miR-324 contributes to Urocortin modulation of apoptosis during myocardial ischemia and reperfusion

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Background/Introduction: Compelling evidences have confirmed the important role of microRNAs as regulators of different cardiovascular processes. However, little is known about their role in cardiac protection against myocardial ischemia and reperfusion (I/R) injuries.

Purpose: The objective of this study was to examine the role of miR-324 in the cardioprotection afforded by urocortin (Ucn-1) added in reperfusion.

Methods: Ucn-1 was infused at the onset of reperfusion in vivo in Wistar rat subjected to transient left coronary artery ligation (40 minutes) to induce I/R, and in vitro in isolated cardiac myocytes undergoing simulated protocol of I/R.

Results: The administration of Ucn-1 significantly restored cardiac function, as evidenced by the recovery of ejection and shortening fractions, which confirm the cardioprotective effect of Ucn-1. Moreover, the addition of Ucn-1 to isolated cardiac myocytes undergoing I/R protocol enhanced cells viability, prevented necrosis but it stimulated apoptosis. Next, we found that the addition of Ucn-1 in reperfusion, significantly enhanced the expression of miR-324, both in animal model and in isolated cardiac myocytes. These observed upregulation of miR-324 by Ucn-1 involved the activation of corticotropin-releasing factor receptor-2, Epac2 and ERK1/2. Moreover, the transfection of cardiac myocyte with miR-324 mimics promoted significant dysregulation of several genes’ expression involved in cell death and apoptosis such as STAT2 and BIM, which confirmed the observed effect of Ucn-1 on apoptosis.

Conclusion: Our data unveil a novel role of urocortin in myocardial protection and apoptosis, involving posttranscriptional regulation with miR-324.