Objectives Evidence exists that the increase of TNF α is associated with reperfusion injury in patients with myocardial infarction after PCI. Adiponectin (APN) is anti-inflammatory and cardioprotective protein suppressed by TNF α , and is significantly reduced during MI/R. Whether neutralising TNF α 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 α 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

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