



Queendom

The ultimate
endometrial test

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Integrated Genetic Laboratory Services
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About IGLS

Our philosophy



IGLS Genetic and immunology testing laboratory

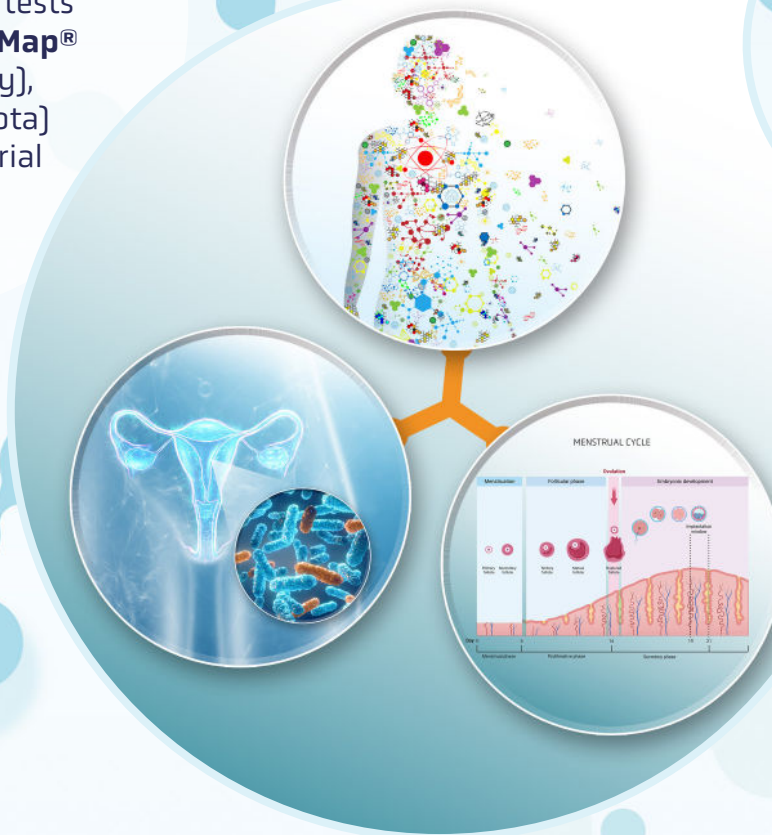
All our efforts, resources and cutting-edge technology are aimed at offering reliable solutions adapted to the needs of assisted reproduction centres, hospitals and other healthcare institutions all over the world.

On a daily basis, our reproductive genetics team puts its expertise at the service of research in labs.

Our **specialists in molecular genetics, biotechnology and immunology work hand in hand with our medical professionals** to find real solutions to a wide variety of fertility problems.

Their daily commitment is to bring all research breakthroughs into the clinical setting, in the form of high-quality diagnostic tests.

It is par excellence, the most complete **endometrial study**, with the advantage that **from a single medical act, one biopsy** allows the three tests to be carried out, i.e. **ER Map[®]** [Endometrial Receptivity], **MicroBioMap[®]** [Microbiota] and **Im Map[®]** [Endometrial Immunology].



Scope of testing

The tests described below are especially useful, both in cases of implantation failure, recurrent miscarriages, patients with chronic endometritis and for in-vitro fertilisation treatments, as well as for any patient seeking a healthy pregnancy.

ER Map[®] NXT

Endometrial receptivity study, to identify the window of implantation, the ideal moment for embryo transfer.

MicroBioMap[®]

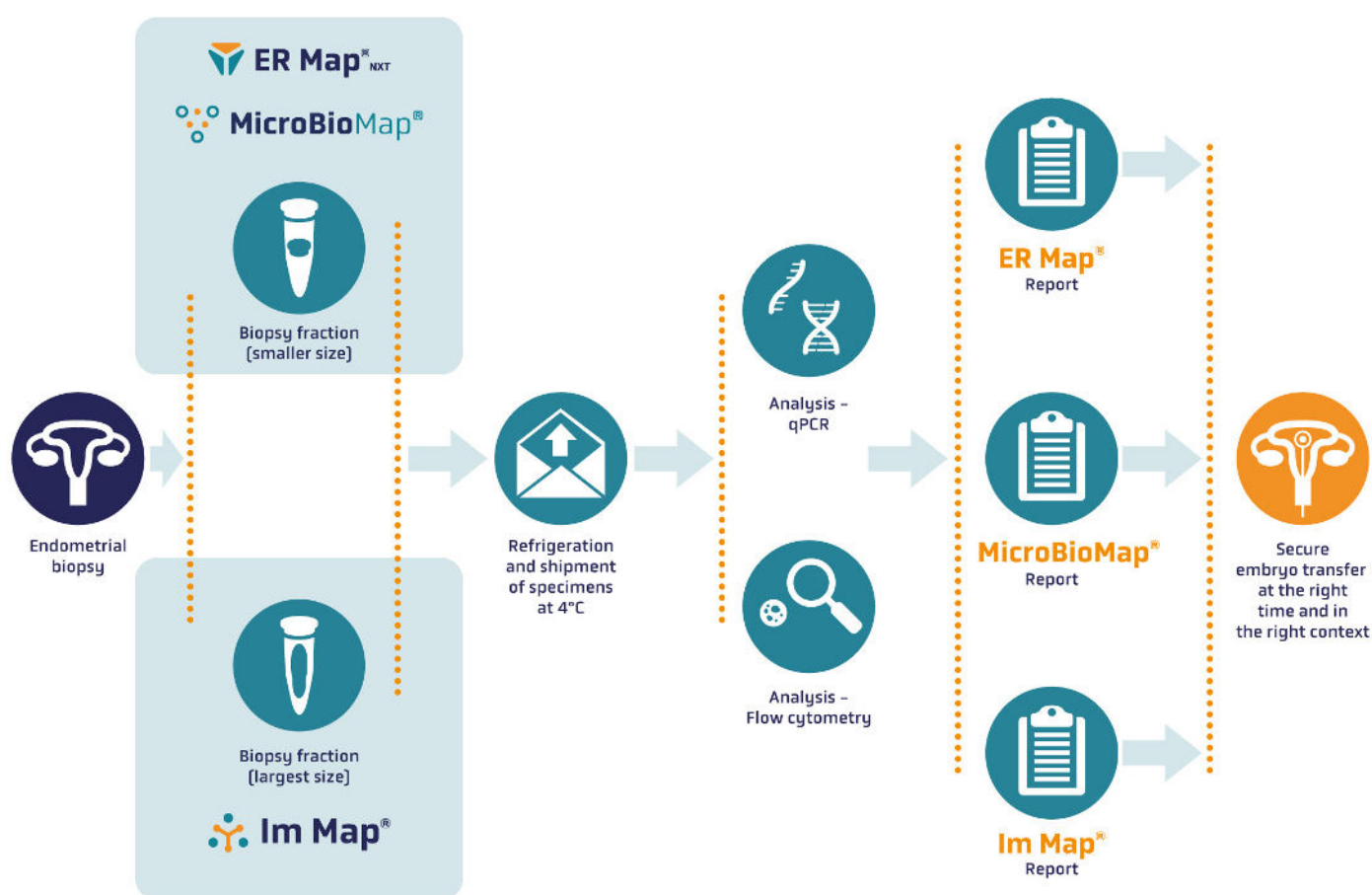
Comprehensive analysis of the endometrial microbiological environment. Crucial information used by the physician in determining the optimal treatment.

Im Map[®]

Immune mapping detects and describes the maternal endometrial immune profile. The result helps the doctor to define the appropriate therapy.

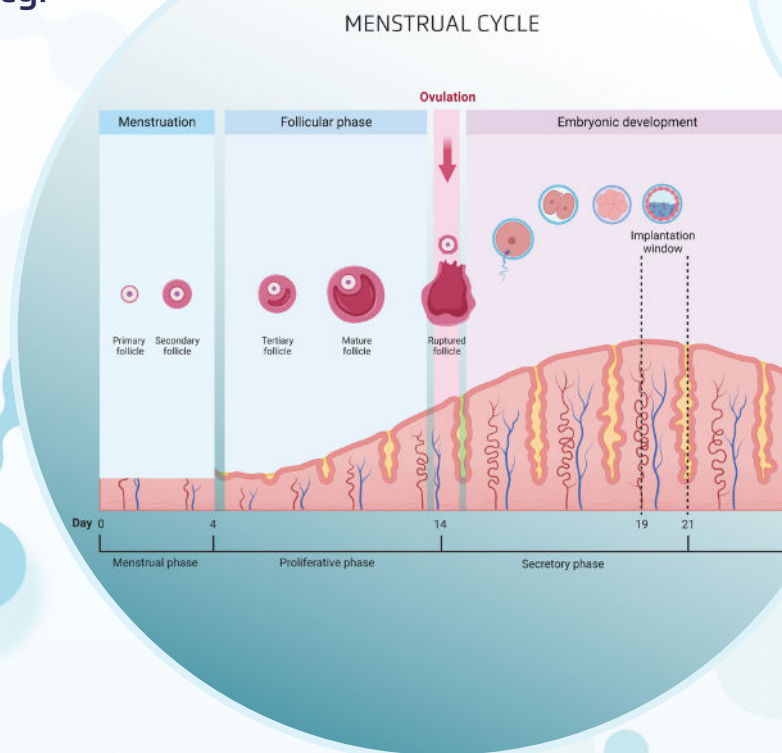
Global process diagram

The three tests can be performed independently, at the discretion of the physician and according to the age and clinical history of the patient, or grouped in packs, the latter option being of interest to patients who need more complete studies, with the advantage that they can all be performed from a single medical act, a biopsy that will be divided into two, for subsequent processing and analysis.



Add quality and confidence to your assisted reproduction treatment: go one step further by including **Queendom[®]** in your process.

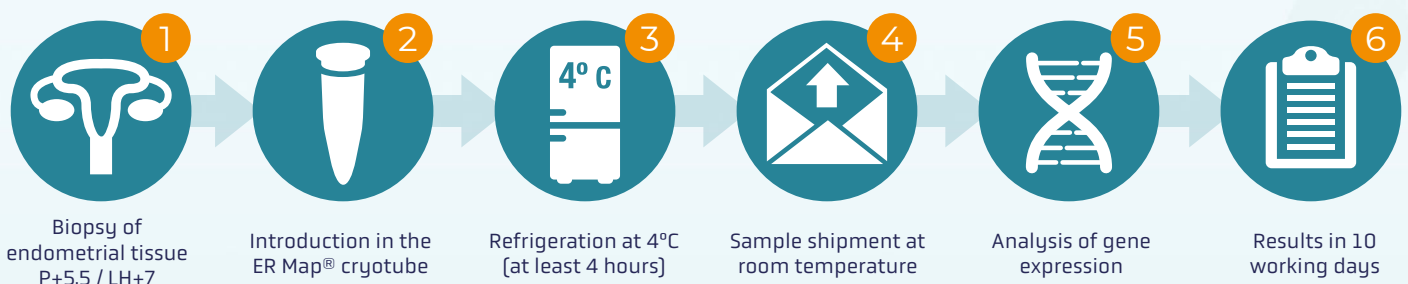
The ER Map[®] test identifies the optimal endometrial timing for embryo transfer at the moment most likely to result in pregnancy.



We know that the endometrium is refractory to pregnancy in other moments of the menstrual cycle outside the so-called "Window Of Implantation" (WOI). Recent studies have shown a specific gene expression profile during the WOI and this transcriptomic signature can be used for the endometrial function test¹.

ER Map[®] is a molecular tool based on the analysis of the genes' expression with functional relevance in the process of endometrial receptivity and the immunological response associated with successful embryo implantation.

The process



Endometrial Receptivity

The endometrium is the inner layer of the uterus where embryo implantation takes place. It undergoes periodic changes throughout the menstrual cycle and it reaches a receptive status, when it is ready for embryonic implantation, around day 19–21 of the cycle. This period of time is known as the “Window Of Implantation” (WOI).

ER Map® test description

Endometrial Receptivity Map can assess the endometrial status of patient and determine if it is receptive or not at the time of the biopsy¹. ER Map® results allow the precise timeframe identification of the WOI. Based on the test results, a personalised embryo transfer can be performed at the highest endometrial receptivity moment, increasing the chances of ART success².

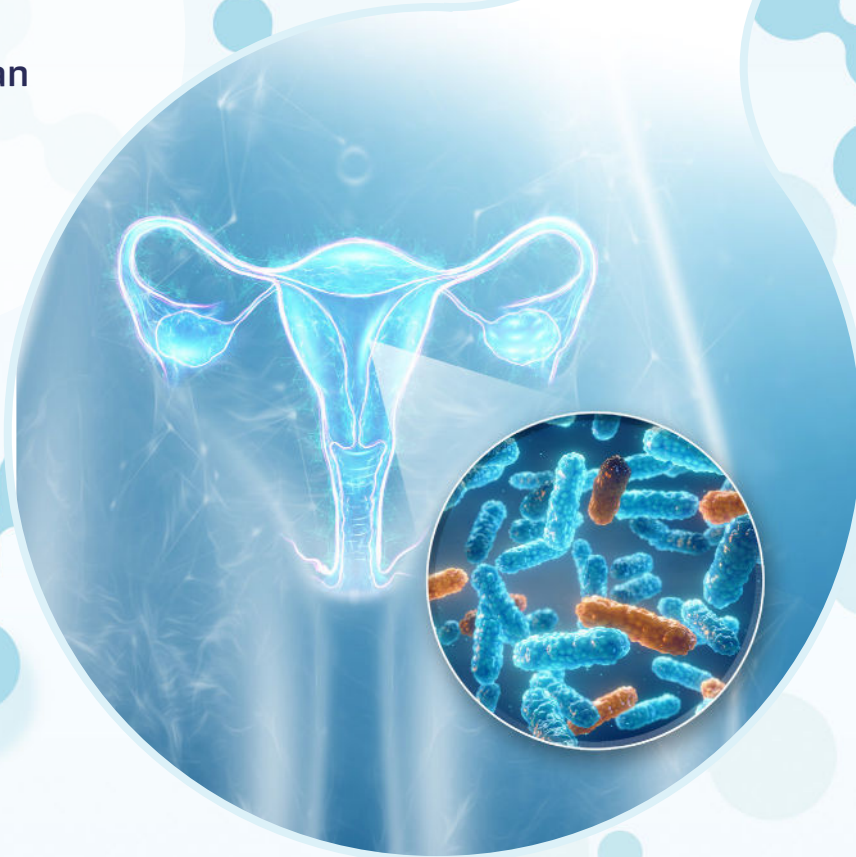
Benefits & value-added

ER Map® distinguishes itself from other endometrial receptivity testing tools by offering unique benefits that make it an outstanding choice for patients undergoing assisted reproduction treatment. Its main differences include specificity, accuracy, customisation, reproducibility and the achievement of satisfactory results. These aspects add value to ER Map®, and it is especially recommended for couples who have experienced failed cycles or pregnancy loss after transferring good quality embryos.

Indications

Classical histologic dating of the endometrium is quite subjective and presents limitations in determining which is the best endometrial moment to perform the embryo transfer. Molecular diagnosis of endometrial status by ER Map® provides a more reliable method to determine specific stages of an endometrial cycle.

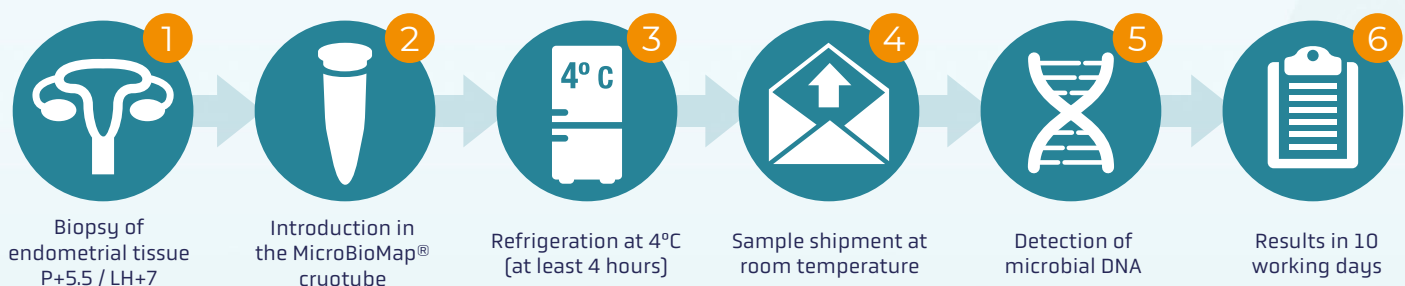
MicroBioMap® is a molecular test that analyses the microbial composition of the endometrium with an influence on female fertility.



This test analyses the presence of a set of microorganisms selected for their effects on female reproductive health using high-resolution quantitative PCR from an extraction of the microbial DNA present in the endometrium, and the level of each of the detected species is standardised per human cell.

The relative abundance of each of the detected microorganisms as a proportion of the total microbial community identified in the sample is also calculated.

The process





The endometrial microbiota

The study of the endometrial microbiota provides valuable information about the uterine environment and its suitability to receive the embryo. The presence of pathogens in the endometrial environment has been shown to be detrimental, being associated with Chronic Endometritis (CE). CD, in turn, is a factor considered to have a high impact on implantation failure, recurrent miscarriages and other pathologies or complications of pregnancy. Furthermore, the dominance of lactobacillus in pathogenic endometria may improve reproductive outcomes.

MicroBioMap® test description

MicroBioMap® is a molecular test that analyses the endometrium for the presence of 18 pathogenic microorganisms (fungi, bacteria and protozoa) involved in the development of chronic endometritis and, in addition, detects 4 species of lactobacillus, described as beneficial for reproductive health.

Benefits & value-added

The detection of pathogenic species potentially causing CD by means of the MicroBioMap® test allows the physician to choose a specific treatment for their elimination, preventing the development of the pathology and also achieving a significant improvement in the chances of success of assisted reproductive techniques in women suffering from this condition.

According to recent studies, Lactobacillus predominance may be an important marker of uterine health, associated with successful reproductive outcomes. The bacterial balance in the endometrium related to the richness of Lactobacillus in this tissue is also studied using the MicroBioMap® test.

Indications

MicroBioMap® is very useful for patients who have experienced implantation failure, recurrent miscarriages, suspected CD or for any patient undergoing an assisted reproduction cycle who wants to improve their reproductive options.

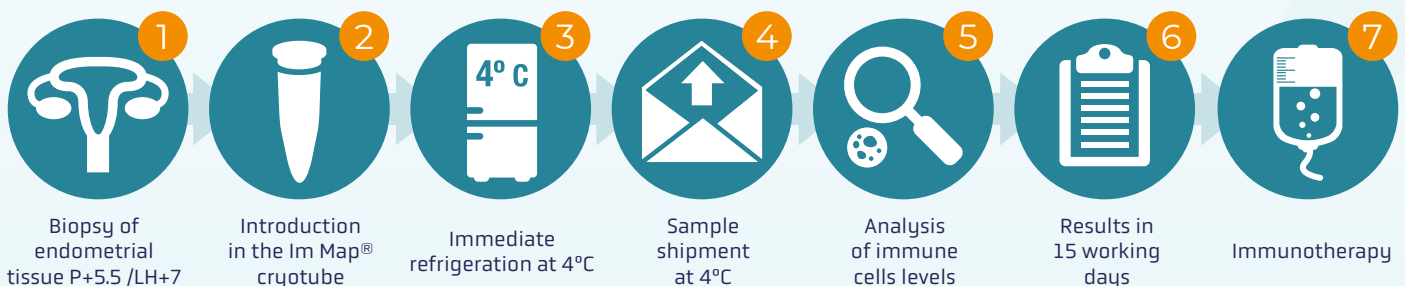
1. Cicinelli et al. 2017, 'Chronic endometritis in patients with unexplained infertility: Prevalence and effects of antibiotic treatment on spontaneous conception', Am J Reprod Immunol, 2018;79:e12782.
2. Vitagliano et al. 2022, 'Chronic Endometritis in Infertile Women: Impact of Untreated Disease, Plasma Cell Count and Antibiotic Therapy on IVF Outcome—A Systematic Review and Meta-Analysis', Diagnostics, 12, 2250.
3. Vomstein et al. 2022, 'Uterine microbiota plasticity during the menstrual cycle: Differences between healthy controls and patients with recurrent miscarriage or implantation failure', J. Reprod. Immunol, 151 (2022) 103634.
4. Moreno et al. 2022, 'Endometrial microbiota composition is associated with reproductive outcome in infertile patients', Microbiome, 10:1, 1–17.
5. Benner et al. 2018, 'How uterine microbiota might be responsible for a receptive, fertile endometrium', Hum. Reprod. Update, 24:4, 393–415.

Im Map[®] is a cellular test that determines immune populations in the endometrium.



Im Map[®] can identify the different immune subpopulations present in the endometrium, so that alterations in their levels can be identified and patients can be offered specific immunotherapy to restore the immune balance in the endometrium and increase foetal tolerance, implantation and the probability of a successful pregnancy.

The process



Tissue and vascular remodelling

Immune cells present in the endometrium are essential for the proper regulation of trophoblast invasion, tissue remodelling, angiogenesis and embryo growth. These processes are carried out through the specific secretion of fetal growth stimulating factors and tissue and vascular remodelling.

Altered levels and activation of immune subpopulations have been shown to be associated with impaired vascular and tissue remodelling causing implantation failure, miscarriages, as well as pre-eclampsia, preterm delivery and fetal growth restriction 1,2 .

Pro-inflammatory/anti-inflammatory balance

Immune cells secrete small proteins called cytokines that regulate the inflammatory state of the endometrium. These can be classified into pro-inflammatory cytokines, which act as active agents in the induction of the immune response, and anti-inflammatory cytokines, which regulate this response. The synthesis of both cytokines will allow the establishment of the pro-inflammatory/anti-inflammatory balance present in the endometrium during the implantation window.

The study of the pro-inflammatory/anti-inflammatory balance is essential, as, for successful implantation, the maternal endometrium must present a specific inflammatory state that promotes this process. Indeed, dysregulation of the pro-inflammatory/anti-inflammatory balance has been associated with pregnancy loss, preterm birth, or preeclampsia ³. Additionally, other studies have shown that women with recurrent miscarriages have increased levels of pro-inflammatory cytokine-producing cells compared to women with successful pregnancies ^{4,5,6}.

Fetal tolerance

The embryo expresses paternal components that can be recognized by the maternal immune system and may cause embryo rejection during pregnancy. To ensure reproductive success, the endometrial maternal-fetal area presents a characteristic immune profile that promotes immunosuppression and ensures fetal tolerance and survival ⁷.

Various studies have demonstrated how an alteration in the immune subpopulations involved in regulating the immune response, and consequently, a change in tolerance, occurs in patients who have suffered spontaneous miscarriages during the first trimester ⁸.

How do we test Im Map®?

This is carried out through an endometrial biopsy in the luteal phase for diagnosis.

The endometrial biopsy sample can be obtained in parallel with the biopsy for our endometrial receptivity analysis test, ER Map®, on LH+7 in a natural cycle, on P+5.5 in a substituted cycle, and hCG+7 in a modified natural cycle.

The samples are analyzed using multiparametric flow cytometry. Flow cytometry is a biophysical technology used to detect immunological markers and carry out the counting of cellular populations.

This technique allows for the simultaneous multiparametric analysis of the physical and chemical characteristics of millions of cells in just a few minutes. In cases where abnormal levels of immune cells are detected, various appropriate immunotherapy options can be offered for each patient.

1. Quenby S. et al. – Fertil Steril 2005, 84(4), 980–984.

2. Tuckerman E. et al. – Hum reprod 2007; 22: 2208–2213.

3. Saito S. et al. – Am J Reprod Immunol 2010 63(6), 601–610.

4. Kwark-Kim J.Y.H. et al. – Hum Reprod 2003; 18(4): 767–773.

5. Nakagawa K. et al. – Reprod Med Biol. 2017(16), 297–301.

6. Nakagawa K. et al. – Am J Reprod Immunol. 2019(82), e12142.

7. Sadeghpour S. et al. – Immunopharmacology and immunotoxicology. 2020; 42: 632–642.

8. Rafie M. et al. Iran. J. Immunol 2015 [12]: 251–262.



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