**GENETIC-DISRUPTION OF *Npr1* LEADS TOCARDIAC HYPERTROPHY AND REMODELING: ROLE OF PRO-INFLAMMATORY CYTOKINES**

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Genetic-disruption of guanylyl cyclase/natriuretic peptide receptor-A (GC-A/NPRA) gene (*Npr1*) exhibit cardiac hypertrophy and congestive heart failure similar to those seen in untreated human hypertensive subjects. The objective of this study was to determine whether ablation of NPRA/cGMP signaling in mice alters the expression of pro-inflammatory cytokines including; interleukin-6 (Il-6), tumor necrosis factor-alpha (TNF-alpha), and transforming growth factor-beta1 (TGF-beta1) leading to cardiac hypertrophy and remodeling in Npr1 homozygous null mutant (*Npr1*-/-) mice. The levels of Il-6, TNF-alpha, and TGF-beta1 in the left ventricular tissues were assayed by ELISA, Western blot analysis, and ribonuclease protection assay. The results showed that Il-6 and TNF-alpha levels were enhanced by 3-fold to 5-fold in the *Npr1-/-* mice hearts as compared with wild-type (*Npr1+/+*) mice hearts. The expression of TGF-beta1 and its receptor (TGF-beta1R) levels were greatly stimulated by almost 4-fold and 8-fold, respectively, in the hearts of *Npr1* null mutant mice as compared with *Npr1* wild-type control mice. The findings demonstrated that the reduced cGMP signaling results in the activation of pro-inflammatory cytokines gene expression, which leads to the development of cardiac hypertrophy and congestive heart failure in *Npr1* null mutant mice. The results suggest that disruption of the *Npr1* gene leads to the augmented expression of cardiac nuclear factor kappa B (NF-kB)-mediated-signaling pathways that provoke the pro-inflammatory cytokines and promote the development of cardiac hypertrophy and remodeling in mice lacking GC-A/NPRA.