# Pediatric Immunotherapy Discovery & Development Network(PI-DDN)

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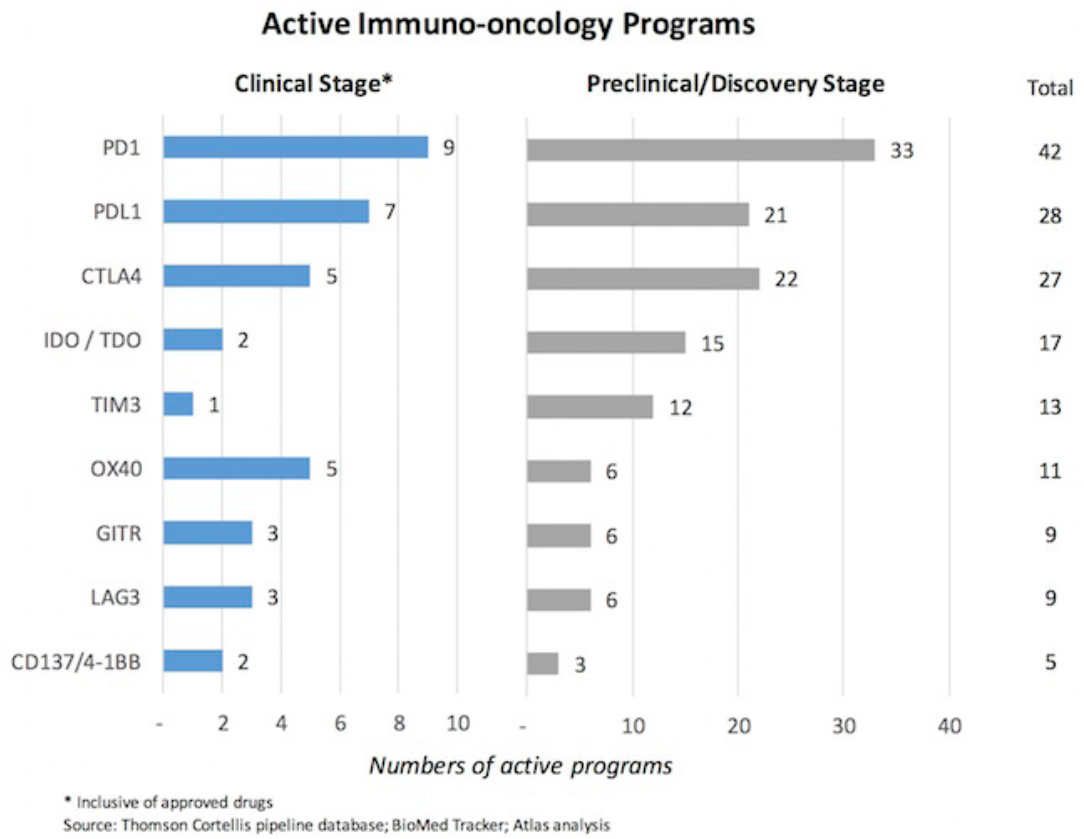
NIH NATIONAL CANCER INSTITUTE

June 2017

# Pediatric Immunotherapy Background

- The focus of adult immuno-oncology research is primarily on agents that boost the immune response to tumor neoantigens




These approaches may have limited applicability for childhood cancers

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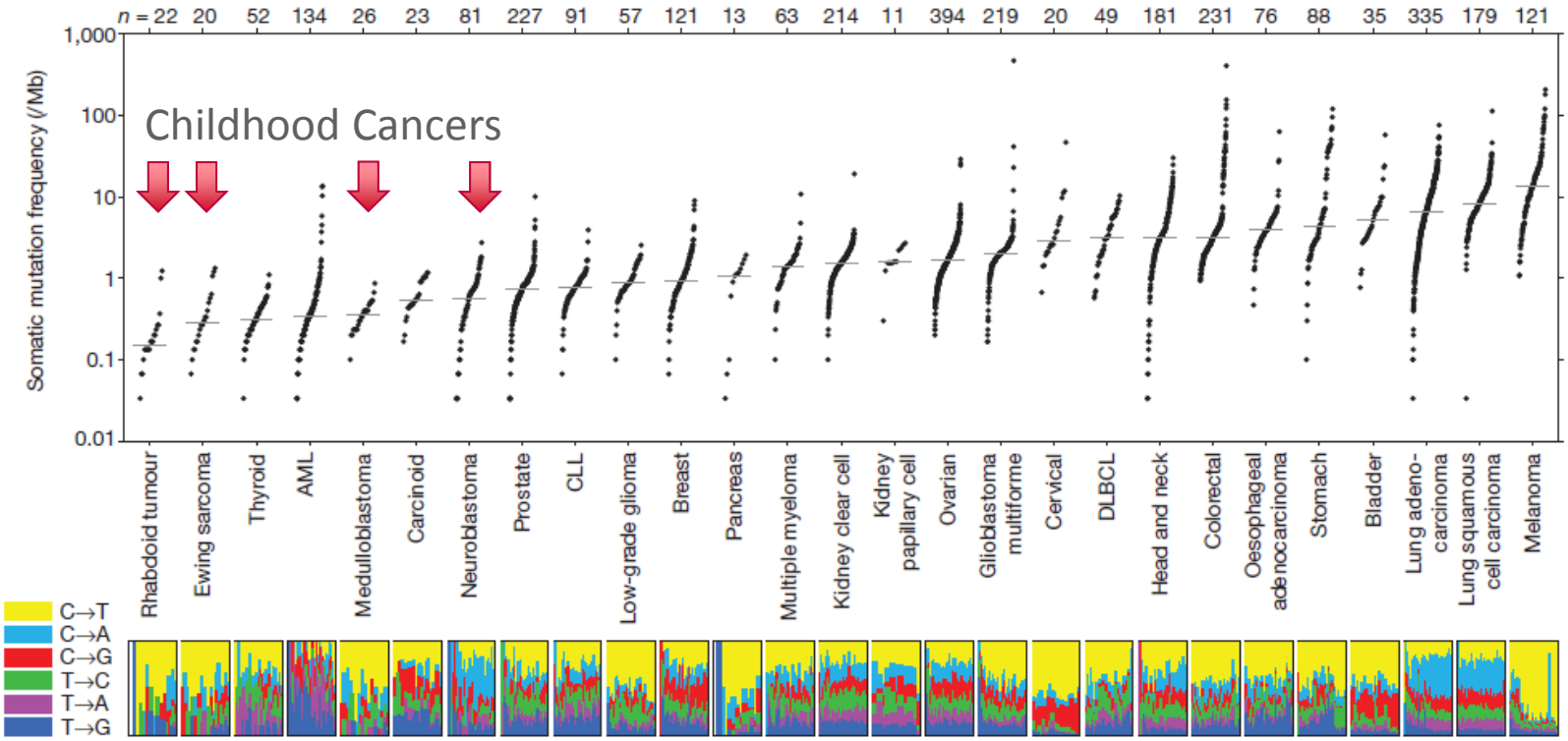
- Pediatric cancers generally have low mutation burdens and corresponding low rates of neoantigens resulting from somatic mutations



# Pediatric Immunotherapy Background

- Pediatric immunotherapy research is distinctive from adult immunotherapy research
- Pediatric cancers generally have low mutation burdens and corresponding low rates of neoantigens resulting from somatic mutations
- Focus of pediatric immunotherapy research on identifying and targeting:
  - Embryonal antigens with low expression in post-natal tissues
  - Antigens expressed on cells that are temporarily “expendable” (e.g., CD19, CD22)
- Primary therapeutic translation is engaging immune mechanisms to target non-mutated epitopes differentially expressed in pediatric cancers

# Examples of Immuno-Oncology Agents for Children

- Brentuximab vedotin
  - Antibody-drug conjugate
  - Targeting CD30
  - Hodgkin lymphoma and anaplastic large cell lymphoma
- Blinatumomab
  - Bispecific T-cell Engaging antibody (BiTE)
  - Targeting CD19
  - Acute lymphoblastic leukemia (ALL)
- CAR T-cells
  - Targeting CD19 and CD22
  - Acute lymphoblastic leukemia (ALL)
- BUT, resistance develops and need agents for pediatric solid tumors

# Examples of Areas of Research Focus for the Pediatric Immunotherapy Discovery and Development Network

- Identification of antigenic epitopes that are uniquely and abundantly expressed on childhood and adolescent cancers.
- Development of optimized, highly specific binders for novel pediatric cancer immunotherapy targets.
- Development of candidate novel immunotherapy agents.
- Identification of cancer cell intrinsic and extrinsic mechanisms of immune evasion that limit the effectiveness of immunotherapy interventions against pediatric cancers.
- Development and application of approaches for in vivo preclinical testing of novel immunotherapy agents, including immune competent pediatric cancer models and humanized mouse models.

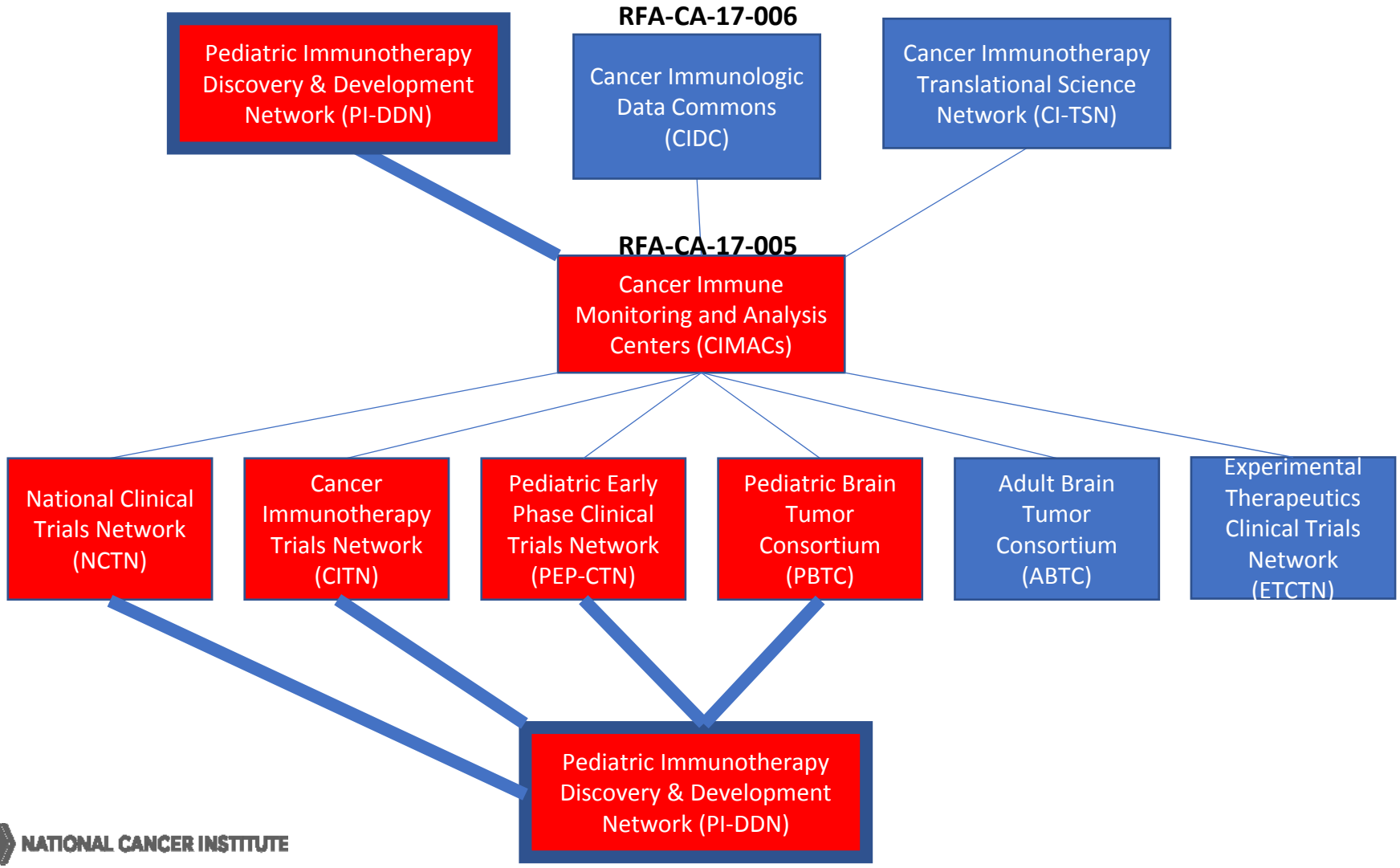
# Pediatric Immunotherapy Discovery & Development Network

- A Collaborative Research Network with planned annual meetings to promote collaboration
- U54 multi-component programs to support collaborative investigator teams addressing two or more relevant synergistic areas of focus.
- U01 research projects to support discrete, individual or multi-PI projects addressing a relevant area of focus such as mechanisms of immune evasion, model development, validation of a single target, etc.
- NCI core services such as manufacturing and toxicology testing of agents developed by Network teams to support advancement to clinical testing in children.
- Funds set-aside for supplements for collaborations across the network for years 2-5.

# Budget Considerations

- U54 multi-component programs (n = 1-2) at $4 million total costs per year for 5 years
- U01 research projects (n = 6-8) at an annual total cost of $4 million for all awards for 5 years
- Collaboration supplements for years 2-5 ($1 million total per year)
- Single receipt date in FY18 and FY19

# NCI Cancer Immunotherapy Networks (Comprehensive)



# Markers of Success

- Discovery of new antigenic epitopes uniquely and abundantly expressed in pediatric cancers
- Development of highly specific binders for novel antigenic epitopes
- Development of novel immunotherapy agents
- Development of models for preclinical testing of immunotherapy agents
- Discovery of mechanisms of resistance
- Establishment of new collaborations for discovery and development of pediatric immunotherapy agents
- Entry of novel immunotherapy agents into pediatric clinical testing



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