Request for Proposals (RFP)
Adverse Childhood Experiences and Breast Cancer Risk

California Breast Cancer Research Program
California Breast Cancer Prevention Initiatives

Deadline to apply
May 11, 2017

Table of Contents

About the California Breast Cancer Research Program and the California Breast Cancer Prevention Initiatives

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

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

- The 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
- The CBCRP is funded through the tobacco tax, 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 $8.5 million for breast cancer research.
- Ninety-five percent of our revenue goes directly to funding research and education efforts
- The CBCRP supports innovative breast cancer research and new approaches that other agencies may be reluctant to support.
- Since 1994, the CBCRP has awarded over $267 million in 1009 grants to over 130 institutions across the state. With continued investment, the CBCRP will work to find better ways to prevent, treat and cure breast cancer.

CBCPI Priority Areas

In 2004, the CBCRP launched its Special Research Initiatives. The CBCRP's Breast Cancer Research Council devoted 30 percent of CBCRP research funds to support coordinated, directed, and collaborative research strategies that increase knowledge about and create solutions to both the environmental causes of breast cancer and the unequal burden of the disease.

In March 2010, CBCRP's Council decided to build on the existing SRI by devoting 50 percent of CBCRP research funds between 2011 and 2015. This new effort is titled the California Breast Cancer Prevention Initiatives (CBCPI). Approximately $24 million will be dedicated to directed, coordinated, and collaborative research to pursue the most compelling and promising approaches to:

1. Identify and eliminate environmental causes of breast cancer.
2. Identify and eliminate disparities/inequities in the burden of breast cancer in California.
3. Population level interventions (including policy research) on known or suspected breast cancer risk factors and protective measures.
4. Targeted interventions for high-risk individuals, including new methods for identifying or assessing risk.

To focus these research efforts, the CBCRP issued a Request for Qualifications (RFQ) to fund a team to collaborate with the CBCRP to develop and implement the California Breast Cancer Prevention Initiatives

planning process. In 2010, the grant was awarded to Tracey Woodruff, PhD, MPH, Professor and Director of the University of California, San Francisco, Program on Reproductive Health and the Environment (PRHE).

In March 2015, CBCRP's Council approved fifteen (15) concept proposals to stimulate compelling and innovative research in all four topical areas of the CBCPI (environmental causes, health disparities, population-level interventions and targeted interventions for high risk individuals). A series of funding opportunities will be released over the next two years reflecting these concepts.

Adverse Childhood Experiences and Breast Cancer Risk

Available Funding

This initiative aims to investigate if adverse circumstances during childhood are associated with subsequent breast cancer incidence.

CBCRP intends to fund one project, with a maximum direct cost budget of $600,000 and a maximum duration of 3 years.

Completed responses to this RFP are due by the deadline: Thursday, May 11, 2017. Signed face pages of submitted applications must be emailed to RGPOgrants@ucop.edu by May 18, 2017. The project start date is August 2017.

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

There has been recent and dramatic growth in theoretical frameworks and plausible biological pathways underlying the relationship between childhood adversity and later health outcomes. Growing evidence shows childhood adversity not only shapes adult risk through its impact on health behaviors in adults (e.g. smoking, alcohol abuse, nutrition behaviors; Felitti et al., 1998; Cohen et al., 2010) but that it may also affect early life biological processes (e.g. accelerated cell aging; epigenetic changes, immune dysregulation; allostatic load; hyperinsulemia and hyperinflammation) (Baumeister et. al., 2016; Cole et. al., 2012; Fagundes et. al, 2013; Johnson et. al., 2013; Szyf, 2009; Tyrka, Price, Kao, Porton, Marsella, and Carpenter, 2010; Rose and Vona-Davis, 2012; Muti et al., 2002).

Although there is little consensus for the definition and conceptualization of childhood adversity, adverse childhood experiences (ACEs) often refers to exposures occurring during childhood to poverty; psychological, physical, or sexual abuse; neglect; drug abuse; incarceration of close family member(s); violence against a mother; parental loss; and mental illness in the household. In fact, exposure to these types of adversity have lasting effects in later life especially in chronic disease and genetic changes related to metabolic control and stress regulation (Szyf, 2009). Studies also indicate that childhood conditions can be important for later development of hypertension and cardiovascular disease (Barker

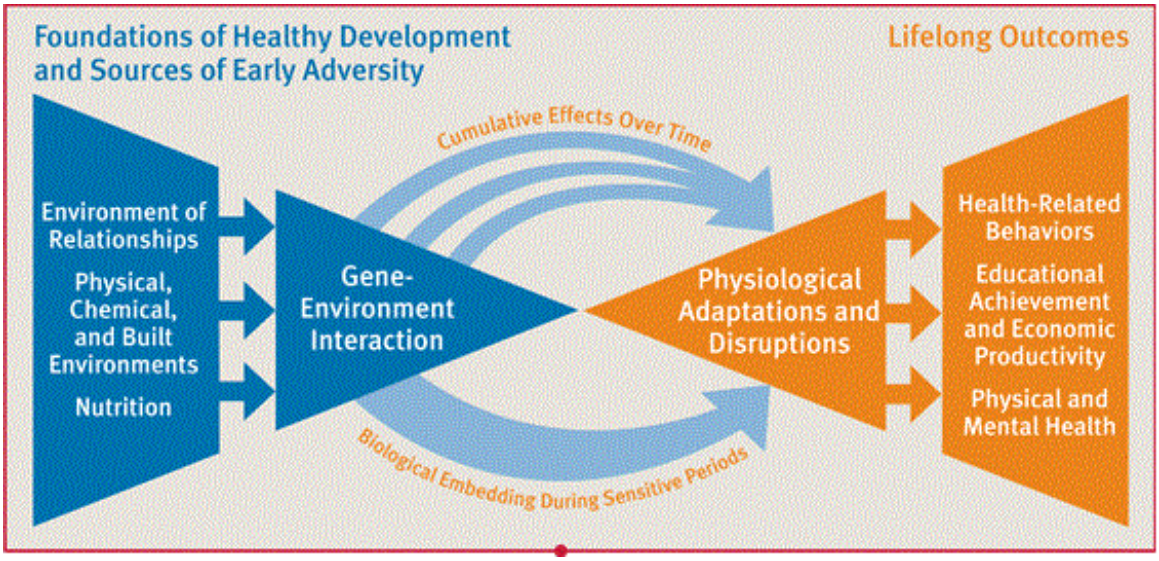
1995), cancer and lung disease (Felitti, et al 1998; Fuller-Thomson & Brennenstuhl, 2009; Morton et al 2012, etc.), while some others reported no such association (e.g.,Korpimaki, Sumanen, Sillanmaki, & Mattila, 2010). This discrepancy may be associated with how adversity is measured.

Toxic stress, an unfortunate byproduct of abuse, poverty and familial violence and/or mental instability, is also related to health outcomes later in life including depression, asthma, autoimmune disease and cancers (Johnson et. al., 2013; Luecken et. al., 2013). In addition to affecting behavioral, neurobiological and cognitive processes, evidence shows caregiving has an effect on physiological responses to stress (Luecken et. al., 2004).

Descriptive data also suggest varied and sometimes contradictory results on the relationship between childhood adversity and race/ethnicity with some studies report no difference in frequency of one or more ACEs between White and African American children (Flaherty et al., 2006), and other studies do with 50.3% of White children experiencing 1 or more ACE, compared to 61.2% African American children, and 57.1% Hispanic children (Felitti, et al., 1998). The relationship between ACEs and race/ethnicity may be mediated by other factors including poverty.

The Biodevelopmental Framework introduced by Harvard's Center for the Developing Child posits "biological embedding" during various "sensitive time periods" (Figure 1). The interplay between environmental and individual level factors in health and disease is focused on the cumulative impact or damage on an individual's physiology, health outcomes, achievement/productivity, and health related behaviors. Windows of susceptibility are periods over the life course where individuals are more susceptible to certain exposures. Windows of susceptibility is a promising area to investigate in order to advance understanding of breast cancer etiology. Two specific time periods, early childhood and puberty, are periods that may with the introduction of strong, frequent or prolonged adverse experiences create a toxic stress response that may negatively impact cognitive and physical development as well as cell development related to disease later in life.

Figure 1. Biodevelopmental Framework



Accessed through http://developingchild.harvard.edu

Relatively few studies to date have specifically investigated the possible connection between childhood adversity and breast cancer. Crosswell and colleagues (2014) assessed a possible association between childhood adversity and elevated inflammation (a predictor of breast cancer mortality) in breast cancer survivors and found a positive association between elevated inflammation with three types of adversity – abuse, neglect and unstable, unstructured home environments, with the association of inflammation and unstable home environment suggesting the impact of adversity on individuals can occur even when the adverse experience is not directed specifically at an individual but 'around them' (Crosswell et. al., 2014). Findings indicate that parental loss may be a predictor of breast cancer in women (Jacobs & Bovasso, 2000) and studies have linked childhood physical abuse to higher odds of cancer as an adult (Crosswell et.al, 2014; Fuller Thompson & Brennenstuhl, 2009; Morton et al., 2012).

Additional evidence suggests that ACEs could be causal factors of breast cancer risk pathways (e.g. childhood abuse linked to adult obesity; Mamun et al., 2007; Greenfield & Marks, 2009). Oxytocin, key in human functions such birth and milk ejection during lactation, is also important to social interaction, where oxytocin can be both shaped by and shapes mother-infant bonding and by negative and positive social experiences early in life (Alves et. al. 2015; Feldman, 2012; Olff et. al., 2013; Taylor et. al., 2014; Cushing and Kramer, 2005). Research has also shown a higher risk for early onset menarche, often linked to breast cancer risk, and the level of severity of childhood sexual abuse in early life, while physical abuse is associated with both early and late onset menarche (Boynton-Jarrett, 2013).

These developments in our understanding of the impact of ACEs on health raise a number of questions relevant to breast cancer. For instance, how might childhood adversity influence pre-menopausal and post-menopausal breast cancer development? Or, do all adverse experiences act equally across conditions (e.g. age at which they occur, severity, presence or absence of interventions to mitigate the impact)? Does exposure to adverse experiences occurring during childhood windows of susceptibility lead to an increase in breast cancer risk in later life?

Further empirical data is needed to fill gaps in knowledge regarding how childhood adversity leads to vulnerability to disease later in life (Luecken et. al., 2004). The growing ACE evidence, coupled with our understanding of windows of susceptibility in the development of breast cancer, opens a potentially fertile new avenue through which to explore prevention of and disparities in breast cancer.

Project Guidelines

The aim of this initiative is to investigate whether childhood adversity contributes to increased breast cancer risk, risk of specific breast cancer subtypes, and/or major risk factors for breast cancer.

Guidelines

Applicants should present research to stimulate this emerging field. Although creating and following a cohort of girls over time to document their ACEs and breast cancer outcomes is out of scope for this initiative, it is possible to assess childhood adversity retrospectively.

A project responsive to this solicitation could utilize an existing cohort of women, including women already diagnosed with breast cancer (with identified subtypes, pre/post-menopausal, ER/PR/Her2 positive and negative) and appropriate controls or the investigator(s) can propose a sound method to identify controls.

Methods to analyze existing cohort data to explore the relationship with ACESs during windows of susceptibility and breast cancer could:

- Use previously collected data to ascertain adverse childhood experiences (e.g. if established study has recorded data on parental loss, childhood economic hardship);
- Administer appropriate survey tools (e.g. Adverse Childhood Experiences instrument) to the cases and controls from an existing cohort of women to collect data on childhood adversity or breast cancer incidence;
- Link address data (e.g. Census data) to administrative/surveillance data (e.g. Behavioral Risk Factor Surveillance System or BRFSS data) to characterize childhood environments (e.g. residential neighborhood poverty) for an existing cohort of women;
- Leverage existing cohorts to examine the relationship between ACEs and breast cancer with larger samples of women; or
- Delineate the pathophysiology of pre- and post-menopausal breast cancer for ACE effects.

Applicants may select at least 1-2 ACEs or a composite of ACEs to study. The ACE selection must be justified and supported by existing literature and/or preliminary results of previously conducted research. Applicants can also include immigrant and foster care populations; as these populations are disproportionately impacted by ACEs.

Applicants should also identify how the results of the proposed research may seed policy or intervention development to prevent ACEs or to mitigate ACE effects in the prevention of breast cancer or breast cancer risk. Thus, the application should illustrate how the findings from the proposed research may elucidate where culturally grounded interventions are likely to have an impact in preventing breast cancer.

A Note about Advocacy Involvement in Research

Advocacy involvement is a requirement for the research funded under this initiative. Therefore, applicants should select a breast cancer or other appropriate community advocate(s), affiliated with an organization, to be actively involved in the proposed research. 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, in-person 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.

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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 comprised of scientists from relevant disciplines and breast cancer advocates and other community representatives. These reviewers assess the following scientific merit criteria:

- **Innovation** Extent to which the project explores new and potentially useful information about the relationship between ACEs and breast cancer. Are the concepts and hypotheses speculative and exploratory? Are methods novel and original? Has(ve) the investigator(s) thought creatively about how to measure and analyze ACEs, any indicators or variables related to this relationship?
- **Impact:** Potential for the project, if successful, to change our understanding of adverse childhood experiences and breast cancer and/or breast cancer risk pathways. Does the research have the ability to translate to population-level change? Will the data yielded by the research be to sufficient to inform policy or to move the field forward?
- **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? Is the outcome of breast cancer sufficiently defined (pre- and post-menopausal, receptor status)?
- **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 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 PI to the stated intent of the selected Initiative? Compare the PI's statements on the Other Review Criteria form and the content of the Lay and Scientific Abstracts to the CBCPI topic area. (A score of "0" for Responsiveness is an automatic disqualification.)

- **Dissemination and translation potential.** The degree to which the applicant's statements on the Other Review Criteria form provides a convincing argument that the proposed research has the potential to inform the development and/or implementation of policy or interventions to address the issue.

- **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?

- **Advocacy Involvement.** Are the named advocate(s) and advocacy organization appropriate for the proposed research project? 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 Process and Instructions

Submission Deadline: Applications must be submitted through proposalCENTRAL (https://proposalcentral.altum.com/) by Thursday, May 11, 2017.

Signed face pages of submitted applications must be emailed to RGPOgrants@ucop.edu by 5pm May 18, 2017.

proposalCENTRAL Online Submission Instructions

Formatting Instructions

All submissions must be in **English**.

Follow these format requirements for written text (consistent with NIH/PHS 398 form):

- The height of the letters must not be smaller than 11 point. Times New Roman or Arial are the suggested fonts.
- Type density must be no more than 15 characters per inch (cpi).
- Page margins, in all directions, must be at least 1/2 inch.
- PI(s) last names and first initials must be in a header, on each page, flush right.

Deviations from the page format, font size, specifications and page limitations are grounds for the CBCRP to reject and return the submission without peer review.

Online Application (Proposal) Management

The CBCRP requires applications be submitted via an online system: proposalCentral. Following are instructions on how to register and how to submit your response to the RFP. The submission deadline is May 11, 2017. *Note*: the proposalCENTRAL site shows East Coast times. Do NOT wait until the deadline to submit your application; if you miss the deadline, the system will not allow you to submit.

If you have any problems using proposalCENTRAL, please contact the proposalCENTRAL help line at (800) 875-2562.

Online Registration

The PI as well as the institution's signing official, contracts & grants manager and fiscal contact must be registered in proposalCENTRAL: https://proposalcentral.altum.com/. Start with "Click here to register". Fill out all the necessary fields on the registration page: First Name, Last Name, Email Address, User ID (can be your name), Password (case-sensitive), Challenge Question, and Answer.

Click BOTH BOXES on the bottom of the page to confirm your agreement with their "Terms of Service" and "Acceptable Use Policy." Click on the "Register" button. ProposalCENTRAL will send you an email with your username, password and a confirmation number. Once confirmed, you can login and the first time you enter the system, it will ask you to enter the confirmation number. You won't need that number again.

Online Forms and Fields

Once logged on, select the "Grant Opportunities" (gray) tab on the top of the page. Open up the filter and scroll down to California Breast Cancer Research Program. Sort the available funding by CBCRP and all of the funding opportunities for CBCRP will be showing. Choose the CBCPI-ACEs Initiative and click on "Apply Now" at the far right of the line.

Portions of the application are prepared using pre-formatted web pages in proposalCENTRAL (Proposal Sections 1 and 3-8). To move from section to section you can click the "Next" button to both save your work and go to the next section, or click "Save" and then click on the next section.

Proposal Section 2 allows you to download the Templates and Instructions for the CBCRP forms. After completing the forms on your computer, Proposal Section 9 allows you upload each one as PDF to attach it to your application.

❒ Title Page

On the "Title Page" enter the Project Title in the space provided (do not exceed 60 characters). Enter the total budget amount requested for the project, including indirect costs, if eligible. The projected start date for this project is August 2017. Enter the end date of the project (up to 3 years).

❒ Download Templates & Instructions

This section includes these instructions as well as the relevant application forms. You will need these forms in order to respond to this RFP.

❒ Enable Other Users to Access this Proposal

Note: A person must be registered in proposalCentral before s/he can be given access.
Read the instructions on this page thoroughly to understand the different levels of access. At the bottom of that page, in "Proposal Access User Selection," type in the email address of other individuals who will be working on the RFP, then click "Find User." Select the desired level of access and Click "Accept Changes" to save.

❒ Applicant/PI

Click on "Applicant/PI" and make sure that all required fields (identified with a red asterisk) are complete. (Click "Edit Professional Profile" to enter any missing data.)

Click “Return to Proposal” after entering missing data. Enter the % effort that the PI will devote to this project. The minimum effort for Principal Investigator is 10% FTE. Click “Save.”

❒ **Institution & Contacts**

On the “Institution & Contacts” page, make sure that all required fields (identified with a red asterisk) are complete, including the Signing Official, Contracts and Grants Official, and Fiscal (Accounting) Contact for the applicant institution. To complete these fields select the name or enter the email address of the individual in each of those roles and click “Add.”

If you add someone, the “Contact Screen - Applicant Institution” screen will open. Make sure that all required fields (identified with a red asterisk) are completed. Click “Save”, then click “Close Window.” Then click “Save” on the Institution & Contacts page.

❒ **CSO Codes and Keywords**

On this page you should select and add CSO codes. At www.icrpartnership.org/CSO.cfm you will find the seven major CSO categories, each with 4-9 sub-categories. Choose a major heading for your research and read the subcategory description. Choose the one that most closely fits. If your project fits under more than one CSO category, add a second code. The second code should represent a different, but integral, part of the research and about half of the total effort.

In addition, add three key words (1-3 words) that describe your project’s main topic, technology, or methods. This helps to place it in the appropriate review committee and assign reviewers. Please use words not in the title.

❒ **Budget**

Provide the total costs for the entire funding request for the grant year on this page. Make sure the budget numbers are exactly the same as those in the provided Excel Budget Summary form that you upload.

❒ **Organization Assurances**

Provide any required information for Human Subjects. If assurances will be required and have not yet been received, mark “pending” and enter the (proposed) date of submission in the “Approved or Pending Date”.

❒ **Upload RESEARCH PLAN and Other Attachments**

This page contains a duplicate list of the forms and instructions that are in Download Templates and Instructions (above and Proposal Section 2). This is where you will upload the CBCRP forms and any other attachments to your proposal; the required items are listed.

To upload attachments, fill in the fields at the top of the page:

- **Describe Attachment:** Provide a meaningful description, such as Jones CV.
- **Select Attachment Type:** From the drop down menu, select the type of form that is being attached.
- **Allowable File Type:** Only Adobe PDF document may be uploaded. Do not Password Protect your documents. Help on converting files to PDF can be found on the proposalCentral site at https://proposalcentral.altum.com/FAQ/FrequentlyAskedQuestions.asp.

- **Select File From Your Computer to attach:** The Browse button allows you to search for the PDF on your computer; click Open to select the file.

Note: Explicit instructions on the content of the documents to be uploaded follow in the "Instructions for CBCRP Forms" section.

❒ **Validate**

This function allows you to check whether all required items have been completed and attached. Don't wait until the last minute to check! Validate often during the course of completing your application so you have time to address missing items. Clicking the "Validate" button will either result in a link to missing items so you can easily go to the page and complete them, or a message at the top of the page "Has been validated and is ready to submit."

❒ **Print Face Page When Application Complete**

Applicants must print application's Face Page and obtain the necessary PI and institutional signing official signatures within a week of the electronic submission (see below).

❒ **Submit**

Submission is only possible when all required items have been completed and all required forms have been attached. Once an applicant hits "Submit," the application cannot be recalled.

❒ **Email Face Page Submission**

The PI, institution's signing official, Contract and Grants official and Fiscal (or Accounting) official all must sign the printed Face Page. Scan the signed form as a PDF and email to RGPOGrants@ucop.edu before 5 pm (Pacific Time) by May 18, 2017.

CBCRP Uploaded Form Instructions

Lay Abstract (REQUIRED)

This item is evaluated mainly in the programmatic review. The Lay Abstract is limited to one page and 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 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 you advocate partner to read this abstract and provide feedback.

Scientific Abstract (REQUIRED)

This item is evaluated mainly in the peer review. The Scientific Abstract is limited to one page and 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.

Other Review Criteria (REQUIRED)

This item is evaluated in the 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 CBCPI research area as outlined in the specific RFP

Program 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.

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(s) of Commitment (REQUIRED)

This item is evaluated in the programmatic review. Please use the template as a basis for commitment letters from the advocate(s). Limit the text to two pages.

Budget Summary (REQUIRED)

Please enter the budget for the presented categories by year into the summary sheet (Excel format). Additional instructions are presented on the form.

The maximum duration and direct costs may not exceed the following for the RFP *Adverse Childhood Experiences and Breast Cancer Risk.*

One Project: 3 Years & $600,000

Note: The amount of the 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 cap by the amount of the F&A costs to the subcontracted partner's institution.

Personnel. List the PI for the application and "individuals who contribute in a substantive way to the scientific development or execution of the project, whether or not salaries are requested." (NIH definition). Include those at the level of postdoctoral fellow and higher. Upload a NIH "Biographical Sketch and Other Support" form for each individual listed. The minimum "Months Devoted to Project" required for the PI is 1.2 months (= 10% FTE).

Other Project Expenses. Enter the costs associated with each category presented on the template (description to be provided in Budget Justification).

Advocate(s) Expenses. Include any travel, meeting, and consultation costs/fees associated with advocate engagement.

Equipment. Purchases up to $10,000 are allowed. Only include individual items >$5,000. Any items less than $5,000 must be purchased under the "supplies" budget category above.

Travel Expenses. Requested travel costs must be broken down and justified as Project-related, Annual meeting (third year only) or Scientific meeting (PI only capped at $2,000 per year).

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. Both categories require additional description (Budget Justification) and documentation (Appendix).

Service Agreements and Consultants. Both categories require additional description (Budget Justification) and documentation (Appendix).

Pooled Expenses. The RGPO takes a conservative budgeting approach to the allocation of pooled expenses. Pooled expenses such as insurance surcharges, system wide networking surcharges, and other pooled training and facilities expenses are generally disallowed as direct costs. Pooled expenses may be allowed at the discretion of the RGPO Program Director if the grantee can show that: 1) the project to be funded 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 (e.g. it is not allowable to charge a new indirect expense such as "facilities" as a direct line item in order to recoup funds lost due a poorly negotiated rate agreement). No indirect cost recovery will be allowed on pooled expenses.

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 25% MTDC*

**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.*

Please see the RFP under **Allowable Indirect (F&A) Costs** for more information.

Budget Justification & Facilities (REQUIRED)

This item is evaluated in the peer review. Limit the text to two pages. Follow the instructions on the template. The minimum "Months Devoted to Project" required for each PI is 1.2 months (= 10% FTE).

Key Personnel (REQUIRED)

This item is evaluated in the peer review. Limit the text to one page. Follow the instructions on the template.

Biographical Sketch & Other Support (REQUIRED)

This item is evaluated in the peer review. Use the NIH form. Limit the length of each biosketch to *no more than* five (5) pages.

Research Plan (REQUIRED)

This section is the **most important** for the peer review. Note carefully the page limits, format requirements, and suggested format.

Page limit: 12 pages

An additional 3 pages is allowed for References.

Format issues: Begin this section of the application using the 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 at least ½ inch.

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

Applicants should be clear in describing how their proposed research project adheres to, and/or builds on, approaches/methods described in the RFP including the expectations at the end of the Pilot. A proposed research project may include to one or more of these interest areas.

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 CBCPI 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, multi-generational studies and ethnic groups.

Research Design and Methods: Provide an overview of the experimental design, the methods to be used, and how data is 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 timeline at the end will demonstrate how the aims are interrelated, prioritized, and feasible. Explain the use of human subjects and vertebrate animals and show their relationship to the specific aims.

Resources and Facilities: Describe the resources and facilities to be used (e.g., laboratory space, core facilities, major equipment, access to populations, statistical resources, animal care, and clinical resources) and indicate their capacities, relative proximity and extent of availability. Include an explanation of any consortium/ contractual arrangements with other organizations regarding use of these resources or facilities. Describe resources supplied by subcontractors and those that are external to the institution. Make sure all of the research needs described in the research plan are addressed in this section.

Human Subjects (REQUIRED)

This item is evaluated in the peer review. **This form is required only for applications that use Human Subjects, including those in the "Exempt" category. Use additional pages, if necessary. For applications requesting "Exemption"** from regular IRB review and approval please 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 Institutional Review Board (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 falls 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 CBCPI Application Face Page 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 appendix, 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 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, but **no later than August 1, 2017.** 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 NIH 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.

Appendix List (OPTIONAL)

Follow the instructions and items list on the template. **The appendix may not 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.

General Funding Policies

Eligibility and Award Limits

1. Any individual or organization in California may submit an application. The research must be conducted primarily 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.
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. PIs who have previously been funded by CBCRP are welcome to apply, but the research aims must be distinct from their previous CBCRP grants.
4. Multiple applications and grant limits for PIs. A PI may submit more than one application, but each must have unique specific aims. For Cycle 23 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 Research Initiative grants are not included in this limit. A PI may have more than one Research Initiative grant in a year.

Policy on Applications from PIs with Delinquent CBCRP Grant Reports

PIs with current CBCRP 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 a Cycle 23 application to possible 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 the CBCRP to allow an extension of any report deadlines.

Application Revision Guidelines

A revised application must have the same principal investigator as the original application. When possible it should have the same title as the original application. However, if the specific aims of the project have changed sufficiently, then a modified title may be chosen. A revision submission for all eligible award types (except CRCs) must include a section of not more than 2 pages uploaded as a part of the Research Plan. This section is a summary of the substantial additions, deletions, and changes that have been made. It must also include responses to criticisms in the previous Review Committee evaluation. This material does not count towards the normal page limit for the Research Plan. We also recommend emphasizing in the Research Plan any relevant work done since the previous application. CRC applicants should follow the directions in the CRC application materials regarding resubmissions.

Confidentiality

The 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 the 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 the CBCRP’s annual report, (iii) the project abstract and progress report abstracts on the CBCRP Web site. 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.

Human Subjects and Vertebrate Animal Use

If a project proposes activities that pose unacceptable potential for human and animal subject risks, then a recommendation either not to fund or to delay funding until the issue is resolved may result.

IRB approval, human subject "exemption" approval, or animal assurance documentation must be provided prior to funding, but is not needed for application review. Applicants are encouraged to apply to the appropriate board or committee as soon as possible in order to expedite the start of the project, and you must do so before or within 21 days of notification that an award has been offered. If all reasonable efforts are not made to obtain appropriate approvals in a timely fashion, funds may be reallocated to other potential grantees' proposed research projects.

Award Decisions

Applicants will be notified of their funding status by July 1, 2017. The written application critique from the review committee, the merit score average, component scores, percentile ranking, 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). Details concerning the appeals procedure may be obtained from the appropriate Research Administrator (with whom the applicant is encouraged to discuss his/her concerns), the CBCRP Director, or by contacting us through the CBCRP Web site: www.cabreastcancer.org/. The period open for the appeal process is within 30 days of receipt of the application evaluation from the Program office. Contact the CBCRP to obtain full information on the appeals process.

Final decisions on application funding appeals will be made by the UCOP Research Grant Program Office (RGPO) Executive Director Dr. Mary Croughan. 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.

Pre-funding Requirements

Following notification by the 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:

- Verification of Principal Investigator status from an appropriate institutional official.
- Documentation of 501(c)(3) non-profit organization status for the organizations.
- Documentation of the DHHS-negotiated (or equivalent) indirect cost rate for non-U.C. institutions.
- Supply up-to-date documentation for approved indirect rate (F&A costs) agreements as of the grant's start date and any derived calculations, if applicable.

- Supply any missing application forms or materials, including detailed budgets and justifications for any subcontract(s).
- IRB applications or approvals pertaining to the award.
- Resolution of any scientific overlap issues with other grants or pending applications.
- Resolution of any Review Committee and Program recommendations, including specific aims, award budget, or duration.
- Modify the title and lay abstract, if requested.

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 below:

RGPO Open Access Policy

The UCOP Research Grants Program Office (RGPO) is committed to disseminating research as widely as possible to promote the public benefit. To that end, all RGPO grantee institutions and researchers grant RGPO a nonexclusive, irrevocable, worldwide license to exercise any and all rights under copyright and in any medium for all scholarly articles and similar works generated as a result of an RGPO grant award, and agree to authorize others to do the same, for the purpose of making their articles widely and freely available in an open access repository. This policy does not transfer copyright ownership, which remains with the author(s) or copyright owners.

Scope and Waiver (Opt-Out)

The policy applies to all scholarly articles and similar works authored or co-authored as a result of research sponsored by an RGPO grant, except for any articles published before the adoption of this policy and any articles for which the grantee institution and/or researchers entered into an incompatible licensing or assignment agreement before the adoption of this policy. Upon express written request of the institutional grantee and/or researcher, RGPO will waive the license for a particular article or delay "open access" to the article for a specified period of time.

Deposit of Articles

To assist the RGPO in disseminating and archiving the articles, the grantee institution and all researchers to the grant award will commit to helping the RGPO to obtain copies of the articles that are published as a result of an RGPO sponsored grant award. Specifically, each author will provide an electronic copy of his or her final version of the article to the RGPO by the date of its publication for inclusion in an open access repository, subject to any applicable waiver or delay referenced above. Notwithstanding the above, this policy does not in any way prescribe or limit the venue of publication.

Grant Management Procedures and Policies

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 Web site: http://www.ucop.edu/research-grants-program/grant-administration/index.html.