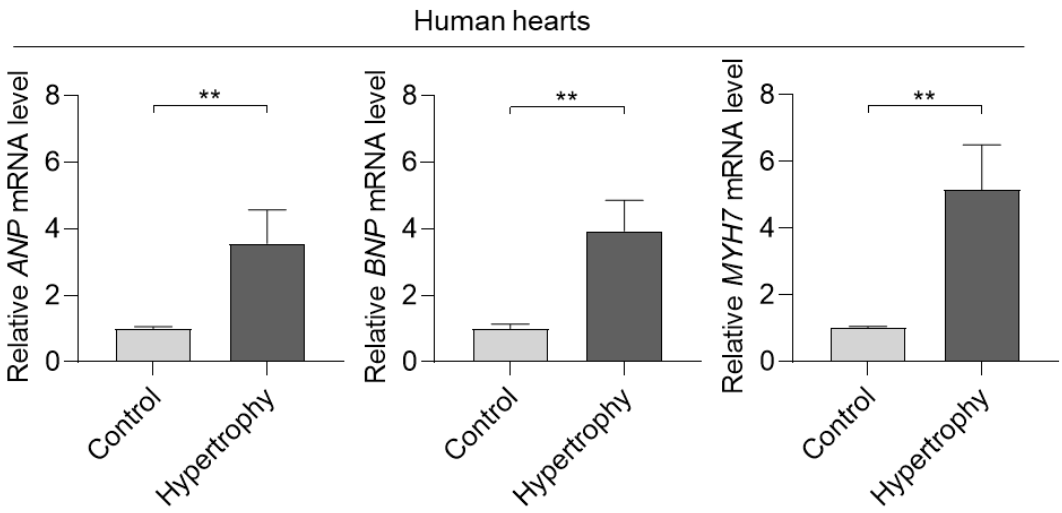
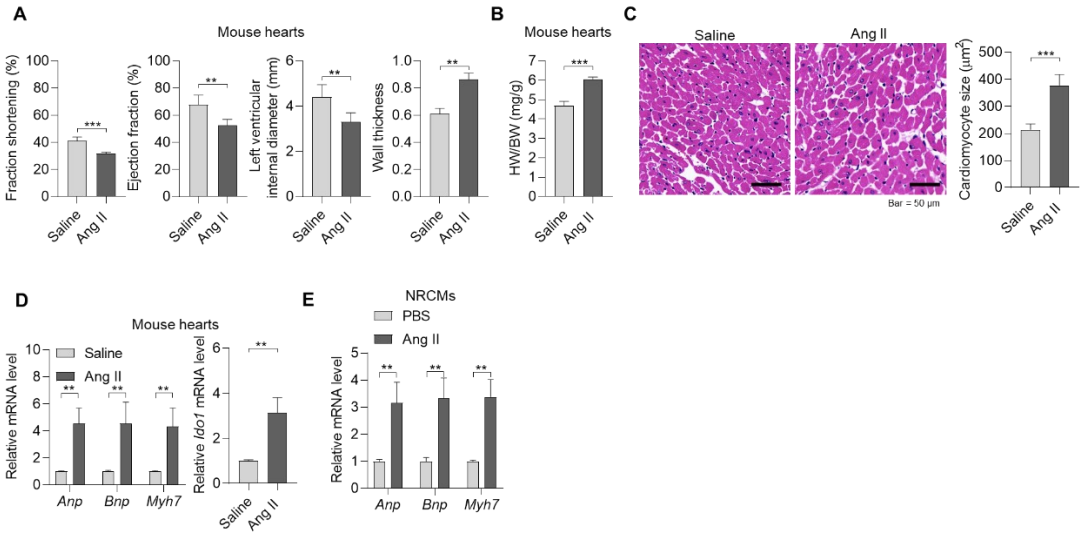
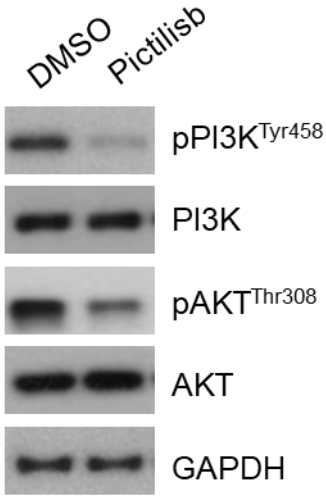


Supplementary Figure 1 Expression of hypertrophic fetal genes in control and hypertrophy heart tissues of humans. RT-qPCR analysis of the expression of hypertrophic genes (*ANP*, *BNP*, and *MYH7*) in the control and hypertrophic hearts of humans. n=5 in each group. ***p*<0.01 by Student's *t* test. *ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide; MYH7, β-myosin heavy chain*.



Supplementary Figure 2 Validation of hypertrophic growth of mouse hearts and rat cardiomyocytes. (A)Fraction shortening, ejection fraction, left wall thickness, and left ventricular internal diameters of mice with/without cardiac hypertrophy. Cardiac hypertrophy was induced by subcutaneously chronic infusion of Ang II (1.3 mg/kg/day) for 28 days. Ang II, angiotensin II. n=5 in each group. ***p*<0.01, ***p<0.001 by Student's *t* test. (B)Heart weight-to-body weight ratio of mice with/without cardiac hypertrophy. Cardiac hypertrophy was induced by subcutaneously chronic infusion of Ang II (1.3 mg/kg/day) for 28 days. n=5 in each group. ***p<0.001 by Student's *t* test. (C)Haematoxylin and eosin (H&E) staining show the increased

cardiomyocyte size in mice with cardiac hypertrophy. Cardiac hypertrophy was induced by subcutaneously chronic infusion of Ang II (1.3 mg/kg/day) for 28 days. Then the heart tissues were harvested and subjected to H&E staining. n=5 in each group. ***p<0.001 by Student's *t* test. (D) qRT-PCR shows the expression of hypertrophic genes (*Anp, Bnp, Myh7*) in control and hypertrophic neonatal rat cardiomyocytes (NRCMs). Cardiomyocytes were treated with Ang II (1 μM) for 48 hours to induce cardiomyocyte hypertrophy. n=3 in each group. ***p*<0.01 by Student's *t* test.



Supplementary Figure 3. Inhibitors effects on PI3K pathway.
Cardiomyocyte cells were with/without PI3K inhibitor pictilisib (100 nM; Panel C) for additional 48 hours. Then, western blot was performed to test the effects.