

## 2. Abstract

Adaptation to chronic hypoxia is in addition to ischemic preconditioning one of the two known cardioprotective mechanisms. The precise molecular basis of these processes is still not fully explained. There are some studies that suggest the possible involvement of the adenosinergic signaling system in this adaptation.

In this work, we focused on the characterization of the adenosinergic system in the myocardium of rats adapted to two regimens of chronic hypoxia - a protective continuous normobaric hypoxia (CNH) and non-protective intermittent hypoxia (INH/R, 23 h hypoxia and 1 h normoxia). Initially, we compared the total amount of adenosine receptors in samples from different groups of adapted animals. We discovered changes mainly at A<sub>2B</sub> receptor, which increased at CNH and declined in INH/R. This result suggests the possible involvement of A<sub>2B</sub> receptors in cardioprotection afforded by adaptation to chronic hypoxia.

Furthermore, we investigated the distribution of various types of adenosine receptors and transporters in the plasma membrane of cardiac cells. We observed that A<sub>2A</sub> and A<sub>3</sub> localize in membrane microdomains together with membrane enzyme CD73 that produces adenosine in the extracellular space by degrading AMP. A<sub>1</sub> and A<sub>2B</sub> receptors similarly as nucleoside transporters ENT1, ENT2 and CNT2 were localized rather in the bulk (non-raft) plasma membrane fraction. These results indicate that the selection of a given adenosine receptor for signaling may be associated with the origin of adenosine released as a signaling molecule.

**Keywords:** adenosine adenosine receptors, adenosine transporters, chronic hypoxia, heart