

RFA for an NF1-Related MPNST Data Coordination Center to Support Patient-Derived Model Development and Testing Centers

The **NF Research Initiative at Boston Children's Hospital** is focused on accelerating therapeutic development for NF1-related Malignant Peripheral Nerve Sheath Tumors (MPNSTs) www.nfresearch-childrens.org

Funding Opportunity Description

Purpose of this RFA:

The purpose of this RFA, and the companion RFA for Patient-Derived Model Development and Testing Centers (MDTCs), is to produce actionable pre-clinical data about response to single agent and combination agents using patient-derived NF1-related MPNST models such as PDX and organoids, with the goal of informing human clinical trials for NF1-related MPNST. This award would support a project similar to the National Cancer Institute's (NCI) PDX-Net.

Background

The desired deliverable for this RFA is a proposal for a Data Coordination Center (DCC) to interact with and coordinate with Patient-Derived Model Development and Testing Centers (MDTCs) that are being established through a companion RFA. The pre-clinical data will involve response to single agent and combination agents using patient-derived NF1-related MPNST models such as PDX and organoids, and the goal of the DCC is to identify correlates between drug response and the "genomic signature" of individual human tumors to inform human clinical trials for NF1-related MPNST.

The Lead PI applying for this award could be from an institution that is separate from the PIs of the MDTCs. Alternatively, the Contact/Lead PI of the DCC could serve as the Contact/Lead PI for the companion RFA for MDTCs. Even if the MDTC application involves multiple sites contributing and testing models, there must still be a single site designated as the DCC, and that should be at the same institution as the Contact/Lead PI of the multi-site Model Development and Testing team.

Proposals for the MPNST DCC must include the following components:

1. Description of the Plan for Coordination of Data
 - a. The DCC has an important role in collecting and analyzing data from multiple models, and potentially across sites. The proposal will need to outline how the DCC will provide administrative and logistical coordination support for collection and analysis of the data.
 - b. Proposals will need to include a plan for adherence to community data standards (e.g., PDXNet for PDX models).

2. Description of Leadership

- a. Documentation of the experience and expertise of the DDC Contact/Lead PI and team members for analysis of data related to patient-derived pre-clinical models, specifically PDX and organoids.
- b. The DCC Contact/Lead PI must provide scientific oversight to the planning and execution of data generation to ensure that high quality data is delivered from the MDTCs.

3. Description of Bioinformatics Capabilities

- a. The DCC must provide appropriate bioinformatics and biostatistics expertise, and computational resources, to support the analysis and integration of complex data from multiple experimental platforms.
- b. Necessary expertise includes an understanding of the clinical variables related to MPNST and the patient-derived models.
- c. It is expected that the DCC will integrate the findings of individual MDTCs into actionable recommendations for the design of human clinical trials for MPNST.

Award Information

Source of Funds: The NF Research Initiative (NFRI) at Boston Children's Hospital is funded by a philanthropic donation.

Award Period: The funding period will be December, 2019 to December, 2021.

Award Budget: Application budgets for direct costs (including fringe benefits on salary) must not exceed \$200,000 per year. In addition, institutional IDC will be provided at a rate of 20%.

Important Dates:

1. Submit a 1-page LOI by Thursday, August 22, 2019 at noon EDT
2. Response to LOI (invitation to submit) within 1 week of receipt of LOI
3. Full application (if invited) by October 14, 2019 at noon EDT
4. Award notice: November 27, 2019
5. Funds available as of January 1st, 2020 (pending contract).

Budget Considerations for Data Coordination Center:

- A single Contact PI will be the Project Lead. Team members related to the DCC must be at the same institution as the Contact PI. Lead PI can request salary support up to 20% of the NIH maximum (and fringe, included as a direct cost). A Co-PI can request salary support up to 10% of the NIH maximum (and fringe, included as a direct cost). All salary costs and fringe are to be included in the total budget.

- Budget must include all expenses related to compute infrastructure and data storage.

Project Governance

Similar to NCI's PDXNet, investigators must agree to a governance model that is designed to facilitate coordination and cooperation, avoid unwarranted duplications of effort, and provide a diversity of scientific input (e.g., about selection of drugs and models to be tested).

1. The MDTC RFA stipulates the creation of a Steering Committee that includes each funded PI, the NFRI Director, and 2 outside advisors (at least one of these consultants to be appointed by the NFRI Director).
2. The Lead/Contact PI for DCC must serve on the Steering Committee.
3. The Steering Committee will assist with scientific direction of the project (e.g., selection of models and drugs to test, serve to monitor progress, and provide feedback to optimize the outcome of the coordinated project).
4. Stipend for the 2 outside consultants, costs for travel to an in-person Steering Committee meeting, and administrative support for scheduling of quarterly teleconference meetings will be provided by NFRI separately from this project budget.

Data Sharing

Cooperating Institution(s) are expected to share data from this project with the NF research community at the end of the embargo period. The NF Research Initiative is following the Synodos model created by the Children's Tumor Foundation, which has partnered with NTAP and contracted with Sage Bionetworks to support the NF Data Portal. The MDTC will coordinate with Sage Bionetworks to make sure all data is available to the NF data portal as well as other specific repositories sharing similar data. The ability to share data through the NF Data Portal at Sage Bionetworks will be provided at no additional cost to the investigators, and does not need to be included in the Project Budget. Sharing of the data on the NF Data Portal requires that the investigators (1) upload their raw data files in a timely manner ahead of sharing within the NFRI community, (2) format the data files in accordance to the NF Data Portal SOPs for data sharing, and (3) describing the data files accurately through the NFDP metadata dictionary.

Eligibility:

- Applications from academic and industry settings will be considered.
- Applicants must be addressing pre-clinical research questions intended to identify new effective therapies for NF1-related MPNSTs.

Structure of the Proposal (if invited, and further details will be provided)

- Background of expertise in analysis of drug screening data and bioinformatics capabilities at the proposed DCC site.
- Brief description of data analysis and coordination plan.
- Collaborators and Key Personnel: describe each person's role, and provide letters of support and biosketches for each.
- Statement of potential COI during the screening and review processes: list all individuals, other than collaborators and key personnel, who may have a COI in the review of the application
- Page Limit: 4 pages (single-spaced)

Selection Process: LOI will be screened by the NFRI leadership. Investigators submitting LOI in line with the stated goals will be invited to submit a full proposal. Proposals will be sent for peer review. Scoring will be according to the plan for data analysis and coordination, and investigator/team commitment and qualifications. Appropriateness of budget related to planned research will be considered secondarily. The NFRI Scientific Advisory Committee will assess the peer reviewer recommendations and make final decisions for the awards.

To Apply:

- Email a one page letter of intent (LOI) with:
 - Contact information of the Lead/Contact Principal Investigator
 - A one paragraph description of the background and expertise of the Lead PI and team relevant to this proposal, bioinformatics capabilities at the institution, and brief description of the compute infrastructure.
- Further application instructions will be sent with the response to LOI, and you can anticipate an application length of 4 pages or less (including references and figures, but not including budget justification or biosketches)

Email: NFresearch@childrens.harvard.edu

Website: <https://www.nfresearch-childrens.org/>

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Boston Children's Hospital**