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Szkoła Główna Gospodarstwa Wiejskiego

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Ekspresja mRNA czynników wzrostu i transformacji fibroblastów w błonie śluzowej macicy klaczy względem nasilenia endometrozy i zmian histopatologicznych

Expression of mRNA of growth factors and fibroblast transformation markers in equine endometrium regarding endometrosis severity and occurrence of histopathological lesions

Rozprawa doktorska

Doctoral thesis

Rozprawa doktorska wykonana pod kierunkiem

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Summary

Horses, among other farm animals, have the lowest fertility rates, which may be caused by age–associated abnormalities. Uterine diseases are considered the main cause of decreased fertility in mares. Endometrosis, a degenerative process in endometrium is associated with fibrosis of extracellular matrix (ECM) and degeneration of endometrial glands, which is associated with decreased histotroph production, resulting in early embryonic death. Diagnosis can be performed only using histopathological assessment of endometrial biopsy. The disease may be categorized with Kenney and Doig classification system depending on severity of lesions. Pathogenesis of endometrosis is yet unknown, while the only confirmed risk factor is age. Thus, aims of this study are: assessment of the impact of *THY1*, *IGF1*, *PDGFRA*, and *MKI67* expression on the severity of endometrosis, occurrence of histopathological changes in endometrium affected by endometrosis, assessment of interactions between them, interactions between their expression of reference genes known for their involvement in endometrosis, as well as interactions between their expression and histopathological changes in endometrium affected by endometrosis. 47 full–thickness uterine sections were collected post–mortem. They were used to prepare histological slides stained with hematoxylin and eosin, and to quantify gene expression of *THY1*, *IGF1*, *PDGFRA*, *MKI67*, *TGFB1*, *ACTA2*, *ESR1,* and *PGR* with qPCR. Histological slides were categorized according to Kenney and Doig. Apart from that, all present endometrial lesions were evaluated separately, including morphological alterations and inflammatory infiltration. *THY1* expression increases in the early stages of endometrosis and with the destruction of the basement membrane, suggesting that THY1 influences enhanced cell interaction with the ECM and intensifies signaling via extracellular vesicles. *IGF1* expression is negatively correlated with the histopathological criteria for assessing endometrosis, including the severity of inflammatory infiltration, suggesting a reduced influence of IGF1 on degenerated endometrium and inhibition of regenerative processes. *PDGFRA* expression is positively correlated with *ACTA2*, *MKI67*, *THY1*, and *ESR1* expression, suggesting the involvement of PDGFRα–related signaling in fibroblast differentiation and activation. The evaluation of co–occurring histopathological changes in endometrium affected by endometrosis may be a useful diagnostic tool in assessing disease progression.

Key words: *endometrosis, pathogenesis, Thy1, IGF1*, *PDGFRα, Ki67, equine*