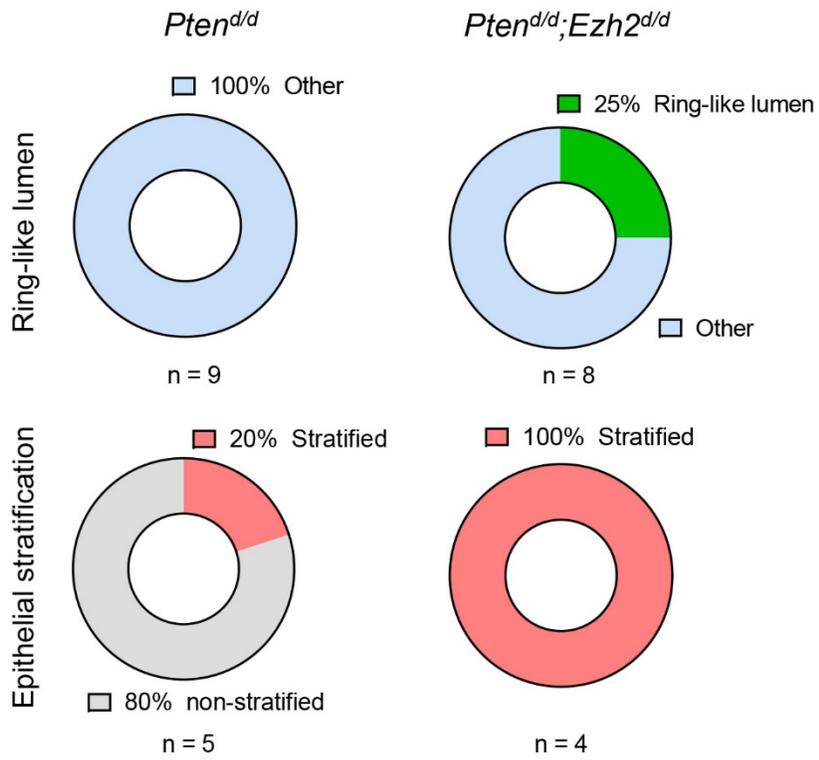
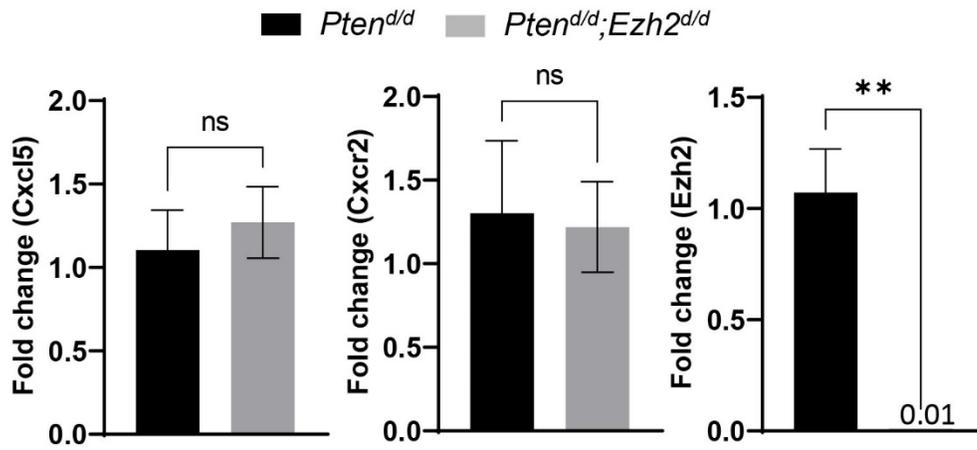


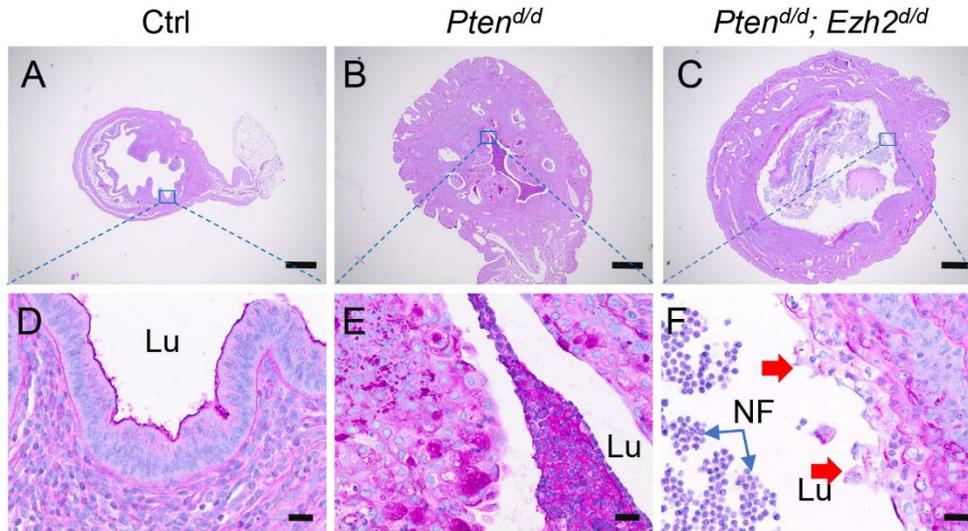
**Figure S1.** Generation and validation of mice with conditional deletion of *Ezh2* and *Pten*. **(A)** Analysis of DNA recombination of *Ezh2* and *Pten* alleles in the uteri of *Pten<sup>ff/ff</sup>* (Ctrl), *Pten<sup>d/d</sup>*, and *Pten<sup>d/d</sup>; Ezh2<sup>d/d</sup>* mice at 2 weeks of age. 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<sup>ff/ff</sup>* (Ctrl), *Pten<sup>d/d</sup>*, and *Pten<sup>d/d</sup>; Ezh2<sup>d/d</sup>* mice. At least three independent samples were examined for each genotype. Scale bar = 20  $\mu$ m (B-M). **(N)** Western blot analysis of H3K27me3 in the uteri from 2-week-old *Pten<sup>ff/ff</sup>*, *Pten<sup>ff/ff</sup>; Ezh2<sup>ff/ff</sup>*, *Pten<sup>d/d</sup>*, and *Pten<sup>d/d</sup>; Ezh2<sup>d/d</sup>* 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.



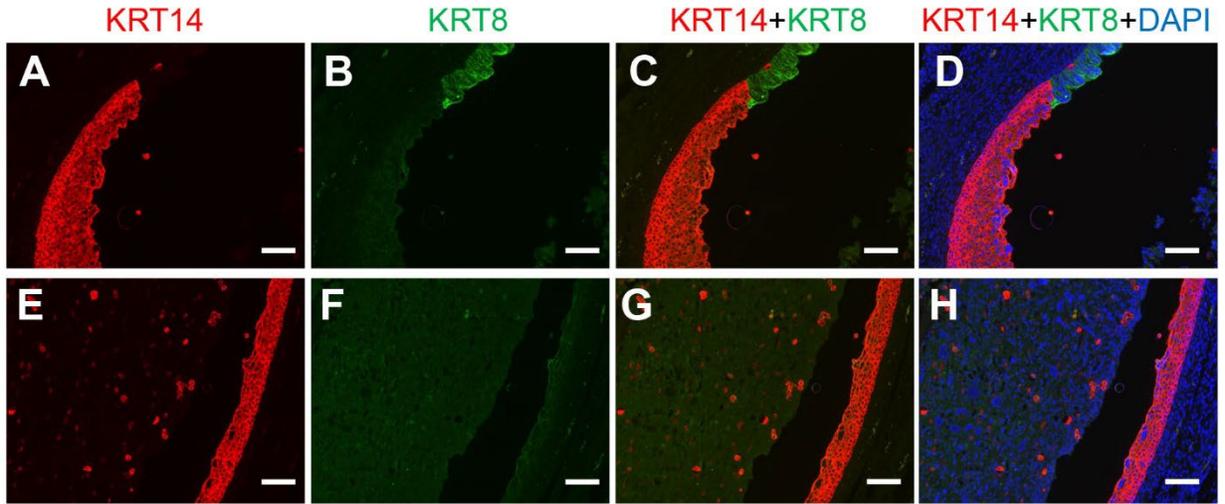
**Figure S2.** A summary of uterine histological features in *Pten*<sup>d/d</sup> and *Pten*<sup>d/d</sup>; *Ezh2*<sup>d/d</sup> mice at 1 month of age. The percentage of mice is used for the pie chart.



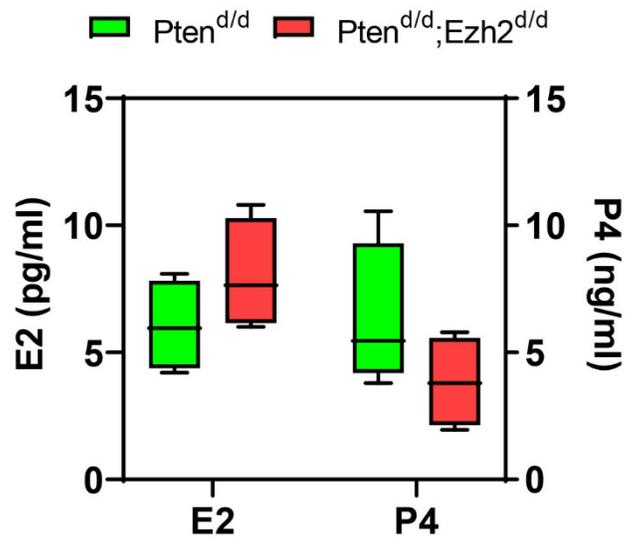
**Figure S3.** Levels of *Cxcl5*, *Cxcr2*, and *Ezh2* transcripts in uterine epithelial cells isolated from *Pten*<sup>d/d</sup> and *Pten*<sup>d/d</sup>;*Ezh2*<sup>d/d</sup> mice. Data are mean  $\pm$  s.e.m. n = 4-5. \*\**P* < 0.01. ns, not significant.



**Figure S4.** Intraluminal neutrophil infiltration in the uteri of *Pten*<sup>d/d</sup> and *Pten*<sup>d/d</sup>; *Ezh2*<sup>d/d</sup> mice. (A-F) PAS staining of uteri from 9-week-old Ctrl, *Pten*<sup>d/d</sup>, and *Pten*<sup>d/d</sup>; *Ezh2*<sup>d/d</sup> 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  $\mu$ m (D-F) and 500  $\mu$ m (A-C).



**Figure S5.** Immunofluorescence of KRT14 and KRT8 using uteri from 1-month-old *Pten<sup>d/d</sup>; Ezh2<sup>d/d</sup>* mice. DAPI was used to counterstain the nuclei. Scale bar = 100  $\mu$ 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.