Report from the Acting Director

Douglas R. Lowy
Acting Director, National Cancer Institute,
National Institutes of Health
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.
Precision Medicine in Cancer Treatment

- President Obama has proposed $70 million in his FY16 budget for the Precision Medicine Initiative in Oncology (PMI-Oncology).

- Future workshop to explore the translational potential for the specific re-activation and/or replacement of tumor suppressor gene activities.
Precision Medicine 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 cervical cancer incidence from 4 randomized controlled trials of cytology (control arm) vs. HPV testing (experimental arm)

Precision Medicine 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

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<thead>
<tr>
<th></th>
<th>Non-Users</th>
<th>Regular aspirin users</th>
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<tbody>
<tr>
<td>All CRC</td>
<td>1.0</td>
<td>0.73 (0.62-0.86)</td>
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<tr>
<td>High 15-PGDH CRC</td>
<td>1.0</td>
<td>0.49 (0.34-0.71)</td>
</tr>
<tr>
<td>Low 15-PGDH CRC</td>
<td>1.0</td>
<td>0.90 (0.63-1.27)</td>
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</table>

**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*
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

- 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\textsuperscript{a,b,c}, Martina L. Veigl\textsuperscript{b,c,1}, Vinay Varadan\textsuperscript{a,b,1}, Arman Nosrat\textsuperscript{d}, Lakshmeswari Ravi\textsuperscript{d}, James Lutterbaugh\textsuperscript{d}, Lydia Beard\textsuperscript{d}, James K. V. Willson\textsuperscript{e}, W. David Sedwick\textsuperscript{b,c,d}, Zhenghe John Wang\textsuperscript{b,f}, Neil Molyneaux\textsuperscript{f}, Alexander Miron\textsuperscript{f}, Mark D. Adams\textsuperscript{g}, Robert C. Elston\textsuperscript{b,h}, Sanford D. Markowitz\textsuperscript{b,c,d,i,2,3}, and Joseph E. Willis\textsuperscript{b,c,i,l,2}

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“...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. “

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
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
## Competing RPG & NCI Total Obligations

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</thead>
<tbody>
<tr>
<td>Competing RPGs - Obligations</td>
<td>414,003,721</td>
<td>403,944,814</td>
<td>450,476,095</td>
<td>-</td>
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<tr>
<td>Competing RPGs - Count</td>
<td>1,085</td>
<td>1,095</td>
<td>1,207</td>
<td>-</td>
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<tr>
<td>NCI Total Obligations</td>
<td>5,067,341,795</td>
<td>4,789,014,389</td>
<td>4,932,368,225</td>
<td>4,953,028,000</td>
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</table>

- **Competing RPGs - Obligations**
- **NCI Total Obligations**
Recent modifications to RPG pool

- Decreasing the cuts to modular grants from 17% to 8.5%.

- Outstanding Investigator Awards: will increase the average size of the awards
NCI Cancer Centers

- P30 core grants
Ras pathway clones

- 2 sequence-validated Gateway Entry clones for each gene (for generating N or C terminal fusions)
- 180 total genes
  - 17 not available commercially in the most biologically relevant isoform
  - 32 additionally not available without non-silent mutations
- 350 of 360 clones completed by July 17th
- Clones available through Dom Esposito: espositod@mail.nih.gov
▪ NCI has begun the recompetition of the Operations and Technical Support (OTS) contract that runs NCI’s Federally Funded Research and Development Center (FFRDC)

▪ Leidos Biomedical Research, Inc. currently administers the contract

▪ Information concerning the competitive process will be announced on FedBizOpps as well as at the FNLCR Acquisition Portal

▪ Pre-Proposal Conference Oct. 1 – 2, 2015

▪ Please help spread the word – we are doing our utmost to ensure a fair and open contract competition
Recent Personnel Changes

Retirements
- Bob Wiltrout, Center for Cancer Research (CCR)
- Joe Tomaszewski, Division of Cancer Treatment and Diagnosis (DCTD)
- Susan Erickson, Office of Government and Congressional Relations (OGCR)

New Leadership
- Toby Hecht, Deputy Director, DCTD
- Lee Helman, Acting Director, CCR
- Glenn Merlino, Acting Scientific Director (Basic), CCR
- MK Holohan, Acting Director, OGCR
- Peter Garrett, Director, Office of Communications and Public Liaison (OCPL)
New Version of Cancer.gov and Cancer.gov/espanol
NCI-MATCH Targeted Treatment Clinical Trial Launches at ASCO

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 CANCER LETTER
NCI-MATCH to Bring in Public, Private Funds, Giving NCI New Urgent Scientific Agenda
By Paul Goldberg

Los Angeles Times
Cancer trials aim to shore up 'precision medicine's' base of evidence

Shanghai Daily
U.S. announces schedule of trial for linking targeted cancer drugs to gene mutations
Jun 02, 2015