Blue Ribbon Panel Recommendations

A. Establish a network for **direct patient involvement**

B. Create a translational science network devoted to **immunotherapy**

C. Develop ways to overcome **resistance to therapy**

D. Build a national cancer **data ecosystem**

E. Intensify research on the major drivers of **childhood cancer**

F. Minimize cancer treatment's debilitating **side effects**

G. Expand use of proven **prevention and early detection** strategies

H. Mine past patient data to predict future **patient outcomes**

I. Develop a 3D **cancer atlas**

J. Develop new cancer **technologies**

Immuno-Oncology Translational Network

Blue Ribbon Panel Immunotherapy and Prevention

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.

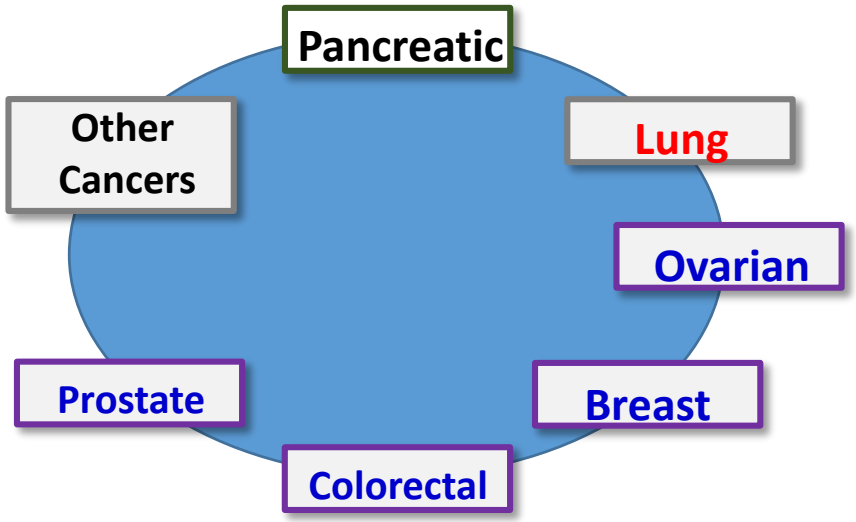
Recommendation: Create a translational science network devoted to immunotherapy

Implementation Plan: Build a collaborative network focused on:

- Discovering and evaluating novel immune-based approaches to increase the number of patients that benefit from immunotherapy; and
- Developing and validating early intervention vaccines to prevent cancers of all types
- Incorporating multi-disciplinary approaches to improve immunotherapy

Cancer Immunotherapy Research Projects (U01)

Cancer Immunotherapy Sub-Networks



Objectives:

- Define immune interactions in tumor microenvironments.
- Identify novel immune checkpoints, tumor-specific T cell receptors and their cognate tumor targets (neoantigens).
- Uncover intrinsic and extrinsic resistance pathways.
- Test improved immunotherapies, (vaccines, checkpoint inhibitors, cellular or viral therapies, bispecific antibodies)
- Studies should be largely **pre-clinical** involving clinically-relevant models and endpoints for rapid translation.

Immuno-Oncology Translational Network (IOTN)

- Current Immunotherapy Projects -

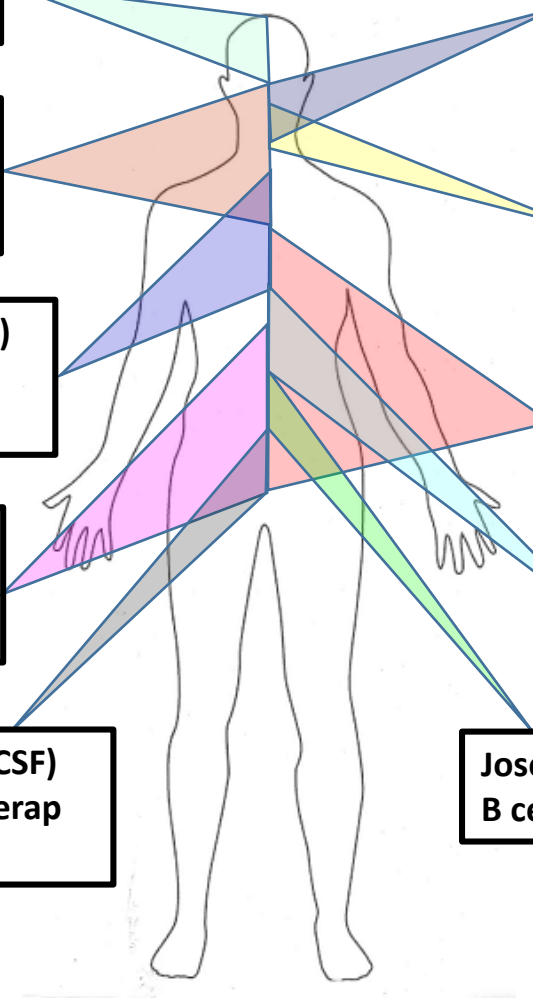
Catherine Bollard (Children's Research Institute DC)
Enhancing cell therapy for BRAIN Tumors

Zac Morris and James Weichert (UWisc - Madison)
Overcome an immuno-suppressive TME [MEL, HNSCC, and SARC] using combination MTRT and IT

Michael Demetriou (University of California – Irvine)
N-glycosylation bi-specific T cell engagers for cancer immunotherapy [BREAST, MEL, others]

Don Kufe and KK Wong (DFCI and NYU)
MUC1-C is a target for reversing immune evasion and resistance to immunotherapies [CRC, PROSTATE, OVARY]

Eli Van Allen and Lawrence Fong (DFCI and UCSF)
Molecular and immune drivers of immunotherap responsiveness in PROSTATE cancer



Stephen Schoenberger, SJ Gutkind, A Rao (La Jolla),
Stimulating Neo-Antigen Specific T Cell Responses in HNSCC

Andrew Sikora and Ananth Annapragada (Baylor)
Targeting the immunosuppressive TME to enhance efficacy of immuno-radiotherapy for ORAL cancer

Owen Witte, GM Crooks, and Yi Xing, Yi (UCLA)
Targeting alternative splicing for TCR discovery in LUNG and PROSTATE small cell carcinomas

Michael Karin (UCSD)
Immunosuppressive mechanisms in non-viral LIVER cancer and control of its response to ICB

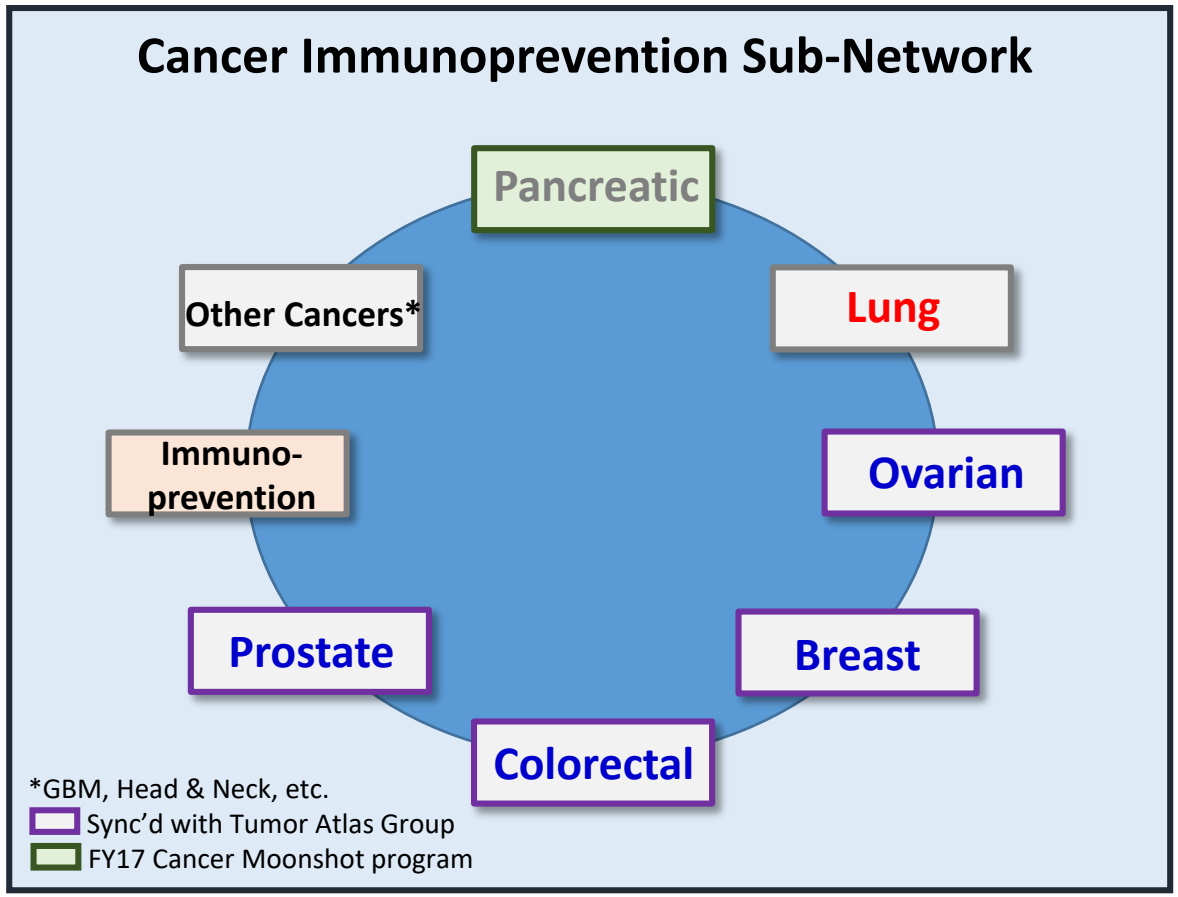
Jose Conejo-Garcia (H. Lee Moffitt Cancer Center)
B cell-dependent anti-tumor immunity in [redacted] cancer

Cancer Immunotherapy Research Projects (U01)

Scientific Goals of the Cancer Immunotherapy Projects

- Define factors underlying escape from immune surveillance
- Improve antigen presentation and priming of anti-tumor cytotoxic T cells
- Discovery and optimization of novel immunotherapies and/or combinations
- Investigate mechanisms of acquired resistance following immunotherapy
- Identify adjuvant therapies that target the gut microbiome to enhance anti-tumor efficacy or reduce toxicity of immunotherapies
- Identify effective immunotherapy approaches in both the periphery and the CNS
- Avoiding or reducing off-target or immune-related adverse events

Cancer Immunoprevention Research Projects (U01)



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

Strategy:

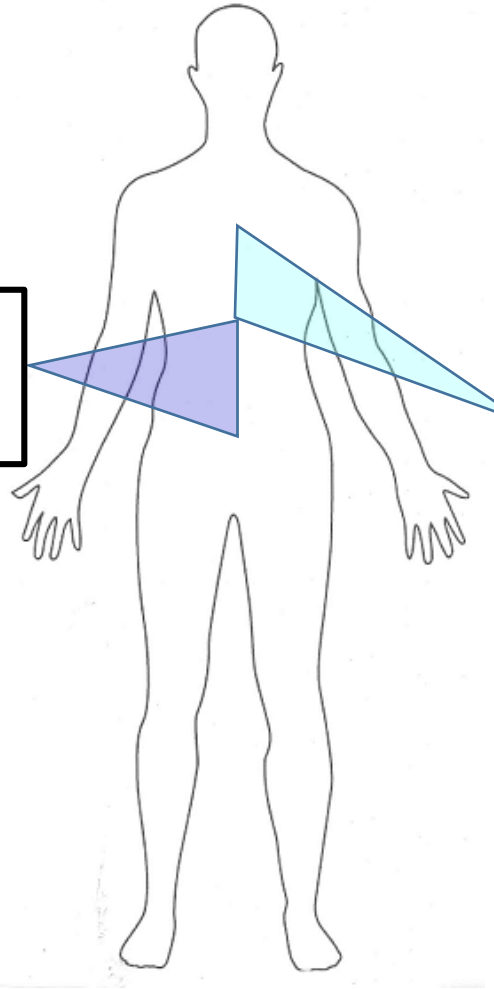
Focus on cancers that occur in specific organ sites in high-risk cohorts.

- Lynch Syndrome (colon and endometrial cancer)
- Familial Adenomatous Polyposis (colon cancer)
- BRCA1/2 Carriers (breast and ovarian cancer)
- NF and TSC (neurologic and other cancers)
- Other Genetic Predisposition Syndromes
- Populations exposed to environmental carcinogens
- Other definable high-risk cohorts

Immuno-Oncology Translational Network (IOTN)

- Immunoprevention Funding Plan -

Steven Lipkin (Weill Cornell)
Neoantigen Vaccination for Lynch Syndrome Immunoprevention [CRC]



Shadmehr Demehri (MGH)
Epithelium-derived alarmins role in BREAST cancer immunoprevention

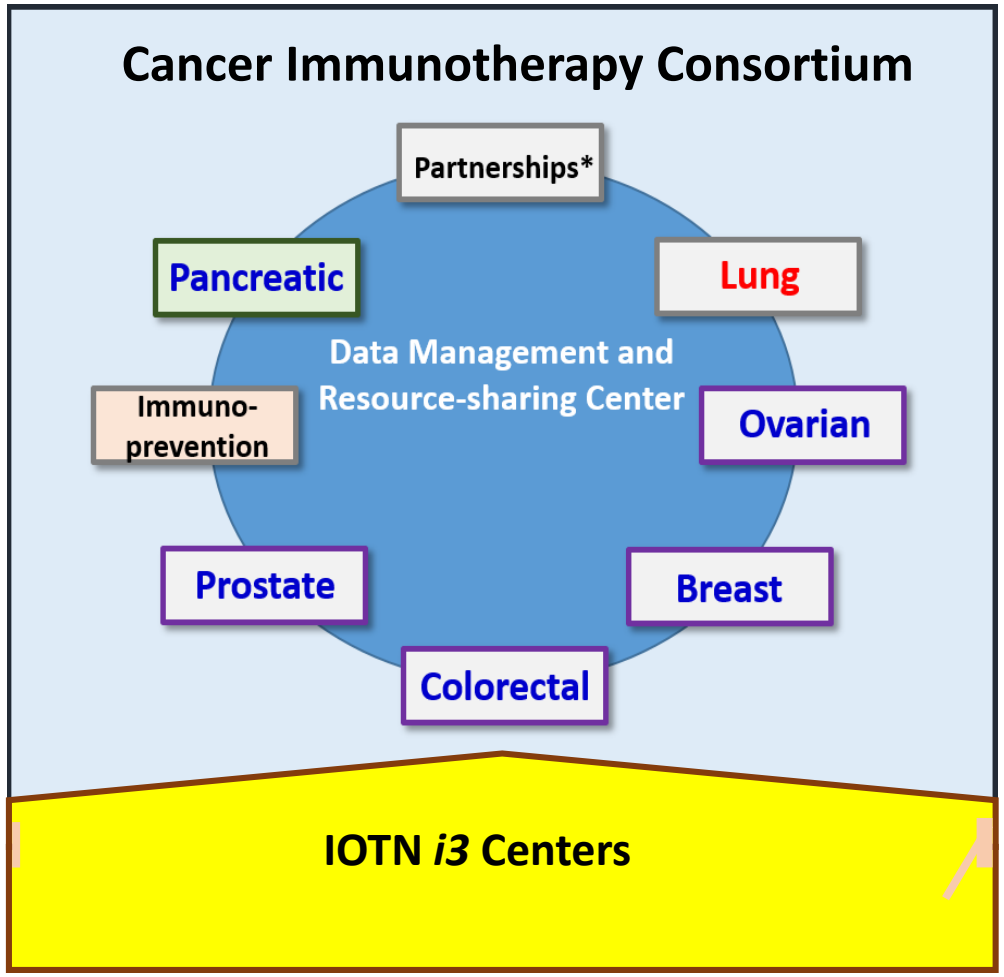
Cancer Immunoprevention Research Projects (U01)

Scientific Goals of the Cancer Immunoprevention Projects

- Define an experimental setting that enables the definition of changes in potential immune targets as a function of time during carcinogenesis.
- Evaluate the validity of identified targets for immunoprevention as a function of time.
- Devise interventions with practical potential for translational studies.
- Produce the preclinical reagents necessary for demonstration of cancer preventive efficacy.
- Demonstrate and reproduce preventive efficacy in preclinical models.

Immuno-Engineering to Improve Immunotherapy (*i3*) Centers

- New Funding Opportunity -



Goal:

- Support multi-disciplinary teams that incorporate bioengineering and systems biology approaches in the IOTN framework.
- Quantitatively understand the physical basis of immune system function
- Build predictive models
- Regenerate compromised immune systems for therapeutic benefit
- Enable precise control of desired immune responses that are **more effective, safer, and more broadly available.**

Immuno-Engineering to Improve Immunotherapy (*i3*) Centers

***i3* Centers should consist of multi-disciplinary teams that incorporate cancer biology, bioengineering and/or systems biology approaches. The i3 centers will contribute to and support the IOTN, using a U54 mechanism,**

Up to 3 Projects in each center:

Examples

- artificial APCs and/or lymphoid structures
- biomaterials to control how, where, and when immune cells are stimulated *in vivo*
- next-gen gene editing and cell therapy engineering
- "universal" immune effector cells
- improved multi-specific proteins & scaffolds for safe and effective engagement of immune cells with tumor cells
- modeling/predictive analyses of immune response attributes to cancer, cancer vaccines, or other immunomodulatory interventions or responses to therapy.
- The projects in any one *i3* Center will be synergistic.

Each center must also include an Administrative Core:

- Manage and coordinate the Center's research activity
- Liaison between each IOTN *i3* Center and IOTN U01s.

Questions?