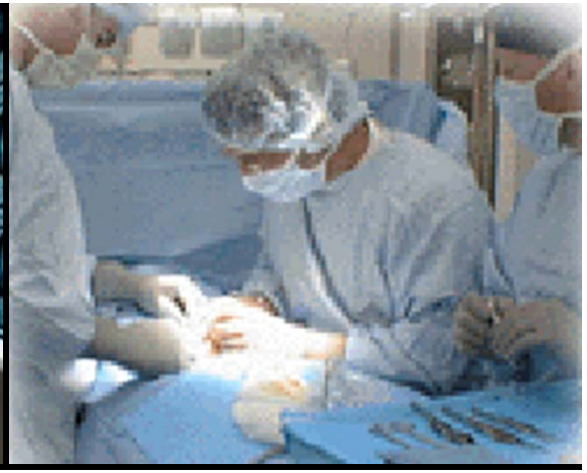
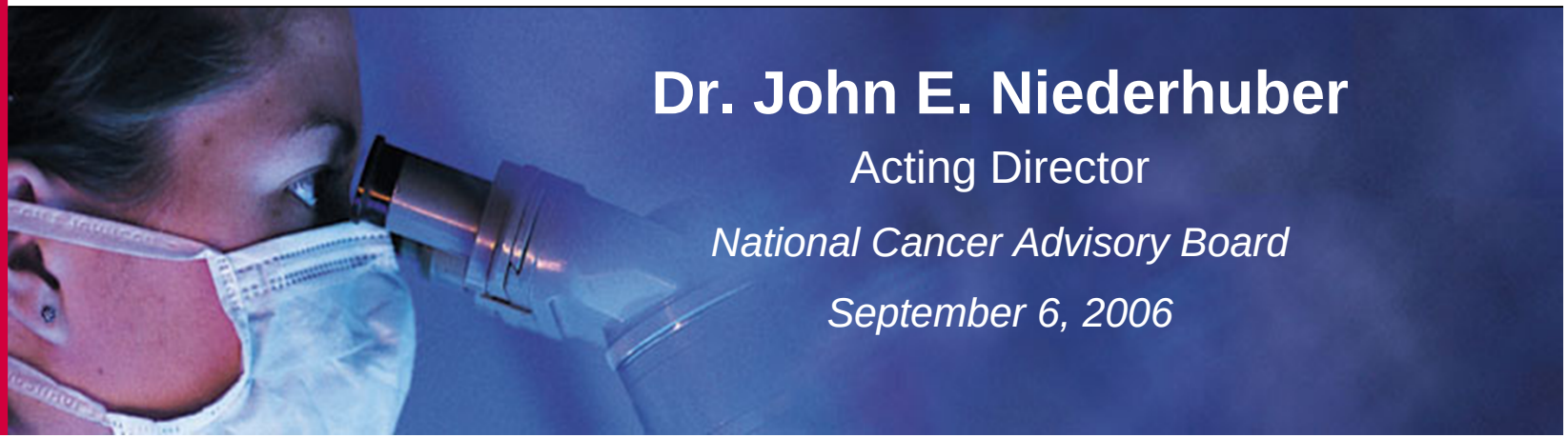
National Cancer Institute





Director's Update



Dr. John E. Niederhuber

Acting Director

National Cancer Advisory Board

September 6, 2006

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health


Dr. Folkman

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% l record**
- **SPOREs are 2% below FY essentially flat with FY05**
- **Training is 1% above the**

EC, June 26, 2006

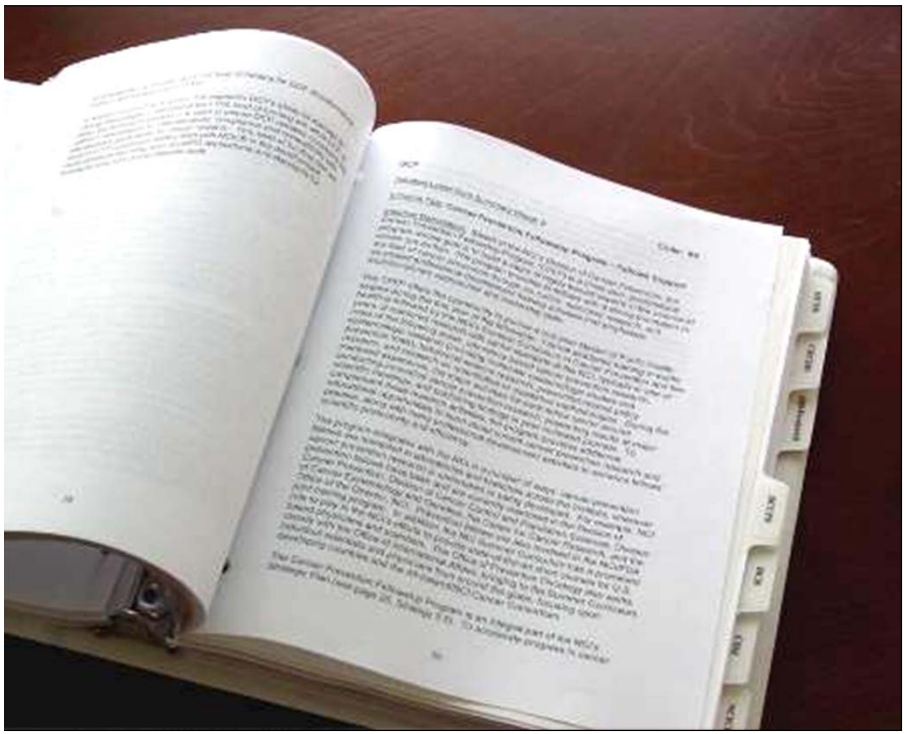
Payline for RO1 raised to 12th percentile

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.



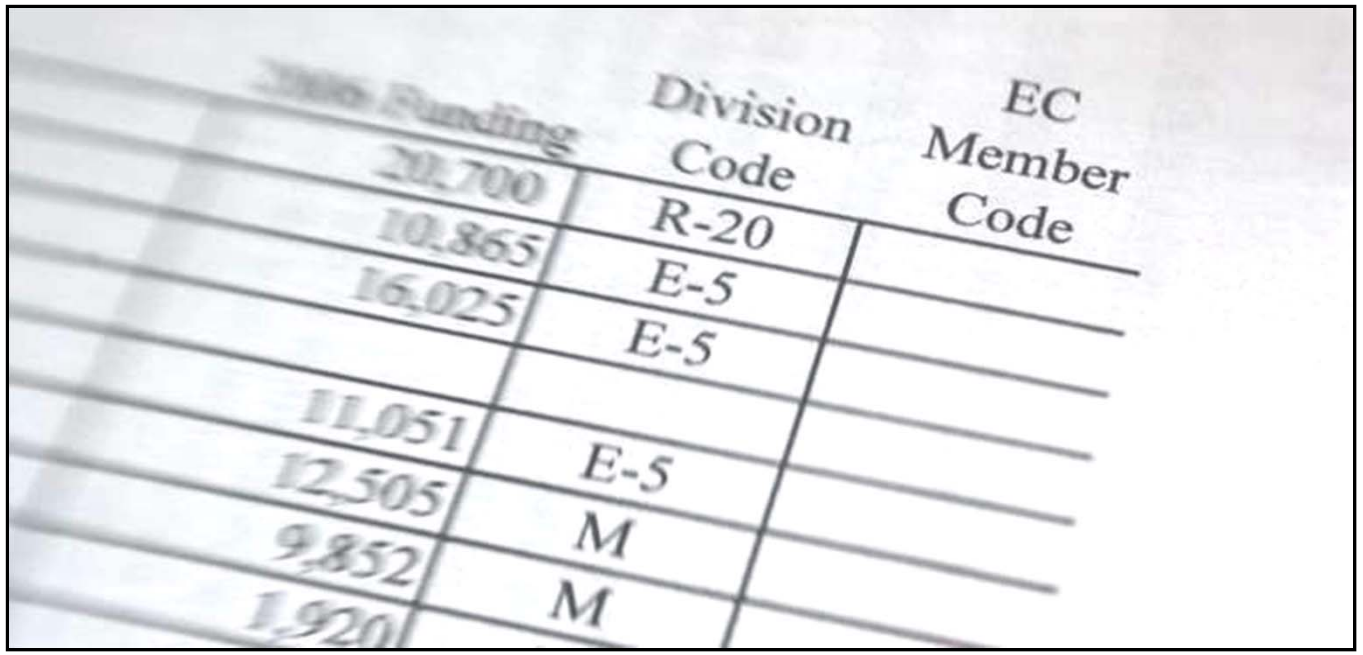
Division Directors' retreat June 7 & 8

- **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

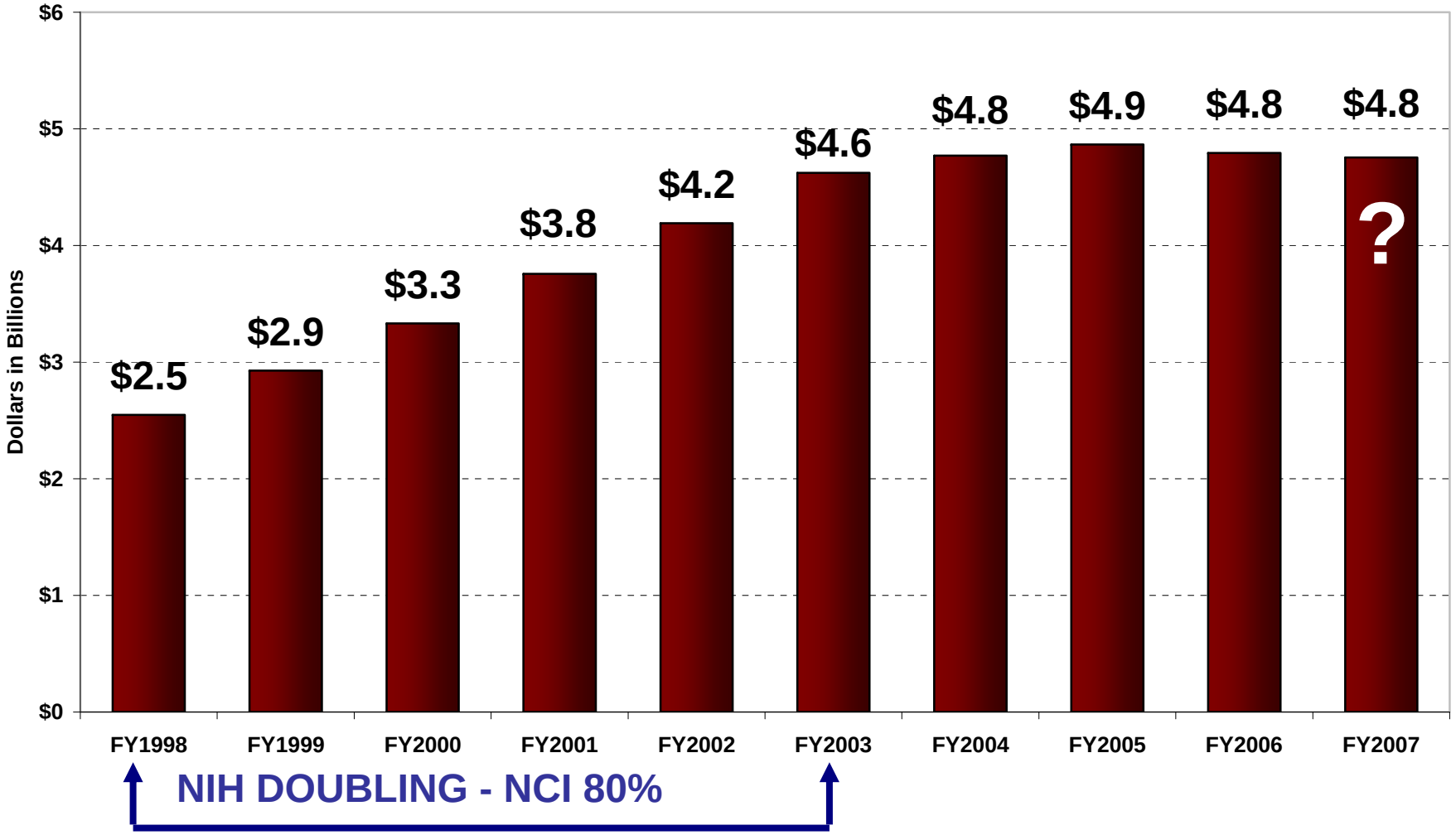
Phase 2 = early August

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



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**

Oncology Biomarkers Qualification Initiative (OBQI): February 2006

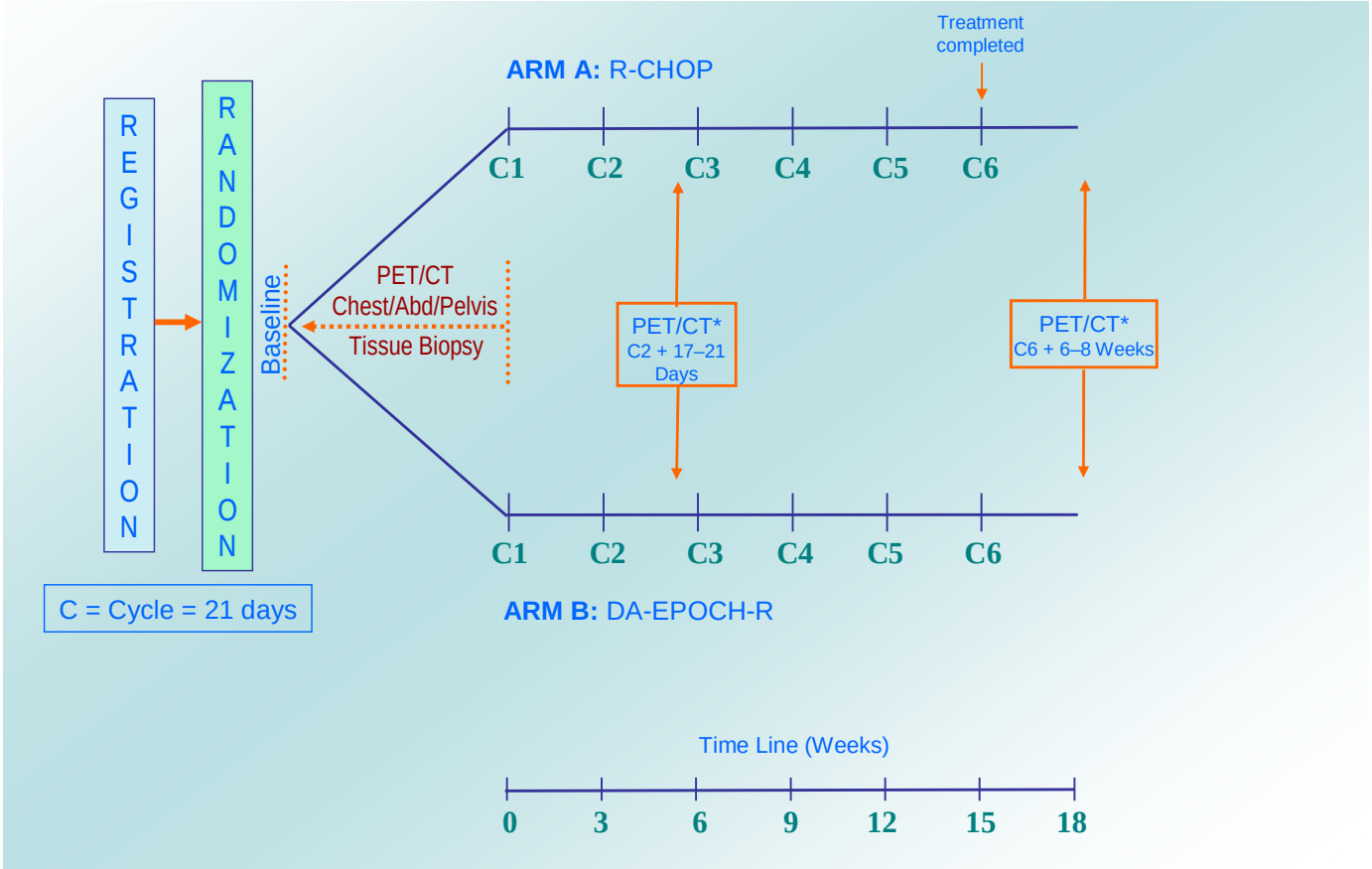
NATIONAL CANCER INSTITUTE	FDA	CMS CENTERS for MEDICARE & MEDICAID SERVICES
Develop biomarker technologies and validation protocols to improve detection, diagnosis, treatment, and prevention of cancer	**Develop guidance for the use of biomarkers to facilitate cancer drug development**	**Make informed decisions about reimbursement for new or existing cancer treatment regimens based on biomarker-guided knowledge**

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**

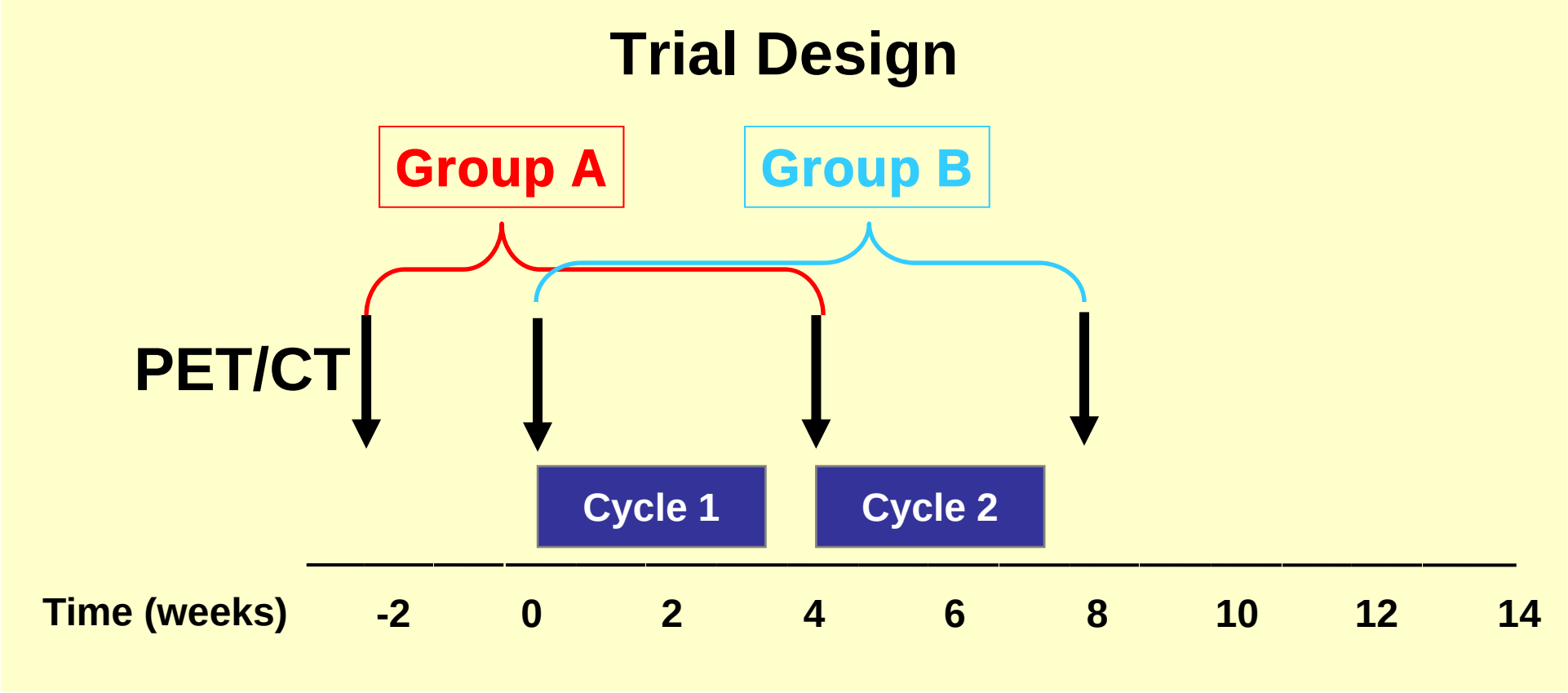
Initial OBQI Projects: Imaging-Based Biomarkers

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



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**

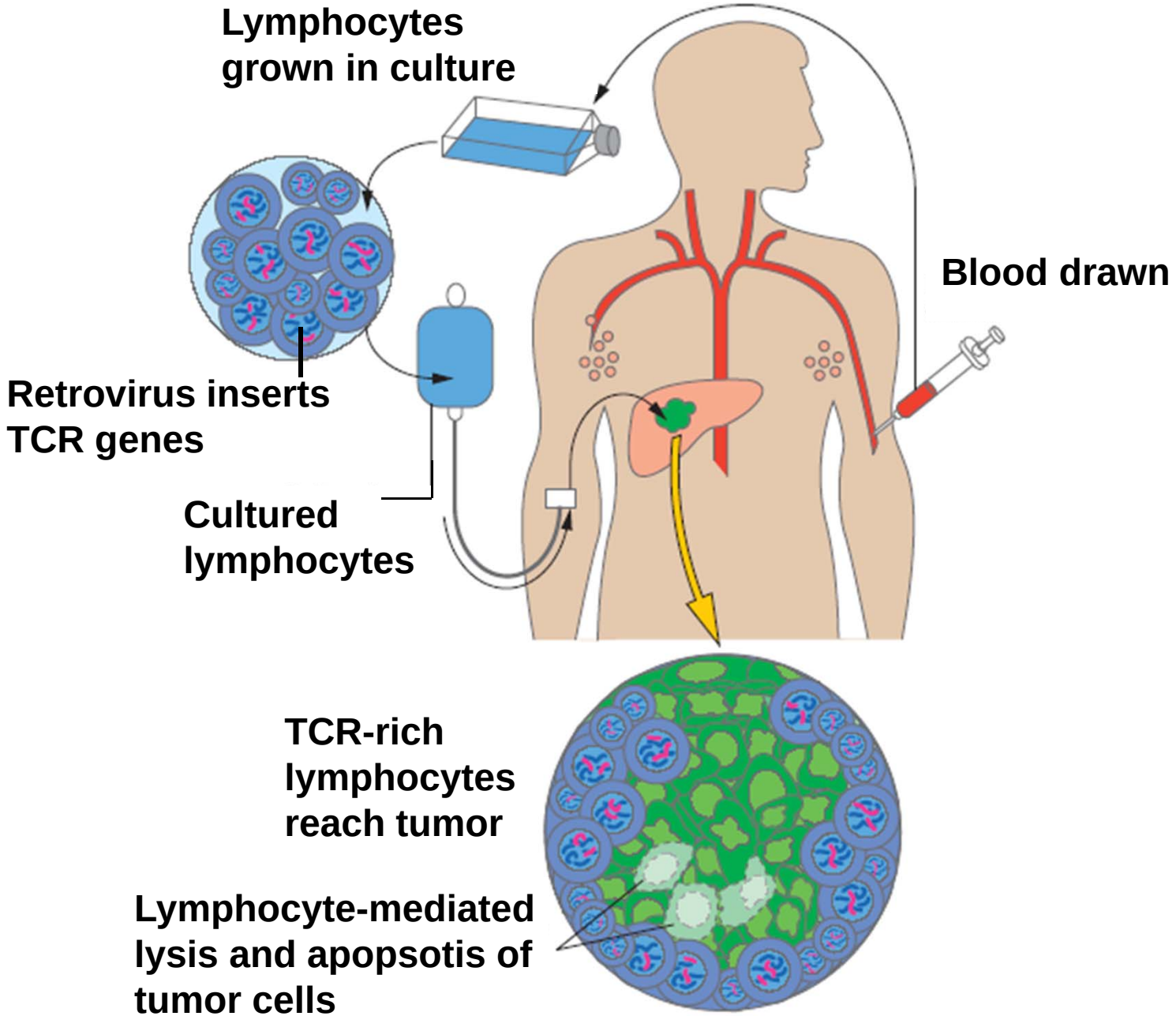
- **Has demonstrated 50% objective response in patients with advanced melanoma**
- **Has shown success in melanoma patients resistant to IL-2 and chemotherapy**
- **Has, until now, been useful only in melanoma patients**
- **Has required patients to have a population of tumor reactive lymphocytes**

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**

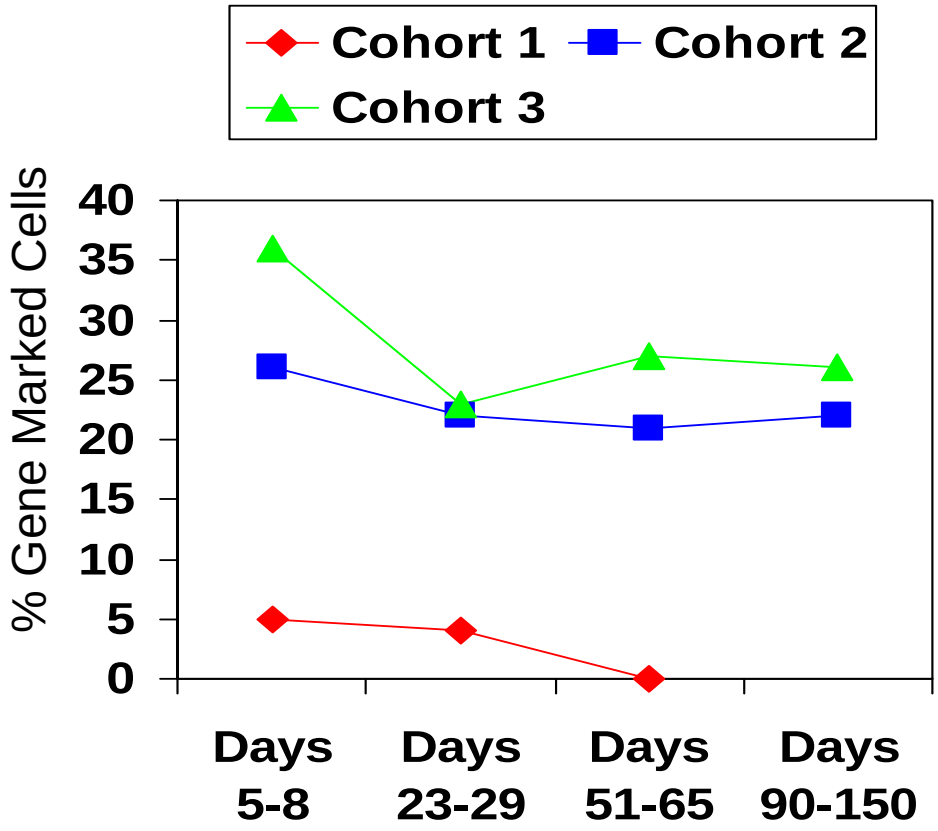
Dr. Steve Rosenberg

TSR Adoptive Transfer Therapy



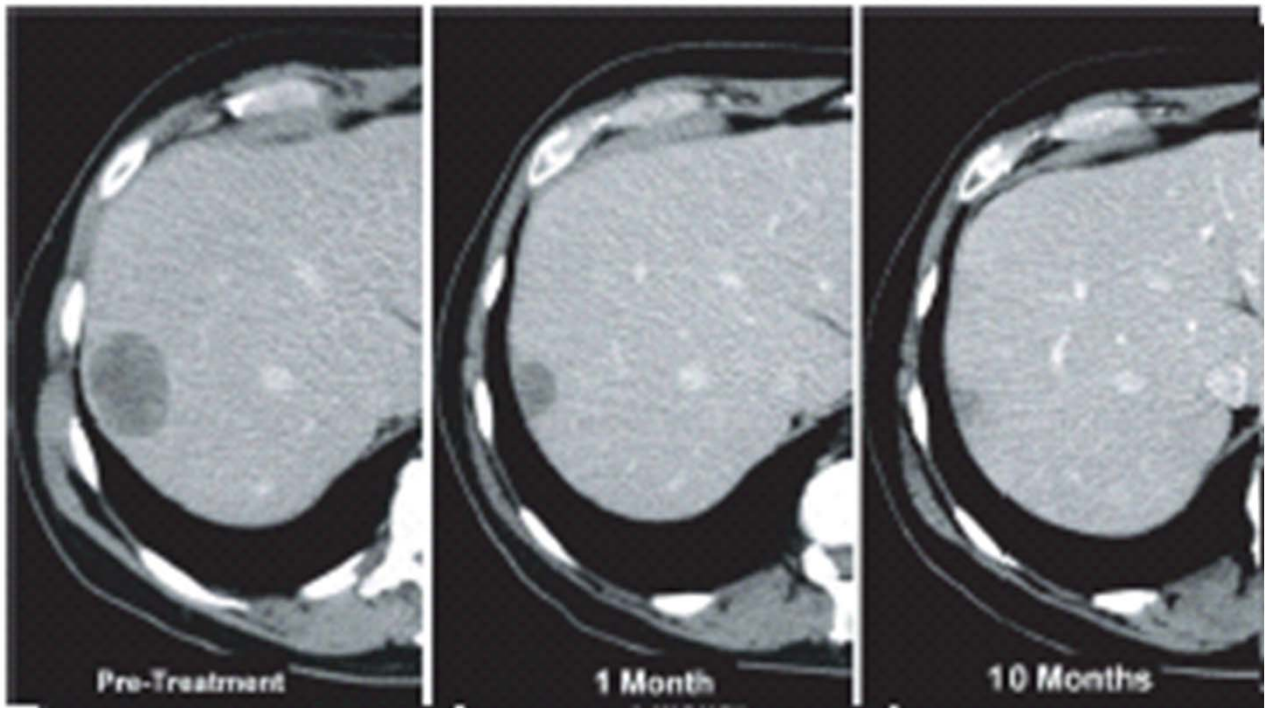
Advances in Immunotherapy: Gene Therapy Enhances Adoptive Cell Transfer

- 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



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

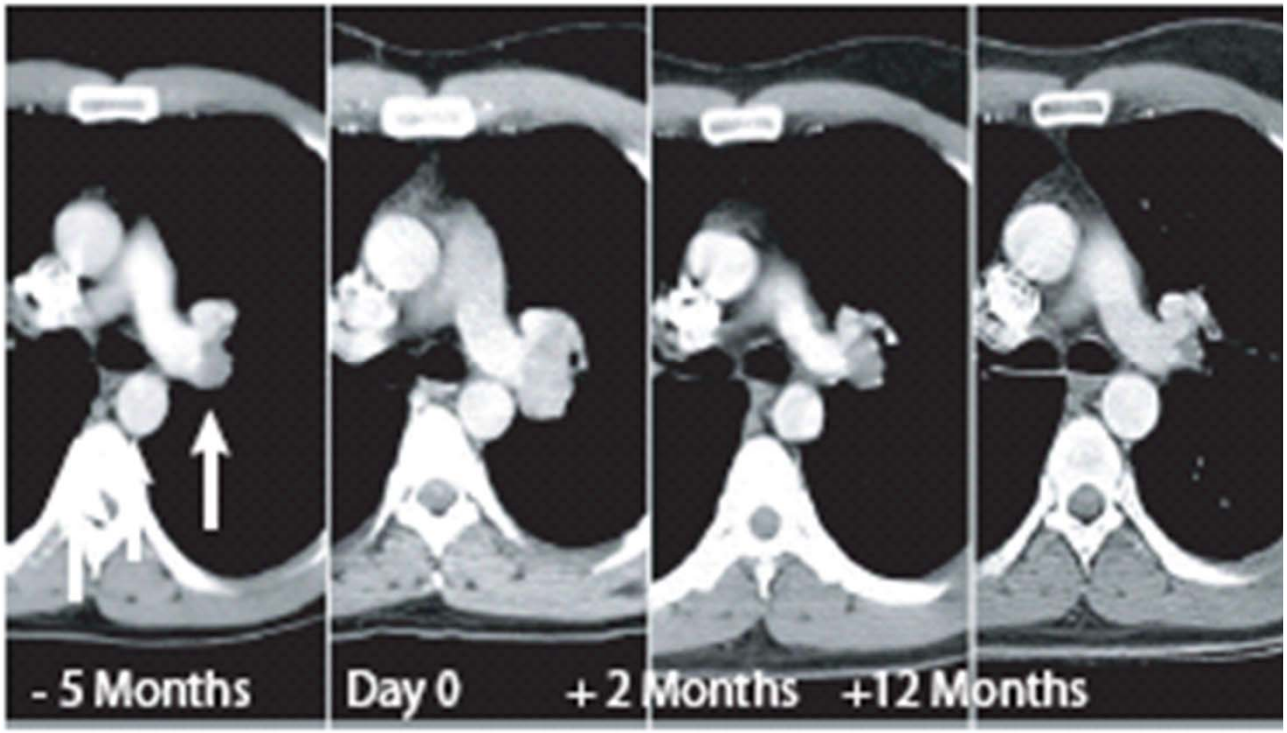


52-year-old male with liver mass

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

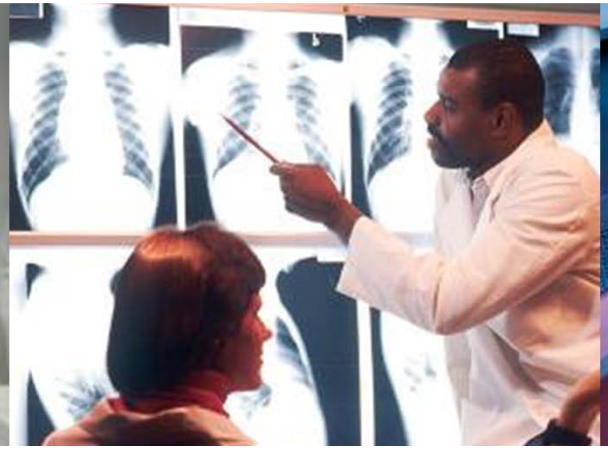
Rosenberg et al. Science, 313(5791), 2006

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