ora™ Non-Invasive Endometrial Receptivity Test

Personalizing embryo transfer timing with a simple blood draw

Highlights:

- Over 30% of women undergoing IVF treatment have been shown to have a displaced window of implantation (WOI), leading to implantation failure
- ora™ utilizes novel miRNA biomarkers that have been shown to have over 90% (Chen et al., 2021)[1] accuracy in identifying displaced WOI as cause for repeated implantation failure
- ora™ 's biomarkers target over 700 endometrial receptivity related genes for a comprehensive analysis
- Clinically validated with an accuracy of over 95.9% in predicting the right window of implantation

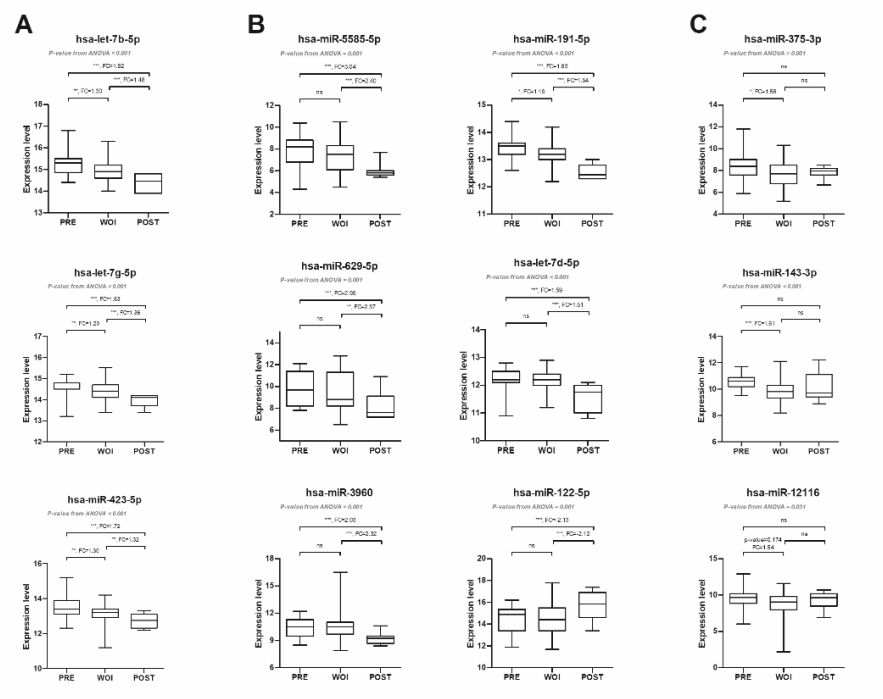
Introduction to Endometrial Receptivity

During in vitro fertilization (IVF) treatment, a variety of factors influence the success or failure of embryo transfer such as embryo quality, immune factors, and uterine conditions. One of the key factors to consider for uterine conditions is the endometrial receptivity status. An accurate assessment of endometrial receptivity identifies the optimal window of implantation (WOI) for embryo transfer. Over 30% of patients undergoing IVF treatment have been found to have a displaced WOI, meaning their optimal time for embryo transfer occurs earlier or later than WOI.

Traditionally, assessment of endometrial receptivity has been done by ultrasound analysis, pathology lab analysis, or analyzing genetic biomarkers in endometrial tissue biopsies. While genetic analysis identifies informative biomarkers from individual patients, obtaining the endometrial tissue biopsies poses discomfort and pain for the IVF patients. The goal of ora™ is to provide a precise, accurate, and painless solution for identifying WOI.

Development of ora™

By harnessing the stability of microRNA (miRNA) biomarkers in the bloodstream and its important function in regulating the embryo implantation process, ora™ was developed to identify the optimal WOI with a simple blood draw instead of needing an endometrial tissue biopsy. In a recent publication, the development process of ora™ was shown to involve utilizing endometrial tissue samples grouped into the three different endometrial receptivity stages (pre-receptive, receptive, and post-receptive) that were confirmed to have successful pregnancy results (Chen et al., 2023)[2]. By utilizing next generation sequencing technology, 135 miRNA biomarkers in the bloodstream were found to be stably expressed across these three different endometrial stages.



Highlighted above are a few of the differentially expressed miRNAs that were found to be correlated with changing endometrial stages.

1	Gland development
2	Response to oxygen levels
3	Cell cycle G1/S phase transition
4	Response to decreased oxygen levels
5	Response to hypoxia
6	G1/S transition of mitotic cell cycle
7	Mitotic cell cycle phase transition
8	Epithelial cell proliferation
9	Cellular response to oxygen levels
10	Regulation of apoptotic signaling pathway

The miRNA biomarkers that ora™ utilizes have been found to regulate various biological processes critical to endometrial function and embryo development. These biomarkers govern processes such as gland development and secretion, response to oxygen levels (crucial for maintaining physiological homeostasis and mitigating inflammation), cell proliferation, and utero embryonic development. By comprehensively analyzing these biomarkers, ora™ offers a holistic assessment of endometrial receptivity in combination with the patients' physiological status.

Clinical Validation of ora™

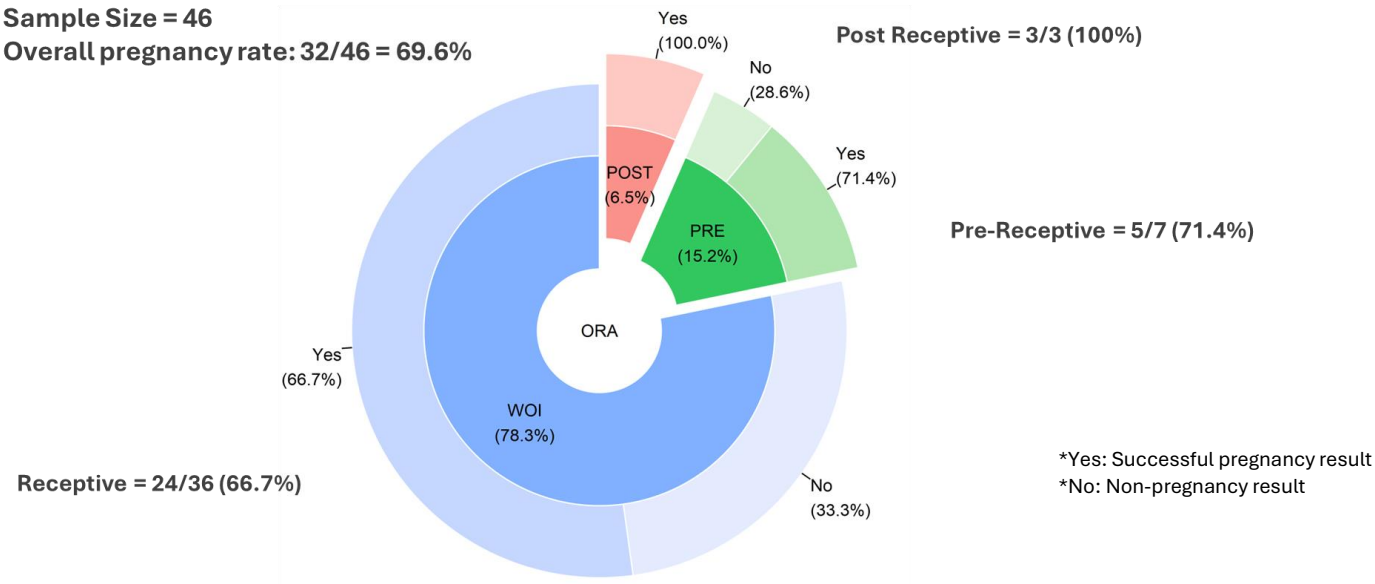
Following the identification of the 135 miRNA biomarkers to target for ora™, an algorithm was trained utilizing 111 clinical samples. After achieving 91.9% accuracy in the training set, a separate set of clinical samples was used to validate the accuracy of ora™.

		Known endometrial status							
		Pre	Rec	Post	Sensitivity	Specificity	PPV	NPV	Accuracy
Predicted result	Pre	2	2	0	66.7%	97.1%	50.0%	98.6%	95.9%
	Rec	1	64	0	97.0%	85.7%	98.5%	75.0%	95.9%
	Post	0	0	4	100.0%	100.0%	100.0%	100.0%	100.0%
							Overall Accuracy		95.9%

The validation set of clinical samples showed that ora™ achieved over 95.9% accuracy in correctly identifying the window of implantation (Chen et al., 2023)[2].

Real World Clinical Data

Preliminary real world clinical data have been collected from clinics utilizing ora™ as a part of their treatment regimen. A total of 46 patients underwent ora™ to identify their personalized WOI and had an overall successful pregnancy rate of 69.6% after following ora™'s recommended embryo transfer timing. Of these 46 patients, 22% of them were identified to have a displaced WOI, with 15.2% in the pre-receptive group and 6.5% in the post-receptive group. Following ora™'s recommended personalized embryo transfer timing, the successful pregnancy rates were 66.7% for the receptive group, 71.4% for the pre-receptive group, and 100% for the post-receptive group.



The efficacy of ora™ can be seen through the high successful pregnancy rates for all three endometrial stages, showing promise in fulfilling its goal of providing a non-invasive, painless solution for IVF patients. A bigger sample size could warrant further validation.

Reference:

1. Chen, C.H. et al. (2021) 'A novel platform for discovery of differentially expressed micrornas in patients with repeated implantation failure', Fertility and Sterility, 116(1), pp. 181–188. doi:10.1016/j.fertnstert.2021.01.055.
2. Chen, M.-J. et al. (2023) 'Development of a predictive model for optimization of embryo transfer timing using blood-based microrna expression profile', International Journal of Molecular Sciences, 25(1), p. 76. doi:10.3390/ijms25010076.