in type 2 diabetes provides a strong link between the high fat phenotype, and reduced energetic capacity of type 2 diabetic mitochondria.

Furthermore, delaying the activation of A1AR to 15 or 30 min post-reperfusion significantly reduced infarct size compared to IR control.

The co-administration of DPCPX (200 nM) with 2′-MeCCPA (10 nM) at the onset of reperfusion significantly attenuated the 2′-MeCCPA mediated infarct. The concomitant administration of 2′-MeCCPA with DPCPX at either 15 or 30 min post-reperfusion also abrogated 2′-MeCCPA induced cardioprotection.

Co-administration of Wortmannin (100 nM) with 2′-MeCCPA (10 nM) at the onset of reperfusion also significantly reduced the 2′-MeCCPA mediated infarct size as well as the co-administration at 15 or 30 min post-reperfusion reversed the cardioprotection.

Conclusion This is the first study to display how 2′-MeCCPA, a highly selective A1AR agonist, when administered at reperfusion, 15 or 30 min post-reperfusion can limit the infarct size development and how the RISK cell signalling pathway is also associated with cardioprotection.

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ADENOSINE A1 RECEPTOR ACTIVATION CAN PROTECT THE MYOCARDIUM FROM ISCHAEMIA REPERFUSION INJURY POST REPERFUSION

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**Introduction**

In response to ischemia, type 2 diabetic hearts are less able to upregulate anaerobic glycolysis and show poorer contractile function. Pharmacological activation of Hypoxia-Inducible Factor (HIF) may be beneficial for the diabetic heart, as it may promote glycolysis, improve function and tolerance of ischemia.

Methods Control and type 2 diabetic rats were given five oral doses (5 mg/kg daily) of PHD-selective HIF activator BAY85-3934. Hearts were perfused ex vivo and subjected to low-flow (0.35 ml/min/gw) ischaemia-reperfusion (IR). Glycolysis, palmitic acid oxidation and function were measured throughout. Mitochondrial oxidation was measured in isolated mitochondria using a Clark-type electrode.

**Results**

Diabetic hearts showed decreased rate-pressure product following ischemia-reperfusion. Pre-treatment with BAY85-3934 resulted in increased glycolytic rate in diabetic hearts, paired with improved functional recovery post-IR. BAY85-3934 treated diabetic rats showed increased hematocrit, indicating systemic activation of HIF signalling. Blood glucose levels remained unchanged with treatment despite changes in cardiac glycolytic rate.

**Conclusion**

This study has shown that treatment with HIF activators may provide a novel avenue to improve metabolism and functional recovery in the diabetic heart following ischemia-reperfusion.