National Cancer Institute Priorities

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

**Males**

Liver & IBD: 2.6*
Melanoma of the Skin: 0.8*
Pancreas: 0.4*
Soft Tissue inc. Heart: 0.2
Urinary Bladder: 0
Esophagus: -0.3
Kidney & Renal Pelvis: -0.4*
Brain & Other Nervous Syste: -0.8*
Leukemia: -1.1*
Myeloma: -1.3*
Oral Cavity & Pharynx: -1.8*
Lung & Bronchus: -2.3*
Larynx: -2.5*
Non-Hodgkin Lymphoma: -2.7*
Colon & Rectum: -2.9*
Stomach: -3.4*
Prostate: -3.5*

**Females**

Liver & IBD: 1.5*
Pancreas: 0.4*
Corpus & Uterus: 0.3*
Urinary Bladder: -0.4*
Lung & Bronchus: -0.6*
Kidney & Renal Pelvis: -0.9*
Brain & Other Nervous Syste: -0.9*
Ovary: -1.3*
All Sites: -1.4*
Leukemia: -1.5*
Esophagus: -1.7*
Breast: -1.9*
Cervix Uteri: -1.9*
Gallbladder: -2.3*
Myeloma: -2.3*
Oral Cavity & Pharynx: -2.3*
Stomach: -2.7*
Colon & Rectum: -2.9*
Non-Hodgkin Lymphoma: -3.4*

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

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

- Improved outcomes
  - >15 year horizon
    - Public sector
  - <5 year horizon
    - Public & private sectors
  - 5-10 year horizon
    - Public & private sectors
  - >15 year horizon
    - Public sector
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.

• 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 multiforme*
- 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)

• 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

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Thank you!