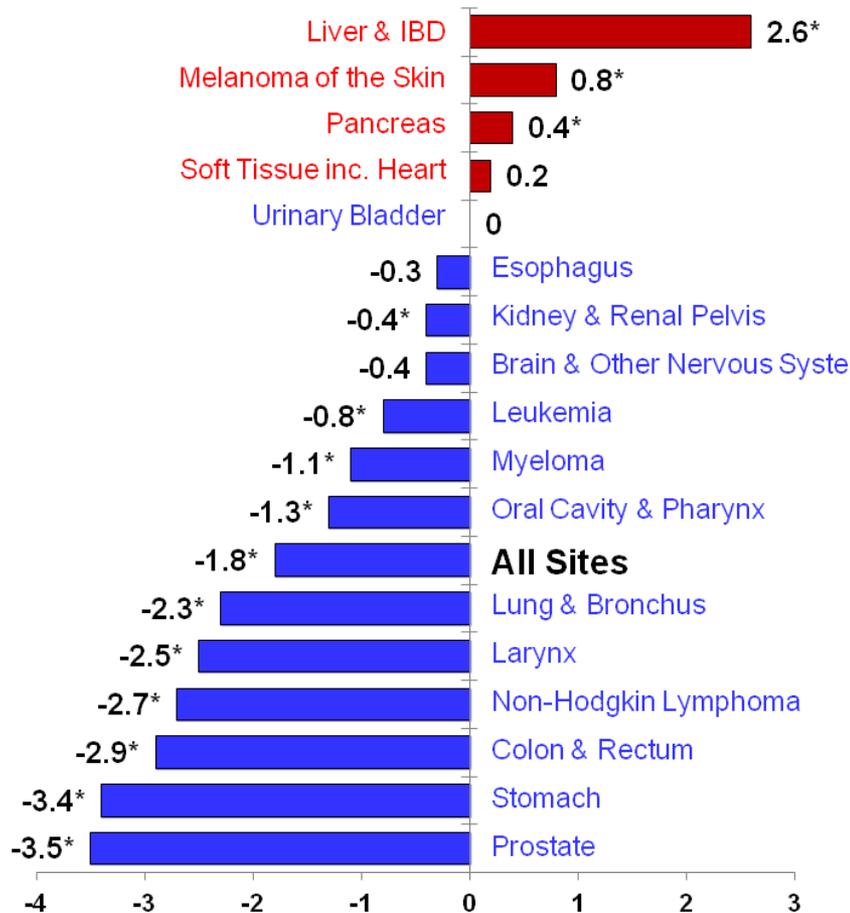
Douglas R. Lowy
Deputy Director, NCI

SBIR Workshop on Federal Resources
May 7, 2013

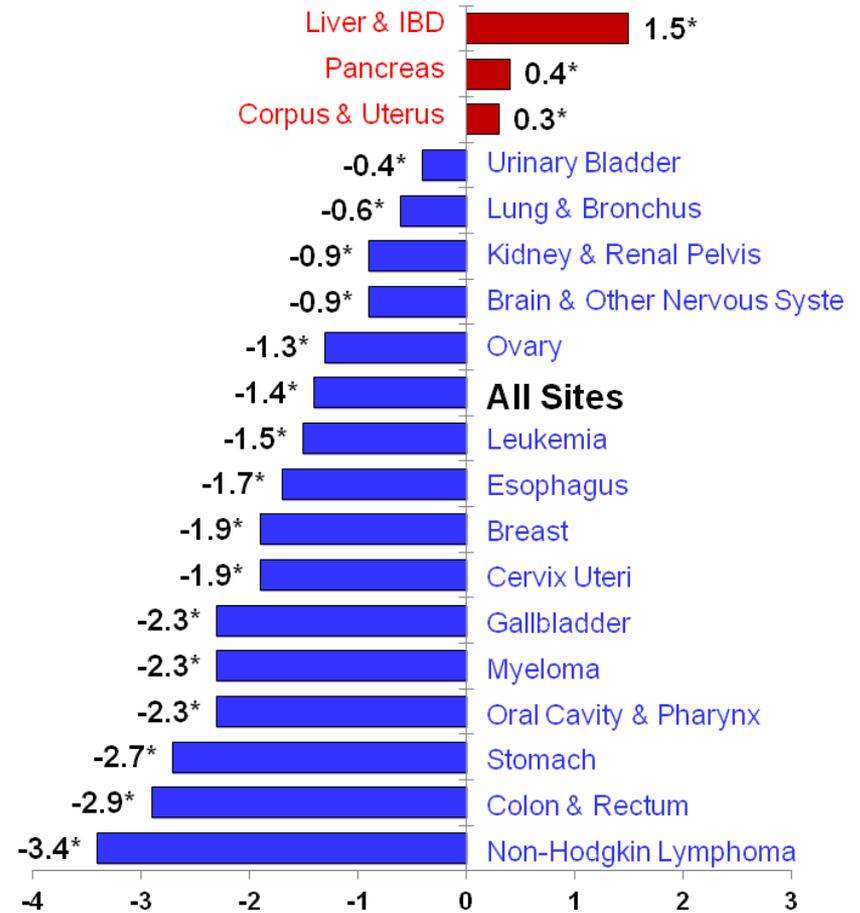
Long-Term US Mortality Trends with Average Annual Percentage Change 2000-2009 By Cancer Site*



Males



Females

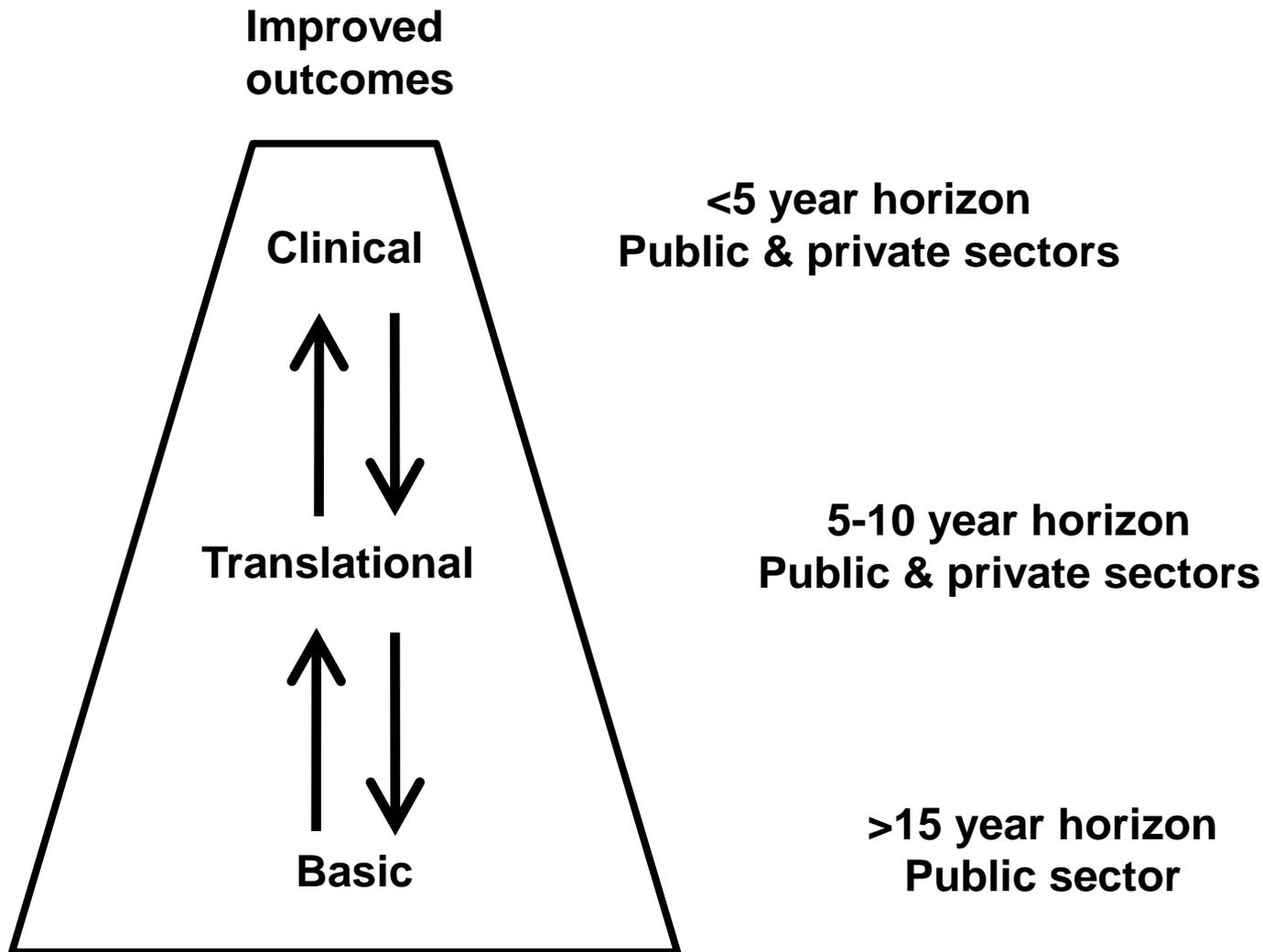


Average Annual Percent Change 2000-2009

From *The Annual Report to the Nation on the Status of Cancer*, J Natl Cancer Inst, Feb 6, 2013

* 10 year AAPC is statistically significant from 0 ($p < .05$) based on joinpoint model. Incidence data from SEER 13, mortality data from NCHS.

From Basic Research to Improved Cancer Control



B-raf Inhibitors: a Multiyear Journey from Basic to Applied

- **2011: FDA approval of vemurafenib (Zelboraf), a B-raf kinase inhibitor, for treatment of metastatic melanoma**
 - Mutant B-raf present in other tumors, variable response to B-raf inhibition
- **2002: B-raf gene found to be frequently mutated in melanoma, increasing its kinase activity**
- 1988: Identification of B-raf gene
- 1984: Identification of c-raf, the cellular gene from which v-raf was derived
- **1984: v-raf is a kinase**
- 1982: Transforming **mouse retrovirus** isolated: its oncogene is designated v-raf

Some Current Priorities

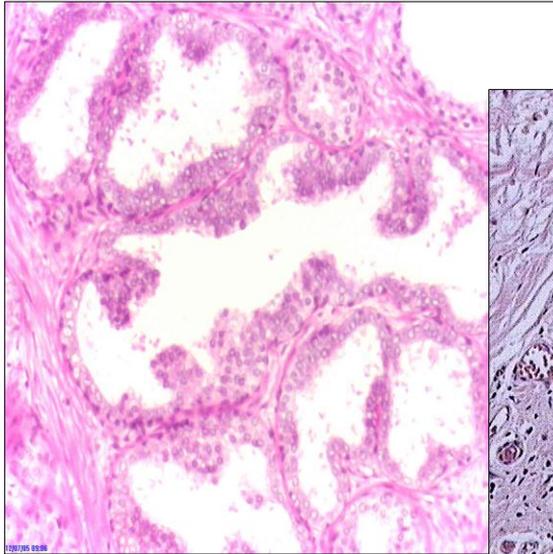
- **Maintaining a vigorous investigator-initiated research portfolio**
- **The Provocative Questions Initiative**
- **SBIR & STTR program**
- **Center for Cancer Genomics**
- **Center for Global Health**
- **The Ras project**
- **Health disparities**

The Provocative Questions Initiative

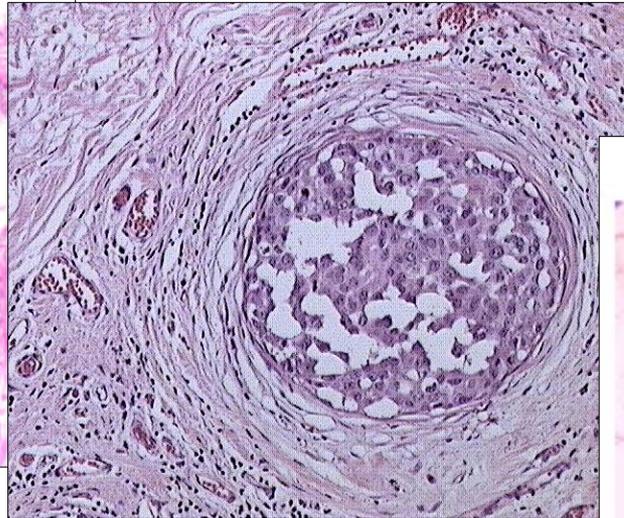
- Development of a list of important but non-obvious questions that will stimulate the NCI's research communities to use laboratory, clinical, and population sciences in especially effective and imaginative ways.
 - *Varmus & Harlow, Science funding: Provocative questions in cancer research. Nature 481:437-7 (2012)*
- The proposals should:
 - Build on specific advances in our understanding of cancer and cancer control
 - Address broad issues in the biology of cancer that have proven difficult to resolve
 - Take into consideration the likelihood of progress in the foreseeable future (e.g. 5 to 10 years)
 - Address ways to overcome obstacles to achieving long-term goals

WHAT PROPERTIES OF NON-MALIGNANT LESIONS (IN SITU CA'S) PREDICT THE LIKELIHOOD OF INVASIVE DISEASE?

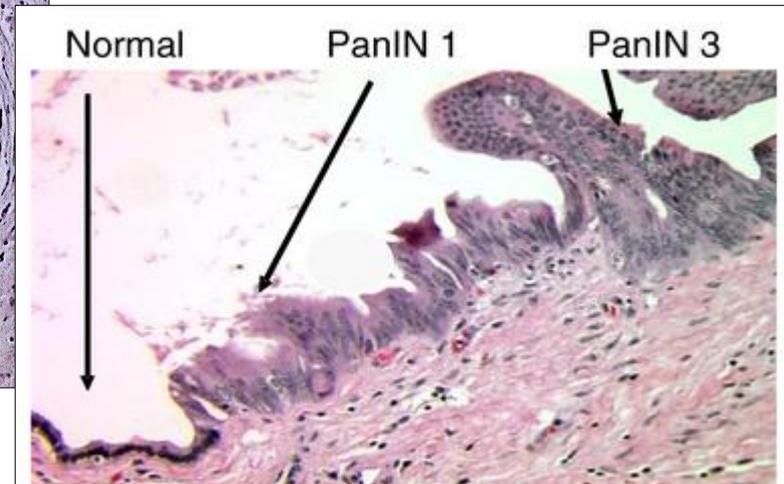
Prostatic
Intraepithelial
Neoplasia (PIN)



Ductal Carcinoma
In Situ (DCIS)



Pancreatic Intraepithelial
Neoplasia (PanIN)



SBIR & STTR Programs

- Goals: support cancer research, prevention, screening, diagnosis, treatment
- Early stage R & D
 - Stimulate technological innovation, increase small business participation in federally funded R&D, including participation by minority and disadvantaged companies
- A range of initiatives
 - E.g., Diagnostic and therapeutic agents, biomarkers, medical devices, imaging, bioinformatics, nanotechnology, proteomics

The Cancer Genome Atlas (TCGA)

- A large community research project sponsored by NCI & NHGRI
- Analyze the genomic changes in a large number of cancers to discover the spectrum of genes implicated in each form of cancer
- Learn how specific combinations of genes work together in the cancer
- Apply this information to suggest new uses for existing drugs and development of new drugs

TCGA Adult Tumor Types

First Goal = Comprehensive Genomics for 25 tumor types @ 500 tumors per type



- AML
- Breast Ductal*
- Breast Lobular/Breast Other
- Bladder (pap and non-pap)
- Cervical adeno & squamous
- Colorectal*
- Clear cell kidney*
- Diffuse Large B-cell Lymphoma
- Endometrial carcinoma*
- Esophageal adeno & squamous
- Gastric adenocarcinoma
- Glioblastoma multiform*
- Head and Neck Squamous
- Hepatocellular
- Lower Grade Glioma
- Lung adeno
- Lung squamous
- Melanoma
- Ovarian serous cystadenocarcinoma*
- Papillary kidney
- Pancreas
- Prostate
- Sarcoma (dediff lipo, UPS, leiomyosarcoma)
- Papillary Thyroid*

*Reached 500 tumor goal

 Research papers published or in preparation

And Rare Tumor Project Launched 2012

- Adrenocortical Carcinoma
- Adult ALL (B-cell and T-Cell)
- Anaplastic Thyroid
- Cholangiocarcinoma
- Chromophobe kidney
- High Risk MDS (del 5q- cases)
- Mesothelioma
- MPNST
- Paraganglioma/Pheochromocytoma
- Small Cell Lung Cancer (biopsy)
- Testicular Germ Cell
- Uterine Carcinosarcoma



Cancer is Very Heterogenous

- Even within the same tumor type, there may be many variations
- However, some variations may be amenable to therapeutic intervention
- Two key issues:
 - Must demonstrate patients with the identified abnormality will benefit from the treatment
 - When possible, use a molecular test to identify those patients

Bringing Genomics to the Patient

- Incorporation of genomic analysis into clinical trials
 - Genomic analysis of patients whose response to treatment and course of disease is known
 - Molecular analysis of tumors in patients who become drug-resistant; determine new treatment on the basis of that analysis
- How to integrate genomic information into patient management?
- Genomic analysis of premalignant lesions may help inform cancer screening

Center for Global Health

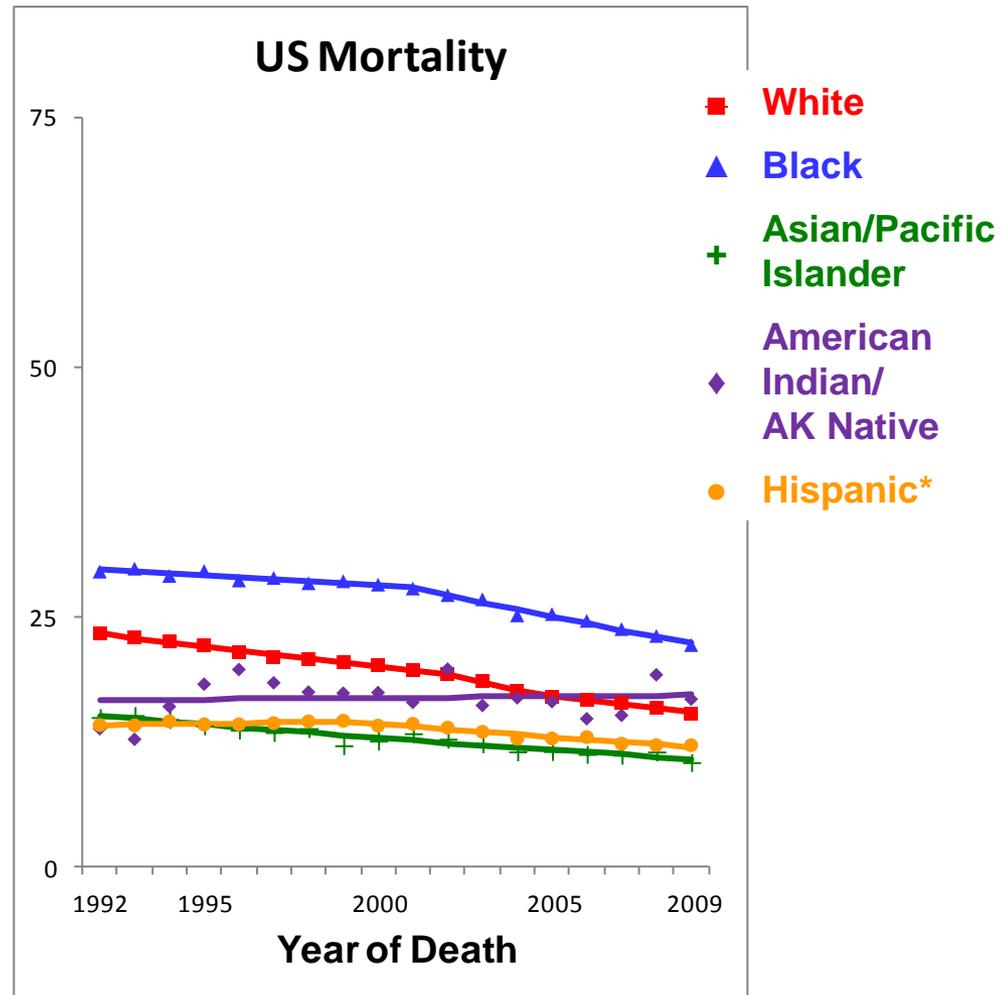
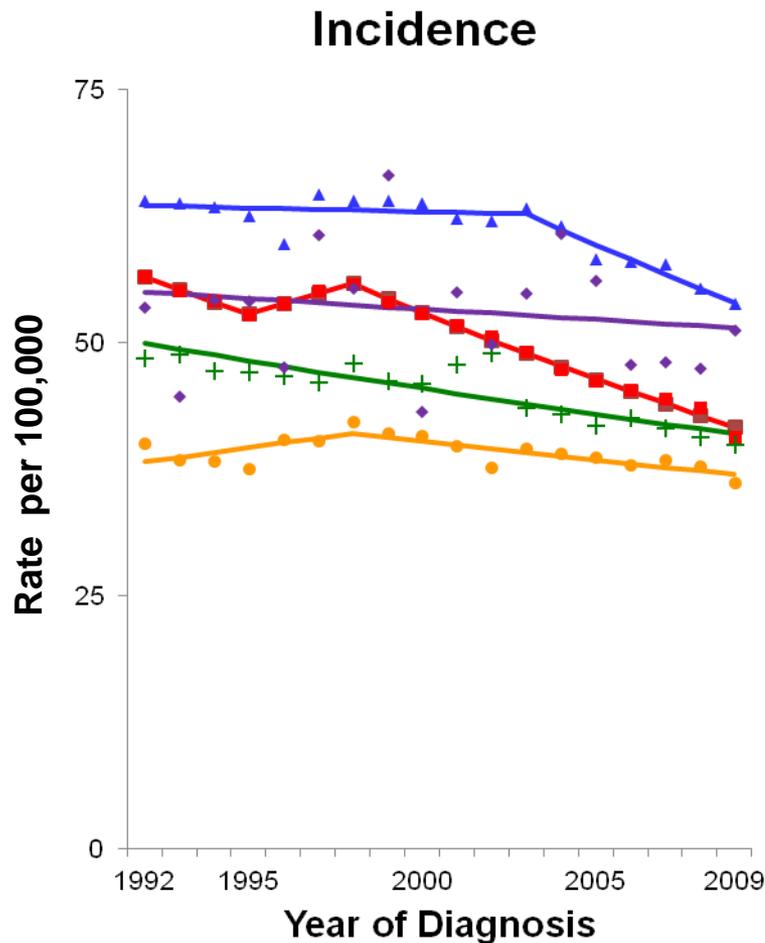
- Organize and coordinate NCI's efforts in global health research (developing world)
 - *Varmus & Trimble, Integrating cancer control in global health. Sci Transl Med 3:101cm28 (2011)*
- Cancer registries/national cancer plans
- Research opportunities: e.g., cancers attributable to infection, implementation
- Potential to partner with NCI cancer centers active in developing world
- Planned SBIR funding for diagnostics and treatment approaches relevant for developing world

The Ras Project

- ***The overall goal:*** to develop treatment that will improve the outlook for patients whose tumors have a mutant ras gene
- ***The importance:*** ras is mutated in ~30% of human cancers and is usually associated with a poor prognosis
 - >90% of pancreatic cancer, >40% colorectal cancer, >25% lung cancer, many other forms of cancer
 - ras was the first oncogene found to be mutated in human cancer (1982)
- ***The problem:*** no successful treatment for tumors with mutant ras, despite many efforts in the public and private sector
- ***The hope:*** A coordinated effort by multiple labs may be able to make progress towards the overall goal

Colon & Rectum

Incidence and Mortality Age-Adjusted Trends



From The Annual Report to the Nation on the Status of Cancer, J Natl Cancer Inst, Feb 6, 2013

Thank you!