**ABSTRACT IN ENGLISH**

The ischemia-reperfusion (I/R) injury, which is a consequence of myocardial infarction, represents a major cause of death worldwide. One of the most effective cardioprotective interventions increasing the resistance of hearts to the I/R injury is the adaptation to a chronic hypoxia (CH). However, the molecular mechanisms of CH are still not well understood. The most important factors responsible for the I/R injury are reactive oxygen species (ROS) produced by complexes I and III within the mitochondrial electron transport chain. Potential candidates maintaining ROS at a low level are mitochondrial creatine kinase (mtCK) and two hexokinase isoforms (HK1 and HK2). These enzymes highly support the mitochondrial oxidative phosphorylation by increasing the availability of ADP for complex V of the respiratory chain. In addition, the HK binding to mitochondria inhibits binding of the pro-apoptotic protein BAX, thereby protecting cardiac cells against apoptosis. Besides the mitochondrial CK isoform, there are two cytosolic CK (CKM and CKB) present in cardiomyocytes that help to maintain energy homeostasis. Based on the known anatomical and physiological differences between the left (LV) and the right (RV) ventricles, the first study focused on the comparing ventricles in terms of the energy metabolism and the HK co-localization with mitochondria. Further, the level of activated AKT kinase, which facilitates interaction of HK2 with mitochondrial membrane, was determined. The results of this study indicate that the RV has a higher activity of aerobic glycolytic metabolism and may be able to respond faster and more powerfully to stressful stimuli than the LV. The results also suggest that AKT activation is a necessary but not a sufficient condition for the enhancement of the interaction of HK2 with mitochondria and that yet another mechanism may be involved. Next, this study aimed at the effect of the normobaric hypoxia on the CK and HK expressions and enzyme activities and the HK co-localization with mitochondria in both ventricles. Rats were adapted for 3 weeks to protective and non-protective regimens of 10% normobaric hypoxia. The results showed that the adaptation to the normobaric hypoxia leads to the activation of glycolysis and phosphocreatine (PCr)/CK system to maintain energy homeostasis under the reduced oxygen concentration. This may suggest that CK and HK can be involved in the stimulation of the oxidative phosphorylation, which reduces the production of ROS. Although no differences were found between protective and non-protective phenotypes, it cannot be ruled out that CK and HK may play a role in the cardioprotective mechanisms induced by the normobaric hypoxia. Interestingly, HK1 and HK2 co-localizations with mitochondria remained unchanged in the LV as well as in the RV after adaptation of rats to a protective regimen,

continuous normobaric hypoxia (CNH), suggesting a stabilization of the HK bond with mitochondria. Then, rats adapted to CNH were subjected to the I/R insult. The HK activity significantly increased in the CNH LV after the I/R insult, which can suggest that the HK can possibly participate in the establishment of the ischemia-resistant phenotype of chronically hypoxic hearts. Finally, the last objective of the study was to investigate the role of CK and HK enzymes in the LV and RV of rats adapted to a hypobaric hypoxia (7000 m). The hypobaric hypoxia represents a greater stress for the myocardium compared to the normobaric hypoxia. The results verified the response of energy metabolism to the reduced oxygen level independently on the degree of stress. In addition, the HK1 and HK2 co-localizations with mitochondria markedly increased in both ventricles after adaptation of rats to hypobaric hypoxia, which was confirmed by the immunofluorescence technique as well as by the fractionation and Western blot method. In conclusion, the protective mechanism of the HK, which lies in its binding with mitochondria, seems to be activated under the hypoxia which is marginal for the fatal cell damage, representing by present hypobaric model. This dissertation study provides a novel insight in the CK and HK function and co-operation under different hypoxic adaptations. And it also provides new information related to cardioprotective mechanisms of adaptation to hypobaric hypoxia, which includes increased binding of the HK with mitochondria. Targeting the HK binding with mitochondria thus represents a potential approach for future therapeutic uses.