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

Robert Croyle, PhD
Division Director
Gary Ellison, PhD
Program Director
Division of Cancer Control and Population Sciences

Board of Scientific Advisors
June 22, 2009
Overview

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

- 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
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
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
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

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


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


Prenatal exposure to BPA in mice up regulated genes related to the immune system and changed genes related to differentiation.
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
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
**Rationale for Continued Follow Up of Cohort of Young Girls ages 6-8 at Baseline**

<table>
<thead>
<tr>
<th>Developmental Milestone</th>
<th>2009</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attainment of Tanner Breast Stage 2 (B2)*</td>
<td>45%</td>
<td>100%</td>
</tr>
<tr>
<td>Attainment of Menarche</td>
<td>9%</td>
<td>&gt;97%</td>
</tr>
<tr>
<td>Establish maturation tempo</td>
<td>5%</td>
<td>90%</td>
</tr>
<tr>
<td>Attainment of peak height velocity</td>
<td>0%</td>
<td>95%</td>
</tr>
<tr>
<td>Achievement of adult height</td>
<td>0%</td>
<td>90%</td>
</tr>
<tr>
<td>Ovulation</td>
<td>0%</td>
<td>75%</td>
</tr>
</tbody>
</table>

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

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

**FY2010**
- $3.0M NCI
- $3.9M NIEHS

**5-year Cost**
- $15.0M NCI
- $21.7M NIEHS
Questions?
Collaborative Within and Across Centers

Environmental and Genetic Determinants of Puberty

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

NCI & NIEHS Scientific & Programmatic Involvement
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

- Risk Assessment
  - Mammary cancer susceptibility

- Mechanisms
  - Biomarkers, Genes

- Breast Cancer Prevention
  - Public Health Messages

**Biology Studies**
Normal mammary development; effects of exposures

- sesame
- Oil
- BPA
- BPA

\( p = 0.004 \)

(176%)

(134%)

Courtesy of Sandra Haslem, PhD, Michigan State University BCERC
## Environmental Agents Studied and the Major Sources of Exposure

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

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

1. Epidemiology Studies on Existing Cohort
2. Environmental Influences during Windows of Susceptibility R01/U01

- Coordinating Center
- Community Outreach & Translation
- Pilot Projects
## Summary

<table>
<thead>
<tr>
<th>Partnerships</th>
<th>Scientific Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legislative Interest</td>
<td>Transdisciplinary Framework</td>
</tr>
<tr>
<td>NIEHS and NCI Collaboration</td>
<td>Continuity</td>
</tr>
<tr>
<td>Community Advocacy</td>
<td>New Scientific Opportunities</td>
</tr>
</tbody>
</table>

National Cancer Institute
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