"TODAYS' DISCOVERIES, TOMORROWS CURES? A CONVERGENCE OF CULTURES"

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WISTAR INSTITUTE
AND
LUDWIG INSTITUTE FOR CANCER RESEARCH

Issues

- **Does the academe have as a goal or an obligation, the development of its discoveries for human benefit?**

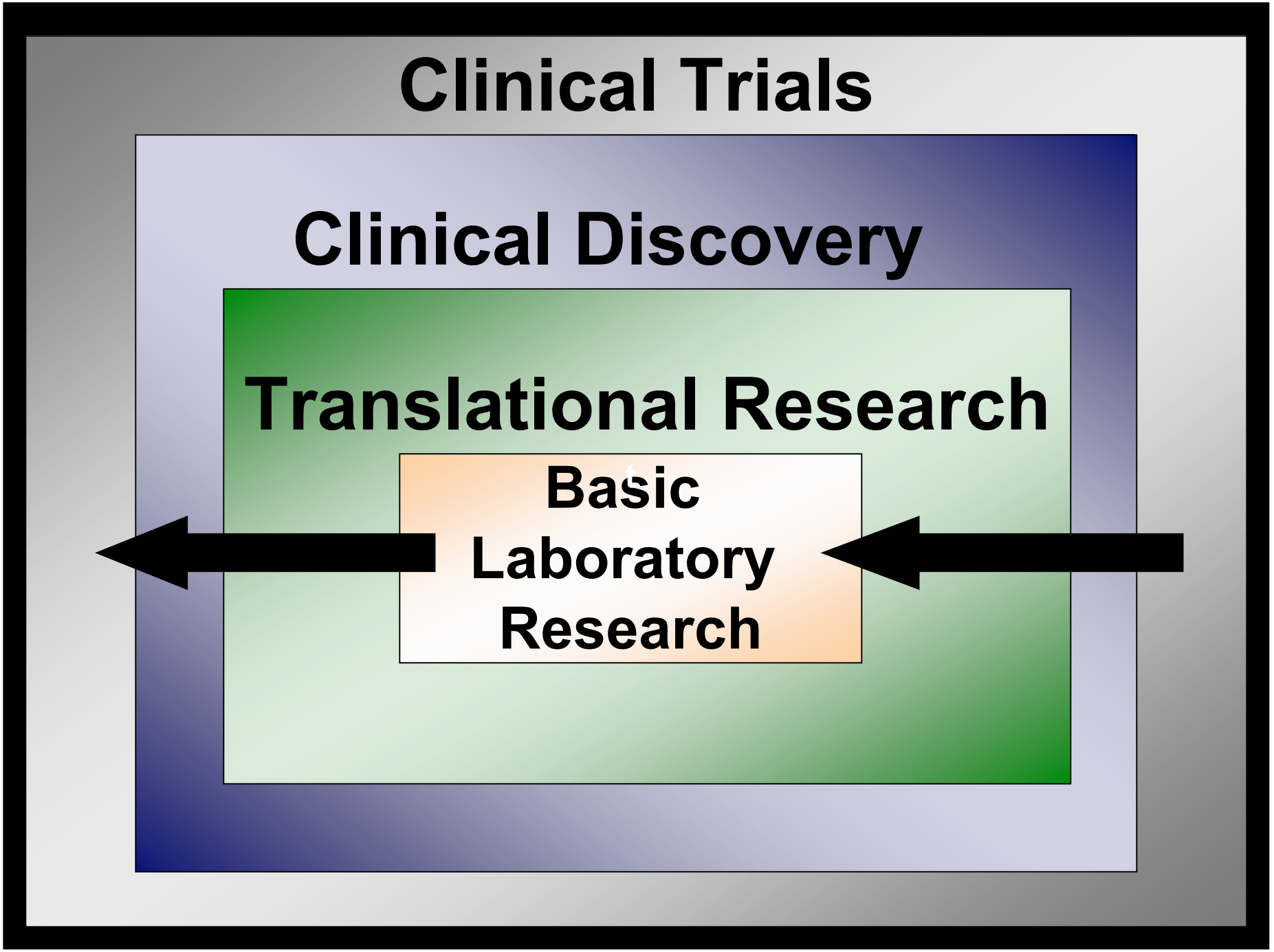
- **Can the academic review process support individual career development in the context of the "teams" required for development of discoveries for clinical benefit?**

Premise

- Clinical observations provide questions for mechanistic studies.
- Basic research provides a pipeline for clinical advances.

Basic Researech

- Provides intellectual framework for rational evidence-based approaches to disease
- Identifies new (drugable) targets
- Biomarkers: diagnostic, prognostic, drug susceptibility
- Surrogate endpoints; drug responsiveness


Clinical Trials
Clinical Discovery
Translational Research
Basic
Laboratory
Research

Does the academe have as a goal or an obligation, the development of its discoveries for human benefit?

- Discovery for the sake of knowledge and for benefit of society
- Individual, institutional, community
- Can it be done? What are the challenges?
  - Individual career development
  - Integration of basic laboratory, translational and clinical science/scientists
  - Integration of science with patient care, data management; statisticians, epidemiologist
  - Infrastructure: standardized reagent and assay development; regulatory affairs; protocol development

Why Not Leave Development to Biotech/Pharmaceutical Industry?

- If too “early” may not get picked up by industry and may be “dropped”
- The more developed the more valuable
- Different motivations
  - Scientific vs. Product Oriented
- Scientific Design vs. Outcome Design

CAN WORK BUT….

- Integrate **EARLY** around:
  - Mechanisms
  - Disease Focus

Requirements For Translational & Clinical Studies

- Institutional Infrastructure-or consultants/contractors
- Select projects for “programmatic” development
- Reagent: Development, production
- Milestones/Decision points
- Scientific oversight

Vaccines

Infectious Disease-Prophylactic

- The number of children who die from I.D. is increasing
- Newly emerging phathogens
- Bioterrorism

Cancer- Therapeutic Vaccines

- Tumor Viruses
- Tumor associated antigens
  - Vaccines (active immunization)
  - Antibody targeting (passive immunization)

Novel Applications

Vaccines Out of Academia: Different "Successful" Models

Wistar Institute: INVESTIGATOR DRIVEN

Rabies Rubella Rotavirus

- Scientific Discovery
- Advanced vaccines from laboratory to clinical trials
- Larger trials by industry

Other vaccines as well as new vaccine delivery systems are currently under development

Goals of the Clinical Trials Program

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- To transition Institute discoveries from the laboratory
- To evaluate discoveries as potential treatment modalities for cancer patients.
- Early to mid-phase clinical trials
  - Safety
  - Establish scientific basis of the study agent
  - Clinical efficacy
- License to commercial partner at enhanced value

Clinical Trials Process

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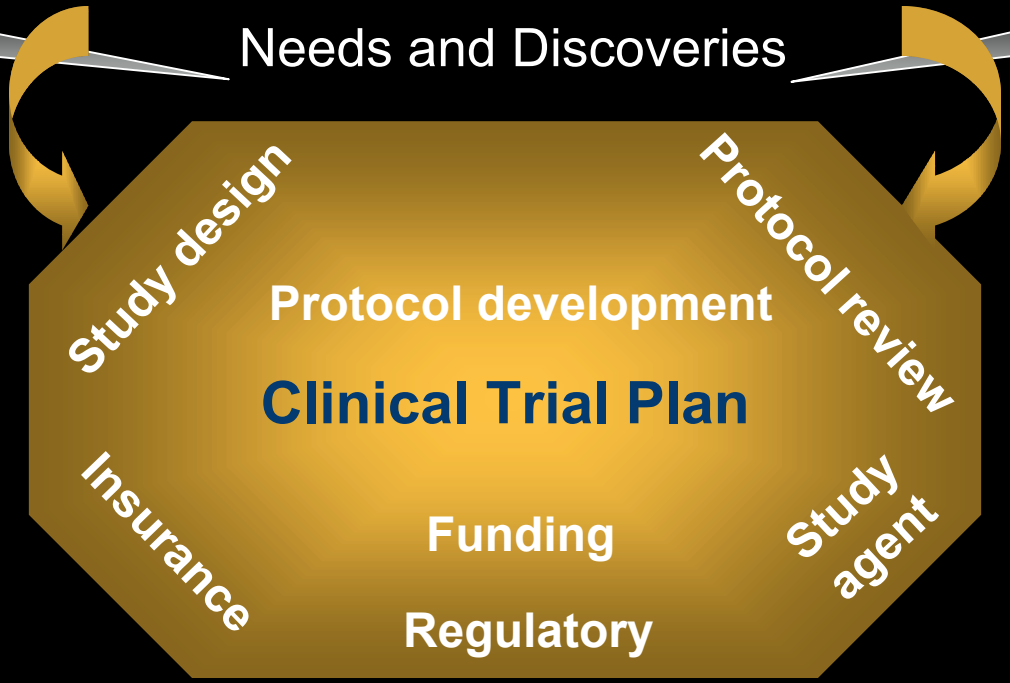
Clinical Strategic Plan

Clinical Investigation Committee(s)

Therapeutic

Scientific

Needs and Discoveries



Office of Clinical Trials Management

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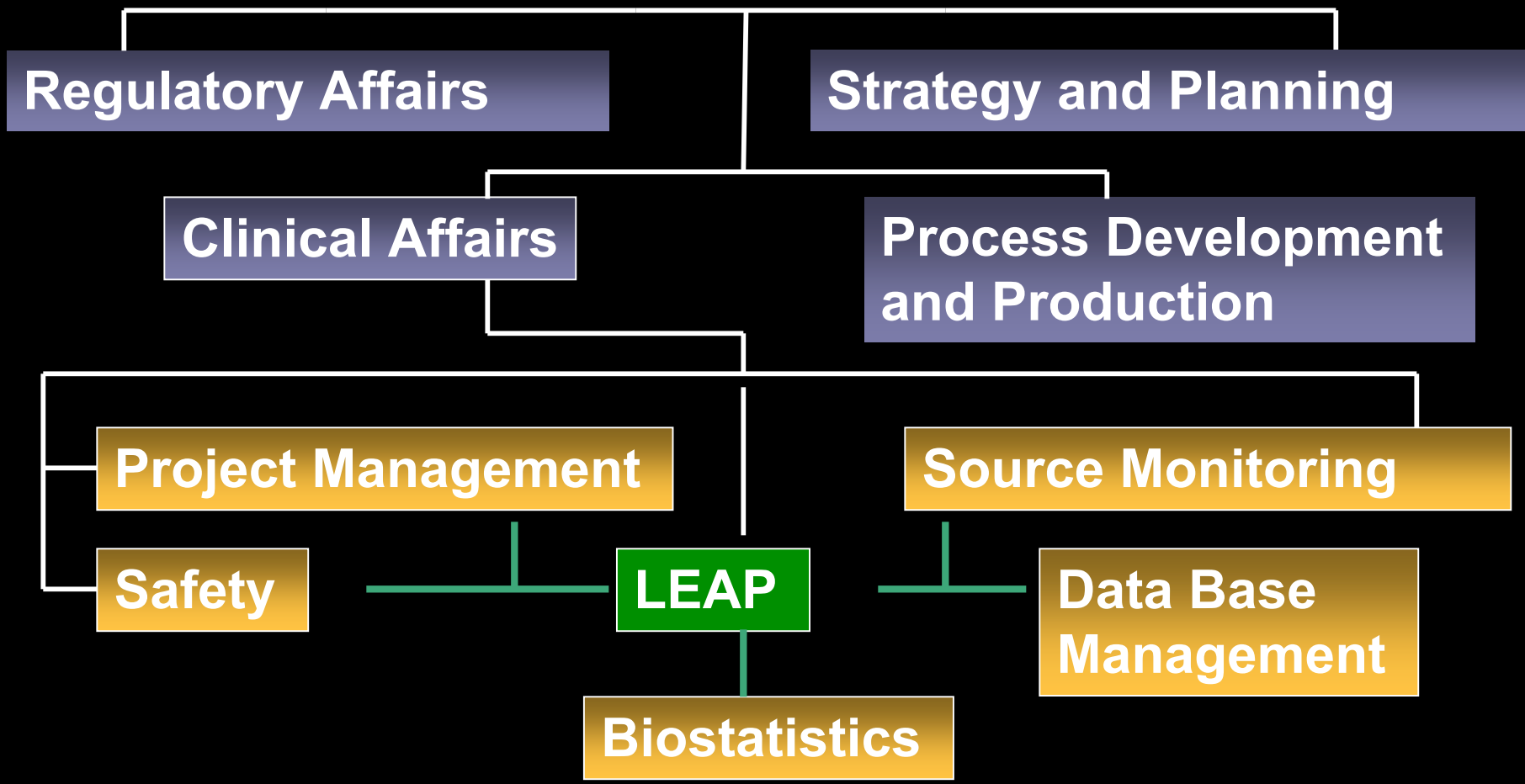

LICR Cancer Immunotherapies:
Antibody Targeting and Cancer Vaccines

- Internal development including reagents, assays, early phase clinical trials
- Partnerships with academic entities
- Partnerships with Biotech/Pharmaceutical Industry
- Government Agencies-USA and International
- Partnerships with not-for-profit funding agencies (CRI)

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Antibody Targeting vs. Antibody Therapy

Academic Approach at LICR

- Target identification
- Targeting (PET)
- Effector mechanisms
  - Internalization
  - Functional Effects
  - Complement fixation
  - ADCC

Industry Approach

- Clinical Outcome

Ludwig Institute for Cancer Research (São Paulo,Brazil)

HPV vaccine

- Scientific Discovery
- Epidemiologic Studies

- Laboratory science for Merck's Clinical Trials

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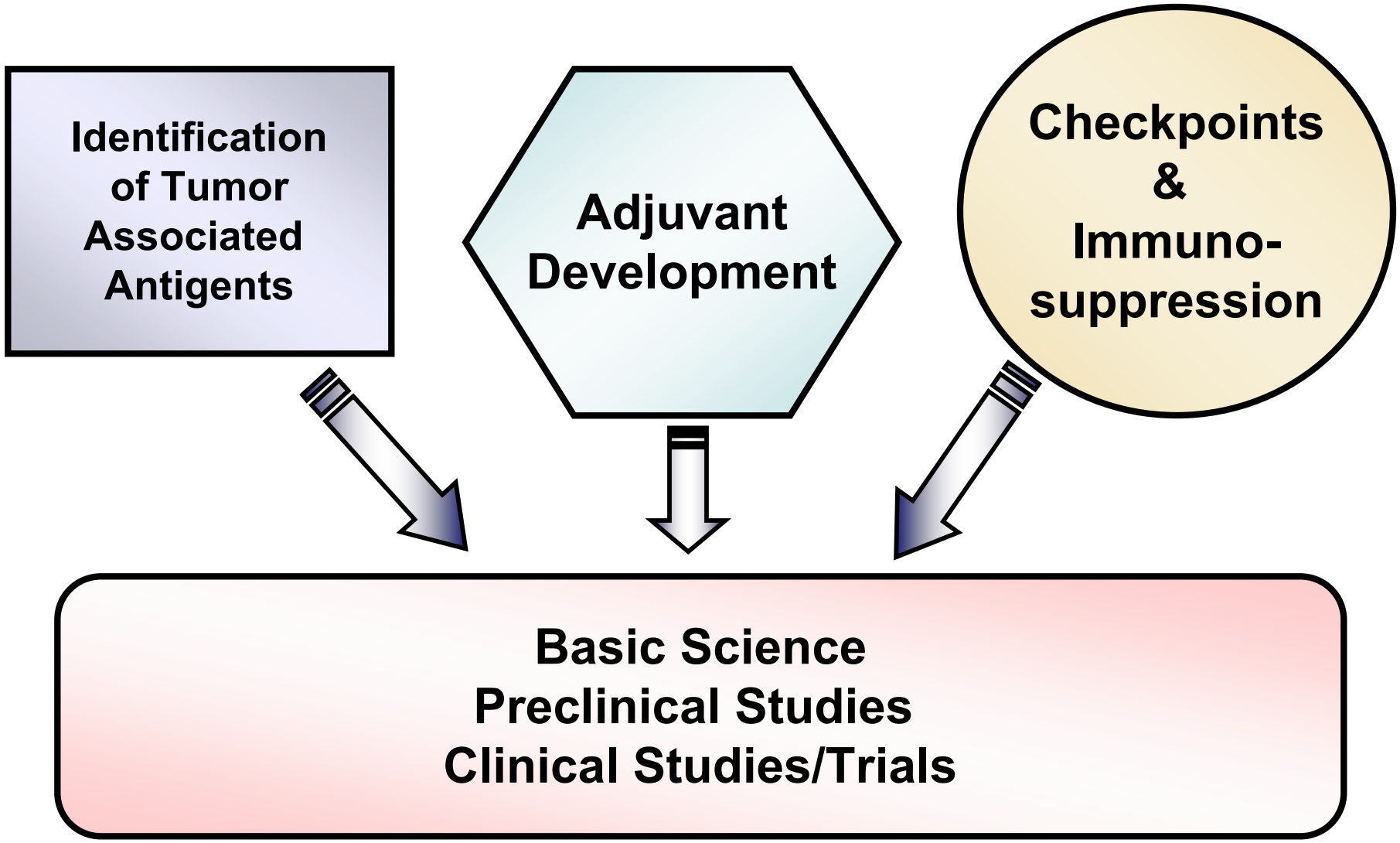
Development of Cancer Vaccines



Evolution of the Cancer Vaccine Collaborative as a New Funding Model

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CRI FUNDING IS UNIQUE

I. Singular focus on Cancer Immunology and Fundamental Immunology (as the pipeline for further advancements in Tumor Immunology)

II. All Career Levels

III. Basic Science Through Clinical Application

IV. Coordination of Participants in Various Grant Programs

Cancer Research Institute Programs

- Predoctoral Emphasis Pathway in Tumor Immunology
- Postdoctoral Fellowship Program
- Investigator Award Program
- Clinical Investigation Program
  - Cancer Antigen Discovery Collaborative
  - Cancer Vaccine Collaborative

CRI STRATEGY

- **Maintain a Pipeline that Keeps CRI at the Forefront of Cancer Immunology by Balancing Distribution of Resources to**
  - **Fundamental Immunology/Cancer Immunology**
  - **Translational and Patient-Oriented-Research**
  - **Clinical Trials**

Need:

- More efficient system for developing effective therapies for cancer

Requires:

- Coordination
- Centralized management by an umbrella entity
- Driven by scientific excellence
- Clinical teams and laboratory science

Model:

- Early-stage clinical research
- Parallel, single-variable trials
- Comparable data, shared and accessible
- Learn from success and failures
- Allow for rapid amendment of ongoing studies

CLINICAL PROGRAMS CAD and CVC

- **Cancer Antigen Discovery:**
  Identify and Characterize Potential Targets of the Immune System on Cancer Cells that can Serve as Basis of Vaccine and Antibody therapies (Translational)

- **Cancer Vaccine Collaborative:**
  Patient-Oriented-Research and Clinical Trials for Cancer Vaccines using:
  - Defined Antigens
  - Standardized Regimens and Monitoring
  - Central Data Collection
  - Parallel single variable protocol designs

Cancer Vaccine Collaborative (CVC)

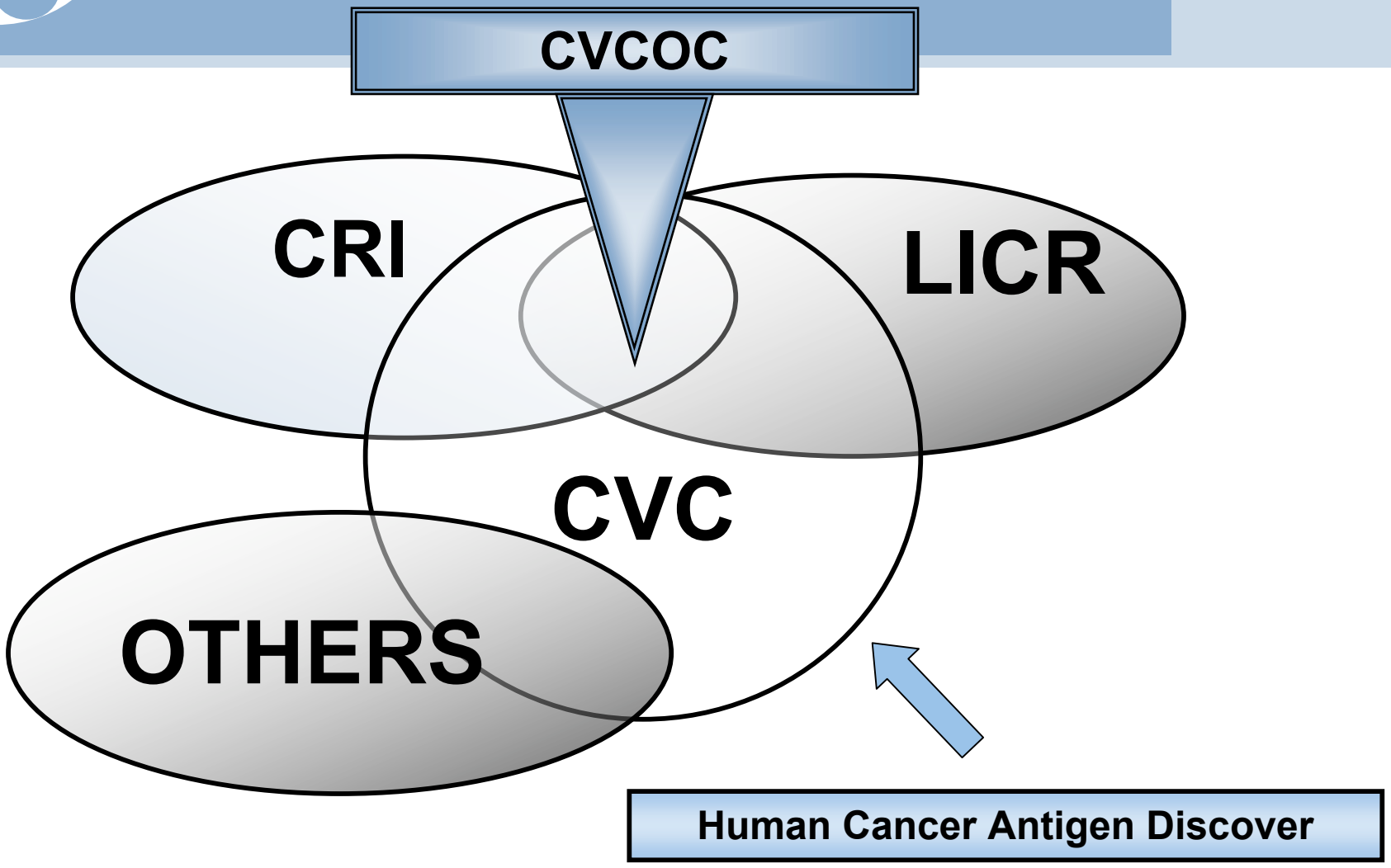
LICR	CRI
Reagent	Funding
Regulatory Infrastructure	Facilitate cooperatively between participants

Actively pursuing incorporation of additional academic partners:

- **Clinical sites**
- **Monitoring- immune response**
- **Novel approaches**

- **CVC Successes**
  - **12 completed, 10 active, 5 pending trials**
  - **Implemented standardized immunological monitoring**
  - **Produced clinical grade vaccines**
  - **Parallel single variable studies**
  - **Confirmed that vaccination leads to a broad integrated immune response**
  - **Compelling data for increased relapse-free survival in melanoma**
  - **Negotiated revenue sharing with LICR (12% of LICR's CVC Net Income)**

CANCER VACINE COLLABORATIVE



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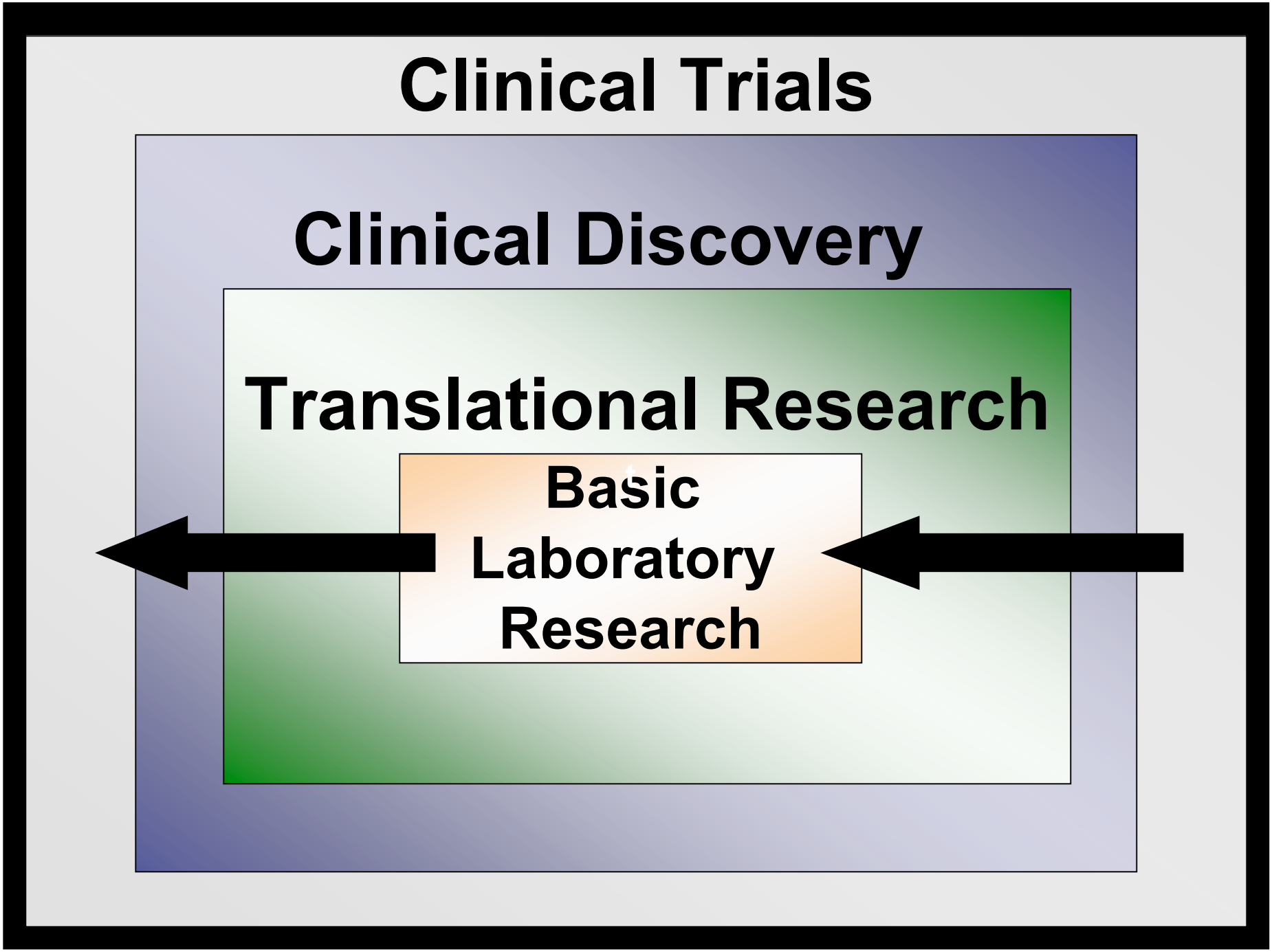
- **Member/Professorial Track:**
  - Basic, translational and clinical scientists
  - Judged on quality of scholarly activities, productivity and creativity
- **Investigator Track:**
  - Provides opportunities for advancement and continuity of staff
  - Judged on scientific quality and productivity

For those who do both, advise they align their clinical and research interests.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