

The understanding molecular mechanism of interactions between macrophages and endometrial fibroblasts in processes related to pathogenesis of endometriosis in mares. (OPUS 19; NSC)

Project PI: dr Anna Szóstek-Mioduchowska

Project description:

Equine endometriosis (endometrial fibrosis, *chronic degenerative condition*) is defined as an active or inactive fibrotic process that develops around the endometrial glands and in the stroma, often associated with pathological alterations in the endometrial glands within fibrotic foci. Generally, fibrosis is characterized by excessive extracellular matrix (ECM) deposition and fibroblast activation. Inflammation is associated to development of fibrosis in a paracrine way by the secretion of profibrotic cytokines and other factors from injured tissues and inflammatory cells. Inflammatory mediators act on endometrial cells and then affect fibrogenesis and ECM remodeling. Macrophages (MΦ) are recruited at the sites of injury or infection and their secretion products affect the surrounding microenvironment. There are at least two different macrophages populations: “classically” activated MΦ1 and “alternatively” activated MΦ2. Both MΦ1 and MΦ2a have been noted to be involved in the pathogenesis of fibrosis in other organs. However, their effect on mare endometrial fibroblasts remains unclear. In our project, we put forward the hypotheses that (a) the endometrial ratio of MΦ1 and MΦ2a is altered in favor of MΦ2 in the course of endometriosis; (b) MΦ1 enhance development of equine endometriosis through effect on secretion of profibrotic inflammatory mediators from endometrial fibroblasts and on myofibroblast differentiation; (c) MΦ2a promote the development of endometriosis by increasing cell proliferation, migration, and deposition of extracellular matrix components (ECM); (d) the action of factors secreted by MΦ1 and MΦ2a is mediated by Hippo signaling pathways and action of metalloproteinase (MMP)-9. The specific objectives of the project include testing the effects of activated MΦ1 and MΦ2a on (1) processes associated with development of mare endometriosis; (2) global proteome and genome *in vitro* and *in vivo* condition and the effect of MMP-9 on equine endometrial fibroblasts in processes associated with development of endometriosis. The main objective of this project is to understand mechanisms underlying the initiation and progression of endometriosis with the aim of developing effective therapeutic strategies in treatment of endometriosis. It would be essential tool to improve horse reproductive efficiency, effective conservation and enhancement of animal genetic resources. Additionally, effective therapies to prevent or even to reverse existing fibrotic lesions are not yet available in any organ. Therefore, the understanding of the common fibrosis pathways would lead to development of these therapies in other organs and species.

Qualifications:

1. Master degree in biotechnology, biology, animal science, veterinary or related discipline;
2. Knowledge in the field of molecular biology, reproduction and immunology;
3. Knowledge in the following techniques: ELISA, Western blot, qPCR and immunofluorescence staining of proteins in the cell and cell culture.
4. Ability to communicate easily in English;
5. Ability to work in a group.