SUPPLEMENTAL MATERIAL

CKIP-1 regulates physiological cardiac hypertrophy through inhibition of HDAC4 phosphorylation

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Supplementary Figure 1: Swimming exercise training promotes physiological cardiac growth. (A) Heart weight (HW) to body weight (BW) ratios in rest and swim mice. **(B and C)** Echocardiographic assessment of ejection factor (EF) (B) and fractional shortening (FS) (C). **(D-F)** Relative mRNA expression of hypertrophic marker genes (ANP, BNP and β-MHC) in the hearts of WT mice after swimming exercise. Values are means ± SEM, n=7~8, ***P*<0.01, ****P*<0.001. Statistical differences between two groups were determined by the unpaired 2-tailed Student's t-test.

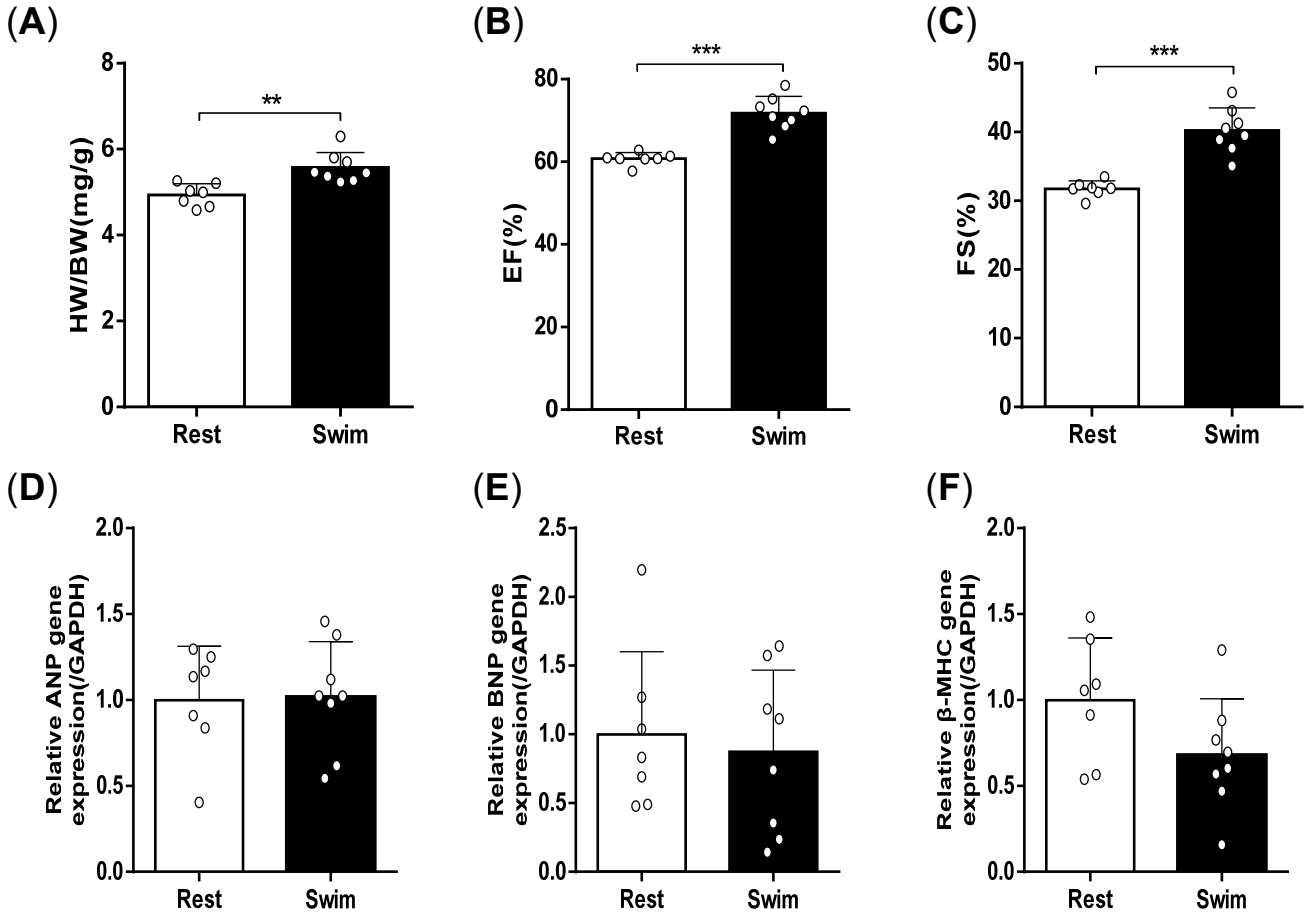
Supplementary Figure 2: Effect of swimming training on the exercise-induced cardiac growth program in CKIP-1 knockout mice. (A) Quantification of interstitial fibrosis in WT and CKIP-1 KO mice after swimming exercise. **(B and C)** Stroke volume (SV) and heart rate (HR) as measured by echocardiography in the mice. Values are means ± SEM, n=8~12, **P*<0.05, ****P*<0.001. Statistical differences among groups were analyzed by two-way analysis of variance (ANOVA) followed by the Bonferroni procedure.

Supplementary Figure 3: Effect of swimming training on the exercise-induced cardiac growth program in CKIP-1 transgenic mice. (A) Quantification of interstitial fibrosis in WT and CKIP-1 transgenic mice after swimming exercise. **(B and C)** Stroke volume (SV) and heart rate (HR) as measured by echocardiography in the mice. Values are means ± SEM, n=4~9. Statistical differences among groups were analyzed by two-way analysis of variance (ANOVA) followed by the Bonferroni procedure.

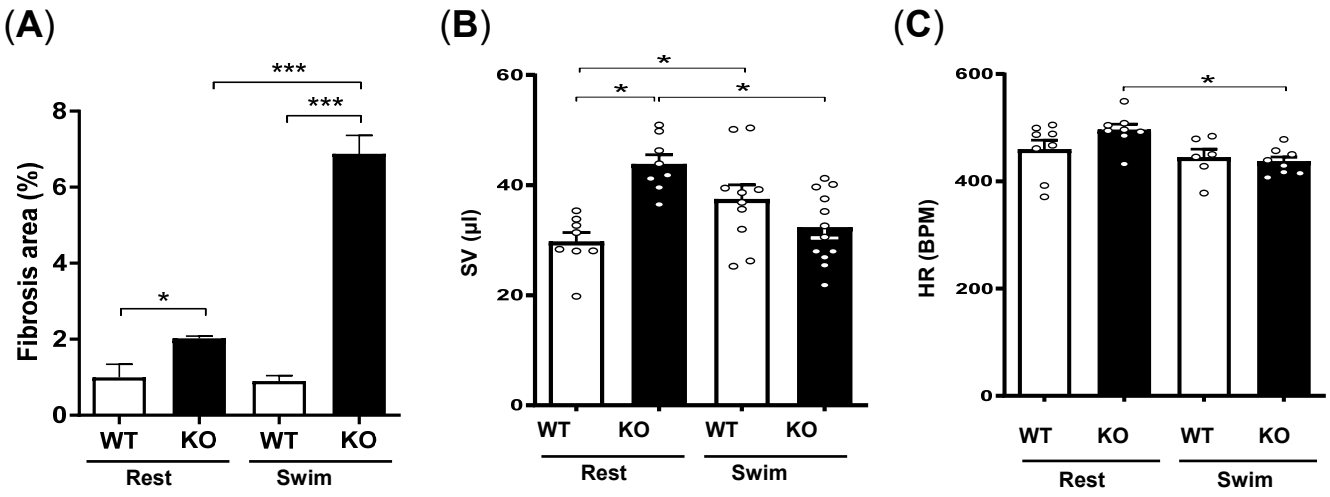
Supplementary Figure 4: CKIP-1 regulates HDAC4 translocation from the nucleus to the cytoplasm in CKIP-1 KO mice heart. Immunohistochemical staining with HDAC4 in CKIP-1 KO mice and WT littermates mice hearts. Scale bars: 10 μm.

Supplementary Figure 5: Expression of phospho-HDAC4/5/9 (Ser 246/259/220) are increased in CKIP-1 KO mice subjected to swimming exercise. Immunoblots showing the expression pattern of phospho-HDAC4/5/9 and HDAC5 in CKIP-1 KO mice and WT littermates mice cardiac tissues.

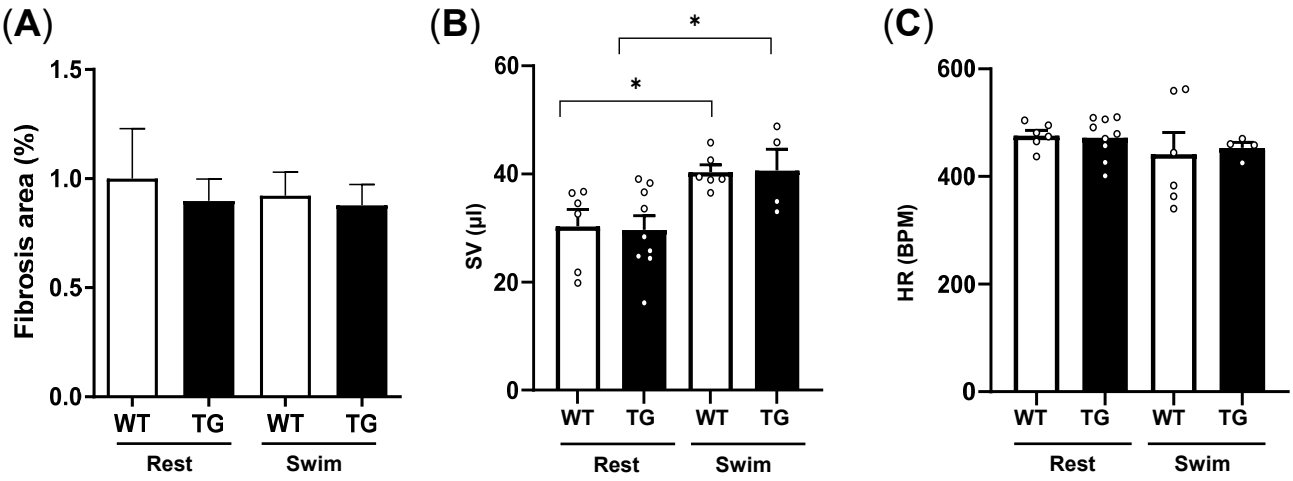
Supplemental Figure 1



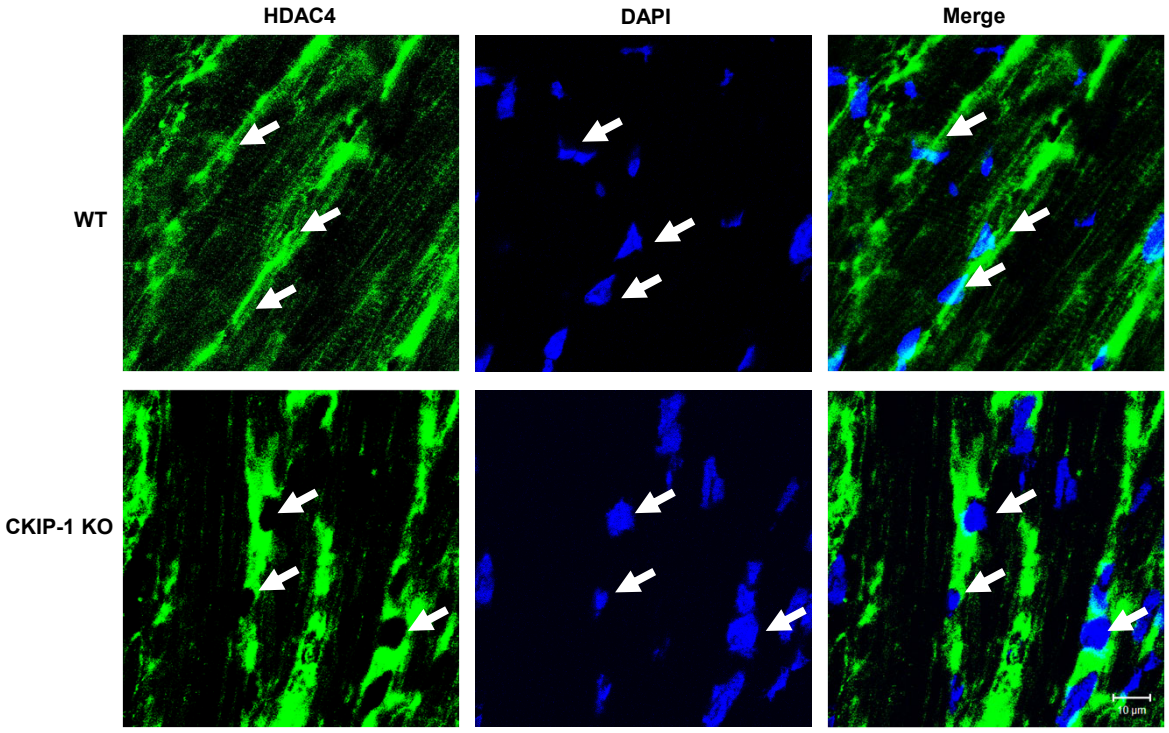
Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4



Supplemental Figure 5