The interaction of T helper cell subset with endometrial fibroblasts in processes associated to development of mare endometrosis

Mare endometrosis (equine 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. Its pathogenesis is not well understood. The pathogenesis of fibrotic disorders is similar in diverse tissues but still tissue-specific.Studies carried out in different species and tissue indicate that T helper (Th) cell subsets contributes to development of fibrosis. Th1 and Th2 cell subset seems 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. In turn, Th17 cell subsets was shown to contribute to dermal and pulmonary fibrosis. Therefore, we suggest that Th cell subsets play an important role in development of endometrial fibrosis in mare. Thus, we put forward the hypotheses that (a) the endometrial ratio of Th1, Th2 and Th17 is altered in favor of the Th2 and Th17 cell subsets in the course of endometrosis; (b) excessive number of Th2 and Th17 cell subsets enhances development of equine endometrosis through the effect of interleukins characteristic for Th2/17 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 three types of Th cell subsets and their mediators on ECM remodeling in 3D fibroblast culture system and endometrial fibroblast properties. In our first aim, we will determine the changes in percentages of endometrial subsets of Th cells in the course of endometrosis in mare. In the second aim, we will investigated the role of Th cell subsets in processes associated to development of endometrial fibrosis. In third aim, the effect of secretory products of Th cells on ECM remodeling and fibrogenesis in mare endometrial fibroblast will be determined will be determined. This project we will broaden basic knowledge about the interaction of T cells and their secretory products with endometrial fibroblasts in the processes associated to the development of endometrial fibrosis in mare. We will establish *in vitro* model to described interaction between T cells and fibroblasts. This could become a starting point for other researchers to study these interaction in physiological and pathological conditions in other organs or endometrium. Far-reaching goal of this project is to provide to therapeutic strategy for mare endometrosis. Currently, it is difficult to provide satisfactory treatment for endometrosis. Understanding of the functions of individual types of Th cells and their effect on ECM remodeling in the context of their plasticity could result in the development of effective therapeutic strategies.