Our Patient Project
Request for LOI (Phase 1 of 2)

Purpose and Overview

Our Patient Project (OPP) is an important translational research element of the MCW Cancer Center (CC)-led Precision Oncology high-impact initiative that is expected to drive discovery over the next three years. The OPP has two goals: 1) To answer a significant unanswered question in the cancer research field or address a major challenge in clinical care by fully characterizing and analyzing samples from a discrete, clinically annotated cancer patient cohort; 2) To develop a rich experimental data set on patient samples annotated with high quality clinical data that can be leveraged by the Principal Investigator (PI), study team, and MCW CC members to foster new multi-disciplinary collaborative research projects funded through extramural sources (*e.g.,* Multi-PI R01s, P-, U- or M-type grant awards, sponsored clinical trials) and that will lead to novel practice-changing cancer prevention and/or therapeutics. This funding program opportunity is anticipated to be open through 2025, with 2-3 full applications funded per year. Each meritorious application will receive up to 4-5 years of funding. Projects will be selected for funding using a two-stage process: a letter of intent (LOI; Phase 1) followed by a full proposal (Phase 2) from invited teams. This document provides a program description and instructions for submitting the LOI. Resubmission of revised LOIs and full proposals are allowed in subsequent rounds.

Program Description

OPP will be a long-running research endeavor of the MCW CC's Precision Oncology high-impact initiative. Funding for the first round of applications is expected to start by September 2022; additional projects will be funded on a rolling basis through 2025 or until further notice.

Successful LOIs will address the following project attributes. ***Attributes 1 and 2 are the most important*** at the LOI stage. A detailed statistical analysis need not be presented in the LOI but data supporting that sufficient accrual can be achieved (or that sufficient high-quality data exists for retrospective analyses) is necessary.

1) The project will answer a major scientific question: Each project will be designed to answer a major question about cancer etiology, cancer prevention, cancer biology, cancer disparities, and/or cancer diagnosis, treatment or survival. The research question must address an unmet need where a definitive answer to the question has not been published.

2)The study cohort will be clearly defined: Central to OPP is the definition of a patient cohort that is represented in or is representative of our catchment area (eastern Wisconsin area; see attached map and list of counties). This cohort can be delineated by a combination of demographic, geographic, clinical and molecular features. The cohort and its issues may not be unique to this area but must represent a group with well-defined unmet needs, relevant to our catchment area, to be addressed by the project. Demographic data will include some combination of age, gender, race, income and education. Clinical features may include some combination of family cancer and other health history, comorbidities, past medical history, smoking history, nutrition/diet, somatic and/or germline mutations, stage at diagnosis, organ of origin, stage at enrollment, pathological grade, and specific aspects of treatment history. For common data elements to be uniformly captured in all cohorts, data acquisition and transfer to a centralized location will be required in order to manage storage and security. This single platform will be developed by the CC; investigators must work with staff to adapt the platform to the needs of the specific project. Projects that can take advantage of automated data transfer from the electronic health record are encouraged.

3) Project will involve a multi-disciplinary team: Each project will be carried out by a multi-disciplinary team. The team may include faculty in medical oncology, surgical oncology, radiation oncology, gynecologic oncology, radiology, pathology, bioinformatics, systems biology, database programming and management, population sciences, translational sciences, clinical sciences, basic sciences, and statistics. The LOI will provide a preliminary

indication of team membership or composition. Also, the team should describe the approximate number and type of trainees (undergraduate students, graduate students, postdocs, staff scientists, clinical fellows) expected to participate and be supported by the project; exact team composition can be finalized during full proposal preparation.

4) The project will interrogate omic-scale molecular features of the cohort and integrate comprehensive data analysis. OPP seeks to fund projects that analyze molecular features of their cohort consisting of genomic, transcriptomic, epigenomic, proteomic, metabolomic, metagenomic, immunomic, lipidomic and/or glycomic tests. This may also include some permutation of somatic mutations, cytogenetics and chromosomal aberrations. It is understood that some of these assays may have already been performed in the course of routine clinical care or as part of a trial. The project will propose to perform additional assays on patient samples and include a general description of data analyses needed to answer the question posed. Feasibility of assays proposed must include expected recruitment rate, statistical evaluation of sample size and technical replicates, evaluation of sample quantity and quality, sample preparation and compatibility with established methods, and pathological assessment of patient samples to be analyzed. The program should also consider additional assays that may be desired or needed in the future and related feasibility parameters necessary to expand the initial scope of the project and/or combine with other projects' data sets.

Additional Considerations

Amendments to a master protocol may be needed. A master protocol will be in place and IRB approved for these studies; however, protocols for projects requiring consent for procedures, data or other items not covered by the master protocol will need to be developed by the team through amendment of the master protocol.

Team formation, cohort definition, assay specification and proposal for data analyses will continue for teams invited to submit a full proposal. For maximal impact and chance of success, reviewers, CC and CTSI leaders, CTO leaders, and Shared Resource directors will work with the PI and senior project team members to optimize investigator team composition; specifics regarding cohort definition, clinical annotation and specimen procurement, processing and storage requirements; specified assays; and proposed data analyses.

Priority Areas

Researchers working in all areas of cancer science are invited to apply. Priority will be given to projects that use multi-disciplinary technologies and approaches, propose to study topics related to understanding or addressing cancer disparities in WI, and address clinically important challenges faced by the WI population and their cancer care givers. Inclusion of correlative studies that utilize MCW Shared Resources are highly encouraged, and when shared resources outside of MCW are proposed, appropriate justification is required.

Eligibility and Evaluation

Eligibility

- Proposed research must be cancer relevant.
- MCW faculty members are eligible to apply. At least one team member must be a CC member.
- Research can take place, and expenditures incurred, only at MCW, Children's Wisconsin, Froedtert Hospital, Versiti BRI, Children's Research Institute or the Zablocki VAMC.
- A clear case for the feasibility of completing the project in a four-year time frame must be made.

Evaluation

LOIs will be evaluated by a panel of physicians and scientists comprising CC leadership, CC Program Leaders, CTO leaders, DOT leaders, Shared Resource directors, and a member of the CC Biostatistics Shared Resource (BSSR), as well as internal and external referees with appropriate expertise, including in areas of pathology, omics, biostatistics, methodology, and with expertise in clinical, basic, population and social sciences.

Review criteria include the following. The first two are most critical at the LOI stage:

- **Importance of the question:** impact of the proposed research question on cancer biology or patient care
- **Cohort characteristics**: relevance to CC catchment area (see attached Wisconsin map and list of counties) and need for reducing cancer health outcomes disparities
- Standard NIH criteria (significance, innovation, approach and investigative team)
- Likelihood that sufficient patients can be recruited or already exist in an accessible database in the timeframe of the research study
- Likelihood that clinical annotation will be available in sufficient detail and quality controlled
- Likelihood that patient samples will be of high quality
- Likelihood that molecular data derived from the study will be high quality
- Validity of statistical analysis plan, including estimates of sample size and power
- Discussion of pitfalls and alternatives
- Likelihood that preliminary results will lead to externally funded research projects, protocols, a LOI from pharma and/or extramural grant funding
- PI and key personnel participation in CC programs (*e.g.,* attend Research Program meetings, serve on CC grant review panels, participate in CC High-Impact Initiatives, participate in recurring seminars or symposia).

Budget

Maximum project budget is $1M total (see also below) over a maximum of 4-5 years. LOI must include anticipated "best estimate" budget for the following categories: personnel (staff, trainees); supplies; sample retrieval, preparation and analysis; assay development and data analysis; data storage and distribution.

Instructions for submitting LOI

Application Format: Use standard 11-point font, single space, and half-inch margins throughout the application. Use pleasing white space. Consecutively number all pages.

- **Cover Page:** To initiate, please email MCWCCResearchPrograms@mcw.edu for a unique link to begin the process. You will be asked to sign into your Faculty Collaboration Database (FCD) and rerouted to our internal system. Certain fields will then be auto populated. Include project title, lead investigators and affiliations. Combine (concatenate) the cover page produced with the remainder of your LOI materials for submission (see below).
- **Scientific Abstract** (250-word limit): Provide a summary of the project.
- **Lay Abstract** (200-word limit): Provide a brief summary of the proposed research project in layman's terms. If funded, this abstract may be distributed to the funding source and used in written correspondence with donors and interested parties.
- **Question** (2-page limit)**:** State concisely the question being addressed. Expand on the question by providing background, description of unmet need, and why the answer is important for cancer biology or patient care, including relevance to the catchment area.
- **Cohort** (1/2-page limit)**:** Describe the patient cohort to be analyzed. Narrow the cohort down by providing as much detail as is reasonable, including sociodemographic characteristics, clinical characteristics, any molecular profiling already available, and treatment history that will define the cohort (see "The study cohort will be clearly defined" above).
- **Analysis** (1-page limit): Describe the planned assays and how the cohort, patient and assay data will be analyzed to address the question. Describe the statistical approach plan envisioned. Consultation with a CC biostatistician at least 30 days prior to LOI submission deadline is required. This can be requested

through iLab.

- **Feasibility** (1-page limit): Provide information about cohort size; availability of detailed clinical data; anticipated recruitment rate; identity of institutions where patients were and/or will be seen; sample procurement, processing and storage; labs or parties to be performing study assays; and data QC that you feel will be helpful in evaluating project feasibility in the allotted time and veracity of conclusions.
- **Future Funding Plans** (250-word limit): State the federal agencies, corporations, non-profit organizations, mechanisms and timing of planned future trials or grant applications that will use the preliminary data produced under this award. State how data from this application will be used to support specific extramural proposals by the PI and/or study team.
- **Budget** (1-page limit)**:** A general budget outline is required for the LOI, but full proposal (if selected) may deviate from the budget included in the LOI.
- **Statement of Collaboration:** A statement from PI and collaborators indicating acknowledgement of participation in this proposal. A statement from the study team indicating that once the initial manuscript stemming (in part or in full) from the proposed work is published, the data will be accessible to all CC members to be queried and be used for development of new hypotheses, projects and grant applications, with appropriate acknowledgement and participation of the original study PI and study team. Guidelines for acknowledgement will be developed together with all awardees during the full proposal stage.
- **Literature Cited** (1-page limit): List references pertinent to the proposed research.
- **Outline and description of project team:** PI, faculty collaborators, staff, trainees, investigators thus far identified, and wherever possible, include their expertise and proposed roles in the project.
- **Biosketches:** Include a standard NIH-format biosketch for each key team member. Include the specific role of the team member in the personal statement. Include information on clinical trial leadership, if applicable.
- **Form D: Return on Investment.** Previous CC Pilot Grant recipients must complete.

Timeline

LOIs are **due by 5:00 pm on March 1 and September 1** of every year through 2024. Please email one PDF file of the LOI to MCWCCResearchPrograms@mcw.edu. CC leadership will contact the PI(s) after peer review regarding a plan for the PI and senior project team members to work with CC leaders, CTO leaders, and Shared Resource directors on optimizing investigator team composition; specifics regarding cohort definition, clinical annotation and specimen procurement, processing and storage; assays specified; and data analyses proposed. **Full proposals will be due the following September 1 and March 1 from LOI submission,** through March 2025. The start date for funding will be dependent on the status of any required human and animal studies protocol approvals, with the understanding that it will not take longer than six months post award notice. Please contact to MCWCCResearchPrograms@mcw.edu with any questions.

Program Expectations

- Publication in a high impact journal
- Presentation of results in a national forum
- Development, submission and award of an investigator initiated clinical trial or other translational/clinical research study with extramural funding support (NIH/NCI or industry sponsored)
- Development and submission of a funding proposal for extramural support; this could include proposals that include a clinical trial or that do not include a clinical trial.
- Final report is required upon project completion, including an outline of project results and clinical trials submitted or planned.
- Awardees will be required to serve on pilot study sections for three years.