

CLAIMS

What is claimed is:

1. A method of determining an endometrial status, comprising: (a) performing an assay on an endometrial sample from a woman to determine a microRNA (miRNA) expression profile of the endometrial sample, wherein the miRNA expression profile comprises expression levels of a plurality of miRNAs; and (b) analyzing the miRNA expression profile to obtain a receptivity predictive score,

wherein the receptivity predictive score classifies the endometrial status of the woman,

wherein the endometrial status comprises a pre-receptive state, a receptive state, or a post-receptive state,

wherein the plurality of miRNAs comprises at least 167 miRNAs having the sequences of SEQ ID NOs:1-167, respectively,

wherein the miRNA expression profile is determined by quantitative PCR (qPCR), sequencing, microarray, or RNA-DNA hybrid capture technology,

wherein the receptivity predictive score is a value produced by a computer-based algorithm, the computer-based algorithm being established by performing data normalization and one or more of the following steps: data scaling, data transformation, prediction modeling, and cross-validation, and

wherein the value of the receptivity predictive score greater than 1 indicates the pre-receptive state, the value of the receptivity predictive score less than -1 indicates the post-receptive state, and the value of the receptivity predictive score from -1 to 1 indicates the receptive state.

2. The method of claim 1, wherein the endometrial sample is obtained from the uterine cavity of the woman.

3. The method of claim 1 or claim 2, wherein the endometrial sample comprises an endometrial biopsy, an endometrial lavage, or combination thereof.

4. The method of any one of claims 1-3, wherein the endometrial sample is obtained (i) seven days after an endogenous luteinizing hormone (LH) surge in the woman or (ii) five days after a progesterone administration in the woman.

5. The method of any one of claims 1-4, wherein the miRNA expression profile is determined by qPCR performed on a cDNA preparation synthesized from the miRNAs in the endometrial sample.

6. The method of claim 5, wherein the cDNA synthesis is performed using a universal reverse transcription primer having a nucleotide sequence represented by the following general formula: 5'-R-(dT)_nVN-3', wherein R comprises SEQ ID NO:168, (dT)_n is an n number of continuous thymine residues, wherein n is 19, V is an adenine residue, a guanine residue, or a cytosine residue, and N is an adenine residue, a guanine residue, a cytosine residue, or a thymine residue.

7. The method of any one of claims 1-6, wherein the receptivity predictive score is calculated using the equation of MIRA score = $f(X \in \text{eq}(C)) = X\beta + \varepsilon$, β being a vector of coefficients, ε being an error, and X being data from the miRNA expression profile.

8. The method of any one of claims 1-7, wherein if the endometrial status is determined to be at the pre-receptive state or the post-receptive state, further comprising: repeating steps (a) and (b) at least once or until the endometrial status is determined to be at the receptive state.

9. The method of any one of claims 1-8, wherein the endometrial sample is from the woman suffering or suffered from an implantation failure.

10. A method of detecting endometrial receptivity for embryo implantation in a woman, comprising: (a) performing an assay on an endometrial sample from the woman to determine a microRNA (miRNA) expression profile of the endometrial sample, wherein the miRNA expression profile comprises expression levels of a plurality of miRNAs; and (b) analyzing the miRNA expression profile to obtain a receptivity predictive score,

wherein the receptivity predictive score determines whether the woman has endometrial receptivity for embryo implantation,

wherein the plurality of miRNAs comprises at least 167 miRNAs having the sequences of SEQ ID NOs:1-167, respectively

wherein the miRNA expression profile is determined by quantitative PCR (qPCR), sequencing, microarray, or RNA-DNA hybrid capture technology,

wherein the receptivity predictive score is a value produced by a computer-based algorithm, the computer-based algorithm being established by performing data

normalization and one or more of the following steps: data scaling, data transformation, prediction modeling, and cross-validation, and

wherein the value of the receptivity predictive score from -1 to 1 indicates that the woman has endometrial receptivity for embryo implantation.

11. The method of claim 10, wherein the endometrial sample is to be obtained from the uterine cavity of the woman.

12. The method of claim 10 or claim 11, wherein the endometrial sample comprises endometrial biopsy, an endometrial lavage, or combination thereof.

13. The method of any one of claims 10-12, wherein the endometrial sample is to be obtained (i) seven days after an endogenous luteinizing hormone (LH) surge in the woman or (ii) five days after a progesterone administration in the woman.

14. The method of any one of claims 10-13, wherein the miRNA expression profile is determined by qPCR performed on a cDNA preparation synthesized from the miRNAs in the endometrial sample.

15. The method of claim 14, wherein the cDNA synthesis is performed using a universal reverse transcription primer having a nucleotide sequence represented by the following general formula: 5'-R-(dT)_nVN-3', wherein R comprises SEQ ID NO:168, (dT)_n is an n number of continuous thymine residues, n is 19, V is an adenine residue, a guanine residue, or a cytosine residue, and N is an adenine residue, a guanine residue, a cytosine residue, or a thymine residue.

16. The method of any one of claims 10-15, wherein the receptivity predictive score is calculated using the equation of MIRA score = $f(X \in \text{eq}(C)) = X\beta + \varepsilon$, β being a vector of coefficients, ε being an error, and X being data from the miRNA expression profile.

17. The method of any one of claims 10-16, wherein the endometrial sample is from the woman suffering or suffered from an implantation failure.

~~18. A kit comprising: one or more microRNA (miRNA) profiling chips targeting a plurality of miRNAs, wherein the kit is configured to contain instructions on (i) determining a miRNA expression profile of an endometrial sample from a woman, optionally using the one or more miRNA profiling chips, and (ii) obtaining a receptivity predictive score based on the miRNA expression profile, using a computer-based algorithm, wherein the plurality of miRNAs comprises at least 167 miRNAs having the sequences of SEQ ID NOs:1-167, respectively,~~

~~wherein the receptivity predictive score classifies an endometrial status of the woman, and
wherein the endometrial status comprises a pre-receptive state, a receptive state, or a post-receptive state.~~

~~19. The kit of claim 18, wherein the one or more miRNA profiling chips comprise primers for detection of expression levels of the plurality of miRNAs.~~

~~20. The kit of claim 19, wherein the miRNA profiling chips are configured to perform a quantitative PCR (qPCR), sequencing, microarray, or RNA-DNA hybrid capture assay, preferably qPCR, to detect the expression levels of the plurality of miRNAs.~~