# Pediatric Immunotherapy Network (PIN)

## RFA; U01 Clinical Trials Optional

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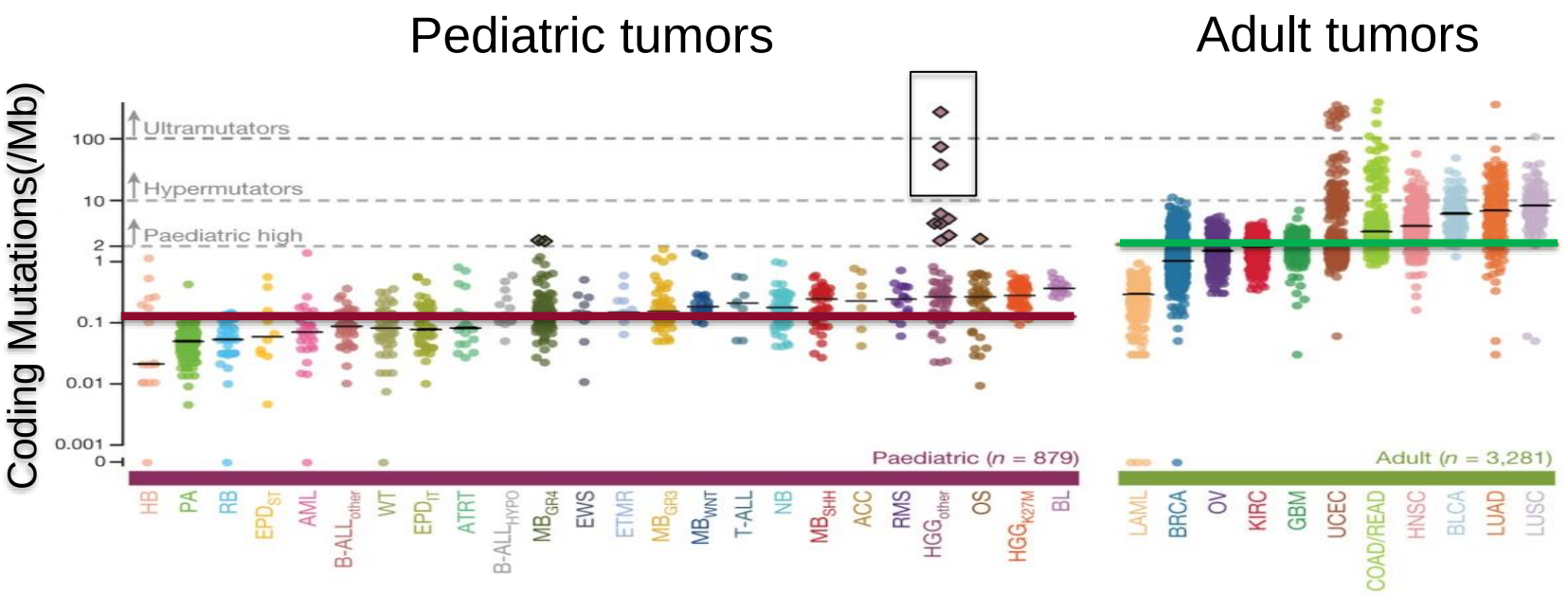
# Pediatric Cancer and Immunotherapy Strategies are Distinct from Adult

- Pediatric cancers mostly arise from misappropriation of normal development processes
- Less environmental exposure, low mutation burden and limited success with immune checkpoint inhibitors
- Distinct immune infiltrates; immunologically cold tumors
- Examples of immunotherapies for children:
  CD19 CAR T cells, CD19 BiTEs, GD2 mAb, CD20 mAb and CD30 ADC



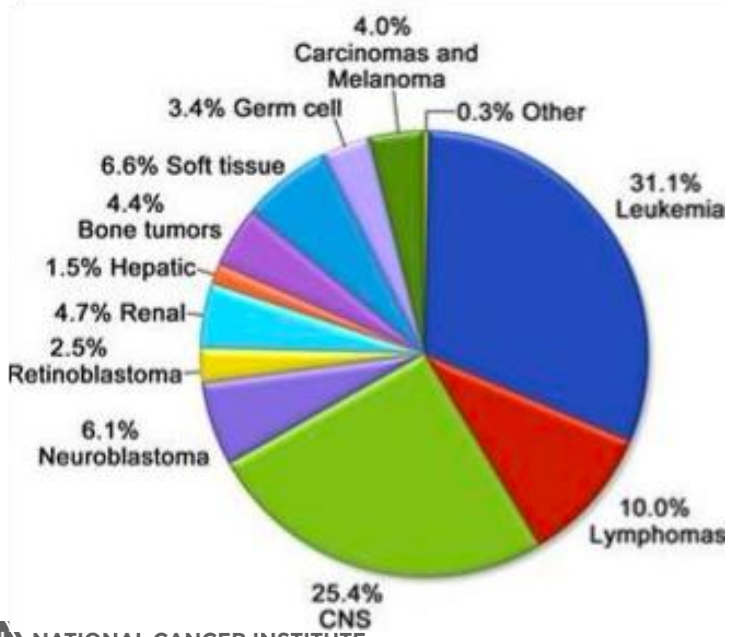

S N Gröbner *et al. Nature* **555** (2018)

# Successes and Challenges for Immunotherapy in Children

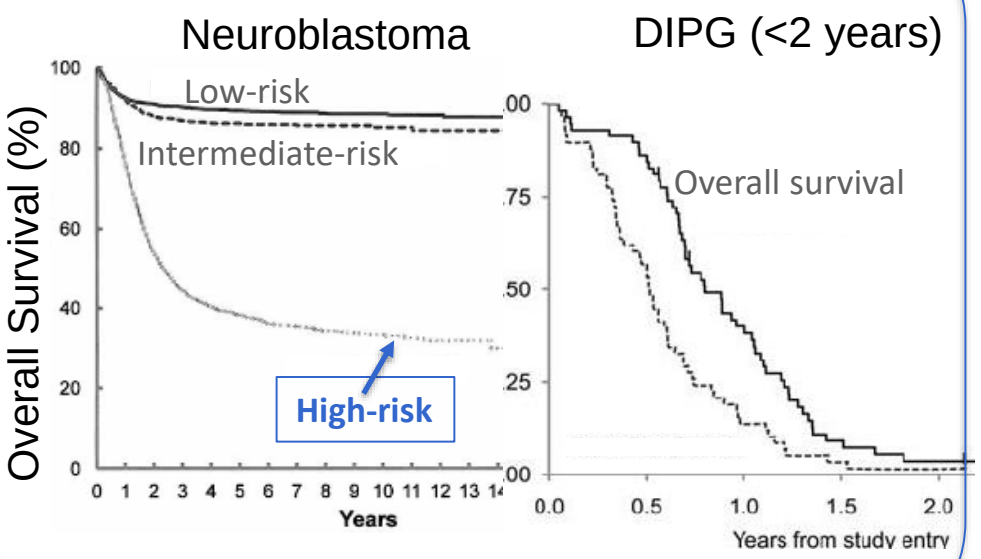
## Some Success for Immunotherapy in Heme Malignancies


Source: Emily WhiteHead Foundation

## Cancer Incidence (0-14 years of age)




## Solid & Brain Tumors: Event-Free Survival



# Challenges for Pediatric Solid & Brain Tumors

- Rare tumors; limited patients for any given tumor indication
- Limited specimen availability; monitoring response to therapy
- Unknown role of the developing immune system
- Poorly understood tumor microenvironment
- Low tumor mutation burden and immunologically cold tumors
- Increased risk for therapy-related toxicities including neurotoxicities
- Lack of appropriate model systems; tumor heterogeneity; blood-brain barrier; lack of known tumor antigens/targets

# NCI Portfolio Analysis
# Pediatric Solid Tumor Immunotherapy (Sept 2021)

| Mechanism | Pediatric Solid Tumor Immunotherapy |
|---|---|
| P01 | 3 |
| R01 | 13 |
| R21 | 3 |
| R35 | 2 |
| R37 | 1 |
| U01 | 4 |
| U54 | 2 |
| Others* | 3 |
| Total | 31 |

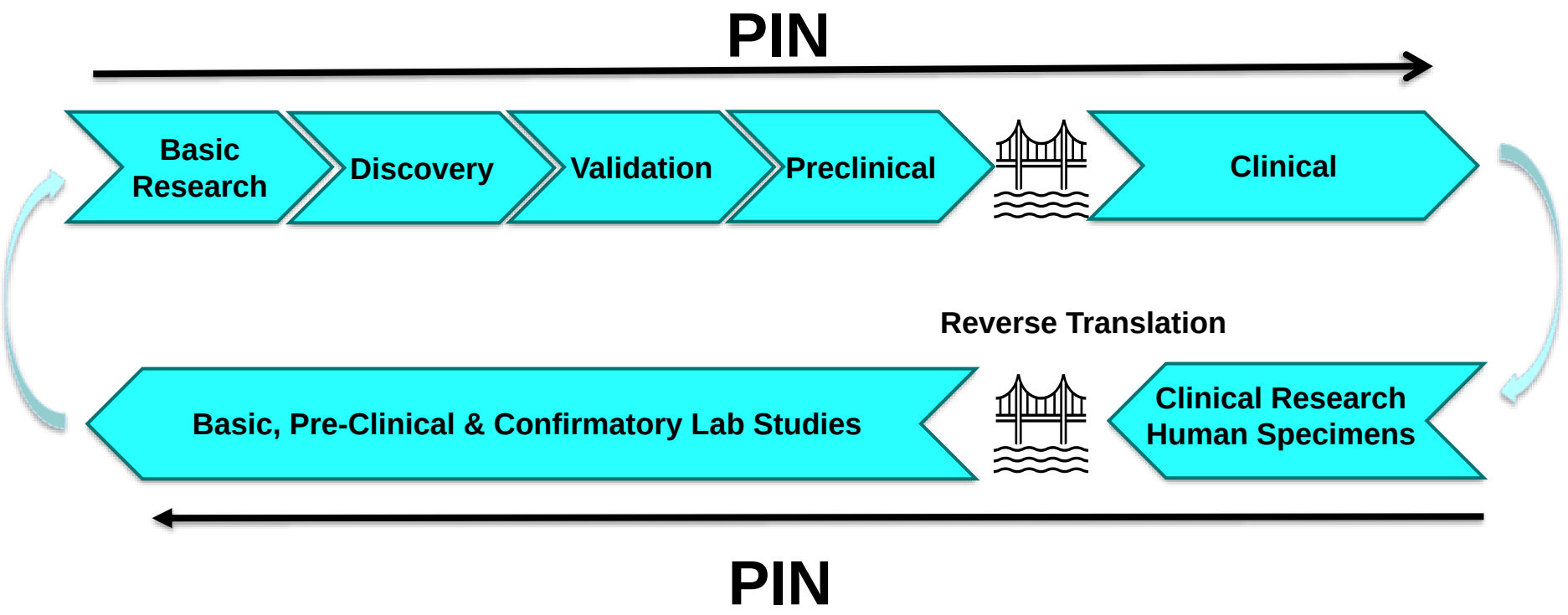
Analysis includes dual assigned grants with NINDS on brain tumors
*Others includes P50 SPOREs

# Gaps and Opportunities Identified by the RFI, NOT-CA-21-086

- Targetable antigenic epitopes, binders and immunotherapy agents
- Elucidation of immune evasion mechanisms
- Pediatric preclinical models especially for brain tumors
- Resources for developing protein therapeutics, IND-enabling studies and cGMP manufacturing
- Predictive biomarkers, analytical technologies for immune monitoring and opportunities for reverse translation

# Pediatric Immunotherapy Network (PIN)

Purpose: To develop translatable novel immunotherapy approaches for children and adolescents with solid tumors including brain tumors toward eventual clinical applications (clinical trials optional)

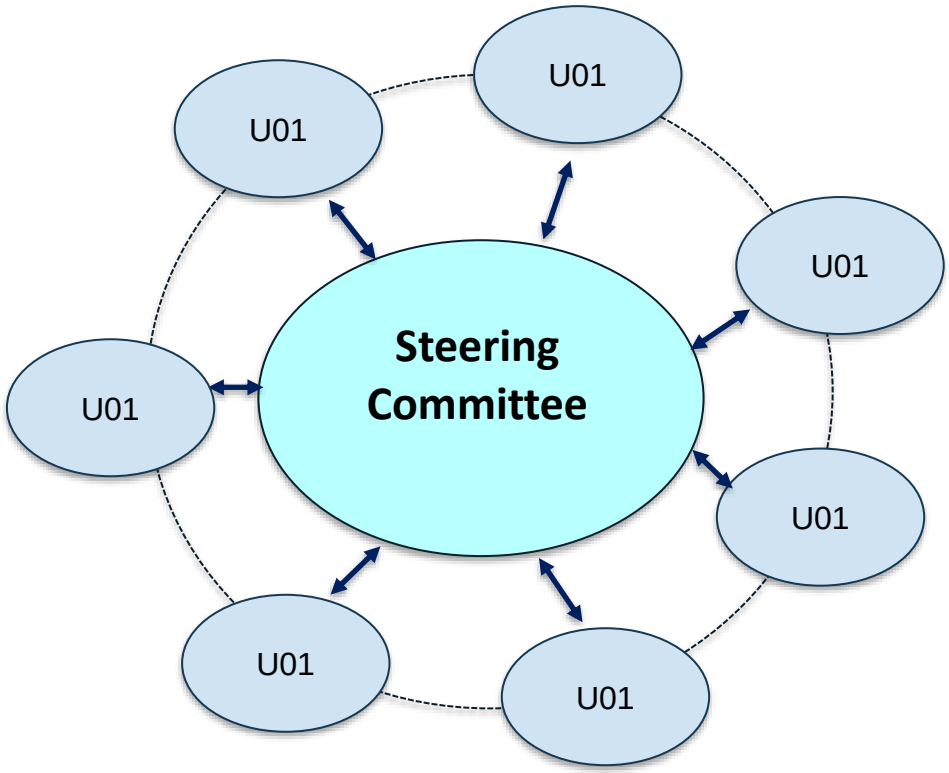


# Implementation Plan for the RFA ( Examples)

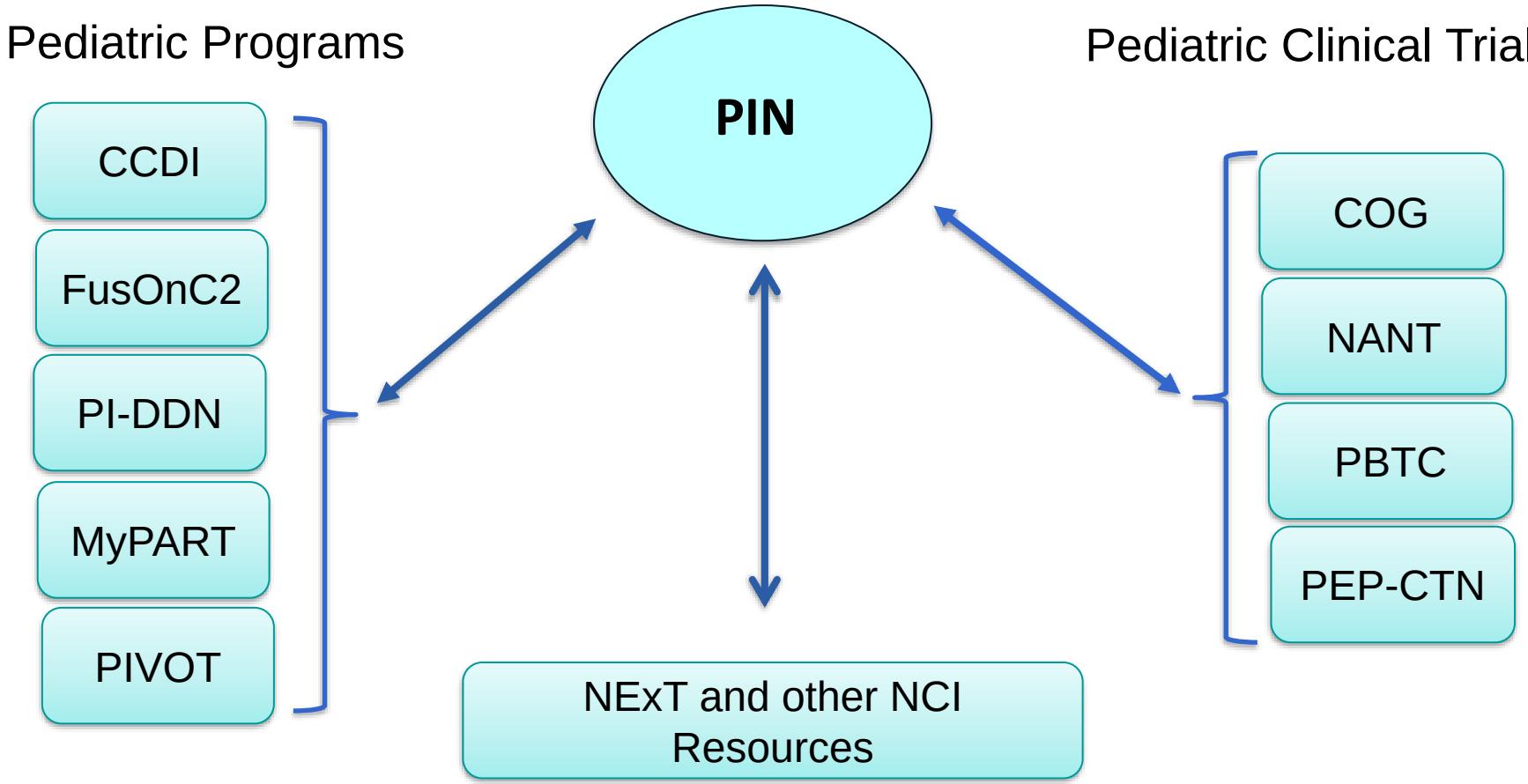
- Discover **novel** pediatric tumor-associated **antigens**
- Analyze **pediatric-specific immune responses** associated with response or resistance
- Molecular and **immune profiling** of pediatric solid tumors
- Strategies to **modulate the pediatric tumor microenvironment** to make immunotherapy agents (e.g., CAR T cells) more effective
- Develop, test, and **optimize preclinical agents** for cold pediatric tumors
- **Reverse translation studies** using **clinical specimens** to interrogate mechanisms of action or resistance to immunotherapy

# Proposed Structure of PIN

- Steering Committee will consist of investigators of U01 projects and NCI staff
- Patient advocates and additional NIH-funded pediatric immunotherapy researchers will be added as associate members
- Administrative coordination for PIN will be provided by one of the U01 sites in partnership with NCI staff



# NCI Pediatric Cancer Networks and Resources




**CCDI**: Childhood Cancer Data Initiative
**FusOnC2**: Fusion Oncoproteins in Childhood Cancer Consortium
**PI-DDN**: Pediatric Immunotherapy Discovery & Development Network
**MyPART**: My Pediatric and Adult Rare Tumor Network
**PIVOT**: Pediatric Preclinical in Vivo Testing program (formerly PPTC)

**COG**: Children's Oncology Group
**NANT**: New Approaches to Neuroblastoma Therapy
**PBTC**: Pediatric Brain Tumor Consortium
**PEP-CTN**: Pediatric Early Phase Clinical Trials Network

# NCI Pediatric Immunotherapy Networks

| | **PI-DDN**<br>Pediatric Immunotherapy Discovery & Development Network | **PIN**<br>Pediatric Immunotherapy Network |
|---|---|---|
| Cancer Types | All diagnoses | Solid tumors including brain tumors |
| Focus | Discovery & Development | Discovery, Development & Translation (Clinical Trial Optional) |
| Timeline | Completion date: 2023-2024 | Earliest anticipated start date: Sep 2023 |

# PIN Budget Considerations (FY 23-27)

| | |
|---|---|
| Number of awards (anticipated) | 6-8 |
| Yearly total cost/award | $450K direct cost/U01 award/year (~$765K total cost/U01 award) |
| Collaborative administrative supplement awards (years 2-4) & network support | $0.5-1.0M total cost/year * |
| Total cost/year | $6.0M |
| Total network cost for 5 years | **$30.0M** |

***** Depending on T1 funding plan - if fewer than 8 awards, NCI program staff may reserve ~$500K to $1.0M for network support and collaborative supplements in years 2-4

# Justification for Use of the RFA Mechanism

- Area of ongoing scientific and clinical need
- Insufficient representation in the NCI portfolio; only 31 grants on pediatric solid tumor immunotherapy (including brain tumor immunotherapy)
- Currently no specialized peer review for pediatric immunotherapy
- Single receipt date will allow for coordinated review and funding of the U01 network

# Justification for Use of the Cooperative Agreement Mechanism

- NCI staff to participate in the Steering Committee
- Monthly Steering Committee meetings to discuss current challenges in pediatric immunotherapy, share results, provide overall advice on future research directions and foster collaboration among awardees
- Collaborations to be established post-award; potential for collaborative funds for years 2-5
- NCI staff to educate Steering Committee members on use of NCI resources such as NExT and other pediatric relevant programs

# Markers of Success/Evaluation Criteria

Successes of PIN at the end of a 5-year cooperative agreement term may include:

- Discovery, development and validation of novel immuno-oncology **targets**
- **Pre-clinical testing** and development of single or combination of immunotherapy agents
- Novel **mechanistic insights** into the tumor microenvironment, response or resistance to immunotherapies
- Conduct of **IND-enabling studies**
- Promotion of novel immunotherapy agent(s) into a **pilot clinical trial**

# Thank you!