

**Objectives** Evidence exists that the increase of TNF $\alpha$  is associated with reperfusion injury in patients with myocardial infarction after PCI. Adiponectin (APN) is anti-inflammatory and cardioprotective protein suppressed by TNF $\alpha$ , and is significantly reduced during MI/R. Whether neutralising TNF $\alpha$  protects against MI/R injury through upregulation of APN level has not been previously investigated.

**Methods and Results** Adult male C57 mice were subjected to 30 min MI followed by 3h or 24h reperfusion or sham MI/R for this study. Etanercept, a TNF $\alpha$  neutralising drug for treating rheumatoid arthritis in clinic, was intraperitoneally injected 10 min before reperfusion. Etanercept administration ameliorated MI/R injury evidenced by increased cardiac function (1 day, 7 day, 14 day  $p < 0.05$  vs vehicle), reduced infarct size ( $p < 0.05$  vs vehicle) and apoptosis ( $p < 0.01$  vs vehicle). Etanercept significantly increased plasma APN concentration at 3 h, 8 h, 1 day and 3 days after reperfusion, respectively (all  $p < 0.05$  vs vehicle) and pAMPK/AMPK ratio at 3 h in myocardium ( $p < 0.05$  vs vehicle). To further investigate whether Etanercept attenuated MI/R injury is related to the APN signalling, additional experiments were performed. Firstly, the siRNA was used to knockdown (KD) the APN receptor 1 & receptor 2 (APN-R1&2) by intramyocardial injection 48 h before MI/R in vivo. APN receptor knockdown attenuated the cardioprotective effect induced by Etanercept supported by decreased infarct size (10% decrease in KD+Etanercept vs 25% decrease in WT+Etanercept), apoptosis (caspase-3 activity 21% vs 35% reduction) and lower pAMPK/AMPK ratio. second, the ob/ob mice, which APN signalling is impaired, were subjected to the MI/R following the same procedure. The cardioprotective effect of Etanercept was attenuated in the ob/ob mice compared with the wild type mice as well.

**Conclusions** Overall, we have demonstrated for the first time that upregulating of adiponectin is involved in the cardioprotective effect of Etanercept, suggesting that using a single administration of Etanercept during PCI might improve the outcome of myocardial infarction patients.

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**UPREGULATION OF ADIPONECTIN IS INVOLVED IN THE CARDIOPROTECTIVE EFFECT OF ETANERCEPT IN MYOCARDIAL ISCHEMIA/REPERFUSION (MI/R) MICE**

Chao Gao, Yi Liu, Qiang Yang, Jingyi Liu, Peilin Liu, Han Wang, Yunping Guo, Lijian Zhang, Sun Lu, Yang Lu, Haichang Wang, Ling Tao *Department of Cardiology, Xijing Hospital, Fourth Military Medical University, Xijing, China*