SUMMARY OF SUPPLEMENTAL FIGURES

Supplemental Figure I

Characteristics of the physiological and pathological cardiac hypertrophy mice model (swimming and TAC). Additional immunohistochemistry of proliferation markers including z-stack orthogonal views.

Supplemental Figure II

Preliminary follow up data on eight transcription factors identified using the Quanttrx screen

Supplemental Figure III

C/EBPβ siRNA and adenoviral over expression data in vitro. ANP/BNP levels and target gene expression with C/EBPβ over expression.

Supplemental Figure IV

AKT over expression in vitro and its effect on C/EBPβ and target genes. Expression levels of exercise-induced genes after TAC surgery. PGC1α over expression and cell sizes.

Supplemental Figure V

CITED4 gain- and loss of function characteristics in vitro and proliferation target gene expression.

Supplemental Figure VI

Characteristics of the C/EBPβ heterozygous mouse including cardiac C/EBPβ levels, target gene expression, heart weight, exercise capacity and proliferation markers.

Supplemental Figure VII

Ultrasound data from C/EBPβ$^{+/-}$ and control mice subjected to TAC. Heart weight and C/EBPβ levels of exercised C/EBPβ$^{+/-}$ mice.

Supplemental Table I

Genes altered in the Quanttrx screen from exercised mice

Supplemental Table II

Genes altered in the Quanttrx screen from mice subjected to TAC

Supplemental Table III

Baseline echocardiac parameters of C/EBPβ$^{+/-}$ mice at baseline.

Supplemental Table IV

List of primers used

LEGENDS TO SUPPLEMENTAL FIGURES

Supplemental figure I

A-D. Data from exercised and TAC-operated mice with respective controls (n=4). **A.** Heart weights normalized to body weights (multiplied by 1000). **B**. Left Ventricular Posterior Wall in diastole (LWPWd) + Left Ventricular Septum in diastole (LVSd). Data presented as mm. **C**. Cell size measurement of cardiomyocytes after cardiac WGA staining in indicated groups. More than 100 cells from each group (n=4) was measured. **D**. mRNA levels of ANP and BNP normalized to 18s levels in indicated groups. **E**. Quantification of CD31 positive cell area relative to total tissue area from exercised and control mice. **F**. Quantification of cells positive with staining using an anti-fibroblast antibody (abcam) in exercised and control mice. **G**. Confocal images of Phospho-histone3 staining (green) counterstained with dapi (blue) and α-actinin (green) in cardiac tissue from exercised mice. Upper left: Cardiomyocyte in prophase with nuclear condensation. Upper right: Cardiomyocyte at end of prophase. Lower left: Cardiomyocyte undergoing cariokenesis and lower right: Cardiomyocyte in telophase after nuclear separation. **H**. Confocal stack of BrdU staining with orthogonal view displaying a nuclei within cardiomyocyte (upper panel) and a nuclei outside cardiomyocyte (lower panel). * indicates $p<0.05$ using students t-test.

Supplemental figure II

A. qPCR validation of Quanttrx-identified transcription factors with expression changes in either the physiological or pathological hypertrophy model (n=4). All changes are $p<0.05$ using students t-test. **B**. Cardiomyocytes and non-cardiomyocytes separated from rat neonatal hearts using density gradient centrifugation. Samples were analyzed for indicated gene expression normalized to 18S, and cardiomyocytes set to 1. **C**. Adenoviral over expression of

indicated genes in rat neonatal cardiomyocytes followed by size measurements. Data is expressed as percent of GFP control. **D**. Western Blot against C/EBPβ in cardiomyocytes (CM) and non-cardiomyocytes with actin as loading control. **E**. Correlation between the percent change seen in the exercise model (y-axis) and the TAC-model (x-axis). All Quanttrx transcription factors significantly altered in either model are included. * indicates $p<0.05$ using students t-test

Supplemental figure III

A. SiRNA knockdown of C/EBPβ in primary cardiomyocytes assayed using RT-PCR. Two siRNA constructs and two control siRNA´s was used. Data is normalized to respective control and 18S. **B**. Western blot against C/EBPβ and tubulin from primary cardiomyocytes transfected with control or C/EBPβ siRNA #2. **C**. mRNA levels of ANP and BNP in rat neonatal cardiomyocytes transfected with control or C/EBPβ siRNA with or without 24 hours treatment with phenylephrine (PE). **D**. Over expression with C/EBPβ adenocirus in primary cardiomyocytes followed by western blot analysis against C/EBPβ. * indicates $p<0.05$ vs respective control and § vs control siRNA +PE using one-way ANOVA.

Supplemental figure IV

A. Normalized mRNA levels of indicated genes following C/EBPβ adenoviral over expression in primary cardiomyocytes. **B-C**. Rat neonatal cardiomyocytes transduced with indicated adenoviral constructs followed by RT-PCR analysis of indicated genes normalized to 18S. **D**. mRNA expression levels of indicated genes from cardiac samples of sham- or TAC operated mice 2 weeks after intervention (n=4). **E**. Rat neonatal cardiomyocytes transduced with PGC1α or GFP expressing adenovirus followed by size measurements. * indicates $p<0.05$ using students t-test (A, D and E) and § marks $p<0.05$ vs AKTwt + GFP using one-way ANOVA (B-C).

Supplemental figure V

A. Pro-proliferative genes up regulated in endurance exercise from expression analysis experiment. **B**. Western blot against CITED4 from rat neonatal cardiomyocytes treated with control or CITED4 expressing adenovirus. **C**. mRNA analysis of CITED4 after transient transfection with control or CITED4 siRNA as annotated. **D**. Normalized SRF mRNA levels with GFP or CITED4 adenoviral over expression. **E-F**. mRNA levels of n-myc and cyclinD1 in heart samples following endurance exercise (**E**) or in rat neonatal cardiomyocytes over expressing CITED4 (**F**). * indicates $p<0.05$ using students t-test

Supplemental figure VI

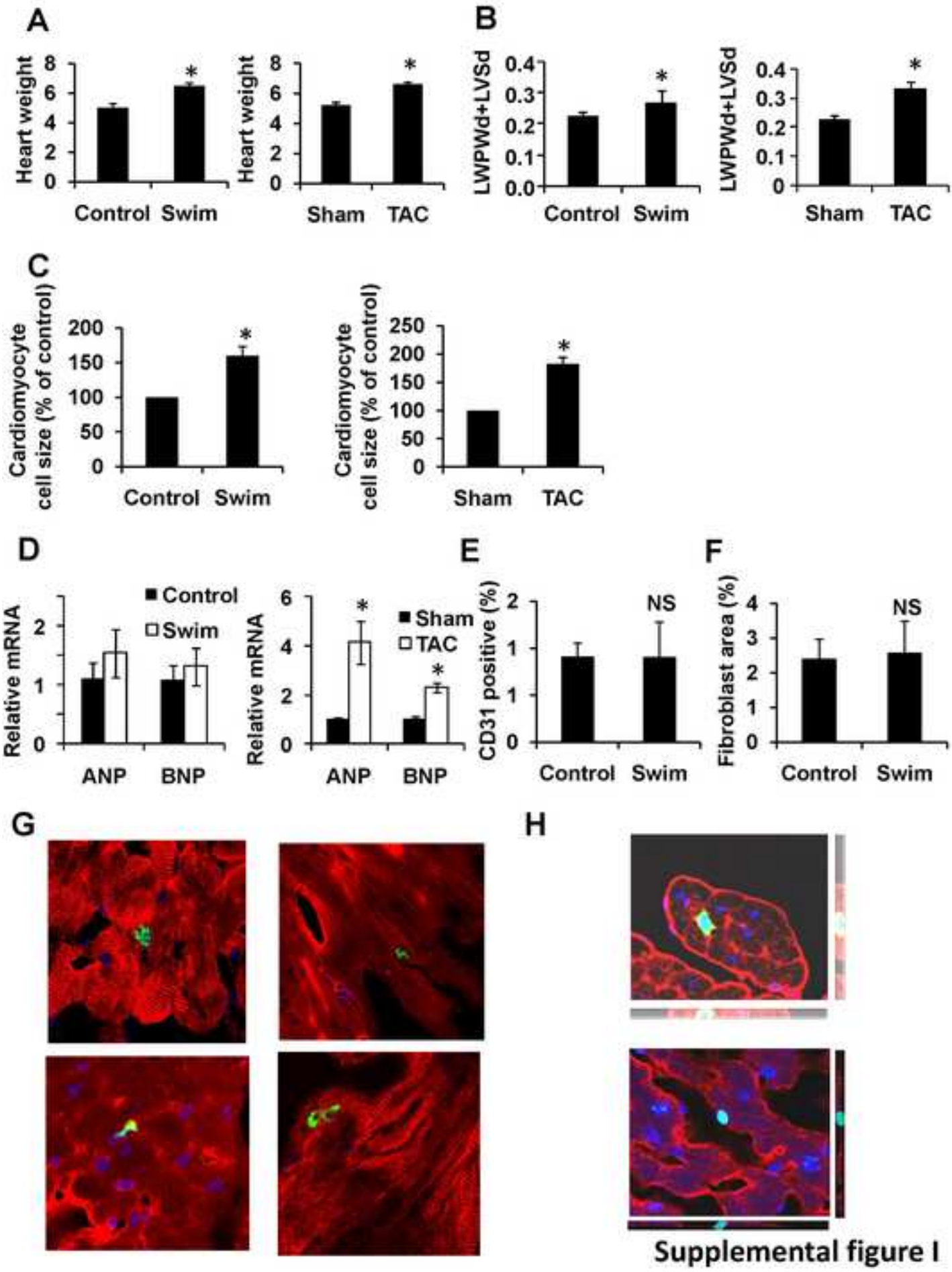
A-B. C/EBPβ mRNA (**A**) and protein (**B**) levels in heart from wild type (n=5) and C/EBPβ$^{+/-}$ (n=7) mice. mRNA levels were normalized to the 18S gene. **C**. Expression of exercise-induced genes in the C/EBPβ$^{+/-}$ mice compared to wild type littermates (n=5 and 7 respectively). **D**. Heart weights of C/EBPβ$^{+/-}$ mice compared to wild type littermates (n=4 and 5 respectively) at baseline. **E**. Maximal exercise capacity measured as described in the method section, in wt and C/EBPβ$^{+/-}$ mice. **F**. PCNA western blot from wt and C/EBPβ$^{+/-}$ mice with sub sequent quantification. Data is presented as PCNA-background normalized to β-actin. **G**. Quantification of ki67 positive cardiomyocyte nuclei (n=5 and 7 mice based on at least 20 images per mouse). * indicates $p<0.05$ using students t-test

Supplemental figure VII

A-B. Echocardiographic characteristics of wild type and C/EBPβ$^{+/-}$ mice after TAC intervention (day 0). **A**. diastolic (left) and systolic (right) Left intraventricular diameter (LVD). **B**. the sum of either diastolic (left) or systolic (right) Intravetricular (IV) and Left Ventricular Posteriar Wall (LVPW) width. **C**. Heart weight in wild type and C/EBPβ$^{+/-}$ mice after TAC intervention. **D**. C/EBPβ expression levels in C/EBPβ$^{+/-}$ and wild type mice after

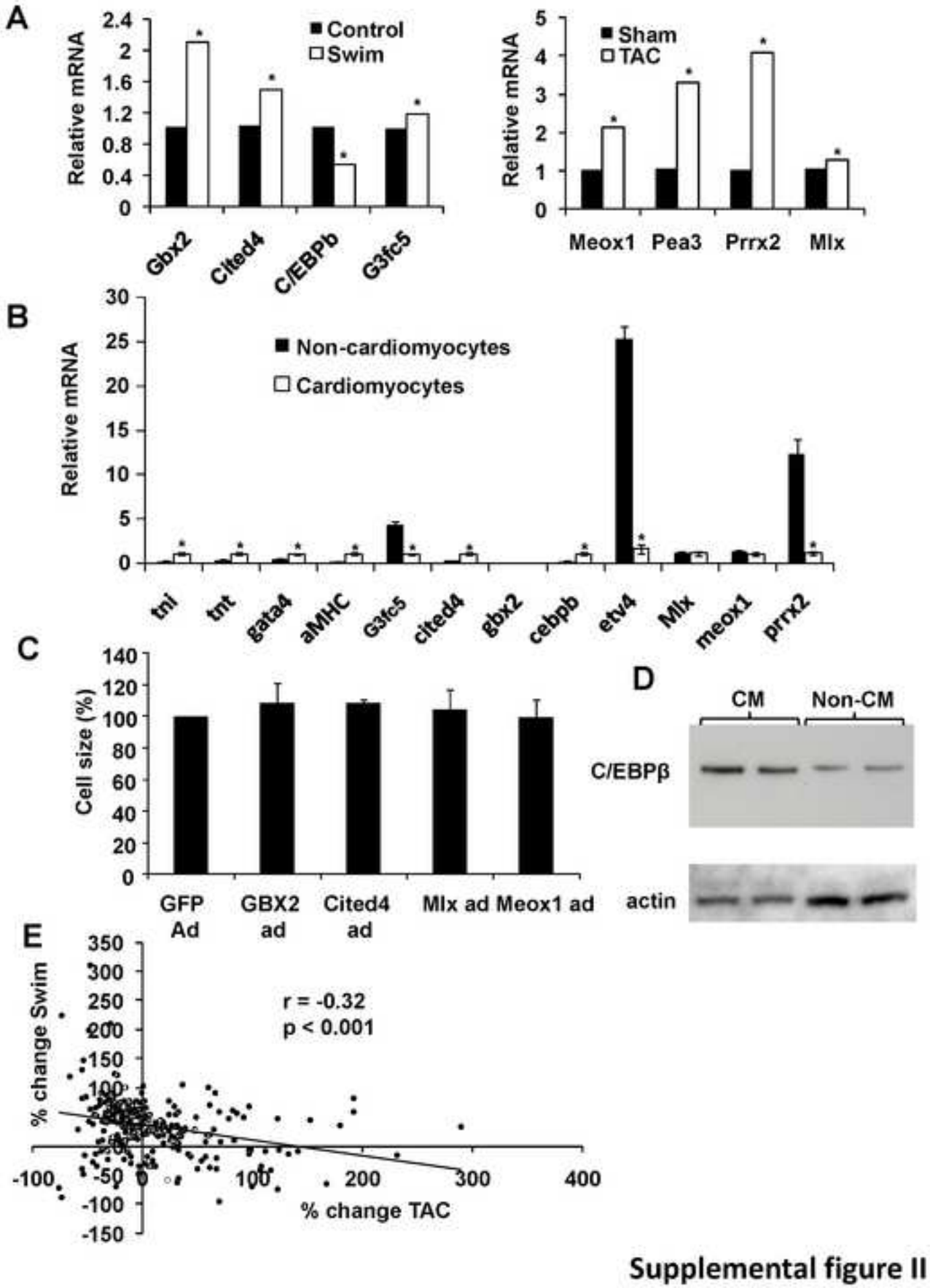
the endurance exercise protocol. **E**. Heart weights normalized to body weight in C/EBPβ$^{+/-}$ and wild type mice after the endurance exercise protocol. * indicates $p<0.05$ using students t-test.

Supplemental Figure 1



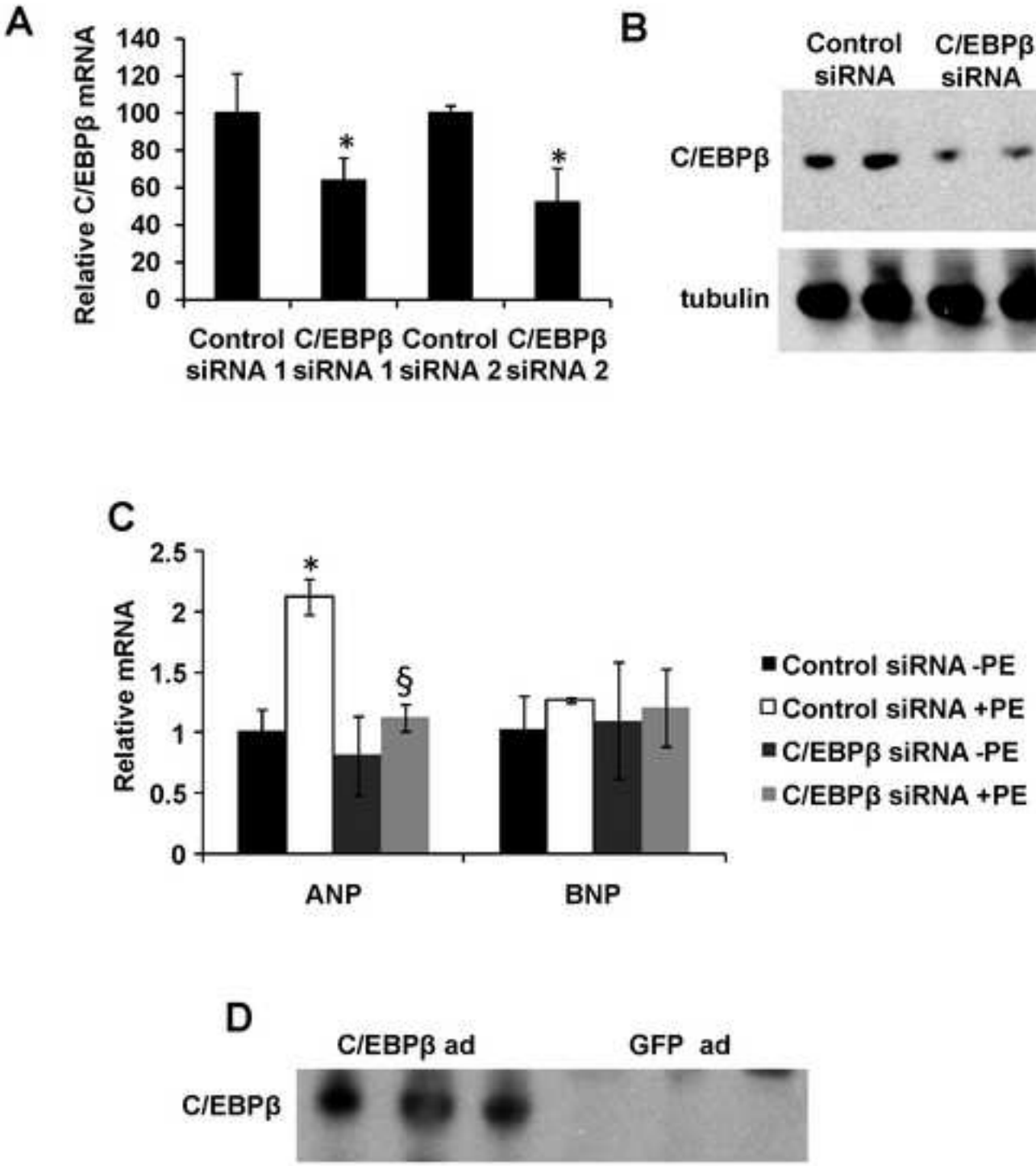
Supplemental figure I

Supplemental Figure 2



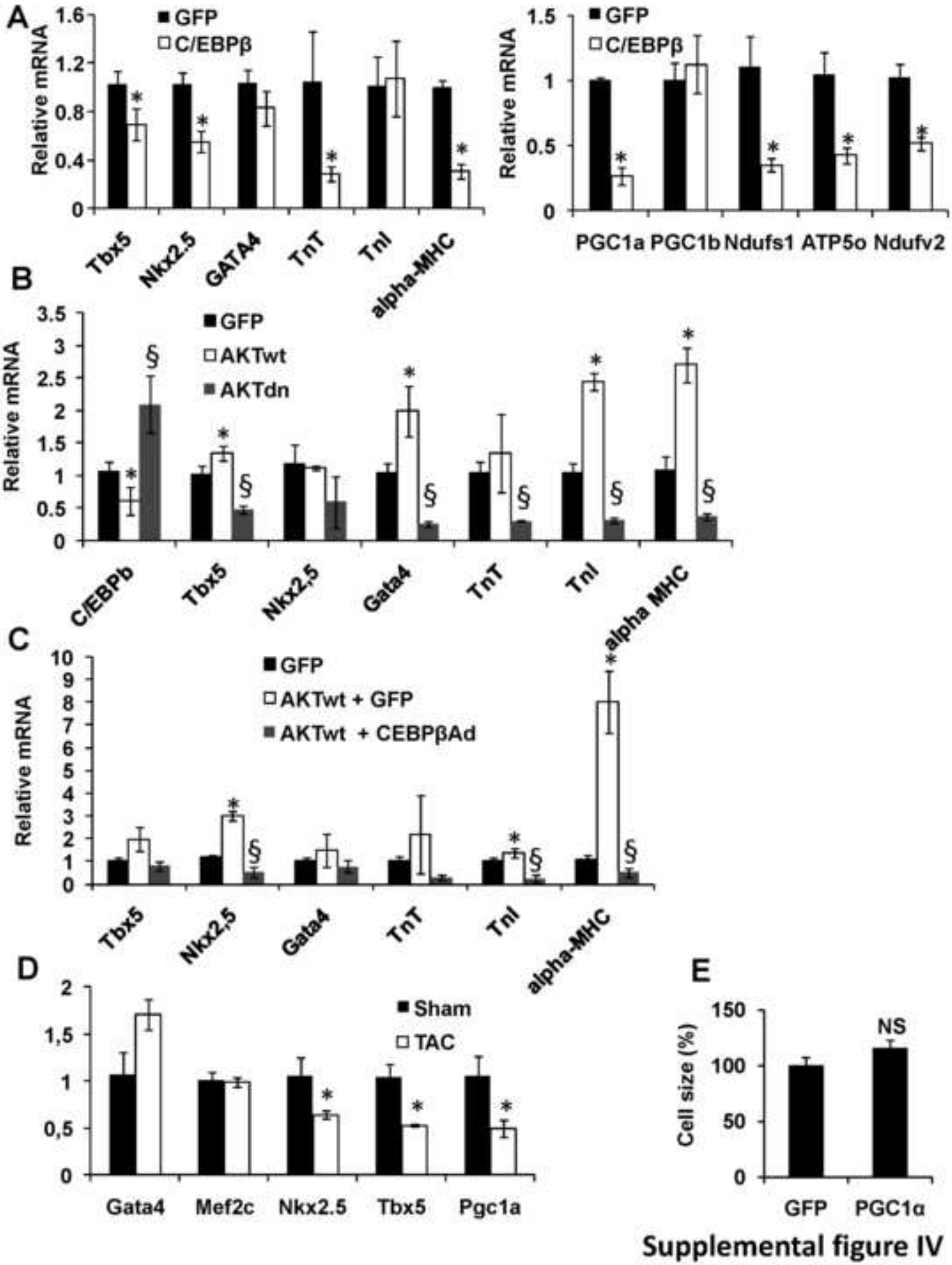
Supplemental figure II

Supplemental Figure 3



Supplemental figure III

Supplemental Figure 4

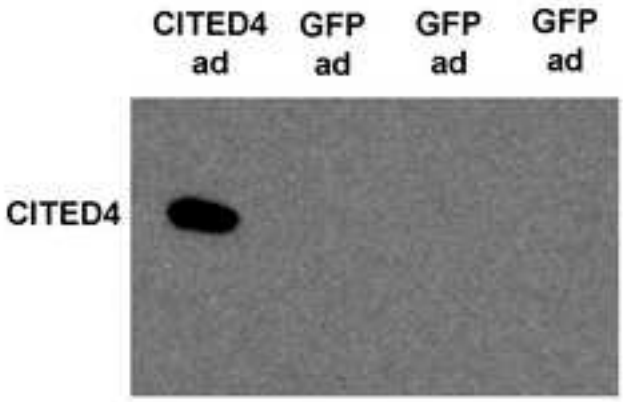


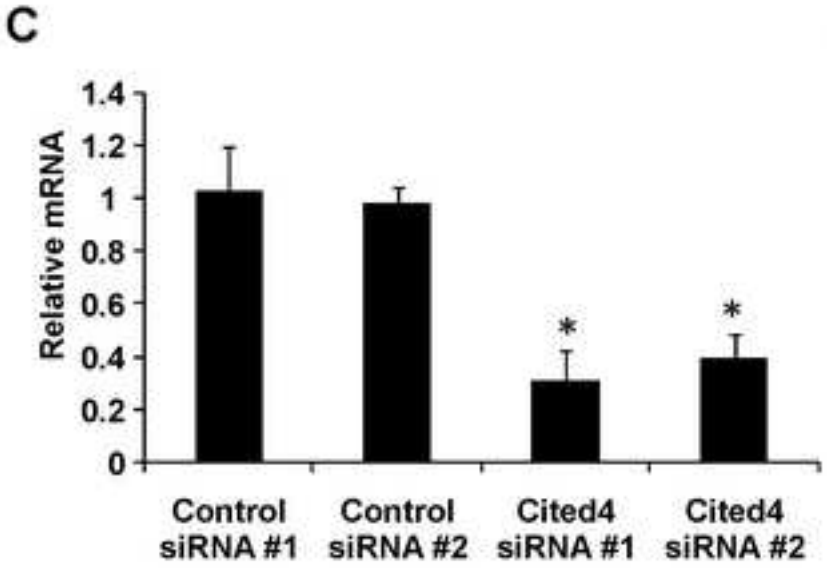
Supplemental figure IV

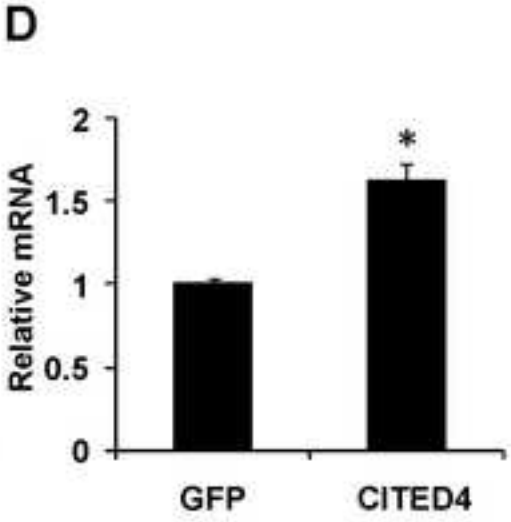
Supplemental Figure 5

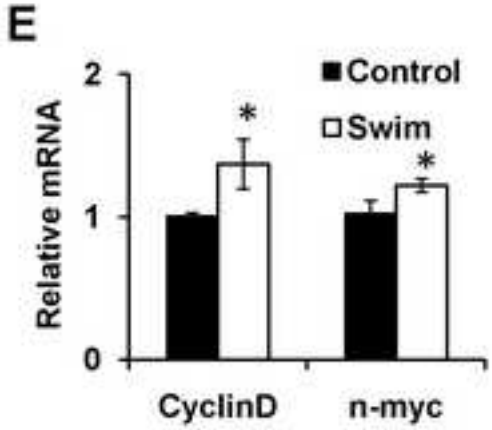
A

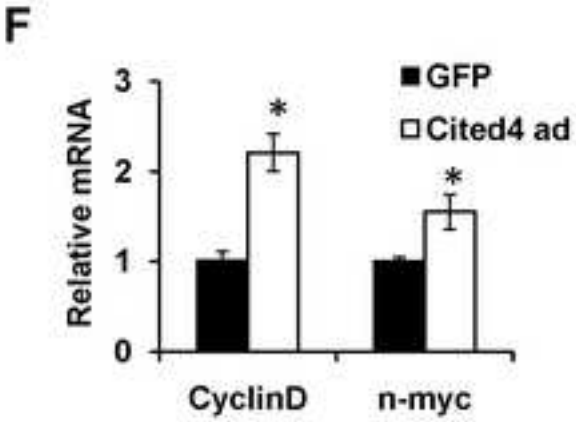
	Fold change swim	p Swim
Mycn	1,37	0,04
Gab1	1,31	0,01
Pa2G4	1,11	0,04
GSK3b	1,46	0,01
Cyclin D1	1,22	0,03
Ndrg3	1,25	0,00
E2f1	1,20	0,00
Bub1b	1,18	0,02
E2f5	1,19	0,01





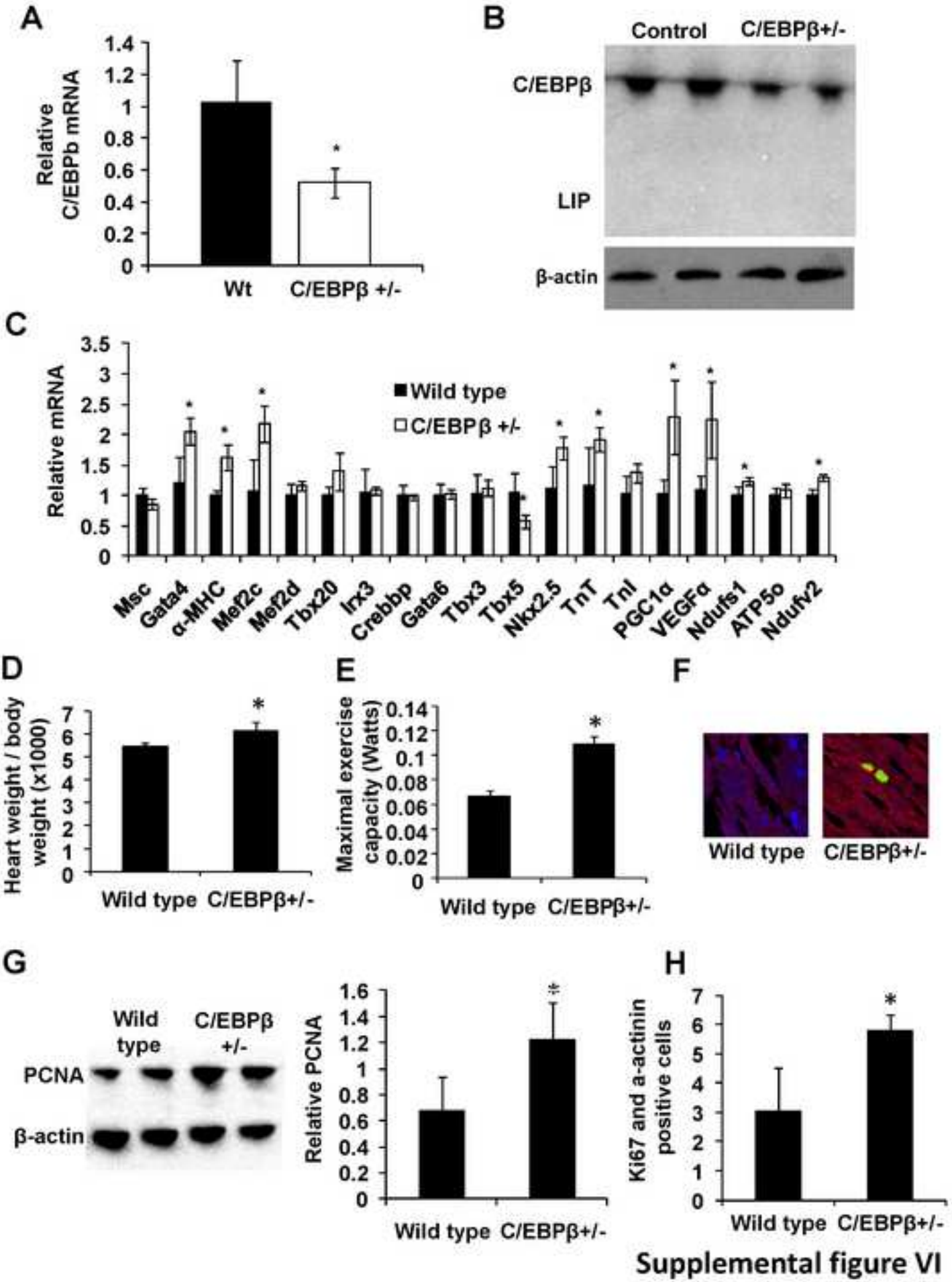






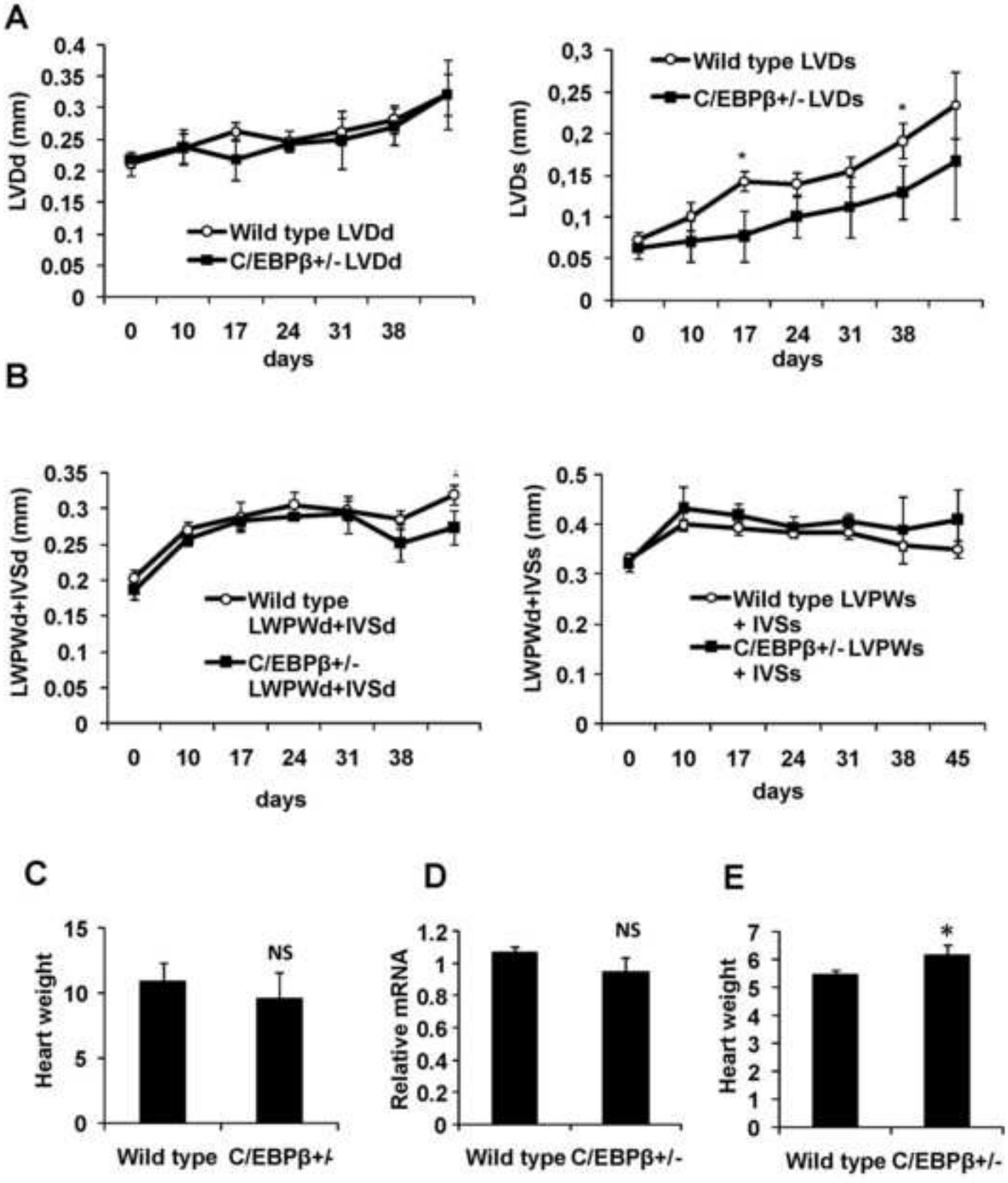
Supplemental figure V

Supplemental Figure 6



Supplemental figure VI

Supplemental Figure 7



Supplemental figure VII