

Figure S1. Generation and validation of mice with conditional deletion of *Ezh2* and *Pten*. **(A)** Analysis of DNA recombination of *Ezh2* and *Pten* alleles in the uteri of *Pten^{ff/ff}* (Ctrl), *Pten^{d/d/d}*, and *Pten^{d/d/d}; Ezh2^{d/d/d}* mice at 2 weeks of age. *n* = 3. **(B-M)** Immunostaining of EZH2 (B-D), PTEN (E-G), pAKT (H-J), and H3K27me3 (K-M) using uteri from 2-week-old *Pten^{ff/ff}* (Ctrl), *Pten^{d/d/d}*, and *Pten^{d/d/d}; Ezh2^{d/d/d}* mice. At least three independent samples were examined for each genotype. Scale bar = 20 μ m (B-M). **(N)** Western blot analysis of H3K27me3 in the uteri from 2-week-old *Pten^{ff/ff}*, *Pten^{ff/ff}; Ezh2^{ff/ff}*, *Pten^{d/d/d}*, and *Pten^{d/d/d}; Ezh2^{d/d/d}* mice. Histone H3 was used as an internal control. **(O)** Quantification of western blot. Data were normalized to the control group (100%). *n* = 4. **P* < 0.05 and ***P* < 0.01. ns, not significant.

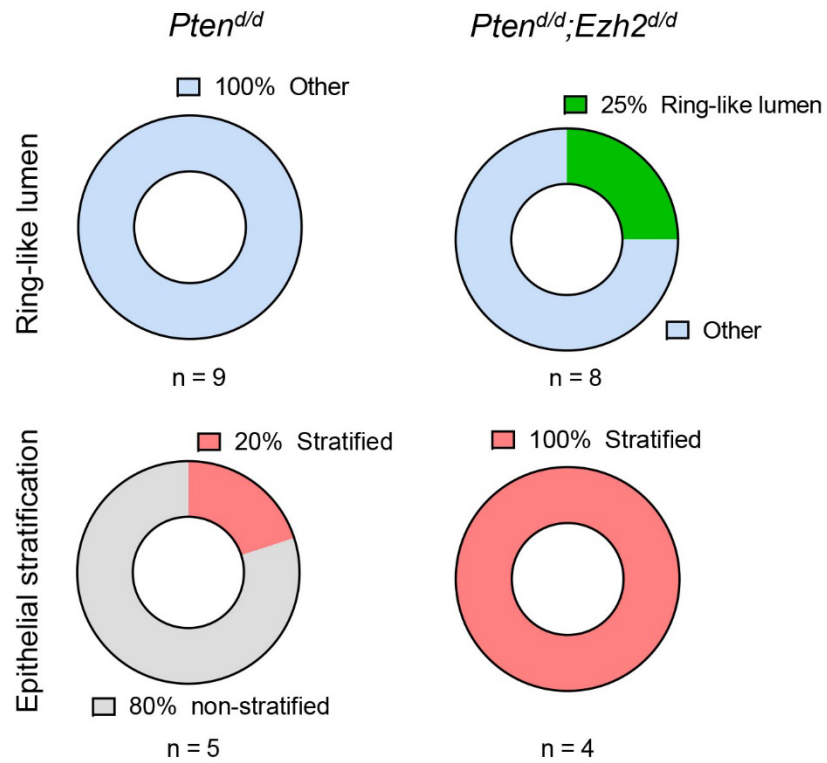


Figure S2. A summary of uterine histological features in *Pten*^{d/d} and *Pten*^{d/d}; *Ezh2*^{d/d} mice at 1 month of age. The percentage of mice is used for the pie chart.

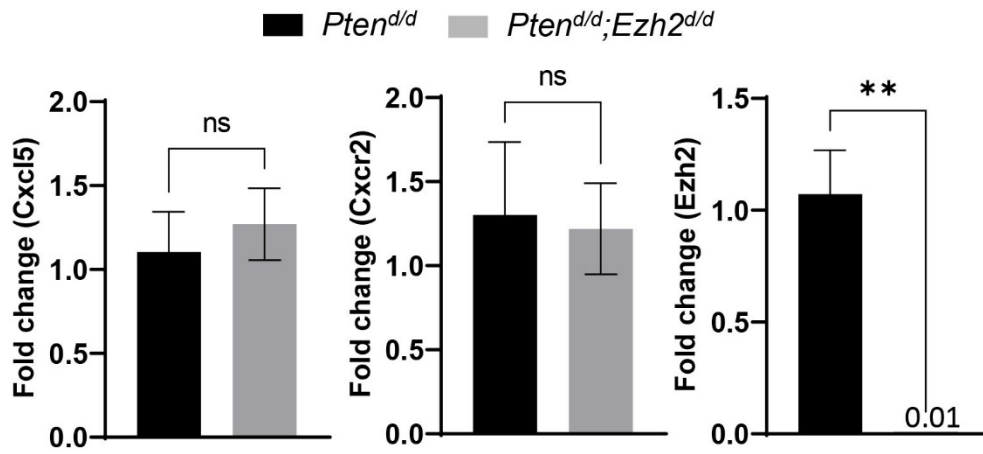


Figure S3. Levels of *Cxcl5*, *Cxcr2*, and *Ezh2* transcripts in uterine epithelial cells isolated from *Pten*^{d/d} and *Pten*^{d/d};*Ezh2*^{d/d} mice. Data are mean \pm s.e.m. $n = 4-5$. ** $P < 0.01$. ns, not significant.

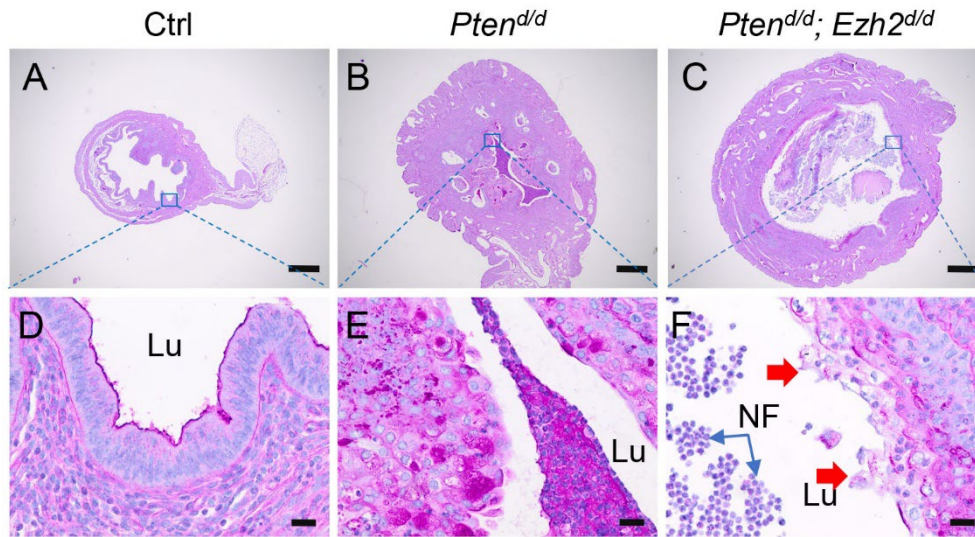


Figure S4. Intraluminal neutrophil infiltration in the uteri of *Pten*^{d/d} and *Pten*^{d/d}; *Ezh2*^{d/d} mice. (A-F) PAS staining of uteri from 9-week-old Ctrl, *Pten*^{d/d}, and *Pten*^{d/d}; *Ezh2*^{d/d} mice. Panels (D-F) are high power images of the boxed areas of panels (A-C), respectively. At least three independent samples were examined for each genotype. Red arrows indicate the sloughing epithelia. Lu, lumen. NF, neutrophils. Scale bar = 20 μ m (D-F) and 500 μ m (A-C).

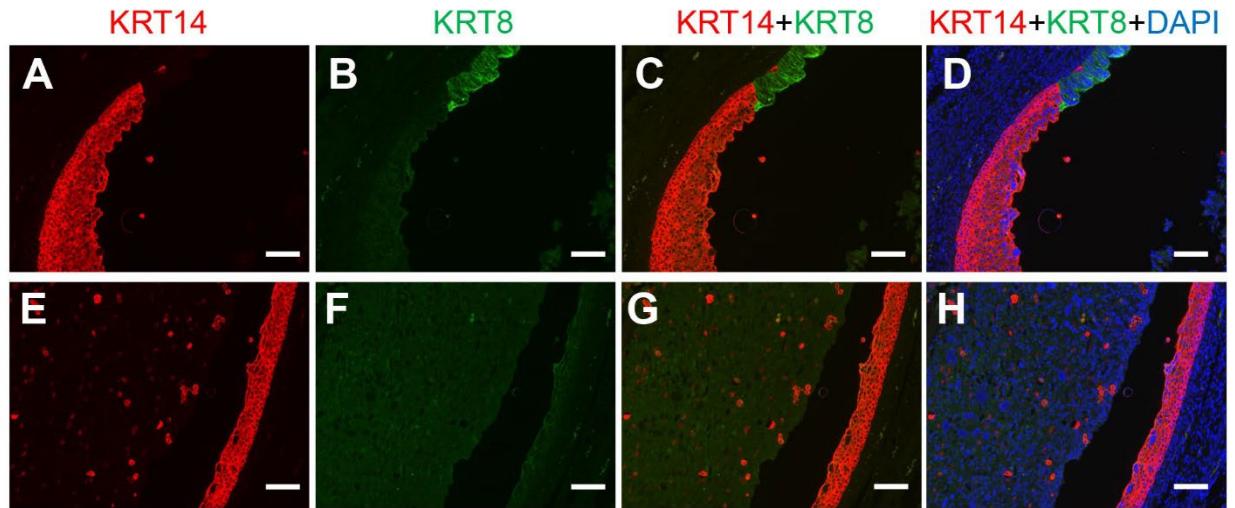


Figure S5. Immunofluorescence of KRT14 and KRT8 using uteri from 1-month-old *Pten*^{d/d}; *Ezh2*^{d/d} mice. DAPI was used to counterstain the nuclei. Scale bar = 100 μ m.

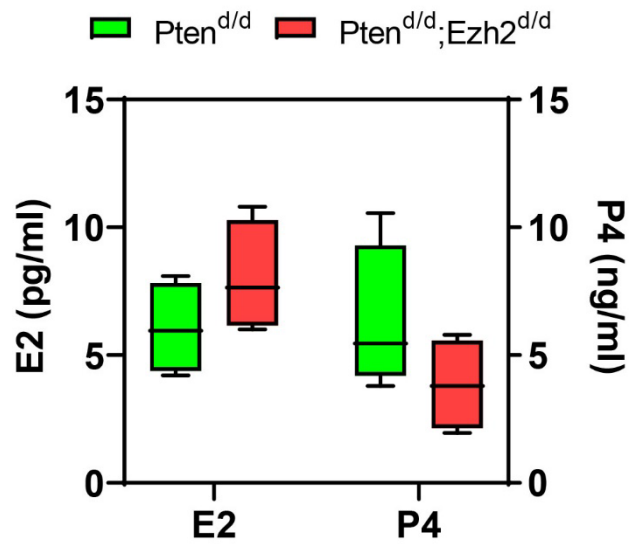


Figure S6. Serum estrogen and progesterone levels in *Pten*^{d/d} and *Pten*^{d/d};*Ezh2*^{d/d} mice. Sera were collected from mice at the age of 9 weeks. n = 4.