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REGRESSION OF PRESSURE OVERLOAD-INDUCED CARDIAC HYPERTROPHY IS ASSOCIATED WITH THE EXPRESSION OF A DISTINCT SET OF GENES

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Regression of cardiac hypertrophy and improvement of functional capacity of failing hearts were reportedly achieved by mechanical unloading in cardiac work. We sought to see whether active transcriptional programs are involved in the regression of cardiac hypertrophy by using a surgical model of regression and gene profiling analysis. In our rat model, cardiac hypertrophy was first induced by transverse aortic constriction (TAC), and then mechanical unloading was achieved by relieving the constriction after significant cardiac hypertrophy had developed. Hypertrophy was significantly regressed at days 1, 3, and 7 after constriction relief in the physiological and molecular level. Gene profiling analysis revealed that 52 genes out of the tested 9,911 arrayed genes were specifically upregulated during the earlyregression period. Among these regression-induced genes, Eyes absent 2 (Eya2) was of a particular interest because it is a transcriptional cofactor involved in the mammalian organogenesis as well as Drosophila eye development. Adenovirus-mediated overexpression of Eya2 in the rat neonatalcardiomyocytes completely abrogated phenylephrine-induced development of hypertrophy as determined by cell size, sarcomere rearrangement and fetal gene re-expression. These data suggest that separate transcriptional programs might be operating during the regression of cardiac hypertrophy, and Eya2 might be a key regulator of one of these programs.

Key Words: Cardiac hypertrophy, Regression, Gene expression, Eya2