Building blocks and energy carriers in the course of mare endometrial fibrosis – identification of metabolic changes and the effect of inflammatory mediators

Mare endometrosis (endometrial fibrosis) leads to changes in tissue architecture and impairment in endometrial function. This condition is one of the main causes of early embryo mortality and thus infertility in mares, resulting in huge losses in the horse-breeding industry. The pathogenesis of endometrosis is not well understood. Fibrosis is a process that occurs in both humans and animals. The molecular mechanisms underlying fibrosis are similar in different tissues but are still tissue specific. Metabolomics is an analytical approach to study changes in the level of small molecules (metabolites) present in living cells. The results of recent studies indicate metabolic changes in lung, liver, kidney and skin fibrosis. The results of our previous study revealed changes in the expression of genes involved in multiple metabolic processes along with the development of fibrosis and possible involvement of interleukin (IL)-4 and IL-13 in the regulation of cellular metabolism. Thus, the objective of this research project is to investigate the metabolic changes occurring in the mare endometrium during the development of fibrosis. We aim to identify alterations in the metabolome profile at each stage of fibrosis and understand the impact of inflammatory mediators, such as IL-4 and IL-13 on the metabolic state of mare endometrial fibroblasts and the level of reactive oxygen species (ROS).

We assume that:

(1) metabolic reprogramming is a characteristic feature of endometrial fibrosis,
(2) IL-4 and IL-13 affect the metabolic state and the level of ROS in connective tissue cells – fibroblasts which are essential in fibrosis development.

The research task will include

(1) the establishment of the metabolome profile of healthy and fibrotic endometrium of the mare,
(2) the evaluation of the changes in endometrial fibroblasts cultured *in vitro* metabolome after treatment with IL-4 and IL-13, and
(3) the determination of the effect of IL-4 and IL-13 on ROS production in mare endometrial fibroblasts.

As part of the project, we will broaden the basic knowledge about the changes in metabolic profile in the mare endometrium at every stage of fibrosis and the potential involvement of IL-4 and IL-13 in the regulation of cellular metabolism. This could become the starting point for other researchers in investigation into endometrial and another organ fibrosis. The results of this project will form the basis for further research to develop an effective treatment for endometrosis in mares by understanding the changes in metabolic processes in the course of endometrosis.