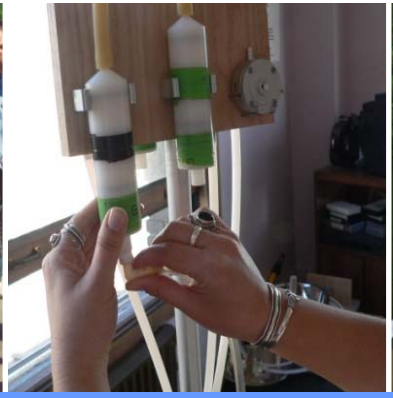

Environmental Chemicals and Breast Cancer

Human Studies

Julia Brody, PhD

Silent Spring Institute

CHE Webinar October 2017

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Cancer is a complex disease influenced across the lifecycle

Breast cancer:

- Before birth
- During puberty
- First pregnancy
- Menopause

Pathways Project for Breast Cancer

Schwarzman et al. 2015, Environ Health Perspectives

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Update:

Human Studies 2007-2017

158 articles

Environmental Research 160 (2018) 152–182

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Environmental chemicals and breast cancer: An updated review of epidemiological literature informed by biological mechanisms☆

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ARTICLE INFO

Keywords:
Endocrine disruptors
Toxicology
Breast development
Mammary carcinogens
Prevention

ABSTRACT

Background: Many common environmental chemicals are mammary gland carcinogens in animal studies, activate relevant hormonal pathways, or enhance mammary gland susceptibility to carcinogenesis. Breast cancer's long latency and multifactorial etiology make evaluation of these chemicals in humans challenging.

Objective: For chemicals previously identified as mammary gland toxicants, we evaluated epidemiologic studies published since our 2007 review. We assessed whether study designs captured relevant exposures and disease features suggested by toxicological and biological evidence of genotoxicity, endocrine disruption, tumor promotion, or disruption of mammary gland development.

Methods: We systematically searched the PubMed database for articles with breast cancer outcomes published in 2006–2016 using terms for 134 environmental chemicals, sources, or biomarkers of exposure. We critically reviewed the articles.

Results: We identified 158 articles. Consistent with experimental evidence, a few key studies suggested higher risk for exposures during breast development to dichlorodiphenyltrichloroethane (DDT), dioxins, perfluorooctanesulfonamide (PFOSA), and air pollution (risk estimates ranged from 2.14 to 5.0), and for occupational exposure to solvents and other mammary carcinogens, such as gasoline components (risk estimates ranged from 1.42 to 3.31). Notably, one 50-year cohort study captured exposure to DDT during several critical windows for breast development (in utero, adolescence, pregnancy) and when this chemical was still in use. Most other studies did not assess exposure during a biologically relevant window or specify the timing of exposure. Few studies considered genetic variation, but the Long Island Breast Cancer Study Project reported higher breast cancer risk for polycyclic aromatic hydrocarbons (PAHs) in women with certain genetic variations, especially in DNA repair genes.

Conclusions: New studies that targeted toxicologically relevant chemicals and captured biological hypotheses about genetic variants or windows of breast susceptibility added to evidence of links between environmental chemicals and breast cancer. However, many biologically relevant chemicals, including current-use consumer product chemicals, have not been adequately studied in humans. Studies are challenged to reconstruct exposures that occurred decades before diagnosis or access biological samples stored that long. Other problems include measuring rapidly metabolized chemicals and evaluating exposure to mixtures.

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2007 Evidence

Brody et al., *Cancer,* 2007, Rudel et al., *Cancer,* 2007,
Xue and Michels, *Lancet Oncology,* 2007; Rudel et al., *EHP*, 2011;
Brody et al., *Science* (letter), 2014; Rudel et al., *EHP*, 2015

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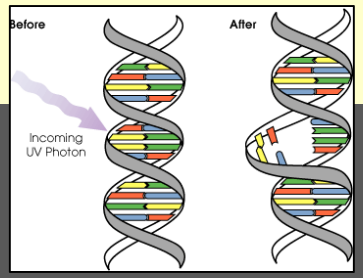
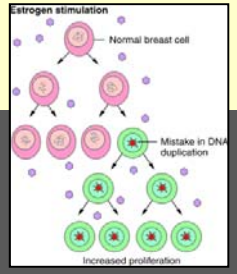
Goals of review:

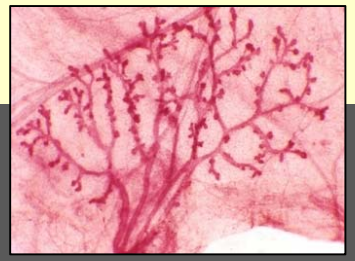
- Learn from unique exposure scenarios that capture questions from biology
- Strengthen “proof of principle”
- Speak to skeptics
- Guide future studies

Review methods:

- Searched literature for 130+ chemicals and breast cancer
- Summarized breast-cancer biology of the chemicals
  - Is this a breast carcinogen? Estrogen-mimic? Does it alter breast growth?
- Analyzed 158 epidemiology studies







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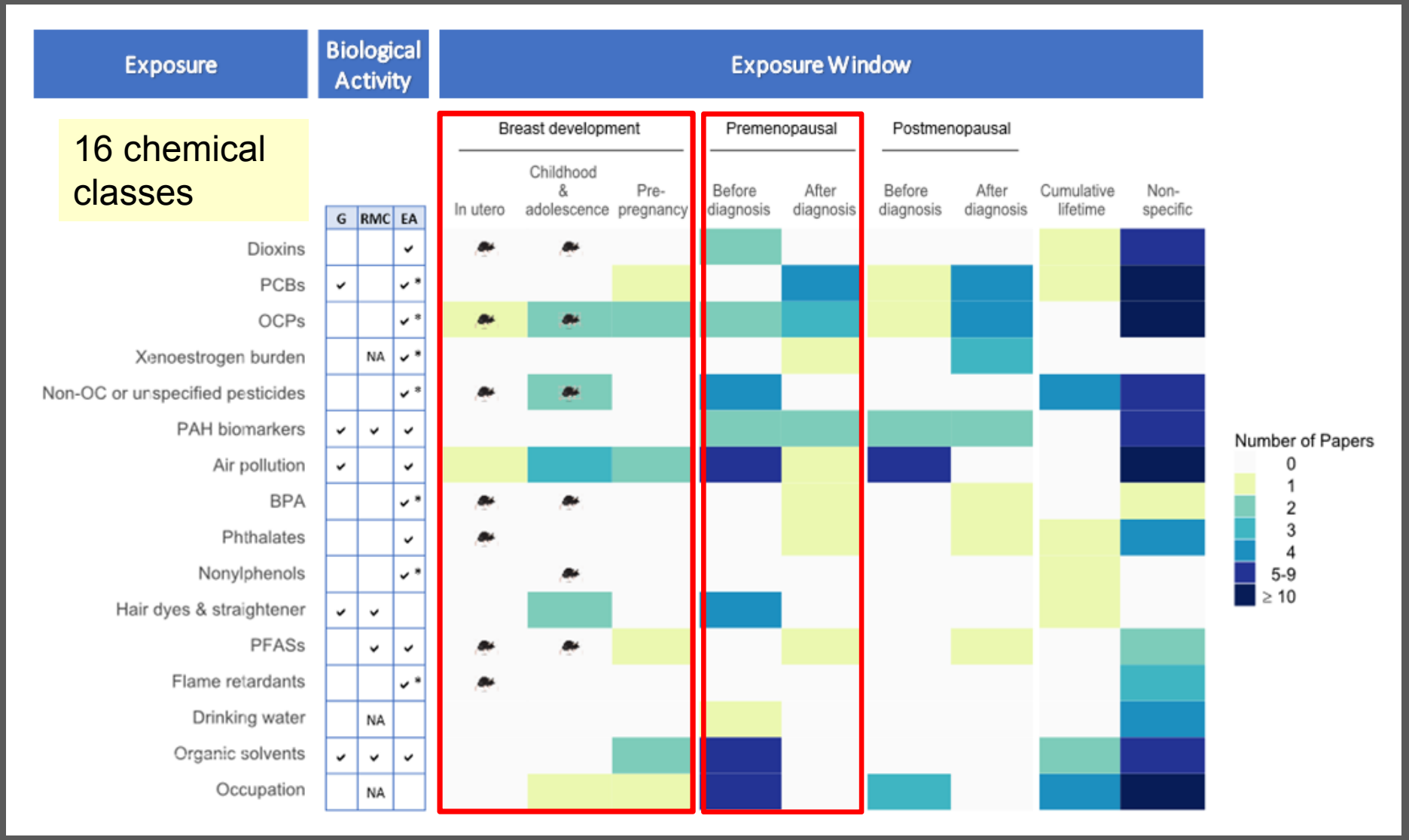
Most studies still miss critical timing



New results - strong studies

- Thank you, cohort members!

Members of CHDS

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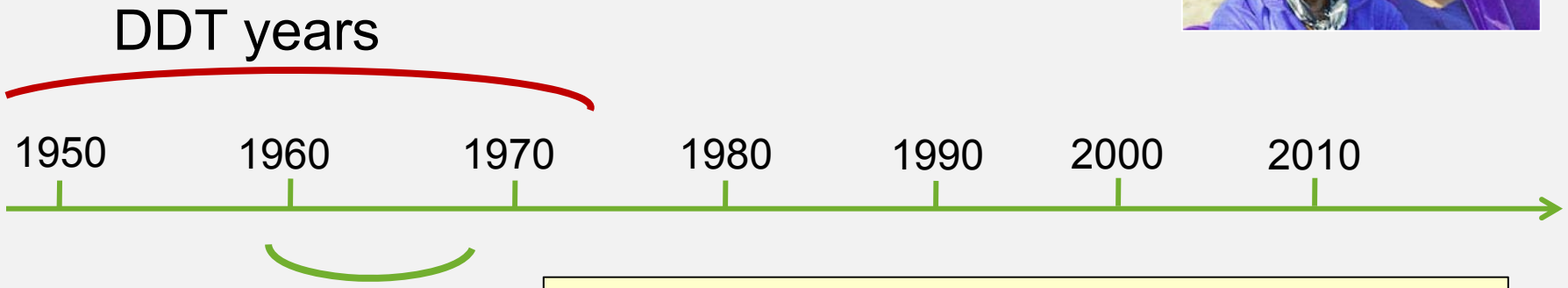
Child Health & Development Studies
Persistent EDCs



Blood sampled after birth

5X higher odds: p,p'-DDT in women < age 14 in 1945

Almost 4X higher odds: o,p'-DDT in daughters

Cohn et al., 2007, 2015

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DDT/DDE/Organochlorine pesticides

Higher odds of breast cancer:

- Long Island - premenopausal breast cancer
- Sister Study - ER+/PR+ tumors

Niehoff 2016, White 2013

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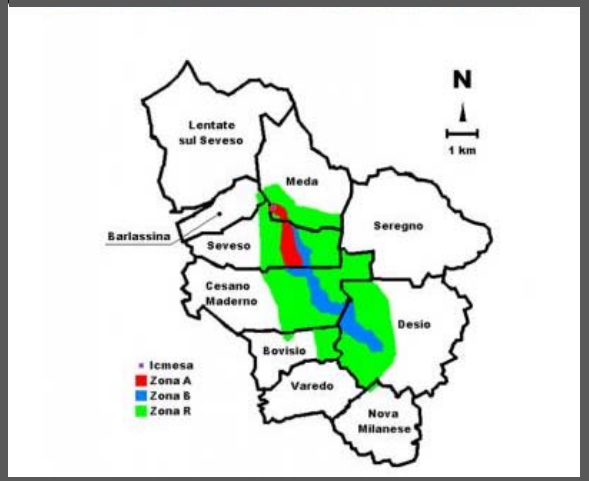
Seveso Women's Health Study
Dioxin - TCDD

Source: toxipedia.org



Women who lived near accident age 0-40

- Higher blood TCDD (dioxin): > 2 X increased risk after 11-20 years of follow up

Warner 2011

Organic Solvents at Work

Source: historicalstockphotos.com

- Early exposure -- before first childbirth, before age 36

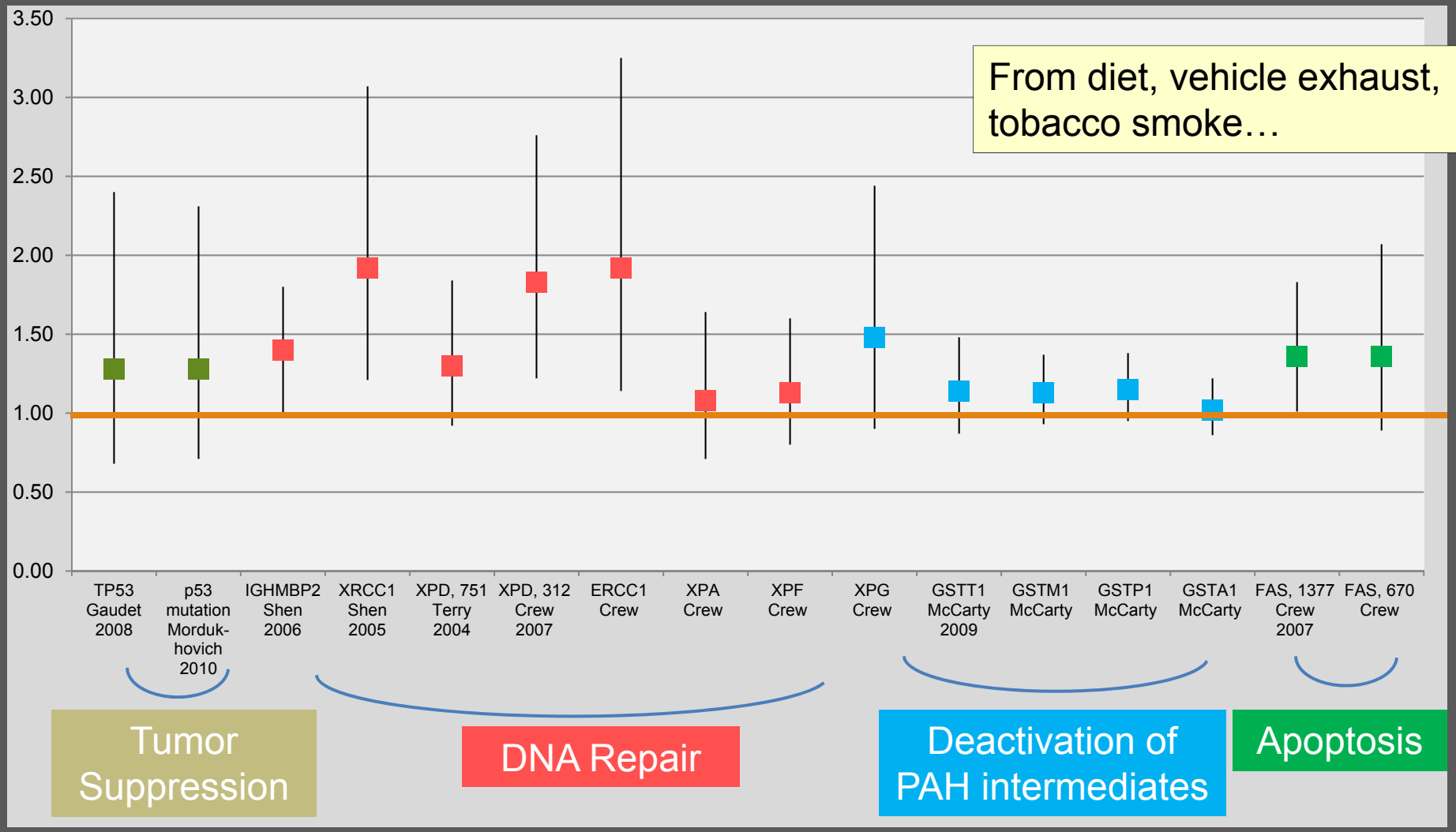
  Ekenga et al., 2014; Glass et al., 2015; Labreche et al., 2010

- Before worker protection rules

  Sung et al., 2007'; Ekenga et al, 2014

Long Island Breast Cancer Study

PAHs X genes



Consumer Product Chemicals
studies increased, but have limitations

Limitations:

- Timing of exposure
- One-time measures of chemicals that are metabolized rapidly
- Mixtures

- Lifetime use of household cleaners and air fresheners (Zota 2010)
- PFOSA at pregnancy associated with breast cancer 10-15 years later – Danish National Birth Cohort (Bonefeld-Jorgensen 2014)

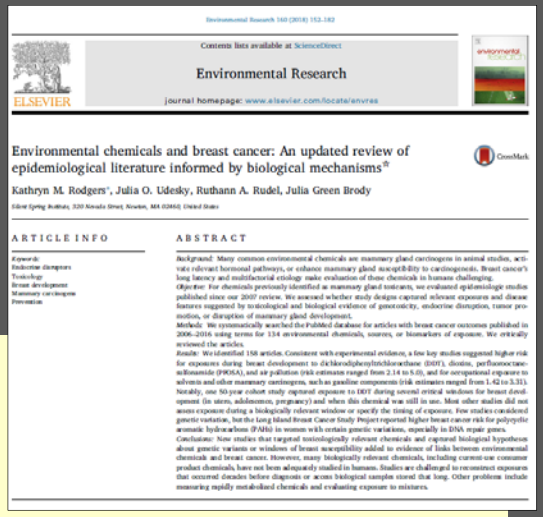
Animal and human studies- generally consistent

+	Stronger evidence of association
(+)	Limited evidence of association
(-)	Limited evidence for no association
-	Stronger evidence for no association

Exposure	Human Breast Cancer	Rodent Mammary Tumors
HRT (E + P)	+	+
HRT (E)	(+)	+
Oral Contraceptives (E + P)	+	+
DES	+	+
Griseofulvin, Furosamide, Metronidazole	(+)	+
Indomethacin, Nitrofurantoin	(-)	+
Ionizing radiation	+	+
Alcohol	+	(+)
Heterocyclic amines (meat)	(+)	+
Sleep disruption	(+)	+
Ethylene oxide	(+)	+
PAH	(+)	+
PAH (polymorphsims)	(+)	Not tested
Solvents (early exposure)	+	+
DDE (adult exposure)	-	-
DDT (early life exposure)	+	Not tested
PCBs (general population)	-	-
PCBs (early life)	(+)	Not tested
PCBs (polymorphism)	(+)	Not tested
Dioxin (early life exposure)	(+)	(+)

Updated from Rudel 2014. Environmental Health Perspectives

Conclusions



Environmental Research

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ARTICLE INFO

ABSTRACT

1. Rely on the strong studies
2. Support unique cohorts
3. Study <u>early effects</u> before breast cancer, <u>mixtures</u>, and <u>interactions</u>
4. Don’t wait: Develop rapid tests to predict chemical effects on the breast

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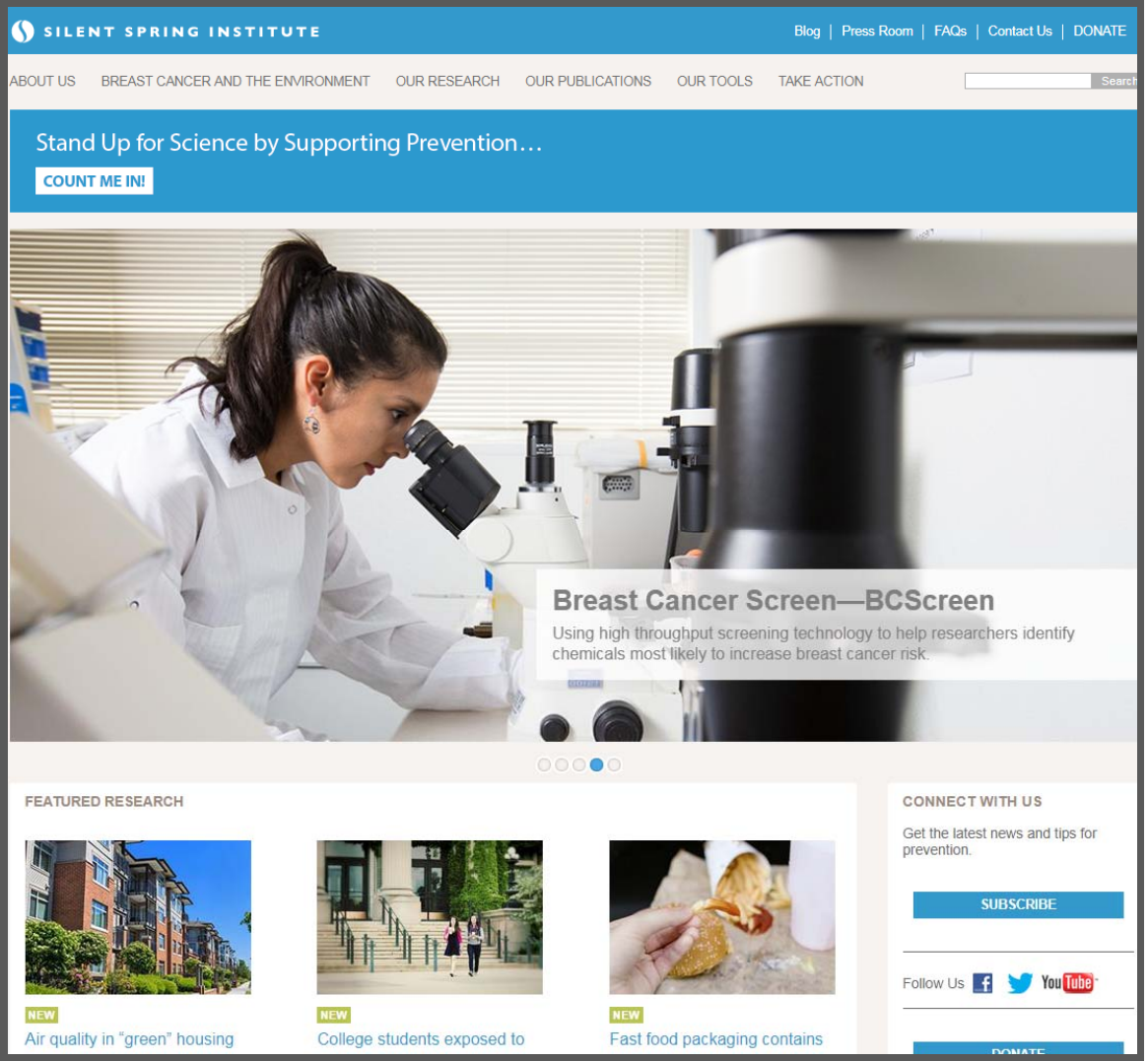
Thank you

Review authors

- Kathryn Rodgers
- Julia Udesky
- Ruthann Rudel



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