

Figure S1. Immunoblot analysis of cardiac-specific overexpression of MKK7 in C57BL/6N mice injected with AAV9-TnT-MKK7. **(A)** Validation of cardiomyocyte specific MKK7 overexpression in the myocardium of C57BL/6N mice injected with AAV9-TnT-MKK7 (N = 1–4); **(B)** Comparable levels of MKK7 expression in other tissues

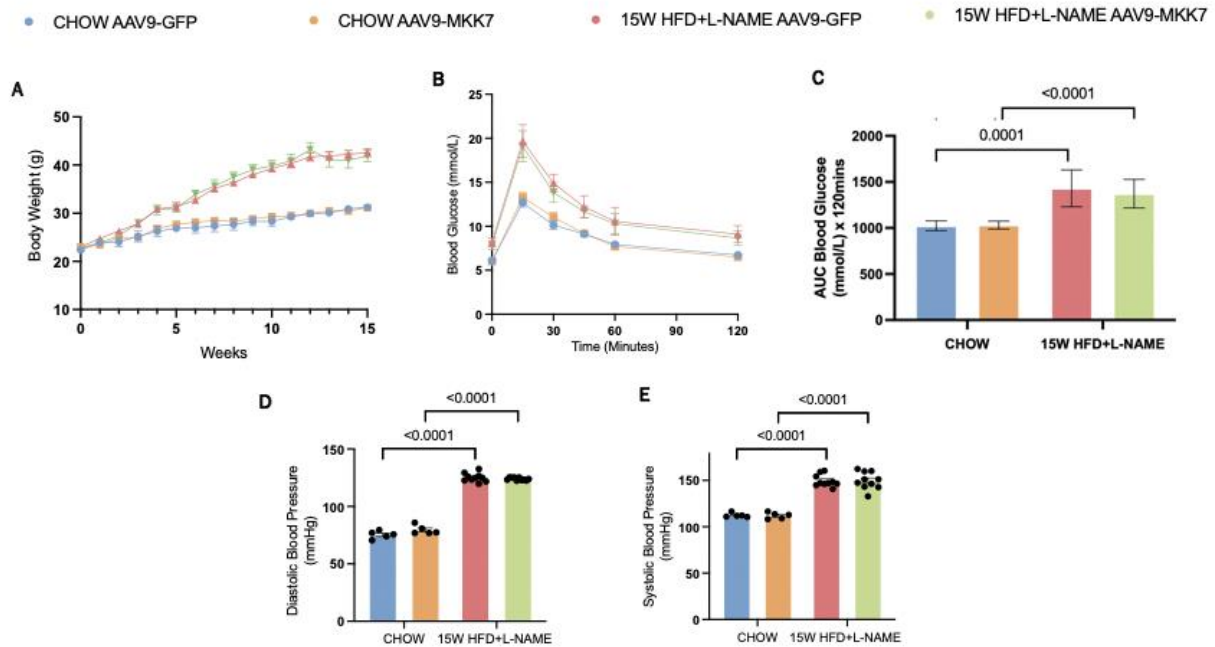


Figure S2: 15-weeks of HFD and L-NAME feeding recapitulates features of clinical HFpEF. (A) Measurement of weekly body weight. (N = 5–10); (B and C) Measurement of glucose tolerance test and area under the curve (N = 5–10); (D and E) Data depicting systolic and diastolic blood pressure using non-invasive blood pressure. (N = 5–10) Presented as mean  $\pm$  SEM.

**Table S1:** Structural parameters of the different mouse groups. End-diastolic interventricular septum thickness (dIVS), end-systolic interventricular septum thickness (sIVS), end-diastolic left ventricular internal diameter (dLVID), end-systolic left ventricular internal diameter (sLVID), end-diastolic left ventricular posterior wall thickness (dPW), end-systolic left ventricular posterior wall thickness (sPW), Left ventricular mass (LV mass). Data presented as mean  $\pm$  SEM.

	CHOW		HFpEF	
	AAV9-TnT- <i>GFP</i>	AAV9-TnT- <i>MKK7</i>	AAV9-TnT- <i>GFP</i>	AAV9-TnT- <i>MKK7</i>
Heart Rate	478 $\pm$ 26.83	491 $\pm$ 30.76	452.8 $\pm$ 18.88	400 $\pm$ 33.66
dIVS	0.84 $\pm$ 0.20	0.84 $\pm$ 0.03	1.04 $\pm$ 0.16	0.72 $\pm$ 0.27
sIVS	1.47 $\pm$ 0.22	1.05 $\pm$ 0.18	1.55 $\pm$ 0.24	1.35 $\pm$ 0.28
dLVID	3.91 $\pm$ 0.16	3.94 $\pm$ 0.20	3.92 $\pm$ 0.37	3.94 $\pm$ 0.29
sLVID	2.25 $\pm$ 0.24	2.08 $\pm$ 0.22	2.29 $\pm$ 0.22	2.36 $\pm$ 0.27
PWd	0.68 $\pm$ 0.18	0.84 $\pm$ 0.03	1.1 $\pm$ 0.18	0.76 $\pm$ 0.18
PWs	1.09 $\pm$ 0.28	1.04 $\pm$ 0.15	1.433 $\pm$ 0.22	1.123 $\pm$ 0.148
LV Mass	3.23 $\pm$ 22.8	3.69 $\pm$ 0.24	3.87 $\pm$ 0.96	2.61 $\pm$ 0.67
RWT	0.35 $\pm$ 0.11	0.41 $\pm$ 0.03	0.56 $\pm$ 0.13	0.38 $\pm$ 0.09