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

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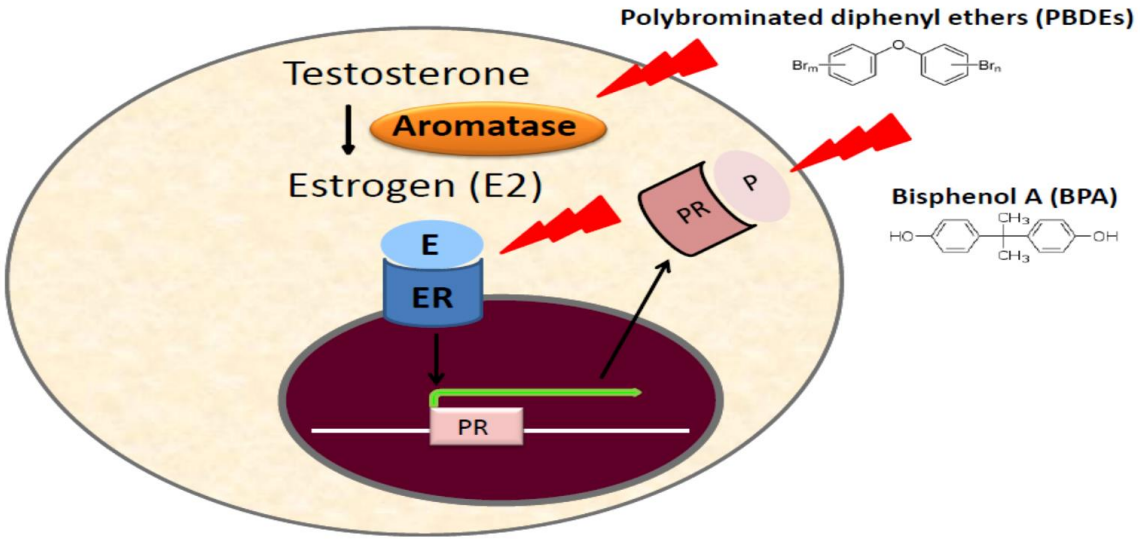
Our BCERP study

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.

Figure 1. PBDEs and BPA can modulate the expression/activity of aromatase, ER and PR activities



S. Chen and S. Neuhausen
NIHU01ES026137 BCERP

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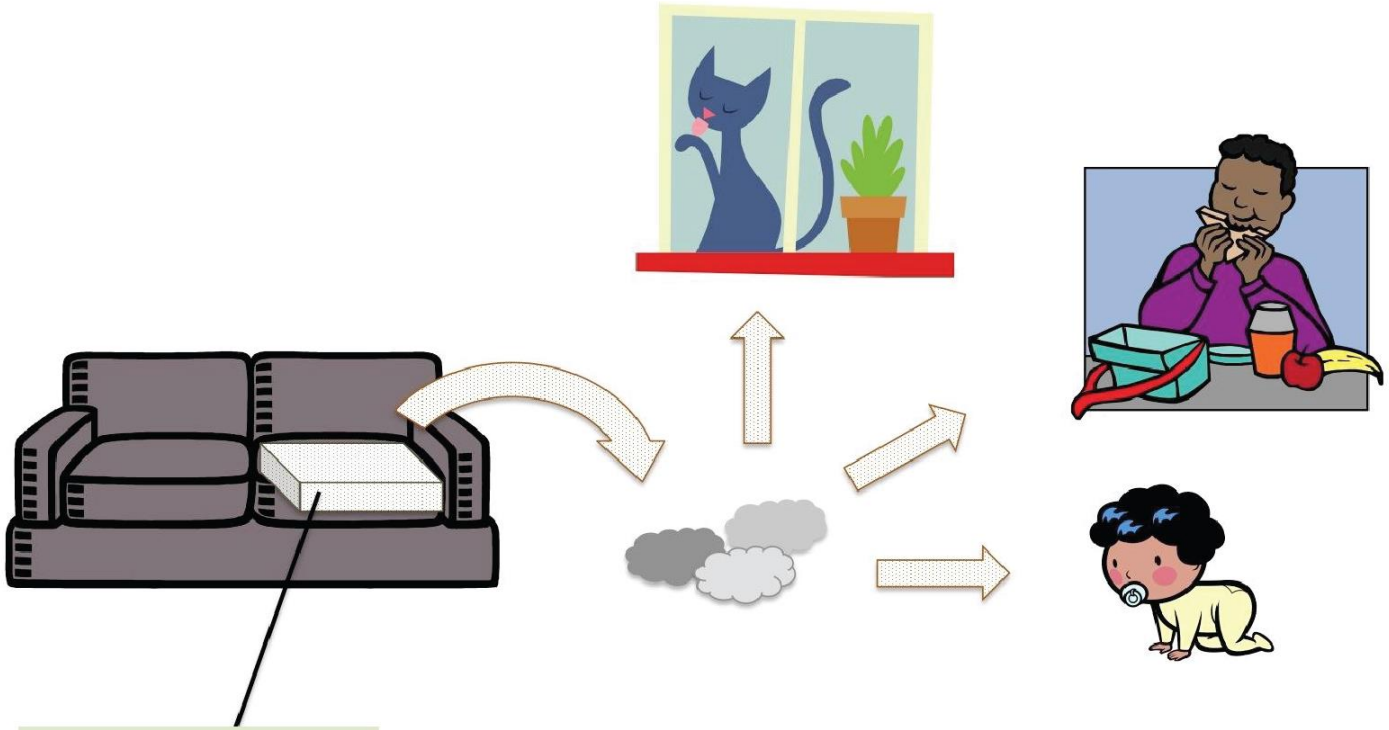
Polybrominated Diphenyl Ethers (PBDEs)

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

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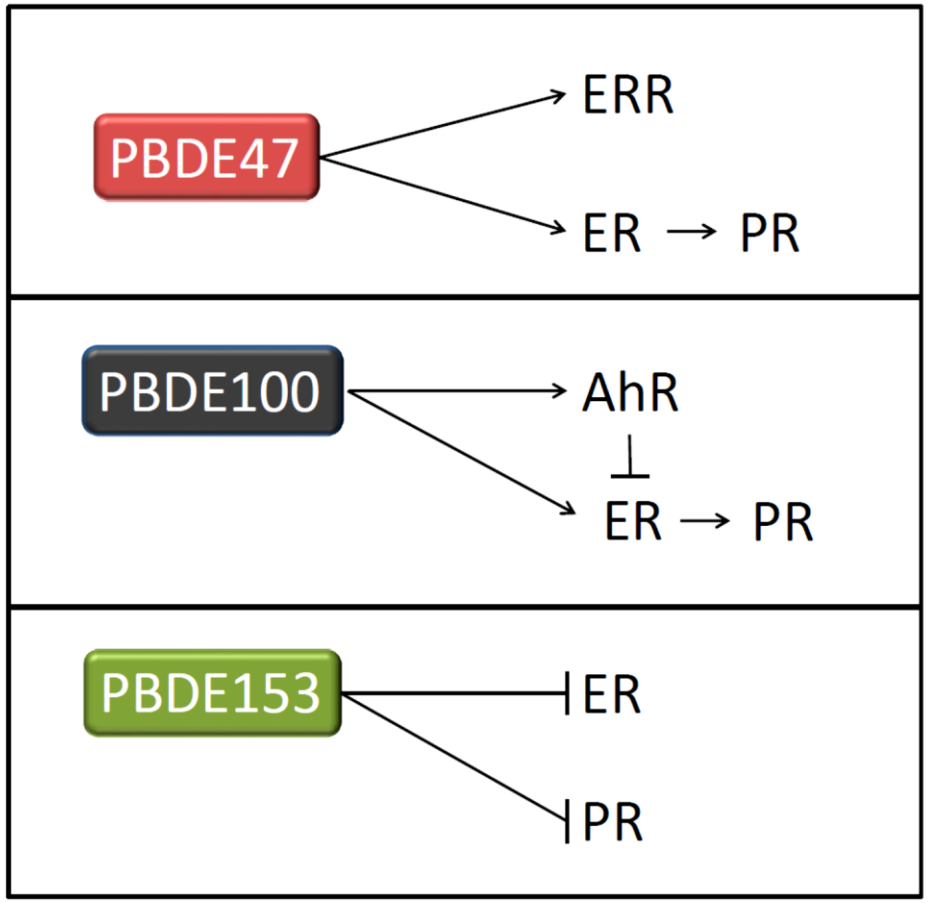
Molecular action of PBDEs



Kanaya et al., Tox Sci, 2019

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COMMUNICATIONS BIOLOGY

ARTICLE

https://doi.org/10.1038/s42003-019-0618-9 OPEN

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

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*]

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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

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Terminal End Bud

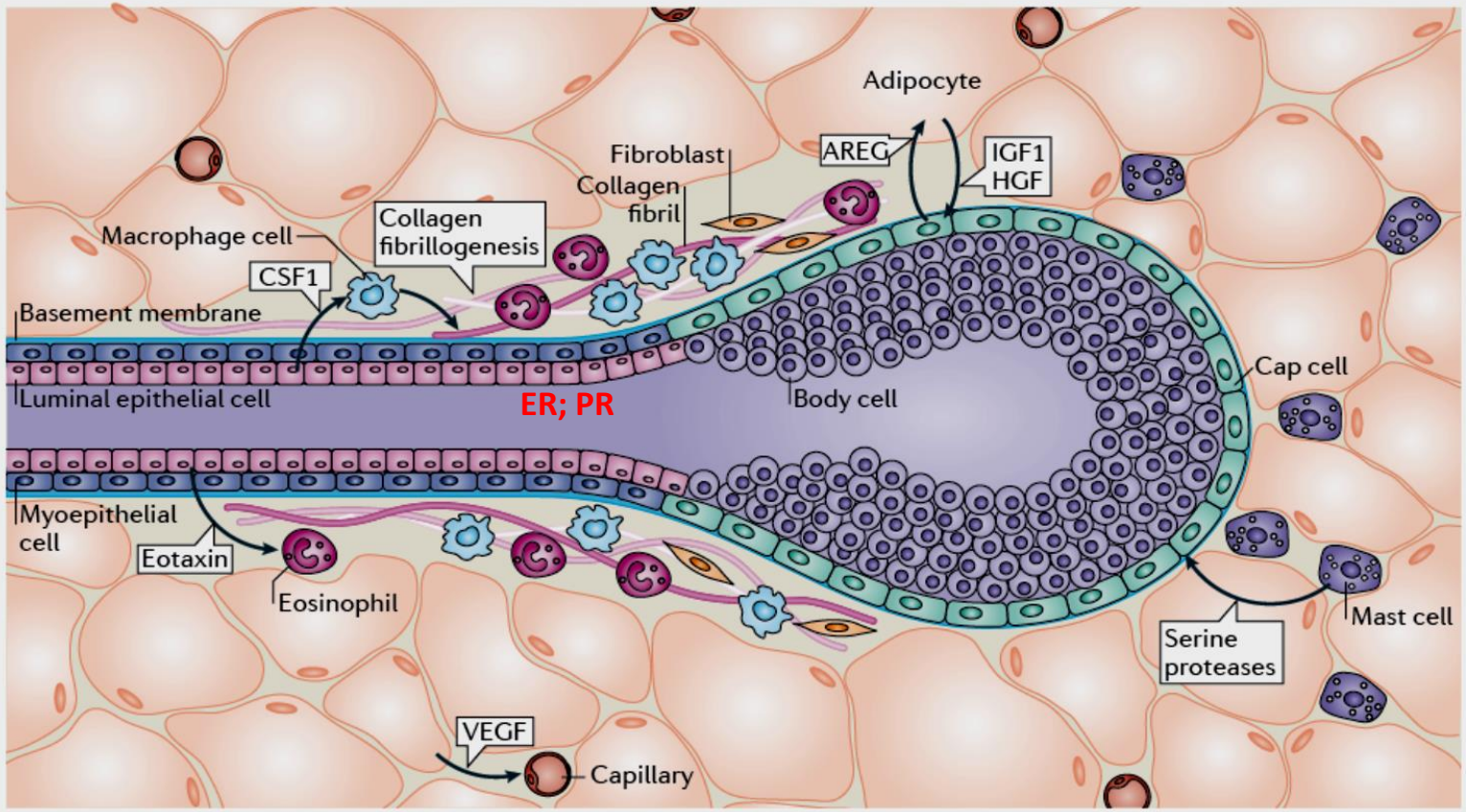

Figure 4 | **Interactions between diverse cell types of the stroma coordinate mammary morphogenesis.**

Gjorevski and Nelson, Nat Rev Mole Cell Biol, 12: 581, 2011

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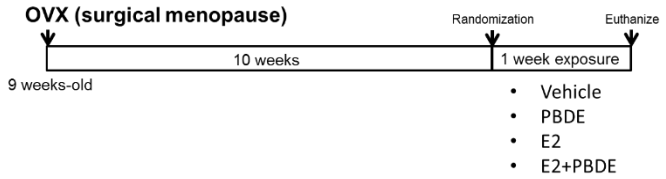
a



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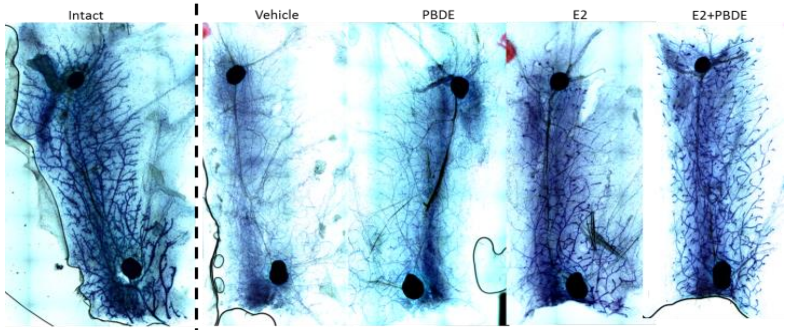
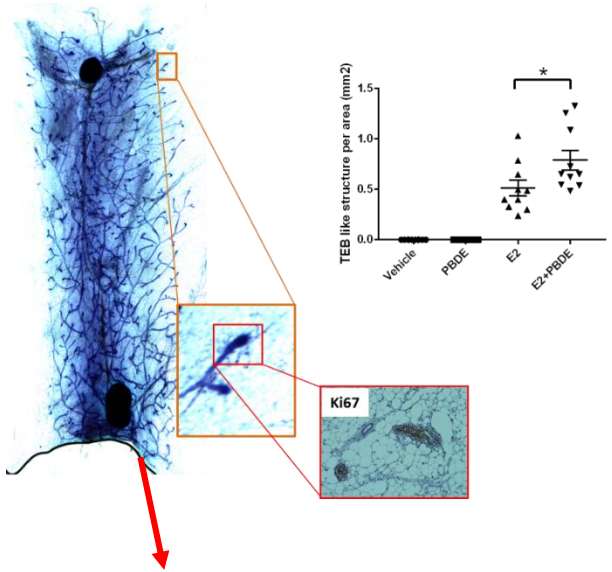


c



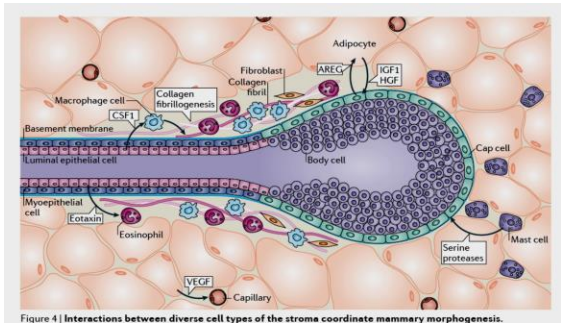
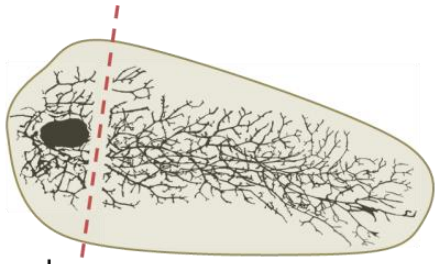


Figure 4 | **Interactions between diverse cell types of the stroma coordinate mammary morphogenesis.**

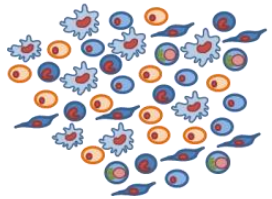
d



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

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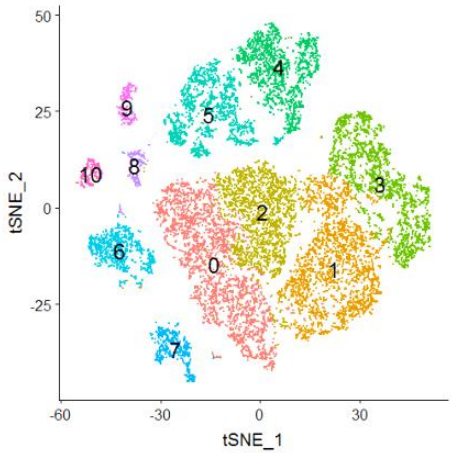
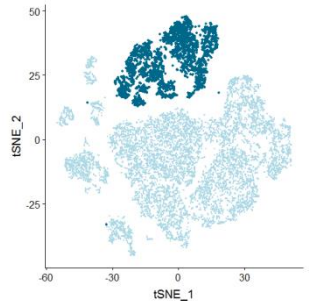
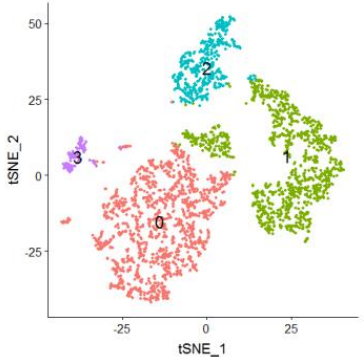
T-SNE plot



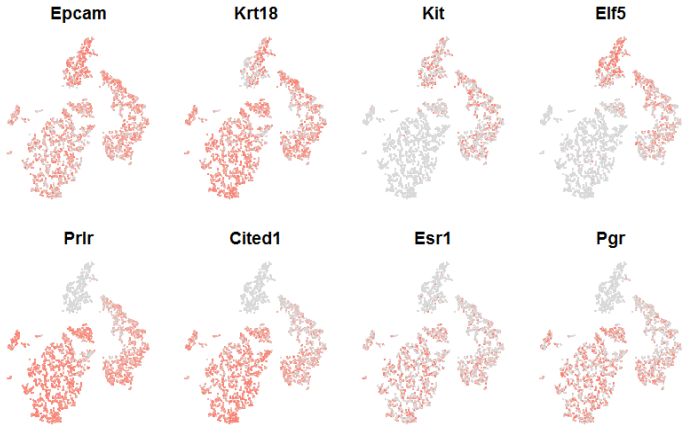
a Luminal cell clusters



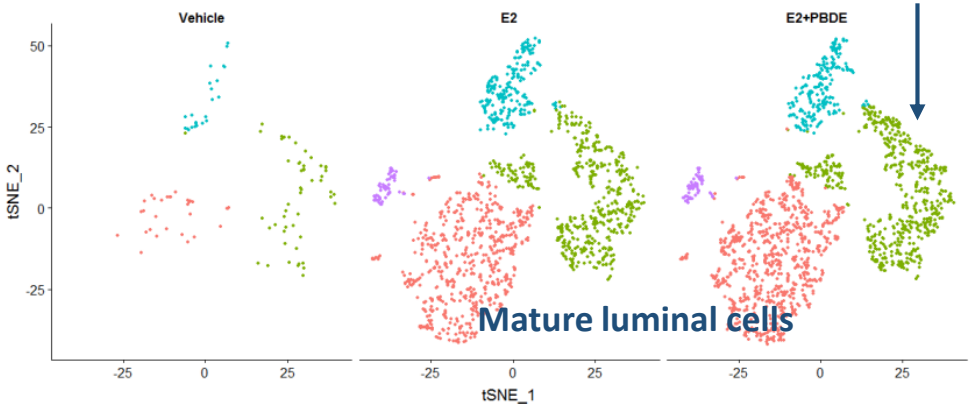
b Re-clustered luminal cells



c Feature plots



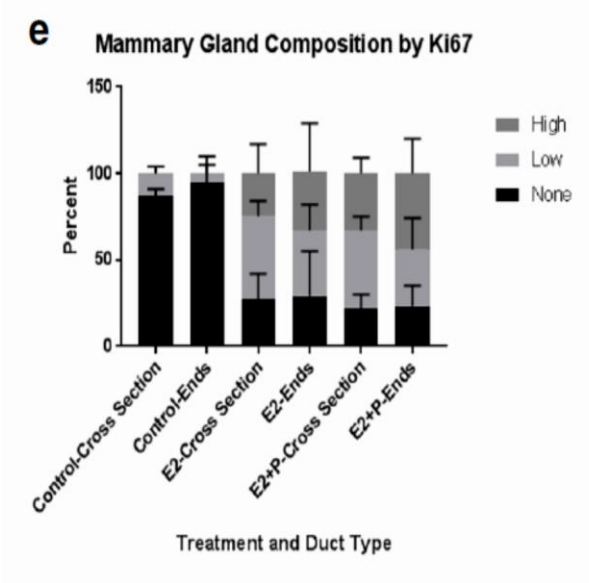
d Treatments

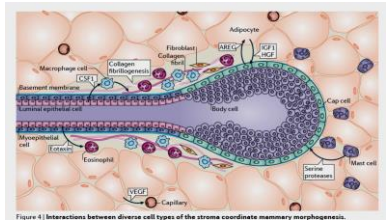


Luminal progenitor cells

Intermediate luminal cells

Mature luminal cells





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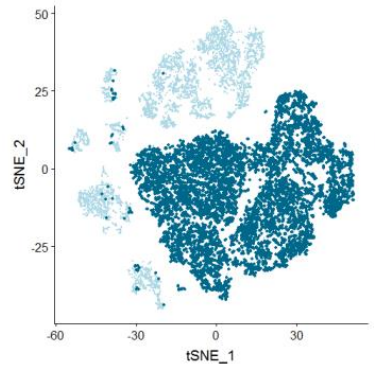
ECM associated and fibroblast cells

a



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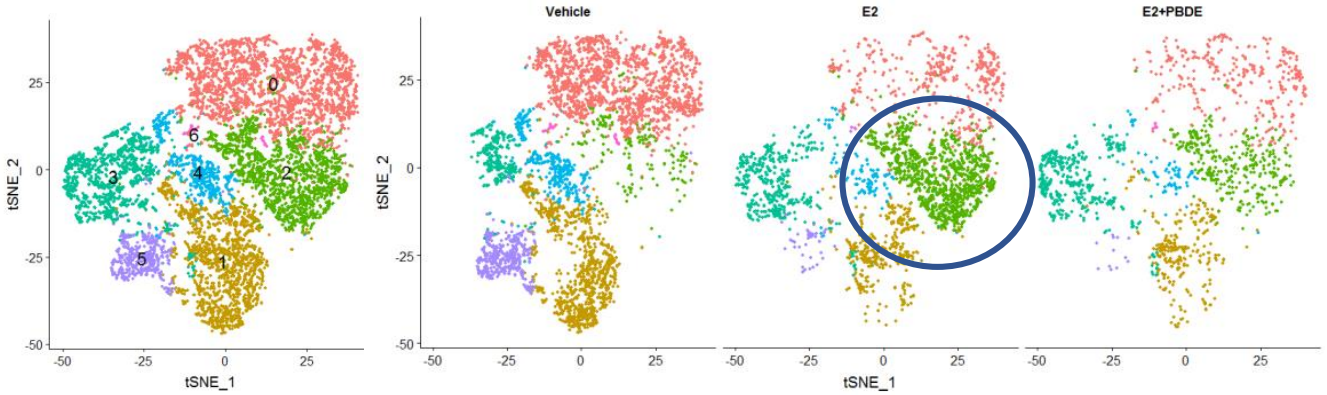

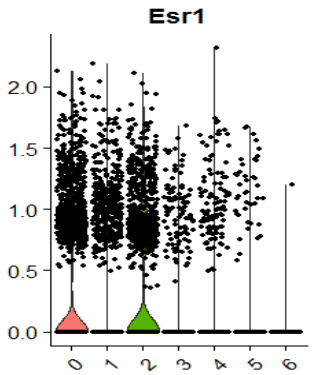

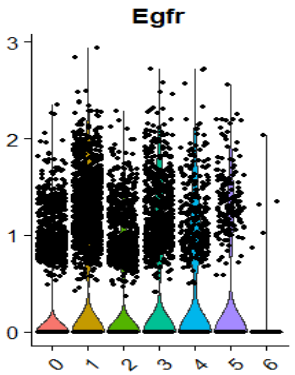

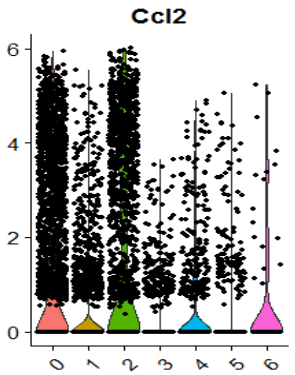

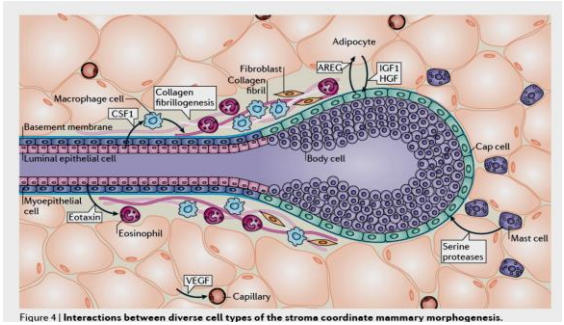

Figure 4 | Interactions between diverse cell types of the stroma coordinate mammary morphogenesis.

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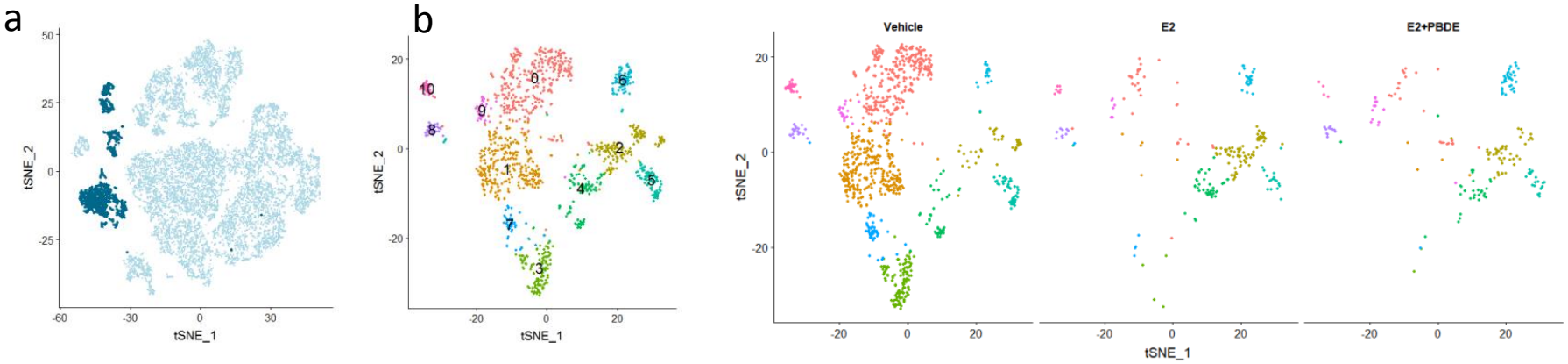
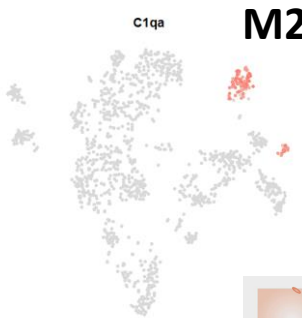
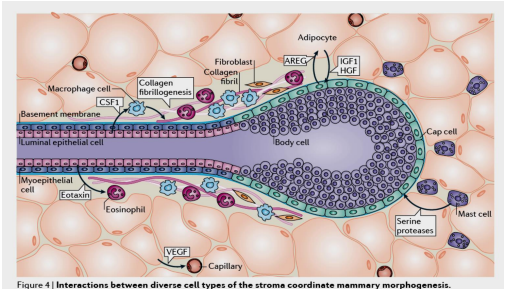
Immune cell clusters





M2



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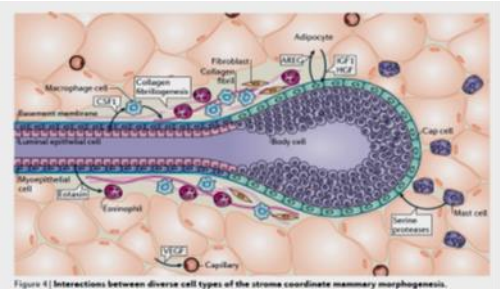

Luminal epithelial cells

ER
PR

AREG

EGFR

Fibroblasts
/stromal cells

Macrophage
polarization

E2+PBDE
Treatment

E2 Treatment

M2 macrophages

PBDE

ER

CCL2

Macrophage
recruitment

Fibroblasts
/stromal cells

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  Dr. Noriko Kanaya
  Ms. Lauren Bernal
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