Supplemental material of Danuglipron ameliorates pressure overload-induced cardiac remodeling through the AMPK pathway.

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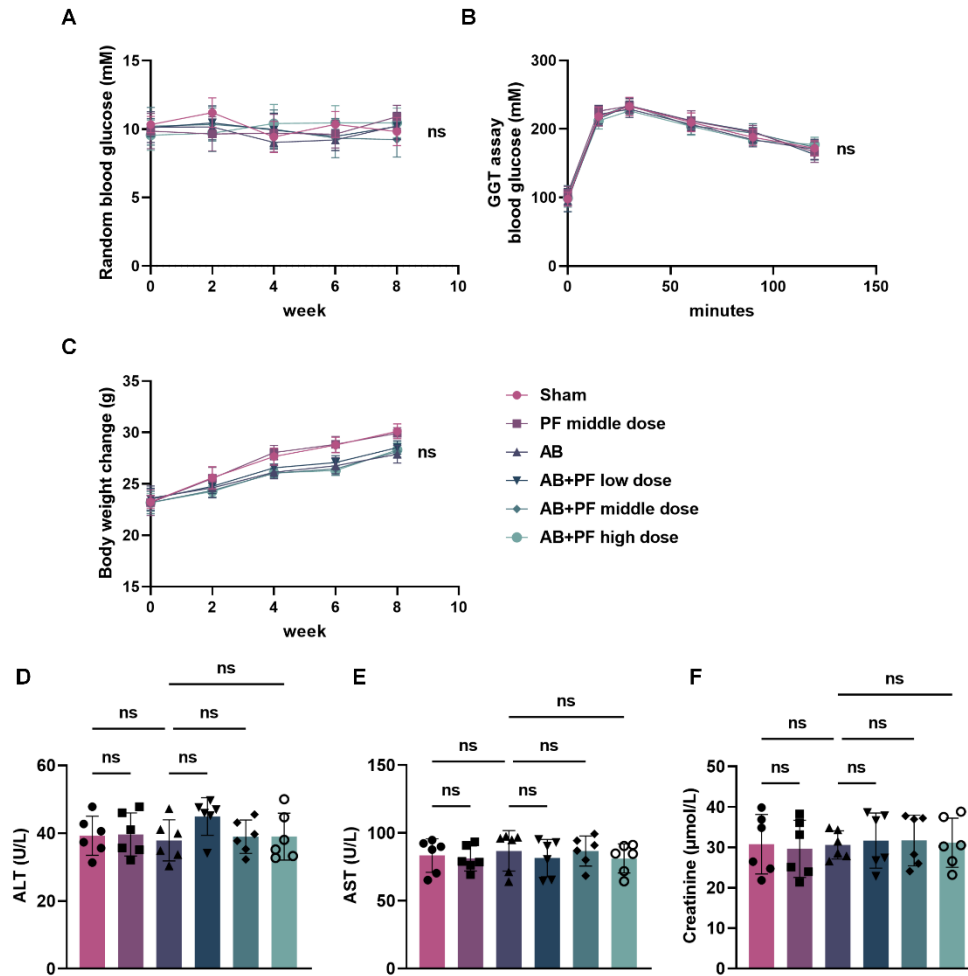[#] These authors contributed equally: Pan Wang, Zhen Guo.

Figure S1 Effects of different doses of PF on body weight, blood glucose, liver and kidney function in mice 8 weeks after AB surgery.

A. Effects on fasting blood glucose in mice treated with different doses of PF every two weeks after sham or AB surgery (*n*=6). **B.** The results of the GTT after 8 weeks of treatment with different doses of PF (*n*=6). **C.** Effect of different doses of PF on body weight of mice after sham or AB surgery (*n*=6). **D-E.** Detection of the liver function indicators ALT and AST after 8 weeks of treatment with different doses of PF (*n*=6). **F.** Detection of the kidney function indicators creatinine after 8 weeks of treatment with different doses of PF (*n*=6). All data are presented as mean±SD. Statistical analysis was performed using one-way ANOVA followed by *post hoc* Tukey test or unpaired *t*-test. *ns* means no statistical significance, $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, $****P < 0.0001$. GTT, glucose tolerance test; ALT, liver enzymes alanine aminotransferase; AST, aspartate aminotransferase.
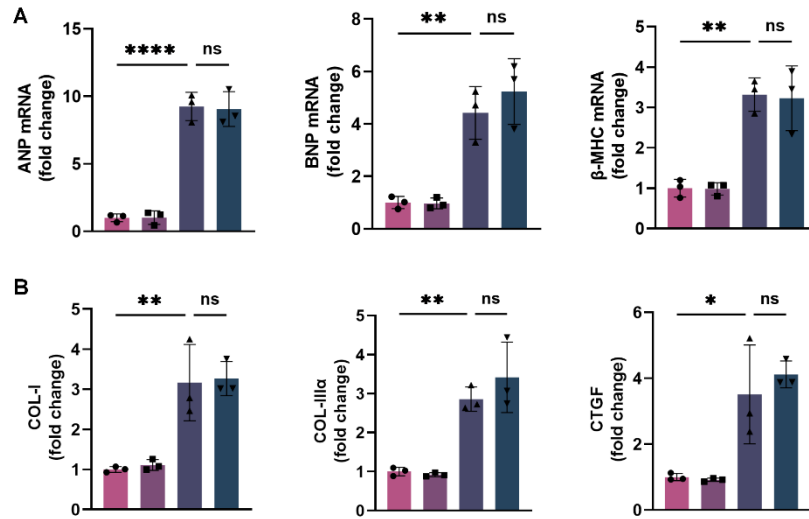
Figure S2 PF is unable to reverse pathological cardiac remodeling in AMPKα2$^{-/-}$ mice.

A. The mRNA expression of hypertrophic markers ANP, BNP and β-MHC in wild-type mice and AMPKα2$^{-/-}$ mice (*n*=3). **B.** The mRNA expression of myocardial fibrosis markers COL-I, COL-IIIα, CTGF (*n*=3). All data are presented as mean ± SD. Statistical analysis was performed using one-way ANOVA followed by *post hoc* Tukey test or unpaired *t*-test. *ns* means no statistical significance, ***$P < 0.001$, ****$P < 0.0001$.
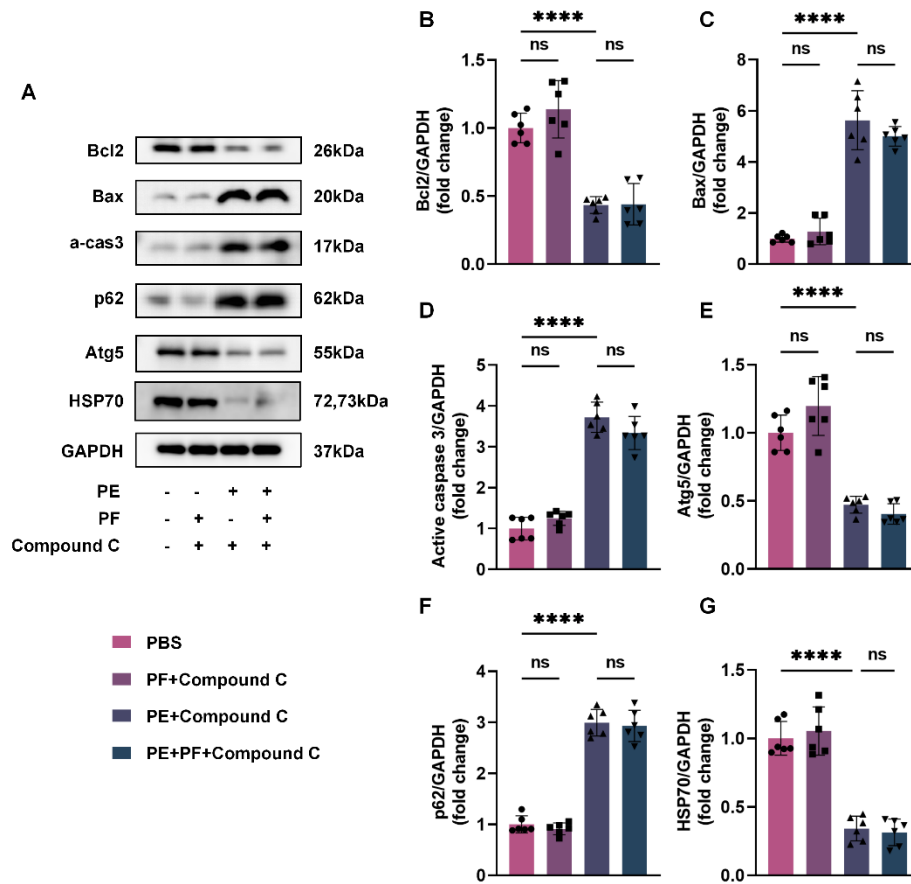
Figure S3 AMPKα inhibitors inhibit the protective effect of PF on cardiac remodeling.

A. The protein expression levels of Bcl-2, Bax, active-caspase3, p62, Atg5 and HSP70 in NRCMs treated with PF (*n*=6). **B-H.** Quantitative analysis of western blot data. All data are presented as mean±SD. Statistical analysis was performed using one-way ANOVA followed by *post hoc* Tukey test or unpaired *t*-test. *ns* means no statistical significance, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, ****$P < 0.0001$.