

# Update on SPORes:

*A work in progress*

James H. Doroshow, M.D.

Toby T. Hecht, Ph.D.

National Cancer Advisory Board

September 8, 2008

## Integrating Translational Research: Implementing TRWG Initiatives

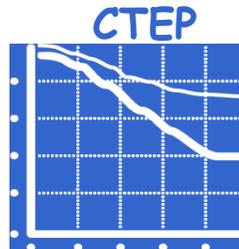
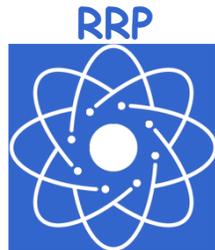
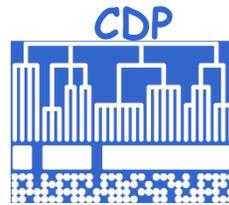
- Make better use of the complex NCI system of programs and resources for translational research; encourage greater sharing of those resources Institute-wide
- Coordinate the various translational research groups across the Divisions, Centers, and Offices of the NCI
- Facilitate portfolio analysis of disease sites; across populations; and across prevention, diagnosis, treatment, and risk assessment
- In context of current NCI budget, assess mechanisms to prioritize and enhance support for translational research

# SPORE Program Transitions

- The Organ Systems Branch (OSB) was moved administratively from the Office of the NCI Director to the Division of Cancer Treatment and Diagnosis (DCTD) and has become a Program: the Translational Research Program (TRP)
  - ✓ This has not meant a greater emphasis on Treatment to the exclusion of other important areas
  - ✓ All NCI Divisions (and the NCI Executive Committee) are participating directly in the oversight of the SPORE Program
- A new TRP leader will be recruited at the Associate Division Director level
- Approximately halfway through an information-gathering process of institutional visits and teleconferences to solicit suggestions from SPORE investigators about how the Program can be improved

# Enhancing SPORE Interactions Across NCI

## DCTD



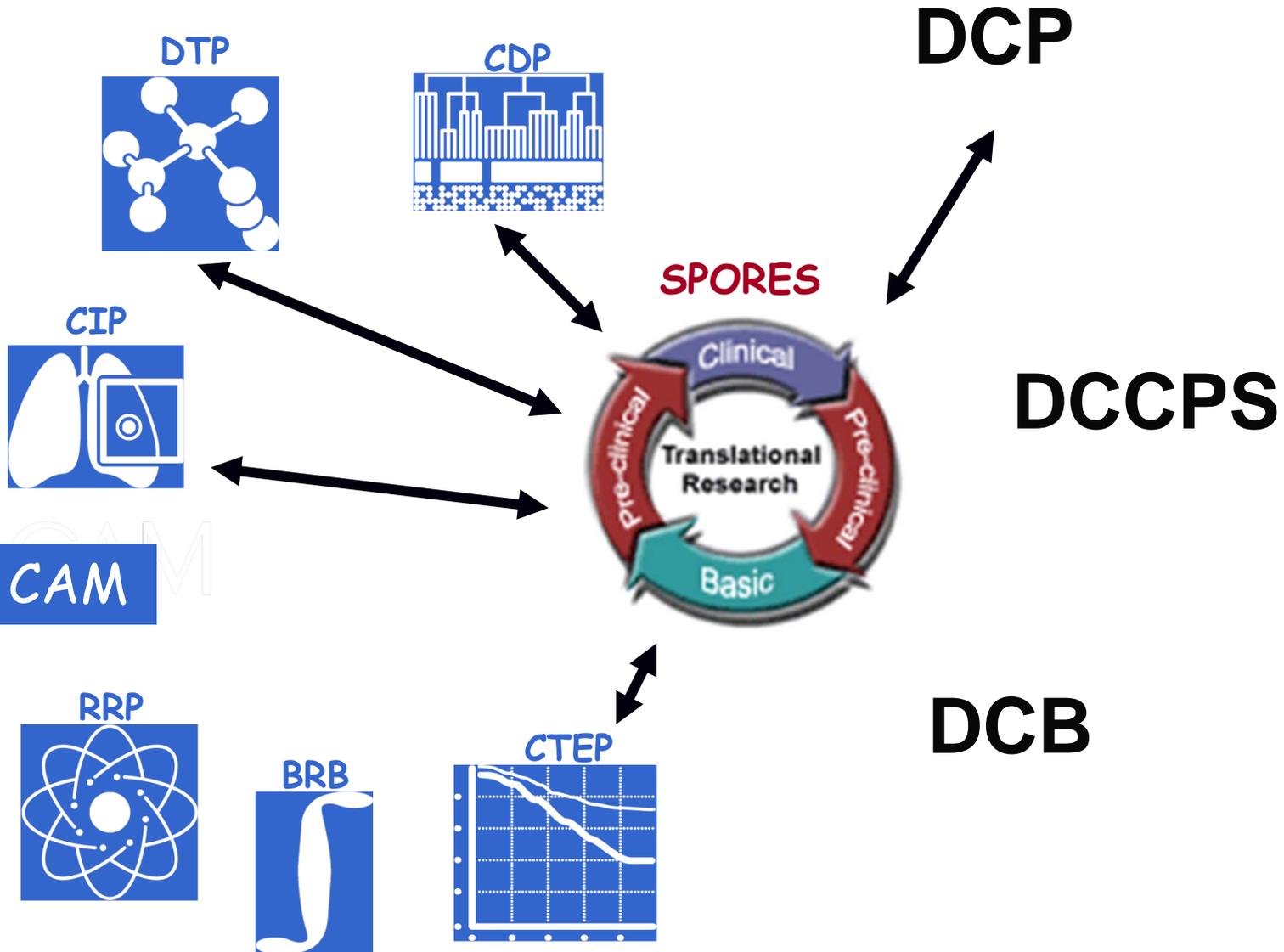
SPORES



DGP

DCCPS

DCB



# Organ Site-Specific SPOREs

(Including Interim Funding)

	<u>07</u>	<u>08</u>		<u>07</u>	<u>08</u>
Bladder	1	1	Leukemia	1	1
Brain	4	4	Lung	7	8
Breast	11	10	Lymphoma	4	4
Cervical	1	1	Myeloma	1	1
Endometrial	1	0	Ovary	4	4
GI	5	5	Pancreas	3	2
Head & Neck	4	4 (1)	Prostate	10	9
Kidney	1	1	Skin	4	5

**TOTAL SPORES 07: 62**  
**08: 60 (1)**

# Revisiting the Guidelines

## Why?

- Cancer Center, Cooperative Group, and SPORE guidelines all currently under review by the Clinical and Translational Research Advisory Committee: Goal is to enhance clinical and translational research coordination
- Part of the reorganization into the Division of Cancer Treatment and Diagnosis:
  - **Aligning the guidelines with the NCI goals for translational science as outlined in the report of the TRWG**
- The fiscal reality of today may make some of the guideline requirements onerous
- The state of science has progressed, opening up new avenues for exploration and collaboration
- Opportunity for feedback from stakeholders
- To make a thriving program even stronger

## The Plan: Stage 1

To visit, in person or by videoconference, four institutions\*:

- o MD Anderson Cancer Center
- o Mayo Clinic
- o Johns Hopkins Oncology Center
- o Harvard Cancer Center

(\*Together these sites hold 31 out of 61 active SPORE grants)

Full and open discussions with the SPORE

Directors about the strengths of the Program and what the leaders would like to see changed in the guidelines and in practice

Completed August 2008

## The Plan: Stage 2

To hold open teleconference session(s) to receive suggestions and comments from SPORE Programs across the country that were not visited

**Complete by mid-fall 2008**

## The Plan: Stages 3 and 4

- Hold comprehensive discussions with the Clinical and Translational Research Operating Committee (CTROC) and the Clinical Trials Advisory Committee (CTAC) to develop formal recommendations
  - The comments and suggestions of the SPORE Directors will be presented and fully discussed
  
- Present recommendations to the NCI Executive Committee for approval

## Guideline Issues

### Moving projects into human studies within 5 years

- Clinical trials very difficult to translate from laboratory observation to patients within 5 years without outside sponsorship
- Re-competition planning often begins 3.5 years into the funding period
- Suggestion: milestone-driven approach with evaluation of whether benchmarks to the clinic are being met (GMP production, toxicology, RAC approval, IND submission, etc.)

**BUT**

- Loosening the requirement might cause loss of SPORE Program's translational focus

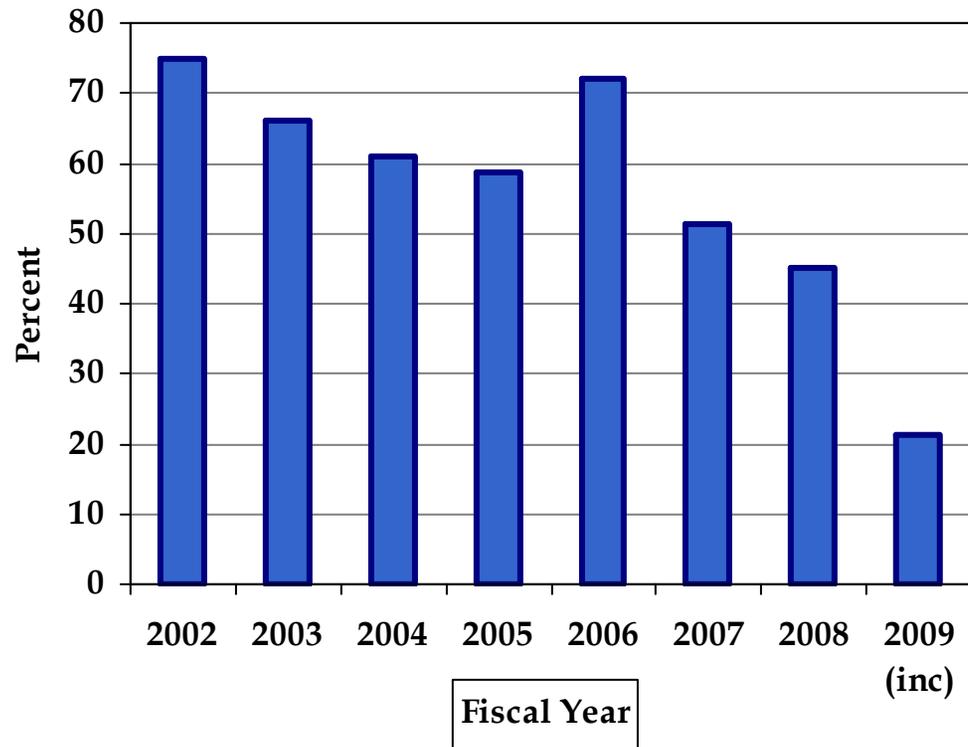
## Minimum Number of Projects

- 4 independent projects build a critical mass and a translational research culture at the institution
- 4 projects allow for greater breadth of research

**BUT**

- A flat budget (with less buying power) means that investigators can do less per project
- Suggestions have included: Minimum of 4 projects for submission and 3 for funding; allows for NCI flexibility in eliminating weak projects

## Percent of Grants Submitted with >4 Projects



## “Required” Project

Early detection; screening; prevention (primary and secondary); population science studies

- Outstanding studies have come from requirement
  - Many studies would NOT have been done if not required
  - Underrepresented in the NCI portfolio
- BUT**
- Not all organ sites have this requirement
  - Required project may not be the strongest project an investigator could propose
  - Population studies often require a larger budget than SPORE grants can provide; need to leverage funds
  - Suggestions include: Could be optional (with or without incentives) or required for the “big 4”: breast, prostate, GI, lung

## Scientific Outcomes of the “Required Project” (a few from a list of many)

- **Poor prognosis basal-like breast cancer: higher frequency in young African-American women than in young Caucasian-American women**
  - **Breast SPORE: University of North Carolina**
  
- **Development of the “Partin Tables” for prostate cancer management and counseling, and the “Pound Tables” for prediction of natural history after surgery; and the translation to clinical practice of AMACR ( $\alpha$ -methylacyl-CoA racemase) as a histochemical marker for prostate cancer diagnosis**
  - **Prostate SPOREs: Johns Hopkins University, University of Michigan, and other institutions**
  
- **An inherited cause of the common form of familial pancreatic cancer identified as a mutation of the BRCA2 gene**
  - **GI SPORE: Johns Hopkins University**

## Organ-Site Focus

- The organ-site focus (as well as the translational requirement) is what makes a SPORE – a SPORE
  - Allows for easier collaboration between SPOREs and for progress in a particular disease
- BUT**
- Broadening organ-site focus would permit non-traditional SPOREs to compete, such as:
    - **AIDS-related malignancies**
    - **Pediatric malignancies**
    - **Pathways of disease common to different organ sites**
  - **Should be guided by the question: Where's the gap?**

## Review Issues

### Questions for discussion:

- Should first-time grants and competitive renewal grants be reviewed under different guidelines and with different review criteria?
- How best to keep “science first” in scoring grants?
- Should the weighting criteria (70:30) be dropped or changed?
  - If retained, what categories should go where?
  - If dropped, how best to instruct the reviewers?

## New Review Instructions for FY09 Grants (Collaboration with the Research Program Review Branch of DEA)

- Reviewers were asked to ignore past and present paylines and to recalibrate (in order to spread) scores.
- Every review element was rated with a numerical score.
- “Science First” policy: Reviewers told to focus on the scientific projects scores and to use the programmatic/procedural elements to “tweak” the scores up or down.
- Assigned reviews gave final sum-up verbally but did not give a final numerical score.

## Results of the 1<sup>st</sup> cycle FY09 SPORE review (n=9)

- The scores were better spread across the range
- The final scores were more in line with the scientific project scores
- Reviewers appeared to adapt well to using the new scoring tool

**We will continue to monitor the results through the next two grant cycles**

# Acknowledgments

## Translational Research Program – DCTD

Peter Ujhazy, MD, PhD  
Andrew Hruszkewycz, MD, PhD  
Ivan Ding, MD  
Igor Kuzmin, PhD  
Rajeev Agarwal, PhD

## Research Programs Review Branch – DEA

Olivia Preble Bartlett, PhD  
David Maslow, PhD  
Shamala Srinivas, PhD  
Caron Lyman, PhD

## SPORE Directors Executive Committee