Table S1. Summary of heart weight, cardiac fibrosis and transthoracic echocardiograph results in adipo-sNaKtide transduced mice.

	Sham (N=8-12)	Sham+adipo-sNaKtide (N=8-10)	PNx (N=11-24)	PNx+adipo-sNaKtide (N=6-9)
Heart Weight (g)	0.132 ± 0.002	0.131 ± 0.004	0.164 ± 0.004**	0.165 ± 0.004**
Cardiac Fibrosis (%)	0.61 ± 0.16	0.62 ± 0.07	2.76 ± 0.29**	2.72 ± 0.12**
Echocardiography				
ESA, mm2	16.4 ± 0.6	14.6 ± 0.8	17.4 ± 0.8	16.3 ± 0.6
ESD, mm	3.12 ± 0.14	3.15 ± 0.07	3.35 ± 0.07	3.35 ± 0.09
PWT, mm	0.52 ± 0.02	0.56 ± 0.01	0.64 ± 0.01**	0.67 ± 0.01**
AWT, mm	0.61 ± 0.01	0.62 ± 0.01	0.73 ± 0.01**	0.75 ± 0.01**
PaVTI, mm	27.8 ± 0.9	29.61 ± 0.7	28.2 ± 0.9	27.6 ± 0.9
PaD, mm	0.96 ± 0.02	1.00 ± 0.02	1.02 ± 0.02	1.05 ± 0.02
RWT, mm	0.25 ± 0.007	0.27 ± 0.002**	0.31 ± 0.003**	0.32 ± 0.003**^
MPI	0.42 ± 0.02	0.39 ± 0.01	0.57 ± 0.02**	0.54 ± 0.01**
FS, %	29.9 ± 2.3	27.8 ± 1.1	23.8 ± 1.0*	23.4 ± 1.5*
EF, %	64.7 ± 3.2	62.3 ± 1.7	55.6 ± 1.7*	54.7 ± 2.5*
LVM, mg	90 ± 2	93 ± 3	112 ± 3**	117 ± 4**
LVMI	3.40 ± 0.11	3.46 ± 0.10	4.17 ± 0.11**	4.45 ± 0.10**

Values are means ± SEM. ESA-end systolic area; ESD-end systolic dimension; PWT-posterior wall thickness; AWT-anterior wall thickness; IVCT-isovolumic contraction time; IVRT-isovolumic relaxation time; PaVTI-pulmonary artery velocity time integral; PaD-pulmonary artery dimension; RWT-relative wall thickness; MPI-myocardial performance index; FS-fractional shortening; EF-ejection fraction; LVMI-left ventricle mass index. * p<0.05, **p<0.01 vs. Sham, ^p<0.05 vs PNx.

Table S2. Summary of heart weight and transthoracic echocardiograph results.

	Sham (N=8-12)	PNx (N=12-24)	PNx+adipo-NaKtide (N=12-13)	4/6-nephrectomy (N=10)
Heart Weight (g)	0.132 ± 0.002	0.164 ± 0.004**	0.132 ± 0.003^^	0.143 ± 0.003^^
Echocardiography				
ESA, mm2	16.4 ± 0.6	17.4 ± 0.8	15.3 ± 0.7	15.9 ± 0.5
ESD, mm	3.12 ± 0.14	3.35 ± 0.07	3.18 ± 0.04	3.25 ± 0.05
PWT, mm	0.52 ± 0.02	0.64 ± 0.01**	0.57 ± 0.01^^	0.60 ± 0.01**^
AWT, mm	0.61 ± 0.01	0.73 ± 0.01**	0.63 ± 0.01^^	0.70 ± 0.01**^$^{\#\#}$
IVCT+IVRT, msec	17.0 ± 0.5	24.5 ± 0.7**	16.8 ± 0.5^^	20.1 ± 0.4**^^$^{\#\#}$
PaVTI, mm	27.8 ± 0.9	28.2 ± 0.9	29.8 ± 0.5	30.2 ± 0.8
PaD, mm	0.96 ± 0.02	1.02 ± 0.02*	0.97 ± 0.01^	1.05 ± 0.02**$^{\#\#}$
RWT	0.25 ± 0.007	0.31 ± 0.003**	0.27 ± 0.002**^^	0.29 ± 0.003**^^$^{\#\#}$
MPI	0.42 ± 0.02	0.57 ± 0.02**	0.38 ± 0.01^^	0.45 ± 0.01^^$^{\#\#}$
FS, %	29.9 ± 2.3	23.8 ± 1.0*	26.9 ± 0.7	25.2 ± 1.1
EF, %	64.7 ± 3.2	55.6 ± 1.7*	60.8 ± 1.0	57.9 ± 1.9
LVM, mg	90 ± 2	112 ± 3**	94 ± 3^^	102 ± 1**^$^{\#}$
LVMI	3.40 ± 0.11	4.17 ± 0.11**	3.65 ± 0.10^^	3.80 ± 0.07**^

Values are means ± SEM. ESA-end systolic area; ESD-end systolic dimension; PWT-posterior wall thickness; AWT-anterior wall thickness; IVCT-isovolumic contraction time; IVRT-isovolumic relaxation time; PaVTI-pulmonary artery velocity time integral; PaD-pulmonary artery dimension; RWT-relative wall thickness; MPI-myocardial performance index; FS-fractional shortening; EF-ejection fraction; LVMI-left ventricle mass index. * p<0.05, **p<0.01 vs. Sham, ^p<0.05, ^^p<0.01 vs PNx, $^{\#}$p<0.05, $^{\#\#}$p<0.01 vs PNx+adipo-NaKtide.

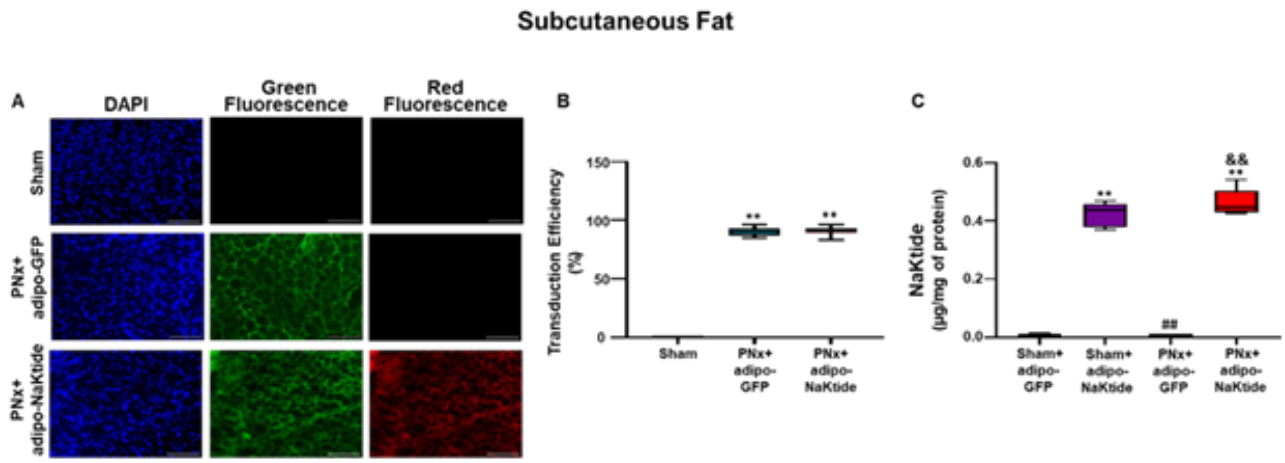

Figure S1. Adipocyte-specific expression of NaKtide in subcutaneous adipose tissues of PNx mice. (A) Immunofluorescence staining demonstrating expression of green fluorescence (GFP) and red fluorescence (NaKtide) in subcutaneous adipose tissues of adipo-NaKtide transduced PNx mice, while adipo-GFP transduced PNx mice showed expression of green fluorescence (GFP) only. No fluorescence was detected in Sham mice without lentiviral transduction. Representative images were taken with a 20X objective lens; the scale represents 100 µm, N=15/group. (B) Transduction efficiency is shown as a percentage of cells transduced by lentivirus construct, N=15/group. (C) NaKtide concentration in subcutaneous adipose measured by competitive ELISA, N=5/group. Each box and whisker plot represents values as maximum and minimum range, upper quartile, median and lower quartile. *p < 0.05 vs. Sham, **p < 0.01 vs. Sham; #p < 0.05 vs. Sham+adipo-NaKtide, ##p < 0.01 vs. Sham+adipo-NaKtide; &p < 0.05 vs. PNx+adipo-GFP, &&p < 0.01 vs. PNx+adipo-GFP.

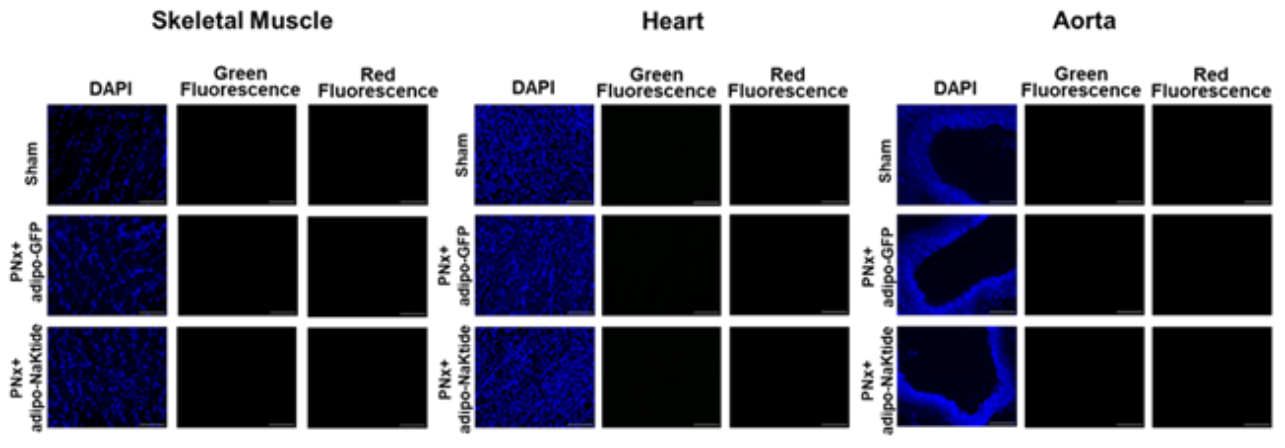

Figure S2. Expression of adipocyte-specific NaKtide in skeletal muscle, heart and aorta of PNx mice. Immunofluorescence staining of skeletal muscle, heart and aorta section showed no detectable green fluorescence (GFP) and red fluorescence (NaKtide) in adipo-GFP or adipo-NaKtide transduced PNx mice, respectively. Representative images of skeletal muscle (N=5/group), heart (N=5/group) and aorta (N=7-9/group) taken with 20X objective lens; scale represents 100 µm.

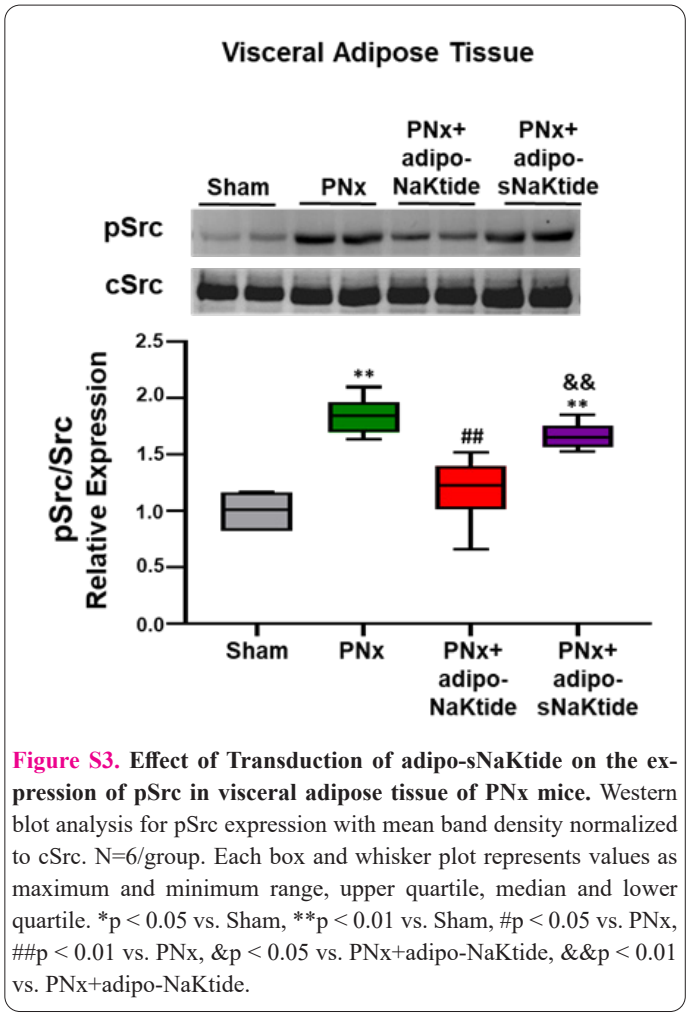

Figure S3. Effect of Transduction of adipo-sNaKtide on the expression of pSrc in visceral adipose tissue of PNx mice. Western blot analysis for pSrc expression with mean band density normalized to cSrc. N=6/group. Each box and whisker plot represents values as maximum and minimum range, upper quartile, median and lower quartile. *p < 0.05 vs. Sham, **p < 0.01 vs. Sham, #p < 0.05 vs. PNx, ##p < 0.01 vs. PNx, &p < 0.05 vs. PNx+adipo-NaKtide, &&p < 0.01 vs. PNx+adipo-NaKtide.

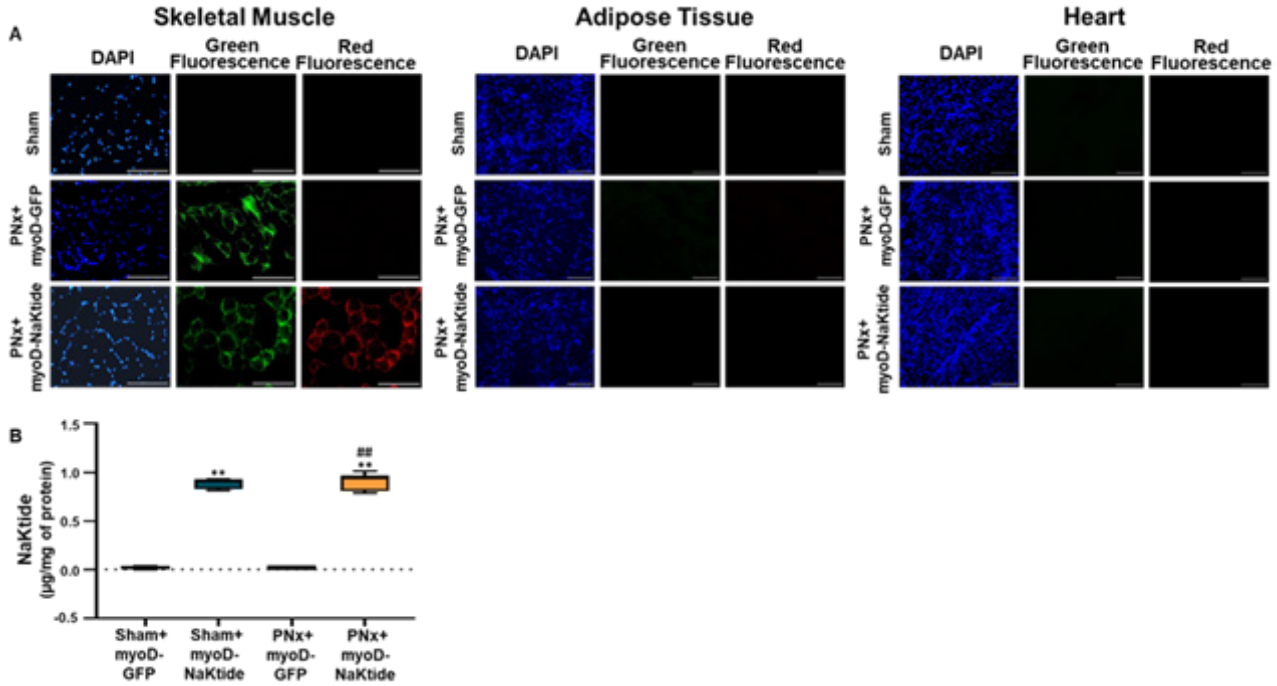

Figure S2. Specificity of NaKtide targeted to skeletal muscle, with MyoD promoter, in PNx mice. (A) Immunofluorescence staining demonstrating expression of green fluorescence (GFP) and red fluorescence (NaKtide) in skeletal muscle of myoD-NaKtide transduced PNx mice, while myoD-GFP transduced PNx mice showed expression of green fluorescence (GFP) only. Expression of myoD-GFP and myoD-NaKtide was undetectable in adipose tissue and heart of PNx mice. Representative images of skeletal muscle (n=3-5/group), adipose tissue (n=5/group) and heart (n=5/group) were taken with a 20X objective lens; the scale represents 100 µm. (B) NaKtide concentration in muscle measured by competitive ELISA. N=4-6/group. Each box and whisker plot represents values as maximum and minimum range, upper quartile, median and lower quartile. **p < 0.01 vs. Sham+myoD-GFP, ##p < 0.01 vs. PNx+myoD-GFP.