WHAT IS NEW AT THE NCI?

• NEW LEADERSHIP
WHAT IS NEW AT THE NCI?

• NEW LEADERSHIP

Doug Lowy
Deputy

Jim Doroshow
Deputy

Barry Kramer
Prevention

Barbara Wold
Cancer Genomics

John Czajkowski
Executive Officer

Ted Trimble
Global Health
WHAT IS NEW AT THE NCI?

• NEW LEADERSHIP

• DIMINISHING BUDGETS

BUT LOTS TO DO AND LOTS THAT CAN BE DONE
WHAT IS NEW AT THE NCI?

• NEW LEADERSHIP

• DIMINISHING BUDGETS

• EXPANSIONS/REARRANGEMENTS OF THE MANDATORY:
  --CENTER FOR CANCER GENOMICS
NCI Center for Cancer Genomics

Develop and apply genome science to better treat cancer patients

DISCOVERY by genomics and functional genomics

- Drug Development
- Pathway Function
- DNA-based Diagnosis

Precision Treatment
Inventing a Pipeline for Comprehensive Characterization

THE CANCER GENOME ATLAS
TCGA Project: Current Status

Nov 2010 Status Vs.
Nov 2011 Status
TOWARDS PRECISION MEDICINE

(NRC REPORT, NOVEMBER 2011)
From microscopes to DNA sequence:

How cancer genomics is beginning to confer precision on treatment for lung cancers.
Path forward to Clinical Sequencing

Arul Chinnaiyan and colleagues: Dec 1, 2011

Timeline

Roychowdhury et al, 2011 Dec 1 Science Transl. Med
Achieving Completeness: *Clinical data should drive more and deeper discovery*

Global Cancer Alliance

Shared knowledge base to which patients can choose to contribute their genomic data, clinical data

*Many challenges, but essential*

E. Lander, TCGA talk 2011
WHAT IS NEW AT THE NCI?

• NEW LEADERSHIP

• DIMINISHING BUDGETS

• EXPANSIONS/REARRANGEMENTS:
  --CANCER GENOMICS
  --CLINICAL TRIALS GROUPS
RE-ENGINEERING COOPERATIVE GROUPS

- CONSOLIDATE GROUPS AND IMPROVE EFFICIENCY
- STRENGTHEN DATA AND SPECIMEN COLLECTION
- INCORPORATE GENOMICS AND OTHER SCIENTIFIC ISSUES INTO TRIALS
- ENFORCE CONNECTIONS WITH CANCER CENTERS
WHAT IS NEW AT THE NCI?

• NEW LEADERSHIP

• DIMINISHING BUDGETS

• EXPANSIONS/REARRANGEMENTS:
  -- CANCER GENOMICS
  -- CLINICAL TRIALS GROUPS

• NEW FOCUS ON THE LESS OBVIOUS:
  -- CANCER AS PART OF GLOBAL HEALTH
GLOBAL CAUSES OF MORTALITY

- 33% infectious and parasitic diseases
- 29% circulatory diseases
- 12% cancer
- 7% perinatal conditions
- 6% respiratory diseases
- 13% other
Cancer Cases Are Rising Globally
Especially in Less Developed Settings

Cancer currently accounts for ~12.5% of ~60 Million global deaths.

Data Source: Globocan 2002
NCI’S NEW CENTER FOR GLOBAL HEALTH

• AMALGAMATE EXISTING INITIATIVES

• GUIDE DEVELOPMENT OF REGISTRIES AND NATIONAL CANCER PLANS

• CAPITALIZE ON ONCOGENIC INFECTIONS: NEW AND EXISTING VACCINES, ETC

• LINK TO TRANS-DISEASE PREVENTION: TOBACCO, OBESITY, ALCOHOL...

• PURSUE OPERATIONAL IMPROVEMENTS: SCREENING, ACCESS TO TREATMENT AND SYMPTOM CONTROL, SURGERY, HEALTH SYSTEMS...

• HARNESS ENTHUSIASM, FIND PARTNERS, AND BUILD CAPACITY
REGIONAL VARIATIONS IN CANCER RATES

GASTRIC

CERVICAL

INFLUENCED BY HPV INFECTION AND SCREENING

LUNG

Prophylactic HPV Vaccines Are L1 Virus Like Particles (VLPs)

L1 Insertion in Baculovirus Expression Vector

Production in Insect Cells

Spontaneous assembly of L1 into VLPs

Induce high titers of virion neutralizing antibodies

Non-infectious, Non-oncogenic

Reinhard Kirnbauer et al. PNAS 1992
IN RWANDA, FUNDS FROM GAVI, AGREEMENT WITH MERCK, PLUS GOVERNMENT SUPPORT HAVE MADE HPV VACCINATION MORE WIDESPREAD THAN IN THE USA
Some NCI-designated Cancer Centers active in Africa

- Fred Hutchinson Cancer Research Center: Uganda
- University of North Carolina: Malawi
- University of Maryland: Nigeria
- University of Michigan: Ghana
- Indiana University: Kenya
2011: FHCRC/UCI PROJECT

50+ YEAR HISTORY OF THE UGI

DENNIS BURKITT

BURKITT’S LYMPHOMA
EBV AND BURKITT'S LYMPHOMA

UNRESOLVED ISSUES:

RELATIONSHIP TO MALARIA?
TARGETABLE MUTATIONS?
IMPROVED AFFORDABLE RX?
BETTER MONITORING FOR RECURRENCE?
SCREENING? VACCINES?
Estimated new cases of EBV-associated cancers worldwide per year

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Number of cases</th>
<th>Attributable to EBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkitt lymphoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developed countries</td>
<td>400</td>
<td>100</td>
</tr>
<tr>
<td>Less-developed countries</td>
<td>7800</td>
<td>6600</td>
</tr>
<tr>
<td>Gastric carcinoma</td>
<td>933,900</td>
<td>84,050</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>62,400</td>
<td>28,600</td>
</tr>
<tr>
<td>Nasopharyngeal carcinoma</td>
<td>80,000</td>
<td>78,100</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>197,450</strong></td>
<td></td>
</tr>
</tbody>
</table>

**WHAT ARE THE PROSPECTS FOR AN EBV VACCINE?**

A NEW PROJECT ON THE NON-OBVIOUS:

PROVOCATIVE QUESTIONS
What is the "Provocative Questions" Project?

• 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
PROCESS

MULTI-DISCIPLINARY WORKSHOPS
AT THE NIH AND AROUND THE U.S.

PQ WEBSITE FOR POSTING, READING, AND RESPONDING TO QUESTIONS

REQUEST FOR PROPOSALS TO ANSWER 24 PQ’S
APPROVED BY BSA FOR RO1’S/R21’S ($15M)

752 APPLICATIONS, SOME FOR EACH PQ

BEING REVIEWED BY NCI SEP’S
EPIDEMIOLOGY
WHY ARE THERE REGIONAL VARIATIONS IN CANCER RATES?

WHAT ENVIRONMENTAL FACTORS CHANGE THE RISKS OF VARIOUS CANCERS WHEN PEOPLE MOVE FROM ONE GEOGRAPHIC REGION TO ANOTHER?

WHY ARE INCIDENCE RATES FOR MANY CANCERS HIGHER IN MEN THAN WOMEN?

<table>
<thead>
<tr>
<th>Type</th>
<th>New Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>All Sites</td>
<td>789,620</td>
<td>739,940</td>
</tr>
<tr>
<td>Oral cavity and pharynx</td>
<td>25,420</td>
<td>11,120</td>
</tr>
<tr>
<td>Esophagus</td>
<td>13,130</td>
<td>3,510</td>
</tr>
<tr>
<td>Liver and intrahepatic bile duct</td>
<td>17,430</td>
<td>6,690</td>
</tr>
<tr>
<td>Larynx</td>
<td>10,110</td>
<td>2,610</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>52,760</td>
<td>17,770</td>
</tr>
<tr>
<td>Thyroid</td>
<td>10,740</td>
<td>33,930</td>
</tr>
</tbody>
</table>

*American Cancer Society
Cancer Facts and Figures, 2010*
Not all cancers increase with age; what determines kinetics?
Why are different tissues so dramatically different in their tendency to develop cancers?

Heart

Prostate

Small Intestine

Large Intestine
Why are different animals with different sizes and different life spans so different with respect to cancer incidence?

- Turtles
- Mice
- Sharks
- Whales...except belugas from the SLE!
WHY ARE PATIENTS WITH CERTAIN NEURODEGENERATIVE DISEASES (PD, HD, AD, FRAGILE X) AT LOWER RISK OF MOST CANCERS?

RISK MODIFICATION
WHY DON’T MORE PEOPLE ALTER BEHAVIORS KNOWN TO INCREASE THE RISK OF CANCERS?

--The message itself is not optimally designed
--The message is not effectively delivered
--The interventions to facilitate behavior change are not optimal
HOW DOES OBESITY CONTRIBUTE TO CANCER RISK?

Trends in Overweight* Prevalence (%), Adults 18 and Older, US, 1992-2008


HOW DOES OBESITY CONTRIBUTE TO CANCER RISK?

### Distribution of Deaths and Death Rates per 10,000 Person-Years*

<table>
<thead>
<tr>
<th>End Point</th>
<th>Matched Subjects</th>
<th></th>
<th>Matched Subjects</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgery Group</td>
<td></td>
<td>Control Group</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(N=7925)</td>
<td></td>
<td>(N=7925)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no./10,000 person-yr</td>
<td></td>
<td>no./10,000 person-yr</td>
<td></td>
</tr>
<tr>
<td>All causes of death</td>
<td>213</td>
<td>37.6</td>
<td>321</td>
<td>57.1</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>55</td>
<td>9.7</td>
<td>104</td>
<td>18.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2</td>
<td>0.4</td>
<td>19</td>
<td>3.4</td>
</tr>
<tr>
<td>Cancer</td>
<td>31</td>
<td>5.5</td>
<td>73</td>
<td>13.3</td>
</tr>
<tr>
<td>Other diseases</td>
<td>62</td>
<td>11.0</td>
<td>89</td>
<td>15.5</td>
</tr>
<tr>
<td>All non-disease causes</td>
<td>63</td>
<td>11.1</td>
<td>36</td>
<td>6.4</td>
</tr>
</tbody>
</table>

*Deaths that were caused by disease include all deaths minus those caused by accidents unrelated to drugs, poisonings of undetermined intent, suicides, and other non-disease deaths.

---

PREVENTION
DO DRUGS THAT ARE COMMONLY AND CHRONICALLY USED FOR OTHER INDICATIONS PREVENT CANCERS AND, IF SO, HOW?

DO DRUGS THAT ARE COMMONLY AND CHRONICALLY USED FOR OTHER INDICATIONS PREVENT CANCERS AND, IF SO, HOW?

Strong Effects

DO DRUGS THAT ARE COMMONLY AND CHRONICALLY USED FOR OTHER INDICATIONS PREVENT CANCERS AND, IF SO, HOW?

Weak or No Effect

DIAGNOSTICS
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)
What is the clinical significance of finding cells from a primary tumor at another site?

THERAPEUTICS
TRADITIONAL CANCER TREATMENTS

Surgery

Chemotherapy

Radiotherapy
WHY ARE SOME DISSEMINATED CANCERS CURED BY CHEMOTHERAPY ALONE?
RÉPUBLIQUE FRANÇAISE

CONTRE LE CANCER

CENTRE RÉGIONAL ANTI-CANCÉREUX
HOSPICE DE LA GRAVE - TOULOUSE - CONSULTATIONS
LUNDI - MERCREDI - VENDREDI à 8 HEURES ET DEMIE

IMP. BARUTEL - TOULOUSE