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N-Acetylcysteine And Allopurinol Up-regulated the Jak/STAT3 and PI3K/Akt pathway via Adiponectin and Attenuated Myocardial Post-Ischemic Injury In Diabetes

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Abstract

N-acetylcysteine (NAC) and allopurinol (ALP) synergistically reduce myocardial ischemia reperfusion (MI/R) injury in diabetes. However, the mechanism is unclear. We postulated that NAC and ALP attenuated diabetic MI/R injury by up-regulating phosphatidylinositol 3-kinase/Akt (PI3K/Akt) and Janus kinase 2/signal transducer and activator of transcription-3 (JAK2/STAT3) pathways subsequent to adiponectin (APN) activation. Control (C) or streptozotocin-induced diabetic rats (D) were untreated or treated with NAC and ALP followed by MI/R. D rats displayed larger infarct size accompanied by decreased phosphorylation of Akt, STAT3 and decreased cardiac nitric oxide (NO) and APN levels. NAC and ALP decreased MI/R injury in D rats, enhanced phosphorylation of Akt and STAT3 and increased NO and APN. High glucose and hypoxia/reoxygenation exposure induced cell death and Akt and STAT3 inactivation in cultured cardiomyocytes, which was prevented by NAC and ALP. PI3K inhibitor wortmannin and Jak2 inhibitor AG490, abolished the protection of NAC and ALP. Similarly, APN restored post-hypoxic Akt and STAT3 activation and decreased cell death in cardiomyocytes. Gene silencing with AdipoR2 siRNA or STAT3 siRNA but not AdipoR1 siRNA abolished the protection of NAC and ALP. In conclusion, NAC and ALP prevented diabetic MI/R injury through PI3K/Akt and Jak2/STAT3 and that cardiac APN may serve as a mediator via AdipoR2 in this process.

Biography

Tingting Wang has completed her Ph.D at the age of 27 years from Wuhan University. During Ph.D studies, she got research training in the Uniformed Services University of the Hearth Sciences in USA for 18 months. Then she has completed her postdoctoral studies from the University of Hong Kong. Now she is an anesthesiologist in Wuhan Union Hospital which is one of the first-class comprehensive hospitals in China. She has published more than 10 research papers in reputed journals and serving as the prestigious reviewer for the Diabetes & Metabolism.