Endometrial Immune Profile

What is an Endometrial Immune Profile?

Endometrial Immune Profile (EIP) is a test to evaluate the molecular immune profile of the lining of the uterus (endometrium) to see if it is properly prepared to promote a successful pregnancy.

Why perform an Endometrial Immune Profile?

In order for pregnancy to be successful the endometrium must undergo two processes: decidualization and placentation. Decidualization is accompanied by substantial recruitment of maternal immune cells with approximately 70% being natural killer (NK) cells. During placentation, embryonic extravillous trophoblastic cells invade into the decidua and actively participate in spiral arteries remodeling that result in increased blood supply to the developing embryo/fetus. Women experiencing recurrent implantation failure have been shown to have an excessive or low count of uterine NK cells and a dysregulation of endometrial levels of interleukin (IL)-15 and IL-18 as well as TWEAK (TNF Weak inducer of Apoptosis) and its receptor, Fn-14 (fibroblast growth factor-inducible molecule) compared with fertile women. IL-15, IL-18 are cytokines involved in activation of uterine NK cells. TWEAK is pro-angiogenic and anti-inflammatory cytokine acting via Fn14. The balance of activating signals versus controlling signals can be measured as IL-18/TWEAK and IL-15/Fn14 ratios. An abundance of uterine NK cells is assessed via CD56 mRNA transcripts quantification. The ratios along with uterine NK cell evaluation have been shown to provide the molecular tools that help to determine whether the endometrium is receptive to accept an embryo for implantation and placentation.

Who should be tested?

- Women who have a history of recurrent implantation failure or recurrent pregnancy loss
- Women with a history of thin endometrial thickness (≤ 6mm)
- Although not as yet tested, there are theoretical reasons to believe that women tested before starting an assisted reproduction cycle with EIP and treated appropriately would experience a higher live birth rate than women not screened and treated.
Frequently Asked Questions

1. In which kind of cycle could the EIP test be performed? How is the endometrial biopsy taken?

The EIP test can be performed with endometrial biopsy sample in either a hormone replacement therapy cycle in preparation of a frozen embryo transfer or a natural cycle. Biopsy of the uterine is performed according to a standard procedure with a Pipelle catheter or similar. About 30 milligrams of tissue is enough for analysis.

2. How is the timing of the endometrial biopsy calculated?

- **Hormone Replacement Therapy cycle:** upon initiation of an HRT cycle, the biopsy is taken after five full days of progesterone treatment or the expected day of frozen embryo transfer. The day for the first intake of progesterone is considered as P+0 and the day of the biopsy is P+5. If you refer to the first day as P+1, the day of the biopsy will be P+6.
- **Natural cycle:** the biopsy is taken 7 to 9 days after the LH surge. The day of the LH surge is considered as LH+0, and the biopsy will be taken at LH+7-9. The best way to identify the LH surge is with the urinary LH tests.

3. What are the possible results obtained from the EIP?

Table 1. Criteria to determine EIP:

<table>
<thead>
<tr>
<th>IL-18/TWEAK</th>
<th>CD56</th>
<th>IL-15/Fn14</th>
<th>EIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Elevated</td>
<td>Any result</td>
<td>Any result</td>
<td>Over-activated</td>
</tr>
<tr>
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<td>Elevated</td>
<td>Any result</td>
<td>Low-activated</td>
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<td>Any result</td>
<td>Low</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Low</td>
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</tbody>
</table>

4. What are some possible treatments according to the EIP result obtained?

This test must be ordered by a physician and the result will be sent to the doctor. The physician who orders the test will be responsible of prescribing treatment. Results of some treatments of women experiencing recurrent implantation failure that have been reported by two centers are summarized in the following graph:
Scientific Publications


