Request for Proposals (RFP)

Novel Approaches to Predict or Prevent the Influences of Environmental Chemicals on Breast Cancer Risk

California Breast Cancer Research Program
Preventing Breast Cancer: Community, Population, and Environmental Approaches

Deadline to apply:
March 02, 2023

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About the California Breast Cancer Research Program and the Preventing Breast Cancer Initiative

The **California Breast Cancer Research Program (CBCRP)** was established pursuant to the 1993 Breast Cancer Act (*AB 2055 (B. Friedman) [Chapter 661, Statutes of 1993]* and *AB 478 (B. Friedman) [Chapter 660, Statutes of 1993]*). The program is responsible for administering funds for breast cancer research in California.

The mission of CBCRP is to eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities.

- CBCRP is the largest state-funded breast cancer research effort in the nation and is administered by the University of California, Office of the President.
- CBCRP is funded through the tobacco tax, a voluntary tax check-off on personal income tax forms, and individual contributions.
- The tax check-off, included on the personal income tax form since 1993, has drawn over $13 million for breast cancer research.
- Ninety-five percent of our revenue goes directly to funding research and education efforts.
- CBCRP supports innovative breast cancer research and new approaches that other agencies may be reluctant to support.
- Since 1994, CBCRP has awarded over $290 million in 1,249 grants to institutions across the state. With continued investment, CBCRP will work to find better ways to prevent, treat and cure breast cancer.

PBC Priority Areas

CBCRP's Program Initiatives integrate expertise and experience from a range of stakeholders to identify compelling research questions and fund research projects that help find solutions to reduce suffering from breast cancer and move science closer to eliminating the disease. The Program Initiatives engage scientists, advocates, people impacted by breast cancer, and the broad community in a dialogue to frame research priorities and fund meaningful research.

In 2004, CBCRP launched its Special Research Initiatives (SRI), devoting 30% of research funds to research to environmental causes of breast cancer and the unequal burden of the disease. Under this initiative, CBCRP funded 26 awards totaling over $20.5 million. In 2010, CBCRP launched its second round of Program Initiatives, the California Breast Cancer Prevention Initiatives (CBCPI), adding population-level prevention interventions as a target area and devoting 50% of its funds to these priority areas. To date, CBCRP has funded 22 awards under CBCPI, totaling over $19 million.

In 2015, CBCRP's Council decided to build on the existing Program Initiatives by devoting 50% of CBCRP research funds between 2017 and 2021 to a third round of Program Initiatives. This new effort is titled Preventing Breast Cancer (PBC): Community, Population, and Environmental Approaches. Approximately $20 million is being dedicated to directed, coordinated, and collaborative research to pursue the most compelling and promising approaches to:

- Identify and eliminate environmental contributors to breast cancer.

- Identify and eliminate fundamental causes of health disparities with a focus on breast cancer in California.
- Develop and test population-level prevention interventions that incorporate approaches to address the needs of the underserved and/or populations experiencing disparities in the burden of breast cancer.

In 2020, CBCRP began releasing a series of initiative based on 10 concept proposals to stimulate compelling and innovative research in all three PBC focus areas.

Novel Approaches to Predict or Prevent the Influences of Environmental Chemicals on Breast Cancer Risk

Available Funding

Biological measurements of environmental exposure and of the molecular pathways involved in transitioning a normal cell to cancer are crucial pieces of knowledge for discovering the causes of breast cancer and informing prevention strategies. The goal of this RFP is to expand the methods and application of biomonitoring beyond the chemicals, populations, and mechanistic pathways that have been well-studied so far and to explore: (1) biomonitoring and links to biological response endpoints in exposed populations and (2) the development/ discovery and application of a novel assay or marker to predict/ prevent risk of breast cancer.

CBCRP intends to fund up to three proposals for a maximum duration of three years and $430,000 maximum total direct costs each.

Completed responses to this RFP are due by Thursday, March 02, 2023, 12 noon PST. The project start date is August 1, 2023.

For more information and technical assistance, please contact:
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Background/Justification

One CBCRP goal is to identify chemical exposures that cause breast cancer so that they can be targeted for reduction or elimination from our environment. Alternatively, understanding pathways and biological responses critical on the pathway to cancer following specific types of exposures allows for intervention if predictive markers of disease are determined. Hundreds of chemicals have been identified in our everyday environment and have been measured in people. A significant number of them are suspected breast carcinogens (Reed and Fenton 2013, Reed and Fenton 2014, Siddique et al 2016, Tucker et al 2018, Terry et al 2019). While there has been significant progress in the identification of hormonally active chemicals and the processes by which chemical exposures cause cancer, there is still a need for mechanistic studies, to elucidate the relationship between chemical exposure and the development of breast cancer.

Environmental epidemiological studies are often considered critical for establishing the impact of chemical exposures on cancer in humans, given that few other studies have the ability to assess relevant exposures and by taking into account their effects in windows of susceptibility across the life cycle (Brody et al 2007, IBCERCC 2013, Rodgers et al 2018, Terry et al. 2019). However, epidemiological approaches alone are insufficient to elucidate how certain chemical exposures drive cancer development. Therefore, advancing scientific understanding of chemicals associated with breast cancer requires multi-disciplinary approaches that include exposure assessment (including biomonitoring), environmental epidemiology, biological mechanism analysis, toxicology, and toxicogenomics/metabolomics, among many disciplines.

Exposure assessment is important, but it relies on modeling or extrapolation of environmental factors, depends on uncertain assumptions, and can result in misclassification. Even human

biomonitoring, which measures exposures directly through analysis of biological media, is limited because for many chemicals, a spot sample only represents exposure at a snapshot in time and may not adequately characterize the level, timing or duration of exposures. In addition, because of the long latency of breast cancer, the relevant exposure may take place decades before cancer diagnosis. Therefore, cell-based molecular characterization and animal models are important to define early exposure markers, as well as assess mechanistic changes and pathways linking exposure to environmental chemicals and breast cancer.

Despite advances in toxicology and analytical chemistry methods, evaluating how exposure to certain environmental chemicals can lead to carcinogenesis remains a challenge today. These obstacles are present due to the fact that these chemicals, by nature, do not act in a singular, specific manner, but rather have multiple biological targets, leading to different effects. Recognizing the critical role of estrogen in breast cancer development, scientists have identified environmental chemicals with estrogenic activity and those known to modulate estrogen biosynthesis. However, breast cancer is not a single disease, but has at least four subtypes: luminal-A, luminal-B, HER2-positive, and triple-negative (TN) breast cancers. Specific assays are needed to evaluate the effect of exposure to environmental chemicals on the development of each subtype, such as assays for ER and PR expression and estrogen-mimic response (linking to luminal A subtype), evaluation of ER and signal transduction pathway cross-talk (linking to luminal B subtype), measurement of HER2 pathway activation (linking to HER2 subtype), and activation of stem cells and DNA repair defect (linking to TNBC). Additional reported targets associated with breast cancer risk include altered mammary gland development (and sexual maturation), progesterone receptor activity, cell cycle/apoptosis changes, and immunotoxicity (Schwarzman et al 2015).

Biomarker assays on human specimens are essential for advancing scientific understanding of the relationship between chemical exposure and breast cancer and have the potential to greatly improve exposure and biological response measurements in epidemiological studies of cancer risk. They have been critically important in prediction of colon and prostate cancer risk, and more studies are needed to identify and test similar biomarkers in breast cancer development. **Figure 1** illustrates the knowledge generation synergies between environmental epidemiology, *in vitro* and *in vivo* studies that collectively advance scientific understanding of how certain environmental chemical exposures can lead to breast cancer. Knowledge from multidisciplinary science of this sort can then help decision-makers develop and prioritize exposure prevention and disease reduction strategies.

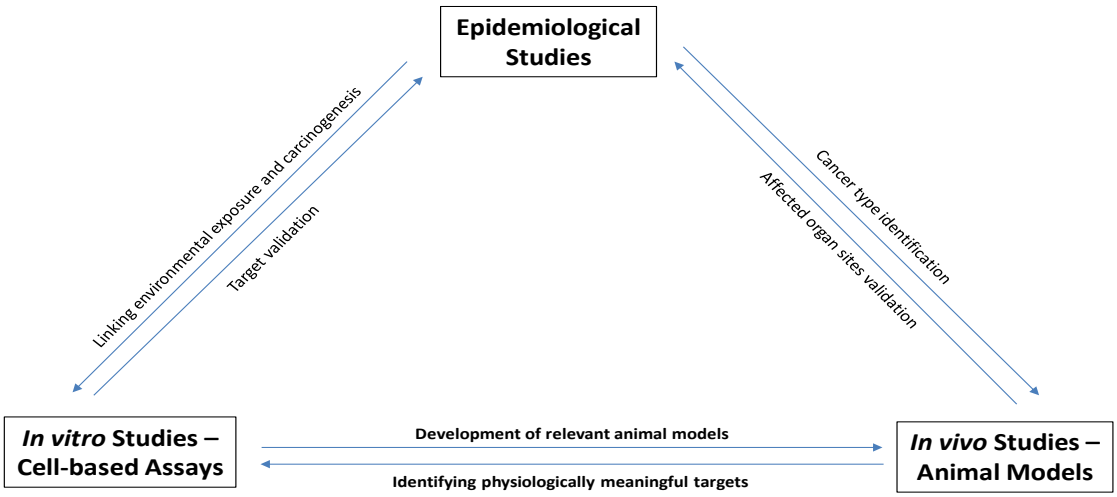

Figure 1. Knowledge generation synergies between environmental epidemiology, in vitro and in vivo studies.

Research Questions

Human biomonitoring for chemicals, that are widely present in our environment, has made major contributions to understanding population exposures over time and within sensitive subpopulations. This has enabled researchers to examine the biological impact of exposure, assess potential synergies among different chemicals, and elucidate relationships between exposures and diseases, including breast cancer.

Despite important scientific progress in this realm of exposure assessment, significant challenges remain including better characterizing novel exposures, combined effects of chemical mixtures, and biological response markers of relevance to breast cancer. Indeed, mechanistic studies to date have been limited mainly to estrogen mimics.

To better understand the role chemicals play in causing breast cancer, CBCRP is calling for proposals in the area of "Novel Approaches to Predict or Prevent the Influences of Environmental Chemicals on Breast Cancer Risk" to cover two main topic areas that are further described below: 1) Biomonitoring and links to biological response endpoints in exposed populations and 2) Development/discovery and application of a novel assay or marker to predict/prevent risk of breast cancer. Accordingly, this RFP encourages applications that may address these research considerations:

A. Expand the scope of inquiry in biomonitoring science beyond well-recognized and well-studied chemical exposures (such as estrogen-mimics) by identifying and characterizing chemical exposures with relevant biological activity linked to breast cancer.
B. Characterize metabolome/exposome-related shifts associated with breast disease and mammary development using non-targeted analytic or artificial intelligence methods.
C. Elucidate functional pathways linking exposure to biological response markers and disease, for spurring action based on human exposure.

Priority projects will use novel methods to address widespread chemical contacts, high exposures to vulnerable groups, or chemicals with high biological activity of relevance for breast cancer.

Approaches and Methods

Biomarkers can be defined as those measurable biologic responses associated with chemical exposures and/or their metabolites, susceptibility (linking to genetic and other predisposition effects of exposure), and prognostic indicators (indicating early events in development of toxicity and breast cancer, ideally for different subtypes). For the purposes of this RFP, we seek proposals from researchers who will focus on: A) identification of biomarkers that predict breast cancer; B) determination of the association between chemical exposure and early biological effects of potential relevance to mammary gland development and breast cancer; or C) development of robust and breast cancer-relevant assays to estimate the relative risk of chemical exposures. This may include, but is not limited to, measures of breast density, markers of chronic inflammation, or recently discovered cancer biomarkers such as exosome miRNA.

Additional areas of interest to CBCRP are chemicals or relevant chemical mixtures previously identified as hormonally active or carcinogenic to the breast, which are still produced in high-volume and present in the environment or in people. We encourage careful consideration of exposure assessment (to include internal dose, regardless of the model system) and how to address inter-individual variability in exposure. A focus on vulnerable time periods and populations is also encouraged.

Topic 1: Biomonitoring in exposed populations

Conduct biomonitoring in populations exposed at high levels to chemicals of interest for breast cancer and use metabolomics or other -omics to identify associations between the exposure and early biological effects. The study should be carried out with relevant female cohorts that have existing chemical exposure data or biospecimens that can be leveraged for such a biomonitoring of exposure/biological response project.

The study should focus on measurements of endogenous processes that are breast-cancer-relevant, as identified by Schwarzman et al. 2015 and other CBCRP chemical testing grantees (see Appendix A), or recently discovered cancer biomarkers such as exosome miRNA. If possible, investigators could develop a proposal that can also demonstrate the relationship in parallel in an animal model. The project should propose specific and definitive end points or outcomes, such as identification of early biological changes, and demonstrate the capability to measure them, so that subsequent studies can connect them to epidemiological studies examining chemical and biomarker response links to clinical breast cancer outcomes. Projects associated with predictive value on breast cancer risk for current use chemicals will be more favorable than research on chemicals banned many years ago.

Topic 2: Develop/discover and apply a novel assay

Develop and apply a novel assay that measures an exposure or biological response relevant to the development of breast cancer or discover a novel biomarker in existing datasets and test its predictive potential for breast cancer in animal or cell-based studies.

Projects will be considered novel if they target an endpoint for which there is currently no good measurement strategy or if they greatly improve on or validate an existing strategy (e.g., reliability, lower cost, more practical, prediction of disease potential, and more human relevance). Examples may include:

A. Develop in vitro or short-term in vivo assays to detect biological activities associated with the characteristics of carcinogenic chemicals—e.g. altered development, chronic inflammation, genomic instability-- in mammary tissue. Assays targeting different breast cancer subtypes are critically needed.

B. Develop a measurement of environmentally relevant mixtures, including vehicle exhaust, diesel, pesticide residues, indoor air (occupational setting), or air pollution that is more interpretable with respect to exposure source and biological effects than current tools. It is expected that the novel tool's measures would be compared to breast cancer risk, metabolomic or transcriptomic marks, or contemporary occupational databases documenting health effects in a female cohort or in animal studies.

C. Discover novel biomarkers linking disease and exposures using artificial intelligence or other bioinformatic tools (pattern recognition or cross-species or cross-strain similarities/differences in existing datasets) and test its predictive potential for breast cancer in animal or cell-based studies.

Resources to Be Used or Considered for Use

A. Expertise. Although lab-based studies are expected, other expertise (bioinformatics, field analysts, or computing specialists) may augment the outcome of the research. Transdisciplinary applications may receive more favorable consideration. Investigators for biomonitoring studies are expected to have permission to access or already be conducting studies in which data would be used to address the aims.

B. Capacity. The investigator(s) should demonstrate that they would have the equipment on hand and capabilities to conduct the proposed research. Costs to purchase access to data sets, conduct animal/cell-based studies, purchase columns for analytical studies, secure data storage space, etc., are appropriate. Purchase of large pieces of equipment to enable the work should not comprise more than 10% of direct costs.

C. Data Sets. Data resources that may be relevant include, but are not limited to 1) female cohorts with biospecimens and/or chemical biomonitoring data that can be leveraged to examine effect biomarkers of relevance to breast outcomes, 2) animal models in which human relevant exposures (especially mixtures or complex contemporary exposures) are delivered during susceptible life stages and followed for risk evaluation for mammary carcinogenesis, 3) advanced cell-based models that consider the molecular features of a certain cancer sub-type, 4) large datasets from published studies that include environmental exposures, -omic(s) data, and/or disease or breast condition information, or 5) occupational biomonitoring studies for which breast outcomes have not been previously interrogated and for which other samples from the cohort population are available.

D. Exposures. Novel or complex exposure biomonitoring is encouraged. Internal dosimetry in animal or cell-based exposure studies are necessary. Modeling of mixtures exposures and biological response outcomes along the trajectory to breast outcomes/cancer are a high priority. Contemporary exposures will be reviewed more favorably.

Dissemination Plan

Each application should identify translational potential or transdisciplinary approaches that are pertinent, research gaps that they intend to fill, potential impact on the field/policy, and the novelty of their proposal. How the findings resulting from the proposal may be applied should be discussed.

Proposals must include plans for dissemination and translation of newly discovered/developed methods and results. The applicants should address the likely relevance to both future research and current policy discussions. The applications should include plans to disseminate results to breast cancer advocates, policymakers, and the larger public, beyond publication in the scientific literature. The project team's community advocate(s) should play a substantive role in formulating and helping carry out the proposed dissemination plan.

Advocacy Involvement

Advocacy involvement is a requirement for the research funded under this initiative. Applications should include a California community advocate affiliated with an advocacy and/or community organization with an interest in the area of biomonitoring, environmental exposures and breast cancer to be actively involved in the project. The community advocate(s) should be involved in the development of the project, goals, aims, and research questions and should drive the identification and definition of community needs and health equity imperatives. Community advocates should be compensated as experts.

Applications will be evaluated on the extent to which advocates are substantively involved in the project including identification of an appropriate advocate(s) for the proposed research; a detailed description of how the advocate(s) will be involved in the project; submission of a Letter of Commitment co-signed by the research advocate(s) and the PI; and a budget line item and justification covering the advocate(s) time, effort, and expenses on the project (e.g. at least quarterly, meetings with the advocate and the investigative team). If needed, CBCRP staff can assist investigators with meeting the advocacy involvement requirement as they prepare their applications.

Budget

CBCRP intends to fund up to three proposals for a maximum duration of three years and $430,000 maximum total direct costs each. The budget may vary for different types of proposals and must be carefully justified.

In addition, if more than one grant is funded in response to this announcement, CBCRP will convene grantees to consider opportunities for synergy and integration. Proposals should include plans to attend a meeting for this purpose.

Indirect (F&A) costs are paid at the appropriate federally approved F&A rate for all institutions except for University of California campuses, which receive a maximum of 30% F&A (25% for off-campus projects). Organizations that do not have a federally approved F&A rate may request a De Minimis rate of 25%.

Supplemental funding is available for funded projects to support promising high school students, undergraduate students and/or community members from groups underrepresented in breast cancer research and/or those who wish to pursue careers focused on questions affecting underrepresented communities to breast cancer research. Applications for these supplements will be accepted during

the prefunding stage of the award and will start August 1, 2023. Visit https://cabreastcancer.org/files/cbcrp-diversity-supplement.pdf to learn more.

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Interagency Breast Cancer and the Environment Research Coordinating Committee. Department of Health and Human Services. Breast Cancer and the Environment: Prioritizing Prevention. Available at: http://www.niehs.nih.gov/about/assets/docs/ibcercc_full_508.pdf. February 2013.

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Terry, M.B., K.B. Michels, J.G. Brody, C. Byrne, S. Chen, D.J. Jerry, K.M.C. Malecki, M.B. Martin, R.L. Miller, S.L. Neuhausen, K. Silk, A. Trentham-Dietz, & on behalf of Breast Cancer and the Environment Research Program (BCERP). 2019. Environmental exposures during windows of susceptibility for breast cancer: a framework for prevention research. *Breast Cancer Research*, https://doi.org/10.1186/s13058-019-1168-2

Tucker, D.K., Bouknight, S.A., Brar, D., Kissling, G., and Fenton, S.E. 2018. Evaluation of prenatal exposure to bisphenol analogues on development and long-term health of the mammary gland in female mice. *Environ Health Perspectives,* 126(8):087003. https://doi.org/10.1289/EHP3189

How We Evaluate RFPs

CBCRP uses a two-tier evaluation process: peer review and programmatic review. It is a combination of (i) the peer review rating, (ii) the programmatic rating, and (iii) available funding that determines a decision to recommend funding.

Peer Review

All applications are evaluated by a peer-review committee of individuals from outside of California. The committee is composed of scientists from relevant disciplines and breast cancer advocates and other community representatives. Applications are rated using

- **Innovation.** Extent to which the project explores new and potentially useful tests for biologically relevant effects of chemicals on breast tissues and development. Are the concepts and hypotheses speculative and exploratory. Are the methods novel and original?
- **Impact.** Potential for the project, if successful to refine or generate novel biomarker assays that will improve current testing modalities for breast cancer relevant chemicals. Does the research address relevant mechanisms, methods and/or models for testing chemicals.
- **Approach.** The quality, organization, and presentation of the research plan, including methods and analysis plan. Will the research planned answer the research questions? Are the design, methods and analyses well-developed, integrated and appropriate to the aims and stated milestones of the project? Does the application demonstrate an understanding of the research question and aims? How well developed is the dissemination plan?
- **Feasibility.** The extent to which the aims are realistic for the scope and duration of the project; adequacy of investigator's expertise and experience, and institutional resources; and availability of additional expertise and integration of multiple disciplines. Does the investigator (and do co-investigators) have demonstrated expertise and experience working in the topic area? Can the project be completed as proposed given the available funding, time frame and the staff knowledge, skills, experience, and institutional resources?

Programmatic Review

This review is conducted by the California Breast Cancer Research Council and involves reviewing and scoring applications with sufficient scores from the peer review process based on the criteria listed below. The individuals on the Council performing this review include advocates, clinicians, and scientists from a variety of disciplines. In performing the Programmatic Review, the advisory Council evaluates **only a portion of the application materials** (exact forms are underlined). Pay careful attention to the instructions for each form. The Programmatic criteria include:

- **Responsiveness.** How responsive are the project and co-PIs to the stated intent of the selected Initiative? Compare the PI's statements on the Program Responsiveness form and the content of the Lay and Scientific Abstracts to the PBC topic area.
- **Critical path/Translation:** The degree to which the applicant's statements on Critical Path and Focus on Underserved Populations form provides a convincing argument that the proposed research fits into and advances a critical path for translation and impact on breast cancer. What barriers must be overcome to take the project to the next level, and what plans are provided for to address these barriers?

- **Quality of the lay abstract.** Does the Lay Abstract clearly explain in non-technical terms the research background, questions, hypotheses, and goals of the project? Is the relevance to the research initiative understandable?
- **Addressing the needs of the underserved.** Do the project and the PI's statements on Critical Path and Focus on Underserved Populations template demonstrate how this research will contribute to health equity by addressing breast cancer issues that disproportionally affect communities who have been historically underserved by research and/or health systems? Does the project address inequities and/or the specific needs of communities who are underserved as they bear a disproportionally high burden of health-related problems due to factors related to race, ethnicity, socioeconomic status, geographic location, sexual orientation, physical or cognitive limitations, age, occupation and/or other factors?
- **Advocacy involvement.** Are the named advocate(s) and advocacy organization appropriate for the proposed research project? Will the advocate provide a perspective that is historically underrepresented in breast cancer research? Were they engaged in the application development process? Are meetings and other communications sufficient for substantive engagement? Are the roles and responsibilities of the PI and the advocate(s) clearly outlined and is the agreement for advocate compensation and reimbursement clear? [The Advisory Council will examine the PI's statements on the Lay and Scientific Abstracts and Advocacy Involvement forms.]

Application Instructions

Application materials will be available through RGPO's SmartSimple application and grant management system beginning on December 1, 2022. Please review the SmartSimple Application Instructions for the technical instructions for accessing and completing your application. This supplemental programmatic instruction document provides guidance for the content of your application.

Application Components

Section 1: Title Page

- **Project Title:** Enter a title that describes the project in lay-friendly language. (Max 100 characters).
- **Project Duration:** Select a duration of 2 or 3 years.
- **Proposed Project Start Date:** Enter a project start date of August 1, 2023.
- **Proposed Project End Date:** Enter a project end date of July 31, 2025 for a 2-year award or July 31, 2026 for a 3-year award

Section 2: Applicant/PI

A required field entitled "ORCID ID" is editable on the Profile page. ORCID provides a persistent digital identifier that distinguishes you from every other researcher and, through integration in key research workflows such as manuscript and grant submission, supports automated linkages between you and your professional activities ensuring that your work is recognized. If you have not already obtain an ORCID ID number, you may do so at http://orcid.org/ Once you have done so, please enter your 16-digit identifier in the space provided on your profile page in the following format: xxxx-xxxx-xxxx-xxxx.

Section 3: Project Information

Please use the following guidelines to differentiate between Lay and Scientific Abstracts:

Lay Abstract (Max 2400 characters)**:** This item is evaluated mainly in the programmatic review. The Lay Abstract must include the following sections:

- A **non-technical introduction** to the research topics
- The **question(s) or central hypotheses** of the research in lay terms
- The **general methodology** in lay terms
- **Innovative elements and potential impact** of the project in lay terms

The abstract should be written using a style and language comprehensible to the general public. Avoid the use of acronyms and technical terms. The scientific level should be comparable to either a local newspaper or magazine article. Avoid the use of technical terms and jargon not a part of general usage. Place much less emphasis on the technical aspects of the background, approach, and methodology. Ask your advocate partner to read this abstract and provide feedback.

Scientific Abstract (Max 2400 characters)**:** This item is evaluated mainly in the peer review. The Scientific Abstract should include:

- A short introductory paragraph indicating the **background** and overall topic(s) addressed by the research project
- The **central hypothesis** or **questions to be addressed** in the project
- A listing of the **objectives or specific aims** in the research plan
- The major research **methods and approaches** used to address the specific aims
- A brief statement of the **impact** that the project will have on breast cancer

Provide the critical information that will integrate the research topic, its relevance to breast cancer, the specific aims, the methodology, and the direction of the research in a manner that will allow a scientist to extract the maximum level of information. Make the abstract understandable without a need to reference the detailed research plan.

Additional information: Applicants must respond to the following categories and discussion points using the online fields provided:

- **Specific aims** (Max 2400 characters/approx. 350 words). List the proposed aims of the project.
- **CBCRP Research Priorities.** Select "Etiology and Prevention" as the CBCRP priority issue that the research addresses.
- **CSO Research Type(s) and Sub-Type(s).** Select the CSO Type and Sub-Type that best represent your project.
- **Subject Area(s).** See SmartSimple submission instructions for more details.
- **Focus Areas(s).** See SmartSimple submission instructions for more details.
- **Research Demographics.** See SmartSimple submission instructions for more details.
- **Milestones.** Add significant milestones that are described in your research plan to this table along with anticipated completion dates and arrange them in chronological order.

Section 4: Project Contacts

Project Personnel. Provide contact information and effort for Key Personnel and Other Significant Contributors on your project including the Applicant Principal Investigator, Co-Investigator, Advocate, Trainee, Consultant, and support personnel, as necessary. Upload biosketches to each of your Key Personnel members in this section, as shown in the SmartSimple instructions. A 5% minimum effort (0.6 months per year) is required for the Applicant PI.

Section 5: Budget

This section contains several sub-tabs: Institution Contacts, Budget Summary, Budget Details, and Subcontract Budget Details. Complete the information in the Institutional Contacts, Budget Summary, Budget Detail and, if applicable, Subcontract Budget Details tab as described in the SmartSimple Application Instructions.

The maximum duration is 3 years, and the direct costs budget cap is $430,000.

Note: The amount of a subcontracted partner's F&A costs can be added to the direct costs cap. Thus, the direct costs portion of the grant to the recipient institution may exceed the award type cap by the amount of the F&A costs to the subcontracted partner's institution.

Additional budget guidelines:

- **Equipment** purchases should not be more than 10% of Direct Costs. Only include individual items >$5,000. Any items less than $5,000 must be purchased under the "supplies" budget category.
- **Other Project Expenses:** Include other project costs such as supplies or **Advocate(s) expenses** (any travel, meeting, and consultation costs/fees associated with advocates) here.
- **Travel**: A minimum of $400 must be budgeted in year 1 for travel to the **CBCRP symposium**. Include in the budget travel to the potential CBCRP convening of initiative grantees (minimum $400). **Scientific meeting travel** is capped at $2,000/yr.
- **Indirect (F&A) costs**. Non-UC institutions are entitled to full F&A of the Modified Total Direct Cost base (MTDC); UC institutional F&A is capped at 30% MTDC*, or 25% MTDC for off-campus investigators (not retroactive to prior grants).

**Allowable expenditures in the MTDC base calculation include salaries, fringe benefits, materials and supplies, services, travel, and up to the first $25,000 of each subgrant or subcontract (regardless of the period covered by the subgrant or subcontract). Equipment, capital expenditures, charges for patient care and tuition remission, rental costs, scholarships, and fellowships as well as the portion of each subgrant and subcontract in excess of $25,000 shall be excluded from the modified total direct cost base calculation. If a grantee or subcontractor does not have a federally negotiated F&A rate at the time of the proposal submission, the grantee and/or subcontractor may request a "De Minimis" F&A rate of 25% MTDC.*

Additional budget guidelines can be found in Appendix B.

Section 6: Assurances

Enter assurance information. If available, enter your institutional Federal Wide Assurance (FWA) code or equivalent for Human Subjects, an IACUC Animal Welfare Assurance code for Vertebrate Animals, and equivalent for Biohazard ad DEA Controlled Substance approvals.

Section 7: Documentation

Complete and upload all required items. All uploads must be in PDF format. Listed below are the forms and templates you download from SmartSimple, enter text, convert to PDF, and, unless instructed otherwise, re-upload to your application in this section.

Upload Item (Template/Form)	Page limit	Required or optional	Peer Review?	Programmatic Review?
Research Plan	**7** *(+ 3 for references)*	**Required**	**Yes**	**No**
Program Responsiveness	**2**	**Required**	**Yes**	**Yes**
Critical Path & Underserved	**2**	**Required**	**Yes**	**Yes**
Advocacy Involvement	**1**	**Required**	**Yes**	**Yes**
Letter of Commitment	**2**	**Required**	**Yes**	**Yes**
Biosketches (All Personnel listed on Key Personnel form)	**5 (each biosketch)**	**Required** *(upload to Project Personnel section)*	**Yes**	**Yes (PI only)**

Facilities	**1 per institution**	**Required**	**Yes**	**No**
Human Subjects	**No Limit**	**Required**	**Yes**	**No**
Vertebrate Animals	**No Limit**	**Optional**	**Yes**	**No**
Appendix list and uploads	**30**	**Optional**	**Yes**	**No**

Detailed Description of Proposal Templates

Research Plan (required)

This section is the **most important** for the peer review. Note carefully the page limits, format requirements, and suggested format. **Limit the text to seven pages, with an additional 3 pages for references.**

Format issues: Begin this section of the application using the download template. Subsequent pages of the Research Plan and References should include the principal investigator's name (last, first, middle initial) placed in the upper right corner of each continuation page.

The Research Plan and all continuation pages must conform to the following four format requirements:

1. The height of the letters must not be smaller than 11 point; Times New Roman or Arial are the suggested fonts.
2. Type density, including characters and spaces, must be no more than 15 characters per inch (cpi).
3. No more than 6 lines of type within a vertical inch.
4. Page margins, in all directions, must be 0.75 inches.

Use the appendix to supplement information in the Research Plan, not as a way to circumvent the page limit.

We ask that applicants describe the proposed research project in sufficient detail for reviewers to evaluate its scientific merit and collaboration elements, as described below. If you don't use all the pages to describe your research plan, it might be best to review what you have written and explain in more detail anything not fully explained. **However, note that a concise, focused research plan of less than the maximum number of pages is preferable to one less concise and made longer by overly elaborate or unimportant details.**

Supporting materials (such as questionnaires, consent forms, interview questions, letters of collaboration) that are directly relevant to the proposal may be included in the Appendix. **The research plan must be self-contained and understandable without having to refer extensively to supporting materials.**

Suggested outline:

Introduction and Hypotheses: Provide a brief introduction to the topic of the research and the hypotheses/questions to be addressed by the specific aims and research plan. The relationship of the project to the specific PBC Project Type and expectations outlined within the RFP should be clear.

Specific Aims: List the specific aims, which are the steps or increments deemed necessary to address the central hypothesis of the research. The subsequent research plan will detail and provide the approach to achieving each of these aims.

Background and Significance: Make a case for your project in the context of the current body of relevant knowledge and the potential contribution of the research.

Preliminary Results: Describe the recent work relevant to the proposed project. Emphasize work by the PI and data specific to breast cancer.

Research Design and Methods: Provide an overview of the experimental design, the methods to be used, and how data are to be collected and analyzed. Describe the exact tasks related to the Specific Aims above. Provide a description of the work to be conducted during the award period, exactly how it will be done, and by whom. Include a letter of commitment if the applicant PI will be using a data set that they do not control/own. Recognition of potential pitfalls and possible alternative approaches is recommended. How will technical problems be overcome or mitigated? Cover all the specific aims of the project in sufficient detail. Identify the portions of the project to be performed by any collaborators. Match the amount of work to be performed with the budget/duration requested. A description of the milestones and timeline will demonstrate how the aims are interrelated, prioritized, and feasible.

Program Responsiveness (required)

This item is evaluated in the peer review and programmatic review. **Limit the text to two pages**. The CBCRP Council (who conducts the programmatic review) will NOT see your Research Plan. The information on this template allows the CBCRP Research Council to rate the application for adherence to the objectives of the PBC research area as outlined in the specific RFP.

PBC Focus (Responsiveness): Provide a clear, brief summary for the CBCRP Council (1 or 2 paragraphs) of how your proposed research addresses the specific RFP topic area, by increasing or building on specific scientific knowledge; by pointing to additional solutions to identify and eliminate environmental causes, and or disparities in, breast cancer; and/or, by helping identify or translate into potential prevention strategies.

Dissemination and Translation Potential: Describe how research findings will be shared with various stakeholder audiences (i.e., policymakers, community members, breast cancer advocates, other researchers/agencies, health care providers, funders etc.). Describe the potential for how the research findings will be translated into policy and/or other practice.

Critical Path & Focus on Underserved Populations (required)

This item is critical to the programmatic and peer reviews. **Limit the text to two pages**.

A. Critical Path

Review the background and rationale described for Program Initiatives at Appendix C and follow the instructions on the template.

B. Focus on Underserved Populations.

Describe the potential for your project to understand and reduce disparities and health inequities in breast cancer risk, incidence, and treatment/prognosis at the individual and community levels. Underserved is defined as communities or individuals who bear a disproportionally high burden of health-related problems due to factors related to race, ethnicity, socioeconomic status, geographic location, sexual orientation, physical or cognitive limitations, age, occupation and/or other factors.

Advocacy Involvement (required)
Follow the instructions on the form, and be sure to address the requested three items (Advocacy Organization/Advocate(s) Selection and Engagement to Date, Advocate(s) Role in Proposed Research and Meeting and Payment Plans). **Limit the text to one page**.

Discuss what involvement, if any, advocates had in the development of this proposal and will have in the project, if funded. Explain how this proposal shows awareness and inclusion of breast cancer advocacy concerns involved in the proposed research.

Letter of Commitment (required)
This item is evaluated in the peer review and in the programmatic review. Please use the template as a basis for commitment letters from the advocate, scientific and/or subcontracting individuals/institutions. **Limit the text to two pages**.

Biographical Sketch (required)
This item is evaluated in the peer review and the programmatic review. **Use the NIH form (version 2015 or later) for each key person and attach it in the Project Personnel section. Limit the length of each biosketch to *no more than* five (5) pages**.

Facilities (required)
This item is evaluated in the peer review. **Limit the text to one page per institution**. Follow the instructions on the template.

Human Subjects (required)
This item is evaluated in the peer review. **This form is required to be completed for applications that use Human Subjects, including those in the "Exempt" category. Applications that do not utilize Human Subjects should state "N/A" on the form and upload, as well.** Use additional pages, if necessary.

For applications requesting "Exemption" from regular Institutional Review Board (IRB) review and approval. Provide sufficient information in response to item #1 below to confirm there has been a determination that the designated exemptions are appropriate. The final approval of exemption from DHHS regulations must be made by an approved IRB. Documentation must be provided before an award is made. Research designated exempt is discussed in the NIH PHS Grant Application #398 http://grants2.nih.gov/grants/peer/tree_glossary.pdf. Most research projects funded by the CBCRP fall into Exemption category #4. Although a grant application is exempt from these regulations, it must, nevertheless, *indicate the parameters of the subject population* as requested on the form.

For applications needing full IRB approval: If you have answered **"YES"** on the Organization Assurances section of the application and designated no exemptions from the regulations, the following **seven points** must be addressed. In addition, when research involving human subjects

will take place at collaborating site(s) or other performance site(s), provide this information before discussing the seven points. Although no specific page limitation applies to this section, be succinct.

1. Provide a detailed description of the proposed involvement of human subjects in the project.
2. Describe the characteristics of the subject population, including its anticipated number, age range, and health status. It is the policy of the State of California, the University of California, and the CBCRP that research involving human subjects must include members of underserved groups in study populations. Applicants must describe how minorities will be included and define the criteria for inclusion or exclusion of any sub-population. If this requirement is not satisfied, the rationale must be clearly explained and justified. Also explain the rationale for the involvement of special classes of subjects, if any, such as fetuses, pregnant women, children, prisoners, other institutionalized individuals, or others who are likely to be vulnerable. Applications without such documentation are ineligible for funding and will not be evaluated.
3. Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records or data.
4. Describe the plans for recruiting subjects and the consent procedures to be followed, including: the circumstances under which consent will be sought and obtained, who will seek it; the nature of the information to be provided to the prospective subjects; and the method of documenting consent.
5. Describe any potential risks —physical, psychological, social, legal, or other. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.
6. Describe the procedures for protecting against, or minimizing, any potential risks (including risks to confidentiality), and assess their likely effectiveness. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects on the subjects. Also, where appropriate, describe the provision for monitoring the data collected to ensure the safety of subjects.
7. Discuss why the risks are reasonable in relation to the anticipated benefits to subjects, and in relation to the importance of knowledge that may be reasonably expected to result.

Documentation of Assurances for Human Subjects

In the Assurances tab, if available at the time of submission, include official documentation of the approval by the IRB, showing the title of this application, the principal investigator's name, and the approval date. Do not include supporting protocols. Approvals that are obtained under a different title, investigator or organization are *not* acceptable, unless they cross-reference the proposed project. Even if there is no applicant institution (i.e., an individual PI is the responsible applicant) and there is no institutional performance site, an USPHS-approved IRB must provide the assurance. If review is pending, final assurance should be forwarded to the CBCRP as soon as possible. Funds will not

be released until all assurances are received by the CBCRP. If the research organization(s) where the work with human subjects will take place is different than the applicant organization, then approvals from the boards of each will be required.

Data and Safety Monitoring Boards (DSMB)

Applications that include Phase I-III clinical trials may be required to provide a data and safety monitoring board (DSMB) as described in the NICI policy release, http://grants.nih.gov/grants/guide/notice-files/not98-084.html. This ensures patient safety, confidentiality, and guidelines for continuing or canceling a clinical trial based on data collected in the course of the studies. The CBCRP may require documentation that a DSMB is in place or planned prior to the onset of the trial.

Vertebrate Animals (optional)

This form is required ONLY for applications involving vertebrate animals.

If your application involves vertebrate animals the following five points must be addressed. When research involving vertebrate animals will take place at collaborating site(s) or other performance site(s), provide this information before discussing the five points. Although no specific page limitation applies to this section of the application, be succinct.

1. Provide a detailed description of the proposed use of the animals in the work outlined in the research plan. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.

2. Justify the use of animals, the choice of species, and the numbers used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.

3. Provide information on the veterinary care of the animals involved.

4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.

5. Describe any method of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. If it is not, present a justification for not following the recommendations.

Documentation of Assurances for Vertebrate Animals

Grants will not be awarded for research involving vertebrate animals unless the program for animal care and welfare meets the standards of the AAALAC or the institution has a U.S. Public Health Service assurance. In the appendix, if available at the time of submission, include official documentation of institutional review committee approval showing the title of this application, the principal investigator's name, and the inclusive approval dates; do not include supporting protocols. Approvals obtained under a different title, investigator, or institution are not acceptable unless they

cross-reference the proposed project. If review is pending, final assurances should be forwarded to the CBCRP as soon as possible. Funds will not be released until all assurances are received by the CBCRP.

Appendix (optional)

Follow the instructions and items list on the template. **The appendix may <u>not</u> be more than 30 pages in length.**

Note that the *research plan must be self-contained* and understandable without having to refer to the appendix. Only those materials necessary to facilitate the evaluation of the research plan or renewal report may be included; the appendix is not to be used to circumvent page limitations of the application.

Appendix A: CBCRP Chemical Testing Projects

Cycle 17 (2011) Special Research Initiatives

Biologically Relevant Screening of Endocrine Disruptors Research Page: Biologically relevant screening of endocrine disruptors (cloudgppnetwork.com)

Xenoestrogen-Specific Perturbations in the Human Breast Research Page: Xenoestrogen-specific perturbations in the human breast (cloudgppnetwork.com)

Cell Bioassays for Detection of Aromatase Gene Activators Research Page: Cell bioassays for detection of aromatase gene activators (cloudgppnetwork.com)

Biomarkers for Environmental Exposures in Breast Cancer Research Page: Biomarkers for environmental exposures in breast cancer (cloudgppnetwork.com)

Building on National Initiatives for New Chemicals Screening. Research Page: Building on National Initiatives for New Chemicals Screening (cloudgppnetwork.com)

Cycle 21 (2015) California Breast Cancer Prevention Initiatives

Human mammary organotypic cultures for chemical screening Research Page: Human mammary organotypic cultures for chemical screening (cloudgppnetwork.com)

Identifying human breast carcinogens using exposomics Research Page: Identifying human breast carcinogens using exposomics (cloudgppnetwork.com)

Chemical Safety During Breast Cancer Susceptible Windows Research Page: Chemical Safety During Breast Cancer Susceptible Windows (cloudgppnetwork.com)

Testing chemicals for likely contribution to breast cancer Research Page: Testing chemicals for likely contribution to breast cancer (cloudgppnetwork.com)

Chemical Testing to Prevent Cancer: Research Translation Research Page: Chemical Testing to Prevent Cancer: Research Translation (cloudgppnetwork.com)

Appendix B: Cost and Expense Guidelines

For all budget categories, clearly label all costs associated with research dissemination activities in the budget justification.

1) Personnel

- The Budget Summary line item for Personnel should reflect the total cost of all individuals identified as supported by the grant and their level of effort. In the personnel section of the application, be sure to name all individuals to be supported by the grant and provide their percent effort (months devoted to the project). All paid individuals must also be listed on the budget.

- Follow the NIH Guidelines and Calculation scheme for determining Months Devoted to Project, available at the links below:
    - NIH Guidelines:
    - http://grants.nih.gov/grants/policy/person_months_faqs.htm
    - NIH Calculation Scheme: http://grants.nih.gov/grants/policy/person_months_conversion_chart.xls

- When computing salary for key personnel, use only the base salary at the applicant organization, excluding any supplementary income (e.g., clinical or consulting incomes). CBCRP does not enforce a salary cap, as long as the overall budget adheres to the costs & expenses guidelines and the amount requested stays within the allowable costs.

2) Student Tuition Fees, Graduate Student Stipends

- For non-fellowship awards: Graduate students may be paid as personnel and may also receive tuition remission. Tuition remission, however, will be considered compensation. The total compensation (salary plus fringe benefits plus tuition listed in this category) may not exceed $30,000 per project year. A maximum of $16,000 per year is allowed for the combined costs of tuition/enrollment fee remission, fringe benefits, and health insurance. Stipend may be budgeted as salary (and included in the MTDC cost calculation) if the institution pays these expenses through a personnel line item.

3) Other Project Expenses

- Include expected costs for supplies and other research expenses not itemized elsewhere.
- Pooled expenses may be allowed as a direct cost at the discretion of the Program with certification of the following: 1) the project will be directly supported by the pooled expenses, 2) the pooled expenses have been specifically excluded from the indirect cost rate negotiation, and 3) the pooled expenses have been allocated consistently over time within the organization. Please explain any requested pooled expense requests in the budget justification.
- Advocate (s) Expenses. Include any travel, meeting, and consultation costs/fees associated with advocate engagement.

4) Equipment (Unit Cost over $5,000)

- Each requested equipment item must be >$5,000 and explain in budget justification.

5) Travel

- **Travel – CBCRP Meeting:** CBCRP may organize an event requiring your travel within the funded grant period. All applicants should budget a one-time minimum expense of $400 under year 1 in the travel budget line labeled: "Travel - CBCRP Meeting".
- **Travel - Project Related:** Project-related travel expenses are allowable only for travel directly related to the execution of the proposed research activities. Label such expenses as "Travel – Project Related." These expenses must be fully justified in the budget justification.
- **Travel - Scientific Meetings:** Scientific conference travel is limited to $2,000 per year (excluding a mandatory allocation of $400 in one year of the project for travel to the CBCRP Conference under Travel - CBCRP Meeting). Label such expenses as "Travel-Scientific Meetings" and explain in budget justification.

6) Service Contracts and Consultants

- Both categories require additional description (Budget Justification).

7) Subcontracts

- In the case of University of California applicants, subcontracts need to be categorized and broken out as one of two types, University of California-to-University of California (UC to UC) sub agreements or transfers; or, Other. A subcontract is not allowed to have another subcontract. Requires additional description (Budget Justification).

8) INDIRECT (F&A) COSTS

- **Indirect cost policy:** Indirect costs are NOT allowed for Conference Awards. For other awards, non-UC institutions are entitled to full F&A of the Modified Total Direct Cost base (MTDC); UC institutional F&A is capped at 30% MTDC (25% for off-campus projects).
- **Modified Total Direct Costs (MTDC)** include salaries and wages, fringe benefits, materials and supplies, services, travel, and up to the first $25,000 of each subgrant or subcontract (regardless of the period covered by the subgrant or subcontract) to an outside institution. MTDC does not include (indirect costs are not allowed on): capital expenditures, charges for patient care, scholarships and fellowships (including postdoctoral stipends), tuition remission and graduate student stipends, rental costs of space, equipment purchases more than $5,000 per item, the portion of each sub grant and subcontract in excess of the first $25,000, and the total cost of any subcontract from one UC to another UC campus. On a non-fellowship award, you may apply indirect costs to graduate student salary (under salary only, not as stipend) but not to tuition & fees.
- For all eligible projects that allow grantees to recover the full amount of their federally negotiated indirect cost rate agreement, grantees must also accept the full federally

recognized F&A rate for all award subcontractors (except for subcontracts to another UC institution, where F&A is not allowed). If a grantee or subcontractor does not have a federally negotiated F&A rate at the time of the proposal submission, the grantee and/or subcontractor may request a "De Minimis" F&A rate of 25% MTDC. A higher indirect rate that has been accepted for state or local government contract or other California grantmaker contract may be approved at the discretion of the Program Director and the Research Grants Program Office Executive Director.

- **INDIRECT COSTS ON SUBCONTRACTS**
  - The award recipient institution will pay indirect costs to the subcontractor.
  - For non-UC subcontracted partners, CBCRP will allow full F&A of the Modified Total Direct Cost (MTDC), as defined above.
  - F&A costs are not allowed for one UC institution's management of a subcontract to another UC institution.
  - The amount of the subcontracted partner's F&A costs can be added to the direct costs cap of any award type. Thus, the direct costs portion of the grant to the recipient institution may exceed the award type cap by the amount of the F&A costs to the subcontracted partner's institution.

Appendix C: Critical Path for CBCRP Program Initiatives

Purpose: The point of asking for the "critical path" is to have the PI place the project on a research continuum (i.e., temporal trajectory) that begins with an idea or hypothesis and continues through development leading to a defined result of practical value (e.g., in the clinic or community). First, ask yourself the question: How will my project and its research goals/milestones lead to a measurable impact on the prevention, detection, diagnosis and treatment, reduction in community and social burden, or improved patient quality of life for breast cancer?

Background: Breast cancer research funding has been successful in the creation of new knowledge. However, the useful application of this knowledge to prevent and detect the disease, and increase survival and quality of life for breast cancer patients could be improved. If funding agencies and researchers are to be accountable to stakeholders, more emphasis needs to be placed on the "critical path" from research-to-practice.

In 2003 Best et al. (*Cancer Epidemiology Biomarkers & Prevention*,12:705-712) distinguished two pathways to practical application of research, "…. it is important to view "translational research" to encompass not only the pervasive view of transfer of basic science discoveries into clinical applications ("bench to bedside"), but also its transfer into effective interventions at the population level with active community participation in the process ("bench to trench"). Collaboration between research producers and research consumers in this translational approach is critical to reduce the cancer burden at the population level, the ultimate measure of benefit to all people."

An early conceptualization and model for a "critical path" between research and action, developed in the context of smoking/tobacco, was advanced in 1985 by Peter Greenwald and Joseph Cullen (*J. Natl. Cancer Inst.*, 74:543-551) who distinguished phases of cancer control research:

Basic Research & Epidemiology
↓
Phase I: Hypothesis development
Phase II: Methods development
Phase III: Controlled intervention trials
Phase IV: Defined population studies
Phase V: Demonstration and implementation
↓
Nationwide prevention and health services programs

In addition, Phases I-V incorporate "feedback loops", so new hypotheses and methods can be generated in concert with novel intervention efforts. The "take home message" from this model is that the CBCRP expects researchers to actively consider where and how their results might find practical applications at the end of the "critical path." Thus, your research decision making and innovative approach should incorporate these elements when planning projects: (i) an awareness of the social (i.e., human and community) needs and environmental determinants of health and disease, (ii) limitations of current prevention, detection, prognosis, and treatment strategies, (iii) the state of the existing science for the topic being addressed, (iv) an understanding of the limitations and

barriers that block translation to a higher level, and (v) a framework for visualizing the desired research outcome and potential benefit (practical uses).

Overview and conceptual framework: The CBCRP believes that each grant should be capable of advancing the topic under investigation along the "critical path." To provide an outline to get you started, we have developed the following chart, which derived and greatly expanded from Table 1 in the FDA's "Challenge and Opportunity on the Critical Path to New Medical Products" (http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html). For the "critical path" dimensions/levels we have added definitions and provided examples of activities relevant to both the "basic science/clinical" and the "public health/community/population/social science" disciplines.

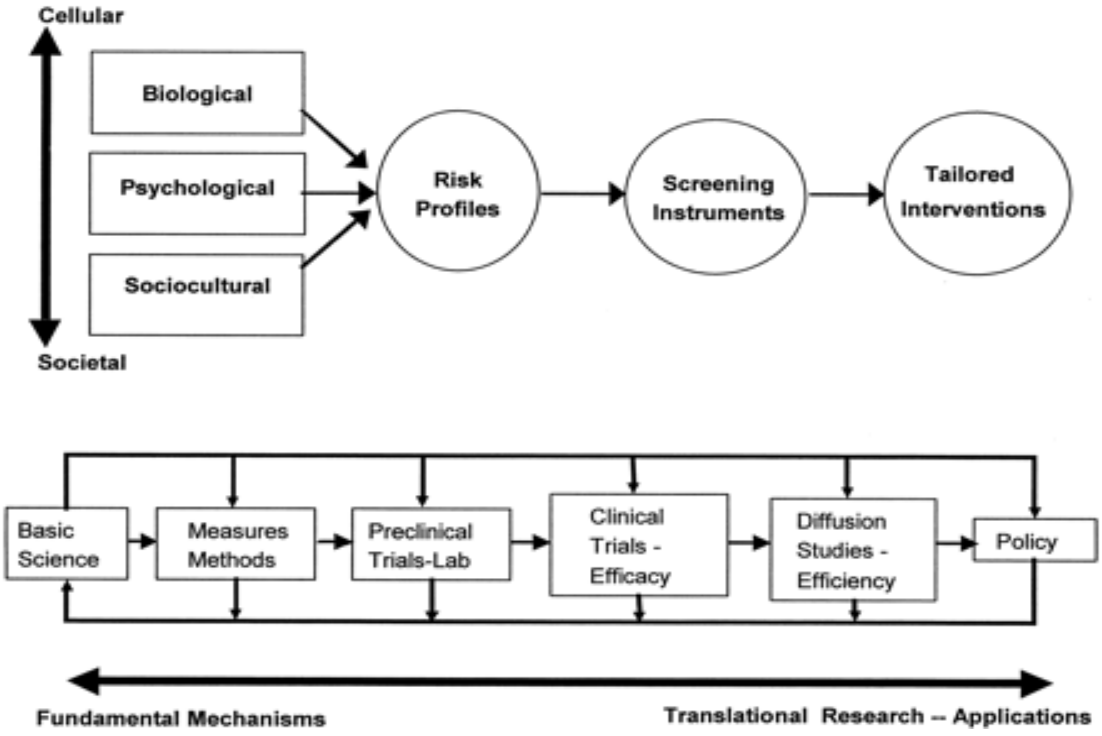
Dimension/Level	**Definitions**	**Examples of activities**
Concept & hypothesis development	Discovery and exploration The links between the hypothesis and a research problem in breast cancer Considering problems from novel perspectives Initial tests in basic systems Establishing the basis for scientist-community interactions	Basic science/clinical track: ○ Assessing background information in breast cancer, other cancer types, and cell/biological models. ○ Developing new information on breast cancer through data collection. ○ Establishing relationships to breast cancer. ○ "Mining" basic science for new treatment, detection, and prognosis concepts. ○ Pilot testing of new compounds and detection/prognosis strategies. Community/population/intervention track: ○ Considering social needs, disparities, and community issues from new perspectives. ○ "Mining" basic science for new epidemiological, behavioral, psychological, sociocultural or policy concepts. ○ Conceptualizing possible interventions. ○ Planning culturally appropriate, acceptable, and feasible delivery approaches for new community-based interventions and prevention strategies. ○ Identifying target populations and establishing new collaborations. ○ Demonstrating or gaining trust and acceptance by the community.

Dimension/Level	Definitions	Examples of activities
		○ Pilot data collection and field methodology developed. (Cancer control phase I --Cullen & Greenwald model)
Methods development and establishing "proof-of-principle"	Obtaining significant data to substantially support the hypothesis and point the direction for future work Establishing direct relevance to breast cancer in the basic science, clinical, or community settings Active scientist-community "partnering" in the research "Multi-disciplinary" collaborations (researchers in different disciplines work <u>independently</u> or sequentially on a common problem) Testing in small populations & initial data gathering	<u>Basic science/clinical track:</u> ○ Studies in model systems. ○ Integration into and challenging existing information on breast cancer. Publication. ○ Early pre-clinical phases (e.g., rational drug design, validate lead compounds). ○ Showing the potential to challenge and improve upon existing therapies and detection/prognosis standards. <u>Community/population/intervention track</u>: ○ Refine prevention strategies and collaborative networks. ○ Preliminary field tests of epidemiological hypotheses, policies or intervention methods and delivery systems. ○ Determination of outcome and process variables. ○ Development of measurement tools and data collection procedures. [Cancer Control Phases II and III (small trials) —Cullen & Greenwald model]
Developmental and testing phase	Formulating a strategy for practical application Stimulate interest in other researchers and "interdisciplinary" collaborations (researchers working	<u>Basic science/clinical track:</u> ○ Significant findings showing a clear connection to the disease. ○ Formulation and testing in animal models. ○ Publication and dissemination. ○ Late pre-clinical studies and early (Phase I & II) clinical trials.

Dimension/Level	Definitions	Examples of activities
	jointly to address a common problem) Generation of derivative concepts (feedback loop) Demonstrating efficacy or utility in a human detection, prognosis, or therapeutic setting. Researchers and community groups "partner" and reach common goals	○ Analysis of target groups and cost effectiveness. ○ Definitive links to target populations for detection, prognosis, treatment strategy. Community/population/intervention track: ○ Larger scale testing of epidemiological hypotheses, policies, or interventions in a well-defined populations enabling generalization to ultimate target populations (efficacy trial). ○ Systematic testing of epidemiological hypotheses, policy proposals, or community-based intervention in a larger population under "real-world" conditions (effectiveness trial). ○ Publication and dissemination. [Cancer Control Phases III (larger trials) & IV—Cullen & Greenwald model]
Implementation & translation	Wide acceptance of concept Improvements for detection, diagnosis, prognosis, and treatment Tangible social benefit New public health policies evolve from community-driven needs and researcher-driven outcomes to decrease disparities in detection, treatment, and disease burden Prevention and lowering risk for breast cancer	Basic science/clinical track: ○ Final basic research studies to validate a new clinical approach. ○ Feedback loop to stimulate new concepts to be tested (level #1) ○ Phase III & IV clinical trials. ○ Application of new therapies and chemoprevention approaches. ○ Advancing the standard of care. Community/population/intervention track: ○ Demonstration and implementation on a large scale. ○ Diffusion studies to other populations and communities. ○ Integration into cancer control health policy. ○ Interventions to lower disease incidence and mortality. (Cancer Control Phase V—Cullen & Greenwald model)

Finally, a major "critical path" limitation is the absence of cross-talk between disciplines. "Basic/clinical" and "public health/social/population/community" researchers often work apart.

Thus, the CBCRP is asking researchers to consider and explore avenues of research communication and common interest that allow the different disciplines to become integrated and lead to practical applications directed at breast cancer. This approach was recently presented by Best et al. (*Cancer Epidemiology Biomarkers & Prevention*,12:705-712),who proposed the term "transdisciplinary research." "*Transdisciplinarity* is a process by which researchers work jointly using a shared conceptual framework that draws together discipline-specific theories into a new synthesis of concepts, methods, measures, and approaches to address a common problem."



Final thoughts: Provide a brief, thoughtful discussion of how your research project would advance along a "critical path" to take your topic from one level to the next and provide practical applications. How might your innovative research "make a significant difference" and provide "transdisciplinary links" between the basic science, clinical, and public health/social/population/community research landscapes?

Appendix D: Other CBCRP Application Policies and Guidelines

Eligibility and Award Limits

1. **Any individual or organization in California may submit an application**. The research must be conducted primarily in California by Principal Investigators who are resident in California. We welcome investigators from community organizations, public or privately-owned corporations and other businesses, volunteer health organizations, health maintenance organizations, hospitals, laboratories, research institutions, colleges, and universities. **Applicants at California-based Nonprofit Institutions**: CBCRP will accept applicants from PIs at non-profit organizations or institutions, provided that the organization can manage the grant and demonstrate financial health. The organization must also meet our liability insurance requirements. If the application is recommended for funding, the University will collect additional information, such as tax ID numbers and financial reports, to review the organization during the pre-funding process to ensure all financial management and project management eligibility criteria can be met.
2. **We encourage researchers new to breast cancer to apply.** Applicants who have limited experience in breast cancer research should collaborate with established breast cancer researchers.
3. **Multiple applications and grant limits for PIs.** A PI may submit more than one application, but each must have unique specific aims. For Cycle 29 applicants are limited to a maximum of two (2) grants either as PI or co-PI, and these must be in different award types. The Program and Policy Initiative grants are not included in this limit. A PI may have more than one Program and Policy Initiative grant in a year.
4. **University of California Campus Employees:** In accord with University of California policy, investigators who are University employees and who receive any part of their salary through the University must submit grant proposals through their campus contracts and grants office ("Policy on the Requirement to Submit Proposals and to Receive Awards for Grants and Contracts through the University," Office of the President, December 15, 1994). Exceptions must be approved by the UC campus where the investigator is employed.

Policy on Applications from PIs with Delinquent Grant Reports

PIs with current RGPO grant support will not be eligible to apply for additional funding unless the required scientific and fiscal reports on their existing grants are up-to-date. This means that **Progress/Final Scientific Reports or Fiscal Reports that are more than one month overdue may subject an application to disqualification** unless the issue is either, (i) addressed by the PI and Institution within one month of notification, or (ii) the PI and Institution have received written permission from CBCRP to allow an extension of any report deadlines.

Confidentiality

CBCRP maintains confidentiality for all submitted applications with respect to the identity of applicants and applicant organizations, all contents of every application, and the outcome of reviews. For those applications that are funded CBCRP makes public, (i) the title, principal investigator(s), the name of the organization, and award amount in a "Compendium of Awards" for each funding cycle, (ii) the costs (both direct and indirect) in CBCRP's annual report, (iii) the project abstract and progress report abstracts on the CBCRP website. If the Program receives a request for additional

information on a funded grant, the principal investigator and institution will be notified prior to the Program's response to the request. Any sensitive or proprietary intellectual property in a grant will be edited and approved by the PI(s) and institution prior to release of the requested information.

No information will be released without prior approval from the PI for any application that is not funded.

Award Decisions

Applicants will be notified of their funding status by July 1, 2023. The written application critique from the review committee, the merit score average, component scores, and programmatic evaluation are provided at a later time. Some applications could be placed on a 'waiting list' for possible later funding.

Appeals of Funding Decisions

An appeal regarding the funding decision of a grant application may be made only on the basis of an alleged error in, or deviation from, a stated procedure (e.g., undeclared reviewer conflict of interest or mishandling of an application). The **period open for the appeal process is within 30 days of receipt of the application evaluation** from the Program office. Before submitting appeals, applicants are encouraged to talk about their concerns informally with the appropriate program officer or the CBCRP program director.

Final decisions on application funding appeals will be made by the Vice President for Research & Innovation, University of California, Office of the President. Applicants who disagree with the scientific review evaluation are invited to submit revised applications in a subsequent grant cycle with a detailed response to the review.

The full appeals policy can be found in the online the University of California, Office of the President, "RGPO Grant Administration Manual – Section 5: Dispute Resolution":

https://www.ucop.edu/research-grants-program/_files/documents/srp_forms/srp_gam.pdf

Pre-funding Requirements

Following notification by CBCRP of an offer of funding, the PI and applicant organization must accept and satisfy normal funding requirements in a timely manner. Common pre-funding items include:

1. Supply approved indirect (F&A) rate agreements as of the grant's start date and any derived budget calculations.
2. Supply any missing application forms or materials, including detailed budgets and justifications for any subcontract(s).
3. IRB applications or approvals pertaining to the award.
4. Resolution of any scientific overlap issues with other grants or pending applications.
5. Resolution of any Review Committee and Program recommendations, including specific aims, award budget, or duration.
6. Modify the title and lay abstract, if requested.

Publications Acknowledgement

All scientific publications and other products from a RGPO-funded research project must acknowledge the funding support from UC Office of the President, with reference to the specific CBCRP funding program and the assigned grant ID number.

Open Access Policy

As a recipient of a California Breast Cancer Research Program (CBCRP) grant award, you will be required to make all resulting research findings publicly available in accordance with the terms of the *Open Access Policy* of the Research Grants Program Office (RGPO) of the University of California, Office of the President (UCOP). This policy, which went into effect on April 22, 2014, is available here: https://www.ucop.edu/research-grants-program/grant-administration/rgpo-open-access-policy.html.

Grant Management Procedures and Policies

All CBCRP grant recipients must abide by other pre- and post-award requirements pertaining to Cost Share, Indirect Cost Rates, Monitoring & Payment of Subcontracts, Conflict of Interest, Disclosure of Violations, Return of Interest, Equipment and Residual Supplies, Records Retention, Open Access, and Reporting. Details concerning the requirements for grant recipients are available in a separate publication, the University of California, Office of the President, "***RGPO Grant Administration Manual***." The latest version of the Manual and programmatic updates can be obtained from the Program's office or viewed on our website: http://www.ucop.edu/research-grants-program/_files/documents/srp_forms/srp_gam.pdf

Contact Information

Technical support and questions about application instructions and forms should be addressed to the Research Grant Programs Office Contracts and Grants Unit:
RGPOGrants@ucop.edu

For scientific or research inquiries, please contact:
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The California Breast Cancer Research Program is part of the Research Grants Program Office of the University of California, Office of the President.