

BASSER
CENTER
FOR BRCA



2020-2022

Grants Program for Penn Investigators

Application Instructions

Letter of Intent Deadline: March 9, 2020

Grant Submission Deadline: April 6, 2020

Request for Applications for Basser Research Awards: \$50,000-\$150,000 yearly x 2 years

Release Date: January 23, 2020

Due Date:

Letter of Intent- March 9, 2020 by 5:00pm

Full Application- April 6, 2020 by 5:00pm

PLEASE NOTE – THERE WILL BE NO EXCEPTIONS

Funding begins: July 1, 2020

Background and Purpose

The Basser Center for BRCA has the unique opportunity to catalyze research to change the paradigm of discovery, innovation, and care for issues related to *BRCA1* and *BRCA2* mutations. Germline mutations in

BRCA1 and *BRCA2* significantly increase the risk of breast and ovarian cancer and also are associated with prostate cancer and pancreatic cancer. Towards this end, the Bassett Center is seeking applications that propose innovative approaches to the focus areas listed below.

Although the Bassett Center will review and consider any application specifically focused on areas relevant to *BRCA1* and *BRCA2*, for this funding cycle we would like to highlight several areas of specific interest:

Focus Area #1: Organoid cultures

The recent advances in *in vitro* 3D culture technologies, such as organoids, have opened new avenues for the development of novel, more physiological human cancer models. Such preclinical models are essential for more efficient translation of basic cancer research into novel treatment regimens for patients with cancer. Importantly, tumor-derived organoids — both phenotypically and genetically — resemble the tumor epithelium they were derived from. Wild-type organoids can be grown from embryonic and adult stem cells and display self-organizing capacities, phenocopying essential aspects of the organs they are derived from. Genetic modification of organoids allows disease modelling in a setting that approaches the physiological environment.

Although drug screens on large 2D cancer cell line collections have provided major insights into genetic predictions of drug response, their fairly poor reflection of native tumor tissue may have contributed to the high failure rate of newly discovered drugs in clinical trials. Patient-derived tumor organoids better recapitulate native tumors and may be superior models to identify and test novel anticancer drugs.

Understanding how germline mutations (e.g. *BRCA1/2*) impact epithelial plasticity, microenvironmental factors, and predisposition to neoplastic transformation is another area where 3D organoid cultures are making headway. This RFA seeks applications that will deploy organoid technology to the study of *BRCA*-related cancers. Use of animal models and/or human tissues is expected, as are studies that propose to understand how *BRCA1/2* mutations effect normal cells-of-origin for organs typically at risk for cancer development due to *BRCA1/2* mutations (breast, ovary/fallopian tube, pancreas, prostate).

Focus Area #2: Haploinsufficiency

Currently the impact of haploinsufficiency on tissue tropism and cancer transformation is not well understood. In this focus area, studies examining the impact of haploinsufficiency and any potential interaction with environmental exposures (for examples aldehydes) are encouraged.

Focus Area #3: Population science

Studies in this focus area can include research related to epidemiology, risk stratification, implementation science, communication, or ethics. Increasing uptake of genetic testing and improving risk stratification of known *BRCA1/2* mutations are important areas of research. Some potential examples include:

- Improving uptake of genetic testing in the community at large or in underrepresented minority populations
- Using EHR-based prompts to identify individuals who are good candidate for *BRCA1/2* testing
- Identifying people at increased risk of *BRCA1/2* mutations through national, state (e.g. cancer registry) or local (e.g. Penn Medicine Biobank or PennOmicsV2) databases
- Ethics and legal implications of doing testing on deceased patient samples

- Examining potential environmental risk factors for cancer in *BRCA1/2* mutation carriers
- Understanding implications of direct to consumer genetic testing
- Utilization of text messaging to improve patient care (ie referral to genetic testing and appointments) or follow-up screening

Submission Guidelines

Eligibility:

- Applicants must be at the Research Assistant Professor level or above.
- Only one application will be accepted per investigator. Investigators may not be Co-PI on more than one application.

Phase I: A mandatory letter of intent (LOI) is due by March 9, 2020.

The LOI must be submitted here: https://www.med.upenn.edu/apps/pgacc/users/sign_in

- Search for program “2020-2022 Basser Center for BRCA Grants for Penn Investigators-Letter of Intent”
- In the “PI/Co-PI” tab, please provide the name of your Co-PI(s), if applicable. ***Each PI needs to be registered in the online submission system, or you will not be able to enter them into the data field.***
- In the “Documents” tab under “Abstract”, please submit a one page letter of intent including:
 - Title of proposed project
 - PI/Co-PI (if applicable) names, degree(s) and position
 - Designation of specific focus area (if relevant):
 - Population Science
 - Haploinsufficiency
 - Organoid cultures
 - Other
 - Description of the project including specific aims and relevance to *BRCA1/2*

The purpose of the LOI is to allow the Basser Center time to assemble appropriate reviewers - not to approve grants for full submission. There will be no feedback provided to applicants regarding the LOI and anyone submitting an LOI is welcomed to follow through with a full grant application.

Phase II: Full grant applications (due April 6, 2020)

1. Applicants must use the Basser Center for BRCA Application Form (located at the bottom of this announcement).
2. Only one application will be accepted per investigator. Investigators may not be Co-PI on more than one application.
3. Applications must be submitted using this website: https://www.med.upenn.edu/apps/pgacc/users/sign_in
 - Under the “Basic Info” tab, please provide the information requested. Standard NIH formatted Biosketches are sufficient. If there are multiple PIs, please combine all Bios *into one single PDF file* and upload.

- Under the “Co-PI(s)” tab, please provide the name of your Co-PI(s), if applicable.
- Under the “Documents” tab, please upload your Research Proposal *as one single PDF file*, using the Bassler Center for BRCA Application Form. Application Forms must include:
 - Abstract
 - Specific aims, not to exceed one page
 - Significance*
 - Background*
 - Research Plan*
 - References
 - Budget with justification

Note: Significance, Background and Research Plan must not exceed **five total pages*

4. Formatting requirements: Arial 11 font, single spaced, no less than ½ inch margins all around.
5. Page numbering is recommended, and should use sequential numbers, e.g., do not use 2a and 2b, etc.
6. Supplemental/Appendix material is limited to letters of support/collaboration and PDFs of papers in press and not yet publically available. Any other additional material will be discarded.

Preparation of Budgets: No specific budget format is required, but be sure to include adequate details and corresponding justification. Awards will be funded for a period of 2 years for \$50,000-\$150,000/year contingent on significant progress year to year. Awards are also contingent on the availability of funds.

Allowable expenditures include:

- Salary support for investigator
- Research supplies and animal maintenance
- Travel when necessary to carry out the proposed research program
- Publication costs, including reprints
- Costs of computer time
- Special fees (pathology, photography, etc.)
- Equipment costing less than \$5,000. Special justification is necessary for items exceeding this amount, and permission must be obtained from the Bassler Center for the purchase of such equipment
- Registration fees at scientific meetings
- Technician/laboratory personnel support

Non-allowable expenditures include:

- Secretarial/administrative personnel
- Honoraria and travel expenses for visiting lecturers
- Per diem charges for hospital beds
- Non-medical services to patients
- Construction or building maintenance
- Major alterations
- Purchasing and binding of periodicals and books
- Office and laboratory furniture
- Office equipment and supplies

- Rental of office or laboratory space
- Recruiting and relocation expenses
- Dues and membership fees in scientific societies

Review Process

The review process will be completed by a committee of outside scientists, which is expected to include a subset of members of the Basser Center External Scientific Advisory Board. Successful applicants will be announced in June 2020. Funding will have a start date of July 1, 2020. Review Criteria will include:

1. **Impact**: What is the likelihood that the proposed research will have a transformative impact on science with a goal toward an impact on clinical care pertaining to BRCA?
2. **Innovation**: Is the proposed application creative and original? If successful, will the work produce dramatic paradigm shifts in research and clinical practice by using novel concepts, methodologies, and/or interventions?
3. **Investigative Team**: Does the proposed PI have a strong track record of leadership of innovative science?
4. **Approach**: Are the general strategies and translational approaches sufficiently rigorous to ensure generation of important data? Is the proposed research BRCA1/2 specific? Are metrics of success and plans for sustainability presented and reasonable?

Ongoing Review and Evaluation

Funded awardees will be expected to submit semi-annual progress reports, which will be evaluated by the Basser Center leadership and Internal Advisory Board and possibly by outside advisors. Metrics of success and progress toward achieving scientific goals will be considered. Continuation of funding will depend on progress.

Link to application form: [2020 Basser Internal Grant Application Form](#)

Link to online submission: https://www.med.upenn.edu/apps/pgacc/users/sign_in

For questions relating to this RFA, please contact:

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