CAMKII IS CRITICAL FOR THE UPREGULATION OF STAT3 SIGNALING IN PATHOGENESIS OF CARDIOMYOCYTE HYPERTROPHY

Poster Contributions
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Background: Signal transducer and activator of transcription 3 (STAT3) pathway is important for cardiac myocyte survival and hypertrophy. Calcium/calmodulin-dependent kinase II (CaMKII) has also been implicated in pathological cardiac hypertrophy. However, the relationship between these two key signaling pathways in pathogenesis of cardiac hypertrophy remains unclear.

Methods: Using H9c2 myocytes, we tested whether CaMKII signaling is essential for the upregulation of STAT3 during cardiomyocyte hypertrophy. H9c2 myocytes were treated with various concentrations of Ang II followed by various molecular assays.

Results: Ang II induced H9c2 myocyte hypertrophy, evidenced by increased cell surface area and increased levels of cardiac hypertrophy markers. Ang II treatment also induced a concentration- and time-dependent increase in both CaMKII and STAT3 phosphorylation (Figure). Antagonists of CaMKII and STAT3 inhibited Ang II-induced cardiomyocyte hypertrophy. Interestingly, CaMKII inhibitor KN-93 abolished STAT3 phosphorylation at both Y705 and S727, whereas the STAT3 blocker WP1066 did not influence CaMKII activity. In addition, CaMKII inhibitor KN-93 also inhibited IL-6 expression induced by Ang II.

Conclusion: Our findings demonstrate that CaMKII can upregulate STAT3 signaling pathway during the induction of cardiomyocyte hypertrophy by Ang II. This may represent a crucial link in the pathogenesis of cardiac hypertrophy and failure and serve as a therapeutic target.