Treg/Th17 balance in murine embryo implantation and pregnancy

Context: Pregnancy implies recognition and tolerance of a foetal 'semi-allograft' by the maternal immune system, a complex process tightly regulated by the immune and endocrine systems.

Objective: This project focuses on two important types of CD4+ T cells, regulatory T (Treg) cells and T-helper 17 (Th17) cells and aims to a better understanding of the role played by their equilibrium in implantation and maternal tolerance of the embryo.

Methods: For the first part (estrous cycle), vaginal smears were performed on virgin mice females in order to determine the phase of the cycle. For the second part (pregnancy), an abortion-prone murine model was used. Pregnant females were killed at different days of pregnancy. Uteri of those mice were taken. Treg and Th17 cell frequencies were first measured by FACS analyses. Quantification of expression of Treg/Th17 specific factors was performed by RT-qPCR.

Results: RT-qPCR study revealed that some Treg and Th17 factors were modified across the cycle. During pregnancy, we did not observe any significant variation of Treg and Th17 cells between abortive and control matings at day 1.5. We observed significant differences between abortive and control mice at later stages of pregnancy. We studied neuropilin-1 expression in uterine Tregs and we observed a variation of the proportion of neuropilin-1 positive Treg cells (thymic Treg) across pregnancy.

Conclusions: Variation of Treg and Th17 factors during estrous cycle seems to imply a hormonal regulation of those cells. Uterine Treg and Th17 cells are not implicated in the early stages of murine spontaneous abortion but later during pregnancy. Thymic Treg (tTreg) cells predominate in cyclic uterus. During pregnancy, peripherally induced Treg (iTreg) cells predominate at the beginning of pregnancy while tTreg cells predominate during middle pregnancy.