

## **Maternal KIR haplotype in donor egg ART**

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The successful adaptation to the semiallogeneic fetus is a complicated process. Maternal tolerance begins at the uterine level, where the local maternal immune system plays an essential role. The maternal immune system dominated by uterine NK (uNK) cells engages a molecular conversation with the embryo.

In oocyte-donation cycles, an increasingly demanded treatment due to advanced maternal age, the incidence of preeclampsia is very high (25%) compared to natural conception (3-5%) and this incidence is not only related to maternal age, as it has been observed even in young patients receiving oocyte-donation.

Assisted reproduction techniques (ART) pregnancies differ from spontaneous pregnancies because patients receive more than one embryo per transfer still in many cases, so more than one paternal (non self) genes per embryo will be expressed, also, donor oocytes, donor sperm, or donated embryos may be used. This implies that more non-self genes (not only paternal – which is obviously non self- but also from the donated oocytes or embryos) are presented to the maternal uterine cells per transfer when compared to spontaneous pregnancies. This overexpression of non self genes by the embryo could be an excessive load and induce poor placentation in some specific “maternal-embryo genes” combinations.

Moreover, the presentation of those embryo non-self genes to the mother’s uterine cells happens much more frequently than in spontaneous pregnancies, as embryo transfer (ET) can be performed even monthly in recurrent implantation failure (RIF) or RM patients.

The donor oocyte-maternal genes, which are different from the oocyte recipient (patient), behaves as a non self genes (similar as the paternal one); thus, the expression of two non-self or ‘paternal’ genes in the embryo is present at uterine level.

Novel findings (Alecsandru et al, 2014,2017) have shown that the combination between maternal and fetal genes (non self genes) have an impact on the live birth rate after IVF cycles, especially when double embryo transfer (DET) and egg donation is used.

A significant drop in LBR per transferred embryo was observed after a DET with donor oocytes in mother-embryo mismatch genetic combination.

The combination of maternal and paternal, donor genes could predict which couple could benefit for the specific donor selection, as it seems that some males or donors have a worst obstetrical outcome with increased risk of recurrent miscarriage and preeclampsia.

Therefore, selecting the right oocyte and/or sperm donors for patients undergoing egg donation, could be significantly more efficient and safer, it could contribute to shorten time to live birth, and minimize the risk of unwanted events such as recurrent miscarriage or preeclampsia and the associated prematurity.