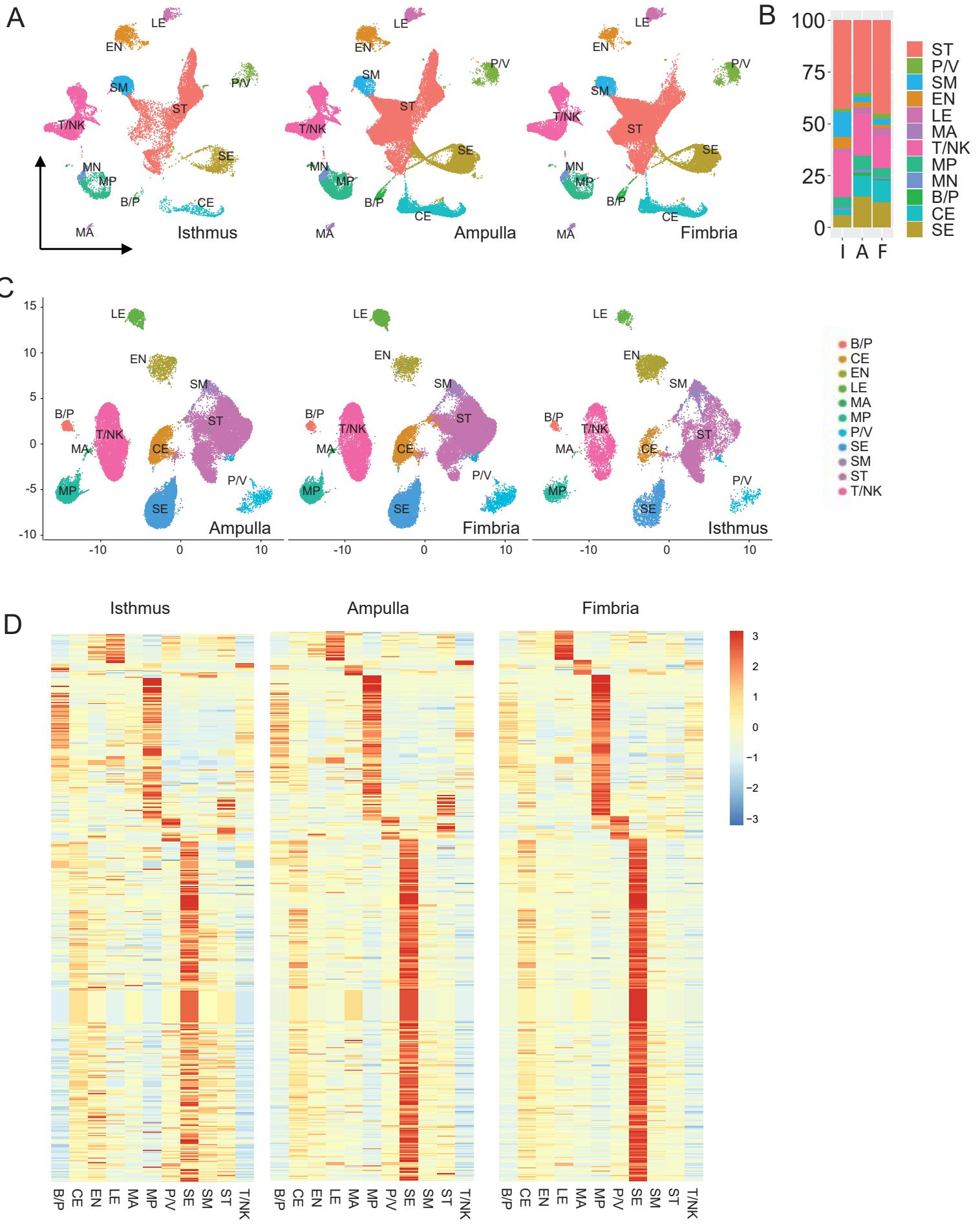


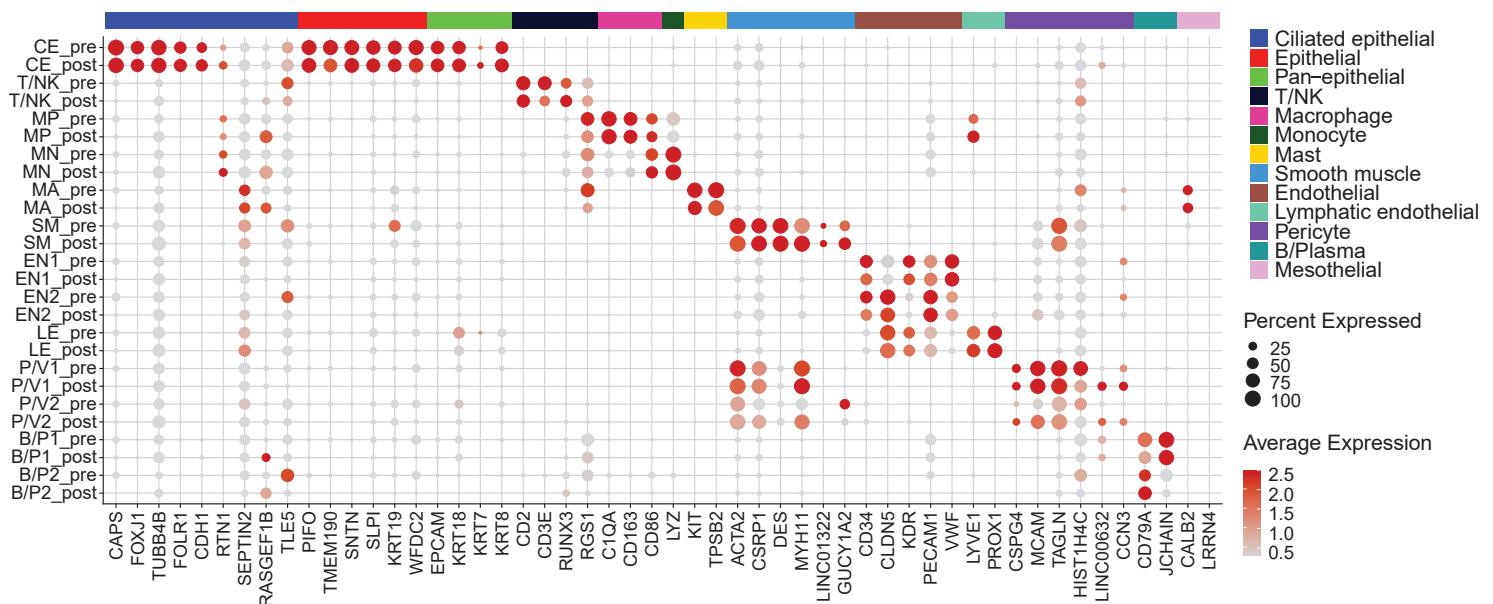
A cell atlas of the human fallopian tube throughout the menstrual cycle and menopause



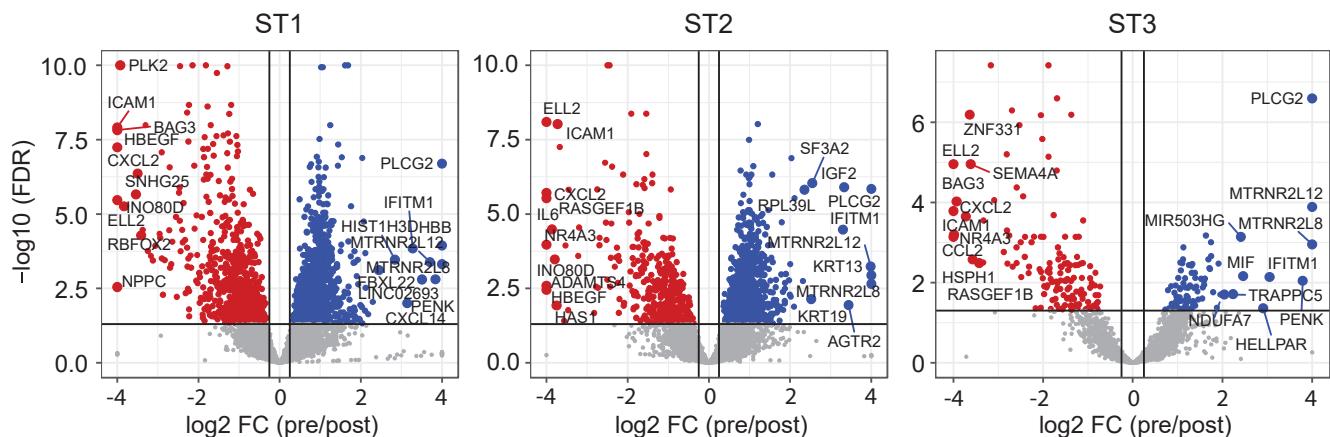
Supplementary Figure 1 (related to Figure 2): Cellular composition of normal pre-menopausal fallopian tube.

- A) Primary cell types found in the isthmus ($n = 5$), ampulla ($n = 10$), and fimbria ($n = 10$) of the normal pre-menopausal fallopian tube. The UMAP plot visualizes the 12 major cell clusters identified using scRNA-seq. Cell clusters are abbreviated as follows: SE = secretory epithelial cells; CE = ciliated epithelial cells; T/NK = T and natural killer cells; MP = macrophages; MA = mast cells; ST = stromal cells; SM = smooth muscle cells; LE = lymphatic endothelial cells; EN = endothelial cells; P/V = pericytes and vascular smooth muscle cells; B/P = B cells and plasma B cells.
- B) Relative abundance of the 12 major cell clusters identified in the pre-menopausal fallopian tube by anatomic site using scRNA-seq. The graph shows the individual percentage of each cell type for all donors combined.
- C) UMAP plot profiling of (A) identifying 11 major cell clusters in the fallopian tube by anatomical site (ampulla: $n = 5$, isthmus: $n = 3$, and fimbria: $n = 5$). The labels are transferred from scRNA-seq data and scATAC-seq specific cluster labels are added.
- D) Heatmaps based on scATAC-seq data. Transcription factor activity by cell type in the different fallopian tube anatomical regions. Heatmap includes all 869 motifs available in the cisBP database.

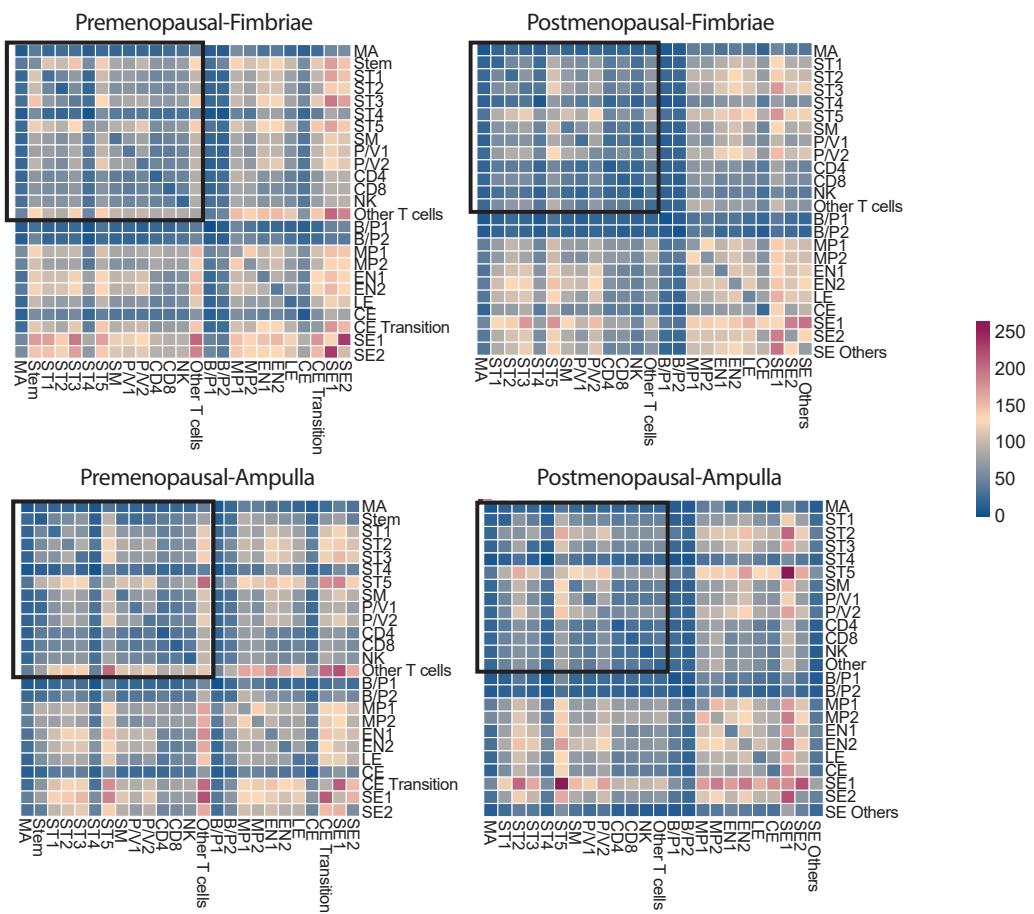
A



B

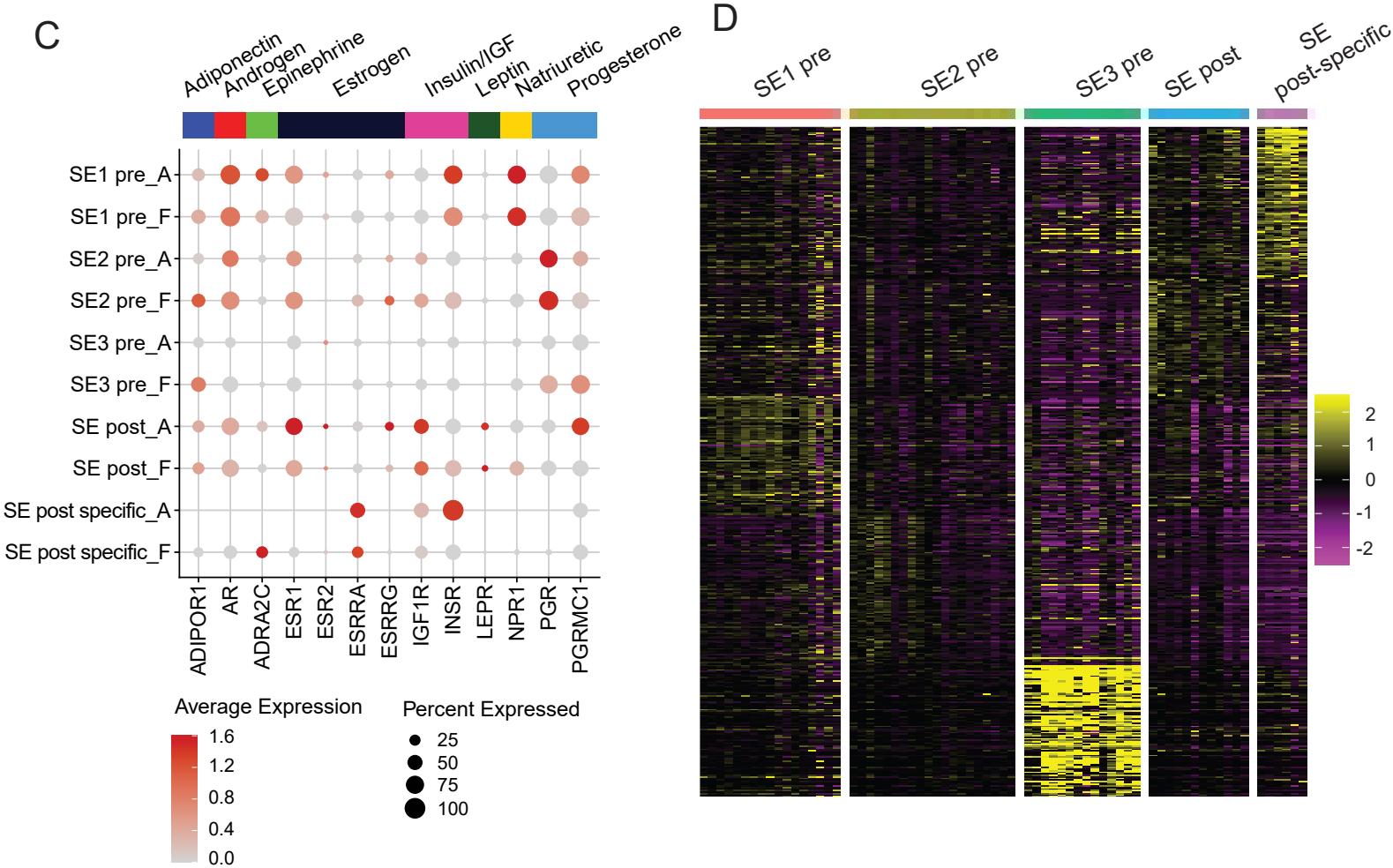
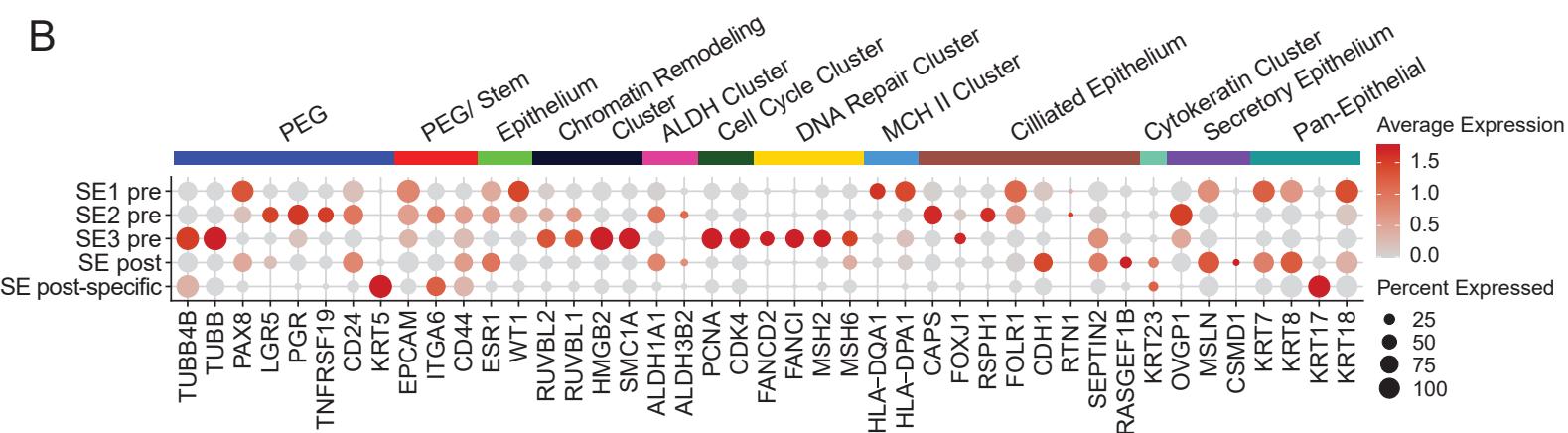
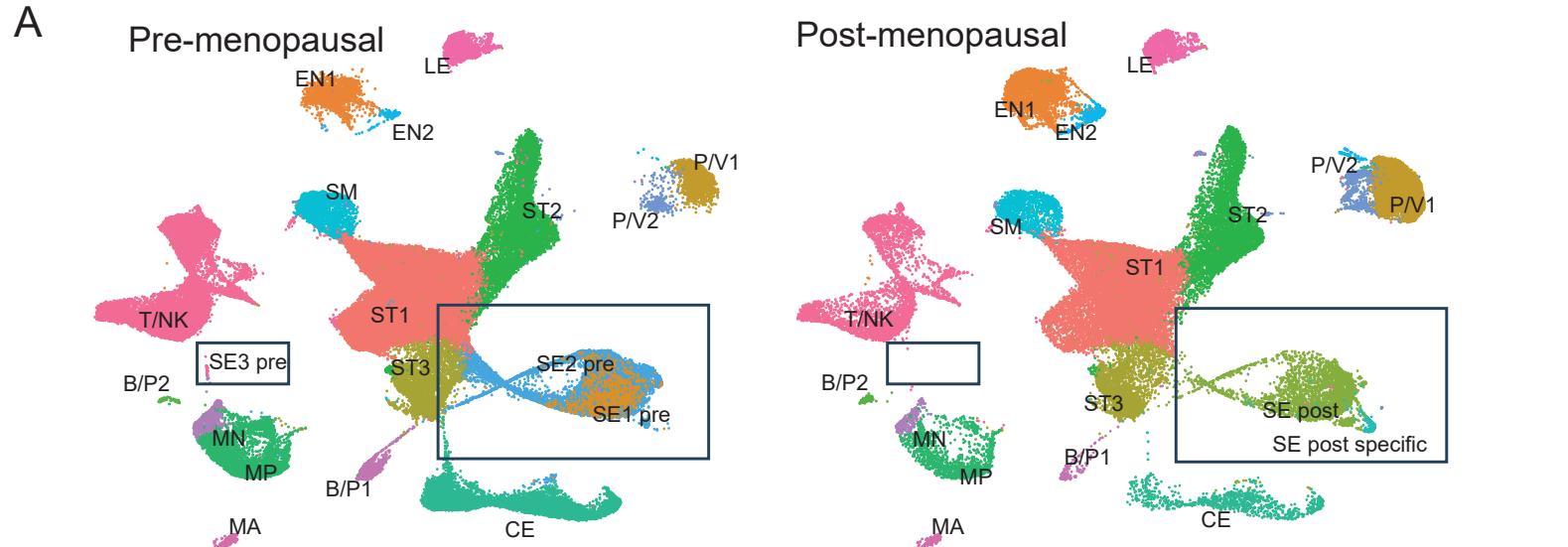


C



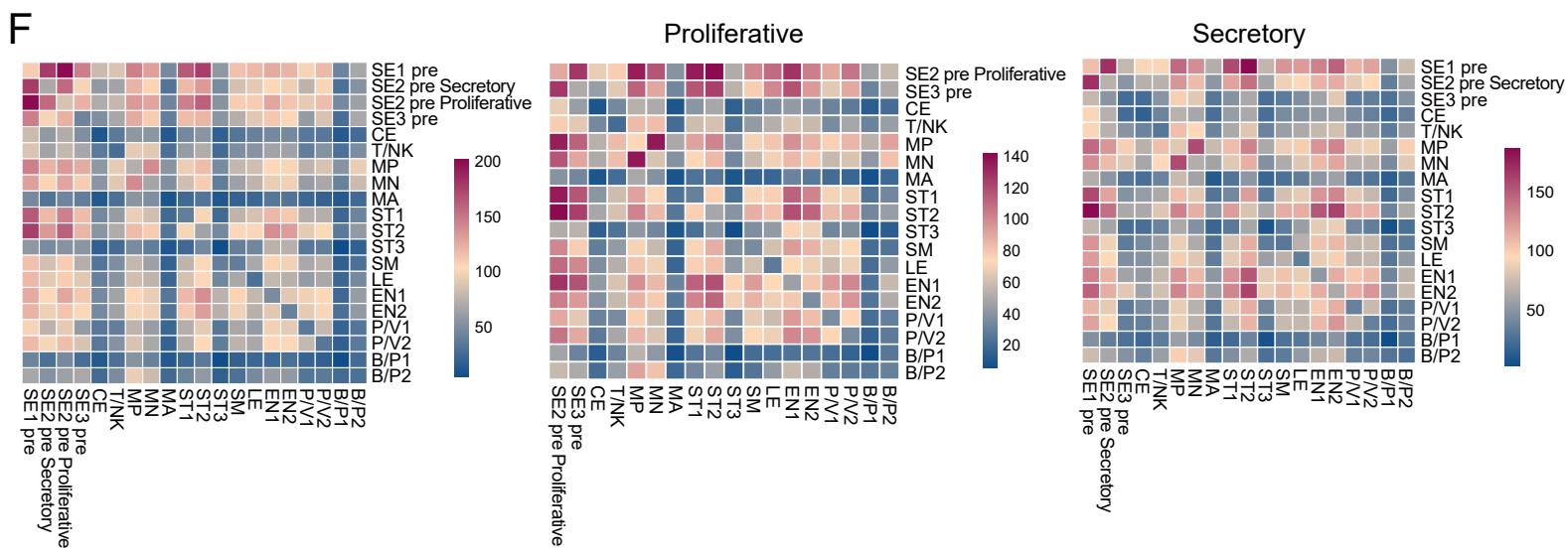
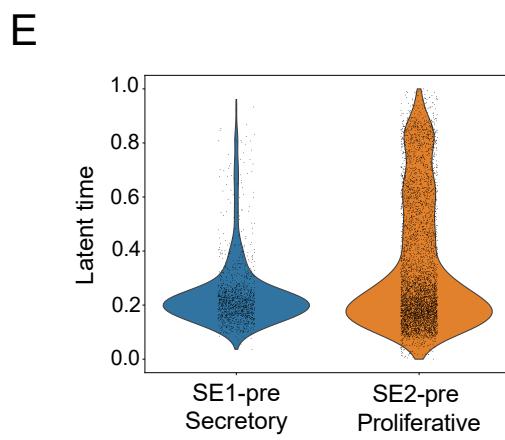
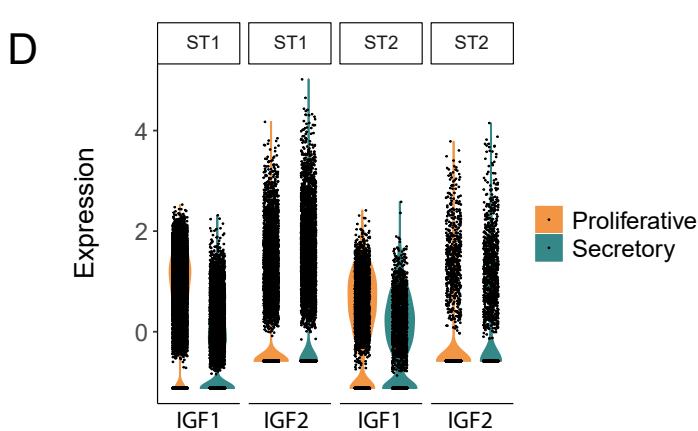
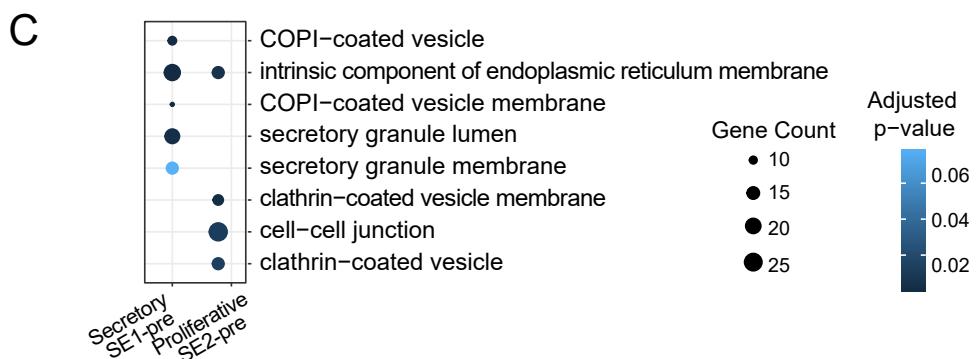
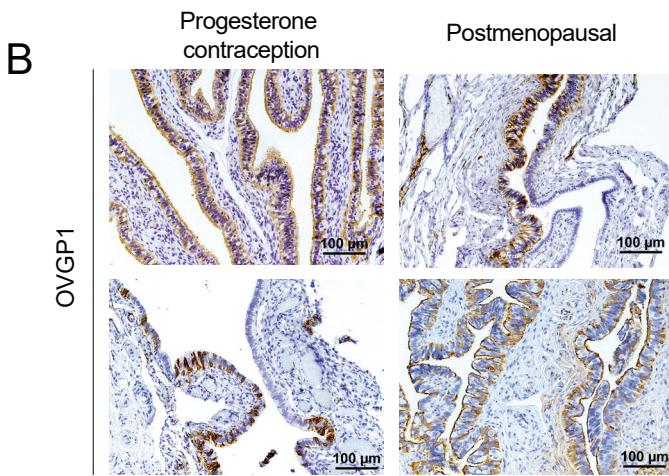
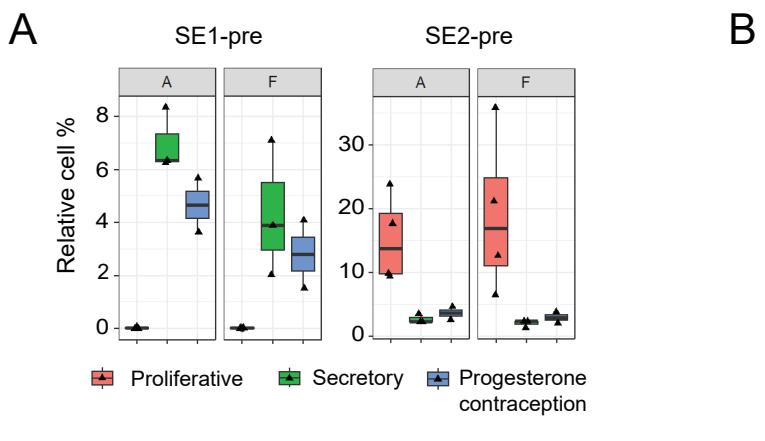
Supplementary Figure 2 (related to Figure 3): Menopause changes gene expression in fallopian tube cells.

- A) Dot plot showing combined (ampulla and fimbriae; pre-menopausal donors: n = 10; postmenopausal donors: n = 7) normalized gene expression levels of known canonical marker genes for each cell type (excluding SE cells) identified in the pre- (n = 20 sample sites) and post- (n = 12 sample sites) menopausal fallopian tube.
- B) Volcano plot derived from pseudo bulk analysis for combined anatomical sites (ampulla and fimbria). The volcano plot is showing the differential gene expression analysis of genes expressed in ST1-3 based on menopausal status. Bigger dot sizes highlight the position of genes of interest.
- C) Heatmaps showing the frequency of interactions among different cell clusters in the pre- and post-menopausal ampulla (n = 6), and fimbriae (n = 6) as imputed by CellPhoneDB from scRNA-seq.



Supplementary Figure 3 (related to Figure 4): Menopause significantly changes secretory epithelial cells.

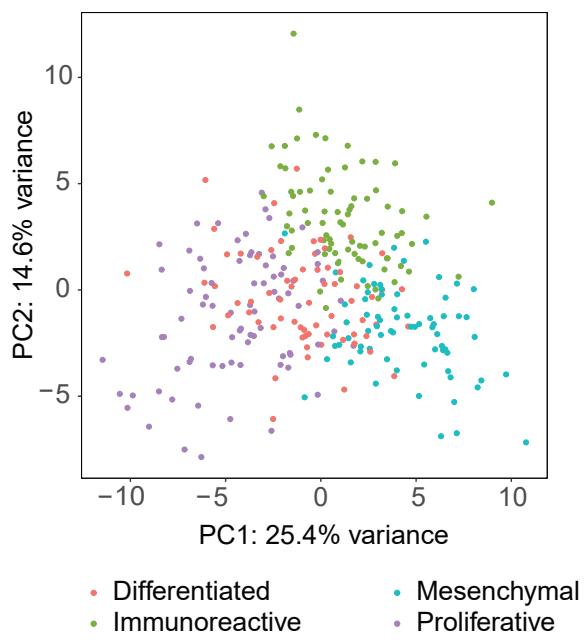
- A) UMAP plot profiling of combined (ampulla and fimbria) fallopian tube samples by menopause status based on scRNA-seq data. UMAP plot identified 19 cell clusters in the pre-menopausal fallopian tube ($n = 20$ patient samples), while 18 cell clusters were identified in the post-menopausal fallopian tube ($n = 12$ patient samples). Boxes highlight changes in SE cell-clusters specific to menopausal status. SE 1/2/3 pre are specific to pre-menopausal fallopian tubes, while “SE post-specific” cells are specific to postmenopausal women.
- B) Dot plot showing combined (ampulla and fimbriae) normalized gene expression levels of known canonical marker genes for SE subtypes identified in the pre- and post-menopausal fallopian tubes.
- C) Dot plot showing normalized hormone receptor gene expression levels in SE subtypes by anatomical site. A = ampulla, F = fimbria.
- D) Heatmap showing the average expression of TP53 consensus genes for SE subtypes at the sample level. Boxes highlight differences in consensus genes specific to SE sub-cell clusters.



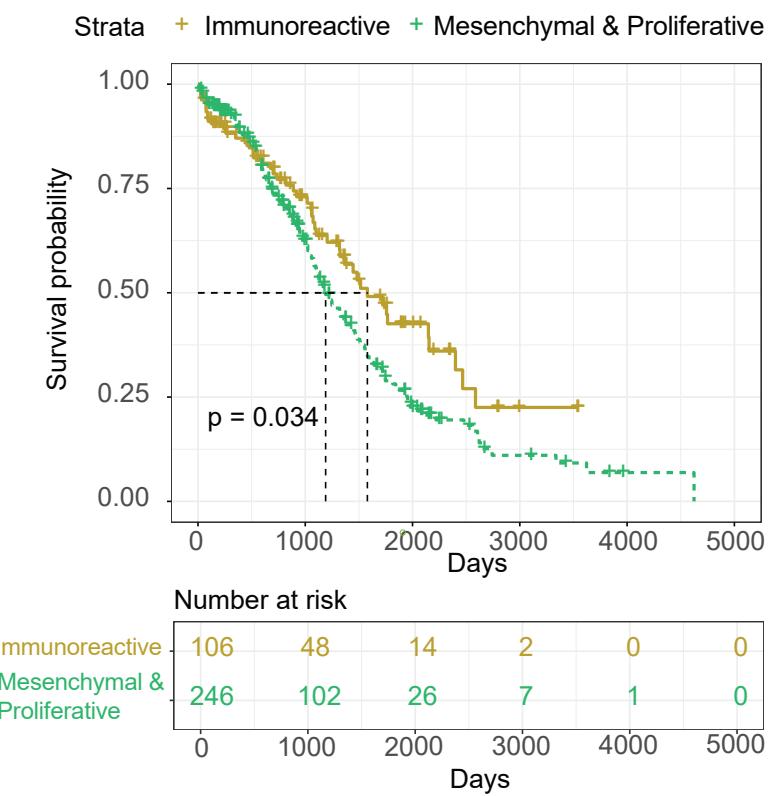
Supplementary Figure 4 (related to Figure 5): Menstrual cycle hormones regulate cellular states in secretory cells.

- A) Cellular proportion differences (in percentages) of SE1-pre and SE2-pre cells based on anatomic region and menstrual cycle phase or progesterone-based contraception in pre-menopausal women. Proliferative phase (n=4/4), secretory phase (n=3/3), progesterone-based contraception (n= 3/3) for ampulla and fimbria respectively.
- B) OVGP1 immunohistochemistry in the fallopian tube of patients on progesterone-based contraception (n = 2) or in post-menopausal women (n = 2).
- C) Dot plot showing the enrichment of selected gene ontology (GO) cellular component terms. Terms are based on differentially expressed genes identified during the proliferative and secretory phases of the menstrual cycle using scRNA-seq data (FDR-corrected p-value <0.05).
- D) Violin plots showing IGF1 and IGF2 gene expression in ST1 and ST2 cells during the proliferative- and secretory phase in pre-menopausal women.
- E) Latent time for SE 1-pre and SE2-pre cells.
- F) Heatmap showing the number of interactions detected by *CellPhoneDB* (ampulla and fimbria combined) among different cell clusters in the fallopian tube by menstrual cycle phase.

A



B



Supplementary Figure 5 (related to Figure 6): Secretory epithelial cell markers can subtype ovarian cancer.

- A) Principal component analysis plot for TCGA samples ($n = 304$) for all four HGSC molecular subtypes (proliferative, mesenchymal, differentiated and immunoreactive) using 186 identified SE-cell markers (SE3; $n = 50$ genes, and SE post-menopausal; $n = 136$ genes).
- B) Survival plot for the immunoreactive molecular subtype against proliferative and mesenchymal subtypes combined.

Supplementary Table 1 (related to Figure 1): Patient cohort.

Patient ID	Age range (years)	Ethnicity	MP age (years)	History of gynecology associated infections ^e	BMI	RNA-seq	ATAC-seq	Visium	Menstrual cycle
D1	70-75	European decent	51	No	27.58	^a A, F, I,	-	-	Postmenopausal
D2	70-75	European decent	52	No	28.47	^a A, I,	-	-	Postmenopausal
D3	60-65	European decent	56	No	31.48	A, F, I,	A, F, I,	-	Postmenopausal
D4	50-55	European decent	53	No	21.45	F, I	F, I	-	Postmenopausal
D5	60-65	Asian	50	No	22.73	A, F, I,	A, F, I,	-	Postmenopausal
D6	60-65	Hispanic	51	No	26.74	A, F, I	A, F, I	-	Postmenopausal
D7	60-65	European decent	52	No	31.31	A, F,	-	-	Postmenopausal
D9	45-50	African American	N/A	Yes	26.67	A, F	-	-	Secretory
D10	40-45	African American	N/A	Yes	53.34	A, F	-	-	Proliferative
D11	35-40	African American	N/A	No	29.27	A, F	-	-	Unknown/ Inactive endometrium ^b
D12	40-45	European decent	N/A	No	28.03	A, F, I	-	-	Unknown/ Inactive endometrium ^c
D13	35-40	European decent	N/A	No	26.41	A, F, I	-	-	Proliferative
D14	30-35	African American	N/A	Yes	32.33	A, F	A, F	-	Proliferative
D15	40-45	African American	N/A	Yes	19.55	A, F	A, F	-	Proliferative
D16	45-50	African American	N/A	Yes	33.11	A, F, I	A, F, I	-	Unknown/ Inactive endometrium ^b
D17	40-45	African American	N/A	No	41.01	A, F, I	A, F, I	-	Secretory
D18	40-45	African American	N/A	No	28.62	A, F, I	A, F, I	-	Secretory
D19	45-50	European decent	N/A	No	26.18	-	-	F	Unknown/ Inactive endometrium ^d

^aDrop-seq data, ^b Depo-Provera, ^c Intra uterine device, ^dProgestin-based, ^eAll infections were previous human papilloma virus infections

All patients were non-smokers.

Abbreviations: donor (D), ampulla (A), isthmus (I), fimbria (F), ovary (O), Menopausal age (MP), Not applicable (N/A).