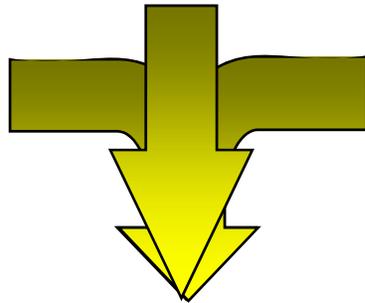


# The Translational Research Working Group (TRWG): Recommendations and Implementation

Lynn M. Matrisian, Ph.D.  
Office of the Director  
National Cancer Institute

# Why convene a Translational Research Working Group?

Major advances in cancer biology



Translational systems that cannot keep pace



# Translational Research Working Group

63 scientists, clinicians, advocates,  
and thought leaders from academia,  
government, and industry

## **Charge:**

Evaluate the current status of NCI's  
investment in translational research  
& envision its future in an inclusive,  
representative & transparent manner

## A Public, Participatory Process 2005-2007

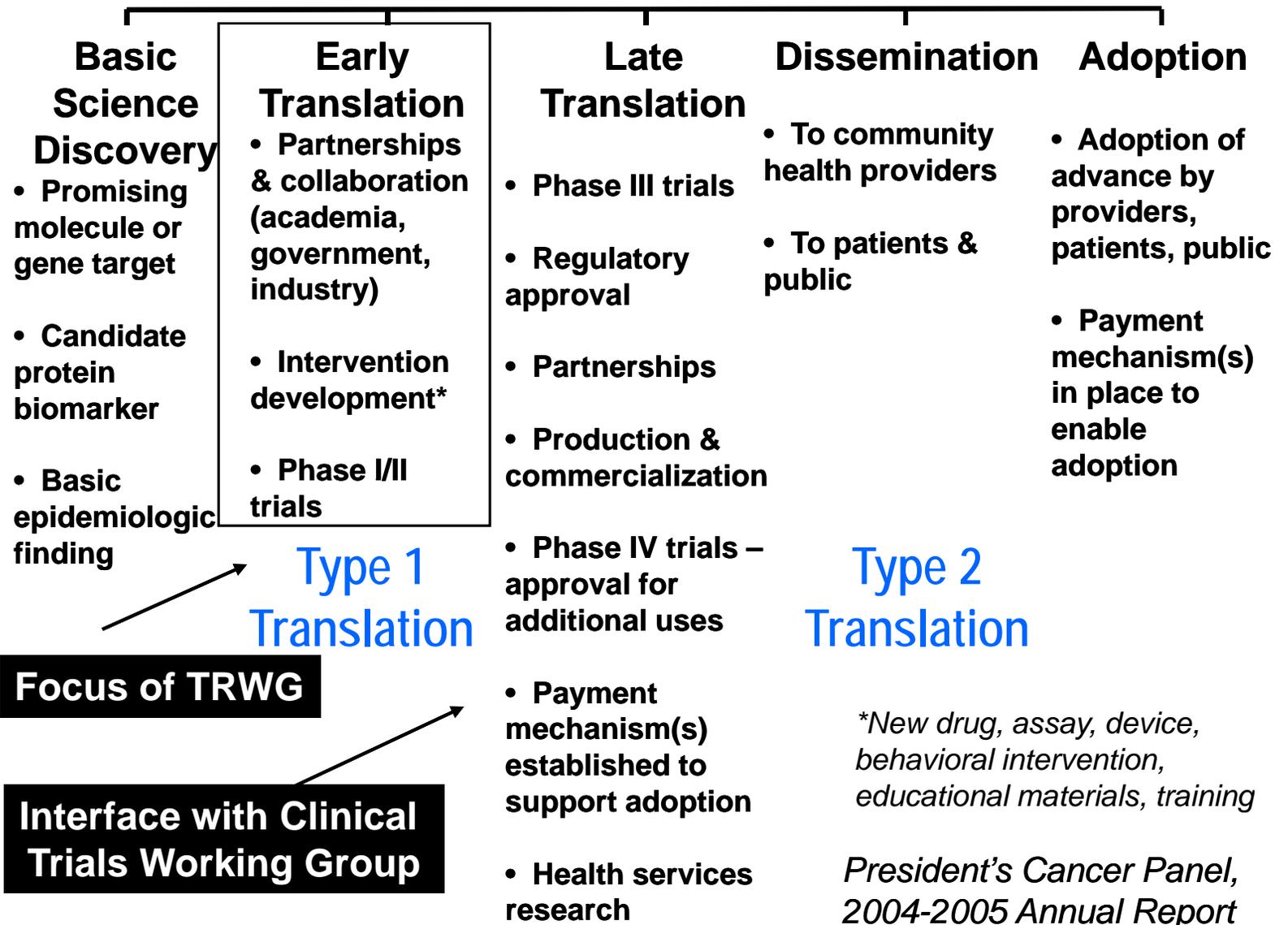
- Reviewed foundational documents
- Analyzed Clinical Trials Working Group process for ideas, challenges & lessons learned
- Gathered public input on key questions & proposed solutions
  - Web-based system
  - 2 Public Roundtables
  - Industry/foundation/society Roundtable (Philadelphia)
- Constituted 6 subcommittees – bimonthly meetings
- 15 recommendations in a 150 page report:  
[www.cancer.gov/trwg](http://www.cancer.gov/trwg)
- Accepted by NCAB June, 2007
- Implementation phase started January 2008

# TRWG Products

- Definition of translational research
- Six developmental pathways to clinical goals
- Process analysis
  - Case studies of 20 examples
- Portfolio analysis
  - FY04 activities
- Fifteen initiatives

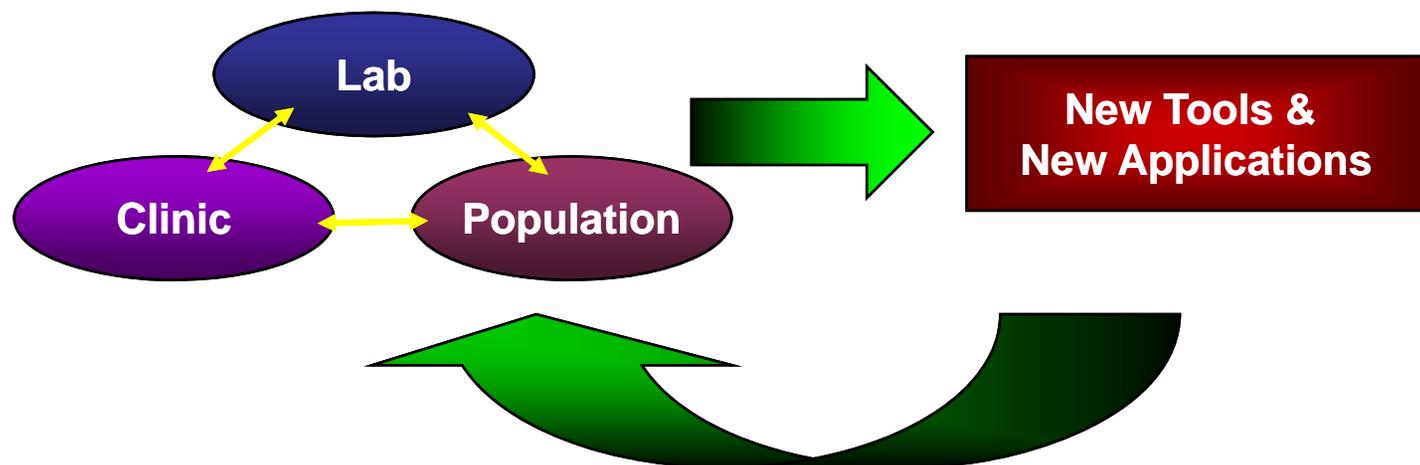


# Defining the Scope of the TRWG: The President's Cancer Panel Translational Continuum

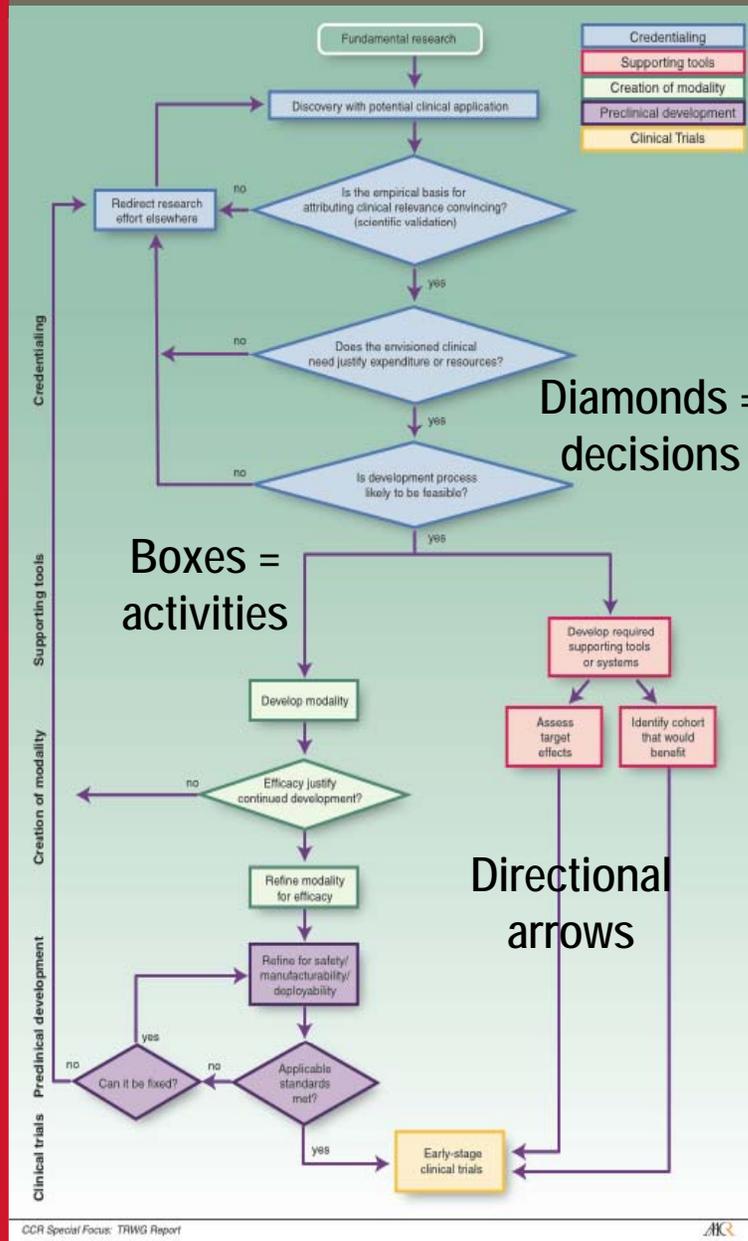


# TRWG's Definition of Translational Research

Research that transforms scientific discoveries arising in the lab, clinic, or population into new clinical tools & applications that reduce cancer incidence, morbidity & mortality



# Operational definition: Pathways to Clinical Goals



## Assessment modalities

(for screening, diagnosis, prognosis, or prediction)

- **Biospecimen-based** (protocols, reagents, instruments)
- **Image-based** (agents, techniques)

## Intervention modalities

(treatment and prevention)

- **Agents** (drugs or biologics)
- **Immune response modifiers** (vaccines, cytokines)
- **Interventive devices** (radiation, surgical devices)
- **Lifestyle alterations** (exercise, nutrition)

*clincancerres.aacrjournals.org*

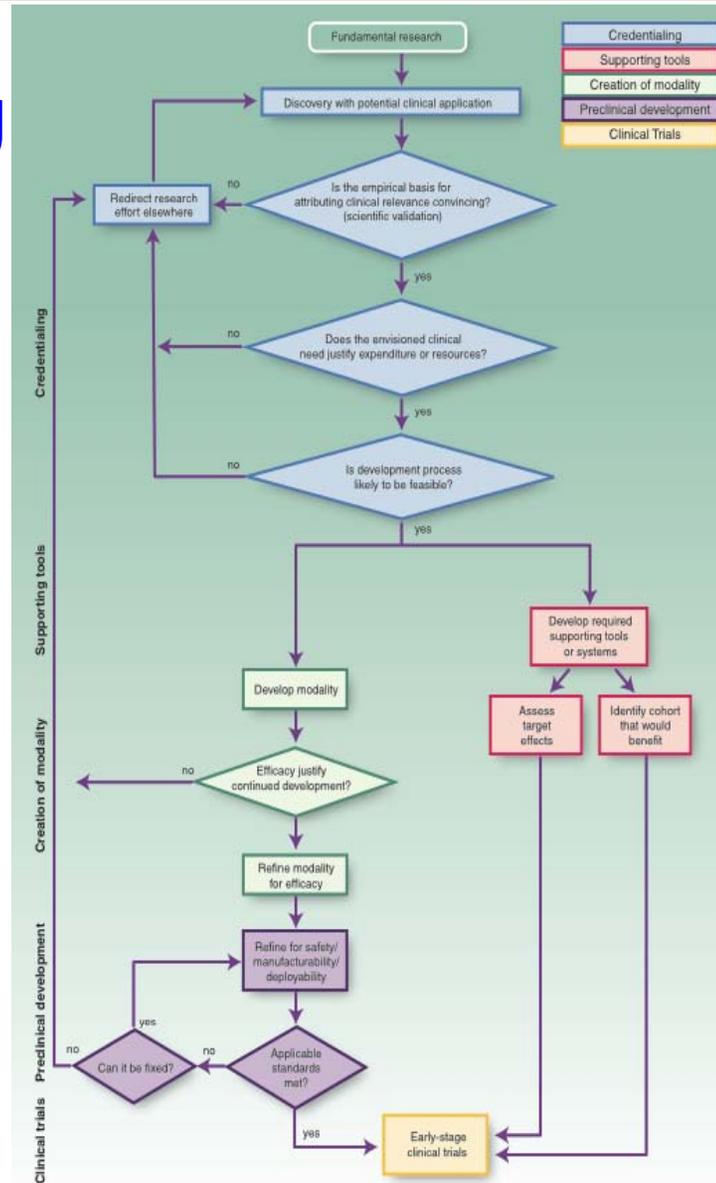
# 5 Domains per Pathway

## Credentiaing

Assess scientific validity, clinical need, & feasibility

## Creation of modality

eg. medicinal chemistry, multi-lab validation



## Supporting tools

eg. animal model, cohort, specimen repository

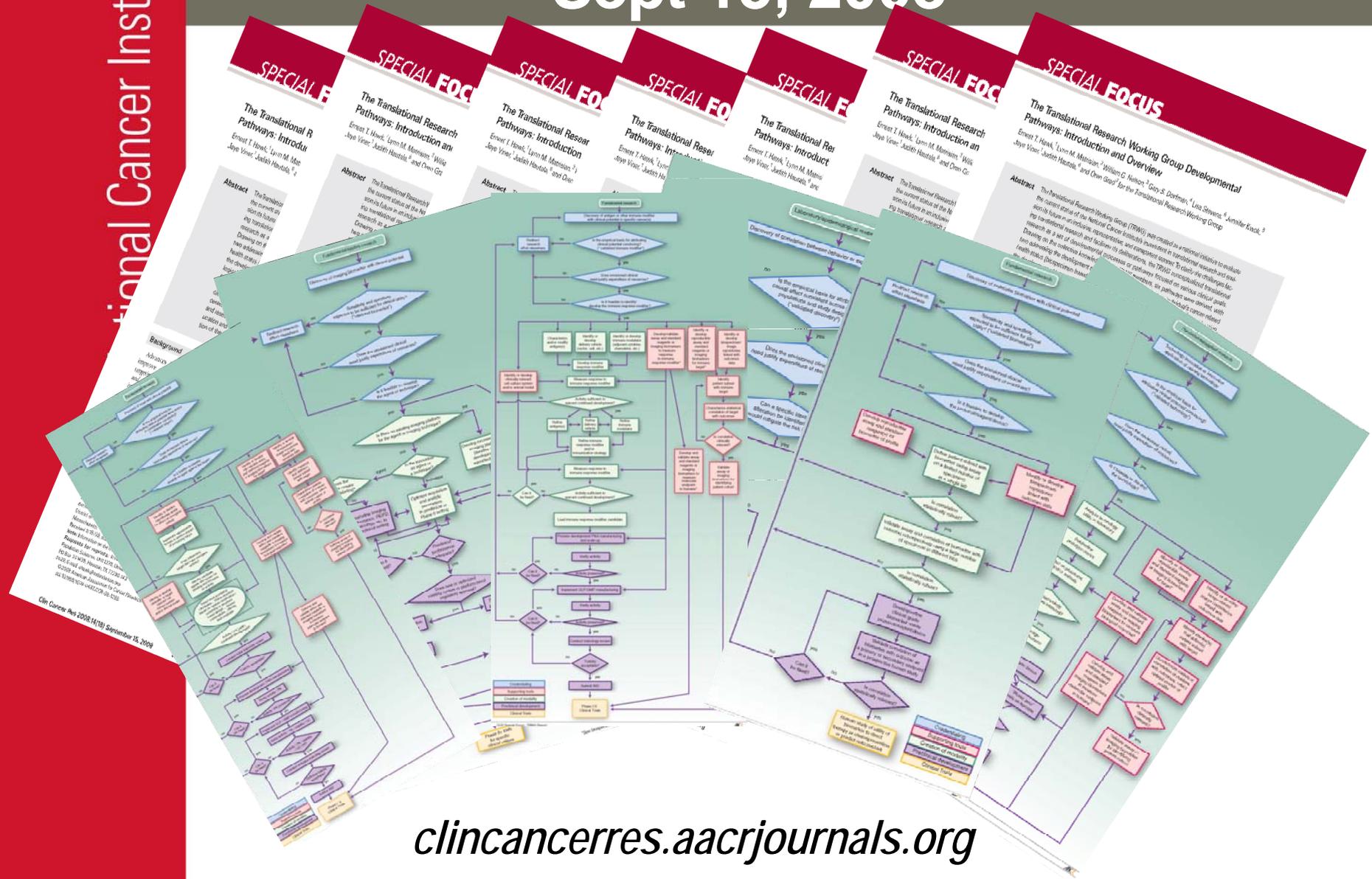
## Preclinical development

eg. toxicology, test on phantoms

## Phase I/II clinical trials

# Clinical Cancer Research

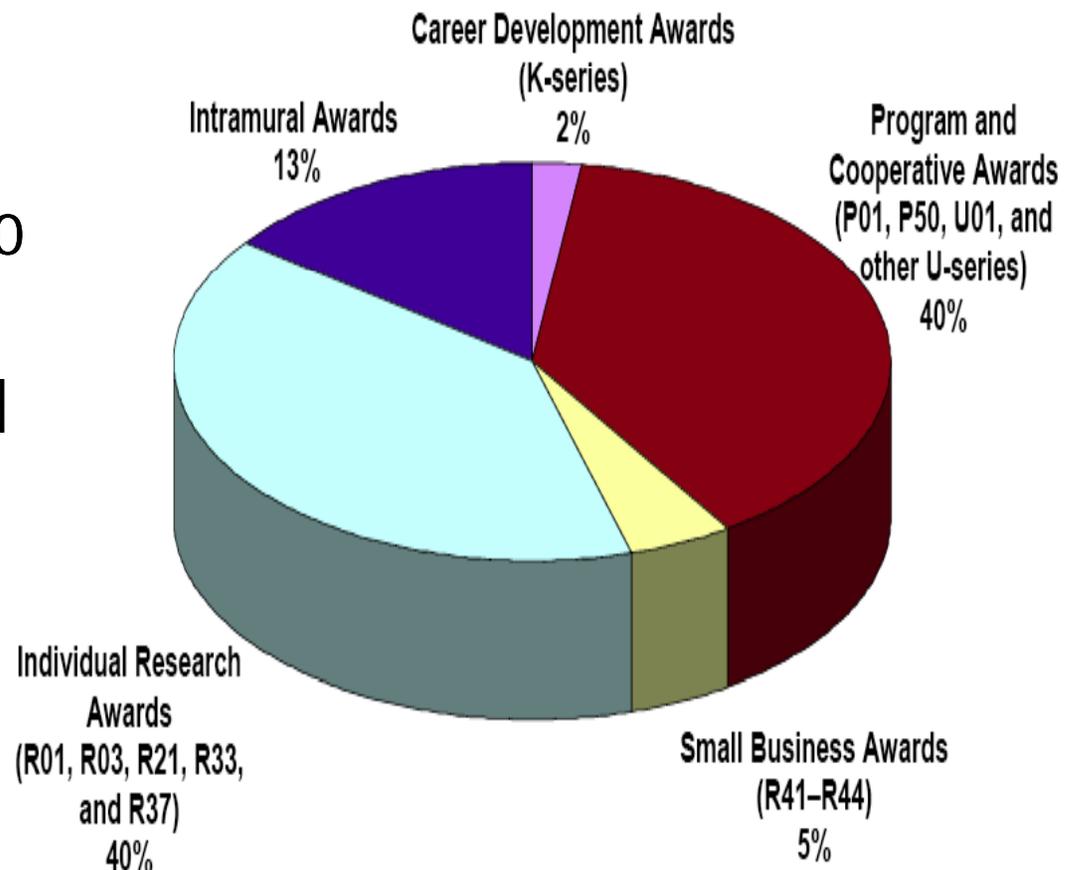
## Sept 15, 2008



[clincancerres.aacrjournals.org](http://clincancerres.aacrjournals.org)  
CCR 14: 5663-5713 (2008)

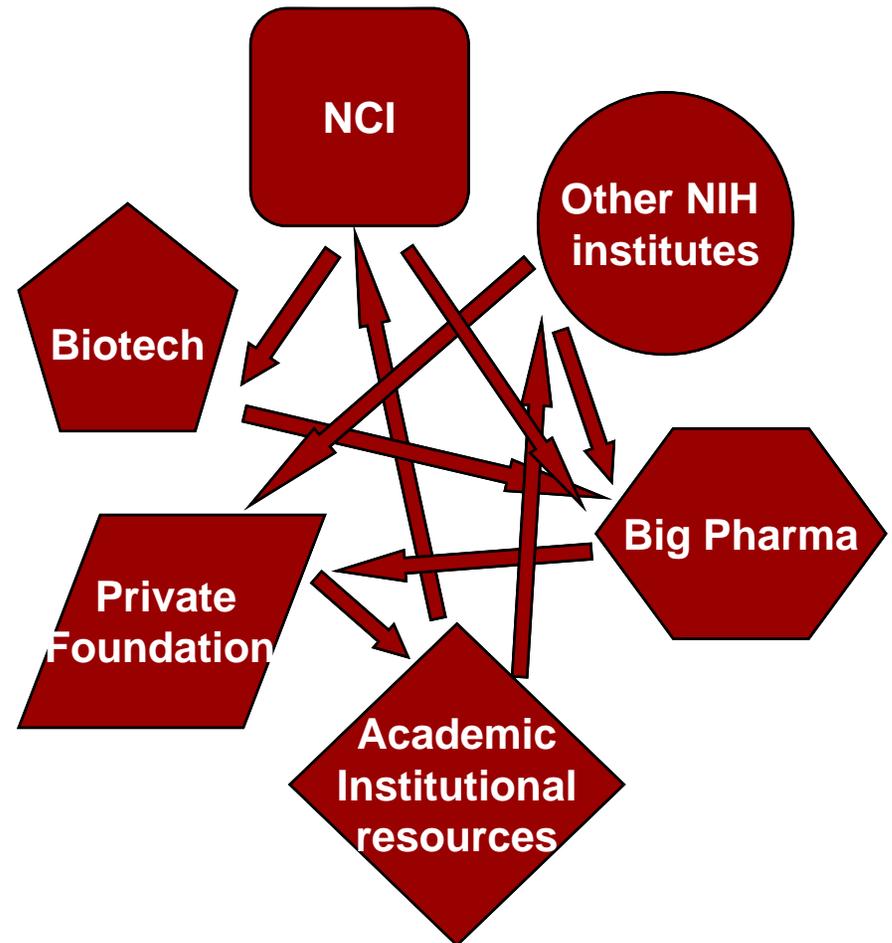
# Portfolio Analysis of NCI's Translational Research Funding (FY04)

- ~30% of NCI budget
- 56% awarded to institutions with NCI-designated cancer centers
- Distributed across funding mechanisms



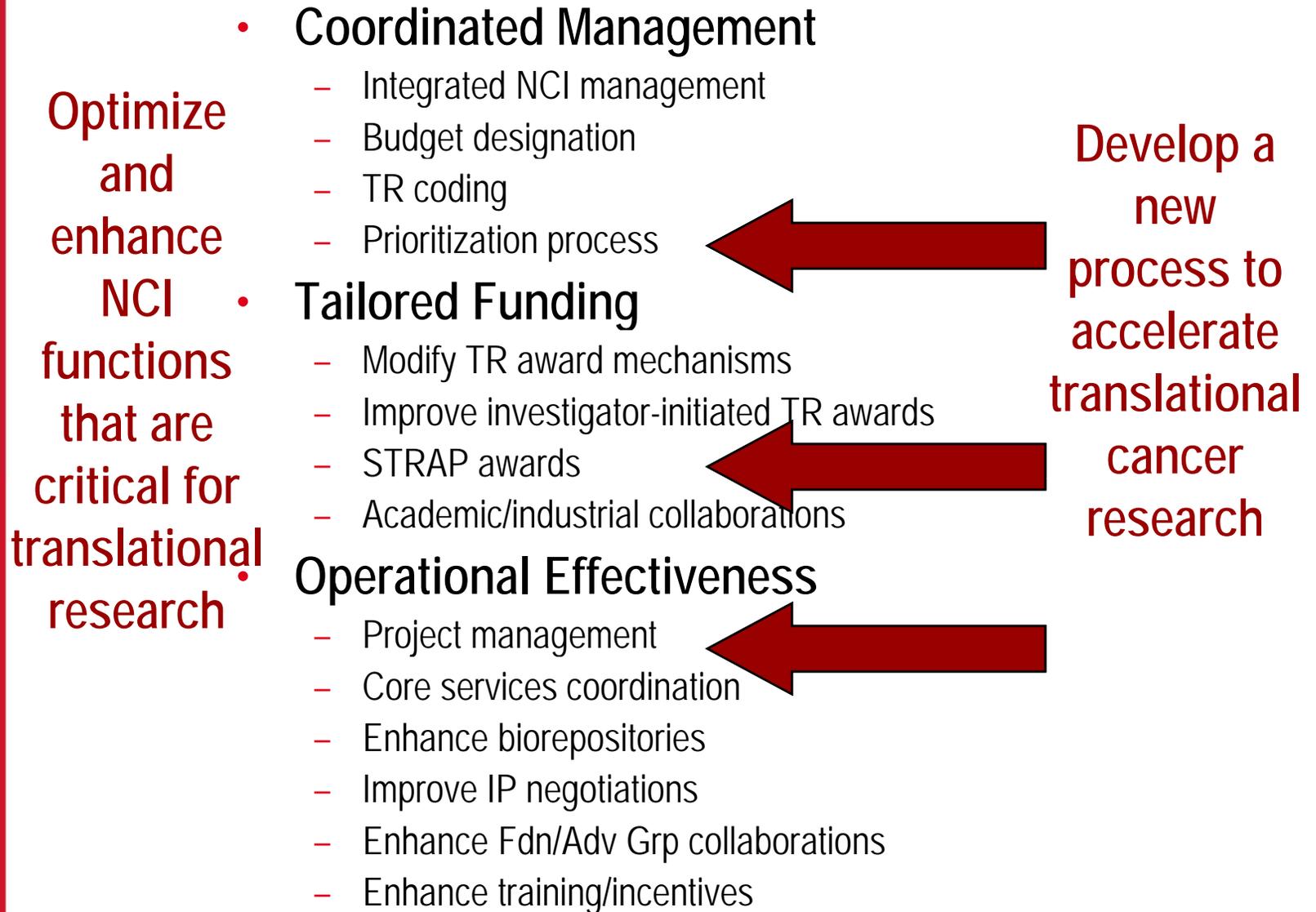
# Process Analysis

- 20 examples of translational research successes
- All Pathways
- Wide variety of mechanisms and funding sources

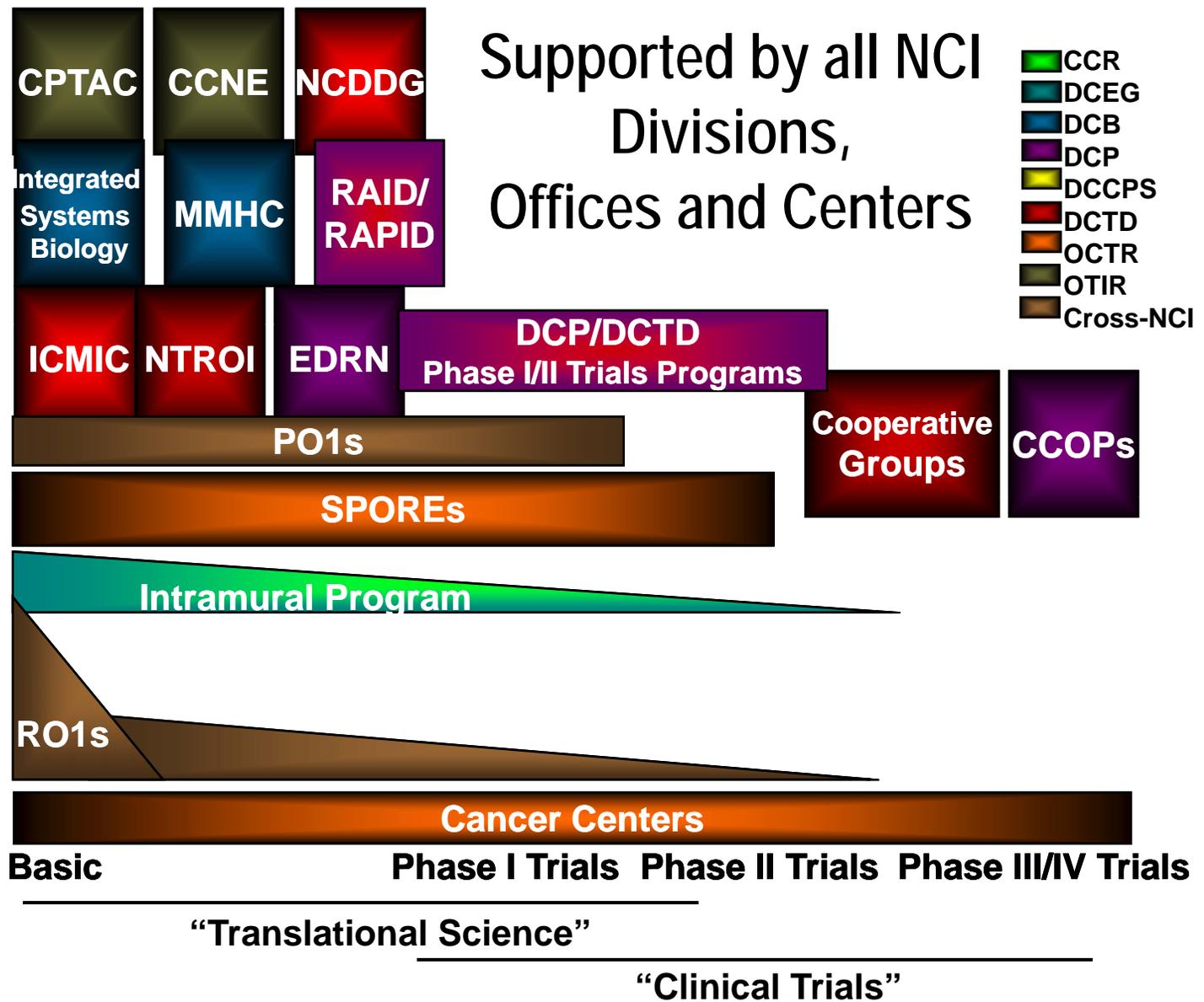


**THERE IS NO FORMULA FOR  
TRANSLATIONAL RESEARCH**

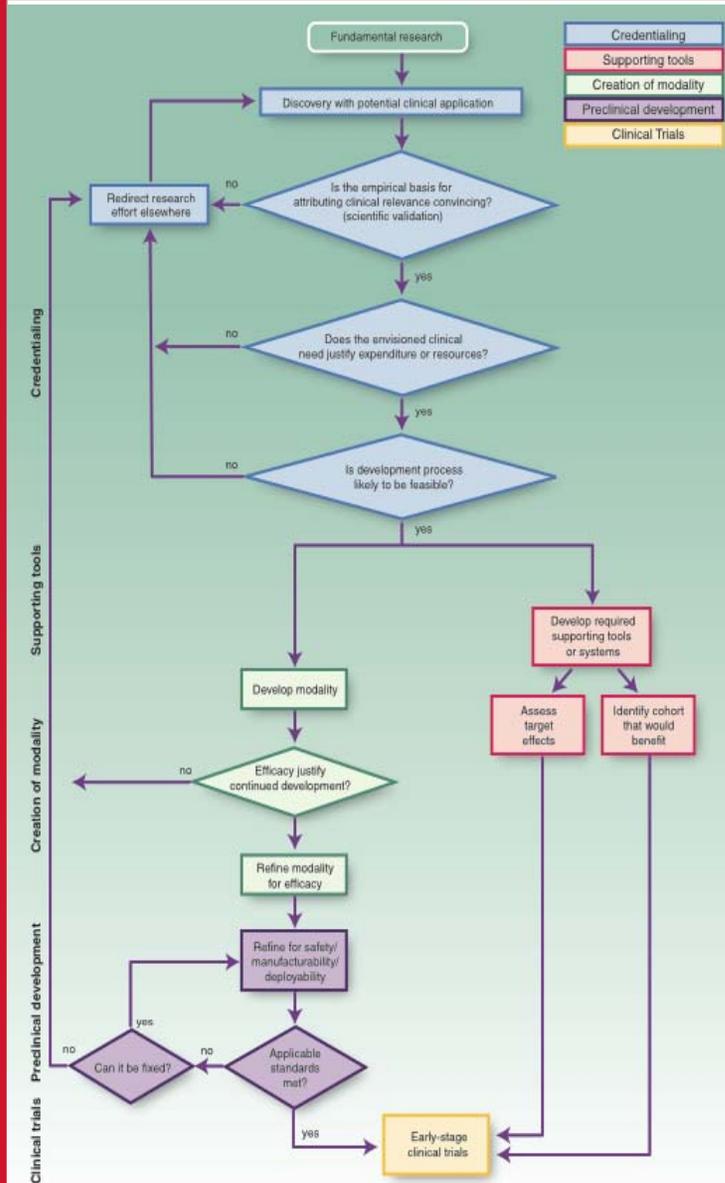
# 15 Initiatives with Implementation Plans



# Current Infrastructure and Funding Mechanisms



# The Challenge of Early Translation

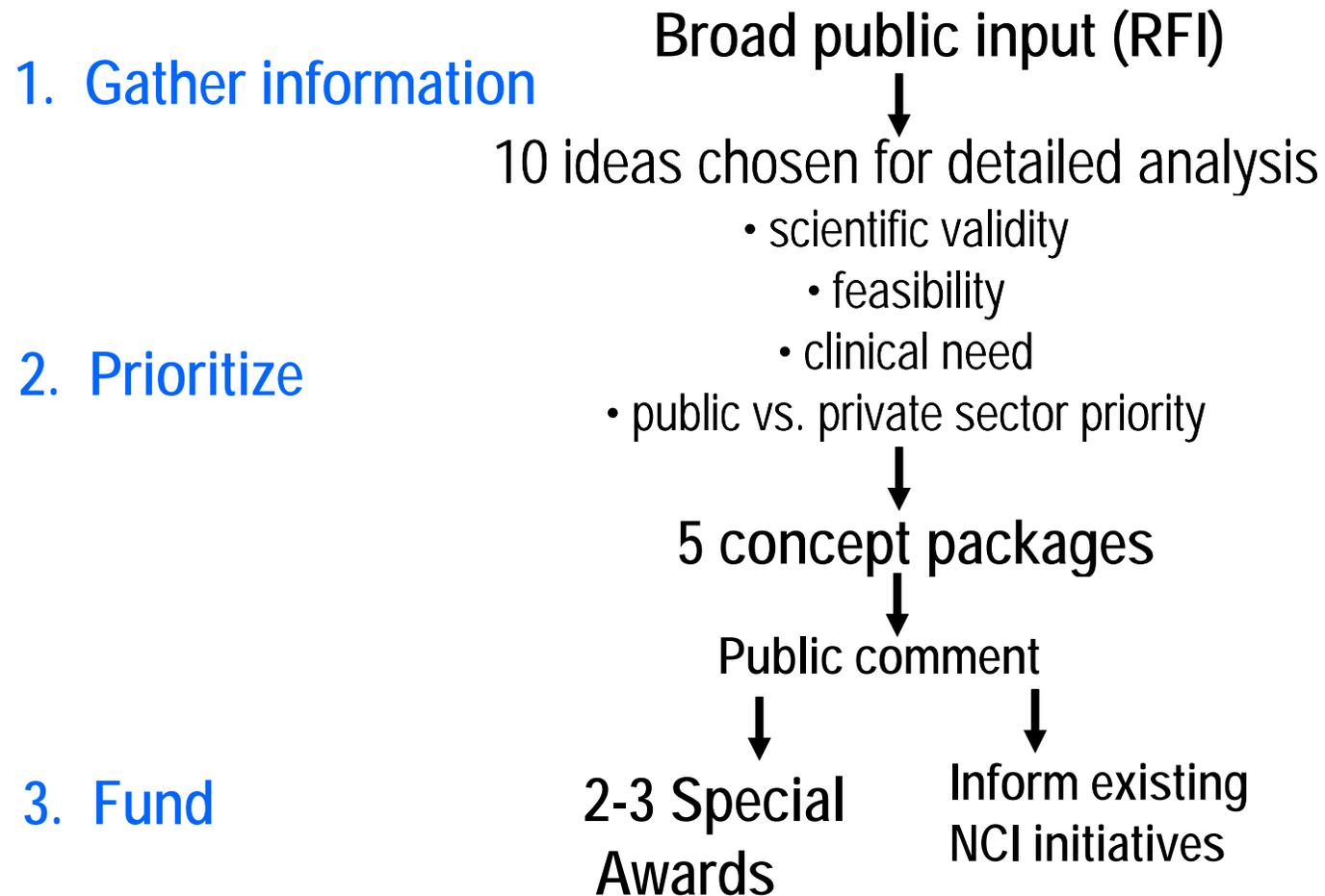


How can we best assure that:

- The most promising concepts enter the developmental pathways?
- Concepts that do enter advance to the clinic or to productive failure?
- Progress is as rapid, efficient, and effective as possible?

# Recommended ADDITIONAL Process for Translational Research

*Select several projects/year that are  
"ripe" for translation*



# Information Gathering



## *NCI Translates NCI-wide Translational Science Meeting*

- November 7-9, 2008 in Washington, DC
- 500 Abstracts submitted by PIs selected by NCI Program Staff
- Advocate involvement
- Working meeting organized around TRWG Pathways to Clinical Goals

*<http://ncitranslates.nci.nih.gov>*

# Purpose

- **Convene experts for a trans-NCI translational science meeting**
  - Expand range of collaborations and interactions between NCI-supported investigators and mechanisms
  - Showcase NCI-supported translational research
- **Initiate the Translational Research Working Group (TRWG) prioritization process**
  - Enhance knowledge and use of the TRWG pathways
  - Produce “Translational Research Opportunities” that can be used to assess the range and quality of promising translational research “concepts”

# Abstract coding

Abstracts were coded to pathways, populations, and organ sites

## Step 1: TRWG Developmental Pathways

Please select at least **one** below.

	ASSESSMENT		INTERVENTIVE			
	Biospecimen	Imaging	Agents	Immune	Devices	Behavioral
Credentialed discovery	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Supporting Tools	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Creation of Modality	<input checked="" type="checkbox"/>	<input type="checkbox"/>				
Preclinical development	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ph/II Clinical trials	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

## Step 2: Select Your Population

Please select at least **one** below.

- At Risk
- Early disease
- Late disease
- Pediatric
- Minorities & Underserved

## Step 3: Select Your Organ Sites

Please select at least **one** below.

- Breast
- Brain
- Colorectal
- Gastrointestinal (other than CR)
- Genitourinary (other than prostate)
- Gynecologic
- Head and Neck
- Hematopoietic
- Lung
- Prostate
- Skin
- Rare (Sarcoma, etc)
- All or most organ sites

# 25 Poster Discussion Sessions



- **Biomarkers**
  - "Omic " Technologies
  - Prognostic & Predictive
  - Early Detection
  - Breast Cancer
  - Prostate & Bladder Cancers
  - Esophagus, Colon & Liver
  - Lung Cancer
  - Hematological & Pediatric Cancers
- **Agents**
  - Biochemical Targets & Drug screening
  - Stem Cells, Gene Expression, & Epigenetics
  - Drug Delivery & Gene Therapy
  - Integrative Biology
  - Prostate Cancer
  - Pancreatic and Breast
  - Hematological Malignancies
  - Head/Neck & Lung
- **Immune Response Modifiers**
  - Antibodies, Cytokines, & Viruses
  - Vaccines
  - Cellular Therapies
- **Interventive Devices**
  - Ionizing & Non-ionizing radiation
  - Devices for surgical ablation & biopsy
- **Lifestyle Alterations**
  - Dietary components
  - Biobehavioral mechanisms
- **Imaging** - Early Detection - Imaging & Therapeutics

# Example: Bortezomib in Multiple Myeloma

Basic: Proteasome identified as potential target in early 1990s

Credentialing: scientific validation, need, feasibility

Supporting tool: in vitro fluorometric assay for proteasome inhibition (PD marker, Proscript)

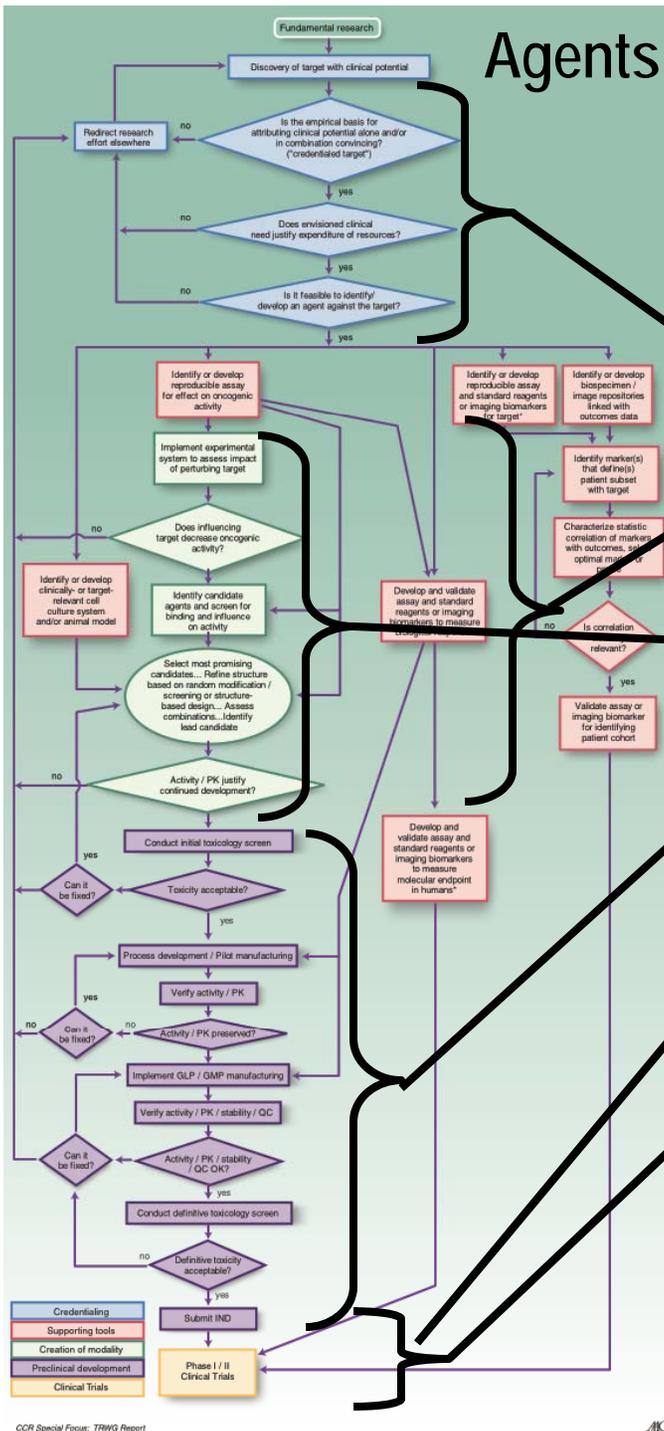
Creation of Modality: PS-341 (Velcade<sup>®</sup>, Proscript and NCI)

Preclinical Development: *Proscript, Inc & NCI Developmental Therapeutics Program*

Phase I: *prostate (CaPCure), myeloma (NCI SPORE)*

Phase II: *multiple myeloma, (Millennium Pharmaceuticals, Inc)*

Late Translation: Phase III clinical trials  
FDA approval 2003



# Translational Research Opportunities



- Focuses on a “**Clinical goal**”
  - A modality (drug, device, biomarker, etc) that can be tested in people
  - Identifies the population/cancer type in which it is tested
- Scientific validity
- Clinical need
- Feasibility: Identifies individuals/research groups with projects or capabilities relevant to pathway domains
  - Creation of Modality
  - Supporting tools
  - Preclinical Development
  - Phase I/II clinical trials

# Implementation Plan

NCI Translates Meeting

Web-based submissions

**OPPORTUNITIES**

*Assess the range and quality of promising translational research "concepts"*

Decision to proceed

yes

Web-based submissions

**PRECONCEPTS**

# Recommended Prioritization Process

PRECONCEPTS



Intra-pathway prioritization

~10 ideas chosen to develop into CONCEPTS

*Detailed analysis of validity, feasibility, need*

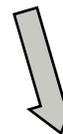


Inter-pathway prioritization

~5 CONCEPTS



Public comment



Executive decisions

RFA for 2-3 special awards    Inform existing

*Clinical goal & population  
impacted specified*

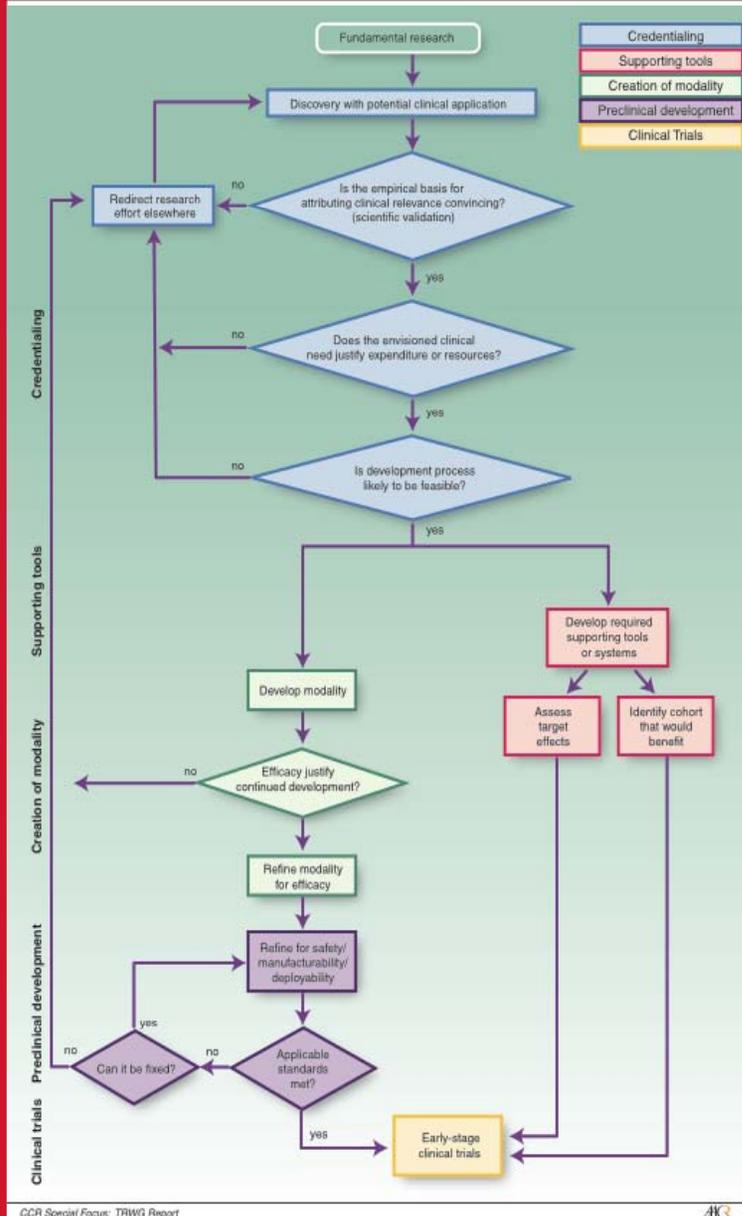
NCI activities

# Proposed New Funding Mechanism

## *Special Translational Research Acceleration Project* *(STRAP)*

- Requirements:
  - Goal of completing early stage human studies
  - Project management plan
  - Specific development milestones and timelines
  - Development/commercialization strategy
- Would provide funds for new or expanded projects as needed
- Project management would link new or existing teams and projects and facilitate hand-offs between groups
- Opportunities to include industry and/or foundation funding or participation

# The Challenge of Early Translation



How can we best assure that:

- The most promising concepts enter the developmental pathways?
- Concepts that do enter advance to the clinic or to productive failure?
- Progress is as rapid, efficient, and effective as possible?

