

Immuno-Oncology Translational Network (IOTN)

BRP Immunotherapy and Prevention Working Group



Recommendation - Accelerate translation of basic discoveries to clinical applications to improve immunotherapy outcomes for both "hot" and "cold" cancers - and to prevent cancers before they occur.

BSA Presentation
June 20th, 2017

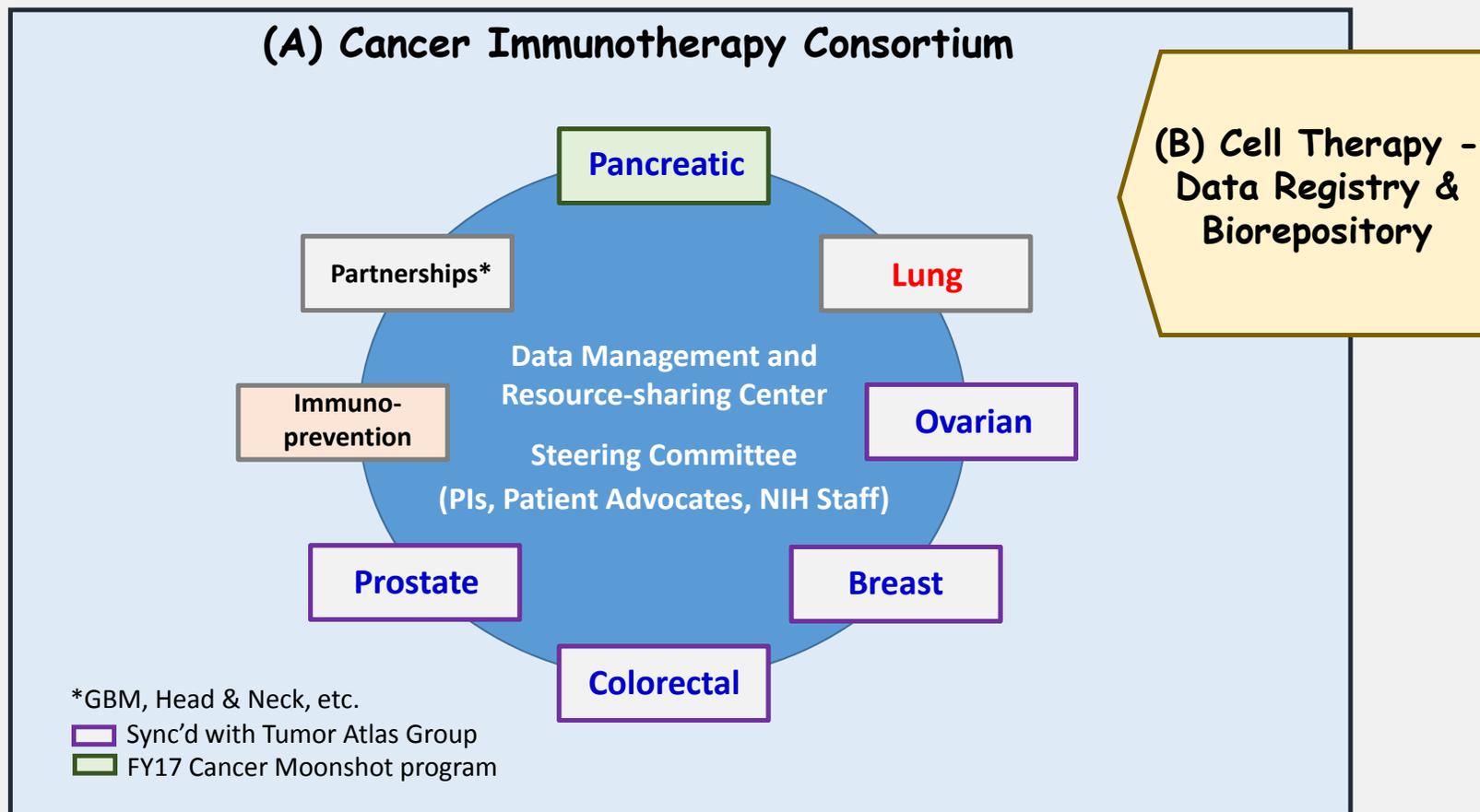
Immuno-Oncology Translational Network (IOTN)

Adult Immunotherapy Implementation Team

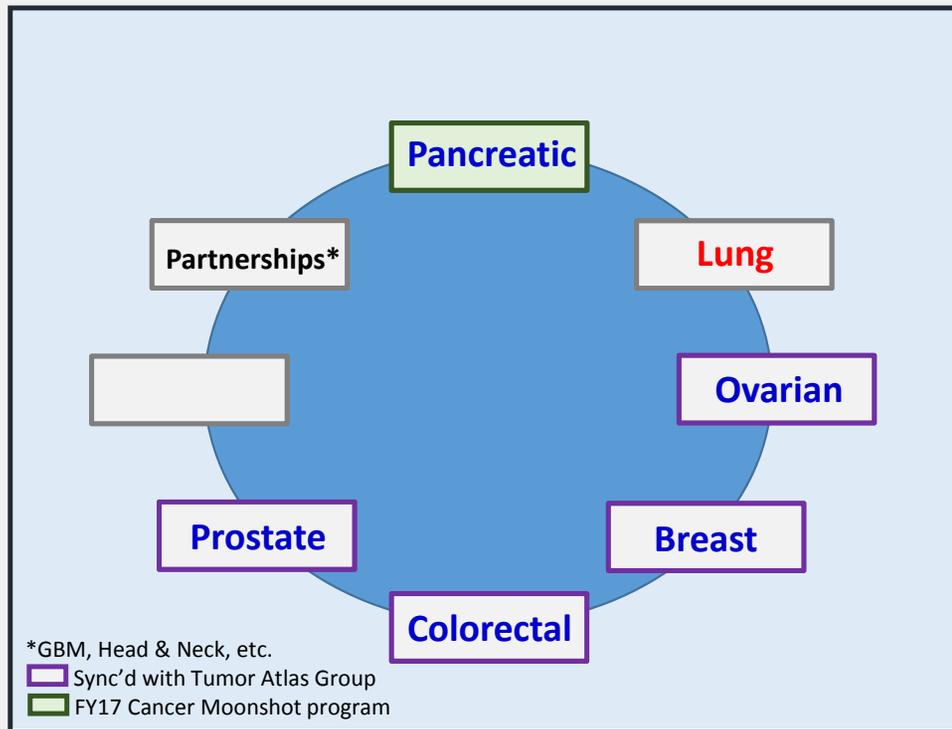


Implementation Plan - Leverage the expertise and resources of a collaborative network of investigators to develop improved immunotherapy approaches including novel combinations.

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Cancer Immunotherapy Consortium



CIC Sub-Networks

U01 mechanism

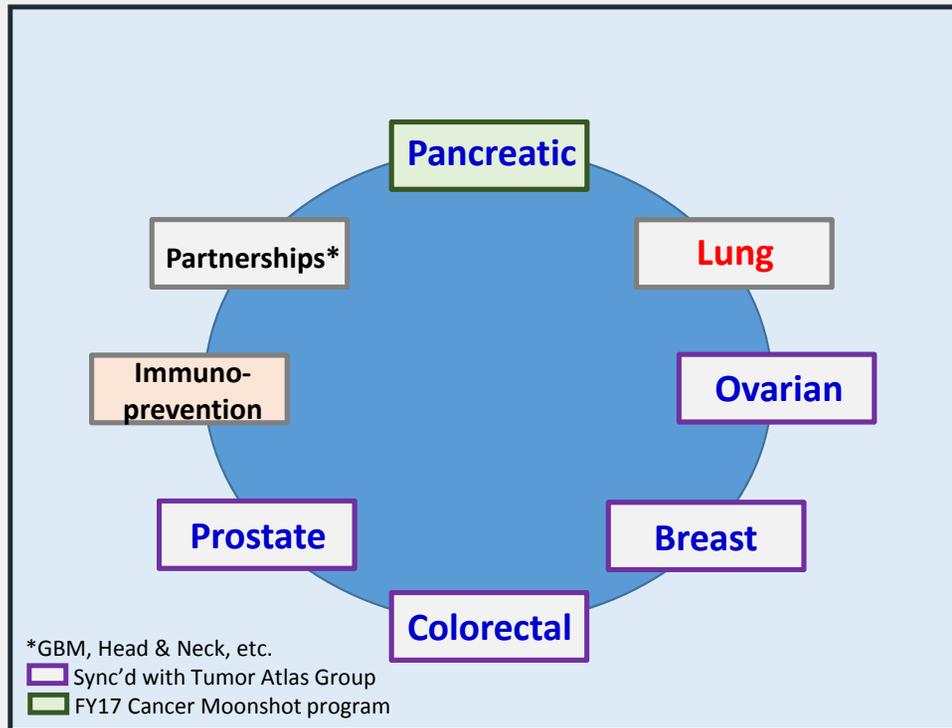
Organ Site-specific Sub-networks

Goal: Develop improved tumor-specific immunotherapy approaches.

Objectives:

- Define immune interactions in the tumor microenvironments.
- Identify tumor-specific T cell receptors and their cognate tumor targets (neoantigens).
- Uncover intrinsic and extrinsic (**immunosuppression**) resistance pathways.
- Test **cancer vaccines, combination therapies, and engineered T cell approaches.**
- Studies will be largely **pre-clinical** including animal models, but with human endpoints and potential for rapid translation into early phase clinical testing.

Cancer Immunotherapy Consortium



CIC Sub-Networks	U01 mechanism
ImPr Sub-Network	U01 mechanism

Cancer Immunoprevention sub-Network

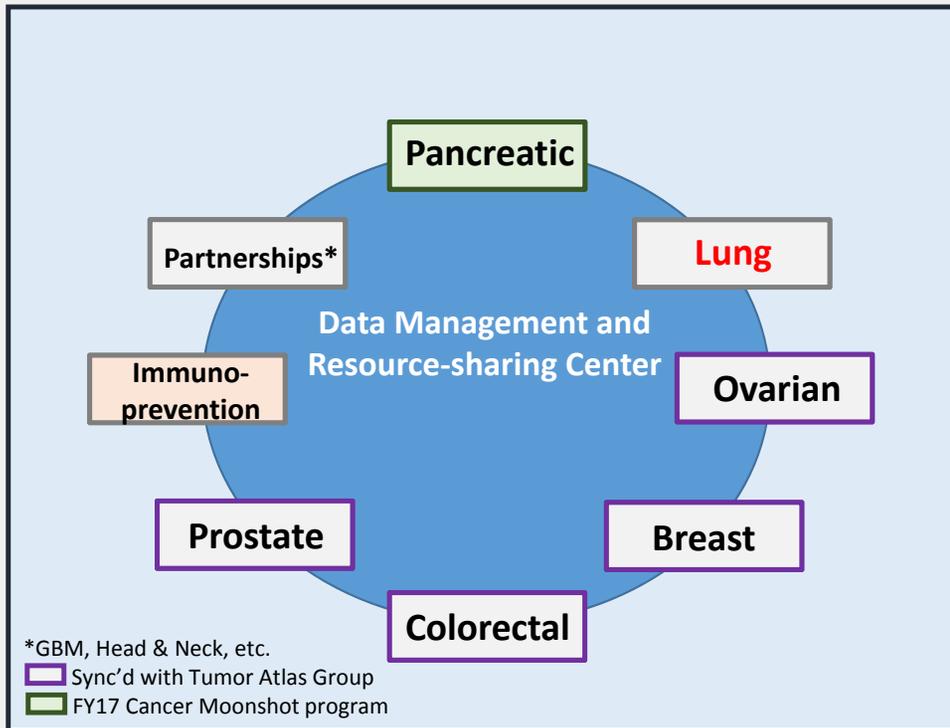
Goal: Identify actionable targets arising in pre-cancerous lesions; develop and validate early intervention vaccines based on these targets.

Objectives:

Focus on cancers that occur in specific organ sites in high-risk cohorts.

- Frameshift Peptides - Lynch S. (colon cancer)
- Fusobacterium nucleatum (colon cancer)
- HER2 (breast cancer)
- EGFR (lung cancer)
- KRAS (lung cancer)
- BRCA1/2 (breast & ovary)
- NF and TSC (neurologic and other cancers)
- Etc.

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CIC Sub-Networks	U01 mechanism
ImPr Sub-Network	U01 mechanism
DMRC	U24 mechanism

The Network will be supported by a **Data Management and Resource-sharing Center (DMRC)**, using a **U24** mechanism, with the following components:

Network Coordinating Center:

- Provide overall administrative support
- Developing a website for consortium members and an outfacing portal for the cancer community.

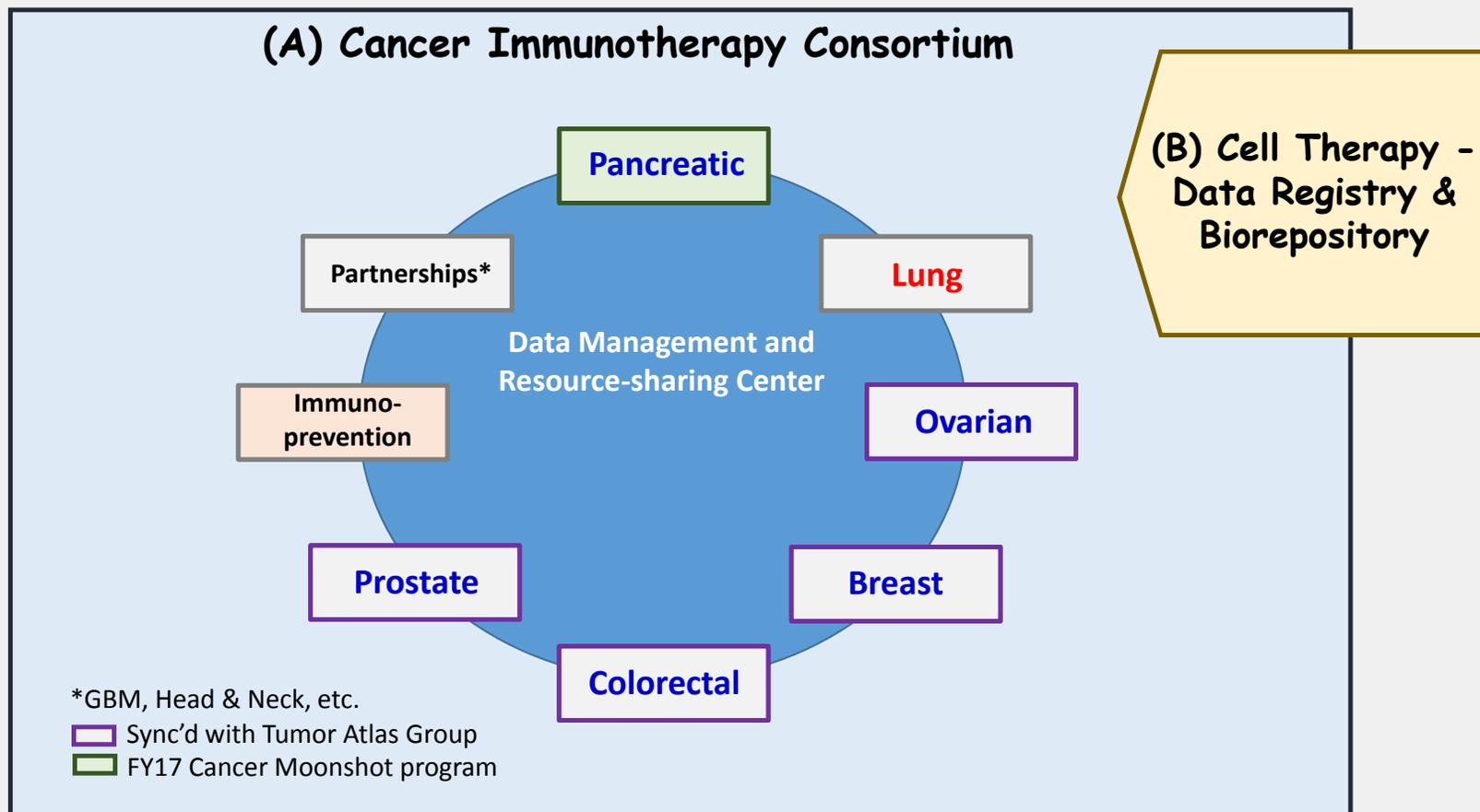
Resource Sharing Center:

- Oversee the tracking and distribution of network biospecimens, models, and resources.

Data Sharing Center:

- Centralized bioinformatics support.
- Establish SOPs and quality control for all network generated data - including genomic data, tumor targets, and cellular analyses to appropriate databases.
 - Coordinate with Cancer Moonshot components (Tumor Atlas, Data Ecosystems, Cancer Immunologic Data Commons, others)

Cell Therapy - Data Registry and Biorepository

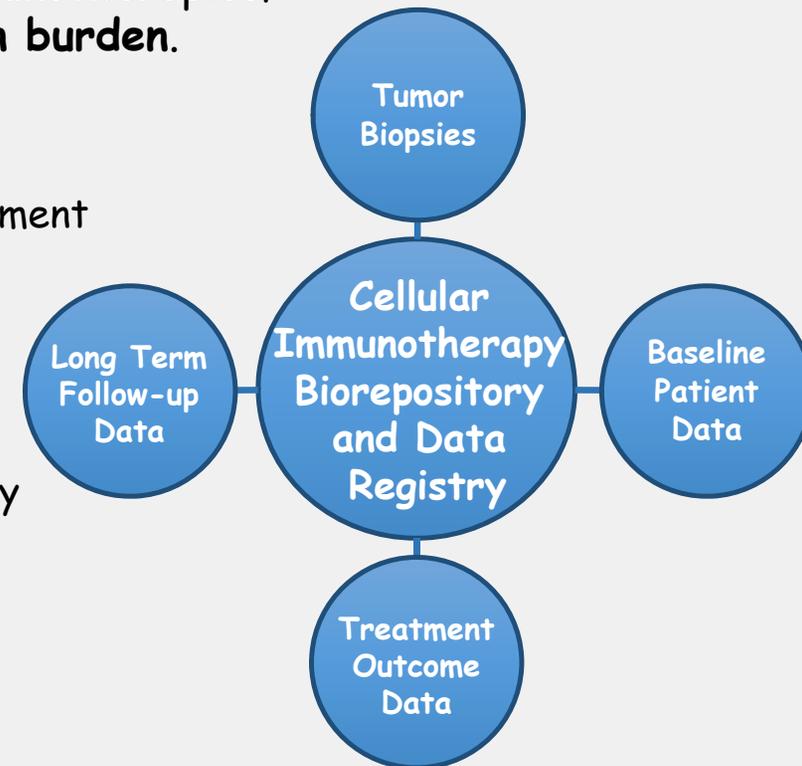


Cellular Immunotherapy - Data Registry and Biorepository

Goal: Accelerate optimization of cell-based immunotherapies;
High impact for cancers with **low mutation burden**.

Objectives:

- **Data Registry** collects baseline patient data, treatment outcomes, and long term follow-up.
- **Biorepository** collects patient normal (PBMCs) and tumor tissue - compare genomic data with clinical outcomes.
- Utilize the **U24 mechanism** to leverage a pilot study through the Center for International Bone Marrow Transplant Registry (CIBMTR).
- Will support all NCI Clinical Trial Networks.



Portfolio Analysis

Text mining of the NCI portfolio for “translational immunotherapy” grants across Lung, Ovary, Breast, Colorectal, and Prostate organs - cross-checked by subject matter experts identified approximately 130 grants.

- Variety of different mechanisms - and no integration of effort.
- Few have combination therapy approaches as primary endpoints.



A network will foster collaborative approaches to enable rapid translation of discoveries to clinical application.

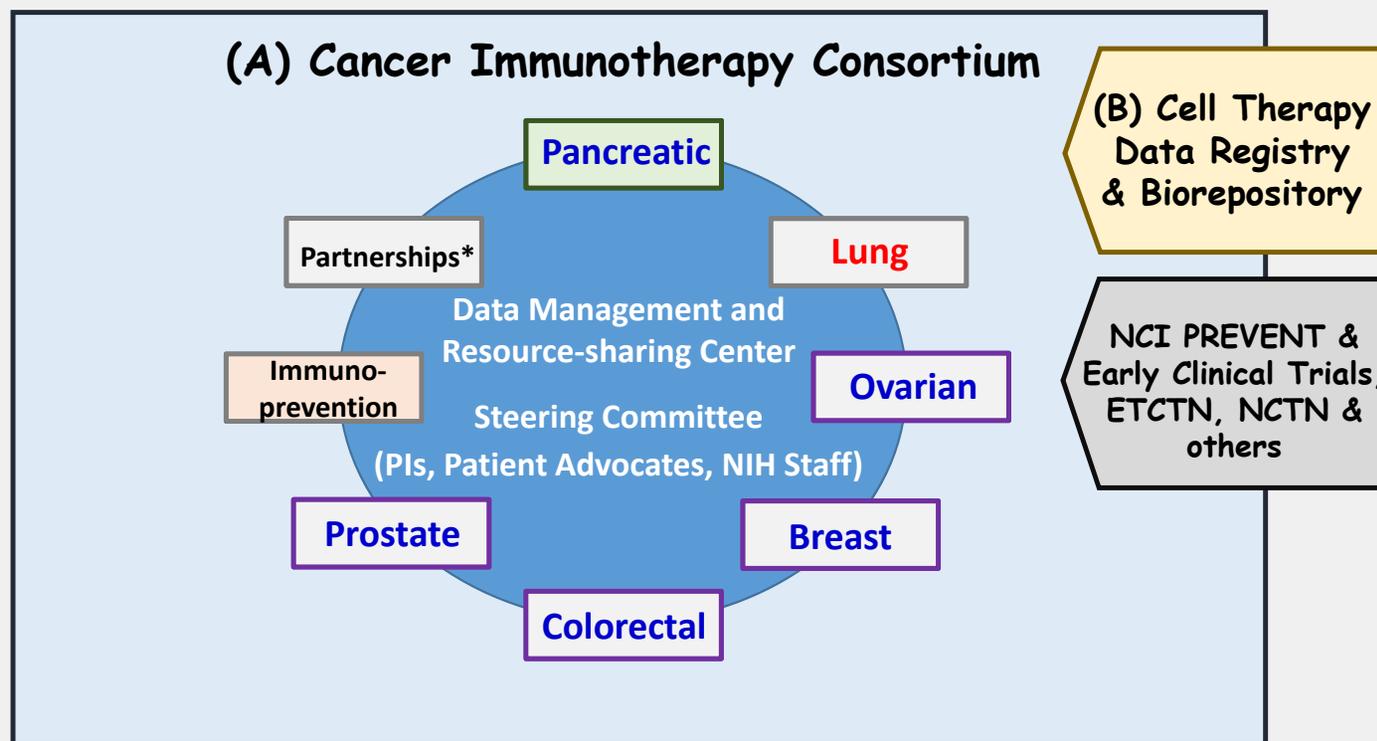
Budget

Cancer	<u>Mechanism</u>	<u>Number of Awards</u>	<u>Direct Costs (M)</u>	<u>FYs</u>
Imm. Consortium				
• Organ Sites	U01 (500K)	8-9	4.33	18-22
• Immunoprevention	U01 (500K)	2-3	1.33	18-22
• DMRC	U24	1	0.75	18-22
Cell Therapy Data Registry & Biorep.	U24	1	1.2	18-22
Program FTE	-	-	<u>0.2</u>	18-22
			\$7.81 M	
• Estimated Total Costs FY18: \$13.0 M				
• Estimated Total Costs FY18-22: \$65 M				

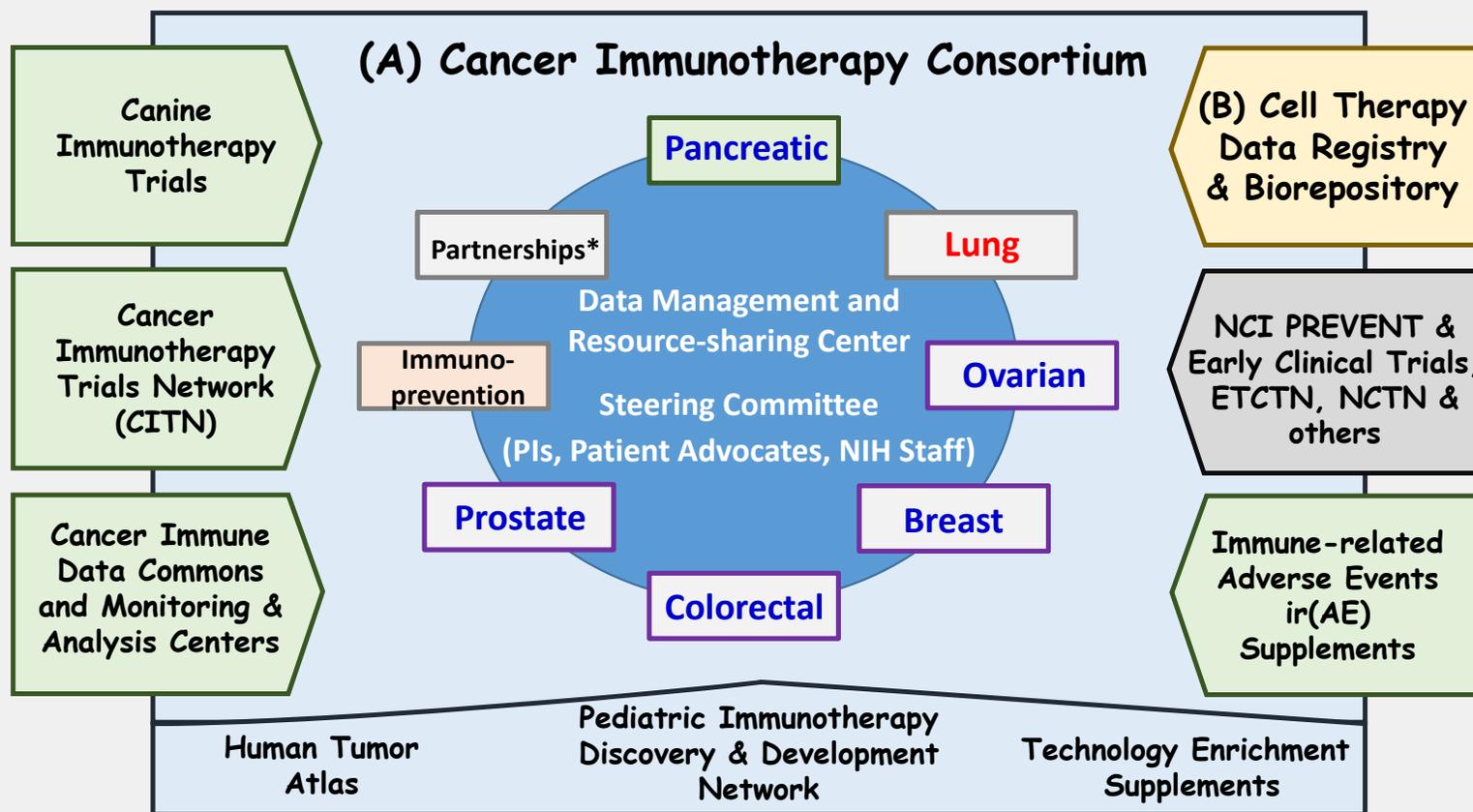
Evaluation Criteria

- Accelerated translation of novel discoveries through collaboration.
- Demonstrate conversion of **cold** tumors to **hot** tumors.
- Validated vaccine approaches for therapeutic or early intervention.
- Novel immunotherapy agents and combination approaches have advanced to early stage clinical application.

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Acknowledgments

BSA Subcommittee Reviewers

Ian Thompson (Chair), Luis Parada, and Mary Lou Smith

- Importance of including animal models in preclinical studies and that immunoprevention is addressed.
- To include patient advocates in the governance of the Network.
- Provide supplement programs in future years to encourage cross-Network collaborations
- Support efforts to address adverse effects associated with immunotherapy.
- Encourage multi-PI and multi-Institution applications.

Adult Immunotherapy Implementation Team

Co-Chairs: Elad Sharon (DCTD) and Kevin Howcroft (DCB)

[Kasia Bourcier \(NIAID\)](#), Nancy Boudreau (DCB), Helen Chen (DCTD), Vik Devgan (DCTD), [Jane Fountain \(NINDS\)](#), [Rebecca Fuldner \(NIA\)](#), James Gulley (CCR), Todd Haim (SBIR), Toby Hecht (DCTD), Christian Hinrichs (CCR), [Kathy Jung \(NIAAA\)](#), Amy Leblanc (CCR), Laura Lunardi (CRS), Marie Mancini (NIAMS), Cheryl Marks (DCB), [Kimberly McAllister \(NIEHS\)](#), John Ojeifo (CRCHD), [Mike Sayre \(NIMHD\)](#), Jeffrey Schlom (CCR), Robert Shoemaker (DCP), [Chiayeng Wang \(NIDCR\)](#), Min Song (DCTD), Magdalena Thurin (DCTD), Jack Welch (CGH)

Questions