LAY ABSTRACT

TITLE: **Single-cell RNA-sequencing analysis of estrogen- and endocrine-disrupting chemical-induced reorganization of mouse mammary gland.**

JOURNAL: Communications Biology (2019) 2:406

AUTHORS: Noriko Kanaya[1], Gregory Chang[1], Xiwei Wu[2], Kohei Saeki[1], Lauren Bernal[1], Hyun-Jeong Shim[1], Jinhui Wang[2], Charles Warden[2], Takuro Yamamoto[1], Jay Li[1], June-Soo Park[3], Timothy Synold[1], Steve Vonderfecht[4], Michele Rakoff[5], Susan L. Neuhausen[6] & Shiuan Chen[1]*

INSTITUTIONS:

1 Department of Cancer Biology, Beckman Research Institute of City of Hope, Duarte, CA, USA.

2 Integrative Genomics Core, Beckman Research Institute of City of Hope, Duarte, CA, USA.

3 Environmental Chemistry Laboratory, Department of Toxic Substances Control, Berkeley, CA, USA.

4 Center for Comparative Medicine, Beckman Research Institute of City of Hope, Duarte, CA, USA.

5 Breast Cancer Care & Research Fund, Los Angeles, CA, USA.

6 Department of Population Sciences, Beckman Research Institute of City of Hope, Duarte, CA, USA.

*Corresponding author

This is attributed to the BCERP grant U01 ES026137.

Lay abstract:

Women are affected by certain chemicals in the environment during menopause. This is because levels of the natural hormone estrogen are lower in the body during menopause, so the body becomes sensitive to chemicals that mimic estrogen. Chemicals in flame retardants in household items like carpet and furniture upholstery mimic estrogen and may affect women during menopause. These chemicals are called polybrominated diphenyl ethers (PBDEs).

We did a study in mice to understand how breast tissue may be affected by these chemicals. We fed the mice PBDE or injected them with estrogen. The levels of PBDE in their blood was designed to be consistent with the levels humans have in their blood from environmental exposure to household items. Mice given these chemicals had more breast tissue growth. These growth changes may make it easier for tumors to grow. This tells us that chemicals in flame retardants may increase risk of breast cancer in women during menopause.

Scientific abstract:

Menopause is a critical window of susceptibility for its sensitivity to endocrine disrupting chemicals due to the decline of endogenous estrogen. Using a surgical menopausal (ovariectomized) mouse model, we assessed how mammary tissue was affected by both 17β-estradiol (E2) and polybrominated diphenyl ethers (PBDEs). As flame retardants in household products, PBDEs are widely detected in human serum. During physiologically relevant exposure to E2, PBDEs enhanced E2-mediated regrowth of mammary glands with terminal end bud-like structures. Analysis of mammary gland RNA revealed that PBDEs both augmented E2-facilitated gene expression and modulated immune regulation. Through single-cell RNA sequencing (scRNAseq) analysis, E2 was found to induce Pgr expression in both Esr1+ and Esr1− luminal epithelial cells and Ccl2 expression in Esr1+ fibroblasts. PBDEs promote the E2-AREG-EGFR-M2 macrophage pathway. Our findings support that E2 + PBDE increases the risk of developing breast cancer through the expansion of estrogen-responsive luminal epithelial cells and immune modulation.