

Knockdown of AMI-related circRCAN2 with siRNAs to elucidate its role during ischemia in porcine cardiac progenitor cells *in vitro*

Kastner N, Mester-Tonczar J, Einzinger P, Traxler D, Hasimbegovic E, Riesenhuber M, Spannbauer A, Zlabinger K, Gyöngyösi M

- Circular RNAs (circRNAs) are non-coding RNAs which functions and role in myocardial infarction are still unknown. RNA-sequencing of the long noncoding circular RNA (circRNA) in our previous pre-clinical experiment revealed that porcine myocardial infarcted tissue exerts significantly differently expressed circRCAN2 as compared to nonischemic porcine heart tissue. Therefore we aimed to elucidate its circular function by knock-down of circRCAN2 by siRNA.

Results

- Lipofectamine transfection with a high concentration of siRNA achieved knockdown of circRCAN2 in pCPCs
- Proliferation markers Ki67 and RhoA were significantly upregulated in normoxic knockdown pCPCs (groups 24h-KD-pCPC and 48h-KD-pCPC) in comparison to untreated pCPCs, which effect was completely abolished after hypoxia.
- Knockdown of circRCAN2 did not affect the expression of the apoptosis marker Cas3 under normoxia, but it led to significant downregulation of Cas3 expression under hypoxia (Fig. 2).

Conclusion

- Knockdown of circRCAN2 in pCPCs led to significant upregulation of the proliferation markers Ki67 and RhoA under normoxic condition, while additional hypoxia revoked it, and resulted in downregulation of the apoptosis marker. Our data suggest a promising opportunity for circRCAN2 as new therapeutic target in patients with heart failure of ischemic and non-ischemic origin.

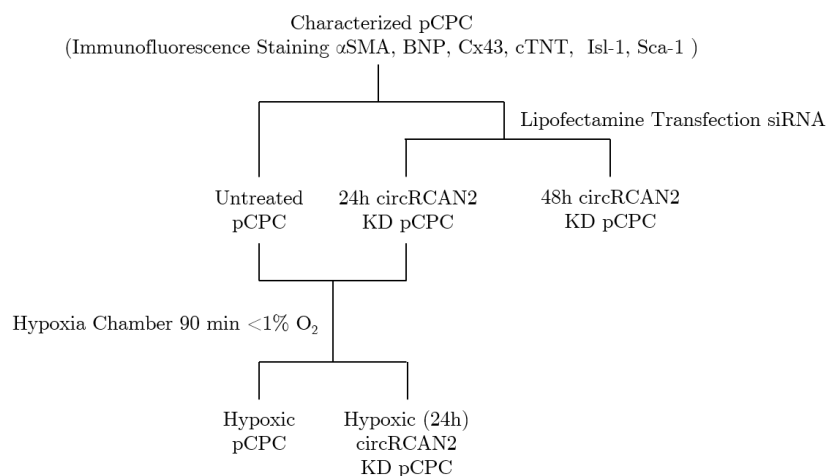


Fig1: Study Design of circRCAN2 knockdown (KD) in pCPCs.

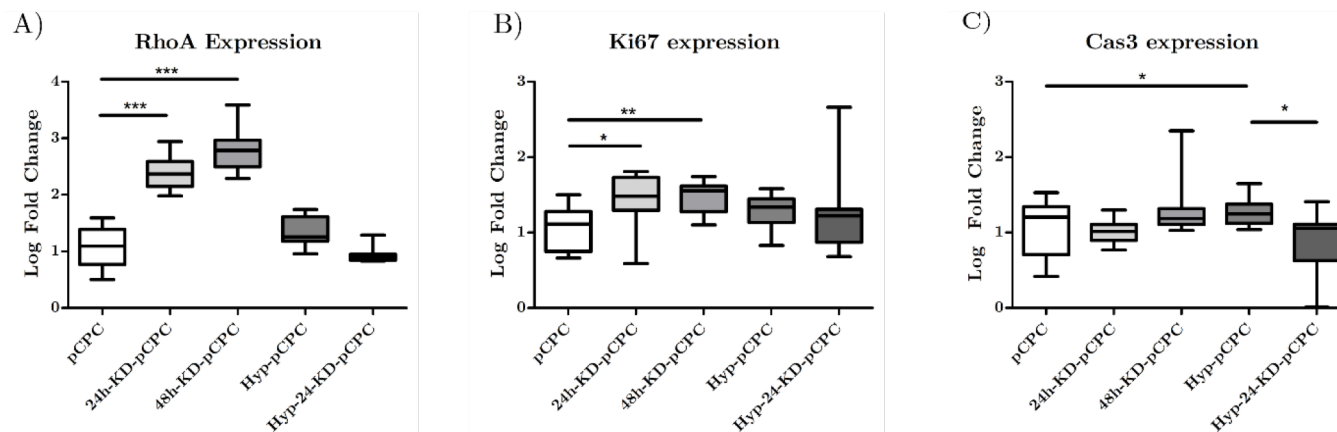


Fig2: Log Fold Changes of Gene Expression in pCPC (untreated normoxic pCPC), 24h-KD-pCPC (24h knockdown of circRCAN2 of pCPCs), 48h-KD-pCPC (48h knockdown of circRCAN2 of pCPCs), untreated Hypo-pCPC (hypoxic pCPCs) and Hypo-24-KD-pCPC (24h knockdown of circRCAN2 of pCPCs).

A) RhoA expression. B) Ki67 expression. C) Cas3 expression