

Special Translational Research Acceleration Projects (STRAPs)

The Immune Response Modifier (IRM) STRAP Experience

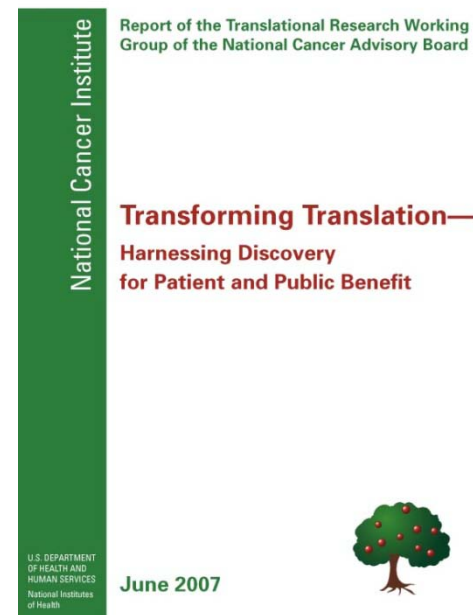
Today's Presentation and Discussion

- Brief overview of the STRAP program
- What we have learned (so far) from
 - IRM STRAP funding opportunity release
 - Submissions from investigators
- Presentations from the investigators on the two awarded IRM STRAPs
 - Dr. Renier Brentjens (MSKCC)
 - Dr. Andrew Raubitschek (City of Hope)
- Discussion: Facilitated by Drs. James Doroshow and Lynn Matrisian*

* Co-Chair of Translational Research Working Group (TRWG)

TRWG STRAP Recommendation

- The TRWG was charged to evaluate the current status of NCI's investment in translational research and envision its future in an inclusive, representative and transparent manner
- The TRWG recommended that NCI establish a program to advance prioritized early translational research opportunities
- NCI initiated the IRM STRAP pilot in response to this TRWG recommendation



www.cancer.gov/trwg

Why are STRAPs Different ?

- S** is for Special
 - Not possible through regular R, P, U, etc mechanisms
 - High probability of significantly advancing field
- TR** is for Translational Research
 - Follows TRWG pathway to early stage clinical trials
 - Includes assessment modalities
- A** is for Acceleration
 - Fast, Facile, and Flexible
- P** is for Project
 - Project Management
 - Timelines and Milestones

IRM STRAP Funding Opportunity Announcement

- Issued May 27, 2010 (<http://grants.nih.gov/grants/guide/notice-files/NOT-CA-10-025.html>)
- Administrative supplements to existing grants
- Scientific areas of IRM Opportunities
 - Adoptive cell therapy
 - Antibody or “T-body” therapy
 - Cancer vaccine targeting a viral antigen
 - Vaccine targeting a cellular antigen (self or tumor)
- NCI provided resources made available
 - IL-12
 - IL-15
- Prioritized list of targets identified by IRM Pathway Prioritization Working Group 2008-2009
 - Antigens
 - Immune Modifying Agents (IMAs)

IRM STRAP Evaluation Criteria

- Is this a clinically significant translational cancer research opportunity that should be accelerated?
- Does the proposal address one of the four prioritized areas in the Notice, and if not, is the opportunity presented well justified?
- Is this an opportunity that would be difficult to accomplish through other available funding approaches?
- Does the research plan address the developmental requirements of an IRM STRAP with components such as a well-described plan, reasonable timeframe/milestones, defined collaboration responsibilities, etc.?
- Is there a reasonable likelihood that the proposed research can reach IND status and clinical testing?
- Does the proposed Research Team have the appropriate expertise and experience to accomplish the IRM STRAP?

IRM STRAP Submission Response

- 23 proposals received
- Half addressed NCI-prioritized antigen or IMA

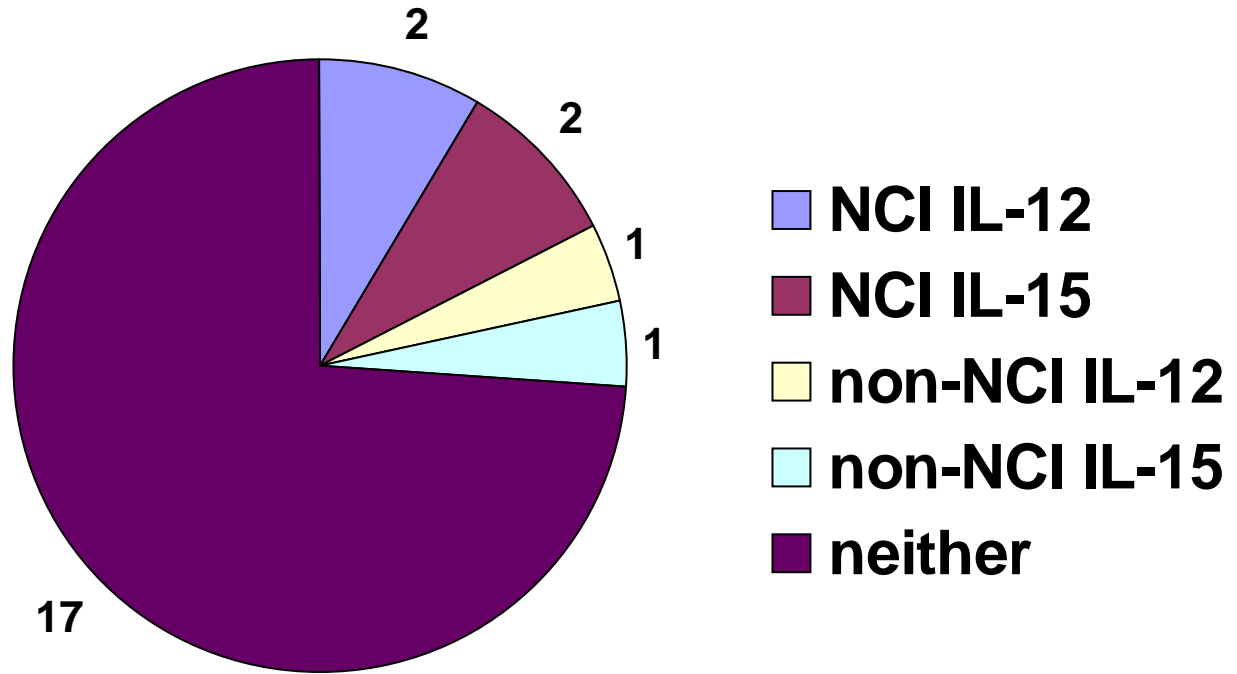
Proposed work addressed at least one NCI-prioritized antigen or IMA		Number of proposals
Antigen	IMA	
yes	yes	6
yes	no	1
no	yes	5
no	no	11

Submission Response to Prioritized List

IDENTIFIED PRIORITIES IN FOA
Prioritized Antigens
HER2, EGFR, CD20, and/or CD19 (Antibody and T-body approaches)
HPV E6/7, HER2, MAGE A3, MUC1, WT1, NY-ESO-1, and/or PSA (for T-cell therapies)
HPV E6/7, HER2, MAGE A3, MUC1, WT1, NY-ESO-1, and/or PSA (for vaccine targeting)
Prioritized Immune Modifying Agents (IMAs)
Antibodies anti-4-1BB, anti-CD20, anti-CD40, anti-CTLA-4, anti-IL-10, anti-PD1, and anti-TGF-beta
Chemokine CCL21
Chimeric Antibody Receptors (CARs)
CpGs
Flt3 Ligand (Flt3L)
1-methyl-tryptophan
Interleukins IL-7, IL-12, IL-15, and IL-21

SUBMISSION RESPONSES
Prioritized Antigens Targeted
CD19
WT1, NY-ESO-1
HER2, WT1, NY-ESO-1
Prioritized IMAs Targeted
anti-CTLA-4
CCL21
CARs
CpGs
Flt3 Ligand (Flt3L)
IL-12, IL-15

Use of NCI-Provided Resources



Characterization of Proposed Research

- Activities required to support a planned clinical trial
 - Laboratory studies to inform design of trial
 - Development of assays to be used in trial
 - Manufacture of agent to be used in trial
 - Conduct of the clinical trial
- Activities that inform future clinical trials
 - Credentialing of a therapeutic concept
 - Laboratory studies to inform future trials
 - Correlative studies conducted as part of planned trial

IRM STRAP Pilot Projects: Getting Over the Translational Research Valley of Death

NEWS FEATURE TRANSLATIONAL RESEARCH

NATURE|Vol 453|12 June 2008



CROSSING THE VALLEY OF DEATH

A chasm has opened up between biomedical researchers and the patients who need their discoveries. **Declan Butler** asks how the ground shifted and whether the US National Institutes of Health can bridge the gap.

IRM STRAP Pilot Awardees

- **A Multi-Center Clinical Consortium to Investigate the Biology and Clinical Efficacy of Autologous T-Cells Genetically Targeted to the CD-19 Antigen in Patients with B Cell Malignancies**
 - Dr. Brentjens, MSKCC
- **Taking iRGD Through the Valley of Death**
 - Dr. Raubitschek, City of Hope

IRM STRAP Pilot: Take Home Lessons

- 12 of 23 submissions addressed at least one of the identified priorities
- 4 of 23 submissions included a request for NCI resources (IL-12, IL-15)
- Requirement that research be within scope of existing parent grant and short “time on street” of FOA may have constrained application of priorities and resources
- The most commonly-proposed developmental activities were agent manufacture and conduct of clinical trials

IRM STRAP Pilot: Take Home Lessons (cont.)

- Most proposals included activities that were not necessary to enable the planned round of human testing, but rather to inform a later iteration
 - Laboratory studies: animal model, in vitro
 - Correlative studies associated with planned trial
- Some of the proposed trials were not first-in-human, but rather tested refinements of a previously-studied regimen
- IRM development often requires iterative human testing to achieve optimal combination of antigen(s) / IMA(s) / delivery vehicle(s)

Discussion of Umbrella STRAP Solicitation

- CTAC advice to NCI
 - Start development of umbrella STRAP solicitation process
 - Initiate prioritization process for other pathways and incorporate into STRAP solicitation as appropriate and feasible