Preclinical evidence for the therapeutic value of TBX5 normalization in arrhythmia control

Authors: Franziska S. Rathjens[1,2], Alica Blenkle[1], Lavanya M. Iyer[1,2] , Anke Renger[3], Fahima Syeda[4], Claudia Noack[1,2], Andreas Jungmann[5,6], Matthias Dewenter[6,7], Karl Toischer[8], Ali El-Armouche[9], Oliver J. Müller[10], Larissa Fabritz[4,11,12], Wolfram-Hubertus Zimmermann[1,2], Laura C. Zelarayan[1,2,*] and Maria-Patapia Zafeiriou[1,2,*]

Affiliations:

[1] Institute of Pharmacology and Toxicology, University Medical Center, Goettingen, Germany

[2] DZHK (German Center for Cardiovascular Disease), partner site Goettingen, Germany

[3] Institut für Erziehungswissenschaften, Humboldt University, Berlin, Germany

[4] Institute of Cardiovascular Science, University of Birmingham, Birmingham, United Kingdom

[5] Internal Medicine III, University Hospital Heidelberg, Heidelberg, Germany

[6] DZHK (German Center for Cardiovascular Disease), partner site Heidelberg/Mannheim, Germany

[7] Department of Molecular Cardiology and Epigenetics, University of Heidelberg, Germany

[8] Department of Cardiology and Pneumology, University Medical Center, Goettingen, Germany

[9] Department of Pharmacology and Toxicology, Faculty of Medicine, University of Technology-Dresden, Germany

[10] Department of Internal Medicine III, University of Kiel, Kiel, Germany.

[11] Division of Rhythmology, Department of Cardiovascular Medicine, Hospital of the University of Münster, Münster, Germany

[12] University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

* To whom correspondence should be addressed. Tel: 0049 551 395777; Fax: 0049 551 395699; Email: patapia.zafeiriou@med.uni-goettingen.de
Correspondence may also be addressed to Tel: 0049 551 3920730; Fax: 0049 551 395699; Email: laura.zelarayan@med.uni-goettingen.de

Supplementary materials and methods

Electrophysiological study of isolated hearts

Hearts were excised under terminal anesthesia, and the aorta was cannulated and retrogradely perfused using 37°C Krebs-Henseleit buffer (in mmol/l; NaCl 118, $NaHCO_3$ 24.88, KH_2PO_4 41.18, glucose 5.55, Na-pyruvate 2, $MgSO_4$ 0.83, $CaCl_2$ 1.8, KCl 4.7) equilibrated with a 95% O_2/5% CO_2 gas mixture. The hearts were mounted on a vertical Langendorff apparatus (Hugo Sachs Electronic-Harvard Apparatus GmbH) and constantly perfused. An octapolar mouse electrophysiologic catheter (CIBER MOUSE; NuMED) was placed in the right atria and ventricles for atrial and ventricular pacing. Three monophasic action potentials (MAPs) were continuously and simultaneously recorded from the right ventricular free wall, septal area and left ventricular free wall epicardium [1]. Atrial S1 pacing was performed to measure activation times from right atrium to right ventricle; endocardial right ventricular pacing was performed to measure ventricular activation times and both for steady-state action potential durations. Ventricular arrhythmia inducibility was performed by programmed ventricular stimulation using a single encroaching premature stimulus (S2). All signals were digitized and stored on digital media for offline analysis. Experiments and analysis were performed blindly (for details [2]).

RNA-Sequencing

Sequence images were transformed with Illumina software BaseCaller to bcl files, which were demultiplexed to fastq files with CASAVA (v1.8.2). Reads were aligned by STAR (2.3.9e) to the GENCODE *Mus musculus* transcriptome (mm10). Counting the reads to each gene was done via HTSeq-count python script. Data was preprocessed and analyzed in the R environment loading DESeq2, gplots, and biomaRt packages. Normalization, estimation of dispersions and testing for differentially expressed genes based on a test assuming negative binomial data distribution was computed via DESeq2. Candidate genes were filtered to a minimum of 0.8 log2fold change and FDR-corrected p-value<0.05. For functional association for the candidates genes were analyzed for gene ontology term enrichment via goseq.

Immunoblot Analysis

Immunoblot analysis was performed as described previously [3]. The following primary and secondary antibodies were used: TBX5 (1:1000; Sigma HPA008786, Hamburg/Germany); TBX5 (1:1000; sc-515536, Santa Cruz Biotechnologies); CX43 (1:1000; AB1728, Millipore, Darmstadt/Germany); GIRK4 (1:250, Sigma HPA017353, Hamburg/Germany), GAPDH (1:50000; Millipore, Darmstadt/Germany); rb-HRP (1:5000; DAKO, Hamburg/Germany); ms-HRP (1:10,000; DAKO, Hamburg/Germany).

Except for the GIRK4 antibody, all blocking and antibody incubation steps were done in in 5% Milk (Applichem) diluted in TBS-T (GIRK4 in 5% BSA (Sigma-Aldrich)).

Chromatin Immunoprecipitation

Adult murine ventricles were minced and crosslinked with 2% formaldehyde (Polysciences) in PBS supplemented with Protease Inhibitors (PI; Complete Mini, Roche). After 30 min, crosslinking was terminated by glycin addition at a final concentration of 125 mmol/l. The suspension was centrifuged at 300 g for 2 min at 4°C, washed with PBS and centrifuged again. Hypotonic buffer (2.38 g/l HEPES, 0.75 g/l KCl, 0.41 g/l $MgCl_2$*6 H_2O, 0.037 g/l EDTA, 0.154 g/l DTT and PI) was added and samples were homogenized in a Tissue Lyser (Qiagen; 30 Hz- 120 sec). NP-40 was added to 1% final concentration, and upon 10 min incubation on ice the samples were centrifuged at 12,000 g for 2 min at 4°C. The pellet was resuspended in hypotonic buffer with 1% NP-40 upon 3 min incubation on ice, centrifuged at 12,000 g for 2 min at 4°C. The resulting pellet was resuspended in sonication buffer I (7.88 g/l Tris-HCl, 2.92 g/l EDTA, 10 g/l SDS, PI, pH 8), incubated on ice for 15 min, and subsequently sonication buffer II (7.88 g/l Tris-HCl, 5.84 g/l EDTA, 10 g/l NP-40, 8.77 g/l NaCl, 0.84 g NaF, PI, pH 8) was added. Samples were sonicated in ice-cold water in Bioruptor Standard (Diagenode) for 30 cycles (30 sec ON/OFF) then centrifuged for 10 min, at 12,000 g and 8°C. The pellet was resuspended in sonication buffer I + II (mixed 1:1 ratio), sonicated and centrifuged as described above. The chromatin-containing supernatant was collected and 500 µl of this fraction was used for each ChIP. Each sample was incubated with 1.5 ml ChIP incubation buffer (7.88 g/l Tris-HCl, 1.46 g/l EDTA, 2.92 g/l NaCl, PI, pH 7.5) containing 2 µg of antibody (TBX5: HPA008786 or ChIP grade rb-IgG - Millipore 12-370) overnight at 4°C. The next day, 50 µl protein A/G coated magnetic beads (Pierce) were added and samples were again incubated for 2 h at 4°C. Magnetic beads were subsequently washed for 5 min each with wash buffer I (7.88 g/l Tris-HCl, 2.92 g/l EDTA, 4.38 g/l NaCl, pH 7.5), wash buffer II (7.88 g/l Tris-HCl, 2.92 g/l EDTA, 7.31 g/l NaCl, pH 7.5) and wash buffer III (7.88 g/l Tris-HCl, 2.92 g/l EDTA, 10.23 g/l NaCl, pH 7.5). Finally, the immunoprecipitated chromatin was eluted by a 30 min incubation in ChIP elution buffer (7.88 g/l Tris-HCl, 1.46 g/l EDTA, 2.92 g/l NaCl, 10 g/l SDS, pH 7.5) at 65°C. The eluate was treated with proteinase K (ThermoScientific) for 1.5 h at 65°C and the chromatin was column purified (NucleoSpin PCR and Gel Clean-Up with Buffer NTB, Macherey Nagel). ChIP-Seq library preparation was performed using NEBNext Ultra DNA library prep kit for Illumina (E7370) according to manufacturer's instructions. Quantitation of DNA libraries was done on an Invitrogen Qubit 2.0 Fluorometer and the size range of DNA libraries was performed on an Agilent Bioanalyzer 2100 (High Sensitivity DNA Assay). DNA libraries were amplified and sequenced by using cBot and HiSeq2500 from Illumina (20-25 million reads per sample).

ChIP-sequencing data analysis

Basic ChIP-Seq analysis was performed on Galaxy [4] on usegalaxy.org. In brief, the sequence reads were aligned to the mouse reference assembly (UCSC version mm9) using Bowtie [5]. Model Based Analysis of ChIP-Seq (MACS2) version 2.1.0.20140616.0, which is the updated version of MACS [6] was used for peak calling; IgG was used as a control file. Bedgraphs obtained from MACS2 were converted to bigwigs and visualized using the Integrative Genomics Viewer IGV 2.3.82 [7, 8]. To calculate the enriched genomic regions in the TBX5-ChIP-Seq dataset 'CEAS: cis-regulatory element annotation system' [9] was used on Cistrome [10]. GREAT analysis was performed to annotate the peaks to genes and calculate enrichment of gene ontology clusters for biological processes and human phenotypes for TBX5 [11]. Heatmaps were generated using deepTools-computeMatrix and heatmapper options for the ChIP-Seq signal (in RPKM) using bamCoverage [12]. Co-Occupancy correlation was statistically analyzed with multibigwig summary and plot correlation on Galaxy. To identify TBX5-peaks, that are overlapping with H3K27ac and POL2, the WindowBed function (500 bp up- and downstream) from BEDTools was used in Galaxy [12, 13]. Motif Enrichment in the ChIP-Seq dataset was tested with AME [14] using known motifs for TBX5, MEIS1 and MEIS2, GATA4 and NKX2.5. Motifs used were identified by previous studies [15, 16] and MotifMap [17, 18]. InteractiVenn [19] was used to analyze the intersection between TBX5 bound genes (found in ChIP-Seq) and genes differentially expressed in TBX5 KO ventricle (cutoff $p<0.05$; Log2-fold-change >0.8 or <-0.8 respectively). Gene ontology/pathway analyses were performed using a minimum of 4 genes per cluster and default parameters and stringency in 'ClueGO': a Cytoscape plug-in [20, 21] and the significant ($p \leq 0.05$) cluster of 'Gene Ontology Biological Processes' were shown. For co-occupancy analysis, TBX5 peaks were compared to public data on active enhancers as H3K27ac and POL2 [22], NKX2.5 [23], GATA4 [23] and the TBX5 repressor TBX3 [23].

Immunofluorescence Staining

Immunofluorescence staining was performed as described previously [3]. Tissues were rinsed in PBS, fixed overnight in 4% formaldehyde (FA) at 4 °C, embedded in paraffin, and sectioned at 4 µm. Sections were deparaffinized, microwaved for antigen retrieval in citrate buffer (2,94 g/l sodium citrate, 0.5 ml/l Tween 20, pH 6.0), blocked in blocking buffer (5 % BSA and 0.1 % Triton-X-100 in PBS) different primary antibodies: TBX5 (1:50; sc-515536, Santa Cruz Biotechnologies), CX43 (1:200; AB1728, Millipore) and cTNT (1:200; ab8295, Abcam) in antibody staining buffer (1 % BSA and 0.1 % Triton-X-100 in PBS). Slides were washed in PBS and incubated with AlexaFluor488- or AlexaFluor594-conjugated secondary antibodies (1:200; Invitrogen). The slides were counterstained with DAPI and mounted with Mowiol 488 (Carl Roth). Images were captured using epifluoresence (IX70, Olympus) or confocal (Zeiss 710 NLO) microscopes. Isolated ventricular murine cardiomyocytes were stained with TBX5 (1:20; HPA008786; Sigma-Aldrich), CX43 (1:20; BD 610062, BD Biosciences), Phalloidin 633 (1:100; Invitrogen) and DAPI.

Cloning and Enhancer Validation Assay

Gja1-enhancer (chr10: 56980696 to 56981259) was cloned into pGL4.25 (Promega) with HindIII and XhoI. Kcnj5-enhancer (chr9: 32313616 to 32314540) was cloned into pGL4.23_GW, which was a kind gift from Jorge Ferrer (Addgene plasmid # 60323) [24], with HindIII and XhoI. TBX5 was cloned into pCMV2c-flag (Sigma) with EcoRI and SalI. Primers are listed in Table S1. All restriction enzymes were FastDigest enzymes (Thermo Scientific).

pCMV2c-flag was used as a control vector for TBX5 co-transfection. The empty vectors of pGL4.25 and pGl4.23_GW were used as controls to exclude effects of TBX5 co-transfection on the vector backbone. The pGL4.23/25 vectors and pCMV2c vectors (250 ng each) and Renilla luciferase expressing plasmid (0.5 ng) were co-transfected in HEK293 cells (100.000 cells per well, 24-well plate, plated 24 hours before transfection) with Turbofect (Thermo Scientific). 24 hours later the Luciferase assay was done with the Dual-Luciferase Reporter Assay System in the Glomax Instrument (both Promega). Values of pCMV2c-TBX5-flag co-transfected samples were normalized to pCMV2c-flag co-transfected samples to calculate increase in activity by TBX5 overexpression.

References and Notes:

1. Fabritz L, Kirchhof P, Franz MR, Eckardt L, Monnig G, Milberg P, Breithardt G, Haverkamp W. Prolonged action potential durations, increased dispersion of repolarization, and polymorphic ventricular tachycardia in a mouse model of proarrhythmia. *Basic Res Cardiol* 2003;**98**:25-32.
2. Wittkopper K, Fabritz L, Neef S, Ort KR, Grefe C, Unsold B, Kirchhof P, Maier LS, Hasenfuss G, Dobrev D, Eschenhagen T, El-Armouche A. Constitutively active phosphatase inhibitor-1 improves cardiac contractility in young mice but is deleterious after catecholaminergic stress and with aging. *The Journal of clinical investigation* 2010;**120**:617-626.
3. Zafiriou MP, Zelarayan LC, Noack C, Renger A, Nigam S, Siafaka-Kapadai A. Hepoxilin A(3) protects beta-cells from apoptosis in contrast to its precursor, 12-hydroperoxyeicosatetraenoic acid. *Biochim Biophys Acta* 2011;**1811**:361-369.
4. Afgan E, Baker D, van den Beek M, Blankenberg D, Bouvier D, Cech M, Chilton J, Clements D, Coraor N, Eberhard C, Gruning B, Guerler A, Hillman-Jackson J, Von Kuster G, Rasche E, Soranzo N, Turaga N, Taylor J, Nekrutenko A, Goecks J. The Galaxy platform for accessible, reproducible and collaborative biomedical analyses: 2016 update. *Nucleic Acids Res* 2016;**44**:W3-W10.
5. Langmead B. Aligning short sequencing reads with Bowtie. *Curr Protoc Bioinformatics* 2010;**Chapter 11**:Unit 11 17.
6. Zhang Y, Liu T, Meyer CA, Eeckhoute J, Johnson DS, Bernstein BE, Nusbaum C, Myers RM, Brown M, Li W, Liu XS. Model-based analysis of ChIP-Seq (MACS). *Genome Biol* 2008;**9**:R137.
7. Robinson JT, Thorvaldsdottir H, Winckler W, Guttman M, Lander ES, Getz G, Mesirov JP. Integrative genomics viewer. *Nat Biotechnol* 2011;**29**:24-26.
8. Thorvaldsdottir H, Robinson JT, Mesirov JP. Integrative Genomics Viewer (IGV): high-performance genomics data visualization and exploration. *Brief Bioinform* 2013;**14**:178-192.
9. Shin H, Liu T, Manrai AK, Liu XS. CEAS: cis-regulatory element annotation system. *Bioinformatics* 2009;**25**:2605-2606.
10. Liu T, Ortiz JA, Taing L, Meyer CA, Lee B, Zhang Y, Shin H, Wong SS, Ma J, Lei Y, Pape UJ, Poidinger M, Chen Y, Yeung K, Brown M, Turpaz Y, Liu XS. Cistrome: an integrative platform for transcriptional regulation studies. *Genome Biol* 2011;**12**:R83.
11. McLean CY, Bristor D, Hiller M, Clarke SL, Schaar BT, Lowe CB, Wenger AM, Bejerano G. GREAT improves functional interpretation of cis-regulatory regions. *Nat Biotechnol* 2010;**28**:495-501.
12. Ramirez F, Dundar F, Diehl S, Gruning BA, Manke T. deepTools: a flexible platform for exploring deep-sequencing data. *Nucleic Acids Res* 2014;**42**:W187-191.
13. Gruening BA. Galaxy wrapper. 2014.
14. McLeay RC, Bailey TL. Motif Enrichment Analysis: a unified framework and an evaluation on ChIP data. *BMC Bioinformatics* 2010;**11**:165.

15. Ghosh TK, Packham EA, Bonser AJ, Robinson TE, Cross SJ, Brook JD. Characterization of the TBX5 binding site and analysis of mutations that cause Holt-Oram syndrome. *Hum Mol Genet* 2001;**10**:1983-1994.
16. Grau J, Posch S, Grosse I, Keilwagen J. A general approach for discriminative de novo motif discovery from high-throughput data. *Nucleic Acids Res* 2013;**41**:e197.
17. Daily K, Patel VR, Rigor P, Xie X, Baldi P. MotifMap: integrative genome-wide maps of regulatory motif sites for model species. *BMC Bioinformatics* 2011;**12**:495.
18. Xie X, Rigor P, Baldi P. MotifMap: a human genome-wide map of candidate regulatory motif sites. *Bioinformatics* 2009;**25**:167-174.
19. Heberle H, Meirelles GV, da Silva FR, Telles GP, Minghim R. InteractiVenn: a web-based tool for the analysis of sets through Venn diagrams. *BMC Bioinformatics* 2015;**16**:169.
20. Bindea G, Galon J, Mlecnik B. CluePedia Cytoscape plugin: pathway insights using integrated experimental and in silico data. *Bioinformatics* 2013;**29**:661-663.
21. Bindea G, Mlecnik B, Hackl H, Charoentong P, Tosolini M, Kirilovsky A, Fridman WH, Pages F, Trajanoski Z, Galon J. ClueGO: a Cytoscape plug-in to decipher functionally grouped gene ontology and pathway annotation networks. *Bioinformatics* 2009;**25**:1091-1093.
22. He A, Gu F, Hu Y, Ma Q, Ye LY, Akiyama JA, Visel A, Pennacchio LA, Pu WT. Dynamic GATA4 enhancers shape the chromatin landscape central to heart development and disease. *Nat Commun* 2014;**5**:4907.
23. van den Boogaard M, Wong LY, Tessadori F, Bakker ML, Dreizehnter LK, Wakker V, Bezzina CR, t Hoen PA, Bakkers J, Barnett P, Christoffels VM. Genetic variation in T-box binding element functionally affects SCN5A/SCN10A enhancer. *The Journal of clinical investigation* 2012;**122**:2519-2530.
24. Pasquali L, Gaulton KJ, Rodriguez-Segui SA, Mularoni L, Miguel-Escalada I, Akerman I, Tena JJ, Moran I, Gomez-Marin C, van de Bunt M, Ponsa-Cobas J, Castro N, Nammo T, Cebola I, Garcia-Hurtado J, Maestro MA, Pattou F, Piemonti L, Berney T, Gloyn AL, Ravassard P, Gomez-Skarmeta JL, Muller F, McCarthy MI, Ferrer J. Pancreatic islet enhancer clusters enriched in type 2 diabetes risk-associated variants. *Nature genetics* 2014;**46**:136-143.

SUPPLEMENTAL FIGURE LEGENDS

Figure S1. Expression of TBX5 in the adult murine heart. A, Co-staining of CX43 (green) and TBX5 (red) shows that besides the prominent atrial and AV node expression (panel I-II) lower levels of TBX5 are present in CX43pos cells throughout the ventricular myocardium (arrowheads, panel III), also in isolated ventricular cardiomyocytes (panel IV). **B,** Immunohistochemistry analysis of TBX5 in a longitudinal paraffin embedded murine heart. Strong TBX5 expression (brown) was detected at the atria and AV node (insert i and ii). Although TBX5 levels were lower in left and right ventricle (insert iii and iv respectively) TBX5 expression was evident throughout the myocardium. **C,** Immunofluorescence analysis of TBX5 expression in a transversal slice of the left ventricle. The different panels show TBX5 expression distributed along the endocardium, working myocardium and outer left ventricle. Secondary antibody incubation with DAPI served as a negative control (yellow color on the negative control is due to cardiomyocyte autofluorescence). Scale bars: 20 µm

Figure S2. Expression of TBX5 and CX43 in different WT and v*Tbx5*KO hearts. A, Co-staining of CX43 (green) and TBX5 (cyan) in different cardiac compartments of wild type and v*Tbx5*KO hearts. Nuclei are depicted by dark blue DAPI staining. Left atria (LA) of v*Tbx5*KO have lower amounts of TBX5 and CX43 in comparison to WT. In contrast to LA right and left ventricular tissue (RV and LV) are completely devoid from TBX5 and its target CX43. Low levels of TBX5 and CX43 are detectable in the endocardial regions of the ventricles. Scale bar: 20 µm **B,** Immunohistochemistry analysis of TBX5 in a longitudinal paraffin embedded v*Tbx5*KO heart that presents TBX5 (cyan) and CX43 (green) expression in the right atria (RA), the bundle of HIS and the septum. Strong TBX5 expression was detected in RA (1) and bundle of HIS (2) while the septum (3) did not express TBX5. The cyan signal observed was unspecific and not nuclear. **C,** Immunohistochemistry analysis of TBX5 (cyan) and CX43 (green) in a longitudinal paraffin embedded v*Tbx5*KO heart slice. The overview picture on the right panel shows the presence of CX43 in both atria and absence from the working myocardium. Insert 1 shows a close-up of LA and LV and insert 2 shows the AV node. Insert 3 and 4 show a closeup view of LA and LV, respectively. LA and AV node show a remaining expression of TBX5 while LV show not TBX5 and sparse CX43 expression. Please note that the AV node does not express CX43. **D,** Immunohistochemistry analysis of TBX5 (cyan) and CX43 (green) in the RA and RV of v*Tbx5*KO heart. After recombination TBX5 and CX43 are expressed in the RA (insert 1) but not the RV (insert 2). **E,** Semi-quantitative analysis of TBX5 positive nuclei in Flox and v*Tbx5*KO hearts. Pictures used for the analysis were taken from left and right atria (Atria), left and right ventricle (ventricles) or compartments of the ventricular conduction system (VCS) as AV node and bundle of HIS. n=4-5 pictures from 3 different mice / group containing 50-100 nuclei. Statistical analysis was performed by one-way ANOVA followed by Sidak's multiple comparison post hoc test. *$P < 0.05$.

Figure S3. Basal functional characterization of *vTbx5*KO mice vs Cre control. A, Echocardiography data from *control CRE* mice supporting no functional deterioration in contrast to v*Tbx5*KO mice (n=10) **B,** No significant fibrosis in the KO animals compared to controls was observed. **C,** Statistical analysis of QT interval and heart rate (HR) obtained by telemetric ECG measurements 1-8 weeks post-rec. Line indicates Cre control mean value ± SEM 4 weeks post-rec. (Cre n=6; Flox n =6; KO n=7-13 biological replicates. The animal number decreased during measurements due to SCD). QT interval significantly increased after TBX5 loss. The HR initially decreased probably due to AV blocks but 8 weeks post-rec the mean HR increased but the variability between the mice increased since some mice presented tachycardias. Statistical analysis was performed by one-way ANOVA followed by Sidak's multiple comparison post hoc test. All values were compared to the values prior recombination (pre). $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$. **D,** *Ex Vivo* burst pacing induced arrhythmia occurrence is higher (60%) in *vTbx5*KO mice vs Flox (23%) and Cre (38%) mice. Statistical analysis was performed by (A, B) paired student's t-test against the pre time point.

Figure S4. Validation of endogenous TBX5 ChIP. A, Successful chromatin-immunoprecipitation was confirmed by qPCR for the known TBX5 binding site downstream of *Scn5a*. **B,** The primers for this qPCR were designed uisng the fragment of the known enhancer for *Scn5a* (left panel). Another putative enhancer was detected between the *Scn5a* gene and the known enhancer (right panel) [21]. Five independent experiments. Statistical analysis was performed by Student's t-test, $^{*}P < 0.05$

Figure S5. TBX5 loss negatively affects blood homeostasis. A, Gene ontology analysis (ClueGO [18, 19]) of biological processes of the upregulated genes in *vTbx5*KO mice mainly include coagulation related genes. **B,** *vTbx5*KO atria 1 month upon recombination are enlarged and contain blood clots.

Figure S6. Peaks on putative TBX5 targets related to cardiac electrophysiology. TBX5 binds to active enhancers (indicated by H3K27ac and POL2 marks from [22]) together with NKX2.5 and GATA4 [23]. The same regulatory regions are bound by repressor TBX3 which is known to occupy the same regions with TBX5 [23]. Upper panels display the approximate genomic location, whereas lower panels show the enlarged region of interest (green bar) enlarged. Genomic regions of **A** *Gja5*, **B** *Kcng2*, **C** *Cacna1g* and **D** *Chrm2* **E** *Gja1* **F** *Kcnj5*

Figure S7. Peaks on putative TBX5 targets linked to cardioprotective genes. TBX5 binds to active enhancers (indicated by H3K27ac and POL2 marks from [22]) together with NKX2.5 and GATA4 [23]. The same regulatory regions are bound by repressor TBX3 which is known to occupy the same regions with TBX5 [23]. Upper panels display the approximate genomic location, whereas lower panels show the enlarged region of interest (green bar). Genomic regions of **A** *Fhl2*, **B** Gpr22, **C** *Fgf16*

Figure S8. Peaks on putative TBX5 targets related to genes involved in cytoskeleton organization. TBX5 binds to active enhancers (indicated by H3K27ac and POL2 marks from [22]) together with NKX2.5 and GATA4 [23]. The same regulatory regions are bound by repressor TBX3 which is known to occupy the same regions with TBX5 [23]. Upper panels display the approximate genomic location, whereas lower panels show the enlarged region of interest (green bar). Genomic regions of **A** *Emilin2*, **B** *Pdlim4*, **C** *Fstl4* and **D** *Cmya5*

Figure S9. Analysis of CX43 and GIRK4 levels in *vTbx5*KO mice in different cardiac compartments. A, CX43 and GIRK4 protein is strongly reduced in *vTbx5*KO ventricles at 4 weeks after recombination **B,** Time-course analysis of protein expression of CX43 and GIRK4 at 1, 2 and 4 weeks after recombination shows a significant protein reduction 1 week post-rec. **C,** *Gja1* mRNA levels remain unchanged in *vTbx5*KO atria. **D,** IGV depicting no TBX5 binding peak at 30 MB distance from the TSS as identified previously as a putative TBX5 enhancer for atrial *Gja1* [23]. Statistical analysis was performed by (A) two tailed tudents' t-test (B) two-way ANOVA followed by Sidak's multiple comparison post hoc test. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.

Figure S10. Heart-specific re-expression of TBX5 leads to robust expression of TBX5 in the ventricle. A, Western blot showing that TBX5 is specifically expressed in the heart, not in liver and spleen. **B,** Cross-sectional area analysis by WGA-FITC showing no cardiomyocyte hypertrophy of KO-RE hearts 8 weeks post AAV injections compared KO-CT (normal mouse cardiomyocytes CSA is about 200-300μm^2) **C,** Heart weight (HW) to body weight (BW) ratio of injected mice is also normal and not indicative of cardiac hypertrophy. Please note that mice were injected with AAVs two weeks after recombination. **D,** Images of KO-CT and -RE mice showing that TBX5 overexpression did not induce any major abnormalities. Scale bar: 1 mm

Figure S11. Heart-specific re-expression of TBX5 leads to robust expression of TBX5 and connexin 43 in the ventricle. A, Overview of cross-sectional slices of 3 KO-CT (left) and 3 KO-RE (right) showing that TBX5 re-expression leads to robust CX43 re-expression in the whole heart. **B,** High magnification confocal images of 3 KO-CT (up) and 3 KO-RE (down) showing robust TBX5 and CX43 re-expression in KO-RE vs KO-CT.

Supplementary Tables

Table S1. Primer Sequences

name	Use	primer fwd	primer rev
TBX5 rec	RT-(q)PCR	AGGCAGGGAGGAGAATGTTT	GGCTCTGCTTTGCCAGTTAC
Gja1	RT-(q)PCR	CACCACTTTGGCGTGCCGGCTT	TCAACCGCTGTCCCCAGGAGCC
Kcnj5	RT-(q)PCR	AGAAGTTAGCCCCAAGGGTTC	ATGCTCCCAAGTACACCCTG
Kcng2	RT-(q)PCR	AATTCAGGAAAGTGAAAAGTCTTGG	TTGGTCCTCCGTTGAGCTTG
Cacna1g	RT-(q)PCR	AGGAGAAGCAGATGGCCGA	GTACACAGGTGGTGGACGAG
Chrm2	RT-(q)PCR	CAGACTCCACCAGATCGCAG	GGATCCAGCCACAAGGACAA
Fhl2	RT-(q)PCR	AAGGAGGAGAACCCACACTG	GTGCCGATCCTTGTAGGACA
Gpr22	RT-(q)PCR	GTGAGCCCAAAGGCCCATAA	CGCACCGTGACGTTTGATTC
Fgf16	RT-(q)PCR	TGATCAGCATCAGGGGAGTG	CAAGGTGGAGGCATAGGTGT
Fstl4	RT-(q)PCR	CCACGTCCTGCAGGTGAAT	GCCAAGAGGGAGAGCTGTTT
Cmya5	RT-(q)PCR	CTGCCGCGTTCTCACTTTTC	TGGGGTTCTAGTCTGGGAGG
Emilin2	RT-(q)PCR	GCAGCTTGTGGAACTGCATC	TCGGTTGCTTCTGAGGGTTC
Pdlim4	RT-(q)PCR	CGGGATCGTGGGAACCATTG	CCACATCATATCCCTCCGGC
Gapdh	RT-(q)PCR	ATGTTCCAGTATGACTCCACTCACG	GAAGACACCAGTAGACTCCACGACA
Scn5a	ChIP-PCR	GGTGTGAATGAGGGAGGCAG	GGGTGTCTGGGACAGGAGAT
Gja1-enh	cloning	TATCTCGAGGTTGTAACATCAACTTTATAATGAAATATC	TATAAGCTTACCACTTGTGCCTGCTG
Kcnj5-enh	cloning	CTCGAGGAGGCAGGGCTAGAGAAGA	GAAGCTTGGTGGGTGAGTTTTGAGCAG
Tbx5-CDS	cloning	GCTATAGAATTCTGGCCGATACAGATGAGGG	TATAGTCGACGCTATTCTCACTCCACTCTG

Full list of down- and upregulated genes: as Excel-file S2

Table S3: Gene Ontology Analysis of downregulated genes in v*Tbx5*KO ventricles

GO-Term	Term p-value corrected		Associated genes
muscle adaptation	550.0×10^{-6}	4.12 %	[Casq1, Cmya5, Il15, Nppb]
potassium ion trans-membrane transport	370.0×10^{-6}	3.17 %	[Cnga3, Kcng2, Kcnip2, Kcnj5, Kcnv2, Stk39]
muscle system process	120.0×10^{-9}	3.32 %	[Adra1b, Cacna1g, Casq1, Chrm2, Cmya5, Ctgf, Gja1, Il15, Kcnj5, Myl1, Nppb, Scn5a]
regulation of muscle system process	360.0×10^{-6}	3.03 %	[Adra1b, Casq1, Chrm2, Cmya5, Ctgf, Scn5a]
regulation of blood circulation	10.0×10^{-6}	3.83 %	[Adra1b, Cacna1g, Chrm2, Ctgf, Dbh, Gja1, Kcnj5, Scn5a]
striated muscle contraction	18.0×10^{-6}	4.35 %	[Adra1b, Cacna1g, Casq1, Ctgf, Kcnj5, Myl1, Scn5a]
heart contraction	9.0×10^{-6}	3.98 %	[Adra1b, Cacna1g, Chrm2, Ctgf, Gja1, Kcnj5, Myl1, Scn5a]
regulation of heart rate	830.0×10^{-6}	4.44 %	[Adra1b, Cacna1g, Kcnj5, Scn5a]
cell communication involved in cardiac conduction	95.0×10^{-6}	9.76 %	[Cacna1g, Gja1, Kcnj5, Scn5a]

Table S4: Gene Ontology Analysis of upregulated genes in v*Tbx5*KO ventricles

GO-ID	GO-Term	Term p-value corrected		Associated genes
GO:0007596	blood coagulation	3.2×10^{-6}	3.72 %	[F5, Fermt3, Gp9, Hpse, Itga2b, P2ry12, Plek]
GO:0030168	platelet activation	9.2×10^{-6}	5.38 %	[F5, Fermt3, Itga2b, P2ry12, Plek]

Full list of intersecting genes: as Excel-file S5

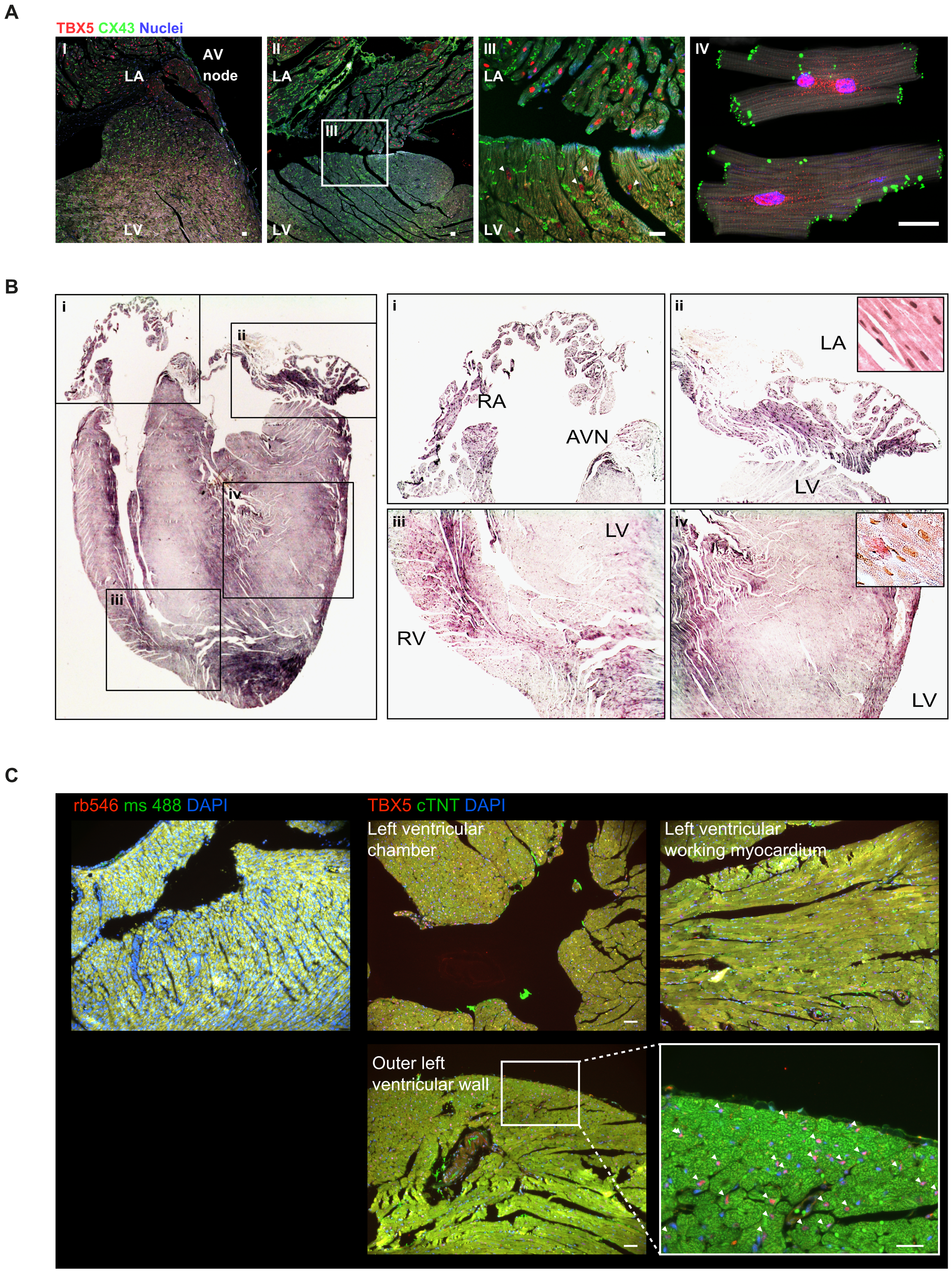

A
TBX5 CX43 Nuclei
I
LA
AV
node
LV
II
LA
III
LV
III
LA
LV
IV
B
i
ii
iv
iii
i
RA
AVN
ii
LA
LV
iii
LV
RV
iv
LV
C
rb546 ms 488 DAPI
TBX5 cTNT DAPI
Left ventricular
chamber
Left ventricular
working myocardium
Outer left
ventricular wall

Figure S1

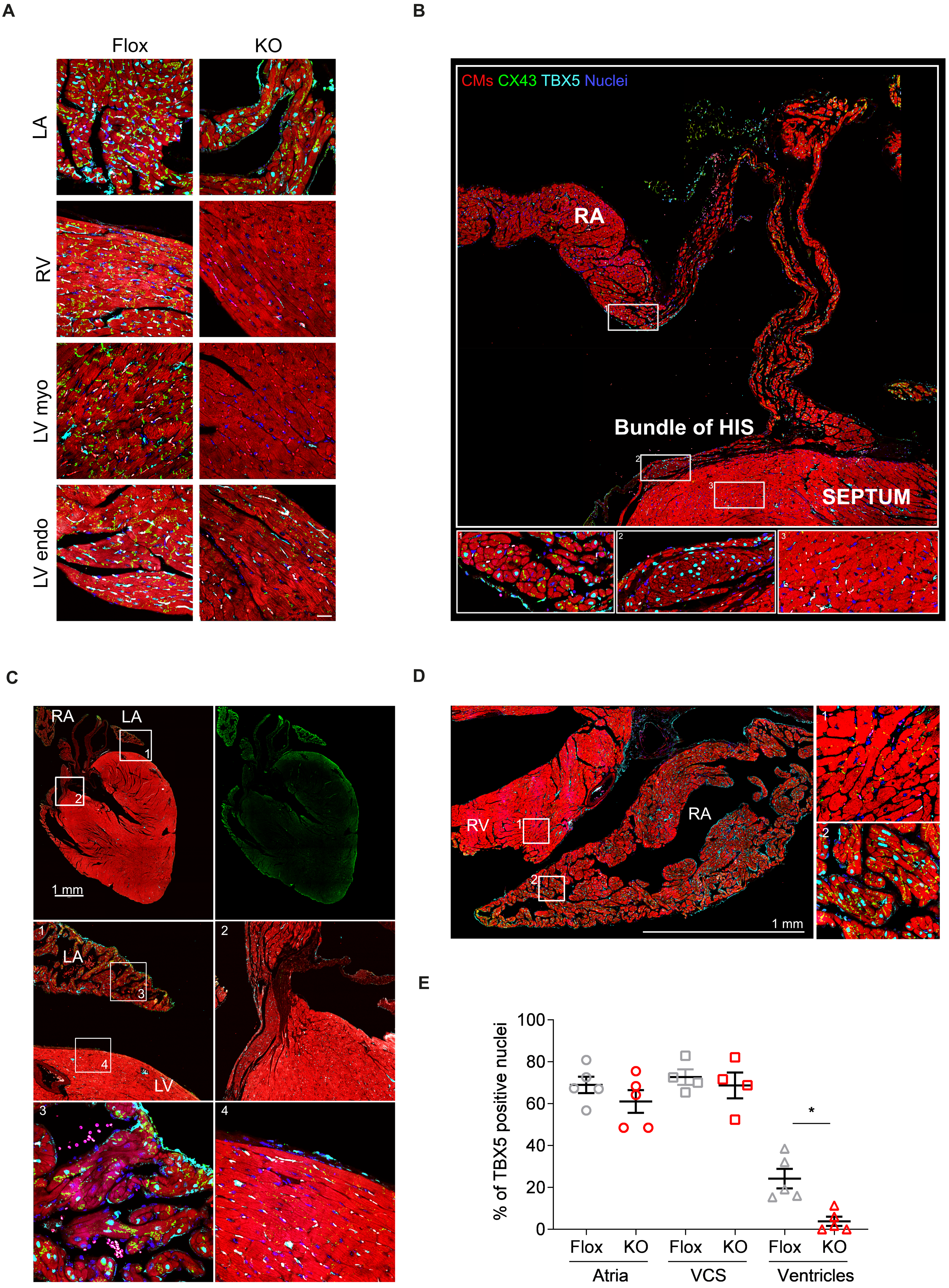

A
Flox
KO
LA
RV
LV myo
LV endo
B
CMs CX43 TBX5 Nuclei
RA
Bundle of HIS
SEPTUM
1
2
3
C
RA
LA
1
2
1 mm
1
LA
3
4
LV
2
3
4
D
RV
RA
1
2
1 mm
E
% of TBX5 positive nuclei
100
80
60
40
20
0
*
Flox
KO
Flox
KO
Flox
KO
Atria
VCS
Ventricles

Figure S2

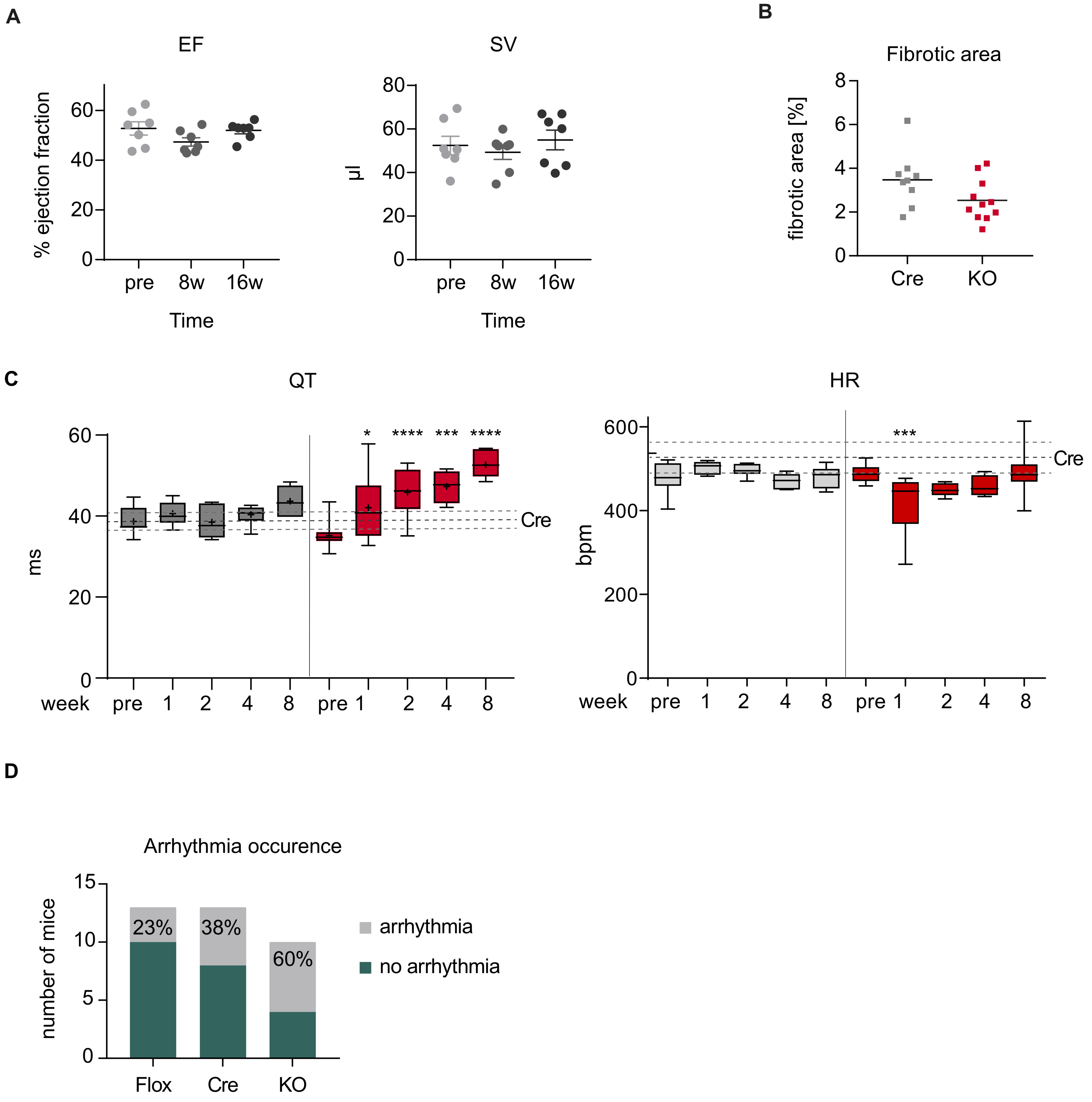

A
EF
% ejection fraction
60
40
20
0
pre
8w
16w
Time
SV
µl
80
60
40
20
0
pre
8w
16w
Time
B
Fibrotic area
fibrotic area [%]
8
6
4
2
0
Cre
KO
C
QT
ms
60
40
20
0
*
****
***
****
Cre
week
pre
1
2
4
8
pre
1
2
4
8
HR
bpm
600
400
200
0
***
Cre
week
pre
1
2
4
8
pre
1
2
4
8
D
Arrhythmia occurence
number of mice
15
10
5
0
23%
38%
60%
Flox
Cre
KO
arrhythmia
no arrhythmia

Figure S3

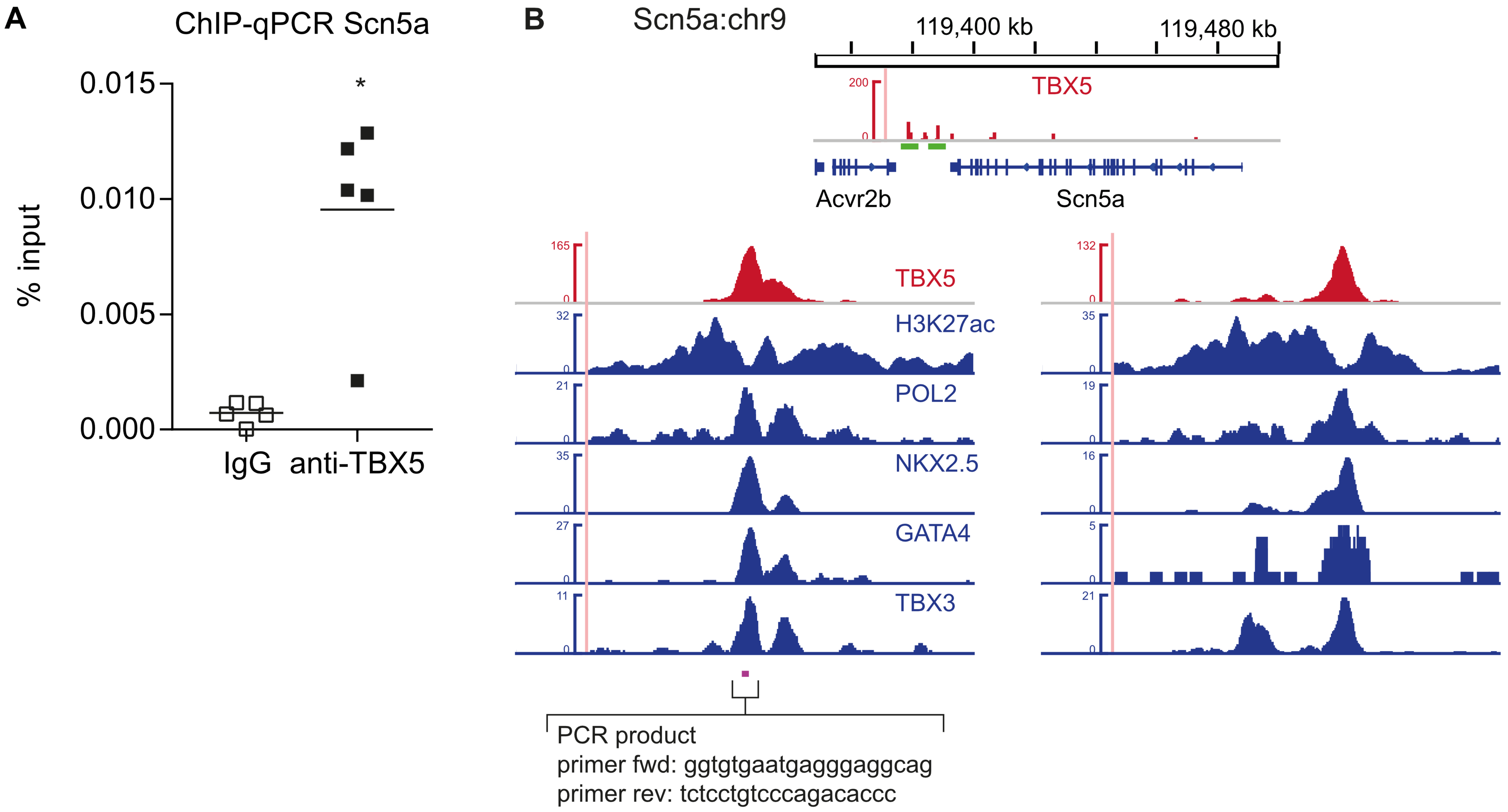

A
ChIP-qPCR Scn5a
0.015
0.010
0.005
0.000
% input
*
IgG
anti-TBX5
B
Scn5a:chr9
119,400 kb
119,480 kb
200
0
TBX5
Acvr2b
Scn5a
165
0
TBX5
32
0
H3K27ac
21
0
POL2
35
0
NKX2.5
27
0
GATA4
11
0
TBX3
132
0
35
0
19
0
16
0
5
0
21
0
PCR product
primer fwd: ggtgtgaatgagggaggcag
primer rev: tctcctgtcccagacaccc

Figure S4

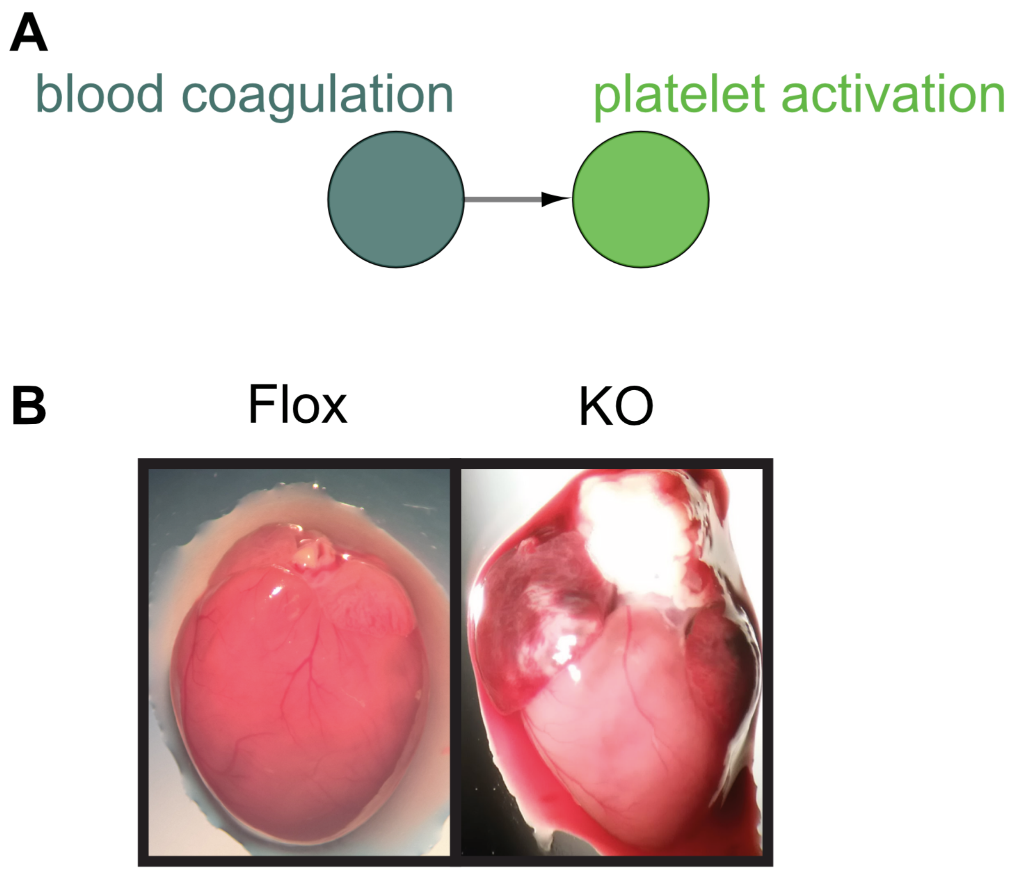


Figure S5

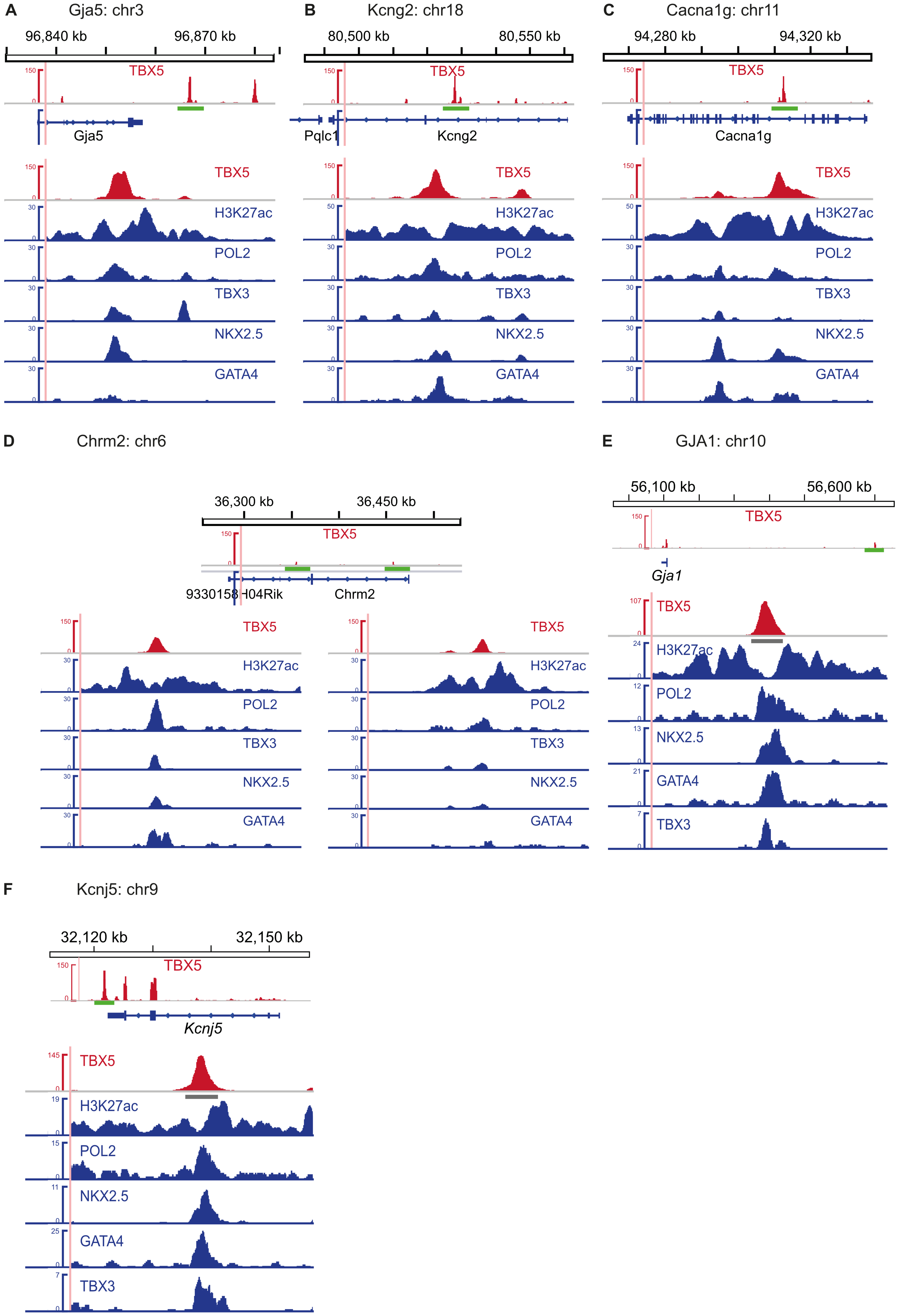

A
Gja5: chr3
96,840 kb
96,870 kb
TBX5
Gja5
TBX5
H3K27ac
POL2
TBX3
NKX2.5
GATA4
B
Kcng2: chr18
80,500 kb
80,550 kb
TBX5
Pqlc1
Kcng2
TBX5
H3K27ac
POL2
TBX3
NKX2.5
GATA4
C
Cacna1g: chr11
94,280 kb
94,320 kb
TBX5
Cacna1g
TBX5
H3K27ac
POL2
TBX3
NKX2.5
GATA4
D
Chrm2: chr6
36,300 kb
36,450 kb
TBX5
9330158H04Rik
Chrm2
TBX5
H3K27ac
POL2
TBX3
NKX2.5
GATA4
TBX5
H3K27ac
POL2
TBX3
NKX2.5
GATA4
E
GJA1: chr10
56,100 kb
56,600 kb
TBX5
Gja1
TBX5
H3K27ac
POL2
NKX2.5
GATA4
TBX3
F
Kcnj5: chr9
32,120 kb
32,150 kb
TBX5
Kcnj5
TBX5
H3K27ac
POL2
NKX2.5
GATA4
TBX3

Figure S6

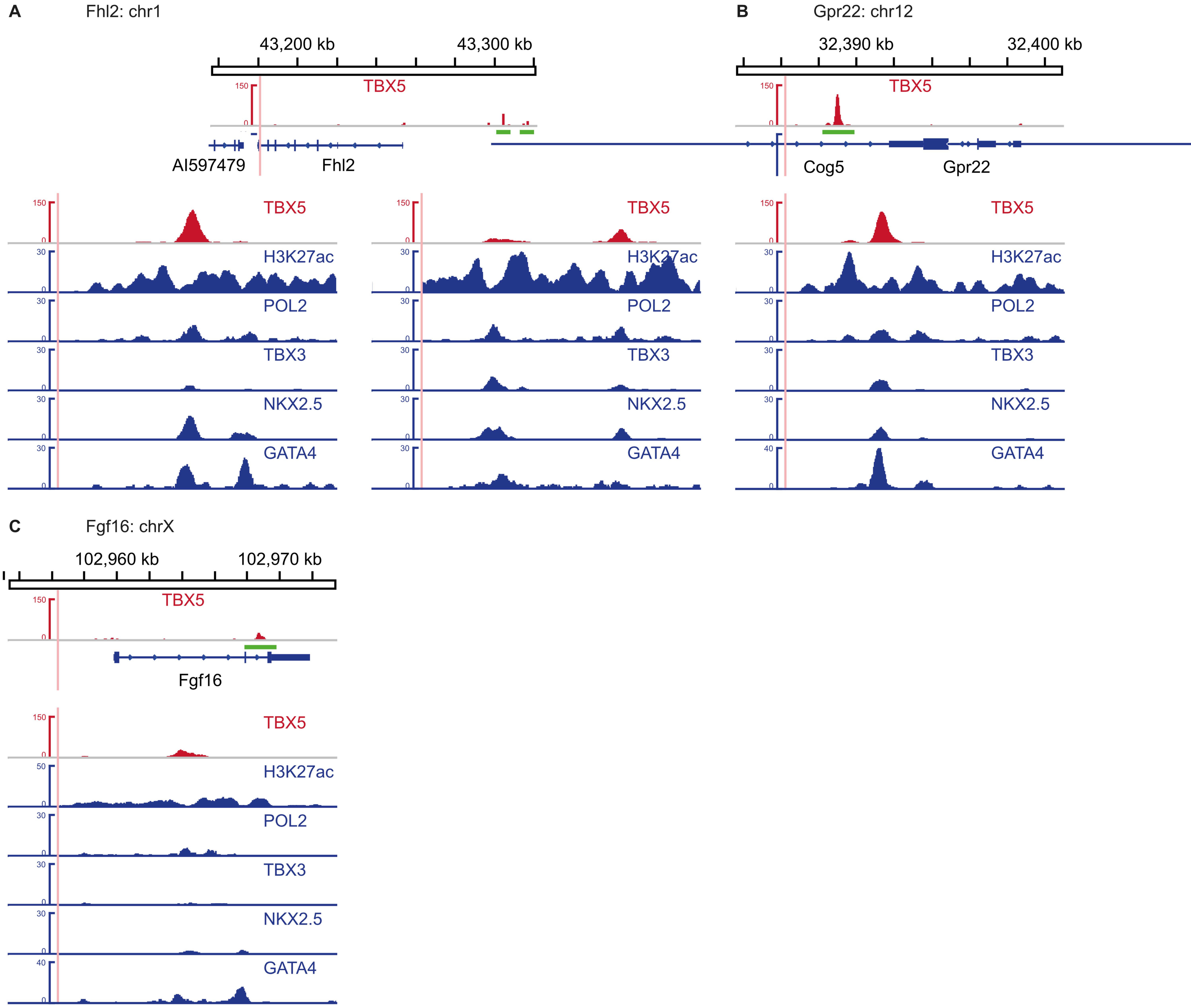

A
Fhl2: chr1
43,200 kb
43,300 kb
150
0
TBX5
AI597479
Fhl2
B
Gpr22: chr12
32,390 kb
32,400 kb
150
0
TBX5
Cog5
Gpr22
TBX5
H3K27ac
POL2
TBX3
NKX2.5
GATA4
150
30
40
0
C
Fgf16: chrX
102,960 kb
102,970 kb
150
0
TBX5
Fgf16
TBX5
H3K27ac
POL2
TBX3
NKX2.5
GATA4
150
50
30
40
0

Figure S7

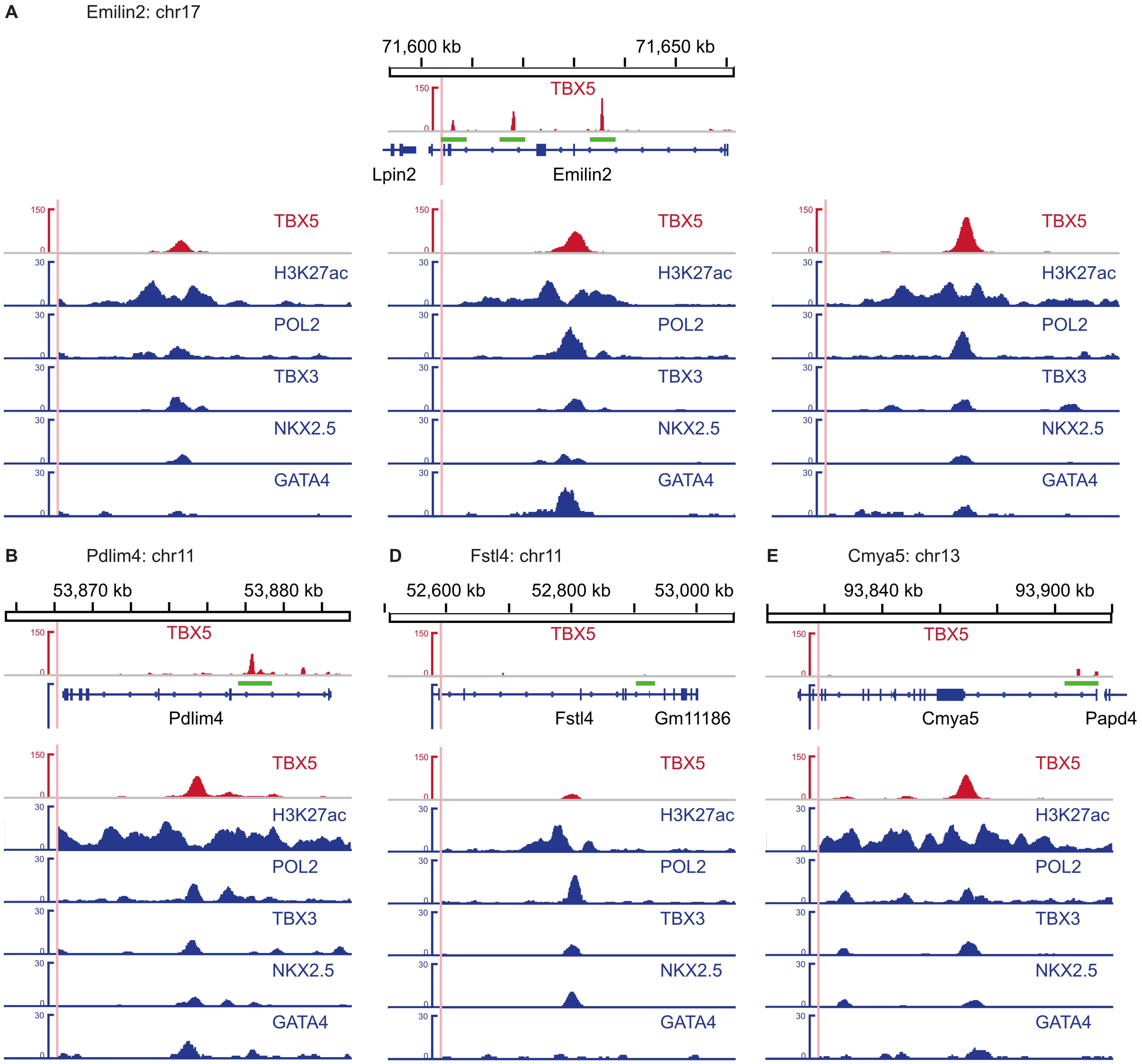

A
Emilin2: chr17
71,600 kb
71,650 kb
TBX5
150
0
Lpin2
Emilin2
H3K27ac
POL2
TBX3
NKX2.5
GATA4
30
B
Pdlim4: chr11
53,870 kb
53,880 kb
Pdlim4
D
Fstl4: chr11
52,600 kb
52,800 kb
53,000 kb
Fstl4
Gm11186
E
Cmya5: chr13
93,840 kb
93,900 kb
Cmya5
Papd4

Figure S8

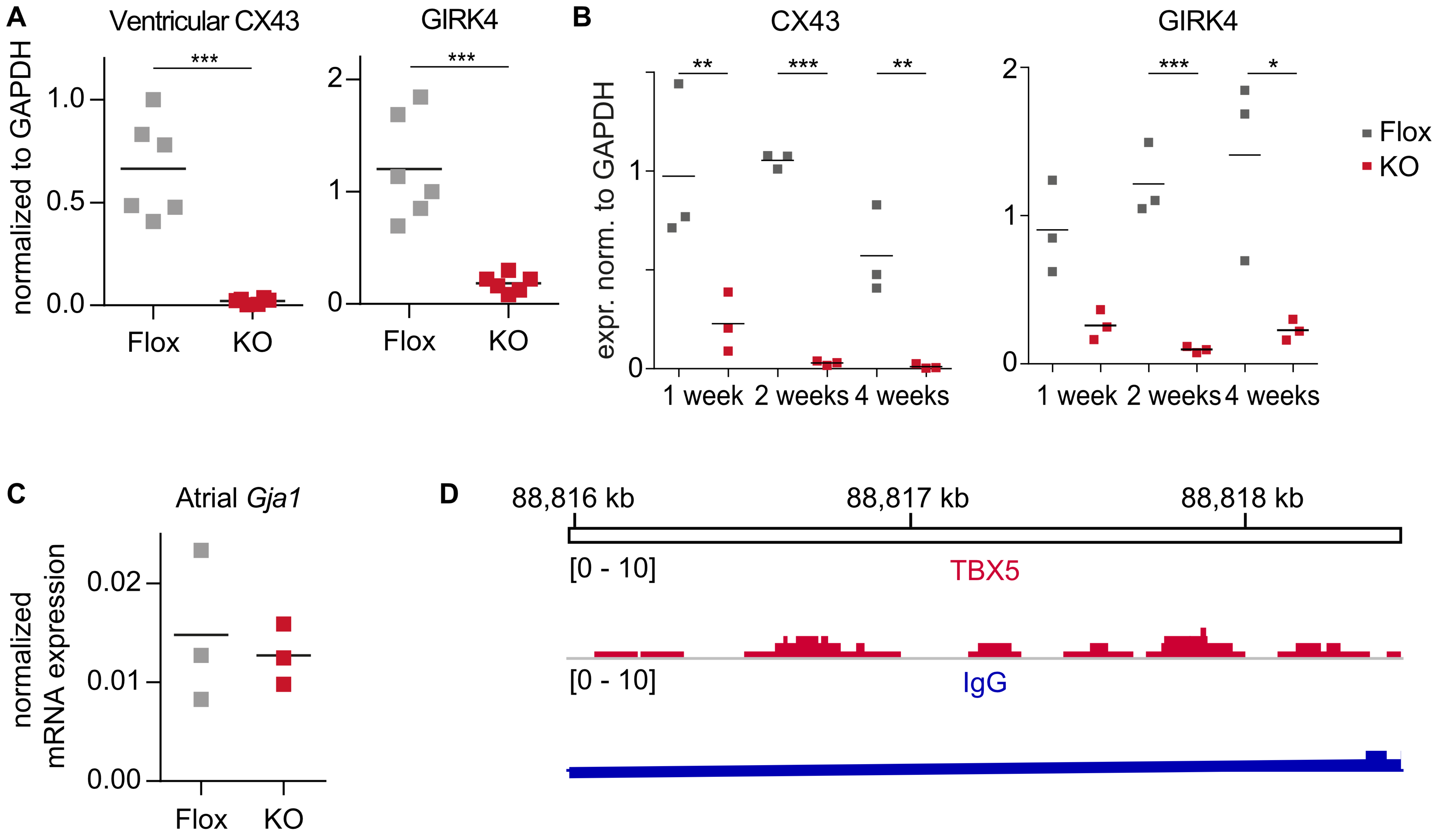

A
Ventricular CX43
normalized to GAPDH
1.0
0.5
0.0
***
Flox
KO
GIRK4
2
1
0
***
Flox
KO
B
CX43
expr. norm. to GAPDH
1
0
**
***
**
1 week
2 weeks
4 weeks
GIRK4
2
1
0
***
*
1 week
2 weeks
4 weeks
■ Flox
■ KO
C
Atrial Gja1
normalized mRNA expression
0.02
0.01
0.00
Flox
KO
D
88,816 kb
88,817 kb
88,818 kb
[0 - 10]
TBX5
[0 - 10]
IgG

Figure S9

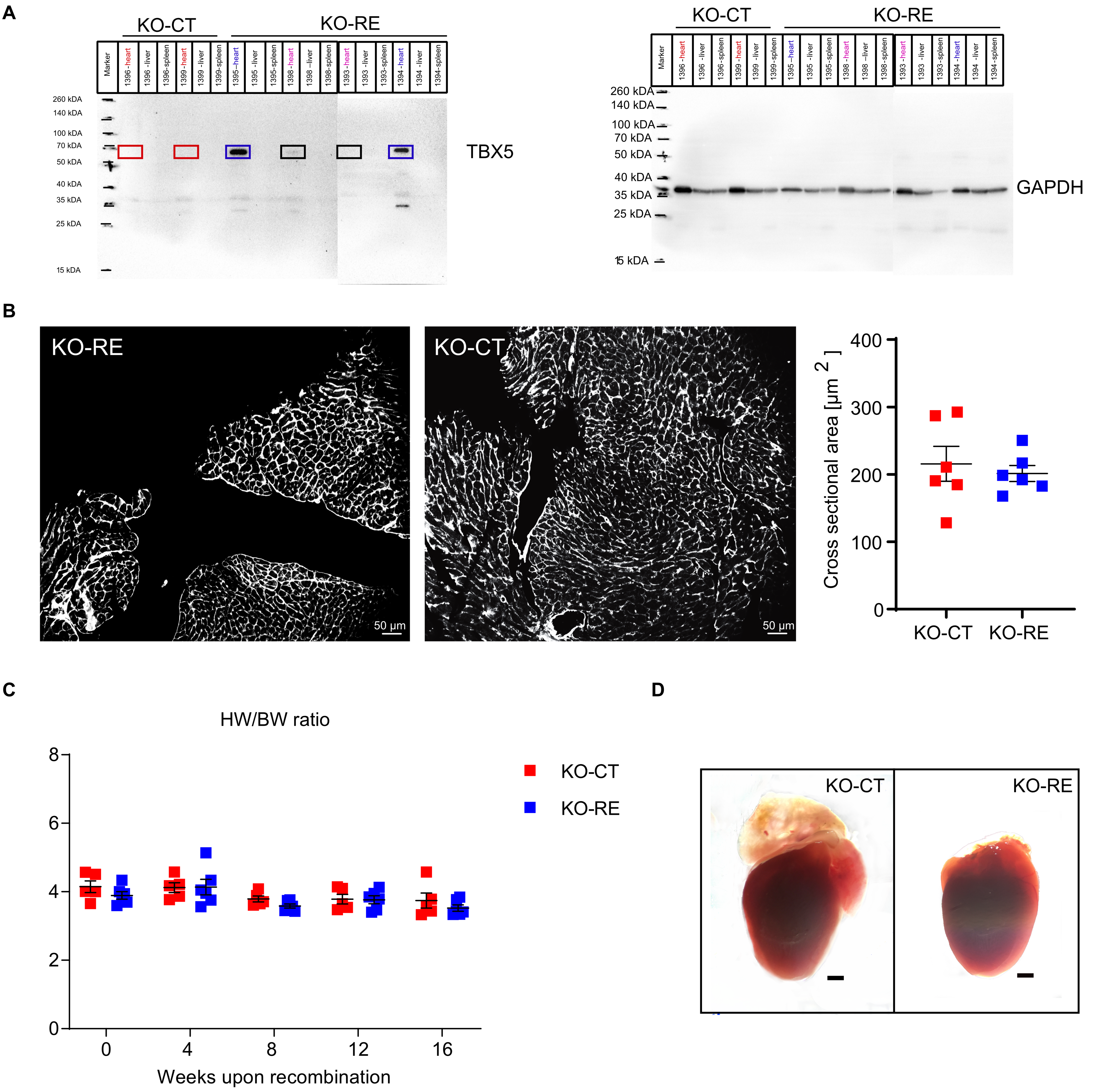

A
KO-CT
KO-RE
Marker
1396 -heart
1396 -liver
1396-spleen
1399 -heart
1399 -liver
1399-spleen
1395 –heart
1395 -liver
1395-spleen
1398 -heart
1398 –liver
1398-spleen
1393 -heart
1393 -liver
1393-spleen
1394 -heart
1394 -liver
1394-spleen
260 kDA
140 kDA
100 kDA
70 kDA
50 kDA
40 kDA
35 kDA
25 kDA
15 kDA
TBX5
GAPDH
B
KO-RE
KO-CT
50 µm
50 µm
Cross sectional area [µm 2]
0
100
200
300
400
KO-CT
KO-RE
C
HW/BW ratio
0
2
4
6
8
0
4
8
12
16
Weeks upon recombination
KO-CT
KO-RE
D
KO-CT
KO-RE

Figure S10

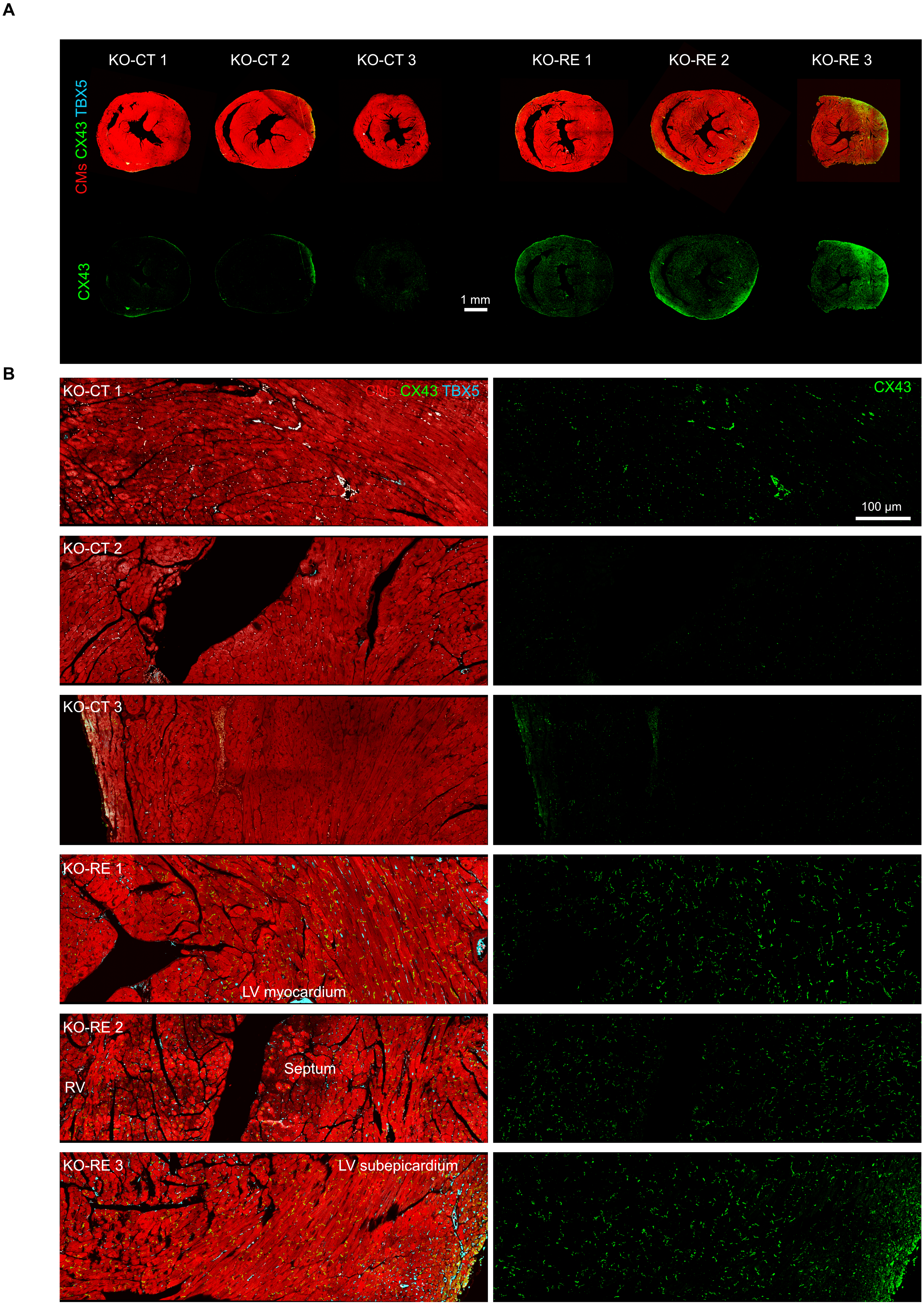
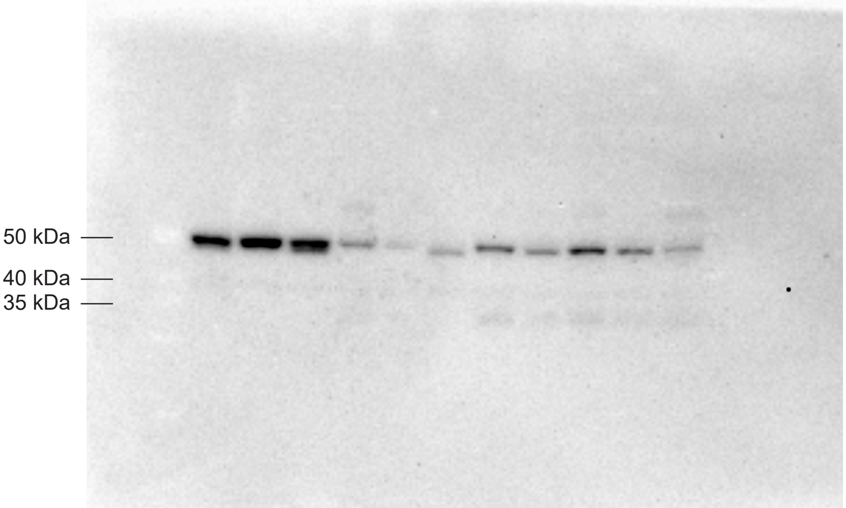

A
KO-CT 1
KO-CT 2
KO-CT 3
KO-RE 1
KO-RE 2
KO-RE 3
CMs CX43 TBX5
CX43
1 mm
B
KO-CT 1
CMs CX43 TBX5
CX43
100 µm
KO-CT 2
KO-CT 3
KO-RE 1
LV myocardium
KO-RE 2
Septum
RV
KO-RE 3
LV subepicardium

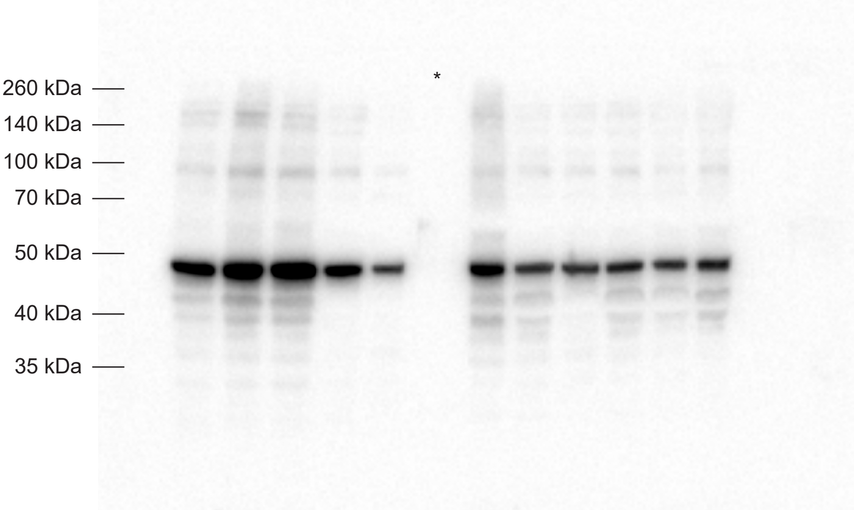
Figure S11

full blots of Figure 1

TBX5



CASQ2

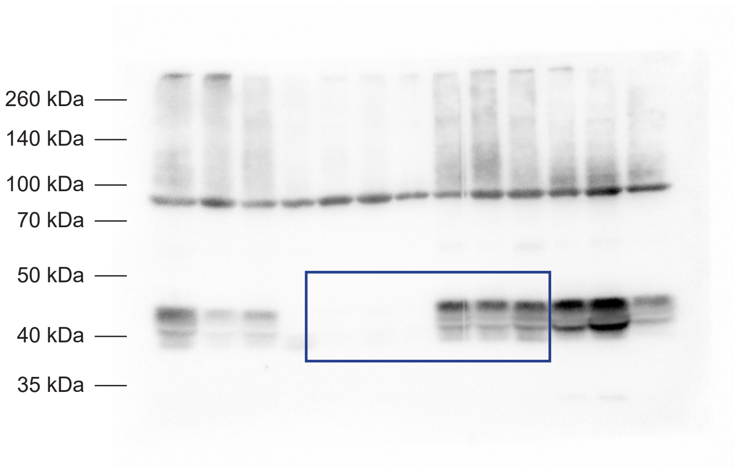


* empty lane

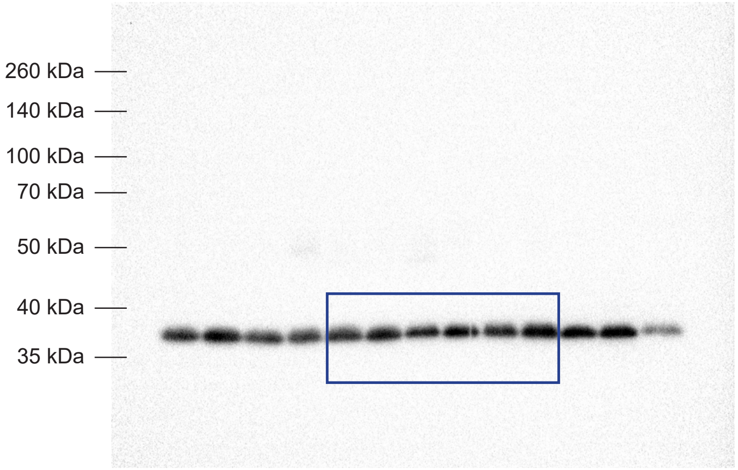
GAPDH

full blots of Figure 6

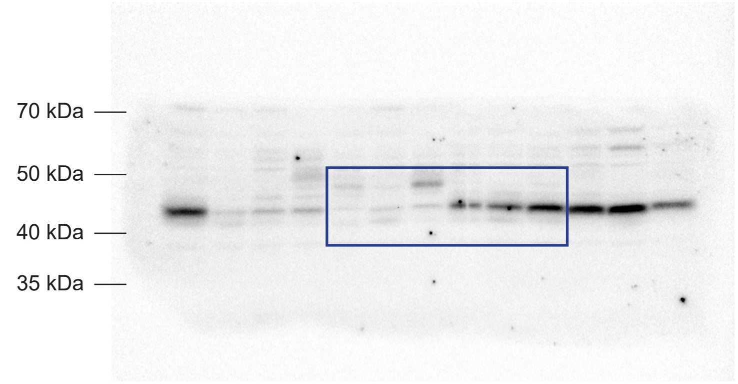
CX43



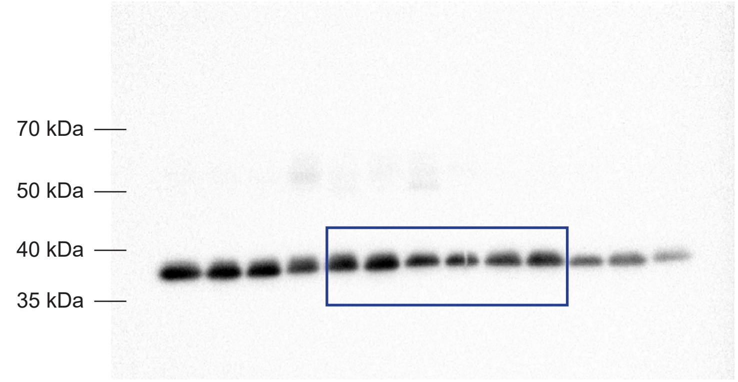
GAPDH



GIRK4

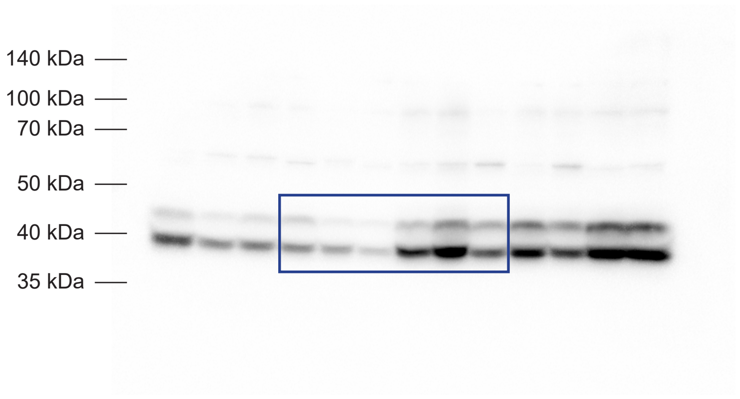


GAPDH

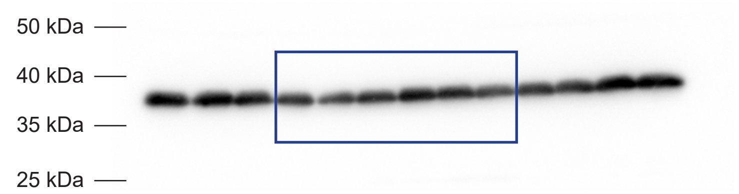


full blots of Figure 7

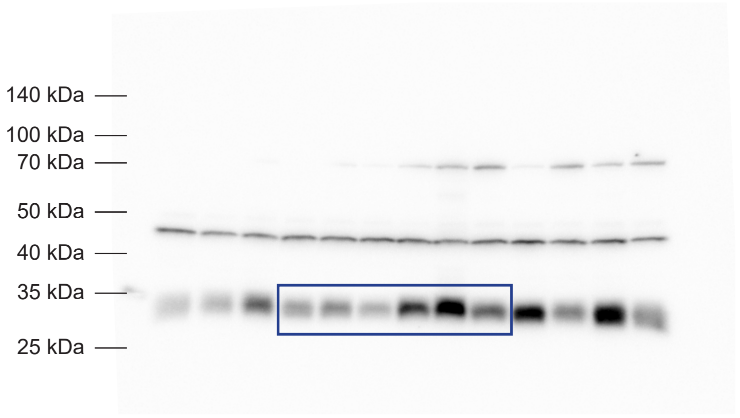
CX43



GAPDH



FHL2



Upregulated genes in
vTBX5KO ventricles
Log2foldchange >0.8

ensembl_gene_id	external_gene_id	description	entrezgene	chromosome_name	start_position	end_position	length	baseMean	log2FoldChange	padj
ENSMUSG00000072324	**Gm8420**	predicted gene 8420 [Source:MGI Symbol;Acc:MGI:3645594]		1	51940650	51941261	612	42,59	3,15	4,73E-20
ENSMUSG00000034028	**Cd226**	CD226 antigen [Source:MGI Symbol;Acc:MGI:3039602]	225825	18	89197431	89270201	72771	60,66	1,93	1,17E-07
ENSMUSG00000078307	**AI593442**	expressed sequence AI593442 [Source:MGI Symbol;Acc:MGI:2143099]	330941	9	52673044	52679429	6386	94,21	1,75	5,63E-08
ENSMUSG00000029372	**Ppbp**	pro-platelet basic protein [Source:MGI Symbol;Acc:MGI:1888712]	57349	5	90768518	90770060	1543	97,36	1,65	3,63E-05
ENSMUSG00000085772	**D630024D03Rik**	RIKEN cDNA D630024D03 gene [Source:MGI Symbol;Acc:MGI:3041224]		11	31790113	31824524	34412	17,32	1,58	5,45E-05
ENSMUSG00000026579	**F5**	coagulation factor V [Source:MGI Symbol;Acc:MGI:88382]	14067	1	164151838	164220277	68440	40,88	1,56	3,62E-04
ENSMUSG00000090622	**A930033H14Rik**	RIKEN cDNA A930033H14 gene [Source:MGI Symbol;Acc:MGI:2444562]		10	69209762	69213098	3337	43,51	1,50	9,10E-07
ENSMUSG00000052013	**Btla**	B and T lymphocyte associated [Source:MGI Symbol;Acc:MGI:2658978]	208154	16	45224315	45252895	28581	18,50	1,49	1,59E-04
ENSMUSG00000016255	**Tubb1**	tubulin, beta 1 class VI [Source:MGI Symbol;Acc:MGI:107814]	545486	2	174450695	174457882	7188	50,62	1,41	1,55E-03
ENSMUSG00000057666	**Gapdh**	glyceraldehyde-3-phosphate dehydrogenase [Source:MGI Symbol;Acc:MGI:95640]	14433	6	125161853	125166467	4615	98,23	1,40	8,28E-06
ENSMUSG00000050447	**Lypd6**	LY6/PLAUR domain containing 6 [Source:MGI Symbol;Acc:MGI:2443848]	320343	2	50066429	50193569	127141	22,66	1,28	1,51E-03
ENSMUSG00000026014	**Raph1**	Ras association (RalGDS/AF-6) and pleckstrin homology domains 1 [Source:MGI Symbol;Acc:MGI:1924550]	77300	1	60483191	60567104	83914	1480,02	1,22	4,56E-04
ENSMUSG00000027322	**Siglec1**	sialic acid binding Ig-like lectin 1, sialoadhesin [Source:MGI Symbol;Acc:MGI:99668]	20612	2	131069220	131086765	17546	120,08	1,21	3,52E-04
ENSMUSG00000081822	**Gm15626**	predicted gene 15626 [Source:MGI Symbol;Acc:MGI:3783070]		5	83299585	83300452	868	57,12	1,19	1,93E-03
ENSMUSG00000034664	**Itga2b**	integrin alpha 2b [Source:MGI Symbol;Acc:MGI:96601]	16399	11	102453297	102470122	16826	75,64	1,18	1,38E-02
ENSMUSG00000027326	**Casc5**	cancer susceptibility candidate 5 [Source:MGI Symbol;Acc:MGI:1923714]	76464	2	119047119	119105501	58383	32,08	1,16	9,43E-04
ENSMUSG00000027656	**Wisp2**	WNT1 inducible signaling pathway protein 2 [Source:MGI Symbol;Acc:MGI:1328326]	22403	2	163820861	163833146	12286	150,03	1,16	2,41E-06
ENSMUSG00000038801	**Scgb1c1**	secretoglobin, family 1C, member 1 [Source:MGI Symbol;Acc:MGI:2655401]	338417	7	140845565	140846768	1204	213,95	1,16	1,93E-05
ENSMUSG00000065145	**Vaultrc5**	vault RNA component 5 [Source:MGI Symbol;Acc:MGI:2673990]		18	36801866	36802008	143	54,90	1,15	7,36E-03
ENSMUSG00000026726	**Cubn**	cubilin (intrinsic factor-cobalamin receptor) [Source:MGI Symbol;Acc:MGI:1931256]	65969	2	13276338	13491924	215587	95,45	1,15	8,81E-04
ENSMUSG00000073555	**Gm4951**	predicted gene 4951 [Source:MGI Symbol;Acc:MGI:3644953]	240327	18	60212080	60247820	35741	30,20	1,14	1,22E-03
ENSMUSG00000021751	**Acox2**	acyl-Coenzyme A oxidase 2, branched chain [Source:MGI Symbol;Acc:MGI:1934852]	93732	14	8225511	8259353	33843	24,36	1,14	4,62E-03
ENSMUSG00000062319	**Gm10115**	predicted gene 10115 [Source:MGI Symbol;Acc:MGI:3641675]		2	6950453	6951680	1228	45,53	1,13	1,25E-02
ENSMUSG00000044258	**Ctla2a**	cytotoxic T lymphocyte-associated protein 2 alpha [Source:MGI Symbol;Acc:MGI:88554]	13024	13	60934155	60936625	2471	408,98	1,13	5,02E-09
ENSMUSG00000026357	**Rgs18**	regulator of G-protein signaling 18 [Source:MGI Symbol;Acc:MGI:1927498]	64214	1	144752683	144775435	22753	44,49	1,13	1,69E-03
ENSMUSG00000097588	**Gm17388**	predicted gene, 17388 [Source:MGI Symbol;Acc:MGI:4937022]		4	136355774	136359440	3667	33,54	1,12	1,46E-02
ENSMUSG00000030159	**Clec1b**	C-type lectin domain family 1, member b [Source:MGI Symbol;Acc:MGI:1913287]	56760	6	129397297	129409335	12039	24,93	1,12	2,66E-02
ENSMUSG00000030054	**Gp9**	glycoprotein 9 (platelet) [Source:MGI Symbol;Acc:MGI:1860137]	54368	6	87778136	87779762	1627	18,41	1,11	2,78E-02
ENSMUSG00000023341	**Mx2**	myxovirus (influenza virus) resistance 2 [Source:MGI Symbol;Acc:MGI:97244]	17858	16	97536083	97560899	24817	64,99	1,11	2,56E-04
ENSMUSG00000064451	**Snora23**	small nucleolar RNA, H/ACA box 23 [Source:MGI Symbol;Acc:MGI:3819494]		7	110046364	110046547	184	25,39	1,10	8,82E-03
ENSMUSG00000021636	**Marveld2**	MARVEL (membrane-associating) domain containing 2 [Source:MGI Symbol;Acc:MGI:2446166]	218518	13	100595957	100616971	21015	27,69	1,09	4,12E-03
ENSMUSG00000022598	**Psca**	prostate stem cell antigen [Source:MGI Symbol;Acc:MGI:1919623]	72373	15	74714839	74717063	2225	17,20	1,09	2,26E-02
ENSMUSG00000063254	**B230325K18Rik**	RIKEN cDNA B230325K18 gene [Source:MGI Symbol;Acc:MGI:2442200]		7	127983079	127985701	2623	39,23	1,07	1,73E-02
ENSMUSG00000082292	**Gm12250**	predicted gene 12250 [Source:MGI Symbol;Acc:MGI:3649299]		11	58183843	58190198	6356	158,85	1,06	2,90E-03
ENSMUSG00000089542	**Gm25835**	predicted gene, 25835 [Source:MGI Symbol;Acc:MGI:5455612]		11	69668852	69668995	144	192,81	1,06	2,12E-04
ENSMUSG00000074056	**Gm10615**	predicted gene 10615 [Source:MGI Symbol;Acc:MGI:3642102]		9	110117703	110119916	2214	20,29	1,05	1,32E-02
ENSMUSG00000080542	**Gm22710**	predicted gene, 22710 [Source:MGI Symbol;Acc:MGI:5452487]		1	118459141	118459265	125	61,30	1,04	2,69E-03
ENSMUSG00000097772	**5430416N02Rik**	RIKEN cDNA 5430416N02 gene [Source:MGI Symbol;Acc:MGI:1918676]		5	100420842	100429516	8675	22,86	1,04	1,80E-02
ENSMUSG00000054135	**A430110L20Rik**	RIKEN cDNA A430110L20 gene [Source:MGI Symbol;Acc:MGI:3036249]		1	181225986	181228498	2513	20,56	1,04	3,01E-02
ENSMUSG00000035208	**Slfn8**	schlafen 8 [Source:MGI Symbol;Acc:MGI:2672859]	276950	11	83002158	83020810	18653	16,00	1,03	3,97E-02
ENSMUSG00000065822	**Snord15a**	small nucleolar RNA, C/D box 15A [Source:MGI Symbol;Acc:MGI:3645887]		7	99482785	99482932	148	128,63	1,02	9,62E-05
ENSMUSG00000086825	**Gm15675**	predicted gene 15675 [Source:MGI Symbol;Acc:MGI:3783117]		1	130429781	130437191	7411	35,66	1,02	2,30E-02
ENSMUSG00000036353	**P2ry12**	purinergic receptor P2Y, G-protein coupled 12 [Source:MGI Symbol;Acc:MGI:1918089]	70839	3	59216271	59262831	46561	62,07	1,02	1,51E-03
ENSMUSG00000037921	**Ddx60**	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60 [Source:MGI Symbol;Acc:MGI:2384570]	234311	8	61928087	62037701	109615	212,09	1,02	1,72E-10
ENSMUSG00000028989	**Angptl7**	angiopoietin-like 7 [Source:MGI Symbol;Acc:MGI:3605801]	654812	4	148495183	148500460	5278	334,87	1,02	6,64E-04
ENSMUSG00000034317	**Trim59**	tripartite motif-containing 59 [Source:MGI Symbol;Acc:MGI:1914199]	66949	3	69035288	69044755	9468	34,40	1,00	1,99E-02
ENSMUSG00000031997	**Trpc6**	transient receptor potential cation channel, subfamily C, member 6 [Source:MGI Symbol;Acc:MGI:109523]	22068	9	8544196	8680565	136370	31,16	1,00	2,28E-02
ENSMUSG00000020838	**Slc6a4**	solute carrier family 6 (neurotransmitter transporter, serotonin), member 4 [Source:MGI Symbol;Acc:MGI:96285]	15567	11	76998603	77032340	33738	26,13	1,00	2,85E-02
ENSMUSG00000037725	**Ckap2**	cytoskeleton associated protein 2 [Source:MGI Symbol;Acc:MGI:1931797]	80986	8	22168152	22185819	17668	23,01	1,00	3,60E-02
ENSMUSG00000089788	**Gm16586**	predicted gene 16586 [Source:MGI Symbol;Acc:MGI:4415006]		1	178321108	178324171	3064	371,81	1,00	9,42E-05
ENSMUSG00000036192	**Rorb**	RAR-related orphan receptor beta [Source:MGI Symbol;Acc:MGI:1343464]	225998	19	18930605	19111196	180592	73,58	0,98	1,36E-02
ENSMUSG00000036913	**Trim67**	tripartite motif-containing 67 [Source:MGI Symbol;Acc:MGI:3045323]	330863	8	124793019	124834713	41695	58,41	0,98	2,65E-03
ENSMUSG00000088059	**Mir1949**	microRNA 1949 [Source:MGI Symbol;Acc:MGI:3837022]		18	35554492	35554632	141	106,50	0,98	9,50E-03
ENSMUSG00000090222	**Gm16340**	predicted gene 16340 [Source:MGI Symbol;Acc:MGI:3840117]		1	173775837	173802720	26884	61,99	0,98	1,34E-02
ENSMUSG00000009185	**Ccl8**	chemokine (C-C motif) ligand 8 [Source:MGI Symbol;Acc:MGI:101878]	20307	11	82115185	82116799	1615	32,36	0,98	2,54E-02
ENSMUSG00000026077	**Npas2**	neuronal PAS domain protein 2 [Source:MGI Symbol;Acc:MGI:109232]	18143	1	39193731	39363234	169504	23,70	0,98	4,74E-02
ENSMUSG00000018654	**Ikzf1**	IKAROS family zinc finger 1 [Source:MGI Symbol;Acc:MGI:1342540]	22778	11	11685003	11772926	87924	40,42	0,97	4,40E-03
ENSMUSG00000078493	**A930039A15Rik**	RIKEN cDNA A930039A15 gene [Source:MGI Symbol;Acc:MGI:3641728]		1	153905301	153916910	11610	28,51	0,97	1,74E-02
ENSMUSG00000001020	**S100a4**	S100 calcium binding protein A4 [Source:MGI Symbol;Acc:MGI:1330282]	20198	3	90603770	90606045	2276	83,64	0,96	4,96E-03
ENSMUSG00000065226	**Gm25791**	predicted gene, 25791 [Source:MGI Symbol;Acc:MGI:5455568]		9	15314845	15314981	137	244,22	0,94	6,00E-05
ENSMUSG00000065725	**Gm26165**	predicted gene, 26165 [Source:MGI Symbol;Acc:MGI:5455942]		2	144261589	144261726	138	59,21	0,93	1,21E-02
ENSMUSG00000073489	**Ifi204**	interferon activated gene 204 [Source:MGI Symbol;Acc:MGI:96429]	15951	1	173747293	173766876	19584	136,55	0,92	1,02E-02
ENSMUSG00000034459	**Ifit1**	interferon-induced protein with tetratricopeptide repeats 1 [Source:MGI Symbol;Acc:MGI:99450]	15957	19	34640871	34650009	9139	182,62	0,92	8,19E-05
ENSMUSG00000073409	**H2-Q6**	histocompatibility 2, Q region locus 6 [Source:MGI Symbol;Acc:MGI:95935]	15019	17	35424850	35430055	5206	107,02	0,92	2,82E-03
ENSMUSG00000026380	**Tfcp2l1**	transcription factor CP2-like 1 [Source:MGI Symbol;Acc:MGI:2444691]	81879	1	118627945	118685167	57223	72,68	0,92	1,03E-02
ENSMUSG00000053007	**Creb5**	cAMP responsive element binding protein 5 [Source:MGI Symbol;Acc:MGI:2443973]	231991	6	53573384	53696007	122624	50,40	0,92	8,35E-03
ENSMUSG00000078122	**F630028O10Rik**	RIKEN cDNA F630028O10 gene [Source:MGI Symbol;Acc:MGI:3641813]		X	96239942	96243636	3695	98,51	0,91	1,24E-04
ENSMUSG00000006014	**Prg4**	proteoglycan 4 (megakaryocyte stimulating factor, articular superficial zone protein) [Source:MGI Symbol;Acc:MGI:1891344]	96875	1	150449412	150466165	16754	144,57	0,91	1,51E-04
ENSMUSG00000074415	**2610203C20Rik**	RIKEN cDNA 2610203C20 gene [Source:MGI Symbol;Acc:MGI:1917705]		9	41580741	41617772	37032	138,03	0,91	1,74E-02
ENSMUSG00000025255	**Zfhx4**	zinc finger homeodomain 4 [Source:MGI Symbol;Acc:MGI:2137668]	80892	3	5218526	5415857	197332	43,77	0,91	2,66E-02
ENSMUSG00000027318	**Adam33**	a disintegrin and metallopeptidase domain 33 [Source:MGI Symbol;Acc:MGI:1341813]	110751	2	131050591	131063814	13224	28,25	0,90	3,69E-02

ENSMUSG00000064853	**Gm23442**	predicted gene, 23442 [Source:MGI Symbol;Acc:MGI:5453219]		17	35162563	35162696	134	378,72	0,90	6,35E-04
ENSMUSG00000042167	**Papd4**	PAP associated domain containing 4 [Source:MGI Symbol;Acc:MGI:2140950]	100715	13	93147400	93192283	44884	66,84	0,90	9,12E-03
ENSMUSG00000065637	**Gm26397**	predicted gene, 26397 [Source:MGI Symbol;Acc:MGI:5456174]		8	126944847	126944980	134	344,74	0,89	7,54E-04
ENSMUSG00000038147	**Cd84**	CD84 antigen [Source:MGI Symbol;Acc:MGI:1336885]	12523	1	171839697	171890718	51022	76,39	0,89	4,60E-04
ENSMUSG00000095123	**Gm21781**	predicted gene, 21781 [Source:MGI Symbol;Acc:MGI:5433945]		10	4391587	4396424	4838	76,78	0,89	1,89E-02
ENSMUSG00000020120	**Plek**	pleckstrin [Source:MGI Symbol;Acc:MGI:1860485]	56193	11	16971206	17052381	81176	292,51	0,88	1,62E-02
ENSMUSG00000049744	**Arhgap15**	Rho GTPase activating protein 15 [Source:MGI Symbol;Acc:MGI:1923367]	76117	2	43748824	44395953	647130	53,85	0,88	2,41E-02
ENSMUSG00000031167	**Rbm3**	RNA binding motif protein 3 [Source:MGI Symbol;Acc:MGI:1099460]	19652	X	8138975	8145880	6906	162,89	0,87	6,07E-06
ENSMUSG00000000318	**Clec10a**	C-type lectin domain family 10, member A [Source:MGI Symbol;Acc:MGI:96975]	17312	11	70156197	70170834	14638	100,25	0,87	1,75E-03
ENSMUSG00000020437	**Myo1g**	myosin IG [Source:MGI Symbol;Acc:MGI:1927091]	246177	11	6506548	6520965	14418	32,89	0,86	3,82E-02
ENSMUSG00000060429	**Sntb1**	syntrophin, basic 1 [Source:MGI Symbol;Acc:MGI:101781]	20649	15	55638843	55906949	268107	70,89	0,86	1,53E-03
ENSMUSG00000096696	**Zfp960**	zinc finger protein 960 [Source:MGI Symbol;Acc:MGI:3052731]	449000	17	17064113	17089628	25516	47,84	0,85	5,60E-03
ENSMUSG00000025498	**Irf7**	interferon regulatory factor 7 [Source:MGI Symbol;Acc:MGI:1859212]	54123	7	141262706	141266481	3776	187,95	0,84	8,99E-05
ENSMUSG00000059401	**Mamld1**	mastermind-like domain containing 1 [Source:MGI Symbol;Acc:MGI:3045303]	333639	X	71050256	71156056	105801	87,24	0,84	4,80E-02
ENSMUSG00000029915	**Clec5a**	C-type lectin domain family 5, member a [Source:MGI Symbol;Acc:MGI:1345151]	23845	6	40574894	40585821	10928	38,21	0,84	3,46E-02
ENSMUSG00000024965	**Fermt3**	fermitin family homolog 3 (Drosophila) [Source:MGI Symbol;Acc:MGI:2147790]	108101	19	6998958	7019469	20512	87,91	0,84	3,88E-03
ENSMUSG00000031938	**4931406C07Rik**	RIKEN cDNA 4931406C07 gene [Source:MGI Symbol;Acc:MGI:1918234]	70984	9	15283337	15306448	23112	142,98	0,83	8,67E-05
ENSMUSG00000052572	**Dlg2**	discs, large homolog 2 (Drosophila) [Source:MGI Symbol;Acc:MGI:1344351]	23859	7	91090706	92447003	1356298	59,30	0,83	2,06E-02
ENSMUSG00000035273	**Hpse**	heparanase [Source:MGI Symbol;Acc:MGI:1343124]	15442	5	100679484	100719716	40233	35,85	0,83	3,84E-02
ENSMUSG00000085334	**Gm12940**	predicted gene 12940 [Source:MGI Symbol;Acc:MGI:3702626]		4	127033731	127049398	15668	159,45	0,81	2,69E-02
ENSMUSG00000045932	**Ifit2**	interferon-induced protein with tetratricopeptide repeats 2 [Source:MGI Symbol;Acc:MGI:99449]	15958	19	34550694	34576419	25726	551,97	0,80	1,09E-04
ENSMUSG00000037143	**4930529M08Rik**	RIKEN cDNA 4930529M08 gene [Source:MGI Symbol;Acc:MGI:1926024]	78774	2	145934784	146215039	280256	66,51	0,80	1,66E-02

Downregulated genes in
vTBX5KO ventricles
Log2foldchange <-0.8

ensembl_gene_id	external_gene_id	description	entrezgene	chromosome_name	start_position	end_position	length	baseMean	log2FoldChange	padj
ENSMUSG00000044067	**Gpr22**	G protein-coupled receptor 22 [Source:MGI Symbol;Acc:MGI:1920260]	73010	12	31706867	31713947	7081	1442,01	-2,98	6,57E-33
ENSMUSG00000022442	**Ttll1**	tubulin tyrosine ligase-like 1 [Source:MGI Symbol;Acc:MGI:2443047]	319953	15	83483772	83510893	27122	313,57	-2,60	2,30E-39
ENSMUSG00000028307	**Aldob**	aldolase B, fructose-bisphosphate [Source:MGI Symbol;Acc:MGI:87995]	230163	4	49535995	49549546	13552	121,32	-2,40	2,51E-29
ENSMUSG00000050953	**Gja1**	gap junction protein, alpha 1 [Source:MGI Symbol;Acc:MGI:95713]	14609	10	56377300	56390419	13120	5422,87	-2,23	1,60E-29
ENSMUSG00000036242	**3632451O06Rik**	RIKEN cDNA 3632451O06 gene [Source:MGI Symbol;Acc:MGI:1914669]	67419	14	49681560	49783383	101824	240,43	-2,23	6,43E-33
ENSMUSG00000026605	**Cenpf**	centromere protein F [Source:MGI Symbol;Acc:MGI:1313302]	108000	1	189640599	189688086	47488	783,03	-2,05	2,11E-18
ENSMUSG00000031230	**Fgf16**	fibroblast growth factor 16 [Source:MGI Symbol;Acc:MGI:1931627]	80903	X	105764279	105774939	10661	205,95	-1,91	1,68E-19
ENSMUSG00000000889	**Dbh**	dopamine beta hydroxylase [Source:MGI Symbol;Acc:MGI:94864]	13166	2	27165233	27183200	17968	18,24	-1,79	9,76E-07
ENSMUSG00000032511	**Scn5a**	sodium channel, voltage-gated, type V, alpha [Source:MGI Symbol;Acc:MGI:98251]	20271	9	119483408	119579016	95609	4669,07	-1,78	3,05E-14
ENSMUSG00000073154	**9330158H04Rik**	RIKEN cDNA 9330158H04 gene [Source:MGI Symbol;Acc:MGI:2442094]		6	36209620	36390191	180572	140,55	-1,77	5,60E-18
ENSMUSG00000036264	**Fstl4**	follistatin-like 4 [Source:MGI Symbol;Acc:MGI:2443199]	320027	11	52764634	53188538	423905	33,47	-1,75	6,29E-08
ENSMUSG00000032034	**Kcnj5**	potassium inwardly-rectifying channel, subfamily J, member 5 [Source:MGI Symbol;Acc:MGI:104755]	16521	9	32314783	32344237	29455	1350,47	-1,73	2,72E-27
ENSMUSG00000087129	**Gm16316**	predicted gene 16316 [Source:MGI Symbol;Acc:MGI:3826530]		2	163685004	163692279	7276	16,20	-1,66	7,13E-05
ENSMUSG00000075015	**Gm10801**	predicted gene 10801 [Source:MGI Symbol;Acc:MGI:3641656]		2	98662237	98664083	1847	28,51	-1,51	3,78E-04
ENSMUSG00000047085	**Lrrc4b**	leucine rich repeat containing 4B [Source:MGI Symbol;Acc:MGI:3027390]	272381	7	44429018	44463351	34334	544,60	-1,44	6,12E-08
ENSMUSG00000075270	**Pde11a**	phosphodiesterase 11A [Source:MGI Symbol;Acc:MGI:3036251]	241489	2	75989141	76338774	349634	57,93	-1,41	3,60E-06
ENSMUSG00000043795	**Gm14492**	predicted gene 14492 [Source:MGI Symbol;Acc:MGI:3642289]		7	142491074	142506771	15698	64,39	-1,39	7,91E-07
ENSMUSG00000033849	**B3galt2**	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2 [Source:MGI Symbol;Acc:MGI:1349461]	26878	1	143640664	143650406	9743	393,44	-1,38	1,32E-03
ENSMUSG00000052837	**Junb**	Jun-B oncogene [Source:MGI Symbol;Acc:MGI:96647]	16477	8	84976909	84978748	1840	436,21	-1,36	7,13E-04
ENSMUSG00000072902	**Gm10435**	predicted gene 10435 [Source:MGI Symbol;Acc:MGI:3642820]		11	59002910	59007293	4384	104,62	-1,35	5,45E-05
ENSMUSG00000008136	**Fhl2**	four and a half LIM domains 2 [Source:MGI Symbol;Acc:MGI:1338762]	14200	1	43123074	43163961	40888	15848,77	-1,35	1,64E-11
ENSMUSG00000045613	**Chrm2**	cholinergic receptor, muscarinic 2, cardiac [Source:MGI Symbol;Acc:MGI:88397]	243764	6	36388084	36528414	140331	3813,70	-1,33	1,04E-12
ENSMUSG00000024053	**Emilin2**	elastin microfibril interfacer 2 [Source:MGI Symbol;Acc:MGI:2389136]	246707	17	71252176	71310965	58790	588,43	-1,32	5,82E-08
ENSMUSG00000060716	**Plekhh1**	pleckstrin homology domain containing, family H (with MyTH4 domain) member 1 [Source:MGI Symbol;Acc:MGI:2144989]	211945	12	79029163	79081648	52486	94,05	-1,31	8,03E-07
ENSMUSG00000020388	**Pdlim4**	PDZ and LIM domain 4 [Source:MGI Symbol;Acc:MGI:1353470]	30794	11	54054928	54069014	14087	132,63	-1,31	5,69E-10
ENSMUSG00000085162	**Gm12295**	predicted gene 12295 [Source:MGI Symbol;Acc:MGI:3650535]		11	65277654	65365798	88145	65,06	-1,28	3,11E-06
ENSMUSG00000090157	**Gm16534**	predicted gene 16534 [Source:MGI Symbol;Acc:MGI:4413442]		2	32050086	32064911	14826	28,02	-1,27	2,07E-04
ENSMUSG00000059852	**Kcng2**	potassium voltage-gated channel, subfamily G, member 2 [Source:MGI Symbol;Acc:MGI:3694646]	240444	18	80294546	80364254	69709	1151,07	-1,27	2,11E-19
ENSMUSG00000028195	**Cyr61**	cysteine rich protein 61 [Source:MGI Symbol;Acc:MGI:88613]	16007	3	145646971	145649985	3015	1352,15	-1,23	2,11E-03
ENSMUSG00000028318	**Polr1e**	polymerase (RNA) I polypeptide E [Source:MGI Symbol;Acc:MGI:1929022]	64424	4	45018583	45036565	17983	273,11	-1,23	6,83E-10
ENSMUSG00000022215	**Fitm1**	fat storage-inducing transmembrane protein 1 [Source:MGI Symbol;Acc:MGI:1915930]	68680	14	55575617	55576952	1336	1111,94	-1,21	5,82E-08
ENSMUSG00000003934	**Efnb3**	ephrin B3 [Source:MGI Symbol;Acc:MGI:109196]	13643	11	69554092	69560205	6114	1218,17	-1,19	2,03E-12
ENSMUSG00000030433	**Sbk2**	SH3-binding domain kinase family, member 2 [Source:MGI Symbol;Acc:MGI:2685925]	381836	7	4956134	4964390	8257	62,34	-1,18	4,98E-03
ENSMUSG00000021236	**Entpd5**	ectonucleoside triphosphate diphosphohydrolase 5 [Source:MGI Symbol;Acc:MGI:1321385]	12499	12	84373857	84409029	35173	4953,03	-1,17	3,03E-29
ENSMUSG00000039488	**Cntn5**	contactin 5 [Source:MGI Symbol;Acc:MGI:3042287]	244682	9	9660891	10904775	1243885	72,72	-1,16	7,23E-04
ENSMUSG00000033595	**Lgi3**	leucine-rich repeat LGI family, member 3 [Source:MGI Symbol;Acc:MGI:2182619]	213469	14	70530821	70538323	7503	50,73	-1,15	6,09E-05
ENSMUSG00000008658	**Rbfox1**	RNA binding protein, fox-1 homolog (C. elegans) 1 [Source:MGI Symbol;Acc:MGI:1926224]	268859	16	6809222	7412479	603258	780,07	-1,15	2,86E-15
ENSMUSG00000020866	**Cacna1g**	calcium channel, voltage-dependent, T type, alpha 1G subunit [Source:MGI Symbol;Acc:MGI:1201678]	12291	11	94408391	94474198	65808	237,88	-1,15	1,69E-03
ENSMUSG00000029019	**Nppb**	natriuretic peptide type B [Source:MGI Symbol;Acc:MGI:97368]	18158	4	147985788	147987205	1418	1595,01	-1,15	1,37E-02
ENSMUSG00000075014	**Gm10800**	predicted gene 10800 [Source:MGI Symbol;Acc:MGI:3641657]		2	98666547	98667301	755	317,55	-1,15	1,87E-02
ENSMUSG00000042895	**Abra**	actin-binding Rho activating protein [Source:MGI Symbol;Acc:MGI:2444891]	223513	15	41865293	41869720	4428	1297,84	-1,13	1,98E-04
ENSMUSG00000040247	**Tbc1d10c**	TBC1 domain family, member 10c [Source:MGI Symbol;Acc:MGI:1922072]	108995	19	4184358	4191047	6690	97,21	-1,12	8,35E-08
ENSMUSG00000032224	**Fam81a**	family with sequence similarity 81, member A [Source:MGI Symbol;Acc:MGI:1924136]	76886	9	70089310	70142560	53251	186,88	-1,11	7,57E-08
ENSMUSG00000020926	**Adam11**	a disintegrin and metallopeptidase domain 11 [Source:MGI Symbol;Acc:MGI:1098667]	11488	11	102761439	102780262	18824	69,04	-1,11	7,36E-03
ENSMUSG00000078137	**Ankrd63**	ankyrin repeat domain 63 [Source:MGI Symbol;Acc:MGI:2686183]	383787	2	118699103	118703963	4861	28,03	-1,09	2,90E-03
ENSMUSG00000070570	**Slc17a7**	solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 7 [Source:MGI Symbol;Acc:MGI:1920211]	72961	7	45163921	45176138	12218	195,54	-1,08	5,05E-03
ENSMUSG00000098178	**Gm26924**	predicted gene, 26924 [Source:MGI Symbol;Acc:MGI:5504039]		17	39846958	39848788	1831	6601,61	-1,06	2,26E-02
ENSMUSG00000042961	**Egflam**	EGF-like, fibronectin type III and laminin G domains [Source:MGI Symbol;Acc:MGI:2146149]	268780	15	7206120	7398395	192276	260,28	-1,05	7,75E-12
ENSMUSG00000040990	**Sh3kbp1**	SH3-domain kinase binding protein 1 [Source:MGI Symbol;Acc:MGI:1889583]	58194	X	159627272	159978069	350798	1345,12	-1,04	1,32E-16
ENSMUSG00000047298	**Kcnv2**	potassium channel, subfamily V, member 2 [Source:MGI Symbol;Acc:MGI:2670981]	240595	19	27322588	27337179	14592	397,95	-1,04	3,80E-06
ENSMUSG00000006356	**Crip2**	cysteine rich protein 2 [Source:MGI Symbol;Acc:MGI:1915587]	68337	12	113140236	113145504	5269	8484,92	-1,04	4,64E-04
ENSMUSG00000092201	**A530058N18Rik**	RIKEN cDNA A530058N18 gene [Source:MGI Symbol;Acc:MGI:2444858]		2	114013563	114068324	54762	76,67	-1,03	1,59E-02
ENSMUSG00000053560	**Ier2**	immediate early response 2 [Source:MGI Symbol;Acc:MGI:104815]	15936	8	84661331	84662852	1522	190,10	-1,02	3,38E-02
ENSMUSG00000024063	**Lbh**	limb-bud and heart [Source:MGI Symbol;Acc:MGI:1925139]	77889	17	72918305	72941942	23638	8704,11	-1,02	3,78E-20
ENSMUSG00000035268	**Pkig**	protein kinase inhibitor, gamma [Source:MGI Symbol;Acc:MGI:1343086]	18769	2	163658386	163726158	67773	1745,95	-1,02	1,06E-13
ENSMUSG00000026114	**Cnga3**	cyclic nucleotide gated channel alpha 3 [Source:MGI Symbol;Acc:MGI:1341818]	12790	1	37218336	37263384	45049	108,65	-1,02	3,06E-06
ENSMUSG00000092397	**C130080G10Rik**	RIKEN cDNA C130080G10 gene [Source:MGI Symbol;Acc:MGI:4844008]		2	114054335	114064868	10534	916,23	-1,02	1,49E-14
ENSMUSG00000035357	**Pdzrn3**	PDZ domain containing RING finger 3 [Source:MGI Symbol;Acc:MGI:1933157]	55983	6	101149609	101377897	228289	547,04	-1,01	4,22E-07
ENSMUSG00000027030	**Stk39**	serine/threonine kinase 39 [Source:MGI Symbol;Acc:MGI:1858416]	53416	2	68210445	68472268	261824	2120,65	-1,01	7,95E-15
ENSMUSG00000038417	**Fig4**	FIG4 homolog (S. cerevisiae) [Source:MGI Symbol;Acc:MGI:2143585]	103199	10	41188172	41303241	115070	1064,02	-1,01	2,15E-09
ENSMUSG00000097805	**Gm17473**	predicted gene, 17473 [Source:MGI Symbol;Acc:MGI:4937107]		15	42676260	42704616	28357	19,23	-0,99	2,12E-02
ENSMUSG00000045087	**S1pr5**	sphingosine-1-phosphate receptor 5 [Source:MGI Symbol;Acc:MGI:2150641]	94226	9	21242912	21248443	5532	18,46	-0,99	4,28E-02
ENSMUSG00000045201	**Lrrc3b**	leucine rich repeat containing 3B [Source:MGI Symbol;Acc:MGI:2384996]	218763	14	15357519	15438987	81469	300,26	-0,98	3,77E-03
ENSMUSG00000019997	**Ctgf**	connective tissue growth factor [Source:MGI Symbol;Acc:MGI:95537]	14219	10	24595442	24598683	3242	1453,11	-0,98	4,19E-03
ENSMUSG00000060187	**Lrrc10**	leucine rich repeat containing 10 [Source:MGI Symbol;Acc:MGI:2448063]	237560	10	117045341	117046768	1428	1537,96	-0,96	1,02E-05
ENSMUSG00000037815	**Ctnna1**	catenin (cadherin associated protein), alpha 1 [Source:MGI Symbol;Acc:MGI:88274]	12385	18	35118888	35254773	135886	11420,81	-0,96	4,30E-13
ENSMUSG00000056708	**Ier5**	immediate early response 5 [Source:MGI Symbol;Acc:MGI:1337072]	15939	1	155096367	155099636	3270	915,91	-0,95	2,41E-02
ENSMUSG00000047485	**Klhl34**	kelch-like 34 [Source:MGI Symbol;Acc:MGI:2685234]	245683	X	157818435	157820369	1935	93,29	-0,94	1,09E-04
ENSMUSG00000037949	**Ano10**	anoctamin 10 [Source:MGI Symbol;Acc:MGI:2143103]	102566	9	122175879	122294374	118496	777,61	-0,94	2,74E-13
ENSMUSG00000076612	**Ighg2c**	immunoglobulin heavy constant gamma 2C [Source:MGI Symbol;Acc:MGI:2686979]		12	113285325	113288930	3606	70,27	-0,94	1,78E-03
ENSMUSG00000020256	**Aldh1l2**	aldehyde dehydrogenase 1 family, member L2 [Source:MGI Symbol;Acc:MGI:2444680]	216188	10	83487450	83534140	46691	262,97	-0,93	2,28E-08
ENSMUSG00000082308	**Gm15770**	predicted gene 15770 [Source:MGI Symbol;Acc:MGI:3783212]		5	142852616	142853199	584	37,64	-0,93	4,18E-02

ENSMUSG00000046516	**Cox17**	cytochrome c oxidase assembly protein 17 [Source:MGI Symbol;Acc:MGI:1333806]	12856	16	38346991	38352763	5773	802,53	-0,93	3,72E-08
ENSMUSG00000034574	**Daam1**	dishevelled associated activator of morphogenesis 1 [Source:MGI Symbol;Acc:MGI:1914596]	208846	12	71831078	71992367	161290	2532,15	-0,90	4,03E-09
ENSMUSG00000054469	**Lclat1**	lysocardiolipin acyltransferase 1 [Source:MGI Symbol;Acc:MGI:2684937]	225010	17	73107985	73243368	135384	2136,59	-0,89	1,51E-03
ENSMUSG00000047419	**Cmya5**	cardiomyopathy associated 5 [Source:MGI Symbol;Acc:MGI:1923719]	76469	13	93040713	93144724	104012	25328,39	-0,89	2,13E-03
ENSMUSG00000039640	**Mrpl12**	mitochondrial ribosomal protein L12 [Source:MGI Symbol;Acc:MGI:1926273]	56282	11	120484613	120489065	4453	1241,60	-0,88	4,95E-02
ENSMUSG00000021314	**Amph**	amphiphysin [Source:MGI Symbol;Acc:MGI:103574]	218038	13	18948371	19150913	202543	54,76	-0,88	3,44E-03
ENSMUSG00000097317	**Gm17281**	predicted gene, 17281 [Source:MGI Symbol;Acc:MGI:4936915]		2	91250743	91255995	5253	300,77	-0,87	7,57E-08
ENSMUSG00000064202	**4430402I18Rik**	RIKEN cDNA 4430402I18 gene [Source:MGI Symbol;Acc:MGI:1918036]	381218	19	28901268	28967800	66533	123,86	-0,86	1,98E-03
ENSMUSG00000074227	**Spint2**	serine protease inhibitor, Kunitz type 2 [Source:MGI Symbol;Acc:MGI:1338031]	20733	7	29256331	29281977	25647	205,83	-0,85	3,00E-02
ENSMUSG00000042249	**Adrbk2**	adrenergic receptor kinase, beta 2 [Source:MGI Symbol;Acc:MGI:87941]	320129	5	112910478	113015514	105037	463,14	-0,85	3,80E-06
ENSMUSG00000064302	**Clasp1**	CLIP associating protein 1 [Source:MGI Symbol;Acc:MGI:1923957]	76707	1	118389058	118609432	220375	6451,77	-0,84	1,64E-04
ENSMUSG00000067653	**Ankrd23**	ankyrin repeat domain 23 [Source:MGI Symbol;Acc:MGI:1925571]	78321	1	36530534	36535729	5196	4476,88	-0,83	1,69E-02
ENSMUSG00000004791	**Pgf**	placental growth factor [Source:MGI Symbol;Acc:MGI:105095]	18654	12	85166639	85177296	10658	84,96	-0,82	1,56E-03
ENSMUSG00000042302	**Ehbp1**	EH domain binding protein 1 [Source:MGI Symbol;Acc:MGI:2667252]	216565	11	22005828	22342292	336465	2347,48	-0,82	8,08E-16
ENSMUSG00000061816	**Myl1**	myosin, light polypeptide 1 [Source:MGI Symbol;Acc:MGI:97269]	17901	1	66924295	66945404	21110	239,10	-0,82	3,72E-02
ENSMUSG00000031712	**Il15**	interleukin 15 [Source:MGI Symbol;Acc:MGI:103014]	16168	8	82331637	82403222	71586	712,99	-0,82	2,72E-03
ENSMUSG00000050296	**Abca12**	ATP-binding cassette, sub-family A (ABC1), member 12 [Source:MGI Symbol;Acc:MGI:2676312]	74591	1	71243090	71414910	171821	258,11	-0,81	3,60E-07
ENSMUSG00000026888	**Grb14**	growth factor receptor bound protein 14 [Source:MGI Symbol;Acc:MGI:1355324]	50915	2	64912476	65024987	112512	3169,19	-0,81	4,08E-20
ENSMUSG00000028132	**Tmem56**	transmembrane protein 56 [Source:MGI Symbol;Acc:MGI:1923195]	99887	3	121201761	121283098	81338	91,34	-0,81	9,98E-03
ENSMUSG00000038403	**Hfe2**	hemochromatosis type 2 (juvenile) (human homolog) [Source:MGI Symbol;Acc:MGI:1916835]	69585	3	96525185	96529216	4032	2507,76	-0,81	2,86E-07
ENSMUSG00000050541	**Adra1b**	adrenergic receptor, alpha 1b [Source:MGI Symbol;Acc:MGI:104774]	11548	11	43774606	43901210	126605	480,37	-0,80	4,95E-06
ENSMUSG00000032060	**Cryab**	crystallin, alpha B [Source:MGI Symbol;Acc:MGI:88516]	12955	9	50752758	50756633	3876	12809,92	-0,80	5,13E-03
ENSMUSG00000007122	**Casq1**	calsequestrin 1 [Source:MGI Symbol;Acc:MGI:1309468]	12372	1	172209894	172219868	9975	147,16	-0,80	1,18E-02
ENSMUSG00000025221	**Kcnip2**	Kv channel-interacting protein 2 [Source:MGI Symbol;Acc:MGI:2135916]	80906	19	45791839	45816061	24223	2275,13	-0,80	2,46E-12
ENSMUSG00000004951	**Hspb1**	heat shock protein 1 [Source:MGI Symbol;Acc:MGI:96240]	15507	5	135887919	135889563	1645	581,65	-0,80	7,39E-03

50

downregulated genes

3632451O06Rik
9330158H04Rik
A530058N18Rik
Abca12
Adam11
Aldh1l2
Aldob
Amph
Ano10
B3galt2
C130080G10Rik
Casq1
Cnga3
Cntn5
Ctgf
Cyr61
Egflam
Fam81a
Fig4
Gm10435
Gm10800
Gm10801
Gm12295
Gm14492
Gm15770
Gm16316
Gm16534
Gm17281
Gm17473
Gm26924
Grb14
Ier2
Ighg2c
Il15
Junb
Klhl34
Lgi3
Lrrc3b
Mrpl12
Myl1
Pde11a
Pgf
Polr1e
S1pr5
Sbk2
Sh3kbp1
Slc17a7
Spint2
Tbc1d10c
Tmem56

47

downregulated genes with TBX5 enhancer binding

Ankrd63
4430402I18Rik
Abra
Adra1b
Adrbk2
Ankrd23
Cacna1g
Cenpf
Chrm2
Clasp1
Cmya5
Cox17
Crip2
Cryab
Ctnna1
Daam1
Dbh
Efnb3
Ehbp1
Emilin2
Entpd5
*Fgf16
Fhl2
Fitm1
Fstl4
*Gja1
Gpr22
Hfe2
Hspb1
Ier5
Kcng2
Kcnip2
Kcnj5
Kcnv2
Lbh
Lclat1
Lrrc10
Lrrc4b
Nppb
Pdlim4
Pdzrn3
Pkig
Plekhh1
Rbfox1
Scn5a
Stk39
Ttll1

2308

genes with TBX5 enhancer binding

0610009B22Rik
0610009D07Rik
1110001A16Rik
1110034G24Rik
1110057K04Rik
1200014J11Rik
1500035N22Rik
1600014C10Rik
1700001O22Rik
1700011E24Rik
1700019N19Rik
1700022I11Rik
1700024P16Rik
1700025C18Rik
1700029H14Rik
1700067P10Rik
1700088E04Rik
1700106J16Rik
1810011H11Rik
1810011O10Rik
1810013L24Rik
2010107E04Rik
2010109A12Rik
2010111I01Rik
2010300C02Rik
2210404J11Rik
2210404O07Rik
2310003H01Rik
2310009B15Rik
2310022B05Rik
2310042D19Rik
2310057M21Rik
2410015M20Rik
2510003E04Rik
2510039O18Rik
2810428I15Rik
2900060B14Rik
3110018I06Rik
3110021A11Rik
3110040N11Rik
3110057O12Rik
3222401L13Rik
3425401B19Rik
4632404H12Rik
4732465J04Rik
4921524J17Rik
4930505A04Rik
4930563D23Rik
4930569F06Rik
4930589L23Rik
4933412E24Rik
4933415A04Rik
4933426M11Rik
5031425E22Rik
5031439G07Rik
6030458C11Rik
6430573F11Rik
9030617O03Rik
9130011E15Rik

86

upregulated genes

2610203C20Rik
4930529M08Rik
4931406C07Rik
5430416N02Rik
A430110L20Rik
Acox2
Adam33
AI593442
Angptl7
B230325K18Rik
Btla
Casc5
Ccl8
Cd226
Cd84
Ckap2
Clec10a
Clec1b
Clec5a
Creb5
Ctla2a
Cubn
D630024D03Rik
Dlg2
F5
F630028O10Rik
Fermt3
Gapdh
Gm10615
Gm12250
Gm12940
Gm15626
Gm15675
Gm16340
Gm16586
Gm17388
Gm21781
Gm22710
Gm23442
Gm25791
Gm25835
Gm26165
Gm26397
Gm4951
Gm8420
Gp9
H2-Q6
Hpse
Ifi204
Ifit1
Ifit2
Ikzf1
Irf7
Itga2b
Lypd6
Mamld1
Marveld2
Mir1949
Mx2

7

upregulated genes with TBX5 enhancer binding

A930033H14Rik
A930039A15Rik
Arhgap15
Ddx60
Gm10115
Raph1
Tfcp2l1

* These genes were manually annotated, because automated GREAT annotation did not correctly annotate these genes.

9230102O04Rik
9230112D13Rik
9430016H08Rik
9630014M24Rik
9630033F20Rik
A130010J15Rik
A330017A19Rik
A430033K04Rik
A630007B06Rik
A730013G03Rik
A730049H05Rik
A830005F24Rik
A830073O21Rik
A930002H24Rik
A930004D18Rik
Aacs
Aasdh
AB041803
Abcb8
Abcb9
Abcc3
Abcc9
Abcd2
Abcd3
Abcf2
Abhd12
Abhd17a
Abhd2
Abhd8
Ablim1
Ablim3
Abtb1
Acaa2
Acacb
Acad9
Acap3
Acbd5
Acbd6
Acn9
Aco2
Acot11
Acox1
Acp6
Acsl1
Acss2
Actc1
Actg1
Actl6a
Actn1
Actn2
Actr10
Actr3
Acy1
Acyp1
Ada
Adam17
Adam19
Adamts1
Adamts2
Adamts20
Adamts3
Myo1g
Npas2
P2ry12
Papd4
Plek
Ppbp
Prg4
Psca
Rbm3
Rgs18
Rorb
S100a4
Scgb1c1
Siglec1
Slc6a4
Slfn8
Snora23
Snord15a
Sntb1
Trim59
Trim67
Trpc6
Tubb1
Vaultrc5
Wisp2
Zfhx4
Zfp960

Adamts7
Adamts9
Adamtsl2
Adarb1
Adck1
Adck3
Adcy5
Adcy9
Adi1
Adk
Adora3
Adprhl1
Adra1d
Adrb1
Adrm1
Adss
Afap1
Afap1l1
Afap1l2
Aff1
Ago2
Agpat1
Agpat2
Agpat3
Agpat9
Agtpbp1
Ahcyl1
Ahdc1
Ahi1
Ahr
AI118078
AI317395
AI413582
AI837181
Ajuba
Ak3
Ak4
Akap1
Akap11
Akap13
Akap7
Akap9
Akt1
Akt1s1
Akt2
Aldh1l1
Aldh3a1
Aldh3a2
Aldh9a1
Alpk2
Alpl
Als2cl
Amd1
Amfr
Ammecr1
Amotl2
Amz1
Anapc15-ps
Anapc16
Anapc5
Ank

Ank1
Ank2
Ankef1
Ankrd1
Ankrd13a
Ankrd24
Ankrd26
Ankrd39
Ankrd9
Anks1
Aox1
Ap1m1
Apba3
Aph1b
Apmap
Apob
Apobec2
Apol6
Apom
Appl2
Arf1
Arf6
Arg1
Arhgap11a
Arhgap12
Arhgap19
Arhgap26
Arhgap31
Arhgap32
Arhgap44
Arhgap5
Arhgef1
Arid3a
Arid3b
Arl3
Arl6ip4
Arl8b
Armc2
Armc8
Arnt
Arntl
Arpc2
Arpp19
Arrdc2
Arrdc3
Arrdc4
Art1
Art3
Art5
Arvcf
Asb15
Asb2
Asb8
Ascc3
Aspdh
Atf3
Atf5
Atf6
Atf7ip
Atg13
Atg16l2

Atg3
Atg7
Atg9b
Atoh7
Atoh8
Atp11a
Atp1a1
Atp1b1
Atp2a1
Atp2a2
Atp5b
Atp5e
Atp5h
Atp5j
Atp6ap2
Atp6v1b2
Atp6v1c1
Atp6v1f
Atpaf2
Atr
Atraid
AU019823
Aup1
Auts2
AW209491
Azi2
Azin1
B230118H07Rik
B230120H23Rik
B3galt1
B3galt5
B4galnt3
B4galt1
Bag1
Bag5
Bag6
Bahcc1
Baiap2l1
Banp
Bbip1
BC003331
BC026590
BC027072
BC034090
BC048609
Bcam
Bcar1
Bcas3
Bcat2
Bccip
Bcl10
Bcl11b
Bcl2a1a
Bcl2l1
Bcl2l11
Bcl7a
Bcl9
Bcor
Bcorl1
Bcs1l
Bdh1

Begain
Bend3
Best3
Bhlhe40
Bid
Blk
Blm
Bloc1s4
Bloc1s5
Bmp1
Bmyc
Brd1
Brd9
Bri3
Btaf1
Btbd2
Btbd6
Btg2
C030039L03Rik
C130026L21Rik
C130040N14Rik
C1qtnf7
C230052I12Rik
C230081A13Rik
C2cd3
C2cd5
C3ar1
Cabin1
Cacna1c
Cacnb2
Cacybp
Camk1g
Camk2d
Camta1
Cand1
Cap2
Capn13
Capn2
Capn3
Capn9
Card9
Casp8
Casp9
Casq2
Casz1
Cav3
Cbfa2t3
Cbfb
Cbwd1
Cbx4
Ccbl2
Ccdc103
Ccdc114
Ccdc117
Ccdc142
Ccdc149
Ccdc152
Ccdc159
Ccdc163
Ccdc18
Ccdc39

Ccdc41
Ccdc42
Ccdc71l
Ccdc8
Ccdc96
Cck
Ccl27a
Ccnd1
Ccndbp1
Ccng2
Ccni
Ccnjl
Ccny
Ccrn4l
Cct2
Cct8l1
Cd180
Cd28
Cd34
Cd4
Cd46
Cd47
Cdadc1
Cdc42bpa
Cdc42bpb
Cdca7
Cdh13
Cdh16
Cdh2
Cdh22
Cdh26
Cdh4
Cdk1
Cdk13
Cdk16
Cdk19
Cdk5
Cdk5r1
Cdk5rap1
Cdk8
Cdkal1
Cdkl2
Cdkl3
Cdkn1c
Cdon
Cdyl2
Cebpb
Cep89
Cep95
Cerk
Cetn3
Cgref1
Chac1
Champ1
Chd2
Chd9
Chek1
Chgb
Chit1
Chml
Chordc1

Chrac1
Churc1
Ciapin1
Cish
Cit
Ckap5
Ckb
Ckm
Clasp2
Clcn5
Clcn6
Cldn25
Clec2l
Clic4
Clic5
Clk3
Clta
Cltc
Clu
Clybl
Cmah
Cmip
Cnep1r1
Cnnm2
Cnnm3
Cog6
Col4a1
Col4a2
Col6a3
Colgalt1
Cops5
Coq10a
Coq9
Coro6
Cox15
Cox4i2
Cp
Cpeb2
Cpeb3
Cpeb4
Cpn2
Cpne4
Cpne5
Cpped1
Cpt1a
Cpt1b
Cpt2
Cradd
Crb3
Creb1
Creb3l2
Crebl2
Creld2
Crem
Cryaa
Cryba4
Crygs
Cs
Csf1
Csf2
Csk

Csnk1a1
Csnk1e
Cspp1
Csrnp1
Csrp3
Cstad
Ctcfl
Ctdp1
Ctdsp1
Ctdsp2
Cth
Ctif
Ctnnd1
Ctr9
Ctrb1
Ctsb
Cuedc1
Cuedc2
Cul4a
Cutc
Cux1
Cux2
Cwf19l1
Cxcr6
Cxxc1
Cxxc4
Cyb561
Cyb5r3
Cycs
Cyp26b1
Cyp51
Cyth1
Cyyr1
D10Jhu81e
D11Wsu47e
D1Ertd622e
D430041D05Rik
D4Wsu53e
D5Ertd579e
D730039F16Rik
D930015E06Rik
Dapk1
Dapl1
Dbnl
Dbp
Dbt
Dcaf15
Dcaf4
Dclk2
Dcp1b
Dctn6
Dda1
Ddah1
Ddr1
Ddx20
Ddx25
Ddx5
Ddx50
Defb42
Dennd1a
Depdc1b

Derl2
Des
Dfna5
Dgat2
Dgcr8
Dgka
Dgkg
Dhrs11
Dhrs13
Dhrs3
Dhrs7
Dhrs7c
Dhx8
Diap1
Dip2a
Diras2
Disc1
Dkc1
Dlc1
Dlg1
Dlgap4
Dll1
Dmbt1
Dmrt1
Dmwd
Dmxl1
Dnahc17
Dnaja2
Dnajb11
Dnajb5
Dnajc1
Dnajc11
Dnajc16
Dnajc18
Dnajc6
Dnajc9
Dnali1
Dnlz
Dnmt1
Doc2g
Dock3
Dok7
Dot1l
Dpf3
Dqx1
Drap1
Dsc2
Dscr3
Dsg2
Dsp
Dtd1
Dtl
Dtna
Dusp10
Dusp7
Dync2li1
Dyrk2
Dysf
E030011O05Rik
E130114P18Rik
E2f4

E2f7
E2f8
E330021D16Rik
Eapp
Ears2
Ebf2
Ece1
Ech1
Echdc3
Ecm2
Ect2
Edf1
Edn2
Eed
Eef2k
Efcab11
Efcab2
Efna1
Efna5
Eftud2
Egln1
Egln2
Egln3
Ehd2
Ehmt2
Eif2ak1
Eif2b4
Eif4ebp2
Eif4g1
Eif4g2
Eif4g3
Eif5a
Eif6
Elac1
Elac2
Elf2
Elk1
Emc10
Emg1
Emp3
Emx1
Endog
Eno3
Enpp5
Entpd6
Eogt
Ep400
Epb4.1
Epg5
Ephb1
Ephb2
Ephb3
Ephb4
Eps8l1
Erbb2
Erbb4
Ercc4
Ercc6
Erh
Eri3
Ero1l

Esrra
Esrrb
Etos1
Etv3
Etv6
Eva1c
Evi5l
Exd2
Exoc3l
Exoc3l2
Exoc4
Exog
Extl3
F3
Fabp3
Faf1
Fam104a
Fam105b
Fam109a
Fam120a
Fam122a
Fam126a
Fam134b
Fam160b1
Fam161b
Fam163b
Fam171a2
Fam174b
Fam175a
Fam175b
Fam179a
Fam187a
Fam193a
Fam195a
Fam195b
Fam207a
Fam20b
Fam20c
Fam210b
Fam211b
Fam214a
Fam49a
Fam65b
Fam78a
Fam84a
Fam86
Fam92b
Fancc
Fance
Far1
Farp1
Fars2
Fblim1
Fbrsl1
Fbxo11
Fbxo31
Fbxo32
Fbxo36
Fbxo4
Fbxo40
Fbxo9

Fbxw7
Fdft1
Fem1a
Fer
Fez1
Fgd2
Fgd6
Fgf1
Fgf23
Fgl2
Fhit
Fhod3
Fign
Fkbp5
Flot1
Flrt1
Fndc3b
Fndc5
Fnip2
Fntb
Foxj2
Foxj3
Foxn3
Foxo1
Foxo3
Foxo6
Foxp4
Frat2
Frmd4a
Frmd5
Frmd6
Frmd8
Fsd2
Fth1
Ftsj2
Fuca2
Fuom
Furin
Fv1
Fxn
Fxyd1
Fxyd3
Fxyd7
Fyco1
Fzd3
G6pc3
Gaa
Gabpa
Gabrr2
Gadd45g
Galk1
Galnt18
Galnt2
Galt
Gap43
Garem
Gas1
Gas6
Gata4
Gata5
Gata6

Gatad2a
Gbas
Gc
Gcc2
Gcgr
Gcom1
Gdap2
Gdf9
Gdi2
Get4
Gfod1
Ggnbp2
Ggt7
Ghr
Gid4
Gin1
Gins2
Gipc1
Gipc2
Git2
Gja3
Gja5
Gjd2
Glb1l
Glcci1
Glce
Glis2
Glrx5
Gltscr1
Gltscr1l
Glul
Gm10006
Gm10036
Gm10083
Gm10126
Gm10129
Gm10132
Gm10253
Gm10263
Gm10277
Gm10282
Gm10300
Gm10382
Gm10384
Gm10570
Gm10634
Gm10647
Gm10729
Gm10762
Gm10766
Gm11273
Gm11492
Gm11733
Gm12830
Gm13090
Gm13298
Gm15737
Gm16253
Gm17296
Gm20390
Gm21685

Gm21974
Gm22
Gm355
Gm4450
Gm5174
Gm527
Gm5447
Gm5546
Gm608
Gm6420
Gm6569
Gm6594
Gm6658
Gm6712
Gm6772
Gm6994
Gm7854
Gm815
Gm839
Gm8444
Gm9047
Gm9754
Gm9791
Gm9874
Gm9887
Gm9900
Gm9932
Gm9934
Gm9966
Gmfg
Gmnn
Gmppa
Gna12
Gnat1
Gnb3
Gne
Gnl3
Gnpda1
Golga7
Golga7b
Gorasp2
Gosr1
Got1
Gpatch2l
Gpatch8
Gpc1
Gpcpd1
Gpd1l
Gpr135
Gpr155
Gpr25
Gpr68
Gpr98
Gramd1b
Gramd4
Grasp
Grhl3
Grhpr
Grk6
Grn
Grtp1

Gsap
Gse1
Gspt1
Gstm1
Gtdc1
Gtf2h1
Gtf2h2
Gtf2i
Gtf2ird1
Gtf3a
Gtpbp2
Gtsf1l
Gxylt1
Gyltl1b
Gzmm
H2afb1
H2afy
H2-Ke6
H3f3b
H60c
Habp2
Hadha
Hadhb
Hand2
Hap1
Harbi1
Haus8
Hbegf
Hbp1
Hcfc1r1
Hcls1
Hdac4
Hdac5
Hddc3
Hdgfrp2
Hdlbp
Heatr2
Hebp2
Hectd2
Hemk1
Herpud2
Hes1
Hexim1
Hey2
Heyl
Hhat
Hhatl
Hiat1
Hic2
Hif1a
Hinfp
Hipk1
Hipk2
Hipk3
Hirip3
Hivep1
Hk1
Hk2
Hlf
Hlx
Hmg20a

Hn1l
Hnrnpl
Homer2
Hopx
Hpn
Hps5
Hs6st1
Hsbp1
Hsd3b7
Hsdl2
Hsp90b1
Hspa12a
Hspa4
Hspa8
Hspa9
Hspb11
Hspb2
Hspb7
Hspb8
Htra1
Htra2
Ick
Ict1
Idh1
Idh2
Ido2
Ids
Idua
Ier3
Ifnar1
Ifngr2
Ifnlr1
Ifrd2
Ift81
Igf2r
Igflr1
Igsf3
Igsf9b
Ikbkap
Ikzf2
Il11ra2
Il12a
Il12b
Il12rb1
Il15ra
Il17b
Il1r2
Impa2
Ina
Ino80
Ino80e
Inpp5a
Inppl1
Insr
Ints6
Intu
Ipo5
Ippk
Iqgap3
Iqsec1
Irf2bp2

Irf2bpl
Irgc1
Irs2
Irx3
Irx4
Irx5
Isca1
Ist1
Itga7
Itgb5
Itpr1
Ivns1abp
Iyd
Jak3
Jmjd1c
Jmjd4
Josd2
Jph2
Jtb
Jup
Kalrn
Kank1
Kank2
Kat6b
Kazn
Kcna7
Kcne1
Kcnh2
Kcnh7
Kcnj8
Kcnk2
Kcnk3
Kcnq1
Kctd20
Kdm4b
Kdm5b
Kdm6b
Keap1
Khdrbs3
Kif11
Kif13a
Kif1b
Kif21a
Kif26b
Kif3a
Kif6
Kifc1
Kifc5b
Kl
Klf10
Klf13
Klf14
Klf15
Klf3
Klf9
Klhl21
Klhl22
Klhl25
Klhl38
Klhl8
Kpna6

Krtap11-1
Ky
Lacc1
Lace1
Lactb
Lactbl1
Lag3
Lama2
Lama5
Lamb3
Lamtor1
Larp7
Ldb3
Lemd2
Leprot
Letm2
Letmd1
Lgi2
Lgi4
Lgmn
Lgr4
Lhx5
Limch1
Lims1
Lin37
Lingo1
Lipo1
Lmbr1l
Lmcd1
Lmo7
Lmod2
Lmod3
Lmx1a
Lnpep
Loh12cr1
Lonrf1
Loxl2
Loxl4
Lpcat3
Lpin1
Lpin2
Lpl
Lpp
Lpxn
Lrfn3
Lrig1
Lrig2
Lrp4
Lrrc10b
Lrrc14b
Lrrc2
Lrrc28
Lrrc3
Lrrc42
Lrrc48
Lrrc52
Lrrfip1
Lrrn2
Lsm3
Lsm6
Lsmem1

Ly86
Lypd1
Lyrm4
Lysmd4
Lzic
Lztfl1
M6pr
Mab21l2
Mab21l3
Macrod1
Macrod2
Madd
Maf
Mageh1
Magi3
Maml1
Maml3
Man1c1
Man2a1
Manba
Map1lc3b
Map2k4
Map3k1
Map3k3
Map3k8
Map4k4
Mapk6
Mapkapk3
Mapre2
March7
Mark3
Mark4
Mast2
Mat2a
Max
Mb
Mccc2
Mcf2l
Mcfd2
Mcm2
Mcur1
Mdh1
Med4
Mef2a
Mef2d
Megf9
Mep1b
Mettl7b
Mex3b
Mfhas1
Mfn1
Mfn2
Mfrp
Mfsd8
Mgat4a
Mgea5
Mgll
Mgst3
Mical3
Micall1
Midn

Mier3
Mif4gd
Mios
Mis12
Mis18bp1
Mkl2
Mkln1
Mknk2
Mlf1ip
Mll5
Mllt1
Mllt10
Mlph
Mmab
Mmachc
Mmp24
Mmp28
Mms19
Mn1
Mnt
Mogat2
Mon1a
Morc4
Morf4l2
Morn1
Mov10l1
Mpc1
Mr1
Mrm1
Mrpl14
Mrpl23
Mrpl3
Mrpl33
Mrpl34
Mrpl42
Mrpl48
Mrpl54
Mrps16
Mrps18a
Mrps18b
Mrps23
Mrps27
Mrps5
Mrs2
Msi2
Msl1
Msra
Msrb1
Mt1
Mta1
Mtdh
Mterf
Mterfd3
Mtfr2
Mthfr
Mtl5
Mtmr3
Mtmr6
Mtr
Mtss1
Mtss1l

Mvd
Mvk
Mxd4
Mybpc2
Mybpc3
Myh10
Myh6
Myh7
Myl2
Myl3
Myl9
Mylk3
Myo10
Myo15b
Myo18b
Myo9b
Myocd
Myom1
Myoz2
Mypn
Mzt2
N6amt1
N6amt2
Naa30
Naa35
Nampt
Nans
Narf
Nat8b
Nav2
Nck2
Nckap5
Ncoa3
Ndfip1
Ndufa13
Ndufa8
Ndufb10
Ndufb9
Nedd4
Nedd4l
Nedd9
Neil2
Nek9
Nemf
Nenf
Nexn
Nfasc
Nfatc1
Nfic
Nfkb1
Nfkbia
Nfya
Ngdn
Nhlrc1
Nhlrc2
Nhsl1
Ninj1
Ninj2
Nipal4
Nisch
Nkx2-5

Nkx6-3
Nle1
Nme1
Nme6
Nmnat1
Nmt2
Nnmt
Nodal
Nol10
Nol9
Notch3
Npffr2
Nphp1
Nr1d1
Nr3c1
Nr3c2
Nr4a1
Nr4a3
Nrap
Nrbf2
Nrp1
Nsun5
Nsun6
Nthl1
Ntn1
Ntrk2
Ntsr2
Nubpl
Nudt1
Nudt13
Nudt15
Nudt8
Nuf2
Nup153
Nup210
Nup214
Nup54
Nup93
Nupl2
Nus1
Oard1
Obscn
Ogfrl1
Ogt
Olfml1
Olfr1402
Onecut1
Opa1
Opn3
Oraov1
Osbpl3
Osbpl8
Osr1
Otos
Otud4
Otud7a
Otx1
Ovol2
Oxr1
Oxsr1
P2rx5

P4ha2
Pabpc1
Pabpc4
Pabpc6
Pabpn1l
Pacrg
Pacsin2
Pafah2
Paics
Paip2b
Palld
Pank3
Panx2
Parm1
Parn
Parp1
Parva
Pask
Pbrm1
Pbx1
Pbx3
Pcdh7
Pcdhga11
Pced1b
Pcf11
Pcgf5
Pcid2
Pcnp
Pcnt
Pcnx
Pcp4l1
Pcyt1a
Pdcd4
Pde3a
Pde4a
Pde4dip
Pde6a
Pde7b
Pdgfa
Pdhb
Pdia5
Pdik1l
Pdk2
Pdlim1
Pdp2
Pds5b
Pdss2
Pdzd2
Pdzrn4
Pex14
Pex16
Pfkfb2
Pgbd5
Pggt1b
Pgls
Pgm2
Phactr2
Phf13
Phf17
Phf19
Phf20l1

Phf8
Phlda1
Phldb1
Phospho1
Phox2a
Phox2b
Phrf1
Phyhip
Pias1
Picalm
Pigh
Pigo
Pih1d2
Pik3c2b
Pik3r1
Pik3r3
Pim1
Pim3
Pipox
Pitpnb
Pitpnm2
Pitrm1
Pitx1
Pja2
Pkia
Pkm
Pknox1
Pknox2
Pkp1
Pkp2
Pkp4
Pla1a
Pla2g16
Plcb1
Plcb2
Plcb4
Plcg2
Plekha1
Plekha3
Plekha6
Plekhf1
Plekhm2
Plekhn1
Plin4
Plin5
Pln
Plp2
Plxna1
Plxnc1
Pm20d2
Pnmt
Pnpla2
Pnpla3
Pnpla5
Pnrc1
Pnrc2
Podn
Pold2
Pold3
Pole
Pole4

Poln
Polr2g
Polr2m
Polr3c
Polr3h
Pom121
Popdc2
Ppap2b
Ppapdc2
Ppara
Ppard
Ppargc1b
Ppfia1
Ppfibp2
Pphln1
Ppif
Ppil1
Ppme1
Ppp1r10
Ppp1r12b
Ppp1r12c
Ppp1r13b
Ppp1r14c
Ppp1r15b
Ppp1r35
Ppp1r37
Ppp1r3b
Ppp1r7
Ppp2r2a
Ppp2r5a
Ppp3cc
Ppp4r2
Ppp5c
Pptc7
Pqlc1
Prcp
Prdm11
Preb
Prickle1
Prickle3
Prima1
Prkaa2
Prkab1
Prkab2
Prkaca
Prkag1
Prkch
Prkci
Prnp
Proser2
Prpf18
Prr7
Prrc1
Prss42
Prss52
Prss53
Prtg
Prune2
Psapl1
Psenen
Psma6

Psmd4
Psmd8
Psme1
Psph
Pstpip2
Ptbp2
Ptcd2
Ptch1
Ptgds
Ptgfr
Ptma
Ptms
Ptn
Ptp4a3
Ptpdc1
Ptpn1
Ptpn11
Ptpn14
Ptpn5
Ptprk
Ptprt
Pusl1
Pvrl2
Pwwp2b
Pxk
Pxmp2
Pygb
Pyroxd1
Pyroxd2
Qk
Qser1
R3hcc1
Rab17
Rab18
Rab20
Rab2a
Rab33b
Rab3a
Rab3d
Rab43
Rab5b
Rab6a
Rabac1
Rabl6
Rad51b
Rad9b
Raf1
Ralbp1
Ralgapb
Ranbp2
Rangap1
Rap1a
Rap1gap
Rap2a
Rap2c
Rapgef2
Rapgef4
Rara
Rarb
Rasa2
Rassf7

Raver1
Rbbp6
Rbbp8
Rbfox2
Rbm19
Rbm20
Rbm24
Rbm25
Rbm38
Rbpms
Rc3h1
Rcan1
Rcan2
Rcor1
Rcor3
Reep5
Repin1
Rere
Rexo2
Rexo4
Rftn1
Rgcc
Rgs2
Rgs6
Rhbg
Rheb
Rhoa
Rhob
Ric8b
Rilpl1
Rilpl2
Rimkla
Rin3
Rit1
Rlbp1
Rmnd5a
Rnf111
Rnf115
Rnf122
Rnf14
Rnf145
Rnf167
Rnf19b
Rnf25
Rnf4
Rnf5
Rngtt
Rnps1
Rp9
Rpa1
Rpa2
Rph3a
Rpl18
Rpl27
Rpl29
Rpl34
Rpl36
Rpl36-ps3
Rpl37
Rpl3l
Rpl41

Rplp0
Rplp1
Rprd1b
Rps24
Rps4y2
Rpusd2
Rqcd1
Rrad
Rraga
Rragd
Rreb1
Rrp1b
Rsbn1
Rsph9
Rtca
Rtp3
Rufy3
Runx1t1
Rusc2
Rxrb
Ryr2
S100pbp
Samd1
Samd14
Sardh
Sash1
Satb1
Sbk1
Scaf8
Scai
Scamp5
Scd2
Scd3
Schip1
Sclt1
Scml4
Scn3b
Scrn1
Scyl1
Scyl3
Sde2
Sec14l1
Sec22a
Sec22b
Sec31a
Sec61b
Selenbp1
Sema3b
Sema4b
Senp1
Sepn1
Sept2
Sept7
Sept9
Serbp1
Serinc2
Serp2
Serpinb1c
Serpinb6b
Sertad4
Sesn1

Sesn2
Sesn3
Setd7
Sez6l
Sf1
Sf3a2
Sf3b5
Sfrp5
Sft2d2
Sftpb
Sfxn5
Sgpl1
Sh2b2
Sh2d1a
Sh3bgr
Sh3bp5
Sh3bp5l
Sh3glb1
Sh3rf2
Shb
Shkbp1
Shoc2
Shroom3
Sik1
Sin3a
Sipa1l1
Sipa1l2
Sirt6
Siva1
Skap2
Ski
Skor1
Slain2
Slc10a6
Slc11a2
Slc12a8
Slc16a1
Slc16a10
Slc19a2
Slc1a7
Slc22a1
Slc22a23
Slc22a3
Slc22a4
Slc24a4
Slc25a11
Slc25a12
Slc25a17
Slc25a23
Slc25a29
Slc25a33
Slc25a34
Slc25a39
Slc25a51
Slc26a6
Slc26a7
Slc27a1
Slc28a1
Slc2a2
Slc2a4
Slc30a5

Slc35a5
Slc35b1
Slc35c2
Slc35f1
Slc38a1
Slc38a10
Slc38a2
Slc38a3
Slc38a4
Slc39a13
Slc39a14
Slc39a7
Slc39a9
Slc41a1
Slc44a1
Slc45a1
Slc4a1ap
Slc4a2
Slc4a3
Slc4a4
Slc50a1
Slc5a6
Slc6a6
Slc7a15
Slc8a1
Slc9a3r1
Slco1c1
Slco4a1
Sltm
Smad2
Smad4
Smad5
Smad7
Smap2
Smarcd1
Smarcd2
Smc3
Smco1
Smcr8
Smg1
Smg9
Smim11
Smim13
Smim6
Smoc2
Smu1
Smyd1
Smyd2
Smyd4
Snai3
Snap25
Snap47
Snapc4
Snapin
Snip1
Snrnp35
Snrnp48
Snrpd3
Snta1
Snx17
Snx5

Sobp
Sorbs1
Sorl1
Sowahb
Sox4
Sp4
Spag17
Spag7
Spag9
Spata24
Spc24
Spcs3
Specc1
Speg
Spen
Spesp1
Spink2
Spink4
Spock2
Spop
Spred2
Sprtn
Spry4
Spryd3
Spryd7
Spsb1
Sptb
Sptbn1
Sptbn4
Sptssa
Spty2d1
Sqle
Srcrb4d
Srebf1
Sri
Srl
Srp19
Srrm1
Srrm2
Srrm3
Srrm4
Srsf6
Ssbp2
Ssh2
Sspn
Ssu2
St3gal5
St7
Stag2
Stard13
Stard3
Stard4
Stard7
Stc2
Steap4
Stk11
Stk16
Stk24
Stk36
Stom
Stox2

Stpg1
Stx16
Stx1b
Stx6
Stx8
Styx
Suds3
Sumo2
Sun2
Supt20
Supt5
Susd2
Suv420h2
Svil
Syce3
Syn2
Syne3
Synpo2
Sys1
Syt13
Syt17
Syt2
Syt7
Tac1
Tacc2
Tacr2
Taf10
Taf3
Tanc2
Tango2
Tapbp
Tas1r1
Tbc1d1
Tbc1d14
Tbc1d16
Tbc1d2b
Tbc1d5
Tbc1d7
Tbccd1
Tbx15
Tbx19
Tbx2
Tbx3
Tcam1
Tcap
Tcea3
Tceal1
Tceb1
Tcf7l2
Tcp11
Tcta
Tead1
Tec
Tecpr2
Tecrl
Tef
Ten1
Tenm4
Tesc
Tex14
Tfap4

Tfrc
Tgfbi
Tgfbr3
Tgm2
Thap8
Thbs2
Themis
Thoc6
Thra
Thrb
Tiam1
Ticam1
Timm22
Timp4
Tlcd2
Tle3
Tlr2
Tlr9
Tm2d1
Tm2d3
Tmcc1
Tmed5
Tmem106b
Tmem126b
Tmem136
Tmem147
Tmem150a
Tmem154
Tmem164
Tmem167b
Tmem180
Tmem182
Tmem184b
Tmem191c
Tmem194
Tmem2
Tmem205
Tmem218
Tmem242
Tmem243
Tmem38b
Tmem40
Tmem41b
Tmem51
Tmem57
Tmem63c
Tmem65
Tmem86a
Tmem88
Tmem89
Tmie
Tmod1
Tmpo
Tmtc1
Tmx1
Tnfsf11
Tnik
Tnks
Tnnc1
Tnni3
Tnnt1

Tnnt2
Tnp1
Tns1
Tom1l2
Tomm20
Tomm40
Tomt
Top1mt
Top3a
Tor1aip1
Tpgs2
Tpm1
Tpp2
Tpr
Tpra1
Tprg
Trabd2b
Trafd1
Trak1
Trak2
Trap1
Trappc10
Trappc12
Trdn
Treh
Trib1
Trim11
Trim14
Trim43a
Trim43c
Trim54
Trim63
Trim7
Trim8
Trip12
Trip13
Trmt61a
Trove2
Trp53bp2
Trpm2
Trpm3
Trpm7
Tsc1
Tsc2
Tsc22d4
Tshz1
Tsn
Tstd2
Tsx
Ttc17
Ttc28
Ttc32
Ttc7
Ttc9b
Ttll11
Ttn
Ttr
Tuba4a
Tubg1
Tubg2
Tulp1

Twf2
Twist2
Twistnb
Twsg1
Txlnb
Txnrd2
Tyrobp
Tyw5
U2af1l4
U2af2
U2surp
Uap1
Ubac1
Ubash3b
Ubc
Ube2a
Ube2b
Ube2j1
Ube2q1
Ube2ql1
Ube2t
Ube2z
Ube4b
Ubfd1
Ubl3
Ubp1
Ubtd1
Ubxn6
Uchl5
Uck2
Ufl1
Ugp2
Ulk1
Ulk3
Umps
Unc13a
Unc45a
Unc45b
Uqcc
Uqcrq
Urgcp
Uros
Usp11
Usp2
Usp27x
Usp28
Usp43
Usp53
Usp6nl
Usp8
Usp9x
Utp14a
Utrn
Vac14
Vamp5
Vamp8
Vangl1
Vapa
Vav2
Vcpip1
Vegfa

Vezt
Vgll4
Vldlr
Vmn1r238
Vprbp
Vps13d
Vps37b
Vps8
Vrk1
Vti1a
Wars2
Wasf2
Wasl
Wbp7
Wbscr17
Wdpcp
Wdr18
Wdr25
Wdr3
Wdr62
Wdr76
Wdr81
Wdr95
Wdyhv1
Whamm
Whsc1l1
Wibg
Wipf3
Wipi1
Wiz
Wnk2
Wnt7b
Wwc2
Wwox
Wwp1
Xcl1
Xirp1
Xpo6
Xpr1
Xrcc2
Xrn1
Yars2
Yif1b
Yod1
Ythdf1
Ythdf3
Ywhag
Zadh2
Zbtb12
Zbtb16
Zbtb20
Zbtb3
Zbtb45
Zbtb48
Zbtb7c
Zbtb8a
Zbtb9
Zc2hc1a
Zc3h10
Zc3h6
Zc3h7b

Zc3h8
Zcchc13
Zdhhc11
Zdhhc13
Zdhhc22
Zfand3
Zfat
Zfml
Zfp106
Zfp142
Zfp148
Zfp191
Zfp235
Zfp27
Zfp326
Zfp330
Zfp335
Zfp354c
Zfp36l1
Zfp386
Zfp395
Zfp407
Zfp41
Zfp438
Zfp444
Zfp46
Zfp516
Zfp52
Zfp608
Zfp612
Zfp622
Zfp648
Zfp661
Zfp68
Zfp697
Zfp706
Zfp710
Zfp712
Zfp787
Zfp91
Zfp945
Zfp97
Zfx
Zhx1
Zhx3
Zic1
Zkscan3
Zkscan8
Zmiz1
Zmym2
Zmynd8
Zw10
Zxdc