Study Of The Molecular Changes Between Pathological & Physiological Cardiac Hypertrophy In A Mouse Model

Abstract

Cardiac hypertrophy is defined as an increase in heart mass. The primary cellular basis of cardiac hypertrophy is an enlargement of the cardiac myocyte which is clearly distinguished from hyperplasia in which the cells remain the same size but increase in number. Two categories of cardiac hypertrophy are currently recognized. These are physiological (beneficial) and pathological (detrimental) cardiac hypertrophy. This study was undertaken to establish the roles of different protein kinase-C (PKC) isoforms in the regulation of cardiac adaptation during two types of cardiac hypertrophies. 24 week male Balb/c mice (*Mus musculus*) were used in this study. Phosphorylation of specific PKC-isoforms and expression of their downstream proteins were undertaken in two hypertrophic conditions by Reverse transcriptase-PCR and western blot analysis; M-mode echocardiography for cardiac function analysis was assessed. Our results showed that PKC-δ was significantly induced during pathological hypertrophy while PKC-α was exclusively activated during physiological hypertrophy. PKC-δ activation during pathological hypertrophy, resulted in cardiomyocyte apoptosis leading to compromised cardiac function and on the other hand, PKC-α activation caused cardiomyocyte growth and down-regulated apoptosis resulting in improved cardiac function in case of physiological hypertrophy. Reversal in PKC-isoform with induced activation of PKC-δ and simultaneous inhibition of phospho-PKC-α resulted in an efficient myocardium to deteriorate considerably resulting in compromised cardiac function during physiological hypertrophy via augmentation of apoptotic and fibrotic load.

This is the first report, where PKC-α and PKC-δ have been shown to play crucial role in cardiac adaptation during physiological and pathological hypertrophy respectively and thus transforms a good heart to a bad one by their conditional reversal.