# Understanding the Contributions of Chemical Mixtures to Breast Cancer Risk
# &
# Many Pathways to Cancer: Identifying Exposures Linked to the Key Characteristics of Carcinogens

## Informational Webinar for Prospective Applicants

CALIFORNIA Breast Cancer Research Program

# Agenda

- The California Breast Cancer Research Program (CBCRP)
  - CBCRP Program-Directed Initiatives
  - Preventing Breast Cancer Initiatives (PBC)
- Understanding the Contributions of Chemical Mixtures to Breast Cancer Risk
- Many Pathways to Cancer: Identifying Exposures Linked to the Key Characteristics of Carcinogens
- How Grants are Evaluated
- Important Dates
- Resources for Submitting an Application in SmartSimple

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# California Breast Cancer Research Program (CBCRP)

- Founded in 1993
  - breast cancer activists, scientists, clinicians, state legislators, and University of California officials collaborated to win passage in the state legislature of the California Breast Cancer Act.
  - funded by a tax on tobacco products, voluntary state personal income tax form check-off, and individual contributions.
  - tax check-off has drawn over $13 million for breast cancer research.
- Grown to become one of nation's largest state-funded breast cancer research effort
- Among the largest breast cancer research funders in the world
- Ninety-five percent of our revenue goes directly to funding research and education efforts

**Mission: to prevent and eliminate breast cancer by leading innovation in research, communication, and collaboration in the California scientific and lay communities**

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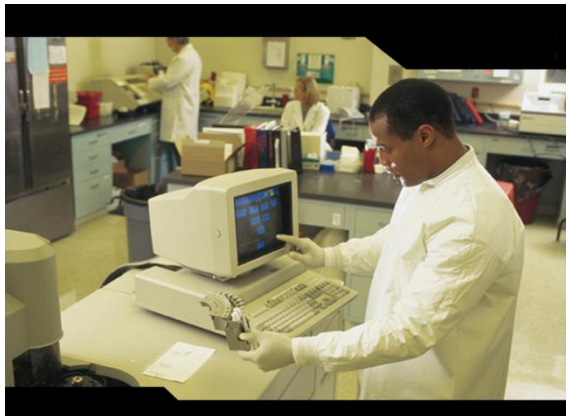
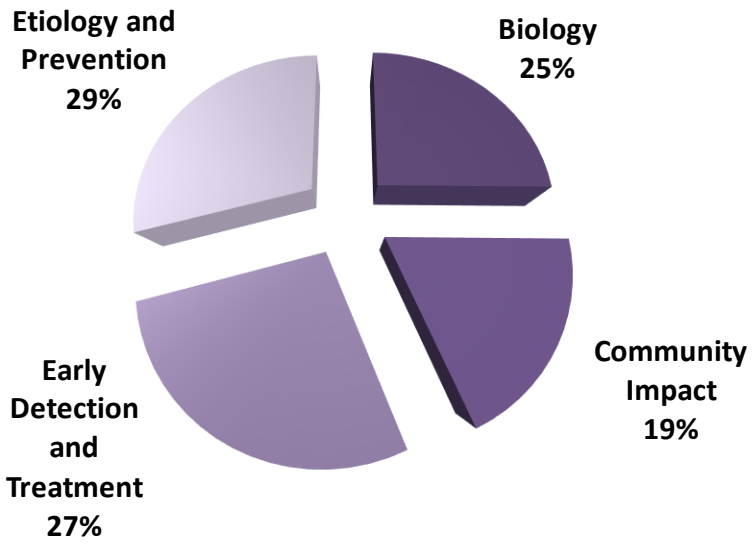
# Since 1994, CBCRP has funded



- Over 1,200 grants
- Totaling over $290 million
- To over 840 academic & community researchers
- At over 140 institutions across the state

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# Program-Directed Initiatives

**Vision**

To identify and support research strategies that increase understanding of, and **create solutions to**, environmental links to breast cancer and fundamental causes of health disparities in breast cancer.

**Goals**

- Support a coordinated statewide effort to explore innovative ideas and new theories
- Leverage California's unique and diverse geographic and population resources
- Undertake critical studies that significantly move these fields forward

*First round launched in 2004; second round in 2010*

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# Preventing Breast Cancer (PBC):
## *Community, Population, and Environmental Approaches*

**In 2015**

CBCRP's Council approved a third round of Program Initiatives, devoting 50% of funds (~$20 million) 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 and 2021**

CBCRP's Council approved 10 concept proposals to stimulate research in these three areas, including:

- Understanding the Contributions of Chemical Mixtures to Breast Cancer Risk
- Many Pathways to Cancer: Identifying Exposures Linked to the Key Characteristics of Carcinogens

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# Chemical Mixtures
## Overview

Overall Aim: To identify chemical mixture exposures associated with risk of breast cancer and/or biomarkers of effect using either:

1. analytical chemistry applications on stored materials from:
   a) a breast cancer cohort; or
   b) women at potential risk of breast cancer (e.g., high mammographic density, atypia, occupational risk; or
2. artificial intelligence, big data methods and/or mining of existing data.

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# Chemical Mixtures
## Overview

**Available Funds:**

CBCRP intends to fund up to two smaller proposals for a maximum duration of 2 years at up to $350,000 maximum direct costs each and one additional laboratory-based proposal for a maximum duration of 3 years at up to $1,000,000 maximum direct costs.

**Eligibility:**

- Any individual or organization in California may apply.
- The research must be conducted primarily in California.

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# Chemical Mixtures
# Research Questions

Applications are encouraged to address the following:

1. Identify complex chemical mixture exposures associated with eventual risk of breast cancer using analytical chemistry applications on stored materials from either (a) breast cancer cohorts or (b) women at potential risk of breast cancer due to their occupation, biomarkers of effect (e.g., high mammographic density, atypia), or residential proximity to carcinogenic exposures.

2. Develop an understanding of the relationship between breast cancer risk and the complex mixture of exposures associated with it using artificial intelligence, big data methods and/or creative mining of existing data.

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# Topic 1 –Novel approaches in analytical chemistry to understand chemical mixtures contributing to breast cancer risk

Approaches will be considered novel if they measure a chemical(s) not previously interrogated, improve on or validate an existing strategy (e.g., reliability, lower cost, more practical, measures multiple chemicals), or apply novel analytical chemistry and/or statistical methods. Examples include:

- Examining stored biospecimens from women who later developed breast cancer or an effect biomarker and determining what in their exposome profiles is associated with increased risk
- Examining environmental samples or applying GIS and exposure modelling to determine novel chemical mixtures or their exposure sources associated with breast cancer risk or effect biomarkers of relevance to breast cancer
- Further defining the exposome in existing studies with stored samples where breast cancer incidence or effect biomarkers of relevance to risk are known.
- Develop relationships between –omics data, exposure and risk to identify markers of a chemical mixture exposure indicating increased risk of breast cancer.

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# Topic 2. Data Mining/Artificial intelligence/Big data methods linking mixture exposures and breast cancer risk using existing data

Examples may include:

- Including bioinformatics in chemical mixture exposure modeling to discover novel exposures linked to disease. Additionally, a novel exposure discovered using artificial intelligence or other bioinformatic tools could be tested for its predictive potential for breast cancer in animal or advanced cell-based studies.
- Updating and expanding previous GIS mapping projects and combining datasets to provide novel insights into exposure mixtures effects.

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# Many Pathways
## Overview

Overall Aim: To address the urgent need to identify chemicals and other environmental exposures that influence the development of breast cancer by

1. developing new assays to fill gaps in coverage for key characteristics of carcinogens relevant for breast cancer;
2. analyzing results from existing assays; and/or
3. identifying new biomarkers relevant to the key characteristics of carcinogens that can be applied as early effect markers for breast cancer in studies in women.

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# Many Pathways
# Overview

**Available Funds:**

CBCRP intends to fund up to three proposals for a maximum duration of three years and $560,000 maximum total direct costs each.

**Eligibility:**

- Any individual or organization in California may apply.
- The research must be conducted primarily in California.

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# Many Pathways
# Research Questions

Applications are encouraged to address the following challenges:

A. Current methods used to screen and test chemicals for carcinogenic properties do not fully encompass the diverse mechanisms by which agents may cause breast cancer;

B. Data that are already available from in vitro and short-term in vivo bioassays could be better leveraged to predict outcomes relevant to breast cancer, prioritize agents for further testing, and improve the identification of new breast carcinogens;

C. There is a need to identify biomarkers for a broader range of effects relevant to breast carcinogens and apply these biomarkers to studies of women to characterize risk in highly exposed populations.

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# Many Pathways
# Possible Approaches

1. Development of new in silico, in vitro, and/or short-term in vivo assays to fill gaps in coverage of the assays for key characteristics of carcinogens relevant for breast cancer causation.

2. Compile published and publicly available results from in silico, in vitro and short-term in vivo assays that are relevant to key characteristics of carcinogens and specifically to breast carcinogenesis.

3. Identify new biomarkers of endpoints relevant to the key characteristics of carcinogens that can be applied in short-term studies of suspected breast carcinogens in women. These biomarkers would focus on biological endpoints of carcinogenic effects, rather than biomarkers of exposure.

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# Both Initiatives
# Dissemination Plan

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

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# Both Initiatives
# Advocacy Involvement Requirement

- Advocacy involvement is a requirement for the research funded under this initiative.
- Applications should include a California community advocate affiliated with an advocacy and/or community organization with an interest in the area of biomonitoring, environmental exposures and breast cancer.
- The community advocate(s) should be involved in the development of the project, goals, aims, and research questions and should drive the identification and definition of community needs and health equity imperatives.
- Applications will be evaluated on advocate involvement:
  - identification of an appropriate advocate for the proposed research
  - a detailed description of how the advocate will be involved in the project
  - submission of a Letter of Commitment co-signed by advocate and the PI
  - a budget line item and justification covering the advocate time, effort, and expenses on the project (e.g. at least quarterly, in-person meetings)
- Additional resources:
  - Learn more about CBCRP's approach and view relevant resources: cbcrp.org/approach/advocacy-involvement
  - CBCRP staff are available to consult with applicants, if needed, about meeting the advocacy requirement

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# Questions?

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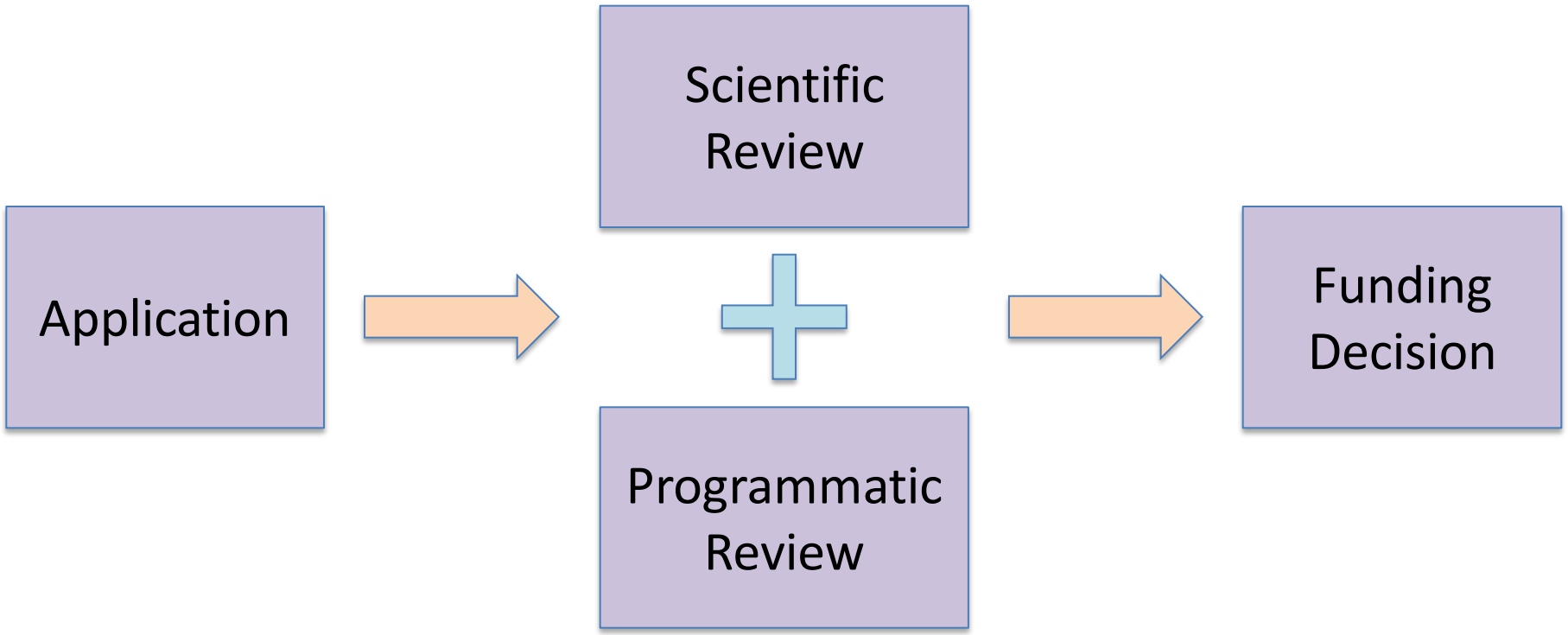
# Two-Tier Evaluation Process

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# Both Initiatives
# Review Criteria

| | **Criteria** |
|---|---|
| **Scientific Review** | • Innovation<br>• Impact<br>• Approach<br>• Feasibility |
| **Programmatic Review** | • Responsiveness<br>• Critical path/Translation<br>• Lay Abstract<br>• Addressing the needs of the underserved<br>• Advocacy Involvement |

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# Application Components

| Form/Attachment | Requirement |
|---|---|
| **Lay Abstract** | Required (Prog Rev) |
| **Scientific Abstract** | Required (Prog Rev) |
| **Budget and Justification** | Required |
| **Research Plan** | Required |
| **Program Responsiveness** | Required (Prog Rev) |
| **Critical Path & Underserved** | Required (Prog Rev) |
| **Advocacy Involvement** | Required (Prog Rev) |
| **Letter of Commitment** | Required (Prog Rev) |
| **Biosketches** | Required (Prog Rev) |
| **Facilities** | Required |
| **Human Subjects** | Required |
| **Vertebrate Animals** | Optional |
| **Appendix** | Optional |

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# Important Dates

| | Date |
|---|---|
| Applications due | November 9, 2023 (12 pm noon PT) |
| Notification of funding status | February 1, 2024 |
| Project start date | March 1, 2024 |

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# Questions?

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# How to submit a proposal in SmartSimple

## Research Grants Program Office (RGPO)

## Contracts and Grants Unit (C&G)

- C&G works in collaboration with CBCRP, serving as interface on administrative and procedural aspects your **Application** submission and review process.
- Contact information:
  - **Email: RGPOgrants@ucop.edu** (Best method)
  - SmartSimple application system: https://rgpogrants.ucop.edu

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# Key Dates & Tips

| Award Type | Application Deadline |
|---|---|
| Understanding the Contributions of Chemical Mixtures to Breast Cancer Risk | November 9, 2023, Noon PT |
| Many Pathways to Cancer: Identifying Exposures Linked to the Key Characteristics of Carcinogens | November 9, 2023, Noon PT |

- All materials must be submitted through SmartSimple
- Detailed instructions are provided on the CBCRP website and in SmartSimple
- **Start early** to become familiar with SmartSimple
- **Submit early:** No late applications will be accepted

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# Biomonitoring Initiative: Questions and Additional Information

**Applications are due no later than November 9, 2023 (12 pm noon PT)!**

Useful links:

- SmartSimple application system: https://rgpogrants.ucop.edu
- Webinar: "How to submit a proposal in SmartSimple"
- Understanding the Contributions of Chemical Mixtures to Breast Cancer Risk: https://www.cbcrp.org/funding-opportunities/sri/chemical-mixtures.html
- Many Pathways to Cancer: Identifying Exposures Linked to the Key Characteristics of Carcinogens: https://www.cbcrp.org/funding-opportunities/sri/many-pathways.html
- Additional funding opportunities: cbcrp.org/funding-opportunities/index.html

For programmatic questions, contact Sharima Rasanayagam, CBCRP Program Officer:

- Sharima.Rasanayagam@ucop.edu

For questions about Smart Simple, technical issues, or application instructions and forms, contact Research and Grants Program Office Contracts and Grants unit:

- RGPOgrants@ucop.edu

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