Effect of Estrogen, Progesterone, and PBDEs on Mammary Gland Structure After Surgical Menopause

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Beckman Research Institute of the City of Hope
Our BCERP study

**Hypothesis**: During the menopausal transition, when natural hormone levels are actively declining, BPAs and PBDEs, acting as endocrine-disrupting chemicals, promote the development of hormone-responsive breast cancers. They may act individually or have additive or synergistic effects.

S. Chen and S. Neuhausen
NIHU01ES026137 BCERP
Polybrominated Diphenyl Ethers (PBDEs)

Traces of PBDEs have been detected in samples of human tissues, human blood and breast milk.

1. Flame retardants are not bound to foam.
2. They off-gas from foam and settle into dust.
3. Dust is ingested through hand-to-mouth contact.
Molecular action of PBDEs

Kanaya et al., Tox Sci, 2019
Single-cell RNA-sequencing analysis of estrogen- and endocrine-disrupting chemical-induced reorganization of mouse mammary gland

Noriko Kanaya¹, Gregory Chang¹, Xiwei Wu², Kohei Saeki¹, Lauren Bernal¹, Hyun-Jeong Shim¹, Jinhui Wang², Charles Warden³, Takuro Yamamoto¹, Jay Li¹, June-Soo Park³, Timothy Synold¹, Steve Vonderfecht⁴, Michele Rakoff⁵, Susan L. Neuhausen⁶ & Shiuan Chen¹*
Characterization of estrogen- and the endocrine-disrupting chemical-induced mouse mammary gland reorganization via single-cell RNA-sequencing

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Communications Biology, 2019
Terminal End Bud

a) OVX (surgical menopause)
- Randomization
- 1 week exposure
- 9 weeks-old
- Vehicle
- PBDE
- E2
- E2+PBDE

b)
- Intact
- Vehicle
- PBDE
- E2
- E2+PBDE

c) Two biological replicates
- OVX (vehicle)
- OVX + E2 (E2)
- OVX + E2 + PBDE (E2+PBDE)

Digestion to single cell suspension

10X Genomics

Sequenced:
Vehicle: 6121 cells, E2: 4952 cells, E2+PBDE: 3783 cells
T-SNE plot

Luminal cell clusters

Re-clustered luminal cells

Feature plots

Mature luminal cells

Intermediate luminal cells

Luminal progenitor cells

Mammary Gland Composition by Ki67

Control: Cross Section

Treatment and Duct Type

Vehicle

Estrogen

Estrogen + Progesterone

City of Hope
ECM associated and fibroblast cells
Immune cell clusters

M2
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