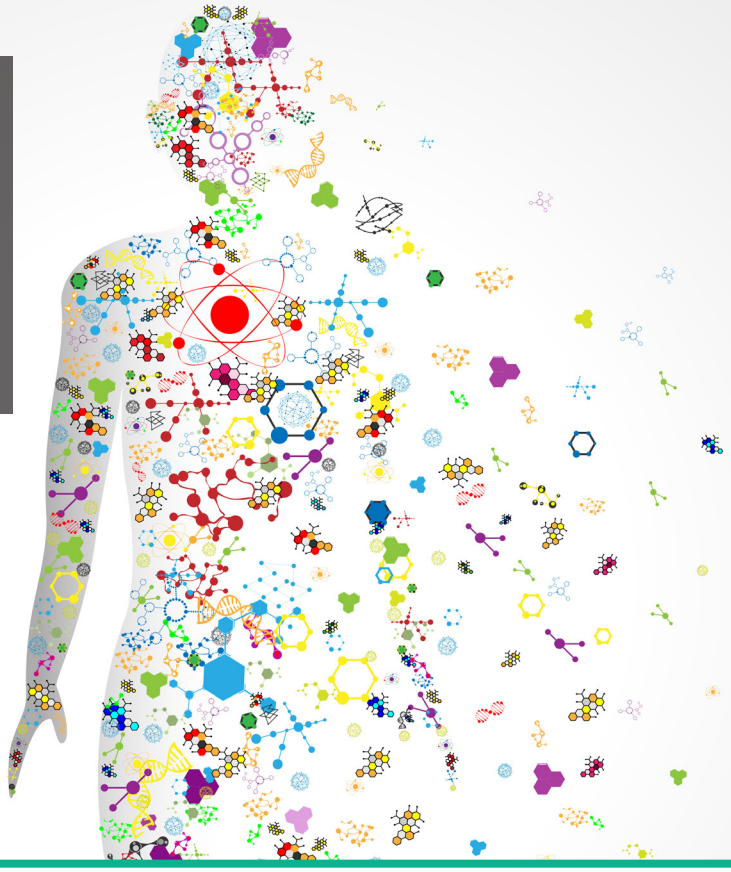
Im Map®

IMMUNOLOGY MAP

Immunologic factors such as an abnormal response to the developing embryo by a woman's immune system may be the cause in many infertility cases



Pregnancy is an exceptional process in which the woman's immune system is not only able to adapt its functions to tolerate the development of the embryo, but also participates actively in implantation and the evolution of pregnancy.To achieve a successful gestation, it is essential that maternal and fetal cells coexist in a finely regulated immune balance. Recent studies have shown that alterations in this balance could lead to the appearance of complications during pregnancy.

ImMap® analyses the levels and activity of various endometrial immune cell subpopulations described as active participants in the gestation process (NK cells, Th1, Th2, Th17 and Treg lymphocytes and B lymphocytes). ImMap® allows the identification of implantation failure or recurrent miscarriage causes in cases where embryonic factors have been previously ruled out.

METHODOLOGY

1. Biopsy of endometrial tissue P+5.5 /LH+7
2. Introduction in the Im Map® cryotube
3. Sample shipment at 4ºC
4. Analysis of immune cells levels
5. Results in 15 working days
6. Immune Therapy

Natural Killer Cells (NK)

NK cells are part of the first line of defence of the immune system and responsible for the identification and destruction of both, foreign cells and self cells infected or under stress conditions.

NK cells are the major cell subtype of the uterine tissue and their proportion varies throughout the menstrual cycle and the gestation process. NK cells increase their presence in the secretory endometrium reaching more than 70% of its cell composition throughout the first trimester of pregnancy.

Uterine NK cells (uNKs) play a key role in embryo implantation and in the vascular and tissue remodelling associated with placental development. Several studies have linked altered levels of endometrial NK cells to implantation failure and miscarriage 1, 2.

Th and Treg lymphocytes

T-lymphocytes are part of the specific immune cell response responsible for the defence against microorganisms. In the endometrium, there are different subtypes of these cells, each with specific functions and proportions and therefore with different influence on the evolution and development of pregnancy.

T-lymphocytes activation leads to cytokines secretion, proteic molecules responsible for the final immune response. Depending on the cytokines profile found in the environment, Th cells may differentiate into different cell types, Th1, Th2, Th17 and Treg, which are ultimately those that define the type of immune response that will be triggered.

- Th1 lymphocytes: secrete pro-inflammatory cytokines promoting an inflammatory environment.
- Th2 lymphocytes: promote humoral responses that originate an anti-inflammatory state.
- Th17 lymphocytes: lead to pro-inflammatory responses and autoimmunity phenomena.
- Treg lymphocytes: suppress the inflammatory response and promote immune tolerance.

Inflammation is necessary for successful implantation, but after this initial stage, it is necessary to generate a tolerant environment that will allow embryonic development. The pro-inflammatory state is mediated by NK, Th1 and Th17 cells in response to paternal antigens present in the embryo, while Treg and Th2 cells will redirect this state into a maternal-fetal tolerant environment.

Since it is necessary for each type of cell to fulfil its functions at a particular point time along the pregnancy process, many studies have assessed the influence of disturbances in these populations on the progression of pregnancy. Abnormal levels of Th1, Th2, Th17 and Treg have been associated with implantation failure, recurrent abortion or preeclampsia 3-8. In addition, the endometrial predominance of Th17 lymphocytes has also been associated with premature birth 5.

B-lymphocytes

B-lymphocytes are the immune cells responsible for defending mucous membranes such as the endometrium by means of antibody production. For implantation to take place, the vast majority of B-lymphocytes must be cleared from the endometrium. Under these circumstances and depending on the subpopulation of B lymphocytes eventually remaining in the tissue, they may contribute to the successful development of pregnancy or the development of adverse outcomes.

B2 lymphocytes produce the so-called protective antibodies, which are able to recognize paternal antigens, but do not trigger any response, preventing maternal immune system activation against the embryo. It has been described that the absence of these antibodies is a dominant feature in patients who have experienced recurrent miscarriage 9.

The B1-a lymphocytes synthesize the denominated natural antibodies, responsible for autoimmune processes. Research has shown that the presence of these molecules in pregnant women increases the risk of complications such as miscarriage, deep vein thrombosis, preeclampsia, or intrauterine fetal death 10.

How do we perform the tests?

ImMap® is performed on a luteal phase endometrial biopsy sample, at day LH+7 in a natural cycle, at day hCG+7 in a modified natural cycle, or at day P4+5.5 in a hormone replacement therapy cycle.

The analysis is performed by flow cytometry and allows the identification and quantification of millions of cells in a few minutes by detecting immune markers, physical characteristics and chemical properties.

The detection of abnormal maternal immune cells levels will enable the establishment of the appropriate immunotherapeutic option for each patient based on the recommendations of our specialised team. These immunological therapies can help to improve the reproductive outcome, increasing the chances of embryo implantation and reducing the probability of suffering complications during pregnancy.

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