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NCI and NIEHS: Breast Cancer and the Environment Research Program (BCERP) Request for RFA Reissuance

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Board of Scientific Advisors
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Overview

- Breast Cancer and the Environment Legislation
- Purpose of Original RFA
- Transdisciplinary Accomplishments
- Discuss the future of BCERP

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Breast Cancer and Environmental Research Act

- P.L. 110-354, Breast Cancer and Environmental Research Act of 2008, signed October 8, 2008
- Establishes Interagency Breast Cancer and Environmental Research Coordinating Committee
- Authorizes $40M for research regarding environmental and genomic factors related to breast cancer etiology
- NCI and NIEHS responsive before legislation signed into law

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Objectives of Original RFA

- Compare normal breast development to environmentally induced developmental changes
- Conduct an epidemiologic study of the timing of pubertal events in girls
- Integrate scientific information so that public health messages can be developed

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Current Structure of Breast Cancer and the Environment Research Centers

- Established network of 4 centers in 2003 through a cooperative agreement
- Each funded center has a biology project and a Community Outreach & Translation Core (COTC)
- Three funded centers have an epidemiology project – pooled cohort of more than 1,200 girls ages 6-8 at baseline
- Projects are interactive and well-integrated
- Multidisciplinary scientists and advocates work on a common problem with a shared conceptual framework

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Rationale for Puberty as a Window of Susceptibility

- Strong biological rationale for a role of chemical exposures in mammary carcinogenesis
- Established risk factors: Age at menarche, age at peak height velocity, age at first full-term pregnancy, age at menopause
- Breast cells rapidly proliferating
- Advocates and general public concern

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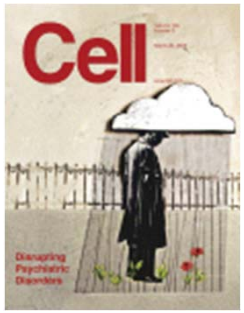
Research Discoveries



Kouros-Mehr H, Slorach EM, Sternlicht MD, Werb Z (2006). GATA-3 maintains the differentiation of the luminal cell fate in the mammary gland. *Cell* 127:1041-55.

Mammary tumors in mice with high GATA-3 expression maintain differentiation and have many estrogen receptors.

Wolff MS, Teitelbaum SL, Windham G, Pinney SM, Britton JA, Chelimo C, Godbold J, Biro F, Kushi LH, Pfeiffer CM, Calafat AM (2007). Pilot Study of Urinary Biomarkers of Phytoestrogens, Phthalates, and Phenols in Girls. *Env Hlth Perspective* 115(1):116-21.

First report of some endocrine disrupting chemicals detected at high levels in young girls.

Moral R, Wang R, Russo IH, Lamartiniere CA, Pereira J, Russo J (2008). Effect of prenatal exposure to the endocrine disruptor bisphenol A on mammary gland morphology and gene expression signature. *J Endocrinol* 196: 101-12.

Prenatal exposure to BPA in mice up regulated genes related to the immune system and changed genes related to differentiation.

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Team Science Illustrated: Rapidly Advancing Science Through Collaboration

Perfluorooctanoic Acid (PFOA)

- High levels found in a sample of young girls
- New cross-center and transdisciplinary collaboration
- Biology projects studying PFOA in animal models
- COTC helped organize and translate findings and key messages through a town hall meeting with the girls' parents

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Evaluation

- NIEHS and NCI
  - Number of publications in high impact journals
  - Evidence of intra- and cross-center collaboration
- Breast Cancer and the Environment Working Group
  - Approximately ten members composed of scientists and breast cancer advocates
  - Positive evaluation
  - Recommends continuation of the study to follow the girls through puberty
- Expansion of Evaluation in Renewal
  - Self-evaluation among projects
  - Scientific productivity
  - Interaction and synergy among basic biology, epidemiology and advocacy components

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Rationale for Continued Follow Up of Cohort of Young Girls ages 6-8 at Baseline

Developmental Milestone	2009	2015
Attainment of Tanner Breast Stage 2 (B2)*	45%	100%
Attainment of Menarche	9%	>97%
Establish maturation tempo	5%	90%
Attainment of peak height velocity	0%	95%
Achievement of adult height	0%	90%
Ovulation	0%	75%

*** An early stage of breast development; endpoint for initial funding period.**

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Breast Cancer & the Environment Research Program (BCERP) –The Next Phase

- Continue to partner with NIEHS on next phase
- Support completion of the epidemiology study in the cohort of more than 1,200 girls in 3 geographic areas – Each area with a dedicated Community and Outreach Training Core
- Expand on recent findings in identifying biomarkers of common exposures, links to genetic polymorphisms, and chemically induced changes to the architecture of the mammary gland through R01s and R21s
- Establish a Breast Cancer and the Environment Research Coordinating Center

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Budget for Renewal

Funding Opportunity Announcement	Mechanism	FY2010 Budget (NCI)
Early Environmental Exposures: Continuing Studies of Human Puberty (U01)	Letter RFA 3 Awards	$1.4M 5 years
Environmental Influences during Windows of Susceptibility and Breast Cancer Risk (U01)	Open RFA 5-6 Awards	$1.2M 5 years
The Breast Cancer and the Environment Research Coordinating Center (U01)	Open RFA 1 Award	$400K 5 years

FY2010	5-year Cost
$3.0M NCI	$15.0M NCI
$3.9M NIEHS	$21.7M NIEHS

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Questions?

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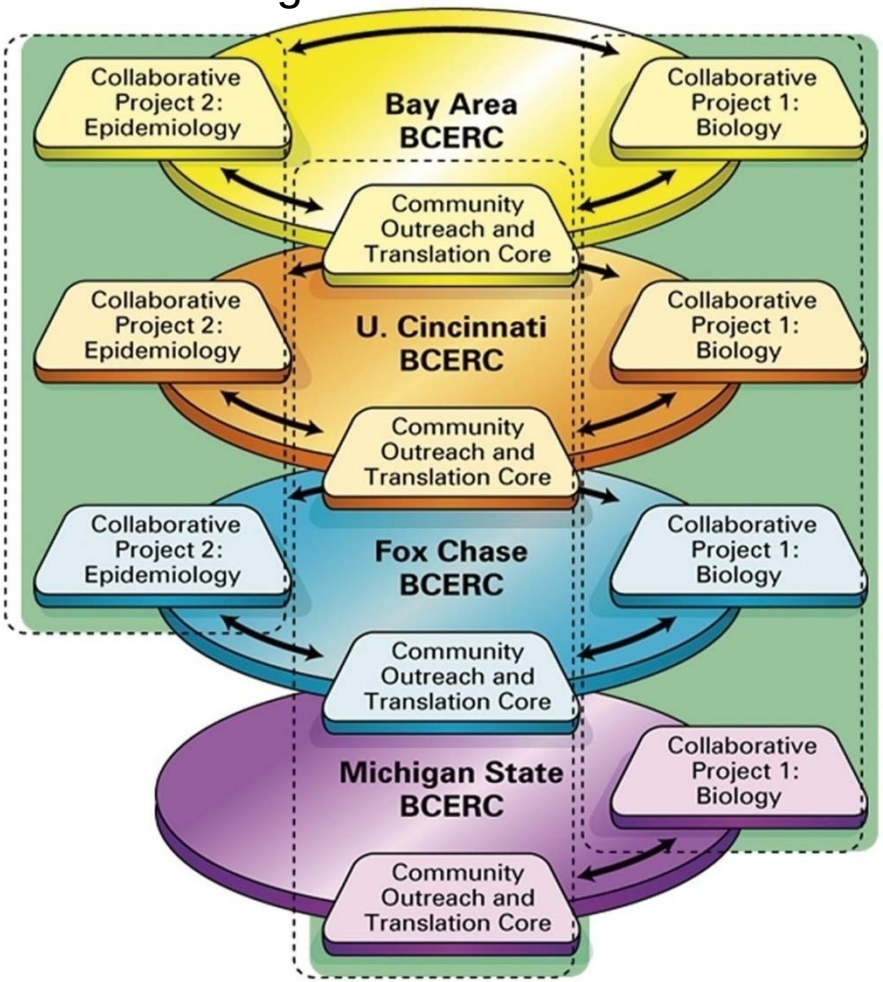
Collaborative Within and Across Centers

NCI & NIEHS Scientific & Programmatic Involvement

Environmental and Genetic Determinants of Puberty



Environmental Effects on the Molecular Architecture and Function of the Mammary Gland across the Lifespan

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Cross-Center Interactions and Integration: BCERC Epidemiology and Biology Studies

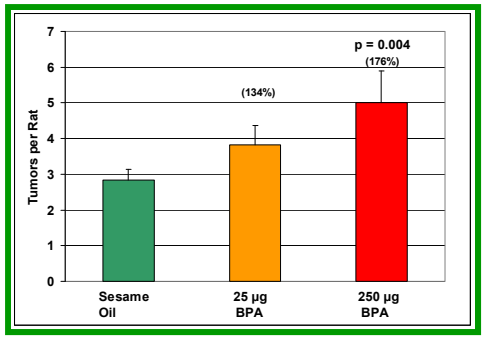
Epidemiology Studies

Identify relevant exposures; effects on pubertal development

Exposures
Chemicals
Endocrine Disruptors
Hormones, Diet

Biology Studies
Normal mammary development; effects of exposures

Risk Assessment
Mammary cancer susceptibility



Mechanisms

Biomarkers, Genes

Breast Cancer Prevention
Public Health Messages

Courtesy of Sandra Haslem, PhD, Michigan State University BCERC

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Environmental Agents Studied and the Major Sources of Exposure

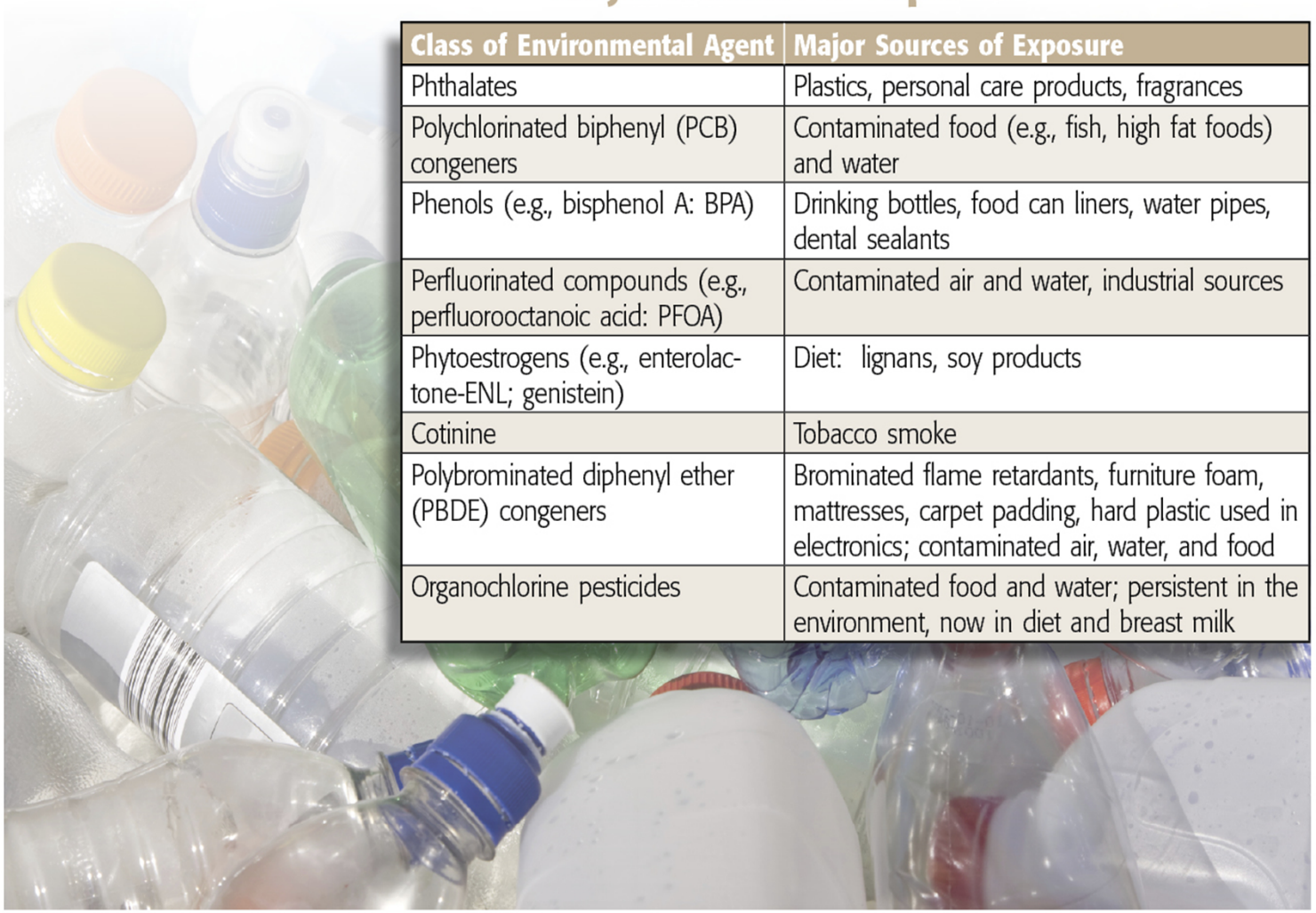

Table 1. Environmental Agents Studied and the Major Sources of Exposure

Class of Environmental Agent	Major Sources of Exposure
Phthalates	Plastics, personal care products, fragrances
Polychlorinated biphenyl (PCB) congeners	Contaminated food (e.g., fish, high fat foods) and water
Phenols (e.g., bisphenol A: BPA)	Drinking bottles, food can liners, water pipes, dental sealants
Perfluorinated compounds (e.g., perfluorooctanoic acid: PFOA)	Contaminated air and water, industrial sources
Phytoestrogens (e.g., enterolactone-ENL; genistein)	Diet: lignans, soy products
Cotinine	Tobacco smoke
Polybrominated diphenyl ether (PBDE) congeners	Brominated flame retardants, furniture foam, mattresses, carpet padding, hard plastic used in electronics; contaminated air, water, and food
Organochlorine pesticides	Contaminated food and water; persistent in the environment, now in diet and breast milk

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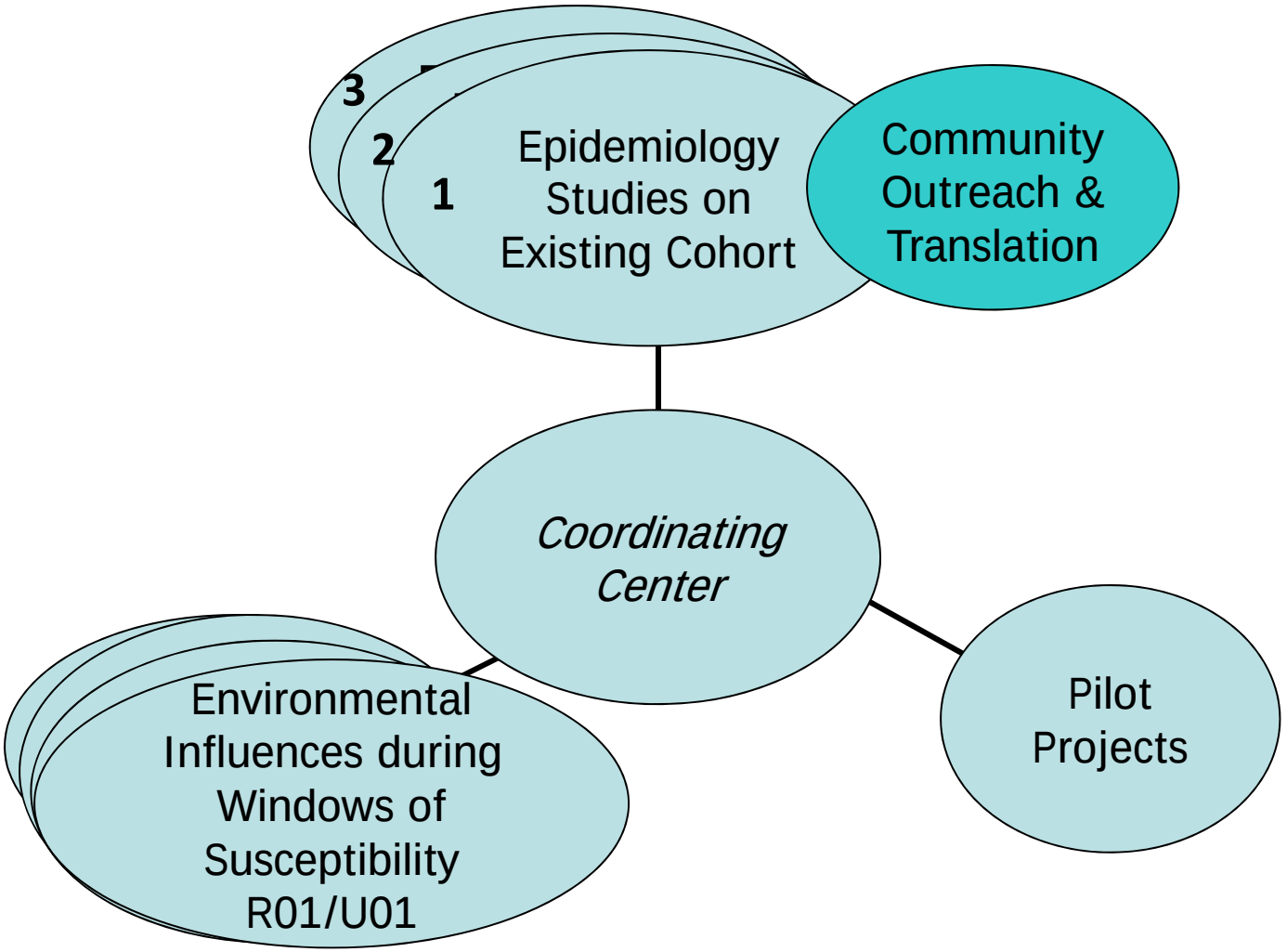
Breast Cancer and the Environment Research Program (BCERP)



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Summary

Partnerships	Scientific Progress
Legislative Interest	Transdisciplinary Framework
NIEHS and NCI Collaboration	Continuity
Community Advocacy	New Scientific Opportunities

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Breast Cancer and the Environment Research Centers

Fox Chase Cancer Center

Center Director

Jose Russo, M.D.

Collaborators

Mount Sinai School of Medicine
University of Alabama at Birmingham

Community Partners

The Renaissance University for Community Education of the Harlem Children's Zone Project: Girls, Inc.
New York City Parks Foundation
Community Science Specialists
Share
Avon Foundation
American Cancer Society
Huntington Breast Cancer Action Coalition, New York
Linda Creed Breast Cancer Foundation, Philadelphia, PA
Helen's Hope Organization, Philadelphia, PA
Great Neck Breast Cancer Coalition, New York
Rose of Hope Scholarship Fund from League of Women Against Cancer, Rydal, PA

Michigan State University

Center Director

Sandra Z. Haslam, Ph.D.

Community Partners

Faith Access to Community Economic Development
Susan G. Komen Breast Cancer Foundation, Lansing, MI Chapter
Michigan Breast Cancer Coalition
Michigan Environmental Council
American Cancer Society, Great Lakes Division

Bay Area – University of California, San Francisco

Center Director

Robert A. Hiatt, M.D., Ph.D.

Collaborators

California Department of Public Health
Kaiser Permanente of Northern California
Lawrence Berkeley National Laboratory
Marin County Department of Health and Human Services
New York University
Roswell Park Cancer Center
San Francisco Department of Public Health
University of Michigan
Zero Breast Cancer

Community Partners

Alameda County Department of Public Health
Bay Area Breast Cancer SPORE Advocacy Group
Bayview Hunters Point Health and Environmental Assessment Task Force
Breast Cancer Fund

University of Cincinnati

Center Director

Robert L. Bornschein, Ph.D.

Collaborator

Cincinnati Children's Hospital Medical Center

Community Partners

Breast Cancer Alliance of Greater Cincinnati
Breast Cancer Registry of Greater Cincinnati
Patterns, Inc.
Pink Ribbon Girls
Susan G. Komen Breast Cancer Foundation, Greater Cincinnati Affiliate
American Cancer Society, Cincinnati Area Office
Breast and Cervical Cancer Screening Project
National Breast Cancer Coalition
Sisters Network Cincinnati
The Wellness Community
YWCA Breast and Cervical Health Network