The role of T helper 1 and 2 subsets in the pathogenesis of endometrosis in mare.

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Mare endometrosis (endometrial fibrosis) leads to the destruction of tissue architecture and impairment of endometrial function. This condition is associated with early pregnancy dysfunction and embryo loss. The pathogenesis of endometrosis remains unclear. Studies carried out in different species and tissues indicate that T helper (Th) cell subsets contribute to development of fibrosis. Th1 and Th2 cell subsets seem to have an opposite effects in fibrotic processes. Interferon (IFN)γ secreted by Th1 acts as a antifibrotic factor, in contrast to IL-4 and IL-13 secreted by Th2. Therefore, Th cell subsets seems to play an important role in development of endometrial fibrosis in mare. Thus, the main hypotheses of this project are that (a) the endometrial ratio of Th1 and Th2 is altered in favor of the Th2 cell subsets in the course of endometrosis; (b) excessive number of cell subsets enhances development of equine endometrosis through the effect of interleukins characteristic for Th2 on extracellular matrix (ECM) components, myofibroblast differentiation and fibroblast properties such as migration and proliferation; (c) secretory products of Th1 cell subsets acts as antifibrotic agents by decreasing ECM components deposition, fibroblast migration and proliferation. The main objective of this project is to determine the effect of two types of Th cell subsets and their mediators on ECM remodeling in 3D fibroblast culture system and endometrial fibroblast properties. In the first aim, the determination of the changes in percentages of endometrial subsets of Th cells in the course of endometrosis in mare will be done. In the second aim, the role of Th cell subsets in processes associated to development of endometrial fibrosis will be investigated. Fibroblasts will be cocultured with Th1 and 2 cells. The expression of ECM components, MMPs and TIMPs will be determined. Additionally, fibroblasts will be co-cultured with Th1/2/17 cells to determine cell properties, (cell proliferation, migration, collagen gel contraction). In third aim, the effect of secretory products of Th cells on ECM remodeling and fibrogenesis in mare endometrial fibroblast will be determined. Fibroblasts culture in 3D culture system will be treated with IFNγ, IL-4 and IL-13. This project we will broaden basic knowledge about the interaction of T cell subsets and their secretory products with endometrial fibroblasts in the processes associated to the development of endometrial fibrosis in mare.