Insulin-like growth factor II receptor (IGFIIR) plays as a risk factor in myocardial cells

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Like insulin-like growth factor (IGF)-I, IGF-II is considered to be a potential candidate for the treatment of heart failure through IGF-I receptor pathway, but its role in signaling transduction through the IGF-IIR is poorly understood. In previous studies, we found that cardiomyoblast apoptosis induced by IGF-I resistance is IGF-II dependent and synergistically enhanced by angiotensin-II (Ang-II). Ang-II even directly induced the activation of IGF-II and IGF-IIR, contributing to H9c2 cardiomyoblast apoptosis and cardiac apoptosis in hypertensive rat by abdominal aorta ligation. We observed increased expression of IGF-II and IGF-IIR in variety situations and the pathological hypertrophy were also found. However, the detail mechanisms and signalings of IGF2R in the regulation of cell apoptosis in response to IGF-II is still unreveil. Using IGF-IR shRNA and Leu27 IGF-II, an analog to specifically activate IGF2R, we investigated the role of IGF-II/IGF2R activation and its downstream signaling. We identified IGF-IIR signaling cross talking with Gαq induced cell hypertrophy and increasing expression of ANP/BNP by activation of PKCα/ CaMKII. In addition, specific activation of IGF2R induced mitochondrial-dependent apoptosis through Gαq and downstream calcineurin signaling in myocardial cells. Moreover, the activation of IGF-IIR induced the matrix metalloproteinase-9 activity and the increase of plasminogen activators expression in H9c2 cardiomyoblast cells. All the evidences provide the new insight into the effects of the IGF2R and its downstream signaling in myocardial cells. The suppression of IGF2R signaling pathways may be a good strategy for the protection against myocardial cell pathological hypertrophy, apoptosis, fibrosis to further alleviate heart failure progression.