Abstract

Hypoxia inducible factor 1 alpha (HIF1A) is a transcriptional factor, which plays a central role in the maintenance of homeostasis under hypoxic conditions. It regulates a wide variety of genes encoding proteins that influence metabolism, extracellular matrix composition, oxidoreductase activity or angiogenesis in response to reduced oxygen levels. When HIF1A protein function is impaired, the organism is unable respond appropriately to hypoxia. Altered HIF1A regulation can result in severe tissue damage and eventually lead to death.

The heart, as an organ with a huge oxygen consumption, is susceptible to various pathologies caused by hypoxic stress. The role of HIF1A in the heart is rather ambiguous and remains to be elucidated. It plays a role in cardioprotective mechanisms but also promotes the development of inflammation and apoptosis. This thesis aims to clarify the role of HIF1A in maintaining physiological functions of the heart during adaptation to hypoxic conditions using a mouse model with heterozygous *Hif1a*$^{+/-}$ deletion. Experiments involving molecular and cell biology methods performed on left ventricular tissue were preceded by bioinformatic analysis of data obtained by RNA sequencing of isolated cardiomyocytes. RNA sequencing data were analyzed using the R scripting language (packages dplyr, DESeq2), software Cytoscape, and a literary search. This approach helped to select candidate genes affected by hypoxia and *Hif1a* mutation for further validation.The results obtained by RNA sequencing, quantitative PCR, Western blot and immunohistochemistry suggest a role for HIF1A in three different processes. First, there are changes in the expression of genes that mediate immune response and inflammation. In the case of global heterozygous deletion of *Hif1a*$^{+/-}$, the migratory capacity of macrophages is impaired. Second, the composition of extracellular matrix is altered – the expression of collagen I and collagen III is upregulated in *Hif1a*$^{+/-}$ mutant. Third, pathways related to metabolism and mitophagy are deregulated; in *Wt* mice in hypoxia the amount of mitochondria is lowered, whereas this response is absent in the deletion mutant.

Key words: heart, cardiomyocytes, HIF1A, hypoxia, transcription factor, RNA sequencing