Request for Proposals (RFP)

Shift Work and Breast Cancer Risk

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

Released: December 01, 2023
Deadline to apply: March 01, 2024

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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.

Shift Work and Breast Cancer Risk

Available Funding

This initiative aims to: determine whether breast cancer risk is higher among individuals in the workforce who occupy low-wage hourly positions with histories of unpredictable shifts (i.e., those controlled by employers) [Project type 1]; and develop intervention(s) for known risk(s) associated with night shift work and test for intervention feasibility and acceptability [Project type 2].

For both types of project, we are expecting investigators to collaborate with workers/community members using community-partnered participatory research methods (CPPR) for the development of study questions and protocols and interpretation (including language) and dissemination of results.

CBCRP intends to fund up to two projects with a maximum duration of two years at a maximum total direct cost of $300,000 for Project 1 and $350,000 for Project 2.

Completed responses to this RFP are due by Friday, March 01, 2024, 12 Noon PT. The project start date is August 01, 2024.

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Background/Justification

There is significant observational epidemiologic data, biological (melatonin levels) and genetic (clock gene function and alteration) studies that support the theory that light at night disrupts the circadian rhythm in women and predisposes them to a higher risk of breast cancer. Shift work at night is a major exposure to light at night and disruptor of circadian rhythm.

Shift Work, Circadian Rhythm, Melatonin and Breast Cancer

In 2007, the International Agency for Cancer Research (IARC) Monograph working group listed shift work that involves circadian disruption as a class 2a or probable carcinogen. This designation put shift work in the same category as anabolic steroids, vinyl fluoride, nitrogen mustard and 62 other agents as class 2a carcinogenic agents. The 2019 IARC Monographs meeting changed the title to Shift Work at Night to better describe the exposure and subsequently re-affirmed the exposures classification as 2a or probable carcinogen. (1,2) The causal link(s) between nighttime shiftwork and breast cancer has yet to be established; however, light at night related circadian rhythm disruption provides a plausible biological mechanism that connects cancer risk with nighttime shift work.

Melatonin

Normal nighttime melatonin levels not only regulate the sleep-wake cycle, but also affect tumor cell differentiation, proliferation and apoptosis and may affect breast cancer invasion through the modulation of specific signaling pathways. *In vitro* studies of melatonin have demonstrated anti-human breast cancer tumor effects. (3) Melatonin exerts an inhibitory effect on breast cancer cell invasion through down-regulation of the p38 pathway, and inhibition of MMP-2 and MMP-9 expression and activity. (4)

Workers who are subject to shift rotations can present a more complex model for understanding the health impact of light at night on the sleep-wake cycle and melatonin production. One study published by Dumont & Lanctôt, for example, attempted to understand the effect of shift rotations, light exposure and melatonin levels. (5) In their study they measured 24-hr urinary excretion of urinary 6-sulfatoxymelatonin (aMT6s) and ambulatory light exposure during both night shift and day/evening shift periods in 13 full-time rotating shift workers. Their results showed that the total 24-h urinary excretion of aMT6s were the same in all shift work groups. However, there was a reversal of the normal sleep-wake levels of aMT6s, which implied that melatonin levels were higher during the day and lower at night, the opposite of what is normally observed in the sleep-wake cycle. With the exception of the reversal in the normal day-night pattern of melatonin production, the same study showed that although the total aMT6s levels in all groups were the same, higher levels of light exposure during night work may result in decreased total melatonin production. This interpretation is consistent with the proposition that circadian disruption, of which decreased melatonin production is only one of the adverse consequences, could be the mediator between night shift work and cancer risks. (5)

Clock genes

The circadian timing mechanism in mammals is controlled by the suprachiasmatic nuclei (SCN). Filipski, et al created a mouse model to evaluate the effect of severe circadian dysfunction (ablation of the SCN) on tumor progression in mice with implants of Glasgow osteosarcoma and pancreatic adenocarcinoma. Both tumor types grew 2-3 times faster in mice with SCN lesions than in sham-operated mice. Survival of mice with SCN lesions was statistically significantly shorter compared with that of sham-operated mice. The study authors concluded that disruption of circadian rhythms in mice was associated with accelerated growth of these malignant tumors, suggesting that the host circadian clock may play an important role in endogenous control of tumor progression. (6)

It has been estimated that 2–10% of all mammalian genes are clock-controlled, indicating extensive circadian gene regulation. (7) Just as disruption of the circadian rhythm affects nighttime melatonin levels, disruptions in the sleep-wake cycle, such as caused by nighttime shift work, may also affect circadian clock-controlled genes. (8) There is a large and growing literature on the effects of circadian gene knockouts (KO) in mice, and polymorphisms in humans, on disease risk. (9,10) These studies suggest the possibility that absent or altered function of circadian genes may increase the risk of some diseases in people. In the first

molecular epidemiologic study of a circadian gene and risk of human cancer, a structural variant in the circadian gene PER3 was detected to be significantly associated with increased risk of breast cancer and may be a potential biomarker for breast cancer (11). This clock–cancer connection was confirmed in later studies, which showed genetic associations between the circadian genes *NPAS2*, *CRY2* and *CLOCK* and breast cancer risk. (12, 13, 14, 15)

Epidemiological evidence

The association between breast cancer and night work has been reported by numerous epidemiologic studies, including cohort studies, case-control studies, and meta-analyses. (2) The CBCRP funded report "Paths to Prevention: The California Breast Cancer Primary Prevention Plan" (available here: California Breast Cancer Plan: Paths to Prevention - Breast Cancer Prevention Partners (BCPP)) summarizes the recent evidence connecting light at night and, in particular, shift work to increased risk of breast cancer.

An important aspect to the assessment of causation from epidemiological studies is the coherence of studies in specific subpopulations with the co-distribution in time and space of the exposure of interest with the disease outcome in the entire population, which is unlikely to occur with long latency diseases such as breast cancer. (16,17). Although coherence between and across studies may not be met (causality), Stevens (17) provides an excellent summary of epidemiological studies in areas that should show an association between night shift work and breast cancer: night shift work, blind women, longer sleep duration, low bedroom light. Mounting evidence supports an association of non-day shift work and breast cancer risk; several studies report lower risk in blind women; long sleep duration is associated with reduced risk in two of three prospective studies; and two studies have reported some association of bedroom light level and risk. (17,18) Other studies have attempted to assess the effect of light at night on a community level.

A last important environment to assess the effect of light at night on health is at the population level. Population analysis attempts to answer the question: is nighttime light level of communities associated with breast cancer incidence in those communities? The first analysis to test this prediction was that of Kloog *et al.* from Israel. They combined into regression models of breast cancer incidence in 147 communities, satellite data on nocturnal illumination from the same communities, as well as information on per capita income, population density, birth rate and ethnic makeup. They also modeled lung cancer incidence as a 'negative control' as a test of the specificity of their method. Nocturnal community light level was significantly associated with breast cancer incidence, and from the model, the highest LAN intensity community had a 73% higher incidence than the lowest. There was no association of LAN and lung cancer incidence. (19)

The Breast Cancer Now Generations Study, which followed 113,000 women over a forty-year period, reported their findings on light at night exposure and breast cancer. When participants entered the study, from 2003 onwards, their exposure to light at night and sleeping patterns were established through questionnaires, classifying light levels in their bedroom as low (too

dark to see your hand, or you wear a mask), medium (light enough to see your hand in front of you, but not to see across the room) or high (light enough to see across the room, but not read, or light enough to read). The Study concluded that exposure to light at night does not increase breast cancer risk. (20)

In Sweden and Germany, studies showed an association between working night shift for more than 20 years and risk for breast cancer. (21,22) However, a dose-response relationship has not clearly emerged among workers exposed to less than 20 years of night work. (23) Lee et al. looking at workers in Korea, concluded that breast cancer in patients with high exposure to night work should be understood to be an occupational disease, and patients should be eligible for workers' compensation, as in Denmark. In Korea, general working hours are longer and night shifts for shift workers are more frequent than in European countries. Therefore, various factors, such as total working hours, the frequency of night work, work schedules (including rotating schedules and rest periods after night shifts), and co-exposure to other occupational carcinogens additional to years of employment in non-day shift work must be considered. Furthermore, they concluded that restrictions on the frequency of night shifts or exposure periods to night work might be considered in order to reduce the risk of breast cancer among night workers in Korea or elsewhere. (23)

Wegrzyn et al. (24), using data from 2 prospective cohort studies, the Nurses' Health Study I and II, examined associations between rotating night shift work and breast cancer risk. In the two cohorts, there were a total of 9,541 incident invasive breast malignancies and 24 years of follow-up. In the Nurses' Health Study I, women with 30 years or more of shift work did not have a higher risk of breast cancer compared with those who never did shift work, although follow-up occurred primarily after retirement from shift work. Among participants in the Nurses' Health Study II, who were younger than participants in NHS I, the risk of breast cancer was significantly higher in women with 20 years or more of shift work at baseline, reflecting young-adult exposure and remained marginally significantly higher when they used updated exposure information. They concluded that long-term rotating night shift work was associated with a higher risk of breast cancer, particularly among women who performed shift work during young adulthood. They called for further studies to explore the role of shift work timing on breast cancer risk.

Conclusion - Although numerous epidemiologic studies have reported a positive association between light at night exposure and breast cancer, other studies report no effect. There is a need to create coherence between study subpopulations and standardize study methodology. In addition, there is a need to measure more precisely the actual disruption of the circadian rhythm and reflect that disruption against health outcome(s) in large cohorts.

Low Wage Shift Work and Breast Cancer

Although the causal link between shift work at night and increased risk of breast cancer has yet to be established, social factors like socioeconomic status have the potential to exacerbate the connection. In July 2013, the Urban Institute released a report titled, "Nonstandard Work

Schedules and the Well-Being of Low-Income Families" that described occupations and industries with the highest share of workers with non-standard schedules. (25) Occupations with high percentages of non-standard schedules included security guards, waiters/waitresses, nurses and home health aides, janitors and laborers. Industries with highest percentages include accommodation and food, arts and entertainment and retail, transporting and warehousing, health, and social assistance. (25) Hansen notes the following sectors with high rates of night work – hospitals, hotels, transportation, security, and industries that depend on 24-hour production schedules. (26)

Schedules that vary from day to day or from week to week (27) and schedule unpredictability occur when the hours or days of work are controlled solely by employers without input from workers. In 2012, almost 3 in 5 wage and salary workers, 75.3 million in total, were paid by the hour. (26) These low-income and part-time workers are often ignored in studies of the effects of shift work. In a survey of problematic scheduling among a large representative sample of early career adults (26 to 32 years of age) working hourly jobs, 41% reported knowing "when they need to work" one week or less in advance of the work week in question. (27) The percentage was even higher for part-time workers (47%).

Lambert, Fugiel, and Henly (2014) found that 45% of mothers with children below the age of 12 years reported that their employers decided their schedule without their input and concluded that women are disproportionately affected by the necessity to arrange childcare. (28)

In a seminal work on shift work and health, Finn was among the first to suggest that unpredictable shift work that is out of the control of workers interrupts endocrine and other physiological processes and that rhythmic adjustments to new work schedules take days to weeks to occur. Consequently, the body is in a constant state of adjustment, with both physical and emotional consequences. (29) This almost certainly is compounded by work-life conflict (30), defined as stress associated with managing work and family responsibilities, such as finding last-minute childcare for working single mothers. In addition, unpredictable work schedules, such as last-minute changes of work shifts, may lead to income instability and such economic volatility may cause additional stress and conflicts for low-wage workers. (31)

The physiological stress produced in individuals who work in low-wage jobs with unpredictable work schedules and the work-life conflict that it produces (e.g., finding last minute childcare, interfering with establishing and maintaining partner or other social relationships, and arranging food shopping and transportation) suggests another route to breast cancer beyond that which comes from light exposure during night shifts. Linnenbringer, Geronimus, and Gehlert and others posit a physiological route through repeated demands on stress hormone system and the ultimate physiological "weathering" that it brings. (32, 33)

Research Questions

The first research aim is to determine whether breast cancer risk is higher among individuals who work in low-wage hourly jobs with histories of unpredictable shifts (i.e., those controlled by employers) than the general population. This work will likely require the use of existing large datasets and secondary data analysis. The second research aim seeks to develop intervention(s) for known breast cancer risk(s) associated with night shift work and test for intervention feasibility and acceptability. This may require original data collection and may require qualitative and quantitative approaches.

For both types of projects, we are expecting investigators to collaborate with workers/community members using community-partnered participatory research methods (CPPR) for the development of study questions and protocols and interpretation (including language) and dissemination of results. Proposals should outline the strategies that will be used to connect with the communities.

Project 1: Low-wage Shift Work and Breast Cancer

Specific aim: Determine whether breast cancer risk is elevated among individuals who work in low-wage hourly jobs with histories of unpredictable shifts (i.e., those controlled by employers) that disrupt circadian rhythm.

Project 2: Night Shift Work and Breast Cancer

Specific aim: Develop and pilot an intervention to reduce or minimize known BC risk(s), particularly light at night associated with shift work and associated body-clock disruptions, and test for the intervention feasibility and acceptability.

Approaches and Methods

Given the knowledge to date, the program is seeking applications related to the topics below. Applicants can submit an application for Project 1 or Project 2 but will only be funded for one.

For each proposal, we are seeking Community Partnered Participatory Research (CPPR) projects with both academic and community Co-PIs.

Project 1: Low-wage Shift Work and Breast Cancer

Specific Aim: Study whether breast cancer risk is higher among individuals who work in low-wage hourly jobs with histories of unpredictable shifts (i.e., those controlled by employers) that disrupt circadian rhythm.

Use secondary data to investigate the link between low-wage unpredictable shift work and breast cancer. The intent of the request for proposals is to explore the possible connection between unpredictable shift work among low-wage workers and breast cancer.

As an example, this might be done by linking data from the California Cancer Registry with state employment data. The O*NET database, sponsored by the US Department of Labor and the Employment and Training Administration, contains detailed information on almost 1,000 occupations. Workers' responses to survey questions are used to create measures capturing a

multitude of different aspects of an occupation, e.g., use of technology, physical demands, customer interaction, skills required - and many, many more. Researchers can add these measures to any dataset by matching on SOC (Standard Occupational Classification) codes, which are commonly used to classify jobs. This allows researchers to incorporate different aspects of job quality into the analysis. Other datasets could also be appropriate.

Project 2: Night Shift Work and Breast Cancer

Specific Aim: Develop and pilot an intervention that has the potential to reduce or minimize the BC risk(s) of light at night associated with shift work and associated body-clock disruptions, and test for the intervention feasibility and acceptability.

Because shift work at night is an important cause of circadian rhythm disruption and because shift work at night affects growing numbers of working women, we seek proposed interventions that modify or reduce the impact that shift work has on the sleep-wake cycle and ultimately the risk of breast cancer. These factors include, but are not limited to, total working hours, the frequency of night work, work schedules (including rotating schedules and rest periods after night shifts). Furthermore, restrictions on the frequency of night shifts or exposure periods to night work might be considered in order to reduce the risk of breast cancer among night workers. We welcome new ideas from communities/stakeholders or from other disciplinary perspectives.

We seek ways of informing interventions that can be tested, that reduce the environmental impact of light at night on the circadian or sleep-wake cycle in women (i.e. architectural design changes, innovative lighting technology, work shift modification or flexibility). These may be at various levels of influence from individual to professional, industry, or local, state, or federal administrative policy.

Since scheduling policies determine nighttime work shift exposure, we welcome pilot intervention projects informed by a careful review of the literature and well-designed stakeholder input to design policies and practices to mitigate exposure to light at night. Ideas might include alternative methods of assigning shifts, changes in work design and lighting, or ways of balancing light exposure during and outside work hours.

The proposal must include a plan for partnering with the community of interest and other key stakeholders. The proposal should describe collaboration with communities and other stakeholders of interest and how they will participate actively in the design and development of the intervention and its initial testing.

Resources to be Used or Considered for Use

Both projects should use a CPPR approach with partners from and with connections to the shift working community.

Project 1: Low-wage Shift Work and Breast Cancer

Specific Aim: Study whether breast cancer risk is higher among individuals who work low-wage hourly jobs with histories of unpredictable shifts (i.e., those controlled by employers) that disrupt circadian rhythm.

- Requires the inclusion of an epidemiologist or statistician with expertise in the use of secondary data sources and in combining administrative data sources.
- Requires large data sets, one of which could be the California Cancer Registry. It also requires sources of employment data, such as the O*NET database. These are example data sets. We welcome the use other data sets.
- Applicants are encouraged to factor in windows of susceptibility in the analysis, such as accounting for age at exposure.

Project 2: Night Shift Work and Breast Cancer

Specific Aim: After a careful review of the literature, in concert with appropriate stakeholders, design and develop an intervention that has the potential to reduce or minimize BC risk(s) associated with exposure to light at night during shift work and associated body-clock disruptions. Test the intervention for feasibility and acceptability.

This project will need:

- Investigative team member with demonstrated expertise in developing interventions and testing their feasibility.
- A team member with experience working night shift work studies.
- Experience using precision assessment and assessment of exposure (e.g. shift timing and shift rotational frequency).
- Team members with experience in conducting qualitative research.
- Organizational or institutional resources to facilitate the development and testing of intervention would be valued. For example, statistical expertise and experience to evaluate intervention effectiveness.
- A track record of recruiting diverse samples of women for research.

Depending on the design of the project, the team may need to include additional expertise. A few examples of situations and expertise are described below. This is not an exhaustive list.

- The inclusion of a health economist to assess the cost and benefit of the intervention may be warranted for some types of studies.

- If investigators seek to reduce the impact of nighttime shift work at the level of policy, then an ideal research team would include expertise in studying formulation of policies that affect shift work design and implementation.
- If investigators pursue interventions involving reducing the effects of light at night through lighting innovation, then demonstrated expertise in industrial lighting and health outcomes would be necessary.

Dissemination Plans

The project plan needs to include a dissemination plan. The dissemination plan should describe how the dissemination activities will be undertaken throughout the project and justify the frequency of the dissemination elements. The plan should specify the personnel devoted to the dissemination team and their roles as well as the target audience including non-research stakeholders, especially workers, their representatives, employers, community members and policy makers. The dissemination plan should take into account audiences, messages, channels, milestones, and appropriate resources to reach milestones. A strong project will have outcomes that have potential to impact policy and/or translational potential.

The dissemination plan should reflect an effort to disseminate the information to an audience that reflects the great diversity of California (geography, race, ethnicity, income level, urban/rural) as well as to the specific communities directly involved in the project. The team should describe potential barriers to dissemination and how the team will address barriers through potential alternative strategies.

Budget

CBCRP intends to fund up to two projects with a duration of two years maximum at a maximum total direct cost of $300,000 for Project 1 and $350,000 for Project 2. Costs commensurate with the Dissemination Plan should be included in the Budget.

University of California campuses receive a maximum of 35% additional indirect (F&A) costs (25% for off-campus projects). All other institutions are eligible for additional indirect costs of up to 25% of total eligible direct project costs or at the rate established for the institution through a U.S. Department of Health and Human Services negotiated indirect cost rate agreement (or another similarly established rate), whichever is higher.

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, 2024. Visit https://cabreastcancer.org/files/cbcrp-diversity-supplement.pdf to learn more.

References

1. IARC Monographs Meeting, Volume 98, Shift work
2. *IARC Monographs* Meeting 124: Night Shift Work (4–11 June 2019)
3. Bondy SC[1], Campbell A[2].*Int. J. Mol. Sci.* **2018**, *19*(8), 2205; Mechanisms Underlying Tumor Suppressive Properties of Melatonin
4. Lulu Mao, Lin Yuan, Lauren M Slakey, Frank E Jones, Matthew E Burow, and Steven M Hill Inhibition of breast cancer cell invasion by melatonin is mediated through regulation of the p38 mitogen-activated protein kinase signaling pathway, Breast Cancer Res. 2010; 12(6): R107.
5. Dumont M, Lanctôt V, Cadieux-Viau R, Paquet J, Melatonin production and light exposure of rotating night workers Chronobiol Int. 2012 Mar;29(2):203-10.
6. Filipski E, King VM, Li X, Granda TG, Mormont MC, Liu X, Claustrat B, Hastings MH, Lévi F. Host circadian clock as a control point in tumor progression, J Natl Cancer Inst. 2002 May 1;94(9):690-7.
7. Storch KF, Lipan O, Leykin I, Viswanathan N, Davis FC, Wong WH& Weitz CJ. 2002Extensive and divergent circadian gene expression in liver and heart. *Nature* **417**, 78–83
8. Suliman Khan,1 Pengfei Duan,2 Lunguang Yao,2 and Hongwei Hou, Shiftwork-Mediated Disruptions of Circadian Rhythms and Sleep Homeostasis Cause Serious Health Problems International Journal of Genomics, Volume 2018 (2018)
9. Kettner NM, Katchy CA& Fu L. 2014Circadian gene variants in cancer. *Ann. Med.* **46**, 208–220.
10. Fonken LK& Nelson RJ. 2014The effects of light at night on circadian clocks and metabolism. *Endocr. Rev.* **35**, 648–670.
11. Zhu Y, Brown HN, Zhang Y, Stevens RG& Zheng T. 2005 Period3 structural variation: a circadian biomarker associated with breast cancer in young women. *Cancer Epidemiol. Biomark. Prev.* **14**, 268–270
12. Hoffman AE, et al.2010CLOCK in breast tumorigenesis: genetic, epigenetic, and transcriptional profiling analyses. *Cancer Res.***70**, 1459–1468.
13. Hoffman AE, et al.2010The core circadian gene Cryptochrome 2 influences breast cancer risk, possibly by mediating hormone signaling. *Cancer Prev. Res.* **3**, 539–548.
14. Zhu Y, Stevens RG, Leaderer D, Hoffman A, Holford T, Zhang Y, Brown HN& Zheng T. 2008Non-synonymous polymorphisms in the circadian gene NPAS2 and breast cancer risk. *Breast Cancer Res. Treat.* **107**, 421–425

15. Philosophical Transaction of the Royal Society B, Biological Sciences. Richard G. Stevens and Yong Zhu Published:05 May 2015 https://doi.org/10.1098/rstb.2014.0120.

16. Hill AB. The environment and disease: association or causation? Proc R Soc Med. 1965;58:295–300

17. Stevens RG. Artificial lighting in the industrialized world: circadian disruption and breast cancer. Cancer Causes Control. 2006;17:501–7)

18. Richard G. Stevens, Light-at-night, circadian disruption and breast cancer: assessment of existing evidence. Int J Epidemiolo. Int J Epidemiol. 2009 Aug; 38(4): 963–970.

19. Kloog I, Haim A, Stevens RG, Barchana M, Portnov BA. Light at night co-distributes with incident breast but not lung cancer in the female population of Israel. Chronobiol Int. 2008;25:65–81.

20. Louise E Johns, Michael E Jones, Minouk J Schoemaker, Emily McFadden, Alan Ashworth, and Anthony J Swerdlow, Domestic light at night and breast cancer risk: a prospective analysis of 105 000 UK women in the Generations Study Br J Cancer. 2018 Feb 20; 118(4): 600–606.

21. Åkerstedt T, Knutsson A, Narusyte J, Svedberg P, Kecklund G, Alexanderson K. Night work and breast cancer in women: a Swedish cohort study. BMJ Open. 2015 Apr 15;5(4):e008127. doi: 10.1136/bmjopen-2015-008127.

22. Pesch B, Harth V, Rabstein S, Baisch C, Schiffermann M, Pallapies D, Bonberg N, Heinze E, Spickenheuer A, Justenhoven C, Brauch H, Hamann U, Ko Y, Straif K, Brüning T. Night work and breast cancer - results from the German GENICA study. Scand J Work Environ Health. 2010 Mar;36(2):134-41. doi: 10.5271/sjweh.2890.

23. Hye-Eun Lee, Jongin Lee, Tae-Won Jang, In-Ah Kim, Jungsun Park, and Jaechul Song, The relationship between night work and breast cancer Ann Occup Environ Med. 2018; 30: 11.

24. Rotating Night-Shift Work and the Risk of Breast Cancer in the Nurses' Health Studies. Wegrzyn LR, Tamimi RM, Rosner BA, Brown SB, Stevens RG, Eliassen AH, Laden F, Willett WC, Hankinson SE, Schernhammer ES. Am J Epidemiol. 2017 Sep 1;186(5):532-540. doi: 10.1093/aje/kwx140

25. María E. Enchautegui. Nonstandard Work Schedules and the Well-Being of Low-Income Families. Low-Income Working Families…Paper 26. Urban Institute, July 2013

26. Hansen, J, “Night Shift Work and Risk of Breast Cancer”, Curr Envir Health Rpt (2017) 4;325-339 DOI 10,1007/s40572-017-0155-y

27. McCrate, E. (2016). Unstable scheduling, precarious employment, and gender: A working paper of the EINet Measurement Group. [https: ssascholars.uchicago.edu/einet]

28. Lambert, S.J., Fugiel, P.J., & Henley, J.R. (2014). Schedule unpredictability among early career workers in the US labor market: A national snapshot.

29. Finn, P. (1981). The effects of shift work on the lives of employees. *Monthly Labor Review*, October 1981.

30. Henly, J.R., & Lambert, S.J. (2014). Unpredictable work timing in retail jobs: Implications for employee work-life conflict. *Industrial and Labor Relations Review, 67(3)*, 986-1016.

31. Vanderpool, et al, "A Narrative Review of the Confluence of Breast Cancer and Low Wage Employment and Its Impact on Receipt of Guideline-recommended Treatment." Global Adv Health Ned. 2013; 2(5) 75-88. DOI 10.7453/gahmj.2013.046, p. 75.

32. Linnenbringer E, Gehlert S, Geronimus AT. Black-White Disparities in Breast Cancer Subtype: The Intersection of Socially Patterned Stress and Genetic Expression. AIMS Public Health. 2017;4(5):526-556. doi: 10.3934/publichealth.2017.5.526. Epub 2017 Nov 24.

33. Schneider, D., & Harknett, K. (2019). Consequences of routine work-schedule instability for worker health and well-being. *American Sociological Review, 84(1)*, 82-114.

Additional Information

- https://www.onetcenter.org/content.html
- US Bureau of Labor Statistics, Characteristics of Minimum Wage Workers: 2012.
- The National Longitudinal Survey of Youth (NLSY97) conducted annually by the National Opinion Research Center under the US Bureau of Labor Statistics.

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 four equally weighted criteria. The first two are categorized as "collaboration elements" and the second two are termed "scientific merit".

- **Partnership** (Collaboration Element)
    - The extent to which the strengths/nature of the proposed community partnership is reflected in leadership and involvement in all phases of the project (e.g. inception to dissemination).
    - The level to which both partners' knowledge and lived experience is integrated into planning and conducting the research.
    - The level to which both co-PIs have engaged with the larger community, including but not limited to cohort membership, to get their input in the application development process.
    - The extent to which agreements have been reached regarding procedures for resolving disagreements among collaborators, ownership of data, and dissemination of results.
    - The potential for capacity-building for any or all of the partners.
    - Demonstrated successful collaboration in previous research projects.
- **Community Benefit** (Collaboration Element)
    - The extent to which the community has been involved in the development of the research idea and questions, and the writing of the research proposal.
    - Plans for how cohort members and the broader community will be involved in the research project during the course of the research, from helping to conceptualize the research question(s) through dissemination of the results.
    - The potential importance and benefit to the broader lay community of the research question(s) and expected outcomes.
    - The potential for the research project to facilitate learning, further collaboration, and systems change.
    - The plan for reporting back results to stakeholders including cohort members in Project 2.
    - The plan for translating the research results into tangible benefits for the community and for engaging the community, local and state stakeholders and

policy decision makers in discussions of the results of the research and the implications for them.

- **Quality of the Research** *(Scientific Merit)*
    - The scientific importance of the research questions, including consideration of the most relevant literature and whether the intervention being researched will result in a breast cancer prevention strategy.
    - The extent to which existing cohorts can be leveraged – especially for Project 2.
    - The appropriateness and integration of the conceptual framework, research methods, and data analysis plan to the research question and aims.
- **Feasibility** (Scientific Merit)
    - The extent to which the project can be successful given the partners' knowledge, skills, resources, and experience.
    - The likelihood of completing the project as proposed given the available funding and time frame.
    - The usefulness (validity and/or importance) of data from previous research and community experience for the proposed research plan.

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? Avoid general references to the requirements of the RFP. Describe how elements of the proposed research plan are linked to one or more of the specific RFP topic areas. Compare the PIs' statements on the Program Responsiveness form and the content of the Lay and Scientific Abstracts to the PBC topic area.
- **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?
- **Diversity, Equity and Inclusion.** Do the statements in the Collaborative Agreements demonstrate a plan for the research team include community members representing groups that are underrepresented in breast cancer research? Do the project and the PIs' statements on the Program Responsiveness form demonstrate how this research will 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? Do the statements in the PIs' Program Responsiveness form describe how the research will affect systems change for historically disenfranchised groups?

- **Community Involvement.** Are the named community PIs and community organizations clearly driving the proposed research project? How well has the team described the strengths/nature of the proposed community partnership and how is it reflected in leadership and involvement in all phases of the project (e.g. inception and application through to dissemination). How well has the team described how both co-PIs have engaged with cohort members and the larger community to get their input in the application development process. Are meetings and other communications sufficient for substantive engagement and collaboration? Are the roles and responsibilities of the PIs clearly outlined and is the agreement for sharing of budget clear? [The Advisory Council will examine the co-PIs' statements on the Lay and Scientific Abstracts, Program Responsiveness form, and Collaborative Agreements.]
- **Dissemination and translation potential.** The degree to which the applicant's statements on the Program Responsiveness form provides a convincing argument that the proposed research has the potential to inform real-world breast cancer prevention efforts.

Application Instructions

Application materials are available through RGPO's SmartSimple application and grant management system. 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 years.
- **Proposed Project Start Date:** Enter a project start date of August 01, 2024.
- **Proposed Project End Date:** Enter a project end date of July 31, 2026.

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 obtained 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. Do not use symbols or other special text, as these will not transfer to the "abstracts" box. 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. Do not use symbols or other special text, as these will not transfer to the "abstracts" box. 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 "2.0 Etiology" as the CSO Type, and please select the corresponding CSO Sub-Type(s) 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.** Complete this table if the research project will involve human subjects. Enter the target demographics of the research participants that you propose to recruit. See the SmartSimple submission instructions for more details.
- **Milestones.** See SmartSimple submission instructions for more details.

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 Investigators (Co-PIs), Co-Investigators, Advocates, Trainees, Consultants, and support personnel, as necessary. Upload biosketches to each of your Key Personnel members in this section, as shown in the SmartSimple instructions. A 10% minimum effort (1.2 months per year) is required for the Applicant PIs (Co-PIs).

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.

Each institution that is a partner in the project must complete a budget. This means the Community Co-PI and the Academic Co-PI will each have their own Budget. If a collaborative partner on the project has a subcontract, then that subcontracting organization can complete a budget or the prime partner can complete the budget for the subcontracting organization. The Submitting Co-PI has the ability to edit all budgets, although the invited Co-PI does not.

Maximum duration is 2 years and the direct costs budget cap is $300,000 for Project 1 and $350,000 for Project 2.

Additional budget guidelines:

- **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.
- **Other Project Expenses:** Include other project costs such as supplies here.
- **Travel**: A minimum of $400 must be budgeted in year 1 for travel to the **CBCRP symposium**. **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 35% 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, they may request a "De Minimis" F&A rate of 25% MTDC.

Additional budget guidelines can be found in Appendix A.

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	10 (+ 3 for references)	Required	Yes	No
Program Responsiveness	3	Required	Yes	Yes
Collaborative Agreements	2	Required	Yes	Yes
Biosketches (All Personnel listed on Key Personnel form)	5 (each biosketch)	Required (upload to Project Personnel section)	Yes	Yes (PIs only)
Facilities	1 per institution	Required	Yes	No
Human Subjects	No limit	Required	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 ten 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 to supporting materials.**

Suggested outline:

Statement of Goals, Research Questions, and Specific Aims. In a short paragraph, describe goals for the research project. Briefly state the research question(s) and hypothesis for the project. Follow with the Specific Aims—the specific tasks that will be undertaken to address the research question(s). These tasks should be very clearly defined and should not include exploratory or development undertakings. The research questions, hypothesis, and aims should have a logical connection.

The relationship of the project to the specific PBC Project Type and expectations outlined within the RFP should be clear.

Background and Significance. Concisely describe the rationale underlying the proposed research strategy; the hypotheses to be investigated; the methodology to be employed; and the experience, knowledge, and skills of the research team. Emphasize positioning the research in the context of existing relevant scientific literature and preliminary data that the team may have collected in preparing for the research. Demonstrate a grasp of the current state of the knowledge relevant to the problem. Provide up-to-date references, acknowledge controversies and contradictory reports, and be comprehensive and accurate. If there is little literature on the topic, draw on information from related fields. Demonstrate the community interest, participation in the plan development from the beginning, and the potential contribution of the proposed research. Briefly state the long-term potential of the research: the problems, issues, or questions which, through the execution of this award, can be further developed, specified, and sharpened into testable hypotheses; and the methodologic approach (or possible approaches that seem at present most appropriate to be used). Keep discussion of the general problem of breast cancer brief; emphasize the specific problem addressed by your research proposal.

Preliminary Data. Describe the prior experience with the issue to be investigated. Emphasize any work by the Co-PIs and data specific to breast cancer. Present any data obtained in detail, with a description of how the data was obtained and analyzed. Describe any pitfalls or

problems that arose, as well as how they were overcome. Provide justification and support for the potential for useful knowledge and interventions to result from the research.

Research Methodology: Research Design, Conceptual Framework, and Data Analysis. Describe in detail the exact tasks listed in the Statement of Goals, Research Questions, and Specific Aims. Provide a detailed description of the work you will do during the Award period, exactly how it will be done, and by whom. For instance, if women are to be surveyed, explain how many women will be surveyed; why you chose this number; how the women will be identified and recruited; why you believe you will be able to reach and recruit this many women; what questions you will ask them; whether you will use face-to-face or telephone interviews, or written surveys and why you will use the method chosen; and, how the data will be collected and analyzed. Be as detailed as possible. Provide this information for each specific task cited in the first section. Discuss potential pitfalls and how you will overcome them should they arise, or alternative methods that you will use if the intended methods are not fruitful. Provide a realistic timeline. Be sure to include a hypothesis and conceptual framework.

Partnership Collaboration Plan and Community Benefit. Begin this section by describing the community of interest for this study. Is the community distinct because of geography, age, gender, associated by disease status or risk, race, sexual orientation, or socio-economic status? Describe the interest of the community in the research question and how they have participated in identifying it. Discuss the importance and benefit to the community of the research question and expected outcome. Specifically answer how the broader community of interest was involved in developing the research proposal. Describe the relationship between the community co-PI and their community organization and the community of interest. How will the community of interest be included on the research team? Discuss how the leadership of the community organization (the Executive Director, the Board of Directors, or the individuals of an informal organization) will ensure that the organization or group is committed to the research project? Describe how the Community Co-PI and the community organization will communicate with one another to facilitate input and decision-making.

Program Responsiveness (required)

This item is evaluated in the peer review and programmatic review. **Limit the text to three 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. Avoid reiterating the requirements of the RFP. Describe how elements of the proposed research plan are linked to one or more of the specific

RFP topic areas. As this is a community-partnered participatory research project, do highlight the strengths/nature of the proposed community partnerships as reflected in the leadership and involvement in all areas.

Diversity and Inclusion: Describe how this research will 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 and how it will affect systems change for historically disenfranchised groups.

Dissemination and Translation Potential: Describe how research findings will be shared with various stakeholder audiences (i.e., workers, their representatives, employers, community members, policy makers, 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 to inform real-world breast cancer prevention efforts.

Collaborative Agreements (required)

This form is reviewed in the peer review and the programmatic review. Applicants should remember that a fully collaborative and power-sharing partnership is a key aspect of this application. **Limit the text to two pages.**

Avoid general references to the requirements of the RFP. Highlight the strengths/nature of the proposed community partnerships as reflected in the leadership and involvement in all areas. Describe how the community PI has been in a leadership role in the application development process and how the team has engaged with the larger community to get their input in the application development process.

The Community Applicant is required to verify the agreements addressed in this form by submitting a statement that the governing body (Board of Directors for a nonprofit organization or the individuals responsible for organizing an informal organization) has reviewed and approved these agreements.

The collaborative agreement should include the following elements:

- **Ownership of Data**: Describe what decision you made about who will own the data and intellectual property rights and why you came to that decision (i.e. what factors you considered, what was important to you in making this decision). If you decide that the data will be owned by only one of the collaborators, please consider that the need to continue to work together will likely extend well beyond the grant period. Will the partner who owns the data be willing to volunteer his/her time well after the grant period to provide access to the data for the other partner? Be sure to discuss ownership of identified and de-identified data, including arrangements both partners have agreed to ensure access to that data by the other partner (including beyond the study period).

- **Handling Disagreements:** Describe what decision you made about the procedures you will go through to handle disagreements during the course of the study and afterwards. Past teams have had to resolve issues around data ownership, conduct of the research, dissemination of data and publications, administrative and budget issues, etc. Describe why you believe your decision on handling disagreements will work for you.
- **Recipient of Grant Award**: Describe what decision you made about whether the grant award will be contracted directly to one partner or to both partners and why you came to that decision. CBCRP suggests that if both applicant agencies have the administrative capacity to manage grant awards, that each agency receives a separate award.
- **Plans for Broader Community Involvement:** Describe how individual community members not on the research team (including staff and board of the community agency applicant as well as community members outside of the organization) will be involved in the planning, conducting, and dissemination of research. Describe how the community co-PI will be overseen by the community applicant and what steps will be taken to select a replacement community co-PI if that were to be needed (please keep in mind that the community co-PI replacement will need to be approved by CBCRP in accordance with the Grants Administration Manual available on the CBCRP website).
- **Plans for Dissemination of Findings:** Dissemination of research findings to both the lay community and the scientific community is important to this research award. This is sometimes a difficult issue as scientific dissemination is often a lengthy process and may impede community dissemination. Please describe how research findings will be disseminated to both the community of interest and the scientific community and what agreements have been made about the timing of dissemination.
- **Plans for Turnover of Personnel:** Describe how the turnover of personnel will be handled (who will hire, fire, etc.) Describe how the community co-PI, specifically, will be overseen by the community applicant and what steps will be taken to select a replacement community co-PI if that were to be needed (please keep in mind that the community co-PI replacement will need to be approved by CBCRP in accordance with the Grants Administration Manual available on the CBCRP website).

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 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 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 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.

Appendix (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; the appendix is not to be used to circumvent page limitations of the application.

Appendix A: 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 explained 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 35% 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 B: 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 30, 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, 2024. 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:
Sharima Rasanayagam, PhD
Environmental Health & Health Policy Program Officer, CBCRP
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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.