Pregnancy outcome affected by immune system genes

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A team of researchers, led by Ashley Moffett, at the University of Cambridge, United Kingdom, has shed new light on genetic factors that increase susceptibility to and provide protection from common disorders of pregnancy, specifically recurrent miscarriage, preeclampsia, and fetal growth restriction.

A key step in the initiation of a successful pregnancy is the invasion of the lining of the uterus by fetal cells known as trophoblasts, which become the main cell type of the placenta. Recurrent miscarriage, preeclampsia, and fetal growth restriction are thought to result from inadequate trophoblast invasion of the uterus lining.

Interactions between maternal cells known as uterine NK cells and fetal trophoblasts - specifically interactions between HLA-C molecules on the fetal trophoblasts and KIRs on the maternal uterine NK cells - are key to determining the extent of trophoblast invasion.

Previous data from Moffett's lab indicated that a particular combination of fetal HLA-C and maternal KIR was associated with increased risk of preeclampsia. In this study, the team has extended this correlation to recurrent miscarriage and fetal growth restriction. Furthermore, they have determined that the presence of other maternal KIRs that combine with the same HLA-C molecule provides protection against the same common disorders of pregnancy.

In an accompanying commentary, Peter Parham and Lisbeth Guethlein, at Stanford University, discuss the importance of these data and how they might explain distinct immune system gene expression patterns in different populations.

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