**LEFT VENTRICULAR HYPERTROPHY AND HEART FAILURE IN HYPERTENSION - MOLECULAR AND CELLULAR MECHANISMS**

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How does hypertension cause cardiac hypertrophy and heart failure? The pressure overload which is the hemodynamic hallmark of hypertension causes concentric left ventricular hypertrophy. Among the important receptor- mediated mechanisms are upregulation of the angiotensin AT1 receptor, the beta-adrenoreceptor, and the endothelin ET-1 receptor. There is evidence, also, for a role for the AT2 and aldosterone receptors. Other ligands which will be discussed are cytokines (gp130-mediated), IGF-1, TNFalpha, and TGFbeta. AT1 receptor activation increases the activity of the transduction molecules MAP kinase and calcineurin. Other important transduction pathways are PKB, STAT 3, and NFkappaB/IkappaB. These will all promote selective transcription of genes controlling cardiac myocyte hypertrophy. The transition from concentric LV hypertrophy to a dilated, failing, ventricle, is a function primarily of matrix metalloproteinase activity, which breaks collagen cross-linkages and allows for pressure-induced dilatation. Several of the transduction molecules may be potential targets for new drugs to prevent LV hypertrophy and remodeling, and heart failure.