### Supplementary table 1. General characteristics of the clinical sample

| Patient No. | Age (year) | Initial pathological Diagnosis | Treatment | Pathological diagnosis and efficacy during treatment every 3 months |
|-------------|------------|--------------------------------|-----------|------------------------------------------------------------------|
|             |            |                                |           | After 3 months                                                   | After 6 months                        | After 9 months                        |
|             |            |                                | Diagnosis | Treatment result | Diagnosis | Treatment result | Diagnosis | Treatment result |
| Case 1#     | 28         | EEC                            | MA        | EAH | PR | secretory reaction | CR | secretory reaction | CR | sensitive |
| Case 2      | 29         | EEC                            | MA        | secretory reaction | CR | secretory reaction | CR | secretory reaction | CR | sensitive |
| Case 3      | 31         | EEC                            | MA        | secretory reaction | CR | secretory reaction | CR | / | / | sensitive |
| Case 4      | 34         | EEC                            | MA+LNG-IUS| proliferation reaction | CR | proliferation reaction | CR | / | / | sensitive |
| Case 5      | 32         | EEC                            | MA+LNG-IUS| EAH | PR | secretory reaction | CR | secretory reaction | CR | sensitive |
| Case 6      | 30         | EEC                            | MA        | EEC | NR | EAH | PR | EAH | PR | insensitive |
| Case 7      | 38         | EEC                            | MA+LNG-IUS| EAH | PR | EAH | PR | EAH + morular metaplasia | PR | insensitive |
| Case 8      | 26         | EEC                            | MA        | EAH | PR | CH | PR | EAH | PR | insensitive |
| Case 9#     | 20         | EEC                            | MA        | EEC | NR | EAH | PR | EEC | NR | insensitive |

EAH, endometrial atypical hyperplasia; EEC, endometrioid endometrial carcinoma; CH, complex hyperplasia; PR, partial response; CR, complete response; NR, no response; MA, megestrol acetate; LNG-IUS, levonorgestrel intrauterine system. #, Representative pathological pictures of the two patients during treatment were shown in Figure 1A.
| Case | Age | Pathological Diagnosis | Endometrial cycle | Height (m) | Weight (Kg) | BMI (kg/m²) | Fertility |
|------|-----|------------------------|-------------------|------------|-------------|-------------|-----------|
| 1    | 50  | Uterine leiomyoma      | Secretory phase   | 1.65       | 68          | 24.977      | G2P1      |
| 2    | 48  | Uterine leiomyoma      | Proliferative phase | 1.63       | 57          | 21.454      | G3P2      |
| 3    | 48  | Uterine leiomyoma      | Proliferative phase | 1.6        | 73          | 28.516      | G4P2      |
| 4    | 34  | Cervical high-grade squamous intraepithelial lesion | Proliferative phase | 1.65       | 60          | 22.039      | G3P1      |
| 5    | 50  | Cervical invasive squamous cell carcinoma | Secretory phase | 1.6        | 55          | 21.484      | G4P3      |
| 6    | 48  | Uterine leiomyoma      | Secretory phase   | 1.57       | 53          | 21.502      | G2P1      |
| 7    | 30  | Uterine leiomyoma      | Proliferative phase | 1.72       | 58.6        | 19.808      | G0P0      |
| 8    | 51  | Uterine leiomyoma      | Proliferative phase | 1.55       | 52          | 21.644      | G3P1      |
| 9    | 50  | Cervical invasive squamous cell carcinoma | Secretory phase | 1.7        | 50          | 17.301      | G2P1      |
| 10   | 45  | Cervical invasive squamous cell carcinoma | Proliferative phase | 1.6        | 54          | 21.094      | G4P3      |
| 11   | 45  | Uterine leiomyoma      | Proliferative phase | 1.55       | 45          | 18.73       | G4P1      |
| 12   | 46  | Uterine leiomyoma      | Proliferative phase | 1.63       | 77          | 28.981      | G1P1      |
| 13   | 45  | Cervical high-grade squamous intraepithelial lesion | Proliferative phase | 1.61       | 72          | 27.777      | G2P1      |
|   |   |   |   |   |
|---|---|---|---|---|
| 14 | 40 | Uterine leiomyoma | Proliferative phase | 1.65 | 58.4 | 21.451 | G1P1 |
| 15 | 45 | Uterine leiomyoma | Secretory phase | 1.56 | 50 | 20.546 | G2P2 |
| 16 | 41 | Cervical invasive squamous cell carcinoma | Secretory phase | 1.63 | 59.3 | 22.319 | G4P1 |
| 17 | 42 | Cervical invasive squamous cell carcinoma | Proliferative phase | 1.62 | 51 | 19.433 | G3P1 |
| 18 | 36 | Cervical invasive squamous cell carcinoma | Proliferative phase | 1.63 | 66 | 24.841 | G3P1 |
| 19 | 48 | Uterine leiomyoma | Secretory phase | 1.5 | 52 | 23.111 | G6P2 |
| 20 | 45 | Uterine leiomyoma | Secretory phase | 1.65 | 58 | 21.304 | G2P1 |
| 21 | 47 | Cervical high-grade squamous intraepithelial lesion | Proliferative phase | 1.58 | 75.4 | 30.203 | G5P1 |
| 22 | 42 | Cervical squamous cell carcinoma in situ | Secretory phase | 1.59 | 54.7 | 21.637 | G3P1 |
| 23 | 36 | Uterine leiomyoma | Proliferative phase | 1.48 | 46 | 21.001 | G3P2 |
| 24 | 38 | Cervical high-grade squamous intraepithelial lesion | Proliferative phase | 1.64 | 58.3 | 21.676 | G1P1 |
| 25 | 29 | Uterine leiomyoma | Proliferative phase | 1.58 | 52 | 20.83 | G1P0 |
| 26 | 44 | Uterine leiomyoma | Secretory phase | 1.62 | 55 | 20.957 | G3P1 |
| 27 | 45 | Cervical invasive squamous cell carcinoma | Proliferative phase | 1.61 | 72 | 27.777 | G2P1 |
| 28 | 45 | Uterine leiomyoma | Proliferative phase | 1.56 | 59 | 24.244 | G4P3 |
| Age | Menstrual Cycle | Diagnosis | Hormone Phase | Hormone Level | Pregnancy Status |
|-----|----------------|-----------|---------------|---------------|-----------------|
| 29  | 49             | Cervical high-grade squamous intraepithelial lesion | Secretory phase | 1.64 | 65 | 24.167 | G3P1 |
| 30  | 37             | Cervical high-grade squamous intraepithelial lesion | Secretory phase | 1.6 | 58 | 22.656 | G1P1 |
### Supplementary table 3. Comparison of basic patient information between Proliferative phase and Secretory phase

|                           | Proliferative phase (n=18) | Secretory phase (n=12) | P value |
|---------------------------|-----------------------------|------------------------|---------|
| Median age (years)        | 45 (29-51)                  | 46.5 (37-50)           | P = 0.0632 |
| BMI (Kg/m2)               | 23.42 ± 3.665               | 21.83 ± 1.940          | P = 0.1811 |
| Uterine leiomyoma         | 10                          | 6                      | P > 0.99 |
| Cervical cancer/HSIL      | 8                           | 6                      |         |

### Supplementary table 4. Target sequences used for gene silencing

| Gene   | Sequence                        |
|--------|---------------------------------|
| siPGR  | GCTTCAAGTTAGCCAAGAA             |
| siNrCAM-1 | GGAGCATGGTGTCCTTTGA         |
| siNrCAM-2 | GAAGGAGTCTATCAGTGTA         |
| siNrCAM-3 | GCAGATCATTCTAGTTTCA         |
| siTET1 | GCTCAACGAGGTCCATTA             |
| Genes    | Primer sequence          |
|----------|-------------------------|
| GAPDH    | 5'-AAGATGTGCCTGTCTGTGTC-3' |
|          | 5'-GCTTTGCTCTGCTTTCTGTCTC-3' |
| PGR      | 5'-TCTACCCGCCCCTATCTCAACTA-3' |
|          | 5'-AGAAGACCTTACAGCTCCCAAC-3' |
| TET1     | 5'-ACCCCCTGTACCTGCTGAGG-3' |
|          | 5'-GCGATGCGCCACCCACCAAT-3' |
| NrCAM    | 5'-AGTGTGTGAGTCTCAGCAGG-3' |
|          | 5'-TGTTGGGTAGTGTTGAGG-3' |
| HAND2    | 5'-CCTCTTCGTCGCTTC-3' |
|          | 5'-AAGATCAAGACACTGCACCT-3' |
| IRF4     | 5'-CGGCTGCGCTTTGAACAA-3' |
|          | 5'-ACACCTTGAGCCGTGAGA-3' |
| NR2F2    | 5'-CGGCTGCGCTTTATG-3' |
|          | 5'-ACAGGCATCTGAGTGGAAC-3' |
| RGCC     | 5'-ACAGACCTCTACCCACGCTT-3' |
|          | 5'-AGAAAGGTGAGTGACGTTT-3' |
| CDH20    | 5'-CAGCACTGTCCCACAGCTAC-3' |
|          | 5'-TATTGCTCGTGTTGGAGG-3' |
| MTIG     | 5'-CTTCTCAGCTTGGA-3' |
|          | 5'-AGGGGTCAAGATTGTAGCAAA-3' |
| SLC28A1  | 5'-CGCCGCAGATGTGCGTAT-3' |
|          | 5'-CCAGTGAAATTTGCCCTTGCC-3' |
| HSD11B1  | 5'-CGAAATCTTGGAGTTCTCTG-3' |
|          | 5'-AAGCTCCAGGCAAGCTGGATA-3' |
| ANGPTL4  | 5'-GCTTCCGCTTCTGCTG-3' |
|          | 5'-AACAGCGCGCTCGAGAAG-3' |
| TRABD2B  | 5'-GGAGATTGACAGCTCTCCG-3' |
|          | 5'-CAGAAAGTGACCTGCTCAGGAA-3' |
| ERVMER34-1| 5'-AGCGGGAGAAAATACCCCAAC-3' |
| Gene  | Forward Sequence | Reverse Sequence |
|-------|-----------------|-----------------|
| WISP1 | 5'-CTACAACAACGGCCAGTCCT-3' | 5'-ACATACCCACTGCTCACAGC-3' |
| CPM   | 5'-GCGCTGGATTTCAACTACCAC-3' | 5'-TCCCGCCCAACAGTCTCAT-3' |
| ITGA10| 5'-AACATACCCACGCTATTCC-3'  | 5'-GTTGTTAGTCACCTAAGTGGC-3' |
### Supplementary table 6. PRB promoter fragment primers used for Hmedip

| Gene | Primer sequence                     |
|------|-------------------------------------|
| PGR1 | Forward: 5’-CAGCCAGAGCCCACAATACA -3’<br>Reverse: 5’- GTTGTGCTGCCCTCCATTG -3’ |
| PGR2 | Forward: 5’- CTTCCCTCGGCCCTGCCAGG -3’<br>Reverse: 5’- AGGGCGCAACAGAGTGTCC -3’ |
| PGR3 | Forward: 5’- ACCCCCTGTCACCTGCTGAGG -3’<br>Reverse: 5’- GGCTTACCCCGATTAGTGAC-3’ |