

# Pediatric Immunotherapy Discovery and Development Network (PI-DDN)(U54 and U01) Pre-Application Webinar

*RFA-CA-17-050*

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# The Cancer Moonshot Initiative



2016 State of the Union Address

## Goals:

- Accelerate progress in cancer, including prevention & screening
  - From cutting-edge basic research to wider uptake of standard care
- Encourage greater cooperation and collaboration
  - Break down silos within and between academia, government, and private sector
- Enhance data sharing
  - Genomic Data Commons
  - Annotated patient-level clinical data and -omics

# The Process



Vice President's Office



Federal Task Force



NCI/NIH



National Cancer Advisory Board



Blue Ribbon Panel



BRP Working Groups (ie Pediatric Cancer Working Group)



# 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**



# Cancer Funding in 21<sup>st</sup> Century Cures Act

- The cancer research portion is named the Beau Biden Cancer Moonshot Initiative
- Allows implementation of the BRP recommendations
- Specifies requirements
  - Data sharing
  - Health disparities

*“To support cancer research, such as the development of cancer vaccines, the development of more sensitive diagnostic tests for cancer, immunotherapy and the development of combination therapies, research that has the potential to transform the scientific field that has inherently higher risk, and that seeks to address major challenges associated with cancer.”*

# Barriers Identified by the BRP Pediatric Cancer WG

- Low mutation burdens, less likely to express neoantigens and be susceptible to immune checkpoint blockade therapies
- Most immunotherapeutic strategies that are in the pipeline of pharmaceutical companies are based on targeting specific antigens expressed on cancers occurring in adults
- Identifying the optimal childhood cancer cell surface antigens for targeting with immunotherapy agents remain a challenge; Little is known about the proportion of the cell surface proteome that is required for tumor cell maintenance;
- Tumors establish a disabling, immunosuppressive TME

## Recommendation B

Development of a pediatric immunotherapy translational science network that would facilitate the testing of new immunotherapy approaches in childhood cancer and establish a robust research pipeline to help further advance this field of study

### **Blue Ribbon Panel Pediatric Cancer Working Group Recommendations:**

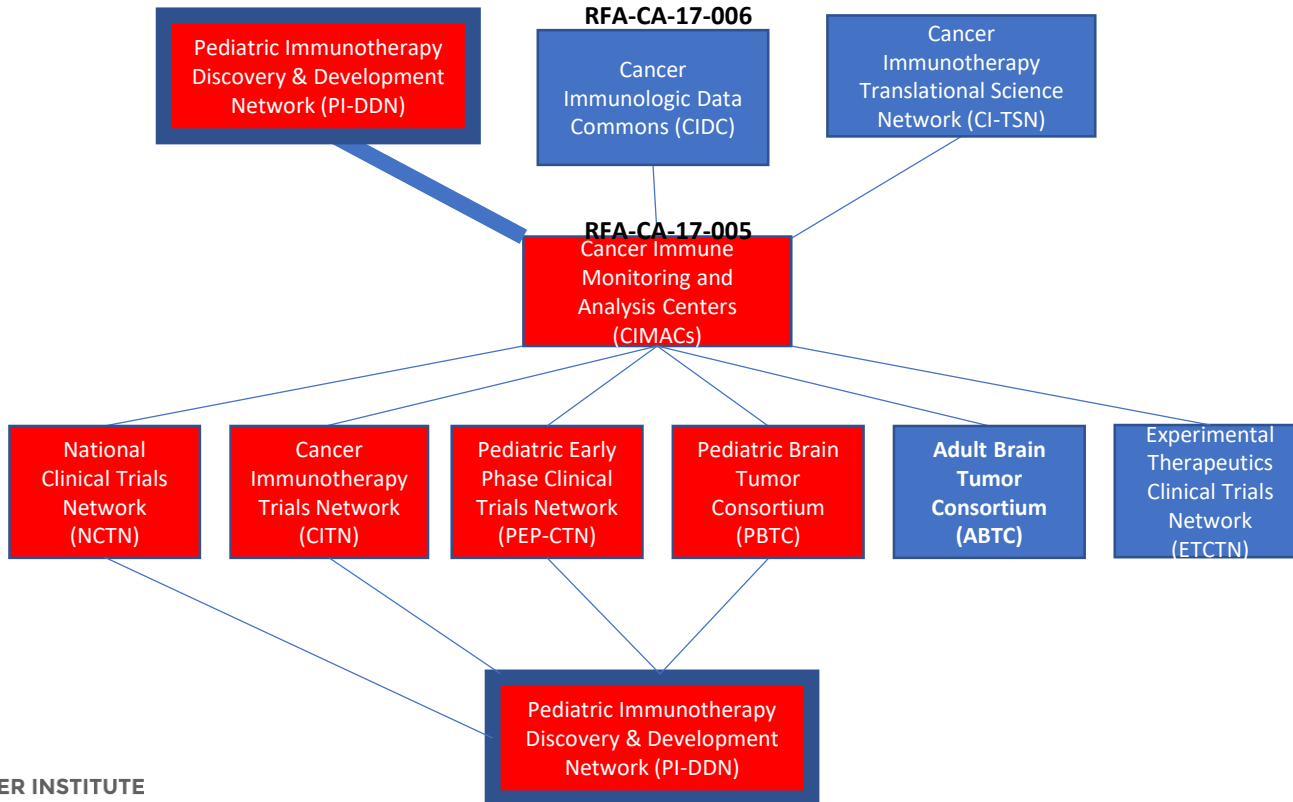
- Identification of antigenic epitopes that are uniquely and abundantly expressed on childhood and adolescent cancers.
- Development of optimized, highly specific binders for novel pediatric cancer immunotherapy targets.
- Development of candidate novel immunotherapy agents.
- Identification of cancer 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 and Development Network (PI-DDN)

- A Collaborative Research Network with planned regular meetings
- 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.
- A set-aside of \$1 million to provide support for collaborative activities across the network for years 2-5.



# NCI Cancer Immunotherapy Networks (Comprehensive)



## Key Dates

- Open Date (Earliest Submission Date): **November 19, 2017**
- Letter of Intent Due Date: **November 20, 2017**
- Application Due Date **December 19, 2017**

(by 5:00 PM local time of applicant organization)

**We strongly suggest that applications be submitted a week in advance!**

- Scientific Merit Review **March 2018**
- Advisory Council Review **May 2018**
- Earliest Start Date **July 2018**

# Specific Requirements for U54 Applications

- Proposed Center must focus on a comprehensive research program that includes both discovery and characterization of pediatric cancer immunotherapeutic targets and identification of paths forward for development of novel therapeutics strategies
- **Conduct of clinical trials is outside the scope of the PI-DDN**
- Centers will include 3 or 4 Research Projects(relevant, complementary and synergistic areas)
- Multi-institutional collaboration is encouraged and to accelerate the pace, but not required
- Center organization should include: administrative core, research projects and shared resource core (optional)
- Expected to work collaboratively with other PI DDN awardees

# Letter of Intent (LOI)

**Due November 20, 2017**

**Highly encouraged**, but not required. *Not binding and does not enter into the review.*

## **Standard elements:**

- Descriptive title of the project
- Name(s), address(es), telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating Institution(s)
- Number and title of this funding opportunity (RFA-CA-17-050)

## **Additional recommended information:**

- **Provide a brief (3-5 sentence) description of the project**
- **Include relevant expertise**

**Email LOI to [mietzj@mail.nih.gov](mailto:mietzj@mail.nih.gov)**

## U54 Budget

Application budgets are limited to \$1.6 million in direct costs per year, and need to reflect the actual needs of the proposed project.

**Funds Available and Anticipated # of Awards:** The NCI intends to commit approximately \$4 million dollars total cost in FY 2018, contingent upon receiving scientifically meritorious applications. One to 2 awards are anticipated to be funded from this solicitation.

**Project Period:** Not to exceed 5 years.

# Mechanism of Support

## **U54**, Specialized Center--Cooperative Agreement

*The spectrum of activities comprises a **multidisciplinary attack** on a specific disease entity or biomedical problem area. These differ from program project in that they are usually developed in response to an announcement of the programmatic needs of an Institute or Division and subsequently **receive continuous attention from its staff**. Centers may also serve as regional or **national resources for special research purposes**, with funding component staff helping to identify appropriate priority needs.*

## **Read Cooperative Agreement Terms**

- Oversight by NCI staff
- Participation in PI-DDN Consortium

## Structure of PI-DDN U54 Centers

- **3-4 Research Projects** that address identifying new targets for immunotherapies, developing new pediatric immunotherapy treatment approaches and defining the biological mechanisms by which pediatric tumors evade the immune system. Each project should focus on relevant, complementary and synergistic areas of immunotherapy.
- **Administrative Core** to manage and coordinate all Center research and activities and serve as the liaisons between the Center and the PI-DDN.
- **Shared Resource Cores** (optional) may be established to provide expertise and resources that support and integrate multiple Research Projects. Each proposed Core must serve 2 or more Research Projects.

## Administrative Details (U54)

- **Note on Eligible Applicants:** Foreign (non-U.S.) institutions are **not** eligible to apply as PD/PI, but foreign components are allowed.
- No late applications will be accepted.
- Page limitations for Research Strategy/Program Plan (in addition to the one page Specific Aims page):
  - 12 pages for Overall component
  - 12 pages for Research Projects (minimum of 3, maximum of 4)
  - 6 pages for Admin Core
  - 6 pages for Shared Resource Cores (optional, maximum of 3)
- Do not use appendix to circumvent page limits.
- **Read all directions carefully!**



# Overall Component for U54 Applications

## **PHS 398 Research Plan (FOA Part 2, Section IV):**

- Instead of standard sections (significance, innovation, approach), focus on overall vision and goals for the proposed PI-DDN Center, including:
  - *Center Overview*
  - *Center Organization and Integration*
  - *Research Projects*
  - *Shared Resource Cores (optional)*
  - *Health Disparities.* If applicable to the type of research project being proposed, the Research Strategy must address how health disparity populations or data will be integrated into the proposed studies.

# Administrative Core for U54 Applications

## Budget:

- Contact PD/PI must commit a minimum of 1.8 person-months effort/year to U54. Other PDs/PIs must devote  $\geq 1.2$  person-months to their respective projects.
- The budget should include funds to support travel for Center and PI-DDN activities, including but not limited to:
  - In the first year, supporting the participation of PD(s)/PI(s) in an initial PI-DDN Planning Meeting and SC meeting
  - Supporting the participation of the PD(s)/PI(s) and other Center members in an annual SC Meeting.
  - Centers are encouraged to include early career scientists in the PI-DDN activities and should include budget to travel at least one graduate student or postdoctoral fellow to the Annual Investigators' Meeting.

## Administrative Core for U54 Applications (Cont.)

### **PHS 398 Research Plan should include (FOA Part 2, Section IV):**

- Plans to support the multidisciplinary research teams, foster synergy and integration in the Center, and support planning and evaluation activities.
- *Management and Communication Plan.*
- *Annual Meeting and Other Consortium Activities.*
  - Brief description of strategies for connecting and integrating the Center with the broader PI-DDN.
- *Outreach plan.*
  - Promote training and career development of researchers in the Center, educate the biomedical community on immunotherapy for childhood cancers, and disseminate advances and capabilities of PI-DDN to broader cancer research community.

## U54 Research Projects

- Each PI-DDN Center should have 3-4 Research Projects

### **PHS 398 Research Plan should include (FOA Part 2, Section IV):**

- Overall strategy for the Research Project
- Concise description of how it fits into organizing framework of the PI-DDN Center
- Standard sub-sections (Significance, Innovation, and Approach)
- Clearly identify any innovative biological concepts proposed to be explored as a potential basis for novel immunotherapeutic strategies for childhood cancer
- Project Timeline: A timeline (Gantt chart) including yearly milestones

## U54 Shared Resource Cores (optional)

- If included, must support at least 2 Research Projects.
- May be physical or virtual infrastructure providing a resource that supports other Center components in their activities. The services and resources provided to other Center components should be clearly defined.
- Issues to be addressed include, but are not limited to: *value* of the Core services to the Center and Research Projects, *integration* between the Core and Projects, *quality control*, procedures for selecting Projects to use the Core and *allocating resources*, cost effectiveness, and increased *efficiency*.
- Training in complex techniques and methods should be described if they are functions of the proposed Core.
- These shared resources ***must not duplicate analogous resources*** already established in the applicant institutions (although supplemental funding to such existing resources may be requested).

# Scientific Review

- Reviewers will provide an overall impact score for the entire PI-DDN Center (Overall Component) and for each individual Research Project.
  - In addition, assigned reviewers will provide individual "criterion scores" for the Overall criteria and for the Research Projects criteria, but not for the other components.
  - The Administrative Core and optional Shared Resource Cores will be evaluated, but each will receive only one overall adjectival (not numerical) rating.
- For the evaluation of the PI-DDN Center application, the Research Projects will be emphasized as the scientific base of each Center, with additional components enhancing and integrating the overall research program.

## Scientific Review (continued)

- **These grants have additional review criteria (see RFA)**
- Appeals of initial peer review will not be accepted.
- Recommended applications will receive a second level of review by the National Cancer Advisory Board.

The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review
- Availability of funds
- Relevance of the proposed project to program priorities

## RFA-CA-17-051: U01 Grants

- Solicits U01 applications for discrete research projects that address relevant research opportunities (e.g., mechanisms of immune evasion, model development, validation of a single target etc)
- NCI intends to fund 6-10 awards, corresponding to a total of \$4 million in total costs for FY 2018, contingent upon receiving scientifically meritorious applications. Future year amounts depend on annual appropriations
- RFA-CA-050 solicits multi-component U54 Center applications
- Successful applicants from both FOAs will become members of the PI-DDN which will address and implement the BRP recommendations



## Participation in PI-DDN

- Both the U54 and U01 are cooperative agreement mechanisms.
- Grantees are expected to actively participate in PI-DDN
- PDs/PIs will serve on the Network Steering Committee (SC), the primary governing body of the Network, to discuss community issues, set policies, and plan and evaluate activities to meet Program goals.
- SC will meet regularly by teleconference, and Network members will meet in person at an Annual Program Meeting.
- Read cooperative agreement terms carefully.

# Addressing the Cancer Moonshot Public Access and Data Sharing Policy:

- Utilizing the provision outlined in the 21st Century Cures Act, NCI has established a data sharing policy for projects that are funded as part of the Beau Biden Cancer Moonshot Initiative that requires applicants to submit a Public Access and Data Sharing Plan that **describes their proposed process for making resulting Publications and, to the extent possible, the Underlying Primary Data immediately and broadly available to the public upon publication** or (if applicable) provides a justification to NCI if such sharing is not possible.
- NCI will give competitive preference and funding priority to applications that comply with the strategy described at [NCI Cancer Moonshot<sup>SM</sup> Public Access and Data Sharing Policy website](#).
- The data sharing plan will become a term and condition of award.

## Agency Contacts (See FOA Section VII)

### Scientific/Research Contacts:

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Division of Cancer Treatment and Diagnosis  
National Cancer Institute (NCI)  
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### Peer Review Contact:

Syed Quadri, Ph.D.  
Center for Scientific Review (CSR)  
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Email: [quadris@mail.nih.gov](mailto:quadris@mail.nih.gov)

### Financial/Grants Management Contact:

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Slides will be posted on the NCI DCB website:  
<https://www.cancer.gov/about-nci/organization/dcb>



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