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Supplemental information

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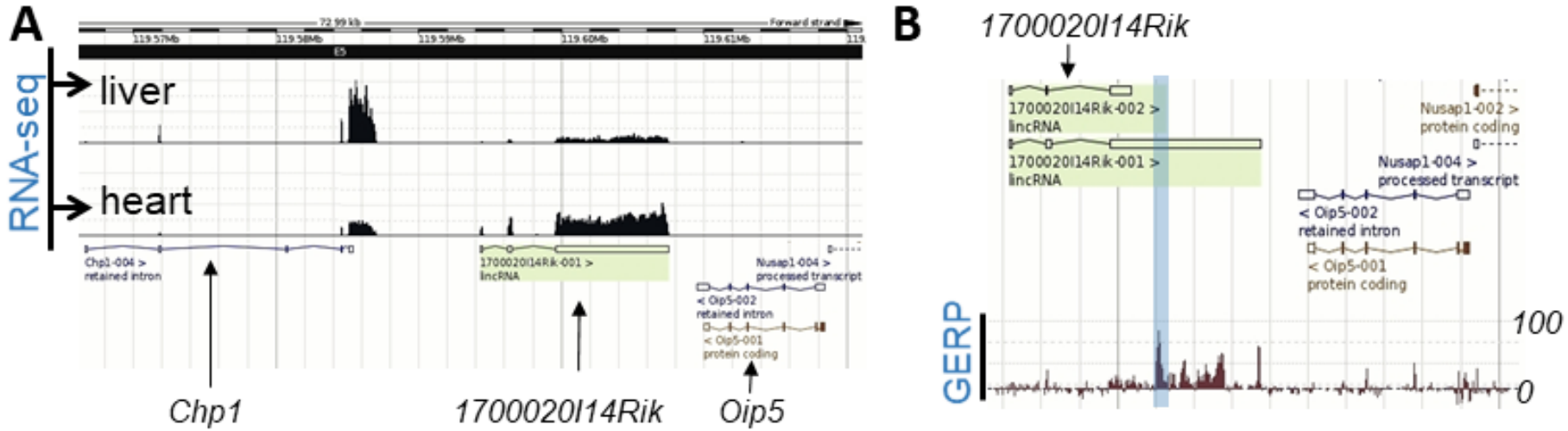
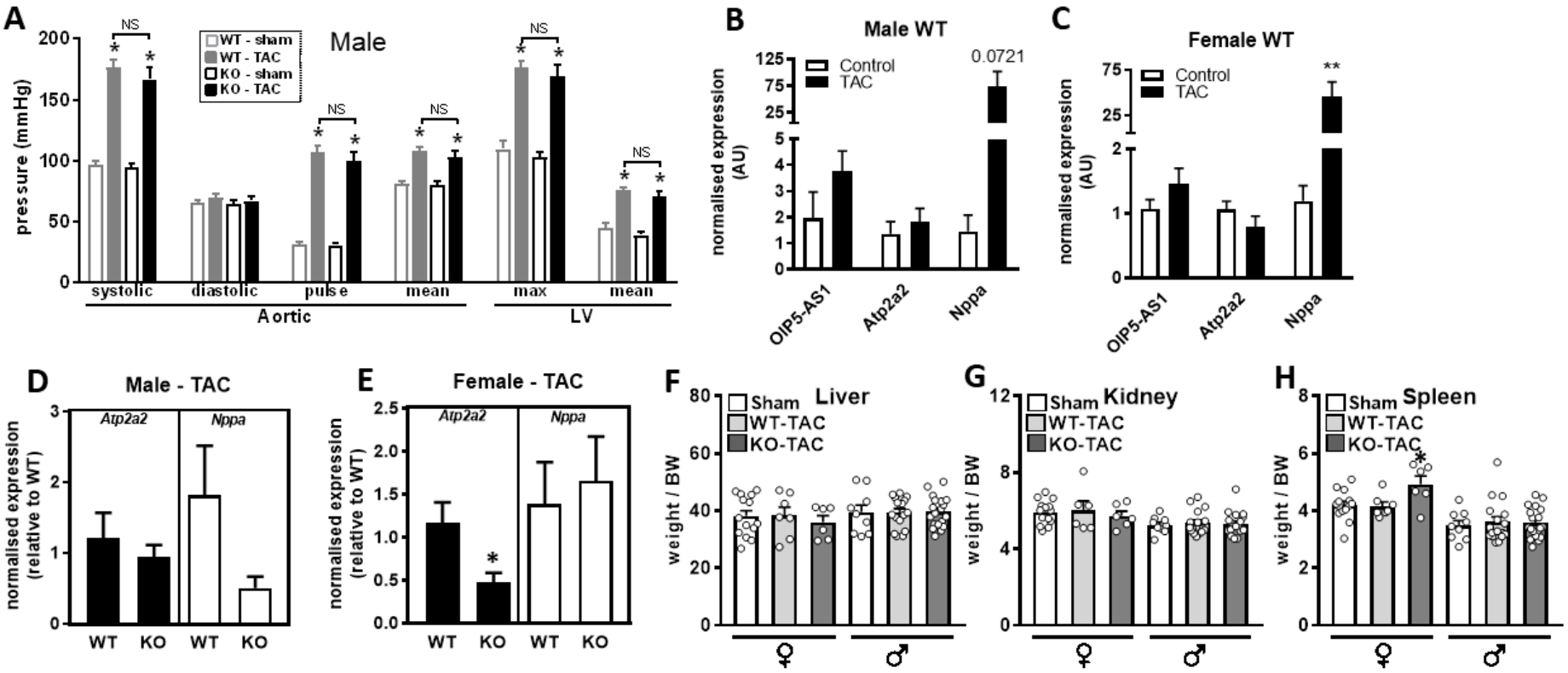


Supplementary Figure S1: Location, expression and homology of OIP5-AS1 (Related to Figure 1)
A. *Ensembl* sourced RNA-sequencing tracks of transcript expression in mouse liver and heart at the OIP5-AS1 locus. **B.** *Ensembl* sourced Genomic Evolutionary Rate Profiling (GERP) data across the OIP5-AS1 gene locus. A greater amplitude in the GERP peak indicates a greater conservation of that region across vertebrate species. Blue box indicates the region of 100% homology in exon 3.



Supplementary Figure S2: Additional phenotyping data from WT and KO mice undergoing Sham and TAC surgery. **(related to Figure 3) A.** Hemodynamic catheter measurements recorded from the aorta and left ventricle (LV) of sham and TAC operated WT and OIP5-AS1 KO male mice (n=3-11/group, mean±SEM), * p<0.05 versus genotype equivalent sham, NS = not significant between WT and KO TAC treated animals. qPCR data from LVs of **B.** male WT and **C.** female WT mice for the genes OIP5-AS1, Atp2a2 (SERCA2) and Nppa (ANP) in either control or TAC operated mice, and in LVs from **D.** male WT v KO TAC or **E.** female WT v KO TAC operated mice for the genes Atp2a2 (SERCA2) and Nppa (ANP). Organ weights adjusted to body weight (BW) in male and female mice 8-weeks post procedure for **F.** liver, **G.** kidney and **H.** spleen. A non-parametric one-way ANOVA with multiple comparisons correction (Dunnet's) was used to test for significance. (n=7-13/group, mean±SEM, * p<0.05 versus sham for relevant sex). Weights for these organs were adjusted to BW.

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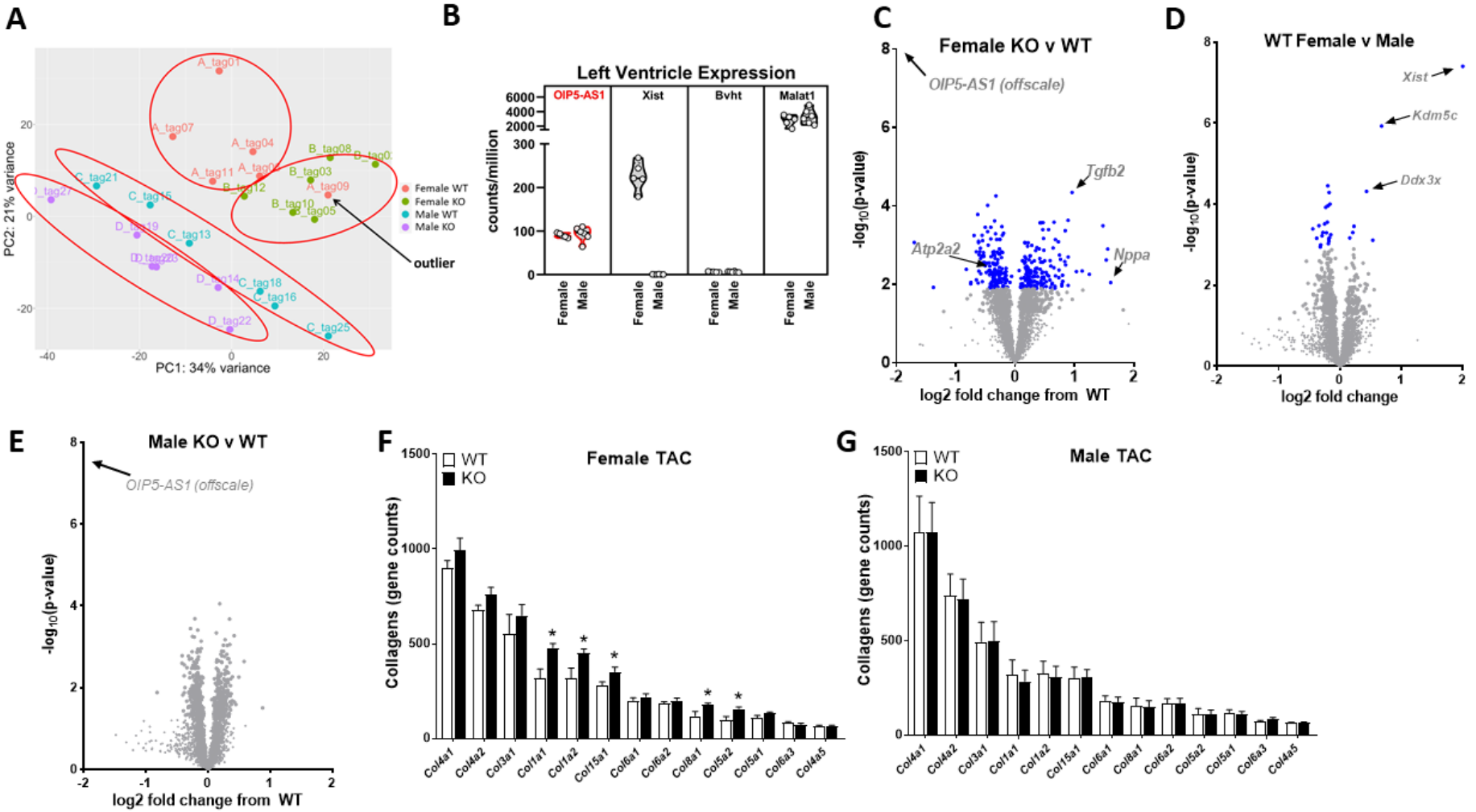

Supplementary Figure S3: Accompanying RNA-sequencing Data Analysis. (Related to Figure 5) **A.** Principle component analysis (PCA) of RNA-sequencing data demonstrating separation of the four groups of samples based on variance (red circles). One sample from the "Female WT" group demonstrated an inconsistent variance compared to its other group members indicating a technical abnormality (black arrow – "outlier") and was subsequently removed from enrichment and network analysis. **B.** Analysis of RNA-seq data demonstrating abundance (counts per million) of OIP5-AS1 compared to three other well-known lncRNAs in cardiac

tissue including Xist, Braveheart (Bvht) and Malat1 across male and female WT hearts (LV). **C.** Volcano plot of genes regulated in LV following TAC between female KO and WT mice (n=5/group for female WT, n=6/group for female KO), grey dots = not-significant, blue dots = FDR<0.1). Arrows demonstrate genes known to be regulated in the setting of heart failure. **D.** Volcano plot of genes regulated in LV following TAC between female and male WT mice (n=5/group for female WT, n=6/group for male WT), grey dots = not-significant, blue dots = FDR<0.1). Arrows demonstrate known sexual dimorphic genes. **E.** Volcano plot of genes regulated in LV following TAC between male WT and KO mice (n=6/group), grey dots = not-significant. Arrow indicates that change in OIP5-AS1 expression is not shown as it is off scale. Absolute transcript abundance of all collagen related genes in LV from RNA-seq data in **F.** female WT and KO mice following TAC and **G.** male WT and KO mice following TAC. A non-parametric one-way ANOVA with multiple comparisons correction (Dunnet's) was used to test for significance. (* $p<0.05$ versus WT, n=5-6/group).