Pre-Application Webinar for Molecular Profiling to Predict Response to Treatment (**MP2PRT**) Program

Retrospective Characterization and Analysis of Biospecimens Collected from NCI-Sponsored Trials of the NCTN and NCORP

Webinar will begin at 3:00 PM Eastern

NCI National Clinical Trials Network
a National Cancer Institute program

December 11, 2020

Website: Program Announcement Available and Webinar Slides / Recording Will be Posted

https://ctep.cancer.gov/initiativesPrograms/nctn.htm

2020 Molecular Profiling to Predict Response to Treatment (MP2PRT) Program Announcement:

Program Title	Documents
NCI Molecular Profiling to Predict Response to Treatment (MP2PRT) Program: Retrospective Characterization and Analysis of Biospecimens Collected from NCI-Sponsored Trials of the NCTN and NCORP	**MP2PRT Announcement** (MS Word) **December 11, 2020 Webinar Information** (PDF) **Cancer Moonshot℠ Initiative**

Closed captioning available:
https://www.captionedtext.com/client/event.aspx?EventID=4664141

Pre-Application Webinar Topics for MP2PRT

1. Program Purpose
2. Key Changes
3. Program Design and Timeline
4. Program Eligibility
5. Application Components
6. Criteria for Review
7. Contact Information

Program Purpose

- MP2PRT program comes out of the Cancer Moonshot^{SM} Initiative and is supported by dedicated funds from the 21st Century Cures Act

- Targets a scientific priority designated by the Blue Ribbon Panel
  - Retrospective analysis of biospecimens already collected from patients enrolled on completed NCI-sponsored clinical trials of the National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP) that have outcome results available

- Successful proposals will be those that are exploratory, hypothesis-generating, or hypothesis-driven, and that propose studies wherein comprehensive molecular analyses could answer a key clinical question or lead to additional important clinical research or trial designs

See program announcement for full information:
https://ctep.cancer.gov/initiativesPrograms/docs/NCI_MP2PRT_Program_Announcement.docx

Key Changes in This Program Announcement

- No set cap on the number of biospecimens included in the proposal
- Clinical trial(s) from which biospecimens are requested must be closed to accrual, but the time period for when outcome results expected is extended to within 18 months of March 2021
- Include ability to include collected & stored images as “clinical data” with funding for appropriate de-identification and submission to TCIA for data sharing

- Reemphasizing that molecular characterization can include sequencing and other characterization, as well as assessment of minimal residual disease
- Reemphasizing that proposals can be **exploratory** (e.g., providing sequencing on a unique dataset in disease area where this type genomic information is not available – diverse population/rare cancer) or **hypothesis generating**

Program Design: Key Elements

- MP2PRT projects are conducted via **subcontracts** to the Group/Research Base for the selected proposal and to subcontracted characterization laboratories and analysis centers as needed
  - Proposals should describe requested molecular characterization techniques and may suggest laboratories capable of conducting the requested characterization, but the laboratories will ultimately be selected through standard contracting processes by the NCI contractor for this project
  - Analyses will be performed as a collaboration between the Group/Research Base and the investigators at the subcontracted laboratories who characterize the samples

Program Design

Proposal selection (anticipated 4 months, by July 2021)

NCTN/NCORP Groups submit proposals to NCI for scientific and feasibility review.

NCI selects proposals to recommend for funding (revisions likely required).

Note: Proposal selection is contingent on successful negotiation of all necessary subcontracts with NCI's contractor, Leidos Biomedical Research, Inc (LBR)

Proposal subcontracting (anticipated 4-6 months, by January 2022)

LBR requests Technical and Cost Proposals for subcontracts needed to carry out the recommended proposals *(e.g., with the Groups and any new contracted laboratories).*

LBR negotiates and executes subcontracts.

Project initiation

LBR holds subcontract kickoff meetings and begins planning regular meetings with all stakeholders.

LBR coordinates the execution of required DUAs and MTAs *(e.g., between the biospecimen bank and the subcontracted laboratories).*

Subcontracted project work is completed (anticipated by December 2023)

Project is registered in the appropriate databases.

Specimens are processed and shipped to the selected characterization laboratories.

Biospecimen and clinical data are shared with the study team and submitted to databases as needed.

Characterization results are returned to the study team and analyzed for publication within 2 years.

Timeline

- Release Date: Wednesday, December 2, 2020
- Webinar: Friday, December 11, 2020, 3-4 PM ET
- Receipt Dates for Proposals: Monday, March 15, 2021
- *Anticipated proposal selection: July 2021*
- *Anticipated execution of necessary subcontracts for selected proposals: January 2022*
- *Anticipated project completion: December 2023*

Program Eligibility

- Limited competition
  - Currently funded NCTN Network Groups and NCORP Research Bases
  - No limit on the number of proposals that can be submitted by each Group/Research Base
- Proposals must be for use of biospecimens collected from fully accrued NCI-sponsored NCTN or NCORP trials in which:
  - Clinical data have already been presented or published **OR**
  - Publication or presentation at a major scientific meeting is expected within 18 months of March 15, 2021 (by September 2023), **AND** any clinical outcome data needed to inform case selection or otherwise inform the project will be available to allow the project to complete within two years
- Proposals must include all of the application components described in the program announcement

Application Components: Overview

- Cover letter signed by NCTN Network Group Chair or NCORP Research Base PI
- Proposal using provided proposal form (should not exceed 10 pages)
- Budget prepared according to the Budget Preparation section in the program announcement
- Letters of support from Statistical Investigator and Biospecimen Bank PI

Application Components: Cover Letter

- Cover letter must be signed by the NCTN Network Group Chair or NORP Research Base PI and must include:
  - Title of the proposed study and title of the clinical trial(s) from which specimens and clinical data will be used
  - Brief description of the proposed study with reference to whether clinical data from the clinical trial(s) are **already available** or **when** they are anticipated to be available
  - **Total budget figure** projected for the study. This total number must be across all years, must include all sub-totals, and must include the **total** anticipated contract costs, including both **direct** and **indirect** contract costs.
  - For NCTN proposals, the cover letter must also include **sub-total budget figures** projected for the **Operations**, **SDMC**, and **Biospecimen Bank** components of the project as applicable (**total contract costs**)

Application Components: Proposal

- Applications must use the proposal form provided in the Program Announcement
- Proposals should not exceed 10 pages, excluding illustrations, appendices, and budgets
- Key proposal components:
  - Objectives and hypotheses
  - Background and justification
  - Justification for characterization of specimens from the requested clinical trial(s), including a brief description of the trial(s)
  - 1-page narrative description of proposed study
  - Information about requested specimens, risk of depletion, and any pathology or enrichment requirements
  - Characterization methods requested
  - Proposed facilities and personnel, including any need for bioinformatic analysis expertise and capacity for storing and analyzing genomic data
  - Endpoints/outcomes and case selection
  - Appropriate statistical analysis plans
  - Information about clinical images, if requested
  - Projected timeline

Application Proposal: Notes for Hypothesis-Generating and Exploratory Proposals

- **Objectives and hypotheses**
  - Studies that are hypothesis-generating or exploratory should clearly indicate this in the objectives and hypotheses sections
- **Appropriate statistical analysis plans and sample size**
  - **Analysis plans:** For hypothesis-generating and exploratory proposals, include an appropriate and sufficiently detailed statistical plan to allow the reviewers to assess the value of the proposed hypothesis-generating/ exploratory analyses. Indicate the specific quantities that will be evaluated and the general statistical framework (e.g., estimation, association, comparison, prediction).
  - **Sample size:** For hypothesis-generating and exploratory proposals, it is understood that there may not be adequate power to assess all proposed exploratory aims. Therefore, please state if you simply request biospecimens from all cases with adequate biospecimen available or if your sample size is based on another rationale. For projects requesting characterization of a large number of specimens, it is recommended that example power calculations be provided if any statistical inference will be reported.
  - Include all requested information in the statistical sections **as applicable**

Application Components: Budget (slide 1)

- Funding for approved proposals will be provided via a contract mechanism, rather than a grant supplement. Proposal budgets should be prepared accordingly.
- The budget must NOT include costs covered any NCTN or NCORP grant.
- Separate budgets sections should indicate which costs would be paid to each NCTN Group grant component. A single budget can be used for NCORP Research Bases.
- Because this program will be conducted through sub-contracts, the budget should clearly identify how much funding is being requested for each distinct institution.

- The budget should use the Form PHS 398 with narrative justification for each cost. The detailed narrative justification for each budget section should:
  - Provide details and rationale for all included costs,
  - Confirm that the indirect cost rate applied is the rate used for contracts, and
  - Include the total costs for each section.

Application Components: Budget (slide 2)

- The budget may include:
  - Biospecimen bank costs for locating, assessing, preparing, and shipping biospecimens to the contracted laboratory
  - Statistical center costs for preparation and transfer of relevant patient-level clinical and outcome data from the trial(s) to the appropriate data repositories and costs to support reasonable biostatistician involvement in the proposed research project
  - Operations center costs for the preparation and submission of clinical images to an appropriate database (if requested) and costs to support reasonable lead investigator and operations staff involvement in the proposed research project

Application Components: Letters of Support

- Proposals must include two letters of support with the following information
  - Statistical Investigator:
    - Verify the availability of the relevant data for sufficient patients with the relevant consent under standard DUA terms in a timely manner
    - Include the sub-total budget figures for the funding requested for the statistical work under the project
    - Verify that the requested funding is not covered by existing NCI grants and will cover the anticipated data costs
  - Tumor Bank:
    - Verify the availability of the specimens for processing and transfer for the project under standard MTA terms in a timely manner
    - Include the sub-total budget figures for the funding requested for the biospecimen bank work, including locating, assessing, preparing, and shipping biospecimens as well as providing biospecimen information to the appropriate databases
    - Verify that the requested funding is not covered by existing NCI grants and will cover the anticipated bank costs

Criteria for Review of Proposals

- **Proposals will be reviewed by NCI for scientific merit and feasibility of the work**
- **Key review considerations:**
  - Inclusion of comprehensive molecular analyses which will answer a key clinical question(s) or fill a gap in existing data and generate valuable data for future research
  - Ability to address the study hypothesis(es) and/or achieve the study's hypothesis-generating or exploratory goals with the number and quality of biospecimens available
  - Inclusion of an appropriate statistical plan for the proposed project, whether exploratory, hypothesis-generating, or hypothesis-driven, with sufficient detail to assure reviewers that the investigators will be capable of carrying out the project
  - Ability of the proposed study to fill a gap in our understanding of health disparities in a special population(s)

Contact Information – MP2PRT

Announcement and Webinar Slides/Video (to be posted):
https://ctep.cancer.gov/initiativesPrograms/nctn.htm

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