



# Breast Cancer and the Environment Research at NIEHS

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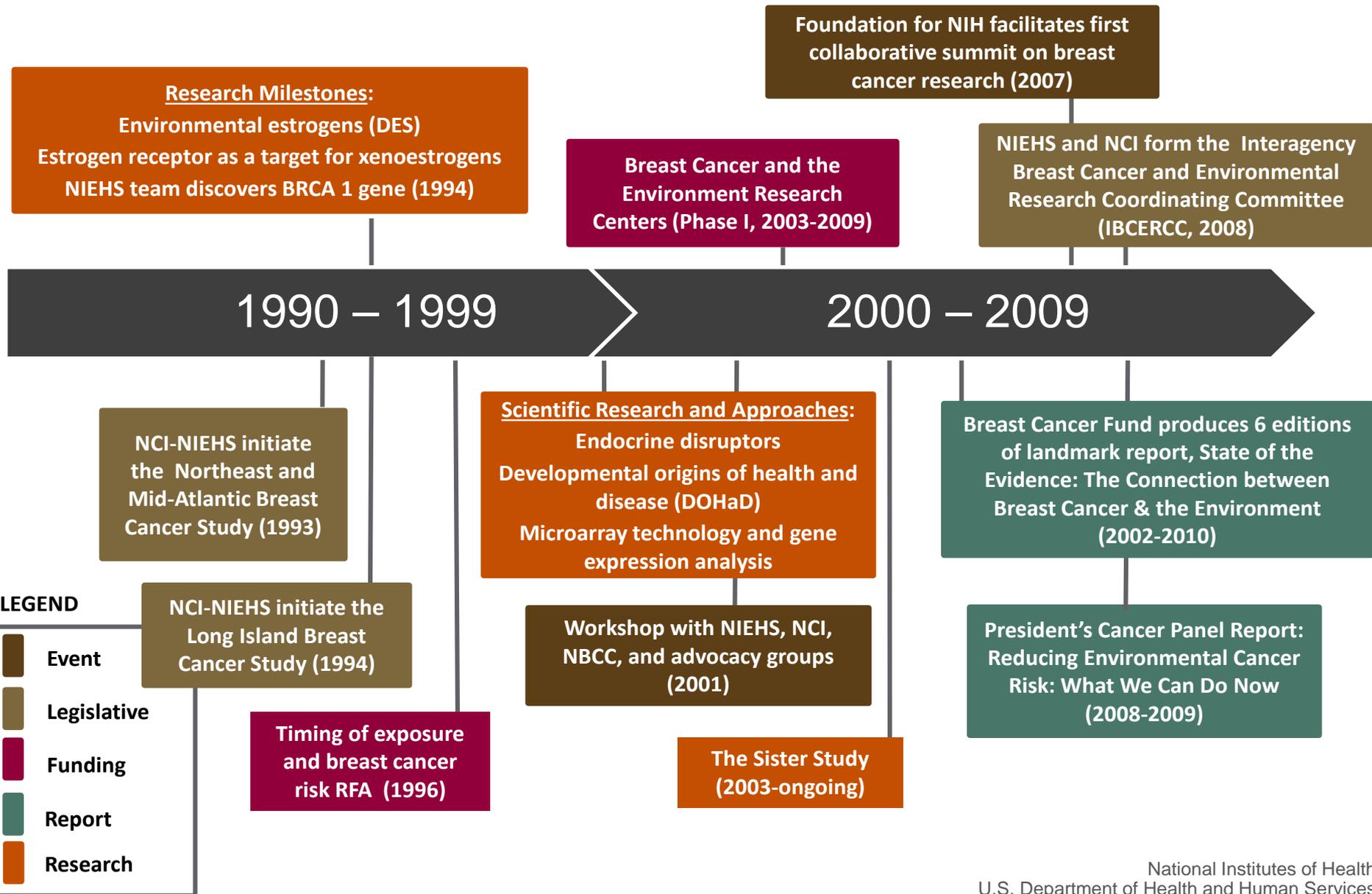
16 November 2017  
Monrovia, CA

# Environmental Factors in Cancer

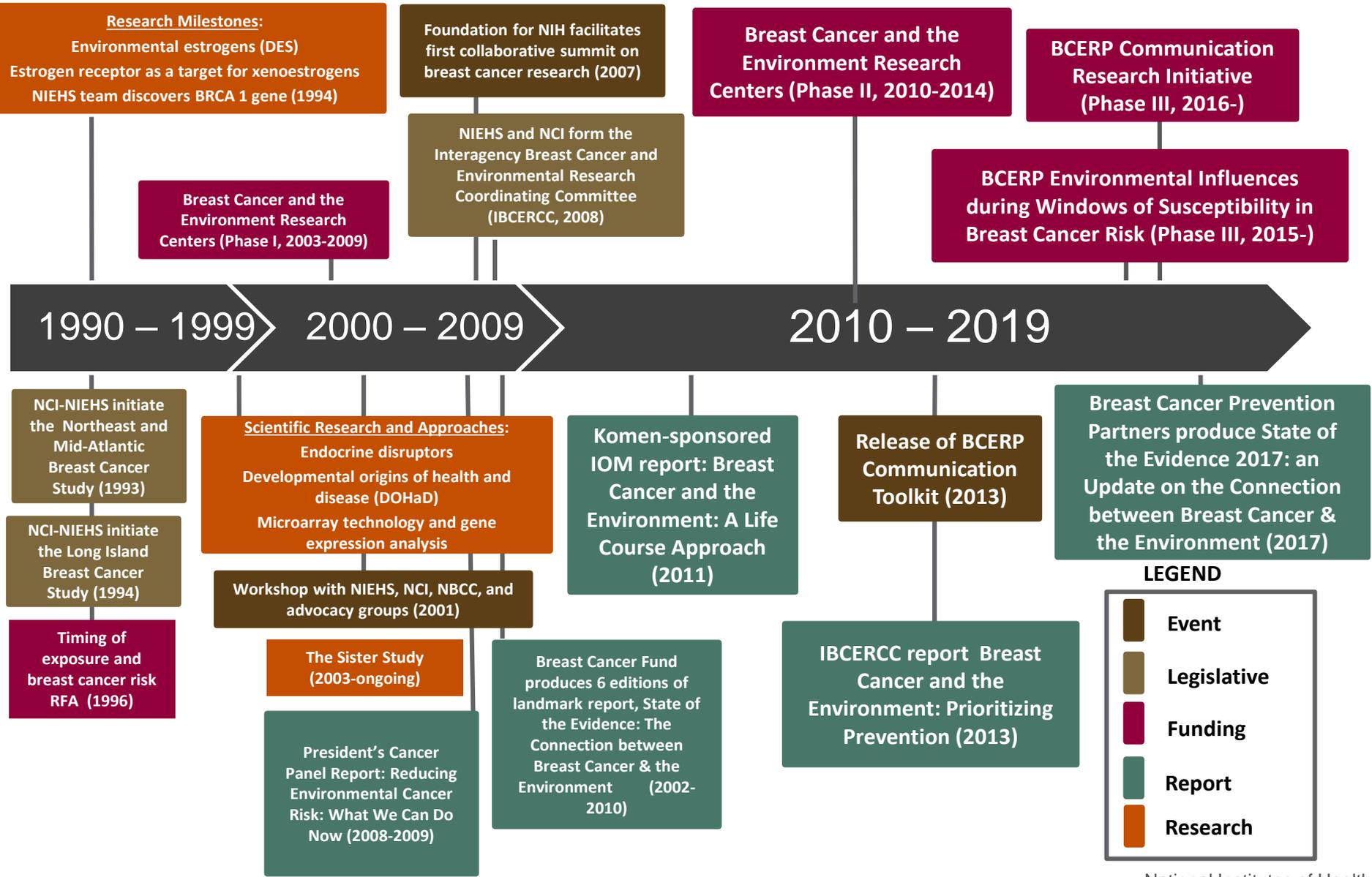
- Environmental factors account for at least 2/3 of cancer cases in the US
- NIEHS defines environmental factors broadly as everything outside the body, including diet, alcohol, cigarette smoke, environmental chemicals, viruses, and bacteria



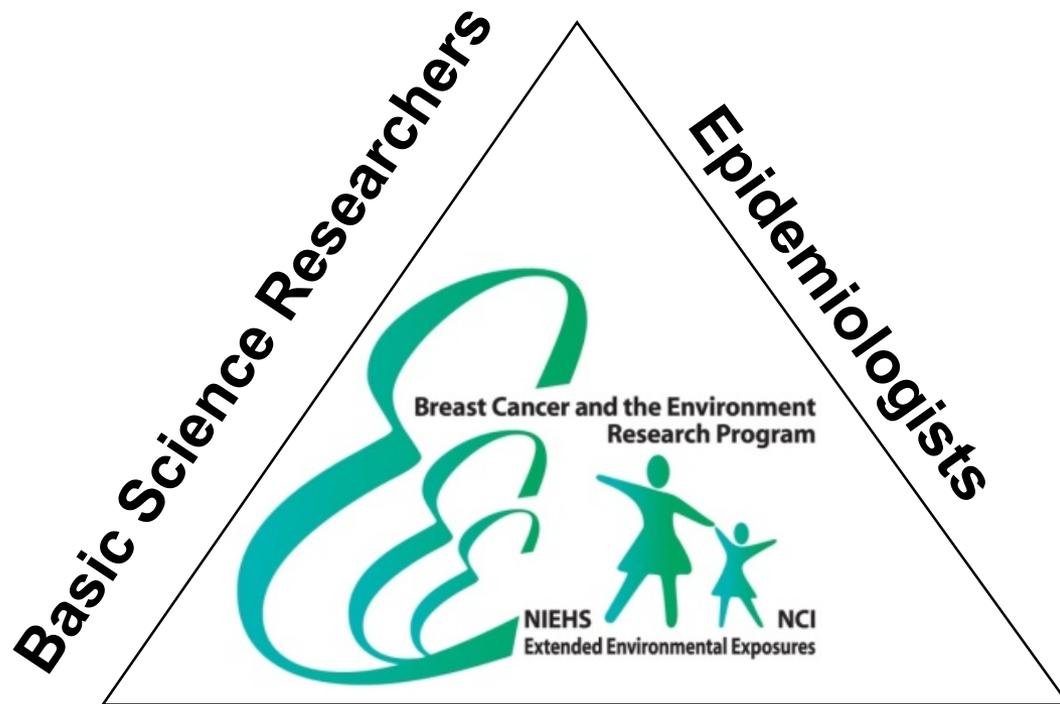
# Milestones Related to Breast Cancer and the Environment Research Program



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## BCERP Partnerships



**Community Advocates and Members**

**Communications Researchers/Dissemination and Implementation Experts**

## Windows of Susceptibility:



Prenatal



Prepuberty



Puberty



Adolescence



Pregnancy/  
Postpartum



Menopause

# Windows of Susceptibility BCERP Projects



## Prenatal

- **Diet & adiposity** (Cincinnati)
- **OC pesticides** (PHI & Columbia)
- **Air pollution, PAHs** (Columbia)



## Prepuberty

- **EDCs** (U. Alabama & Fox Chase, & Ohio State)



## Puberty

- **Diet & adiposity** (Cincinnati & Kaiser)
- **Diet & EDCs** (Mt. Sinai)



## Adolescence

- **EDCs** (UCLA, Silent Spring, Fox Chase, U. Chile)



## Pregnancy/ Postpartum

- **Obesity** (UNC-CH)
- **Air pollution PAHs** (Columbia)
- **Xenoestrogens** (UMass-Amherst)



## Menopause

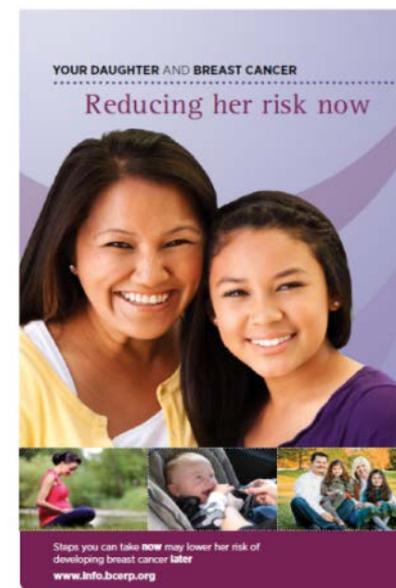
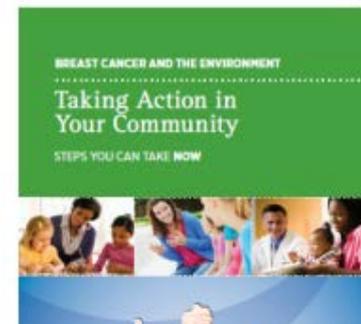
- **EDCs** (BRI-City of Hope)

**PFOA, high fat diet, oxybenzone (MSU)**

**Life Course Genomics (Mt. Sinai)**  
**Mammary Gland Architecture across Lifespan (UCSF)**  
**Genetics of Breast Cancer Risk (U. Wisconsin)**  
**Metals/Metalloids and Density (Georgetown & USUHS)**

# Breast Cancer Risk Communications

- BCERP community partners need evidence-based tools and communication strategies
- The BCERP Community Outreach and Translational Cores (COTCs) engaged in translating BCERP findings into messages for their local communities.
- Communications research grants for assessing and promoting environmental health literacy:
  - Strategies for Communicating the Environmental Risks of Cancer, R03, **Univ. South Carolina**
  - Using Targeted Social Media to Communicate Culturally Sensitive and Interactive Environmental Risk Information about Breast Cancer to Mothers, R21 **George Mason Univ.**
  - Training Pediatric Health Care Providers as a Primary Information Source for Communicating Environmental Risks for Breast Cancer, R21 **Michigan State Univ.**



**BCERP key message toolkits**

## BCERP Success – PFCs in Cincinnati



- BCERP Pilot Project, 2005
- ½ girls >95<sup>th</sup> percentile, PFCs



- Cincinnati & San Francisco:
- 5 PFCs detectable in 95% in 6-8 year old girls
- Cincinnati > San Francisco
- Girls in Northern Kentucky (NKY) highest



- Individual biomarker results sent to the girls



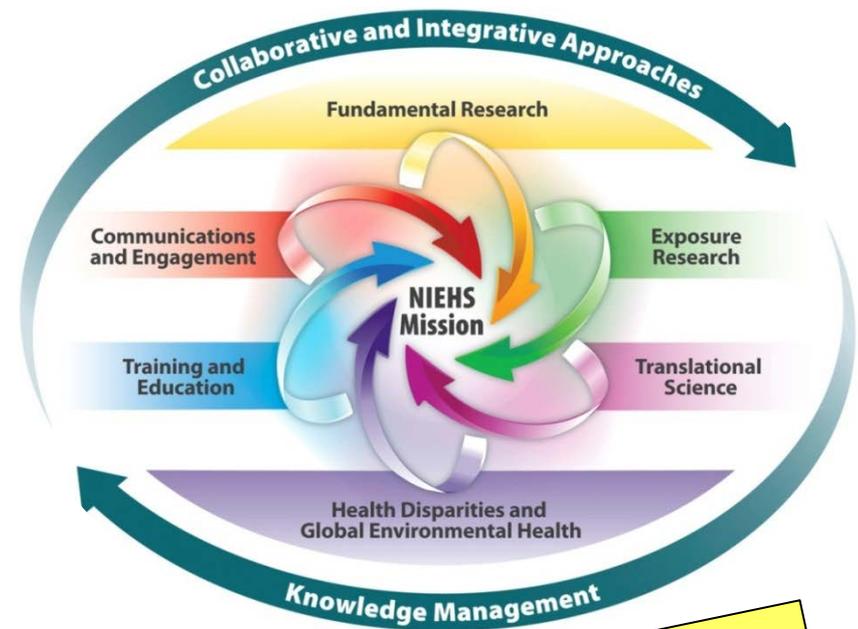
- Stunted mammary development
- Delayed onset of puberty



- Drinking water source of PFCs
- Granular activated carbon filters for water treatment initiated at NKY facilities, 2012

# BCERP Aligns with NIEHS Strategic Plan

- **Goal 1:** Understand fundamental mechanisms and biological pathways of breast cancer
- **Goal 2:** Linking individual susceptibility across the lifespan with risk of breast cancer
- **Goal 6:** Understanding the disproportionate risk of breast cancer research through research in diverse populations
- **Goal 8:** Increase scientific literacy and awareness of risk of breast cancer from environmental exposures
- **Goal 9:** Training a multidisciplinary group of scientists from diverse backgrounds
- **Goal 11:** Improving communication and collaboration between researchers and stakeholders



**2018-2023 Strategic Plan Coming Soon!**

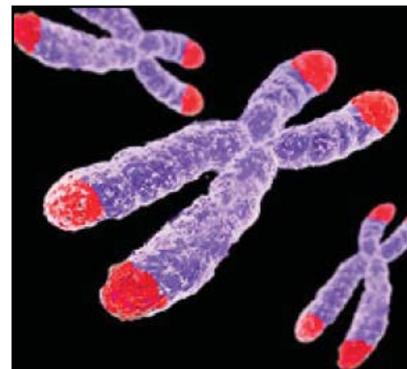
# The NIEHS Sister Study and Two Sister Study

- **Sister Study** examines environmental and familial risk factors for breast cancer in sisters of women who have had breast cancer
- This study enhances the ability to assess the interplay of genes and environment in breast cancer risk and to identify potentially preventable risk factors
- Between 2004-2009 the study recruited nearly 51,000 subjects, 35-74 years of age
- **Two Sister Study** focuses on young-onset breast cancer (below age 50) and is a family-based study
- 1,400 young-onset sisters enrolled along with 1,700 of their sisters in the Sister Study.



## Recent Findings from The NIEHS Sister Study

- Higher level of physical activity at ages 5-19 was associated with lower breast cancer risk
- High levels of vitamin D (serum 25(OH)D levels) and regular vitamin D supplement use were associated with lower rates of postmenopausal breast cancer; SNPs in vitamin D-related genes may modify this association
- Burning either wood or natural gas indoors was associated with moderate risk of breast cancer



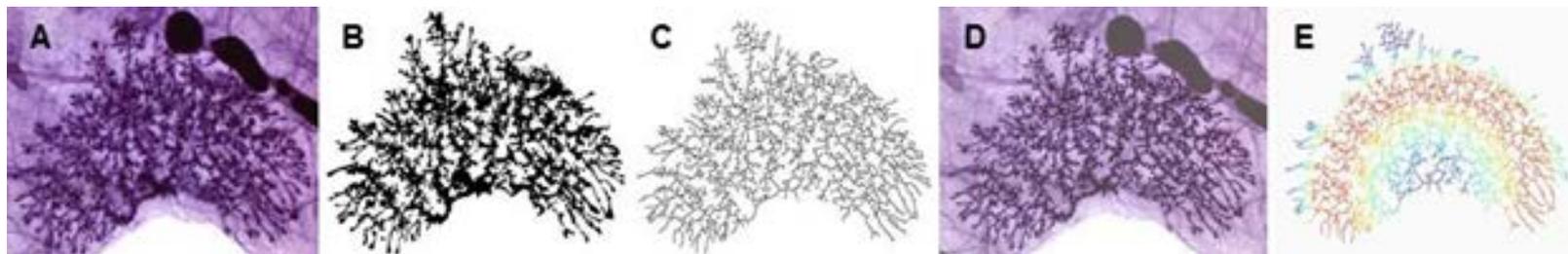
## Recent Findings from the Two Sister Study

- Family-based, genome-wide association study of **young-onset** breast cancer (age<50)
- Identified 3 autosomal SNPs at novel loci with unknown functional roles
- No evidence of maternally mediated, X-linked, or mitochondrial genetic effects
- Of 77 SNPs previously linked to risk of breast cancer at any age, SNPs in TOX3, ESR1, FGFR2, and RAD51B were also found to be associated with young-onset breast cancer
- None were explained by prenatal effects of maternal variants



## NTP: Mammary Branching Density

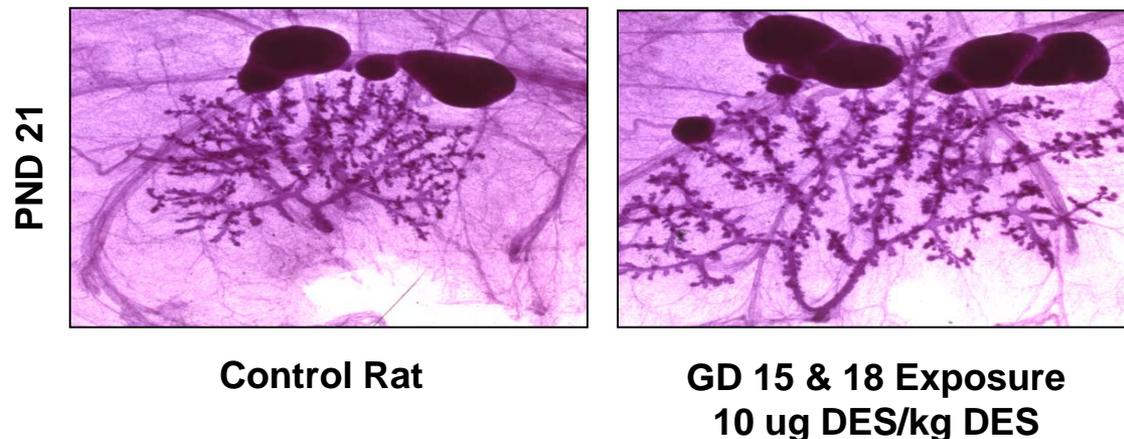
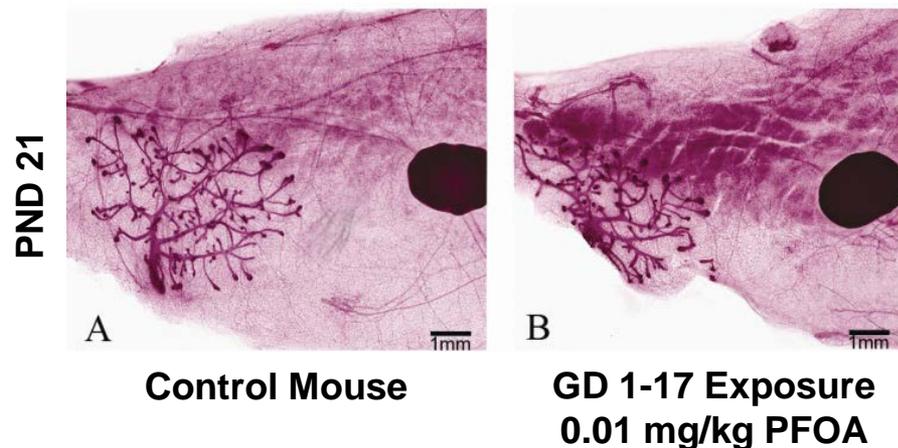
- Sholl method allows for objective quantification of morphological mammary gland branching density as a measure of development in peripubertal rats.



**Stepwise ImageJ processing of mammary gland whole mount image. A) Original whole mount image. B) Binary thresholded image. C) Skeletonized image. D) Overlay of skeletonized image onto original whole mount image demonstrating accuracy of image processing. E) Analyzed image painted as a heat map according to the Sholl profile.**

# NTP Examining Critical Windows in Animal Models

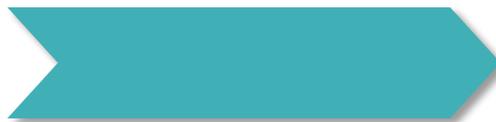
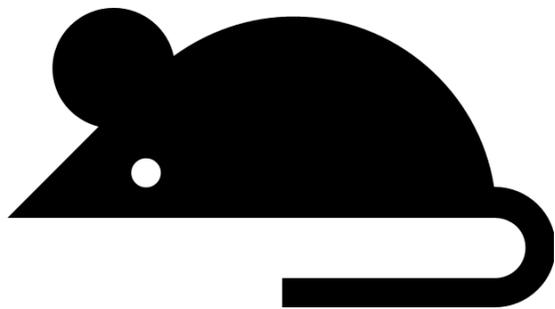
- **Low dose PFOA exposure** during gestation results in reduced mammary gland development in 3 generations of offspring
- **Gestational exposure of DES** results in hypercellularity and altered ER and PR gene expression---  
→ **predictive biomarkers**



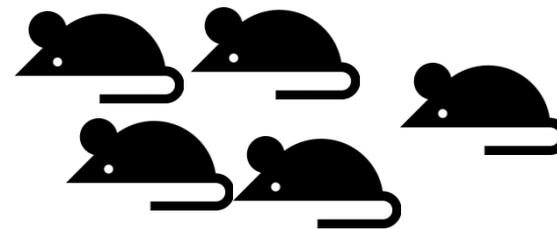
# National Toxicology Program

Fetal Developmental Period

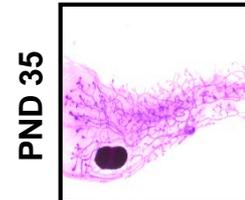
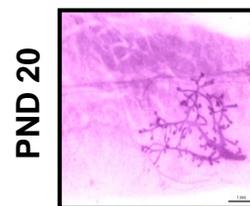
 **BPAF**  
**BPS**



Puberty

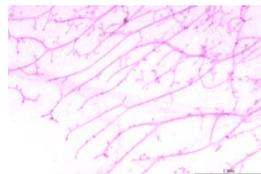


Precocious Development

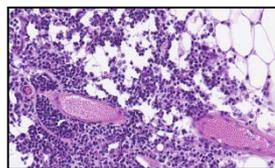


Persistent Terminal End Buds  
Vehicle Treated

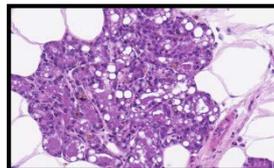
Early Adulthood



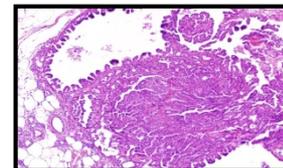
Late Adulthood



Inflammation



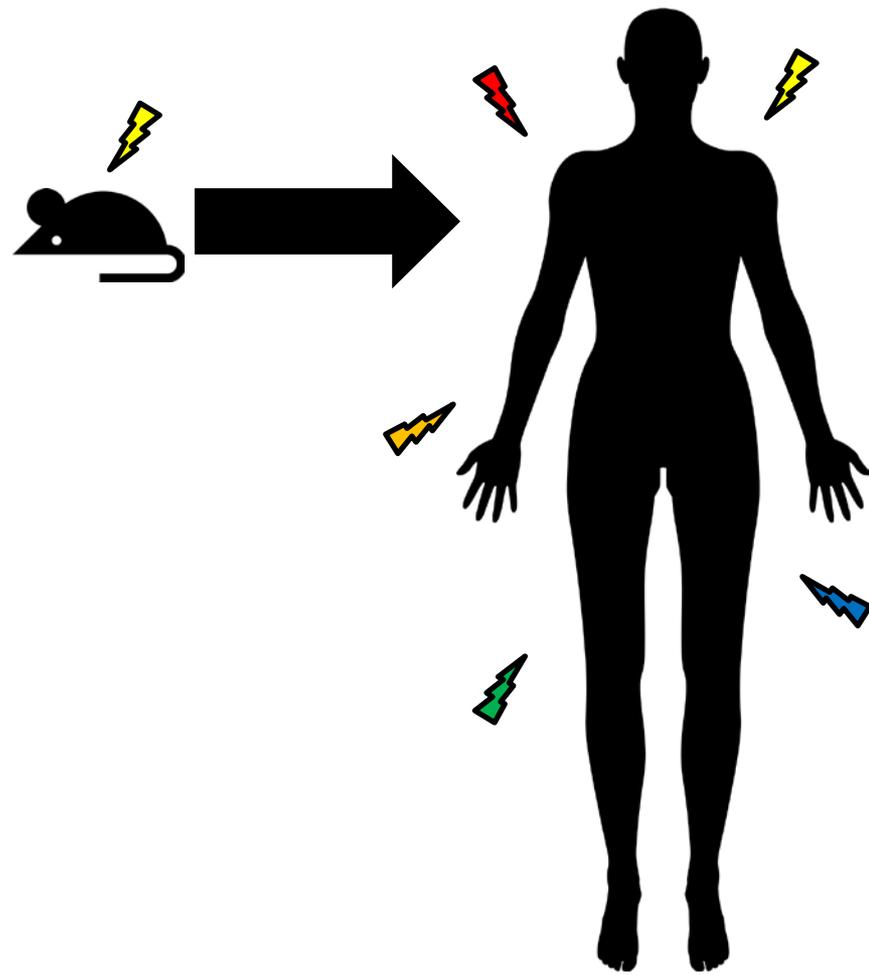
Lobuloalveolar  
Hyperplasia



Adenocarcinoma

## Translational Science

- Women with mammographic densities greater than 75% have a 4- to 6-fold increased risk of breast cancer
- Is mammary branching density in rodent models comparable to human mammographic density?
- 2017 BCERP Opportunity Fund: Translating Rodent Mammary Structure to Human Breast Density: Comparative Digital Analysis of Histology





## Importance of Community-engaged Research

- Advances the research agenda
  - Values local knowledge
  - Traditional Ecological Knowledge
- Builds the capacity all partners
  - Fosters empowerment or “in-powerment”
- Raises the environmental health literacy
- Bolsters youth engagement
  - Develop next generation of EHS researchers
  - Increase diversity of EHS researchers
- Strengthens commitment to partnerships



Photo courtesy of Urban Environment Program, Cornell University Cooperative U.S. Extension-New York City

# NIEHS and BCERP Partner with Communities

**Community Forum** Tonight at 6:30pm

Cooper Auditorium at City of Hope: 1500 East Duarte Road, Duarte, CA 91010

- National, Wisconsin, Massachusetts, Great Neck, Long Island, and Michigan Breast Cancer Coalitions
- Avon Foundation
- Breast Cancer Fund
- WE ACT for Environmental Justice
- Girls Inc of Holyoke
- Rays of Hope Foundation
- La Esperanza – The Hope of Pioneer Valley
- Protect Our Breasts
- Breast Cancer Action
- Breast Cancer Care and Research Foundation
- Black Women for Wellness
- Zero Breast Cancer
- Susan G. Komen for the Cure
- Wisconsin Cancer Council
- Earth Conservation Corps
- Groundwork Anacostia River DC
- Capital Breast Care Center
- Breast Cancer Alliance of Greater Cincinnati
- Huntington Breast Cancer Action Coalition
- Central Carolina Nurses' Council
- First Calvary Baptist Church Health Ministry
- Save Our Sisters
- e-WATCH (Wellness for African Americans Through Churches)
- ACTS (Action in Churches in Time to Save Lives) of Wellness
- NC Breast and Cervical Cancer Control Program
- Pink Ribbon Girls

## Prevention is the Key

- Genetic and environmental factors individually contribute and interact with each other to increase breast cancer risk
- Breast cancer rates can vary with environmental circumstances
- The large majority of cases occur in women with no family history of breast cancer
- Environmental factors are more readily identified and modified than genetic factors and, therefore, present a tremendous opportunity to prevent breast cancer



## Looking Forward to the Meeting

- Susceptible windows of exposure
- Community advocates advancing research and informing the public
- Cosmetics as a source of endocrine disruptors
- Microenvironment and aging
- Epigenetic clock and timing of puberty



Thank you to our hosts from the  
Beckman Research Institute!



National Institute of Environmental Health Sciences  
*Your Environment. Your Health.*

# Thank you!



National Institute of  
Environmental Health Sciences



National Toxicology Program  
U.S. Department of Health and Human Services

NIEHS Strategic Plan Website  
<http://www.niehs.nih.gov/strategicplan>

