hypertrophic agonist, Angiotensin II (AngII) stimulates the expression of transcription factor (TF) POU4F2/Brn-3b (referred to as Brn-3b) in intact mouse hearts and in neonatal rat ventricular cardiomyocyte (NRVC) or embryonic rat heart-derived cell line H9c2. AngII stimulates Brn-3b expression via MAPK/ERK1 signalling pathway whereas known hypertrophic mediator, calcineurin acts via NFAT binding sites present in the gene promoter. Induction of Brn-3b by AngII correlates with expression of hypertrophic markers, atrial natriuretic peptide (ANP) and β-myosin heavy chain (β-MHC) suggesting that increased Brn-3b may be part of the hypertrophic response in these cells. Under these conditions, Brn-3b simulates known target gene, cyclin D1, which is required for hypertrophic responses in cardiomyocytes. However, AngII also stimulates the growth inhibitory p53 protein, which together with pro-apoptotic Bax is associated with apoptotic cell death that characterises progression from pathological hypertrophy to heart failure. Brn-3b cooperates with p53 to enhance Bax expression so may drive apoptosis in cardiomyocytes under these conditions. Thus, stimulation of Brn-3b by hypertrophic agonist, AngII may result in distinct effects on cell fate depending on whether p53 is co-expressed.

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INDUCTION OF BRN-3B/POU4F2 IN CARDIAC MYOCYTES BY ANGIOTENSIN II CAN AFFECT FATE AND SURVIVAL DEPENDING ON CO-EXPRESSION WITH P53

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Early hypertrophic responses help the heart to maintain cardiac output and compensate for increased demand or workload. However, prolonged stresses trigger death of non-dividing cardiomyocytes and accompanying fibrosis, which underlies progression to heart failure. However, the molecular mechanisms associated with transition from compensatory to pathological changes in the heart are not fully understood. Here we demonstrate that the