COORDINATION OF IL-6Rα EXPRESSION OF CD4+ T CELLS BY TROPHOBLAST-DERIVED MVS. INDUCTION OF LOCAL IMMUNE TOLERANCE AT THE FETO-MATERNAL INTERFACE.

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Abstract

Background: Maternal immune tolerance requires the action of regulatory T cells at the feto-maternal interface, whose differentiation is influenced by the local cytokine milieu. Microvesicles (MVs) have been shown to mediate communication between the maternal immune system and the semiallograft fetus. The “Janus-faced” IL-6 plays a central role in the orchestrated immune response during gestation. It has seemingly dual and contradictory effects on the outcome of pregnancy. On the one hand, it is needed to promote the physiological processes in pregnancy, while on the other hand, it inhibits the differentiation of CD4+ lymphocytes toward regulatory T cells. Goals: We assumed that trophoblast-derived MVs regulate both the local cytokine production and the cytokine sensitivity of the lymphocytes.
Methods: We used multicolour flow cytometry for the assessment of induction of IL-6Rα expression in primary human T cells by BeWo choriocarcinoma cell-derived microvesicles, and for the characterization of their differentiation into Treg cells.
Results: In the present work we showed that 1) trophoblast-derived MVs induce IL-6 secretion of lymphocytes 2) we detected lower IL-6Rα expression of CD4+ T lymphocytes and higher IL-10 secretion, meaning that the inhibitory effect of IL-6 on regulatory T cell differentiation is diminished by trophoblast derived MVs. Considering that trophoblast derived MVs target maternal T cells, we propose that the negative influence of IL-6 on regulatory T cell differentiation is compensated by trophoblast derived MVs via the down-regulation of IL-6Rα expression of CD4+ T lymphocytes.
Conclusion: Therefore trophoblast derived MVs contribute to the establishment and maintenance of local maternal immune tolerance, which is a prerequisite for healthy pregnancy.