

Underexpression of activating receptors by uterine NK cells is associated with failures of placental implantation

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Background

Insufficient placental implantation is associated with disorders of pregnancy that ultimately lead to preterm birth, including pre-eclampsia, intrauterine growth restriction and preterm labour. The uterine mucosa is rich in uterine NK cells, which are thought to promote placental implantation and individuals who possess the gene encoding the NK cell activating receptor, KIR2DS1, are at lower risk of pre-eclampsia. We will test the hypothesis that uterine NK cell expression of KIR2DS1 is associated with lower risk of pregnancy disorders characterised by failures of implantation.

Ref. Male & Moffett, 2023. Annu Rev Immunol 41:127

Approach

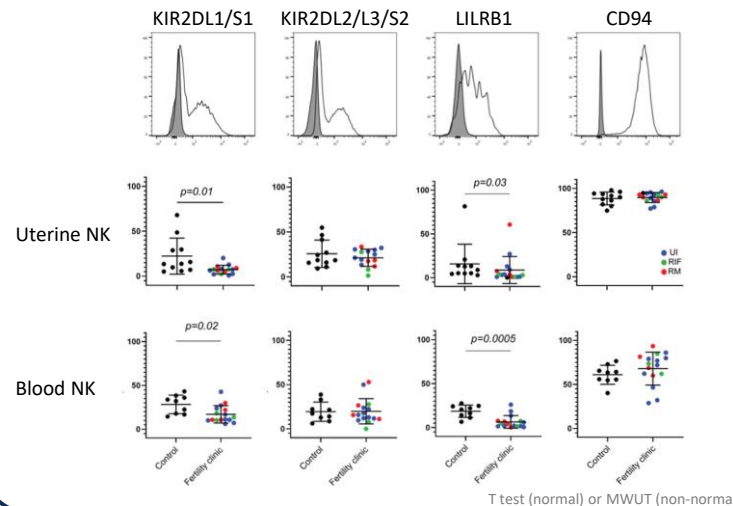
Patients attending the fertility clinic for

- Recurrent Implantation failure (3)
- Recurrent miscarriage (4)
- Unexplained infertility (9)

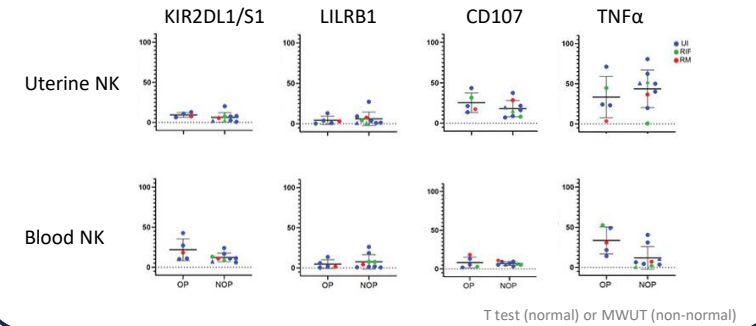
11 controls attending for contraceptive coil fitting

Isolate immune cells and analyse by flow cytometry

Patient NK cells express lower KIR2DL1/S1...



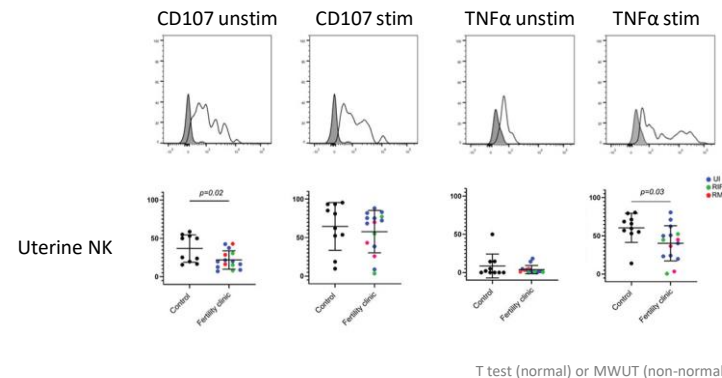
... but uNK parameters do not predict outcome



Implications

Our findings are consistent with previous studies suggesting that lack of expression of NK cell activating receptor KIR2DS1 is associated with failures of implantation, and we also found lower uterine NK cell activity associated with implantation failure. However, our finding that neither uterine NK cell KIR2DS1/L1 expression nor activity predicted pregnancy outcome raises the possibility that the association is not causal. Current work on larger cohorts aims to address this.

...and patient uNK cells are less active...



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