Abstract: **P529**

calreticulin mediated cardioprotection of CTRP3 against I/R injury

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Topic(s):
Ischemia, Infarction, Cardioprotection

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Background
The underlying mechanisms of cardioprotection of C1q tumor necrosis factor-related protein 3 (CTRP3) against ischemia/reperfusion (I/R) injury remain largely unknown. The present study aimed to investigate whether calreticulin (CRT) mediated CTRP3’s cardioprotection against I/R injury.

Method and results
We inhibited mice cardiac CRT expression via intra-myocardial injection of CRT SiRNA, performed transient LAD ligation, measured the cardiac function, apoptosis and oxidative stress to identify CRT’s effects on cardioprotective actions of CTRP3 against I/R injury in vivo. LDH release and expression of CRT were measured in neonatal cardiomyocytes (NCM) subjected to simulated I/R (SI/R) and CTRP3. CRT specific SiRNA was also utilized in vitro. CRT inhibition partially blunted cardioprotection of CTRP3 against I/R injury (evidenced by left ventricular ejection fraction and myocardial infarct size). It also blunted CTRP3’s function against I/R induced apoptosis and oxidative stress (evidenced by TUNEL positive staining and reactive oxygen species production). In addition, SI/R increased LDH release, and administration of CTRP3 attenuated SI/R-induced cell death significantly. However, neither SI/R nor CTRP3 altered CRT expression in NCM. Inhibition of CRT expression blunted cardioprotective action of CTRP3 against SI/R induced apoptotic events (evidenced by TUNEL positive staining, LDH release and Caspase 3 activity). Furthermore, CRT inhibition significantly blunted CTRP3’s anti-oxidative action (evidenced by gp91phox expression and superoxide generation). However, CRT inhibition did not attenuate AMPK phosphorylation by CTRP3 administration in NCM.

Conclusion
Therefore, these novel findings strongly indicate that CTRP3 exerts cardioprotective effects against I/R injury partially via CRT mediated anti-apoptotic and anti-oxidative actions.
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