

Will IVF work for a particular patient? The answer may be found in her blood

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For the first time, researchers have been able to identify genetic predictors of the potential success or failure of IVF treatment in blood. Dr. Cathy Allen, from the Rotunda Hospital, Dublin, Ireland, told the 25th annual conference of the European Society of Human Reproduction and Embryology today that her research would help understand why IVF works for some patients but not for others.

Previous work in this area has looked at gene profiles in such tissues as the uterine lining, but Dr. Allen and her team chose to examine the gene expression patterns in RNA extracted from peripheral (circulating) blood, an easily accessible biological sample. Blood samples were taken at eight different stages during the period around conception and the early stages of the IVF cycle. Five of these samples came from women who achieved clinical pregnancies, three from those who had implantation failure, and three from subfertile women who conceived spontaneously. Analysis showed that 128 genes showed a more than two-fold difference in expression in early clinical pregnancy compared with a non-pregnant state.

The <u>molecular pathways</u> that were most over-represented in this expression were concerned with angiogenesis (the growth of new <u>blood vessels</u>), endothelin signalling (blood vessel constriction), inflammation, oxidative stress (damage to cell structures), vascular endothelial growth factor (signalling processes in blood vessel growth), and pyruvate metabolism (the supply of energy to cells). "All these processes are important in the achievement and maintenance of pregnancy," said Dr.



Allen.

"We found that the gene expression profiles in blood of patients at the time of pituitary down-regulation showed interesting patterns of gene clustering. Over 200 genes were differentially expressed in patients who went on to achieve an IVF pregnancy compared with those who did not," she said.

The researchers found that the peripheral blood gene expression 'signature' (also known as the transcriptome) before IVF was predictive of IVF outcome. This finding demonstrates the power of high-dimensional technology in biomarker discovery, and highlights the potential for developing clinically useful tools, they say.

One of the most difficult decisions for patients who have had unsuccessful IVF treatments is whether they should undergo further attempts at IVF, or if there are ways to optimise chances of success. The researchers hope that the results generated by this work will lead to the development of a test to aid in IVF decision-making. They say that their work will help to identity biomarkers that can identify events occurring at implantation, the maintenance of pregnancy and successful or unsuccessful pregnancy outcome.

"IVF technology has advanced tremendously over the past three decades, yet success after IVF remains an unpredictable outcome," said Dr. Allen. "Our work will help understand whether the implantation of embryos is influenced by the constantly changing expression of human genes."

Previous studies in the field of gene-expression have focused on single genes as opposed to genome-wide screening of all the human genes with high density DNA microarrays, as used by Dr. Allen and her team. The advent of tools like microarrays that can simultaneously probe for up to 29,000 genes has radically changed scientific approaches to this type of



research. "It's like looking at how a team of players perform together rather than focusing on the individual players," said Dr. Allen.

"We intend to look further at the most significant genes we have identified as being important in this field in order to be able to understand their exact biological role in reproductive function. We hope that our work will lead to the development of a clinically useful tool to help doctors counsel their patients in the difficult decision-making involved in IVF," she said.

Source: European Society for **Human Reproduction** and Embryology

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