**Supplemental Materials and Methods**

**Histopathological analyses**

All histopathological analyses were carried out blindly before matching histology numbers to mice genotypes. Criteria for histopathological studies were the thickness of basal-like epithelial cell layer, presence of nuclear atypia with the enlarged nucleus, and stroma invasion as described previously (5). When multiple stages of neoplastic diseases were present, the worst grade of disease was assigned to each mouse.

**Image acquisition and analysis**

Nikon NIS-Elements imaging software (v5.2) was used to obtain images with an Eclipse Ti2 microscope (Nikon Instruments Inc., Melville, NY) equipped with a Nikon DS-Qi2 monochrome and a DS-Ri2 color camera. The microscope was also equipped with calibrated objective lenses. A histology slide with the largest cross-section was used to measure the size of each tumor. Sizes of all cancers in each mouse were summed for total cancer area. An analysis package in Nikon NIS-Elements imaging software (v5.2) was used to calculate cancer size. For the quantification of proliferative and apoptotic cells, approximately 400-600 cells per cancer were analyzed using the NIH ImageJ software.

**Clinical data and statistical analyses**

MSTAT software (version 6.4.2; oncology.wisc.edu/mstat) was used to carry out Wilcoxon rank-sum test for cancer size and Fisher’s exact test for cancer incidence in mice. The Gene Expression Profiling Interactive Analysis (gepia) server (<http://gepia.cancer-pku.cn/>) was used for comparison of *PGR* and *ESR1* mRNA expression levels. For calculation of the mean gene expression and survival and correlation analysis, TCGAbiolinks (2.12.6) was used to import raw counts from TCGA and GTEx. They were then converted to TPM using human genome 38 gene lengths from Rsubread (1.34.7) in R (3.6.1). The ggpubr R package (0.2.5) was used for the Welch’s two-sample unpaired t-test and Pearson Correlation for *PGR* and *ESR1* expression. Survival (3.1-12) and survminer package (0.4.6) were used to fit the Cox proportional hazards model to calculate the hazard ratio and plot the Kaplan-Meier curves for the TCGA data. The Genomic Identification of Significant Targets in Cancer 2.0 (GISTIC 2.0) algorithm-thresholded copy number data were collected from TCGA-CESC primary tumors using the TCGAbiolinks, and pairwise comparisons of *PGR* expression between copy number variation groups were tested using an unpaired Welch’s two-sample t-test in ggpubr. The phi coefficient test was conducted in the DescTools(0.99.38) package in R (3.6.1). The P-value equal to or less than 0.05 was considered to be significant in all experiments.

 **Supplemental References**

1. Song S, Pitot HC, Lambert PF. The human papillomavirus type 16 E6 gene alone is sufficient to induce carcinomas in transgenic animals. J Virol **1999**;73:5887-93

2. Herber R, Liem A, Pitot H, Lambert PF. Squamous epithelial hyperplasia and carcinoma in mice transgenic for the human papillomavirus type 16 E7 oncogene. J Virol **1996**;70:1873-81

3. Winuthayanon W, Hewitt SC, Orvis GD, Behringer RR, Korach KS. Uterine epithelial estrogen receptor alpha is dispensable for proliferation but essential for complete biological and biochemical responses. Proc Natl Acad Sci U S A **2010**;107:19272-7

4. Fernandez-Valdivia R, Jeong J, Mukherjee A, Soyal SM, Li J, Ying Y*, et al.* A mouse model to dissect progesterone signaling in the female reproductive tract and mammary gland. Genesis **2010**;48:106-13

5. Riley RR, Duensing S, Brake T, Munger K, Lambert PF, Arbeit JM. Dissection of human papillomavirus E6 and E7 function in transgenic mouse models of cervical carcinogenesis. Cancer Res **2003**;63:4862-71

**Supplemental Figure Legends**

**Supplemental Figure 1. (A)** Shown are representative images of H&E stained cervical cancer sections. Note that all cancers are well–differentiated. Scale bar, 50 μm. (**B**) The normal epithelium and CIN lesions adjacent to cancers are shown. CIN, cervical intraepithelial neoplasia. Scale bar, 50 μm.

**Supplemental Figure 2. The PR status does not change the expression of cervical cancer biomarkers.** **(A-B)** At least three PR–negative and PR–positive cervical cancers in each genotype were stained for p16Ink4a (**A**) and Mcm7 (**B**). Nuclei are pseudocolored red. The only cancer in the *NTG/Cre/Pgrf/+* genotype was used as a negative control. Dotted lines separate cancer from surrounding stroma. Scale bar, 50 μm.

**Supplemental Figure 3. PR-negative cancers are larger than PR-positive cancers in *E6/E7* mice. (A)** Individual cancer areas and total invasion area in each mouse are shown in box**–**and**–**whisker plots. The group sizes for individual cancer areas were as the following: PR– (n=8) and PR+ cancer (n=5) in *Pgrf/+*, PR– (n=15) and PR+ cancer (n=3) in *Cre/Pgrf/+*, and PR– cancer (n=20) in *Cre/Pgrf/f*. Those for total invasion area were PR– (n=5) and PR+ cancer (n=4) in *Pgrf/+*, PR– (n=8) and PR+ cancer (n=2) in *Cre/Pgrf/+*, and PR– cancer (n=11) in *Cre/Pgrf/f*. **(B)** Cancer size data shown in (**A**) was pooled and divided into PR**–** and PR+ cancer. \*P = 0.05.

**Supplemental Figure 4. (A)** *ESR1* is downregulated in cervical cancer. *ESR1* transcript levels were compared between cervical cancer (n = 306) and normal cervical tissues (n = 13). \*P = 1.7 x 10-10 (Welch’s *t*-test). **(B)** Heterozygous deletion of *PGR* is common in cervical cancer. Copy number variation data is shown in a pie chart (n=292). Each patient was categorized into homozygous deletion (n=5), heterozygous deletion (n=108), normal (n=138), gain (low-level amplification, n=18), or amplification (high-level amplification, n=23). Note that 98.4% of cancers retained at least one *PGR* allele.