ZAK 透過 p38 和 JNK 訊息途徑和 GATA-4 和 c-Jun 轉錄因子活化誘發心肌細胞肥大和腦利鈉尿素蛋白表現

ZAK induces Cardiomyocyte hypertrophy and brain natriuretic peptide expression via p38/JNK signaling and GATA-4/ c-Jun transcriptional factor activation.

Contents

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Abstract

Cardiomyocyte hypertrophy is an adaptive response of heart under varied types of stress. During the period of accumulation of stress, the transition from physiological hypertrophy to pathological hypertrophy resulted in promotion of heart failure. Our previous studies found ZAK highly expressed in heart specimen of myocardial infarction patients and demonstrated that overexpression of ZAK by Tet-on system induced cardiac hypertrophy and elevated the pathiological hypertrophy marker, Atrial natriuretic peptide （ANP） expression. In this study, we firstly applied tet-on ZAK WT H9c2 and treated them with Doxycycline (Dox), finding the increases in both cell size and hypertrophic marker BNP in a dose-dependent manner. ZAK expression was induced by Dox triggering the p38 and JNK pathway and activating the p-GATA4 and p-c-Jun transcription factors, without the involvement of p-ERK or NFATc3. However, tet-on ZAK DN showed no effect on the above signaling. Moreover, by the nuclear immunostaining and nuclear-cytoplasm isolation assay, we further confirmed that activated tet-on ZAK WT H9c2 cell may have highly enhanced the p-GATA4 and p-c-Jun nuclear