# Supplementary data

## Materials and methods

### RNA extraction from endometrial tissue

Endometrial biopsies were obtained by Pipelle catheter (Laboratoire CCD, Paris, France) during laparoscopic surgery, immediately placed into RNAlater (Ambion, USA) and after 24-hour incubation at 4˚C stored at -80˚C until use. Endometrial RNA was extracted using miRNeasy Mini kit (Qiagen) according to the manufacturer's protocol. DNase I treatment was performed on column using RNase-Free DNase Set (Qiagen). Purified RNA quality (RIN) was assigned with Cubit IQ assay (ThermoFisher Scientific). The paired endometrial biopsies of healthy women were obtained and processed as described in [1]. Urinary luteinizing hormone (LH) test was used to determine the day of the LH surge (LH+0). The first of the paired samples was collected one to three days after the LH surge (LH+1/+3), while the second biopsy was performed on days LH+7 to +9 in the same menstrual cycle.

### Gene expression profiling

Fifty-seven endometrial receptivity genes [2] together with four housekeeping genes (*SDHA, CYC1, TBP* and *HMBS*) were assessed by TAC-seq methodology [3]. Briefly, mRNA was converted to cDNA, hybridized with specific oligonucleotide probes and converted to next-generation sequencing (NGS) library. The TAC-seq libraries were sequenced with Illumina NextSeq 500 high output 75 cycles kit.

### Sequencing data analysis and normalization

Raw sequencing reads were processed as described in [4]. Each sample was normalized using geometric mean of four housekeeper genes (*CYC1, HMBS, SDHA* and *TBP*) expression level

using psych (version 1.7.8) package in R (version 3.2.2). TAC-seq data was processed with open-source software (https://github.com/cchtEE/TAC-seq-data-analysis).

**Endometrial receptivity classification with support vector machine (SVM)**

RNA sequencing data from paired LH-dated endometrial samples from 27 healthy fertile women was used to create a model specifically for discrimination of ES (LH+2) and MS (LH+7) phases. Scikit-learn (version 0.19.1) implementation of the SVM was chosen for the sample classification [5]. Cross-validation accuracy assessment was performed via leave-one-out cross-validation and 2-fold cross-validation on the 53 endometrial samples. A linear kernel one-vs-rest classifier with balanced class weights was used as SVM model parameter. Analysed biopsies were classified based on the SVM predicted class with distance (score) from other classes to ES and MS.

**Supplementary table 1**. General characteristics of the study participants

| | *Endometriosis (n=45) | Without endometriosis (n=33) | Healthy women (n=27) |
|---|---|---|---|
| Age (year ± SD) | 31 ± 5 | 32 ± 5 | 30 ± 3 |
| BMI (kg/m2± SD) | 22.2 ± 3 | 23.0 ± 5 | 23.7 ± 4.5 |
| Stage I-II*, n | 25 | - | - |
| Stage III-IV*, n | 20 | - | - |
| Menstrual phase (days 1-5), n | 4 | - | - |
| Proliferative phase (days 6-14), n | 9 | 8 | - |
| Early-secretory phase (days 15-18), n | 9 | 10 | - |
| Mid-secretory phase (days 19-23), n | 10 | 9 | - |
| Late-secretory phase (days 24-28), n | 13 | 6 | - |
| LH+ 1/+3 | - | - | 27 |
| LH+7/+9 | - | - | 27 |

BMI – body mass index, LH –luteinizing hormone. *Endometriosis stage was determined according to ASRM [6].

**References**

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[2] Altmäe S, Koel M, Võsa U, Adler P, Suhorutšenko M, Laisk-Podar T, Kukushkina V, Saare M, Velthut-Meikas A, Krjutškov K, Aghajanova L, Lalitkumar PG, et al. Meta-signature of human endometrial receptivity: a meta-analysis and validation study of transcriptomic biomarkers. Sci Rep 2017; 7:10077.

[3] Teder H, Koel M, Paluoja P, Jatsenko T, Rekker K, Laisk-Podar T, Kukuškina V, Velthut-Meikas A, Fjodorova O, Peters M, Kere J, Salumets A, et al. TAC-seq: targeted DNA and RNA sequencing for precise biomarker molecule counting. Npj Genomic Med 2018; 3:34.

[4] Teder H, Koel M, Paluoja P, Jatsenko T, Rekker K, Laisk-Podar T, Kukuškina V, Velthut-Meikas A, Fjodorova O, Peters M, Kere J, Salumets A, et al. TAC-seq: targeted DNA and RNA sequencing for precise biomarker molecule counting. NPJ Genomic Med 2018; 3:34.

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