ABSTRACT

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Equine Metabolic Syndrome (EMS) is a disease stemming from insulin resistance and deregulation of the insulin signalling pathway. The key organ in the development of insulin resistance is the liver, which due to its function is often referred to as the metabolic centre of the organism. The clinical symptoms of equine metabolic syndrome include insulin resistance, impaired hepatic metabolism, obesity and regional fat deposits, hyperinsulinemia, hypoadiponectinemia, hyperleptinemia, systemic inflammation and hypertension. Laminitis is one of the most severe manifestations of insulin resistance and equine metabolic syndrome. In recent years, the interest in stem cells has increased significantly, in terms of their participation in the pathophysiology of equine metabolic syndrome and laminitis, as well as due to their significant therapeutic potential,. Additionally, a new group of relatively newly discovered biomarkers is the subject of many studies on insulin resistance, as well as other diseases, namely non-coding RNAs (ncRNAs - non-coding RNAs), such as miRNAs (micro-RNAs) and lncRNAs (long non-coding RNAs - long non-coding RNAs).

The aim of the research conducted as part of the doctoral thesis was to select potential miRNA and lncRNA markers that can be used as specific and precise biomarkers of diseases associated with insulin resistance. In addition, the research hypothesis assumed that stem cells of the coronary corium – HPC (*Hoof Progenitor Cells*) are involved in the pathophysiology of laminitis and that the analysis of their response to the inflammatory process and hyperinsulinemia in terms of their unique miRNA secretome can provide valuable information on the pathophysiology of laminitis, its potential diagnosis and therapy. Based on the most recent literature, 6 promising non-coding miRNAs and lncRNAs were selected, which may be sensitive and specific biomarkers of hepatic insulin resistance and metabolic diseases. As part of the conducted research, the process of isolating HPC cells from the area of the coronary

corium was also developed. The morphology, proliferation, differentiation, oxidative stress, mitochondrial metabolism, inflammatory response, apoptosis and unique miRNA secretome of HPC cells were characterized in comparison to the ASC cell model (*Adipose Stem Cells*). Moreover, an assessment of the response of HPC cells to the inflammatory environment and hyperinsulinemia was performed, due to their potential participation in the pathophysiology of the laminitis.

The obtained results of the latest research reports analysis as well as the conducted research indicate that non-coding RNAs are precise biomarkers related to insulin resistance and that the newly isolated and characterized population of HPC cells may play a role in the regeneration of the dermis and epidermis injuries as well as regeneration of the damage to blood vessels occurring during laminitis. Moreover, the results of the conducted research show that the selected miRNAs may have diagnostic and therapeutic potential in the course of laminitis, due to the change in their expression in HPC cells in the course of inflammation and hyperinsulinemia.