
MIRA
miRNA-based Receptivity Analysis

What is MIRA™?

MIRA™ assesses a combination of miRNA biomarkers in order to determine the status of a patient's endometrium receptivity, increasing the chances of IVF treatment success.

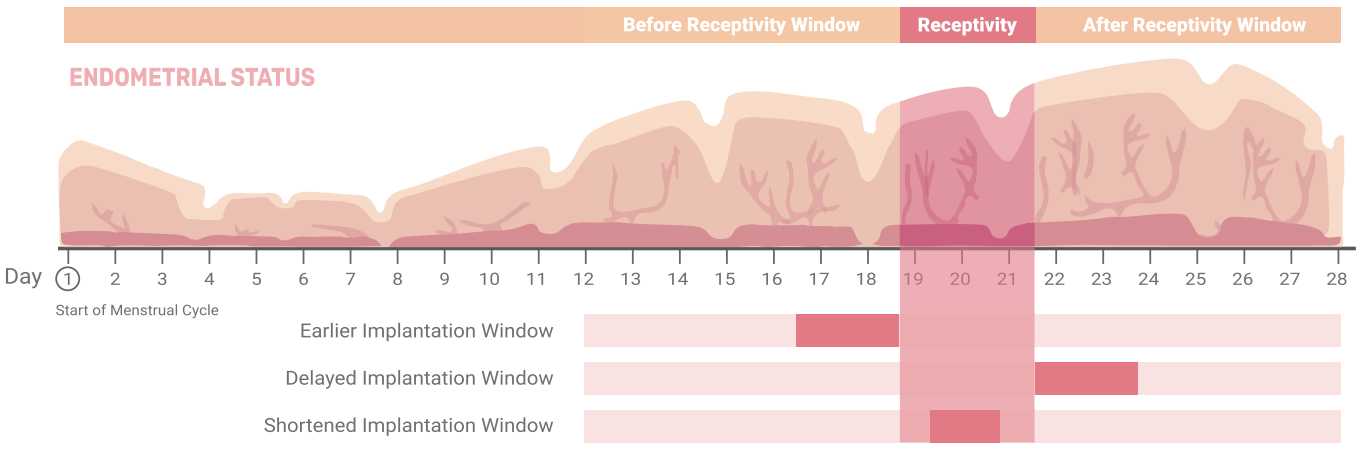
What is endometrial receptivity?

Endometrial receptivity is the period of time when the endometrium is ready for embryo implantation. This typically occurs between days 19 and 21 of the menstrual cycle of fertile women. This interval of receptivity can also be referred to as the window of implantation (WOI).

How does MIRA™ help with the IVF treatment cycle?

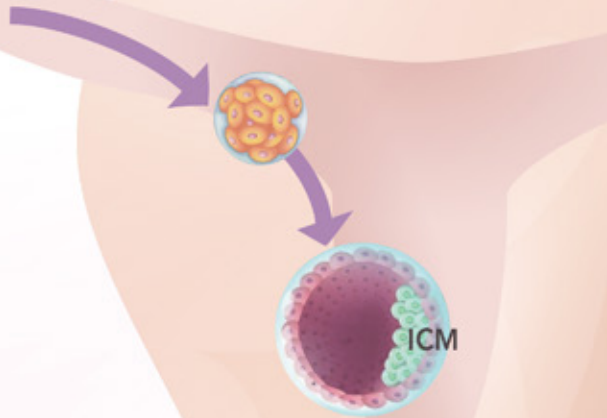
Large scale studies have shown that 30% of infertility patients have a displaced WOI. One of the main causes of implantation failure is the lack of synchronization between embryo and endometrium. MIRA™ has the unique ability to assess endometrial receptivity in order to determine the optimal time for embryo transfer.

The average WOI is between days 19 and 21 of the menstrual cycle. However, this can vary among individuals. 30% of fertile women have a shorter implantation window, or one outside of the average.



miRNA biomarkers

- miRNA is stable compared to mRNA as it is enclosed and protected by proteins, thus allowing analysis of endometrial tissue samples of lesser quality
- miRNA can act as non-invasive biomarkers, opening up the possibility of non-invasive endometrium receptivity testing in the future
- miRNA exhibits higher correlation with the protein level compared to mRNA as miRNA regulates mRNA to suppress protein translation and/or induce mRNA degradation
- Numerous scientific publications have indicated the role of miRNAs in the regulation of the endometrium's status



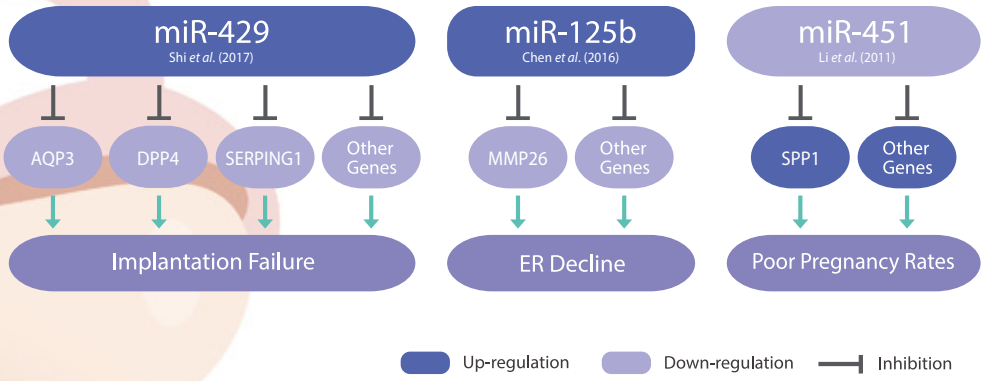
NextAmp™ Analysis System

- Our quantitative amplification-based platform provides highly reproducible and sensitive results compared to other molecular testing technologies
- Turnaround time can be shortened half the time of third party assays
- Less sample input is needed in order to run MIRA™
- It allows for decentralized lab testing as NextAmp™ Analysis System is easy to install in each lab and simple to run

Example Role of miRNAs:
Anti-implantation

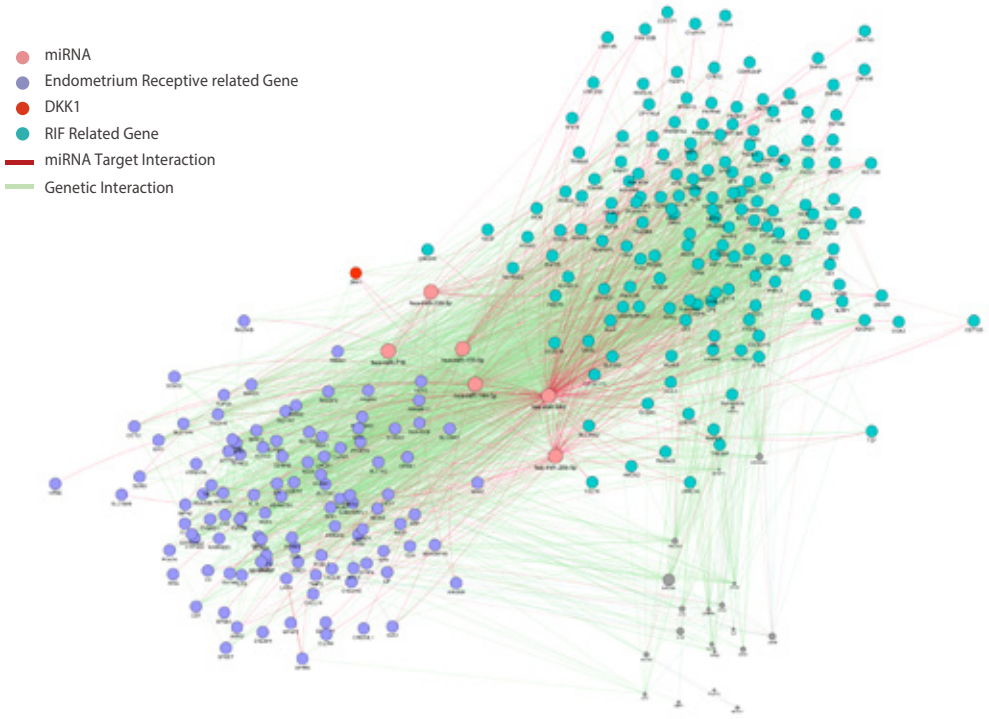
miR-145: High expression of miR-145 also causes implantation failure by blocking the crosstalk between embryonic Igf1 and maternal Igflr.

Others: miR-451, miR-424, miR-125b, and miR-30b become downregulated during high progesterone levels compared to the normal condition, and might have an important role during hormonal regulation.



MIRA™'s panel covers close to 100 miRNA biomarkers that are related to over 600 endometrial receptivity-related genes

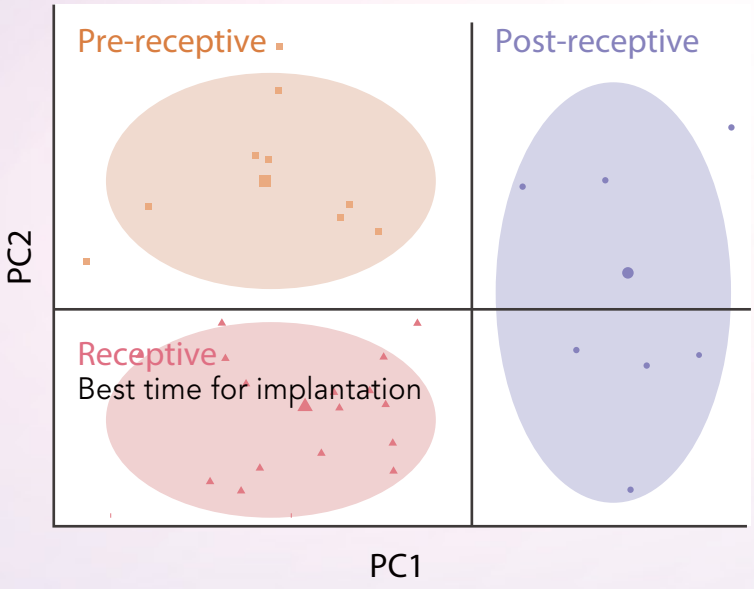
Amongst them are novel miRNAs that have shown an accuracy of around 90% for identifying a displaced WOI as the cause for repeated implantation failure



Reference: Chen, Ching Hung et al. "A novel platform for discovery of differentially expressed microRNAs in patients with repeated implantation failure." Fertility and sterility, S0015-0282(21)00088-1. 3 Apr. 2021, doi:10.1016/j.fertnstert.2021.01.055"

MIRA™ Data

MIRA™ successfully predicts three different stages of endometrial receptivity using its proprietary algorithm, providing the optimal time for embryo implantation down to the hour.



What can MIRA™'s report tell you?

Receptive: Best Time to Implant

In the Window of Implantation (WOI)

A **Receptive** result on the report indicates that the time of the tissue biopsy was the optimal time for embryo transfer and that the same conditions and timing can be used during their subsequent treatment cycles for the most favorable personalized embryo transfer conditions.

Non-receptive: Adjust Implantation Time

NOT in the Window of Implantation (WOI)

A **Non-Receptive** (pre- or post-receptive) result on your report indicates that the time of the tissue biopsy was not in the optimal time period for embryo transfer and that the timing of embryo transfer for the patient should be altered in order to increase the chances of a successful implantation.

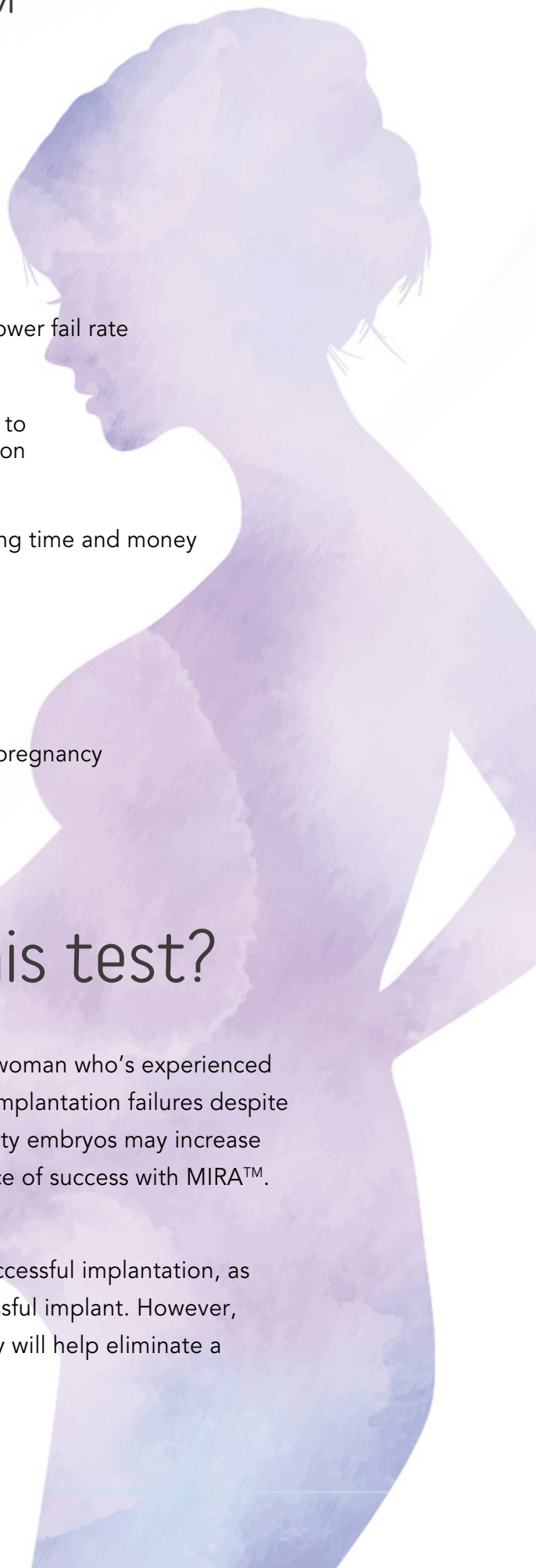
Inconclusive : The analysis was not able to determine the optimal time for embryo transfer. This could be the result of an exceptionally low quality or low quantity biopsy sample. A MIRA™ representative will follow up with you to discuss altering the steps of the biopsy in order to retest your patient for a more comprehensive result. An inconclusive result happens in less than 1% of results.

Benefits of MIRA™

Increased Successful Implantation Rate

40% without MIRA™ >> 70% with MIRA™

- Less invasive – less sample needed with a lower fail rate
- Faster report time – providing faster results to doctors and patients for personalized solution
- Fewer cycles of IVF treatment needed, saving time and money
- Reduce implantation failure rates
- Increase chances of obtaining a successful pregnancy



Who should take this test?

- Any woman that plans to undergo an IVF treatment process may use MIRA™ to increase their chances of successful implantation.
- Any woman who's experienced repeated implantation failures despite good quality embryos may increase their chance of success with MIRA™.

Undergoing the MIRA™ test will not guarantee a successful implantation, as there are many other factors that can affect a successful implant. However, understanding your patient's endometrial receptivity will help eliminate a displaced WOI as a reason for implantation failure.

Sample submission process

1. Fill out the **Sample Submission and Consent Form** (included in the kit).

2. **Endometrial biopsy** should be taken either:
   - After **5 days (120 hours)** of progesterone administration in an **HRT cycle**.
   - Or, after **7 days (168 hours)** from hCG administration in a **natural cycle**.

3. Place the endometrial biopsy in the MIRA™ **cryotube**.

   Optional: Place half of the biopsy into **formaldehyde for staining** to confirm endometrial cells.

4. Label the MIRA™ cryotube with one of the **barcode stickers** included in the kit.

5. Gently invert the MIRA™ cryotube back and forth for **10 seconds**, or **at least 5 times**.

6. Store the MIRA™ cryotube at **4°C** for at least **4 hours**.

7. **Scan and email** a copy of the Sample Submission and Consent Form to your **MIRA™ representatives**

8. Once the sample is ready for shipment, place the MIRA™ cryotube in the **protective vessel**.

9. Place the **protective vessel** inside the padded shipping envelope, along with the **completed & signed Sample Submission and Consent Form**.

10. Ship the package at **room temperature** to the designated shipping address using **priority or next day shipping**.

References / Publications

miRNAs and RIF

Chen CH, Lu F, Yang WJ, Yang PE, Chen WM, Kang ST, Huang YS, Kao YC, Feng CT, Chang PC, Wang T, Hsieh CA, Lin YC, Jen Huang JY, Wang LH. A novel platform for discovery of differentially expressed microRNAs in patients with repeated implantation failure. Fertil Steril. 2021 Apr 3:S0015-0282(21)00088-1. doi: 10.1016/j.fertnstert.2021.01.055. Epub ahead of print. PMID: 33823989.

For tissue miRNA

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For circulating miRNA

Kresowik, J. D., Devor, E. J., Voorhis, B. J., & Leslie, K. K. (2014). MicroRNA-31 is Significantly Elevated in Both Human Endometrium and Serum During the Window of Implantation: A Potential Biomarker for Optimum Receptivity. Biology of Reproduction, 91(1), 1-6. doi:10.1095/biolreprod.113.116590

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MKT-0001-2106E