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Research Article

Prokineticin 2 (PK2) Rescues Cardiomyocytes from High Glucose/High Palmitic Acid-Induced Damage by Regulating the AKT/GSK3β Pathway In Vitro

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Prokineticin 2 (PK2) is a small 8 kDa protein that participates in many physiological processes, such as angiogenesis, inflammation, and neurogenesis. This experiment investigated the effect of PK2 on high glucose/high palmitic acid-induced oxidative stress, apoptosis, and autophagy in cardiomyocytes and the AKT/GSK3β signalling pathway. H9c2 cells were exposed to normal and high concentrations (33 mM) of glucose and palmitic acid (150 μM) with or without PK2 (10 nM) for 48 h. Reactive oxygen species were detected using the fluorescent probes DCFH-DA and DHE. Changes in apoptosis were assessed using flow cytometry, and autophagosomes were detected using Ad-GFP-LC3. Apoptotic proteins, such as Cleaved Caspase3, Bax, and Bcl-2; autophagy proteins, including Beclin-1 and LC3B; and PK2/PKR/AKT/GSK3β signals were evaluated using western blotting. Cardiomyocytes exposed to high glucose/high palmitic acid exhibited increases in intracellular ROS, apoptosis, and autophagosomes, and these increases were robustly prevented by PK2. In addition, high glucose/high palmitic acid remarkably suppressed PK2, PKR1, and PKR2 expression and p-AKT/AKT and p-GSK3β/GSK3β ratios, and these effects were significantly prevented by PK2. Moreover, an AKT1/2 kinase inhibitor (AKT inhibitor, 10 μM) blocked the effects of PK2 on the changes in cardiomyocyte exposure to high glucose/high palmitic acid. These results suggest that PK2 attenuates high glucose/high palmitic acid-induced cardiomyocyte apoptosis by inhibiting oxidative stress and autophagosome accumulation and that this protective effect is most likely mediated by the AKT-related signalling pathway.

1. Introduction

Diabetes is a metabolic disease characterized by hyperglycaemia and is becoming a global health problem [1]. The International Diabetes Federation predicts that the total number of diabetes cases will reach 700 million by 2045 [2]. Type 2 diabetes, which is associated with the disturbed metabolism of glucose and lipids, accounts for 90% of all the cases. Diabetes mainly harms the body's macro- and microcoronary arteries and poses a high risk for cardiovascular morbidity and mortality [3]. Diabetic cardiomyopathy (DCM) is a structural and functional disorder of the heart caused by diabetes that is independent of hypertension, coronary atherosclerotic heart disease, valvular heart disease, and other known heart diseases [4]. However, the mechanisms underlying DCM remain unclear.

Prokineticin 2 (PK2), a secreted 8 kDa protein [5], is involved in a variety of physiological and pathological processes, including nerve growth, immune response, angiogenesis, and inflammation [6–9]. PK2 binds to two receptors, namely, prokineticin receptor 1 (PKR1) and prokineticin receptor 2 (PKR2), which share approximately 85% amino acid identity, which are widely distributed in both mice and humans, and which modulate biological processes, such as neuronal survival and testis development [10–12]. In 2007, Urayama et al. first discovered that PK2 is expressed in