Director’s Update

Dr. John E. Niederhuber
Acting Director
National Cancer Advisory Board
September 6, 2006
NCAB – Director’s Update

- Honors and appointments
- Fourth quarter budget update
- Planning process for 2007
- Roadmap Trans-NIH Strategic Initiative Drive
- Oncology Biomarkers Qualification Initiative
- Scientific updates
Honors
Department of Health and Human Services Honor Award for research on the human papillomavirus

John T. Schiller, Ph.D.
Laboratory of Cellular Oncology, CCR

Douglas Lowy, M.D.
Laboratory of Cellular Oncology, CCR
Honors
Department of Health and Human Services Honor Award for contributions to NCI’s Katrina Relief Team

Norm Coleman, M.D.
Radiation Oncology Branch, CCR DCTD

Lee Helman, M.D.
Pediatric Oncology Branch, CCR
Appointments

Dan Gallahan
Deputy Director,
Division of Cancer Biology

Lenora Johnson
Acting Director,
Office of Liaison Activities
2006 – Final Quarter

- Have been hit with a **mid-year increase in taps** for direct utility costs to NIH of almost $4 million
- RPG **payline running about 11th percentile**;
  15% of the competing pool in reserve for some exceptions
- Type 5s generally **2.35% below the commitment record**
- **SPOREs are 2% below FY2005**
  essentially flat with FY05
- Training is 1% above the FY05 level

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**EC, June 26, 2006**

Payline for RO1 raised to 12th percentile

Payline for *RO1 raised to 18th percentile

Total additional funds committed: $8.3 million
Budget Planning for 2007

Leadership of the NCI is coming together to evaluate programs with an eye toward reduced or flat budgets for the foreseeable future.

Division Directors’ retreat June 7 & 8

• Directors presented and discussed their division’s portfolios
Budget Planning for 2007

Important background for future funding decisions.
Budget Planning for 2007

Ranking by anonymous ballot, to reduce, maintain, or expand each program.

Directors also discussed how to leverage resources, for new initiatives.
Budget Planning for 2007

P: Phase out in 2007
R20: Reduce in 2007 by a minimum of 20%
R10: Reduce in 2007 by a minimum of 10%
R5: Reduce in 2007 by a minimum of 5%
R<5: Reduce in 2007 by 1-4%
M: Maintain in 2007 at current dollar level
E2: Expand in 2007 by <2%
E5: Expand in 2007 by 2%-5%
N: New
Budget Planning for 2007

Phase 2 = early August

Review “infrastructure-like” programs, many of which are housed within the Office of the Director

Phase 3 = September-January

Revisit all scorings multiple times and reprioritize towards a monetary target
NCI’s Congressional Appropriations, FY 1998 to FY 2007

NIH DOUBLING - NCI 80%

John E. Niederhuber, MD
June 2006
Appropriations Bill Status

• House and Senate Appropriations committees have passed an appropriations bill for Labor/HHS
  — neither has come up for a vote by the full House or Senate
  — votes appear unlikely before the November elections
Appropriations Bill Status

• House version: For NIH and NCI, essentially equal to the President's Budget
  – For NCI, $4.754 billion — $40 million less than FY 2006

• Senate version: Subcommittee added $200 million to the NIH request
  – For NCI, $4.799 billion — $9 million more than FY 2006. (Senate adjusted the FY 2006 base downward for the Secretary's transfer from NIH to CMS)

(Above figures for NCI include the NIH Roadmap)
NCI Community Cancer Centers Program

Launching pilot of multiple sites in early 2007

• Bring science to the patient — early phase clinical trials

• Utilization of electronic medical records — a national cohort of patients for clinical research

• Tissue acquisition for TCGA project

• Rapid dissemination of new therapies

• Management of cancer as a chronic disease

• Reduce healthcare disparities
Roadmap Trans-NIH Strategic Initiative Drive

- Identify and develop ideas for a new cohort of Roadmap initiatives for 2008
- Through a “common fund,” up to $50 million per year from the existing Roadmap budget will be allocated for these initiatives
- Common fund will comprise 1.7 percent of the FY 2008 budget
- Growth in future years will not exceed real growth of the NIH
Roadmap Trans-NIH Strategic Initiative Drive

• **Phase 2**: Five consultation meetings to solicit initiative ideas from the extramural community (July/September)

• **Phase 2**: Solicit idea nominations from IC directors and NIH OD program officers (August)

• **Phase 3**: Solicit input and/or idea nominations from the broad stakeholder community, via a Web-based Request for Information (RFI), to be released in October 2006
Roadmap Trans-NIH Strategic Initiative Drive

- Dec. 2006: Dr. Zerhouni will select up to 5 idea categories to be developed into concepts
- Jan.-May 2007: RM development teams will conduct pre-RFA activities to produce initiative-focused science and business plan packages
- May 2007: NIH IC directors and the Advisory Council to the NIH Director will conduct a final review of proposed initiatives
- May 2007: Dr. Zerhouni will make the final selections
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<th>National Cancer Institute</th>
<th>FDA</th>
<th>CMS</th>
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<td>Develop biomarker technologies and validation protocols to improve detection, diagnosis, treatment, and prevention of cancer</td>
<td>Develop guidance for the use of biomarkers to facilitate cancer drug development</td>
<td>Make informed decisions about reimbursement for new or existing cancer treatment regimens based on biomarker-guided knowledge</td>
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The NCI-FDA Interagency Oncology Task Force (IOTF)

- Established in 2003 to enhance efficiency of clinical research and scientific evaluation of new cancer treatments
  - Establish joint training and fellowships
  - Discover & develop biomarkers for clinical benefit
  - Utilize caBIG™ to support standardized & organized clinical trials data reporting; support electronic filing to speed regulatory review
  - Address specific regulatory barriers impeding cancer drug development
Initial OBQI Projects: Imaging-Based Biomarkers

**Project 1:** FDG-PET for prediction of tumor response and patient survival in lymphoma

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Treatment completed

Access to FDG-PET/CT imaging is a requirement for institutions enrolling patients on the F18 FDG-PET validation CALGB 50303 study.

**Initial OBQI Projects:**

- Imaging-Based Biomarkers
- **Project 1:** FDG-PET for prediction of tumor response and patient survival in lymphoma
Initial OBQI Projects:
Imaging-Based Biomarkers

**Project 2:** Phase II study of FDG-PET/CT as a predictive marker of tumor response and patient outcome: prospective validation in non-small cell lung cancer
Why FDG-PET?

• > 50-year body of knowledge about glycolytic pathway in cancer (i.e., Warburg Effect, strong mechanistic rationale)

• In many clinical settings (e.g., NSCLC, esophageal cancer, lymphoma), FDG-PET can provide an early measure of response to treatment with approved therapies

• With a few additional studies, FDG-PET could facilitate drug development and patient care by resulting in shorter phase II trials, accelerated approval in Phase III.
Development of biomarkers consortium

• Public–Private partnership
• NIH-FDA-CMS-Pharma-FNIH
• Consortium’s work will be through individual projects
• FDG-PET lead project
Advances in Immunotherapy: Gene Therapy Enhances Adoptive Cell Transfer

Adoptive cell transfer: the reintroduction, after lymphodepletion, of the patient’s own tumor reactive T-lymphocytes

- Has demonstrated 50% objective response in patients with advanced melanoma
- Has shown success in melanoma patients resistant to IL-2 and chemotherapy
- Has, until now, been useful only in melanoma patients
- Has required patients to have a population of tumor reactive lymphocytes
Advances in Immunotherapy: Gene Therapy Enhances Adoptive Cell Transfer

• Rosenberg group has developed method to retrovirally transfect T-lymphocytes with T-cell receptors that recognize cancer antigens

• T-cells can be made to express receptors that recognize a broad range of cancer antigens, allowing application to cancers other than melanoma

• Reactive T-lymphocytes may be generated in patients that have none of their own
TSR Adoptive Transfer Therapy

Blood drawn

Lymphocytes grown in culture

Retrovirus inserts TCR genes

Cultured lymphocytes

TCR-rich lymphocytes reach tumor

Lymphocyte-mediated lysis and apoptosis of tumor cells
Advances in Immunotherapy: Gene Therapy Enhances Adoptive Cell Transfer

- Cohort 1, with ex vivo culture period of 19 days showed limited persistence of transduced lymphocytes.
- In cohorts 2 & 3, the experimental group, efforts made to isolate lymphocytes during active growth phase
  - Cohort 2: Ex vivo culture period reduced to 6–9 days
  - Cohort 3: Duplicated cohort 1 conditions, followed by a second rapid expansion protocol after 8–9 days

% Gene Marked Cells

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<th>Days</th>
<th>Cohort 1</th>
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Advances in Immunotherapy: Gene Therapy Enhances Adoptive Cell Transfer

2 of 15 patients with metastatic melanoma demonstrated regression of their tumors > 18 months after treatment with engineered T-lymphocytes.

Rosenberg et al. Science, 313(5791), 2006
Advances in Immunotherapy: Gene Therapy Enhances Adoptive Cell Transfer

2 of 15 patients with metastatic melanoma demonstrated regression of their tumors > 18 months after treatment with engineered T-lymphocytes

30-year-old male with hilar mass

Rosenberg et al. Science, 313(5791), 2006
Advances in Immunotherapy: Gene Therapy Enhances Adoptive Cell Transfer

- Normal human resting peripheral blood lymphocytes can be converted into cells capable of recognizing tumor antigens in vitro and capable of mediating cancer regression in vivo.
- Dr. Rosenberg’s groundbreaking work suggests the therapeutic potential of genetically engineered cells for the biologic therapy of cancer.
- Though response rate is lower than in conventional ACT, this method increases the number of patients eligible for ACT.
- Further modification of the transfection procedure may produce greater persistence of the modified lymphocytes and thus increase response.
National Cancer Institute

Patients & Families

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health