The human immune system (IS) is prepared to eliminate anything that it recognizes as foreign in order to offer appropriate protection against pathogens. During pregnancy, the mother’s IS faces an element—the embryo—which presents “non-self” antigens from the father in cases of pregnancies with their own eggs; or from the father and the donor in oocyte donation cases. The ability of the mother’s IS to “tolerate” the embryo, despite recognizing it as foreign, is essential to achieve a successful pregnancy.

Recent studies have revealed that alterations in the immunoregulatory mechanisms of the maternal response to the fetus may be responsible for some cases of female infertility, implantation failure or miscarriage.

KIR-HLAC genotyping is a genetic test that allows to assess the risks of the embryo being rejected by the maternal immune system, and thus to direct medical interventions in order to achieve a successful pregnancy.

**METHODOLOGY**

1. Blood sample from the couple (4ml)
2. Maintenance of blood samples at 4°C until shipping
3. Shipping of the sample at room temperature
4. KIR - HLAC genotyping
5. Results in 15 working days
What is KIR-HLAC genotyping?

There are several factors that are crucial to achieve a pregnancy: a good quality embryo, a uterus prepared to receive it and an adequate immune interaction between both to allow the embryo to implant and develop properly. Maternal immunotolerance towards the embryo is achieved through the interaction between the cells of the maternal immune system present in the uterus (called uterine NK cells) and the embryo. These cells recognize the embryo through receptors located on its surface called KIR, which attach to embryo identification fragments found on its surface called HLA-C, one inherited from the mother and another inherited from the father.

Several studies have shown that certain combinations of KIR and HLA-C are more likely to lead to complications in pregnancy\(^1\-^5\).

KIR and HLA-C genotyping allows determining whether there is a good compatibility between KIR uterine receptors and the "foreign" HLA-C presented by the embryo or not. If so, the process of maternal-fetal tolerance will develop correctly and the pregnancy will evolve without complications. Otherwise, if this compatibility between the embryonic HLA-C and KIR uterine receptors does not exist, the process of embryonic acceptance, and so the pregnancy, will be compromised.

What is KIR HLAC genotyping for?

KIR-HLAC genotyping allows to:

- Identify the cause of recurrent miscarriages and implantation failure.
- Decide the optimal number of embryos to transfer.
- Prevent possible complications during pregnancy.
- Choose a compatible donor for the future pregnant woman, in both, oocyte and sperm donation cases.

How is this test performed?

KIR-HLAC genotyping is performed on the couple’s DNAs. For this, a 4 ml blood sample (collected in a purple lid, EDTA-tube) from each member of the couple is required.

Once extracted, blood samples will be refrigerated at 4°C and shipped to our laboratory at room temperature. Once the sample has arrived, we will proceed to extract the genetic material of the couple and subsequently carry out KIR and HLA-C genotyping of the future mother, and HLA-C genotyping of the father.

In cases of oocyte or sperm donation, donor HLA-C genotyping is required.

What if a couple is KIR-HLAC incompatible?

In the field of fertility immunological incompatibilities may affect essential reproductive processes which, ultimately, may result in implantation failure, recurrent miscarriages and preeclampsia. Several studies have shown that severe pathologies associated with pregnancy increase significantly on pregnant women with an incompatible maternal-fetal combination\(^1\-^3,5\). When the combination of maternal KIR and HLA-C of the future embryo is incompatible, it is advisable to:

- Transfer a single embryo to avoid exposing the mother to a double load of incompatible HLA-C.
- Immunomodulatory treatment can also be prescribed to the expectant mother.
- In cases of oocyte or sperm donation, donor HLA-C genotype and maternal KIR matching is recommended to ensure maternal-fetal compatibility.

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