Summary

Cardiac ischemia is one of the most frequent causes of death in Hungary. In case of oxygen supply injure can cause serious injuries. The aims of our studies were to investigate of pathological mechanism forming in consequence of ischemia/reperfusion and pharmacological approaches.

In the first part of our experiments we examined the protective effect of CO applying different concentration CO treatment. Our results show that low concentrations of exogenous CO protect the isolated ischemis/reperfused heart and act by increasing cAMP and cGMP levels in the myocardium. The significant increase in cGMP levels related to guanylate cyclase activities in CO-treated hearts, and suggests that CO-induced elevation by the guanylate cyclase-cGMP system is essential for cardioprotection.

Carbon monoxide (CO) carriers have been recently developed as a pharmacological tool to simulate the effect of heme oxygenase-1-derived CO. Hearts were treated with different doses of CORM-3, which is third generic CO releasing molecule. The results demonstrate that CO liberated from CORM-3 markedly influences the balance of important ions and, as a consequence of its effect, provides cardiac protection against tissue damage and myocardial dysfunction inflicted by ischemia-reperfusion. Indeed, hearts treated with CORM-3 were less susceptible to potentially life-threatening arrhythmias, as evidenced by the reduced incidence of VF and VT during reperfusion. The observed protection against the incidence of arrhythmias by CORM-3 was proved by a significant reduction in infarct size and improvement in post-ischemic cardiac function.

In the third part of our experiment we investigated the role of TG2 enzyme in the ischemia/reperfusion. Our dates imply that in $TG2^{-/-}$ hearts the maintenance of the high energy-phosphate content is impaired during ischemia/reperfusion. This defect could reflect a failure in mitochondrial ATP production. We precluded the possibility that signal mediated by alpha-1b-adrenergic receptor (AR) would take in part the increasing of sensitivity regarding ischemia/reperfusion. These data provide evidence for a novel function of TG2 participating in the maintenance of the intact mitochondrial respiratory function, the absence of which leads to a serious failure in ATP production.