SUPPLEMENTAL MATERIAL

Supplemental Methods

Generation the ATF3 knockout mice and fibroblast-specific over-expression of ATF3 mice

The generation/characterization of whole-body ATF3-knockout mice was described previously[1]. In brief, ATF3 gene is comprised of five exons A-E. The knockout allele lacks exon B, which contains the AUG initiation codon. The ATF3 knockout mice were backcrossed to the C57BL/6J background over 10 generations. We used a conditional transgenic approach, Cre/loxP recombination system, to generate transgenic mice that over-express ATF3 in a tissue-specific manner. Conditional transgenic founder mice expressing ATF3 gene ($ATF3^{fl/fl}$ TG) were generated by Cyagen Biosciences Inc. (Guangzhou, Guanddong, China) in the C57BL/6 background. Briefly, pRP.ExBi-EF1A-loxp-stop-loxp-mAtf3 vectors were linearized with gel purified, microinjected into fertilized mouse zygotes, and transferred to pseudopregnant females. The scheme for construction of the targeting vectors is shown in Supplemental Figure 4A. PCR for genotyping was performed with primers: 5'-TTCTCCTTGGAATTTGCCCTTT-3'(sense) and 5'-CAAGCTAATTCCTGCAGGTCGA-3'(antisense), which yielded 226 bp products for ATF3 fl/fl TG (Supplemental Figure 4B). The internal control PCR primers: 5'-ACTCCAAGGCCACTTATCACC-3' (sense); 5'-ATTGTTACCAACTGGGACGACA-3' (antisense). The col1a2-Cre/ERT mice, containing a CreER(T) recombinase gene located stream of a proa2(I) collagen promoter/enhancer which confers fibroblast-specific CreER (T) gene expression, were purchased from JAX Lab. $ATF3^{fl/fl}$ mice were bred with col1a2-Cre/ERT mice to achieve fibroblast-specific ATF3 over-expression in the adult. Mice were intraperitoneally treated with 2mg/Kg of tamoxifen dissolved in corn oil (2mg/Kg) for 7 days at 8-10 weeks of age[2].

Bone marrow transplantation

BM transplantation was performed as previously described[3]. Briefly, the 8-week old recipient mice (WT or ATF3KO) were exposed to 10 gray dose total-body irradiation from a cobalt-60 source. BM cells from 8 weeks old sex-matched donor mice (WT or ATF3KO) were collected in RPMI1640 medium. Four hours after irradiation, 1×10^7

BM cells in 200 μl from donor mice were injected into recipient mice via caudal vein. Reconstituted mice were conditioned with drinking water containing 100mg/l levofloxacin and 100mg/L fluconazole for two weeks. 10 weeks after BM transplantation, reconstituted mice were subjected to saline or Angiotensin (Ang) II infusion (1000 ng/kg/min) for 12 weeks. Ang II was purchased Sigma-Aldrich (catalog number A9525). Ang II is a synthetic peptide, with purity noted to be ≥93% (verified by HPLC). The molecular formula is $C_{50}H_{71}N_{13}O_{12}$. The efficiency of BM reconstitution was evaluated by genotyping genomic DNA isolated from BM cells.

Transthoracic echocardiography

Cardiac function was evaluated by the Vevo 770 high-resolution microimaging system (Visualsonic, Toronto, Canada). The heart was viewed from the parasternal short-axis in 2D mode. The left ventricular wall thickness and chamber dimension were measured in M-mode.

Histopathology analysis

Histopathology analysis was performed. Briefly, heart tissues were fixed, embedded, and sectioned into 5μm thick slices. Sections were stained with Masson's trichrome (collagen, blue; cytoplasm, red/pink) for collagen deposition analysis. Sections were stained with wheat germ agglutinin (WGA) to assess cellular hypertrophy. For immunohistochemistry, heart section were incubated with antibodies against α-smooth muscle actin (α-SMA) and SM-22α at 4℃overnight, then with secondary antibodies at 4℃ for 1 hour and detected with 3, 3'-diaminobenzidine, and sections were counterstained with hematoxylin. For immunofluorescence, frozen heart sections or cells were labeled with primary antibodies ATF3, Col1a2, Col1a1, Col2a1, CD31, SM22, α-actinin, and GFP, and then incubated with Alexa Fluor 555-, 488- or 633-conjugated secondary antibody (Jackson ImmunoResearch Laboratories, West Grove, PA). Immunohistochemistry images were captured by a Nikon Eclipse TE2000-S microscope (Nikon, Japan), and analyzed by a person blinded to treatment using Image Pro Plus 3 (Nikon). Immunofluorescence images were captured with Leica ST5 laser scanning confocal microscope.

In situ hybridization

In situ hybridization (ISH) was performed utilizing the Panomics QuantiGene ViewRNA ISH tissue assay (Affymetrix, Santa Clara, CA) as previously described[4]. Mouse hearts were fixed in 10% formaldehyde and embedded in paraffin. 5 micron sections were cut, deparaffinized, boiled in pre-treatment solution, and digested with proteinase K. Heart sections were hybridized for 3 hours at ℃with a custom designed probe against ATF3 and DDR2, ATF3 and CD68 or ATF3 and Col1a1 (Affymetrix, Santa Clara, CA). Bound probes were amplified per protocol from Panomics using PreAmp and Amp molecules. Working Label Probe oligonucleotides conjugated to 6-AP were added. Fast Blue Substrate was used to produce the signal for DDR2 or CD68 or ATF3 (blue dots). AP-Enhancer solution was added to each tissue section after washing. Working Label Probe oligonucleotides conjugated to 1-AP were added; Fast Red Substrate produced the signal for ATF3 or Col1a1 (red dots). Slides were counterstained with Hematoxylin. Images were taken a by Nikon Eclipse TE2000-S microscope (Nikon, Tokyo, Japan).

Human heart samples

Human hypertrophic heart tissue samples were obtained from patients previously diagnosed with HCM, undergoing septal myectomy surgery. Control samples were obtained from normal heart donor left ventricles. All specimens were processed immediately after surgery and stored at less than -80°C, until total RNA and protein were extracted. The local Institutional Review Board of the Institute of Biophysics and Anzhen Hospital approved all studies involving human heart tissue samples.

RNA-sequencing and data analysis

WT mice were infused with Ang II for 0, 7, and 28 days. Hearts were collected for RNA extraction. Cardiac fibroblasts were isolated from heart of WT and ATF3KO mice after Ang II infusion for 7 days. Cardiac fibroblasts were pretreated with p38 inhibitor (SB203580) or control for 1 hour, and stimulated by Ang II for another 24 hours. The total RNA of mouse heart tissue, mouse cardiac fibroblasts, or human heart tissue was extracted by TRIzol method (Invitrogen). The mRNA was reverse transcribed into double strand cDNA fragments. Library construction was performed by Illumina's TruSeq RNA Library Prep Kit per manufacturer's protocol (Illumina, San Diego, CA).

Final library quality control was performed by DNA High Sensitivity Qubit Kit (Invitrogen), the Bioanalyzer High Sensitivity Chip Kit (Agilent), and the qPCR machine (Agilent). qPCR was performed via Illumina Universal Library Quantification Kit (KAPA Biosystems). RNA libraries were then sequenced at 10pM on the Illumina HiSeq 2000 to generate 100 bp pair-end reads. After adaptor-removing and quality control filtering, the clean reads were mapped to mouse genome (Mm9) using Tophat2 (v2.0.9). Cufflink (v2.0.0) was used to identify differentially expressed genes (DEGs) between samples. Significant DEGs of each pairwise comparison were selected (p value<0.05). Pathway analysis, predominantly based on the Kyoto Encyclopedia of Genes and Genomes (KEGG) database, was employed to determine the significant functions and pathways of DEGs. Only pathway categories with a FDR-corrected P-value less than 0.05 were chosen. Path-Net was built per interactions between KEGG database pathways to permit systematic identification of interactions between significant pathways identified in cardiac fibroblast from Ang II-infused ATF3KO mice[5]. The transcriptome data of saline and Ang II infusion model has been uploaded into a public database (accession number GES89712). The transcriptome data of heart tissue from normal and HCM patients has been uploaded into a public database (accession number GSE89714).

Microarray analysis

WT mice were subjected to TAC or sham operation for 28 days. Total mouse heart RNAs were extracted. The mRNA microarray profiling was performed by Affymetrix GeneChip Mouse Genome 430 2.0 Array (Santa Clara, CA). Total RNA labeling, microarray hybridization, and scanning were performed per manufacturer's manual. Raw intensity signals of each mouse were scanned with GenePiX Personal 4000B (Molecular Devices Corporation, Sunnyvale,CA,USA) and quantified using GenePix Pro 4.0 software (Molecular Devices Corporation, Downingtown, PA, USA). Differentially expressed genes between two groups were filtered with criteria p<0.05; fold change >1.5. The microarray data has been uploaded into a public database (accession number GES89493).

Quantitative RT-PCR (qRT-PCR) analysis

Heart tissue and CF RNA was extracted by Trizol reagent method (Invitrogen). Total RNA was used for first-strand cDNA synthesis with M-MLV reverse transcriptase (Promega, Madison, WI). qRT-PCR was performed utilizing SYBR Green Master Mix (Takara, Otsu, Shiga, Japan) on the iCycler iQ system (Bio-Rad). PCR conditions included initial denaturation at 95°C for 5 minutes, 95°C for 45 seconds, and 60°C for 1 minute for 45 cycles. Gene expression levels were normalized to GAPDH. All samples were run in duplicate. The following of primers for genes:

ATF3 5’-GCTGGAGTCAGTTACCGTCAA-3’; 5’-CGCCTCCTTTTCCTCTCAT-3’;

α-SMA 5’-TCCTGACGCTGAAGTATCCGATA-3’; 5’-GGCCACACGAAGCTCGTTAT-3’;

ANP 5’-CACAGATCTGATGGATTTCAAGA-3’; 5’-CCTCATCTTCTACCGGCATC-3’;

Myh7 5’-CGCATCAAGGAGCTCACC-3’; 5’-CTGCAGCCGCAGTAGGTT-3’

Map2K3 5'-CTGAAGCAGGTGGTGGAGGAG-3'; 5'-TGGGCCAGTCCCTATGAATCC-3'

TGF-β2 5’-TCCCCTCCGAAAATGCCATC-3’; 5’-TGAGACATCAAAGCGGACGA-3’

TGF-β3 5’-ATGACCCACGTCCCCTATCA-3’; 5’-ACTCAGACTCCGAGGTCTCC-3’

BMP4 5’-CGGAAGCTAGGTGAGTTCGG-3’; 5’-AGAATCCCATCAGGGACGGA-3’

TGF-βi 5’-GCCCATGATAAGAGGGGACG-3’; 5’-ACATCCGGTCCATGGTGAAC-3’

TGF-βil1 5’-CCTATAGCTGGGCAAGTGGT-3’; 5’-CAAAAGGGAGCCCCATCCTT-3’

Thbs1 5’-CAATTTTCAGGGGGTGCTGC-3’; 5’-CCGTTCACCACGTTGTTGTC-3’

Thbs2 5’-ACCTCAGCAGAGGCAATGTC-3’; 5’-CCAGCCAGGTATGCTTTCCA-3’

Thbs3 5’-TCTTTTTCCCTCCCAGTCGC-3’; 5’-CTTAGCCGGTTCACTACCCC-3’

Smurf2 5’-GGGACATGTCTAACCCCGGA-3’; 5’-TGCACAGAGTACTGTCAGGC-3’

Col3a1 5’-ACGTAAGCACTGGTGGACAG-3’; 5’-CATTAGGCGCAGGAAGGTCA-3’

Col1a1 5’-CGATGGATTCCCGTTCGAGT-3’; 5’-CAGGAGGGCCATAGCTGAAC-3’

IL-6 5’-TCTCTGCAAGAGACTTCCATCC-3’; 5’-TTGTGAAGTAGGGAAGGCCG-3’

Itgb5 5’-AATGTGGAAGTGCCCCCAAT-3’; 5’-TTGAGGCTTTGGAACTTGGC-3’

Serpine1 5’-GACGTTGTGGAACTGCCCTA-3’; 5’-TTCTCAAAGGGTGCAGCGAT-3’

Cst3 5’-TTCGCTGTGAGCGAGTACAA-3’; 5’-ACGAGCTCTCACCACCTGTA-3’

IGF-1 5’-CTCAGAAGTCCCCGTCCCTA-3’; 5’-ATTTTCCGAGTTGCCTCCGT-3’

IGF-bp5 5’-AAAGCAGTGTAAGCCCTCCC-3’; 5’-TCCCCATCCACGTACTCCAT-3’

GAPDH 5’-CATGGCCTTCCGTGTTCCTA-3’; 5’-GCGGCACGTCAGATCCA-3’

Chromatin Immunoprecipitation (CHIP) Assays

ChIP assays were carried out with a EZ-ChIP kit (Millipore, Billerica, MA, USA) per manufacturer's protocol. Briefly, three biological replicates of cardiac fibroblast from ATF3KO mice transfected with Ad-con or Ad-ATF3 for 48 hours were treated with Ang II for 6 hours. Cells were cross-linked with 1% paraformaldehyde, before lysis with cold PBS/protease inhibitor. Chromatin was sheared by 10 seconds of sonication (Covaris 220) interposed with 30 second pauses, repeated 10 times. Immunoprecipitation was performed overnight at 4°C, via 4 μg of specific antibody or immunoglobulin G. Each IP sample was added to protein G agarose beads for 3 hours incubation at 4 °C. After pull-down, beads were washed 5 times. The immunocomplexes were extracted and processed by reverse cross-linking, proteinase K digestion, and DNA precipitation. The following antibodies were used for Chip: rabbit anti-ATF3 antibody (C-19, Santa Cruz), rabbit anti-acetyl-Histone H4 antibody (Millipore), and Ig G (Sigma). The following primers were used for Map2K3 Chip-PCR: forward 5'-CAGGACCACGCCAGCACAATC-3' and reverse 5'-CGGACTGTCACGCACAAACCC-3'.

CHIP-sequencing and Peak finding

Input DNA and CHIP DNA were prepared for ChIP sequencing via Illumina kit per manufacturer's protocol. Briefly, each sample was subjected to end repair, followed by addition of an A base to the 3′ end. Adaptor ligated DNA fragments were size-selected (175–225 bp), PCR-amplified, and further size-selected (175–225 bp). Amplification and size selection were confirmed by a BioAnalyzer. DNA fragments were pooled and sequenced on an Illumina HiSeq-1000 sequencer. CHIP sequencing data was obtained via Illumina Genome Analyzer II. 36 base pairs were analyzed by Illumina's pipeline software for quality filtering, and aligned to the Mm9 reference mouse genome. Only uniquely aligned reads were kept for subsequent bioinformatics analysis. To identify ATF3 peaks, We analyzed the Chip-seq data by the latest version of MACS2 software, with parameters "--d1 3561809 --d2 8108116 -g 60 -l 120" [6]. Analysis commenced a default false discovery rate (FDR) threshold of 0.0001, and a window size set at 1,000 bp. Firstly, we used a DNA input sample to eliminate biases introduced by sequencing,

chromatin structure, and sequence compositions. Secondly, the sample from ATF3-deficient CF transfected with Ad-con was used as unspecific background to identify specific ATF3 binding. Afterwards, BED Tools was used to annotate the genomic location of identified peaks.

Western blotting

Western blotting was performed. Briefly, total protein from heart or cells homogenate was extracted by SDS lysis buffer containing a protease inhibitor cocktail and phosphatase inhibitors (Roche, Mannheim, Germany). The equal samples were loaded, separated, and transferred to a membrane (Pierce). The membranes were blocked and incubated overnight with primary antibody as listed below at 4℃overnight, then incubated with infrared Dye 800-conjugated secondary antibodies (Rockland Immunochemicals, Inc., Gilbertsville, Pa.) for 1 hour at room temperature. The images were quantified by the use of the Odyssey infrared imaging system (LI-COR Biosciences, Lincoln, NE).

Preparation of nuclear extracts and immunoprecipitation

1×10^7 WT cardiac fibroblasts were plated 24 hours prior to transfection with Ad-con or Ad-ATF3. 48 hours later, cells were stimulated with PBS or Ang II (1uM) for 6 hours and harvested. Co-immunoprecipitation was performed using Nuclear Complex Co-IP kit (Active Motif) per manufacturer's protocol. Briefly, the cellular pellet was gently resuspended in 500 μl hypotonic buffer. 25 μl detergent was added, and the entire mixture was centrifuged. The nuclear fraction was resuspended and incubated with 100 ul digestion buffer and 0.5 μl enzymatic shearing cocktail for 90 minutes. The reaction was terminated by 0.5 M EDTA. Insoluble material was removed by centrifugation. The supernatant represented nuclear extract. 0.3 mg of nuclear extract was incubated for 1 hour with protein G sepharose beads (Santa Cruz), followed by 1 hour with 4 μg ATF3 or IgG antibody, followed by 3 additional hours with beads. Finally, beads were washed 4 times in IP washing buffer. Each bead pellet was resuspended in 8 μl of 2× reducing loading buffer. Samples were heated at 95°C for 5 minutes. The supernatant was subjected to western blot against HDAC1 antibody.

Cell Preparation

Cardiac fibroblasts (CF) were isolated from WT or ATF3KO mice by enzymatic digestion and cultured in full DMEM medium as previously described[7]. WT or ATF3KO CF were treated with PBS or Ang II (100 nM) for 48 hours. ATF3KO CF were infected with LV-Map2K3 shRNA or LV-con shRNA for 48 hours and treated with Ang II or PBS for anothor48 hours. ATF3-/- CF were pre-treated with p38 inhibitor (SB203580) or control for 48 hours in the absence or presence of Ang II. CF activation was evaluated via α-SMA and collagen I protein expression. Cardiomyocytes (CM) were isolated from one-week mouse pups by enzymatic digestion and cultured in CM-Medium. 24 hours later, CM was starved with FBS-free CM-medium for 8 hours. The medium was exchanged with fresh isolated conditional medium collected from WT or ATF3KO CF treated with Ang II for 24 hours. CM hypertrophy was analyzed by α-actinin staining and ANP mRNA expression.

Fluorescence-Activated Cell Sorting

Cardiac cell suspensions were prepared as previously described[8, 9]. Heart cells were sorted by flow cytometry (Beckman Coulter MoFlo XDP) into populations of $CD45^-CD31^+$ endothelial cells, $CD45^-PDGFR\text{-}\alpha^+$ cardiac fibroblasts, $CD45^-PDGFR\text{-}\alpha^-CD31^-$ cardiomyocytes, and $CD45^+F4/80^+$ macrophages. Isolated cardiac cells were utilized for RNA or proteins extraction and qRT-PCR and western-blot analysis.

Knocking down of Map2K3 by lentiviral short hairpin RNA (shRNA)

The following Map2K3-targeted short hairpin RNAs were designed and synthesized by Genechem Co. Ltd (Shanghai, China). The recombinant lentivirus of small interfering RNA targeting Map2K3 (Map2K3-RNAi-lentivirus) and control lentivirus (GFP-lentivirus) were commercially prepared. Briefly, a lentivirus transfer vector (GV118) was constructed. The vector contained an ampicillin resistant gene and an enhanced green fluorescent protein gene. Expression of shRNA was driven by a U6 promoter. Packaging of viruses was performed by transient transfection of 293T cells with a transfer plasmid and 3 packaging vectors: pGC-LV, pHelper 1.0, and pHelper 2.0. Three days after transfection, lentiviral particles were collected, filtered, and concentrated by ultracentrifugation at 50,000g for 2.5 hours at 4°C. The lentiviral-shRNA was transfected into cardiac fibroblasts at a final concentration of 50×PFU/cell (after cells

had grown to 30-50% confluence). After 96 hours, the knockdown efficiency of shRNA was evaluated by qRT-PCR. The targeting sequence of the small hairpin RNA: TGATGGAACACCCATTCTT (Map2K3-1#); TCACTATCGGAGACAGAAA (Map2K3-2#); ATGTGAAGATGTGCGACTT (Map2K3-3#).

Adenovirus Gene Transfer

Adenoviral vector encoding the mouse ATF3 gene (Ad-ATF3) and negative control (Ad-con) was constructed, packaged, purified, and titrated at Genechem Co. Ltd. For adenovirus-mediated gene transfer, Ad-ATF3 or Ad-con was transfected into CF from ATF3-/- mice at a final concentration of 200×PFU/cell for 48 hours. After 48 hours, the overexpression efficiency of Ad-ATF3 was evaluated by Western-blot.

Cytokines measurement

Cell culture supernatants were analyzed for mouse IL-6, Edn-1, and FGF-2 levels by sandwich ELISA kit (R&D System, Minneapolis,MN).

Design of LV-ATF3-mir1/133TS vectors and cell transfection

Recombinant LV vectors containing ATF3 with 2 tandem target sequences for mmu-mir1a-3p and mmu-mir-133a-3p introduced at its 3' end (LV-ATF3-mir1/133TS) were constructed in accordance with the manufacturer's instructions. Complementary oligonucleotides contained 2 tandem targeting sequences for mmu-mir1a-3p and mmu-mir-133a-3p:5'-

ataaATACATACTTCTTTACATTCCAcgtaATACATACTTCTTTACATTCCAacgcgtCAGCTGGTTGAAGGGGACCAAAtcacCAGCTGGTTGAAGGGGACCAAAC-3'.

For ATF3-mir-1-mir-133TS vectors, mir-1 and mir-133 TS were annealed and ligated into sites of 3' UTR end of ATF3 expression cassette with EcoRI. Next, ATF3-mir1/133TS were amplified from the carrier vector with the following pairs of primers: 5'-GAGGATCCCCGGGTACCGGTCGCCACCATGATGCTTCAACATCCAG-3'; 5'-CACACATTCCACAGGCTAGGTTTGGTCCCCTTCAACC-3'. The resulting PCR products were subcloned into a LV-pUbi-MCS-psSV40-EGFP vector (using AgeI/ NheI restriction sites) under the control of a pUbi promoter. LV-Control-mir1/133TS vectors replace ATF3 vectors with negative control vectors. All final LV constructs were confirmed by sequencing, purified, dialyzed and titrated in 293T cells. Cardiac

fibroblasts (CF) and cardiomyocytes (CM) were isolated from 1 week-old ATF3KO mouse pups by enzymatic digestion. The LV-Con-mir1/133TS and LV-ATF3-mir1/133TS were transduced into CF and CM at a final concentration of 50PFU/cell (after cells had grown to 30-50% confluence). After 72 hours, the ATF3 expression was evaluated by WB.

Antibodies

The following antibodies were used: ATF3 (SC-188) and Col 1a2 (SC-393573) from Santa Cruz Biotechnology; α-SMA (A5228) and α-actinin (A5044) from Sigma; HDAC1(AB7028), GFP (Ab13970), p-smad3 (Ab52903), Vimentin (Ab8978), CD31 (Ab393573) purchased from Abcam; H4AC (8647), Map2k3 (8535S), p-p38 (4511), T-p38 (9212S), p-MK2 (3007), T-MK2 (3042S), p-JNK1/2 (4668S); T-JNK1/2 (9258S), p-ERK1/2 (4370), T-ERK1/2 (4695), IgG (14708) from Cell Signaling Technology.

Supplemental Tables

Supplemental Table 1. Significant transcriptional factors in the heart, after Ang II infusion 7 days or 28 days and TAC operation for 28 days

Gene_sym	Description	Fold change		
		Ang II7D	Ang II28D	TAC 28D
Aebp1	**AE binding protein 1**	2.3		
Arid5a*	AT rich interactive domain 5A	2.7	2.5	
Arnt2	Aryl hydrocarbon receptor nuclear translocator 2		2.5	
Arntl*†	**Aryl hydrocarbon receptor nuclear translocator-like**	**16.8**	**8.5**	**4.9**
Atf3*†	**Activating transcription factor 3**	**3.3**	**5.5**	**2.1**
Batf	**Basic leucine zipper transcription factor, ATF-like**	3.9		
Bcl11a*	B-cell CLL-lymphoma 11A	2.6	2.3	
Bhlhe40	basic helix-loop-helix family, member e40			2.0
Bnc1	basonuclin-1	0.2		
Cebpd*	CCAAT-enhancer binding protein delta	2.1	2.4	
Clock	circadian locomotor output cycles kaput			1.5
Creb3l1*	cAMP responsive element binding protein 3-like 1	2.9	2.2	
Creb3l3	cAMP responsive element binding protein 3-like 3			2.8
Crem	cAMP responsive element modulator			1.8
Csrnp3	Cysteine And Serine Rich Nuclear Protein 3	0.4		
Dbp*†	**D site albumin promoter binding protein**	**0.0**	**0.3**	**0.5**
E2f1	E2F transcription factor 1	4.3	0.4	1.6
E2f2*	E2F transcription factor 2	6.6	2.2	
Egr1	Early growth response 1		4.4	
Egr2*	Early growth response 2	7.6	6.4	
Etv4	Ets Variant Gene 4	6.9		
Fosb*	FBJ murine osteosarcoma viral oncogene homolog B	6.8	4.0	
Foxd3	Forkhead Box D3	0.3		
Foxm1	Forkhead Box M1	8.9		
Foxo6	forkhead box O6			0.5
Foxs1*†	**Forkhead box S1**	**3.4**	**2.8**	**1.7**
Fus	fused in sarcoma			0.5
Gata3	GATA binding protein 3	0.3		
Gata5	GATA binding protein 5		3.0	
Grhl2*	Grainyhead-like 2	0.2	0.3	
Hic1	hypermethylated in cancer 1			1.9
Hif3a	Hypoxia Inducible Factor 3 Alpha Subunit	0.4		
Hlf*†	**Hepatic leukemia factor**	**0.2**	**0.3**	**0.4**
Hoxa4	Homeo box A4		0.4	

Hoxb9	homeobox B9			2.1
Hoxd9*	Homeobox D9	2.5	2.5	
Hspa1a*	Heat shock protein 1A	2.4	2.5	
Id2	inhibitor of DNA binding 2			1.7
Id4	Inhibitor Of DNA Binding 4	2.5		
Ikzf1	IKAROS family zinc finger 1	2.2		
Ikzf3*	IKAROS family zinc finger 3	3.8	2.7	
Ikzf4*	IKAROS family zinc finger 4	2.4	2.4	
Irf4	Interferon regulatory factor 4	0.4		
Irf7	Interferon regulatory factor 7		0.4	
Junb	Jun-B oncogene			1.7
Kcnip3	Potassium Voltage-Gated Channel Interacting Protein 3	0.4		
Klf15	Kruppel-like factor 15			0.7
Klf5	Kruppel-Like Factor 5		2.2	
Ldb2	LIM Domain Binding 2	2.5		
Lhx2	LIM homeobox protein 2			3.3
Litaf	Lipopolysaccharide Induced TNF Factor	2.5		1.7
Maff	v-maf musculoaponeurotic fibrosarcoma oncogene family, protein F (avian)			1.6
Meox1*	Mesenchyme homeobox 1	5.5	2.6	
Mllt3	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 3			0.5
Mybl1	MYB Proto-Oncogene Like 1	2.5		
Myc*	V-myc myelocytomatosis viral oncogene homolog	2.7	2.1	
Mycl1*	v-myc myelocytomatosis viral oncogene homolog 1 lung carcinoma derived	5.2	4.3	
Mycn	v-myc myelocytomatosis viral related oncogene, neuroblastoma derived (avian)			1.6
Neurog3	neurogenin 3			0.2
Nfatc4	nuclear factor of activated T cells, cytoplasmic, calcineurin dependent 4			1.7
Nfe2l3	Nuclear Factor, Erythroid 2 Like 3	3.2		
Nov	Nephroblastoma Overexpressed	2.1		
Npas2*†	**Neuronal PAS domain protein 2**	**4.8**	**3.0**	**1.8**
Nr1d2*†	**Nuclear receptor subfamily 1 group D member 2**	**0.2**	**0.4**	**0.6**
Nrl	neural retina leucine zipper gene			2.0
Pbx2	pre B cell leukemia homeobox 2			2.0
Scx	scleraxis			1.6
Msx2	Msh homeobox 2		2.0	
Smad7	SMAD family member 7			1.8
Snai3	snail homolog 3 (Drosophila)			0.4
Sox18	SRY-box containing gene 18			1.5

Sox4	SRY-box containing gene 4	0.6
Sox9	SRY-box containing gene 9	2.0
Srebf2	sterol regulatory element binding factor 2	1.9
Stat5a	signal transducer and activator of transcription 5A	0.5
Tbx15	T-box 15	3.2
Tef	thyrotroph embryonic factor	0.5
Trim33	tripartite motif-containing 33	0.5
Tsc22d3	TSC22 domain family, member 3	0.7
Zbtb12	zinc finger and BTB domain containing 12	0.5
Zfp488	zinc finger protein 488	1.7

Asterisk (*) indicates 22 TFs continually changing during Ang II infusion for 7 and 28 days. Dagger sign (†) indicates 7 TFs with common alteration during Ang II infusion and TAC for 28 days.

Supplemental Table 2: Differential expression genes between WT and ATF3KO CF

Gene ID	Gene Symbol	FDR	Fold change of ATF3 KO vs WT	Up-Down
58520	0610007P14Rik	0.000	1.45	UP
67851	1700021F05Rik	0.024	0.67	Down
75623	1700029F09Rik	0.027	0.59	Down
76669	1700128F08Rik	0.029	1258.92	UP
69126	1810022K09Rik	0.001	0.68	Down
70153	2210016F16Rik	0.010	0.75	Down
68544	2310036O22Rik	0.035	0.82	Down
69612	2310037I24Rik	0.009	0.81	Down
71923	2310047M10Rik	0.011	1.62	UP
78890	2310079F23Rik	0.034	1.80	UP
72128	2610008E11Rik	0.009	0.68	Down
67683	2610029G23Rik	0.048	0.81	Down
66578	2610039C10Rik	0.038	0.58	Down
112422	2610305D13Rik	0.032	1.65	UP
78832	2700078E11Rik	0.014	0.79	Down
68026	2810417H13Rik	0.000	0.71	Down
73112	3110003A17Rik	0.007	0.77	Down
66680	3230401D17Rik	0.025	0.74	Down
74041	4632434I11Rik	0.001	0.67	Down
223989	4921513D23Rik	0.008	1.32	UP
68271	4930441O14Rik	0.016	540.60	UP
75939	4930579G24Rik	0.000	0.45	Down
233103	4931406P16Rik	0.000	1.32	UP
229227	4932438A13Rik	0.001	1.32	UP
71101	4933407H18Rik	0.000	1.71	UP
238330	6430527G18Rik	0.000	1.34	UP
231014	9330182L06Rik	0.040	10.78	UP
240185	9430020K01Rik	0.000	1.27	UP
319277	A230046K03Rik	0.008	1.25	UP
319278	A230050P20Rik	0.024	1.44	UP
269855	A430110N23Rik	0.002	1.34	UP
239559	A4galt	0.003	1.88	UP
213993	A630007B06Rik	0.037	1.41	UP
77128	A930001N09Rik	0.049	1.36	UP
223921	Aaas	0.036	0.81	Down
268860	Abat	0.002	1.66	UP
11303	Abca1	0.028	1.20	UP
27403	Abca7	0.002	1.43	UP
217262	Abca9	0.003	1.34	UP

27416	Abcc5	0.007	1.31	UP
76491	Abhd14b	0.027	1.35	UP
320712	Abi3bp	0.000	1.40	UP
107476	Acaca	0.000	1.29	UP
110460	Acat2	0.000	1.72	UP
11421	Ace	0.000	1.73	UP
104112	Acly	0.000	1.58	UP
70025	Acot7	0.013	0.82	Down
74205	Acsl3	0.000	1.40	UP
60525	Acss2	0.000	2.48	UP
11475	Acta2	0.000	0.72	Down
11461	Actb	0.000	0.79	Down
11489	Adam12	0.000	1.25	UP
224697	Adamts10	0.000	1.49	UP
239337	Adamts12	0.003	1.58	UP
240913	Adamts4	0.000	1.77	UP
108153	Adamts7	0.000	1.41	UP
269959	Adamtsl3	0.000	1.25	UP
110532	Adarb1	0.021	1.34	UP
242669	Adc	0.025	1.48	UP
76187	Adhfe1	0.006	1.77	UP
70292	Afap1	0.018	1.27	UP
106877	Afap1l1	0.003	1.91	UP
93736	Aff4	0.000	1.21	UP
231801	Agfg2	0.004	1.35	UP
11603	Agrn	0.007	1.34	UP
226691	AI607873	0.001	1.38	UP
433693	Akirin2	0.026	0.79	Down
19378	Aldh1a2	0.000	1.30	UP
107747	Aldh1l1	0.000	1.49	UP
11670	Aldh3a1	0.020	1.36	UP
212647	Aldh4a1	0.008	1.47	UP
71481	Alpk1	0.004	1.66	UP
52206	Anapc4	0.001	0.81	Down
11601	Angpt2	0.000	1.56	UP
108857	Ankhd1	0.002	1.25	UP
107765	Ankrd1	0.000	0.68	Down
99696	Ankrd50	0.027	0.81	Down
77318	Ankrd55	0.001	1.60	UP
67628	Anp32b	0.000	0.81	Down
16790	Anpep	0.015	1.22	UP
16952	Anxa1	0.000	0.72	Down
319924	Apba1	0.005	1.41	UP
11789	Apc	0.000	1.28	UP

11800	Api5	0.000	0.78	Down
30878	Apln	0.000	1.65	UP
11816	Apoe	0.000	1.28	UP
68316	Apoo	0.001	0.42	Down
106952	Arap3	0.023	1.63	UP
234023	Arglu1	0.048	0.81	Down
228482	Arhgap11a	0.001	0.71	Down
58996	Arhgap23	0.005	1.21	UP
233071	Arhgap33	0.022	2.52	UP
52666	Arhgef25	0.010	1.28	UP
239985	Arid1b	0.027	1.21	UP
65105	Arl6ip4	0.003	0.71	Down
65106	Arl6ip5	0.019	0.83	Down
56443	Arpc1a	0.014	0.80	Down
109689	Arrb1	0.011	1.30	UP
105171	Arrdc3	0.020	1.44	UP
11883	Arsa	0.000	1.39	UP
11881	Arsb	0.011	1.24	UP
230837	Asap3	0.000	1.64	UP
70396	Asnsd1	0.010	0.77	Down
66695	Aspn	0.005	1.45	UP
108888	Atad3a	0.040	0.75	Down
11910	Atf3	0.000	0.00	Down
223922	Atf7	0.049	1.70	UP
76295	Atp11b	0.024	1.31	UP
67126	Atp5e	0.033	0.73	Down
228033	Atp5g3	0.012	0.82	Down
71679	Atp5h	0.023	0.83	Down
108664	Atp6v1h	0.006	0.81	Down
11977	Atp7a	0.009	1.36	UP
11983	Atpif1	0.037	0.83	Down
226255	Atrnl1	0.016	1.26	UP
22589	Atrx	0.000	1.37	UP
20877	Aurkb	0.024	0.78	Down
23821	Bace1	0.004	1.24	UP
56175	Bace2	0.048	1.67	UP
12013	Bach1	0.000	1.50	UP
228536	Bahd1	0.017	1.41	UP
104416	Bap1	0.040	1.23	UP
70508	Bbx	0.006	1.29	UP
229003	BC006779	0.000	1.35	UP
217216	BC030867	0.003	0.56	Down
100568459	Bc1	0.012	2.20	UP
68183	Bcas2	0.004	0.71	Down

12048	Bcl2l1	0.000	0.78	Down
12029	Bcl6b	0.000	2.55	UP
77578	Bcl9	0.033	1.38	UP
20893	Bhlhe40	0.000	1.44	UP
83675	Bicc1	0.000	1.25	UP
11799	Birc5	0.005	0.75	Down
12211	Birc6	0.001	1.21	UP
233016	Blvrb	0.000	0.73	Down
12159	Bmp4	0.015	0.74	Down
12168	Bmpr2	0.005	1.50	UP
12190	Brca2	0.025	0.68	Down
70456	Brp44	0.002	0.60	Down
74007	Btbd11	0.040	0.53	Down
238386	Btbd7	0.000	1.61	UP
226089	C030046E11Rik	0.040	1.31	UP
226777	C130074G19Rik	0.021	2.04	UP
12261	C1qbp	0.001	0.82	Down
56745	C1qtnf1	0.004	1.39	UP
72709	C1qtnf6	0.000	1.33	UP
232371	C1rl	0.002	1.54	UP
50908	C1s	0.000	1.76	UP
12266	C3	0.000	1.48	UP
12268	C4b	0.002	1.37	UP
12301	Cacybp	0.021	0.82	Down
67488	Calcoco1	0.002	1.38	UP
12314	Calm2	0.000	0.82	Down
55984	Camkk1	0.023	2.01	UP
216874	Camta2	0.041	1.25	UP
12334	Capn2	0.000	0.82	Down
12371	Casp9	0.029	1.36	UP
12391	Cav3	0.016	0.57	Down
12402	Cbl	0.042	1.54	UP
109857	Cbr3	0.005	0.67	Down
12417	Cbx3	0.000	0.78	Down
68339	Ccdc88c	0.011	4.53	UP
12424	Cck	0.019	0.08	Down
20292	Ccl11	0.026	1.46	UP
20305	Ccl6	0.024	1.77	UP
20307	Ccl8	0.000	1.82	UP
20308	Ccl9	0.000	1.55	UP
12428	Ccna2	0.001	0.81	Down
268697	Ccnb1	0.018	0.82	Down
12443	Ccnd1	0.000	0.62	Down
12444	Ccnd2	0.000	0.82	Down

12449	Ccnf	0.014	0.72	Down
227210	Ccnyl1	0.012	0.83	Down
12466	Cct6a	0.000	0.82	Down
17079	Cd180	0.029	0.28	Down
70445	Cd248	0.015	0.82	Down
60533	Cd274	0.016	2.94	UP
70333	Cd3eap	0.013	0.71	Down
12505	Cd44	0.000	0.79	Down
17064	Cd93	0.000	1.89	UP
216150	Cdc34	0.001	0.77	Down
104252	Cdc42ep2	0.001	0.71	Down
12544	Cdc45	0.008	0.68	Down
52276	Cdca8	0.000	0.67	Down
12554	Cdh13	0.001	1.91	UP
12560	Cdh3	0.015	0.36	Down
12562	Cdh5	0.000	2.34	UP
12534	Cdk1	0.000	0.75	Down
107951	Cdk9	0.022	0.80	Down
227526	Cdnf	0.015	12.94	UP
57810	Cdon	0.000	1.33	UP
60411	Cenpk	0.005	0.50	Down
70454	Cenpl	0.008	0.52	Down
74107	Cep55	0.037	0.78	Down
28135	Cep63	0.006	0.63	Down
14962	Cfb	0.000	1.47	UP
12628	Cfh	0.000	1.29	UP
12630	Cfi	0.032	1.87	UP
18636	Cfp	0.037	2.80	UP
27221	Chaf1a	0.001	0.73	Down
110749	Chaf1b	0.000	0.57	Down
66121	Chchd1	0.035	0.72	Down
14004	Chchd2	0.039	0.78	Down
72170	Chchd4	0.004	0.47	Down
244059	Chd2	0.001	1.40	UP
71389	Chd6	0.008	1.31	UP
109151	Chd9	0.001	1.42	UP
218865	Chdh	0.003	5.18	UP
12662	Chm	0.015	1.34	UP
76969	Chst1	0.001	2.02	UP
71722	Cic	0.000	1.45	UP
68379	Ciz1	0.007	1.27	UP
54124	Cks1b	0.001	0.71	Down
66197	Cks2	0.001	0.69	Down
26373	Clcn7	0.001	1.30	UP

60363	Cldn15	0.013	1.33	UP
12741	Cldn5	0.002	2.01	UP
224796	Clic5	0.033	3.59	UP
78785	Clip4	0.001	2.25	UP
12759	Clu	0.000	1.63	UP
12785	Cnbp	0.000	0.73	Down
12798	Cnn2	0.000	0.80	Down
12818	Col14a1	0.000	1.29	UP
12822	Col18a1	0.000	1.56	UP
373864	Col27a1	0.007	1.89	UP
12825	Col3a1	0.000	1.28	UP
12833	Col6a1	0.000	1.23	UP
17846	Commd1	0.006	0.68	Down
12866	Cox7a2	0.002	0.76	Down
66142	Cox7b	0.000	0.73	Down
12870	Cp	0.000	1.28	UP
12876	Cpe	0.000	0.79	Down
223978	Cpped1	0.009	0.76	Down
56264	Cpxm1	0.000	1.28	UP
68337	Crip2	0.000	0.80	Down
12931	Crlf1	0.000	0.75	Down
12933	Crmp1	0.001	2.88	UP
110750	Cse1l	0.002	0.83	Down
12977	Csf1	0.000	0.80	Down
12978	Csf1r	0.043	0.61	Down
12982	Csf2ra	0.002	2.22	UP
73720	Cst6	0.033	0.43	Down
14219	Ctgf	0.000	0.83	Down
68588	Cthrc1	0.020	1.58	UP
66965	Ctu2	0.047	0.70	Down
15945	Cxcl10	0.000	9.35	UP
20315	Cxcl12	0.000	1.32	UP
57266	Cxcl14	0.006	0.76	Down
12767	Cxcr4	0.000	2.32	UP
12778	Cxcr7	0.017	1.31	UP
13063	Cycs	0.006	0.82	Down
114886	Cygb	0.000	1.39	UP
13121	Cyp51	0.000	1.37	UP
225995	D030056L22Rik	0.025	0.64	Down
66039	D14Ertd449e	0.000	2.53	UP
27981	D4Wsu53e	0.000	1.33	UP
13134	Dach1	0.010	8.09	UP
59036	Dact1	0.005	1.29	UP
13138	Dag1	0.000	1.31	UP

69635	Dapk1	0.000	1.43	UP
13143	Dapk2	0.036	3.10	UP
27214	Dbf4	0.005	0.76	Down
83703	Dbr1	0.021	0.66	Down
76863	Dcun1d5	0.011	0.80	Down
69219	Ddah1	0.000	0.81	Down
66942	Ddx18	0.017	0.81	Down
228889	Ddx27	0.021	0.79	Down
68278	Ddx39	0.022	0.82	Down
230073	Ddx58	0.000	1.22	UP
234311	Ddx60	0.001	2.57	UP
110052	Dek	0.000	0.73	Down
329727	Dennd2c	0.049	0.46	Down
68184	Denr	0.010	0.79	Down
74754	Dhcr24	0.000	1.56	UP
13360	Dhcr7	0.000	1.73	UP
13361	Dhfr	0.002	0.66	Down
20148	Dhrs3	0.000	1.46	UP
54004	Diap2	0.025	1.34	UP
56419	Diap3	0.027	0.80	Down
66254	Dimt1	0.004	0.58	Down
72662	Dis3	0.048	0.80	Down
54485	Dll4	0.003	2.32	UP
240283	Dmxl1	0.007	1.38	UP
22791	Dnajc2	0.000	0.68	Down
246738	Dnajc28	0.010	4.13	UP
108671	Dnajc9	0.001	0.70	Down
474332	Dnm3os	0.000	1.97	UP
13433	Dnmt1	0.000	0.82	Down
238130	Dock4	0.002	1.64	UP
105445	Dock9	0.000	1.94	UP
83768	Dpp7	0.015	1.29	UP
13495	Drg2	0.039	0.81	Down
13518	Dst	0.000	1.24	UP
80904	Dtx3	0.037	1.35	UP
209200	Dtx3l	0.000	1.50	UP
19252	Dusp1	0.000	1.28	UP
110074	Dut	0.016	0.74	Down
13543	Dvl2	0.030	1.24	UP
13544	Dvl3	0.001	1.45	UP
21648	Dynlt1b	0.040	0.47	Down
13549	Dyrk1b	0.005	1.56	UP
228598	Ebf4	0.018	5.75	UP
68545	Ecscr	0.038	1.24	UP

66967	Edem3	0.000	1.27	UP
13614	Edn1	0.001	1.33	UP
55949	Eef1b2	0.000	0.82	Down
65967	Eefsec	0.018	0.71	Down
13641	Efnb1	0.024	0.75	Down
13644	Efs	0.008	1.50	UP
13649	Egfr	0.000	1.29	UP
13653	Egr1	0.000	1.27	UP
13654	Egr2	0.036	1.31	UP
20918	Eif1	0.000	0.80	Down
13664	Eif1a	0.001	0.82	Down
66235	Eif1ax	0.018	0.82	Down
209354	Eif2b1	0.037	0.79	Down
13665	Eif2s1	0.000	0.81	Down
67204	Eif2s2	0.000	0.79	Down
78655	Eif3j	0.001	0.79	Down
192170	Eif4a3	0.002	0.80	Down
13684	Eif4e	0.003	0.79	Down
13688	Eif4ebp2	0.033	1.29	UP
16418	Eif6	0.006	0.80	Down
15568	Elavl1	0.001	0.77	Down
13714	Elk4	0.025	1.71	UP
13717	Eln	0.000	1.41	UP
170439	Elovl6	0.000	1.48	UP
170757	Eltd1	0.007	1.76	UP
59308	Emcn	0.019	1.45	UP
13726	Emd	0.008	0.76	Down
14791	Emg1	0.023	0.74	Down
100952	Emilin1	0.000	1.29	UP
237711	Eml6	0.037	2.80	UP
13809	Enpep	0.020	1.78	UP
18605	Enpp1	0.001	1.34	UP
13819	Epas1	0.000	1.39	UP
13823	Epb4.1l3	0.001	0.81	Down
13838	Epha4	0.001	2.00	UP
13841	Epha7	0.005	1.49	UP
77781	Epm2aip1	0.019	1.28	UP
13855	Epn2	0.000	1.45	UP
80898	Erap1	0.001	1.32	UP
236930	Ercc6l	0.003	0.66	Down
170942	Erdr1	0.000	0.01	Down
13874	Ereg	0.000	0.66	Down
13876	Erg	0.000	2.66	UP
13877	Erh	0.006	0.81	Down

69524	Esam	0.001	1.94	UP
13885	Esd	0.000	0.73	Down
66580	Esf1	0.002	0.75	Down
75320	Etnk1	0.035	1.24	UP
66362	Exosc3	0.001	0.56	Down
16456	F11r	0.002	1.83	UP
76267	Fads1	0.000	1.26	UP
56473	Fads2	0.000	1.60	UP
66540	Fam107b	0.004	0.74	Down
107373	Fam111a	0.002	0.82	Down
71721	Fam13c	0.020	1.24	UP
109359	Fam175b	0.033	1.30	UP
68659	Fam198b	0.000	0.83	Down
66140	Fam33a	0.024	0.64	Down
320609	Fam40b	0.028	1.86	UP
212943	Fam46a	0.000	1.45	UP
76820	Fam49a	0.013	1.41	UP
69109	Fam58b	0.019	0.56	Down
235461	Fam63b	0.000	1.27	UP
68099	Fam92a	0.000	0.73	Down
14104	Fasn	0.000	1.34	UP
329628	Fat4	0.007	1.46	UP
14113	Fbl	0.000	0.79	Down
14114	Fbln1	0.000	1.35	UP
72194	Fbxl20	0.003	1.39	UP
14137	Fdft1	0.000	1.27	UP
110196	Fdps	0.000	1.31	UP
14156	Fen1	0.000	0.67	Down
232237	Fgd5	0.024	1.65	UP
64654	Fgf23	0.012	2.05	UP
14190	Fgl2	0.011	1.39	UP
14194	Fh1	0.005	0.77	Down
229474	Fhdc1	0.011	0.68	Down
14199	Fhl1	0.000	0.72	Down
231997	Fkbp14	0.009	1.27	UP
30795	Fkbp3	0.005	0.78	Down
14229	Fkbp5	0.049	0.81	Down
55990	Fmo2	0.017	1.59	UP
68655	Fndc1	0.000	1.36	UP
319448	Fndc3a	0.000	1.37	UP
72007	Fndc3b	0.000	1.25	UP
14281	Fos	0.000	1.38	UP
14282	Fosb	0.000	2.31	UP
108655	Foxp1	0.006	0.83	Down

72313	Fryl	0.018	1.27	UP
14325	Ftl1	0.000	0.80	Down
56095	Ftsj3	0.000	0.73	Down
73068	Fut11	0.044	1.29	UP
56188	Fxyd1	0.004	1.95	UP
654820	G530011O06Rik	0.000	0.33	Down
14387	Gaa	0.000	1.23	UP
14388	Gab1	0.021	1.26	UP
102060	Gadd45gip1	0.012	0.75	Down
74246	Gale	0.020	1.46	UP
68147	Gar1	0.003	0.66	Down
14450	Gart	0.017	0.79	Down
14451	Gas1	0.000	1.50	UP
14457	Gas7	0.000	1.33	UP
80909	Gatsl2	0.023	1.45	UP
55932	Gbp3	0.007	1.31	UP
229900	Gbp7	0.011	1.43	UP
236573	Gbp9	0.026	1.70	UP
72972	Gcap14	0.001	1.29	UP
26912	Gcat	0.000	1.59	UP
14630	Gclm	0.000	0.68	Down
68133	Gcsh	0.018	0.71	Down
14567	Gdi1	0.004	1.26	UP
67604	Get4	0.022	0.78	Down
328232	Gfod1	0.001	1.90	UP
14585	Gfra1	0.005	1.54	UP
56316	Ggcx	0.029	1.24	UP
217039	Ggnbp2	0.002	0.81	Down
23887	Ggt5	0.007	1.76	UP
272551	Gins2	0.004	0.63	Down
109145	Gins4	0.008	0.74	Down
109801	Glo1	0.041	0.82	Down
73046	Glrx5	0.024	0.76	Down
100036768	Gm11696	0.019	0.08	Down
628308	Gm14420	0.000	1.33	UP
24083	Gm16515	0.003	1.55	UP
100463512	Gm20594	0.033	1.37	UP
14681	Gnao1	0.007	1.32	UP
230737	Gnl2	0.043	0.81	Down
30877	Gnl3	0.028	0.82	Down
54342	Gnpnat1	0.036	0.76	Down
54214	Golga4	0.000	1.29	UP
224139	Golgb1	0.000	1.33	UP
14732	Gpam	0.000	1.69	UP

14571	Gpd2	0.012	0.73	Down
14758	Gpm6b	0.000	1.35	UP
224792	Gpr116	0.000	1.98	UP
243277	Gpr133	0.042	1.33	UP
381413	Gpr176	0.002	0.82	Down
106512	Gpsm3	0.032	1.55	UP
14778	Gpx3	0.000	1.64	UP
69590	Gpx8	0.000	0.82	Down
14809	Grik5	0.030	1.48	UP
14810	Grin1	0.005	3.77	UP
54645	Gripap1	0.046	1.34	UP
56637	Gsk3b	0.003	1.23	UP
14873	Gsto1	0.000	0.76	Down
29870	Gtse1	0.000	0.74	Down
60596	Gucy1a3	0.001	1.31	UP
54195	Gucy1b3	0.007	1.33	UP
74558	Gvin1	0.000	1.41	UP
14933	Gyk	0.025	1.84	UP
107435	Hat1	0.000	0.67	Down
219072	Haus4	0.001	0.61	Down
68695	Hddc3	0.036	3.10	UP
217026	Heatr6	0.038	1.30	UP
77446	Heg1	0.000	1.26	UP
15201	Hells	0.002	0.68	Down
15204	Herc2	0.001	1.23	UP
226861	Hhat	0.030	2.03	UP
227095	Hibch	0.032	0.69	Down
15251	Hif1a	0.000	1.36	UP
29816	Hip1r	0.023	1.74	UP
110521	Hivep1	0.011	1.28	UP
15361	Hmga1	0.001	0.56	Down
15364	Hmga2	0.017	0.61	Down
97165	Hmgb2	0.000	0.74	Down
15357	Hmgcr	0.000	1.51	UP
208715	Hmgcs1	0.000	1.44	UP
15312	Hmgn1	0.001	0.83	Down
15374	Hn1	0.014	0.80	Down
15384	Hnrnpab	0.000	0.79	Down
15439	Hp	0.000	1.50	UP
15458	Hpx	0.040	10.78	UP
15461	Hras1	0.000	0.72	Down
58240	Hs1bp3	0.047	1.28	UP
15490	Hsd17b7	0.000	1.71	UP
15519	Hsp90aa1	0.000	0.75	Down

50497	Hspa14	0.021	0.79	Down
15482	Hspa1l	0.028	7.01	UP
243912	Hspb6	0.024	0.71	Down
29818	Hspb7	0.039	0.76	Down
15510	Hspd1	0.000	0.76	Down
15528	Hspe1	0.000	0.73	Down
56213	Htra1	0.008	1.24	UP
78558	Htra3	0.000	1.48	UP
330723	Htra4	0.049	0.62	Down
15194	Htt	0.030	1.25	UP
667370	I830012O16Rik	0.000	2.16	UP
15926	Idh1	0.000	1.25	UP
319554	Idi1	0.000	1.51	UP
15932	Idua	0.001	1.71	UP
15936	Ier2	0.005	1.21	UP
15950	Ifi203	0.000	1.66	UP
71586	Ifih1	0.047	1.23	UP
15957	Ifit1	0.000	1.68	UP
15959	Ifit3	0.000	1.52	UP
15982	Ifrd1	0.012	0.75	Down
16000	Igf1	0.000	1.34	UP
16009	Igfbp3	0.000	1.40	UP
16011	Igfbp5	0.000	2.81	UP
210094	Iglon5	0.039	1.90	UP
242050	Igsf10	0.032	1.25	UP
60440	Iigp1	0.002	1.34	UP
56489	Ikbke	0.002	1.54	UP
16186	Il2rg	0.032	1.72	UP
77125	Il33	0.000	1.36	UP
16195	Il6st	0.000	1.29	UP
67781	Ilf2	0.031	0.83	Down
16210	Impact	0.000	1.39	UP
16319	Incenp	0.001	0.79	Down
16323	Inhba	0.001	0.71	Down
231070	Insig1	0.000	1.47	UP
404710	Iqgap3	0.005	0.74	Down
16362	Irf1	0.030	1.34	UP
54123	Irf7	0.000	1.48	UP
54396	Irgm2	0.006	1.29	UP
71780	Isyna1	0.000	1.57	UP
109700	Itga1	0.005	1.38	UP
319480	Itga11	0.013	1.36	UP
16400	Itga3	0.008	1.54	UP
16403	Itga6	0.007	1.82	UP

16414	Itgb2	0.002	1.83	UP
16416	Itgb3	0.011	1.44	UP
16419	Itgb5	0.000	1.23	UP
16425	Itih2	0.003	1.45	UP
320404	Itpkb	0.006	1.41	UP
20403	Itsn2	0.000	1.45	UP
231986	Jazf1	0.028	0.55	Down
16476	Jun	0.000	1.56	UP
16477	Junb	0.000	1.26	UP
16478	Jund	0.003	1.26	UP
16480	Jup	0.000	1.36	UP
545156	Kalrn	0.000	1.64	UP
57814	Kcne4	0.000	1.21	UP
63830	Kcnq1ot1	0.009	1.20	UP
240776	Kcnt2	0.038	1.45	UP
622320	Kctd21	0.036	1.83	UP
105440	Kctd9	0.000	0.69	Down
193796	Kdm4b	0.001	1.44	UP
16542	Kdr	0.000	2.00	UP
16551	Kif11	0.002	0.78	Down
16554	Kif13b	0.008	1.57	UP
16560	Kif1a	0.000	1.31	UP
16565	Kif21b	0.000	2.06	UP
110033	Kif22	0.034	0.81	Down
269152	Kif26b	0.000	1.63	UP
16573	Kif5b	0.000	1.23	UP
16590	Kit	0.000	2.43	UP
118445	Klf16	0.017	0.70	Down
16598	Klf2	0.004	1.42	UP
16599	Klf3	0.000	1.45	UP
75785	Klhl24	0.000	1.72	UP
16669	Krt19	0.041	0.20	Down
237339	L3mbtl3	0.033	1.46	UP
212442	Lactb2	0.042	1.27	UP
16776	Lama5	0.005	1.51	UP
16792	Laptm5	0.008	3.64	UP
214048	Larp1b	0.033	0.68	Down
28036	Larp7	0.000	0.70	Down
16803	Lbp	0.000	1.88	UP
16819	Lcn2	0.001	1.33	UP
18826	Lcp1	0.025	1.76	UP
16835	Ldlr	0.000	1.24	UP
232798	Leng8	0.004	1.30	UP
246316	Lgi2	0.010	1.36	UP

19141	Lgmn	0.000	1.37	UP
16881	Lig1	0.000	0.78	Down
14728	Lilrb4	0.008	2.90	UP
16890	Lipe	0.035	1.56	UP
16891	Lipg	0.000	2.34	UP
217325	Llgl2	0.049	1.63	UP
30937	Lmcd1	0.036	0.80	Down
16905	Lmna	0.000	0.83	Down
16906	Lmnb1	0.000	0.76	Down
380928	Lmo7	0.020	1.78	UP
94352	Loxl2	0.000	1.32	UP
14792	Lpcat3	0.002	1.25	UP
14245	Lpin1	0.000	1.96	UP
16956	Lpl	0.000	1.24	UP
80877	Lrba	0.024	1.46	UP
16971	Lrp1	0.000	1.20	UP
231549	Lrrc8d	0.021	1.27	UP
16987	Lss	0.000	1.73	UP
17022	Lum	0.000	1.40	UP
17101	Lyst	0.002	1.36	UP
17105	Lyz2	0.011	1.50	UP
17149	Magoh	0.007	0.76	Down
67920	Mak16	0.036	0.81	Down
26397	Map2k3	0.000	2.09	UP
225028	Map4k3	0.014	1.21	UP
328329	Mast4	0.000	1.42	UP
17181	Matn2	0.000	1.35	UP
84004	Mcam	0.000	1.89	UP
17216	Mcm2	0.000	0.76	Down
17215	Mcm3	0.000	0.79	Down
17217	Mcm4	0.000	0.78	Down
17218	Mcm5	0.000	0.67	Down
17219	Mcm6	0.000	0.72	Down
17220	Mcm7	0.000	0.78	Down
210711	Mcmbp	0.005	0.81	Down
14013	Mecom	0.010	1.30	UP
17257	Mecp2	0.002	1.36	UP
76199	Med13l	0.010	1.26	UP
69792	Med6	0.029	1.50	UP
80509	Med8	0.041	0.79	Down
80889	Mesdc1	0.047	0.80	Down
17294	Mest	0.014	1.57	UP
56307	Metap2	0.000	0.80	Down
210029	Metrnl	0.001	0.73	Down

76293	Mfap4	0.000	1.63	UP
50530	Mfap5	0.000	0.74	Down
52065	Mfhas1	0.013	0.75	Down
269181	Mgat4a	0.003	1.78	UP
320878	Mical2	0.000	0.82	Down
17318	Mid1	0.000	0.67	Down
67949	Mki67ip	0.003	0.73	Down
17347	Mknk2	0.000	1.32	UP
231051	Mll3	0.044	1.30	UP
17356	Mllt4	0.000	1.32	UP
246198	Mllt6	0.000	1.34	UP
77697	Mmab	0.000	1.73	UP
17380	Mme	0.040	1.58	UP
17388	Mmp15	0.023	2.65	UP
26561	Mmp23	0.020	1.26	UP
17394	Mmp8	0.015	1.45	UP
105450	Mmrn2	0.000	1.64	UP
17476	Mpeg1	0.049	1.71	UP
56282	Mrpl12	0.038	0.80	Down
27397	Mrpl17	0.004	0.79	Down
67681	Mrpl18	0.000	0.71	Down
68611	Mrpl28	0.025	0.75	Down
94062	Mrpl3	0.002	0.72	Down
67270	Mrpl42	0.035	0.78	Down
66407	Mrps15	0.003	0.75	Down
69902	Mrto4	0.000	0.58	Down
17688	Msh6	0.000	0.69	Down
76626	Msi2	0.032	1.26	UP
17748	Mt1	0.000	1.22	UP
17750	Mt2	0.000	1.21	UP
66902	Mtap	0.000	0.71	Down
17754	Mtap1a	0.000	1.31	UP
17760	Mtap6	0.001	0.77	Down
238505	Mtr	0.046	0.70	Down
17777	Mttp	0.032	2.00	UP
192156	Mvd	0.000	1.90	UP
17855	Mvk	0.000	1.43	UP
17857	Mx1	0.002	17.25	UP
56309	Mycbp	0.017	0.57	Down
18109	Mycn	0.035	0.57	Down
66915	Myeov2	0.035	0.69	Down
98932	Myl9	0.000	0.73	Down
107589	Mylk	0.010	1.56	UP
338367	Myo1d	0.000	1.32	UP

17920	Myo6	0.021	1.33	UP
17921	Myo7a	0.002	1.25	UP
270163	Myo9a	0.049	1.21	UP
54169	Myst4	0.016	1.41	UP
212706	N4bp3	0.015	1.82	UP
74838	Naa15	0.000	0.72	Down
59027	Nampt	0.000	1.27	UP
94181	Nans	0.029	0.83	Down
53605	Nap1l1	0.000	0.79	Down
50927	Nasp	0.000	0.69	Down
269198	Nbeal1	0.020	1.46	UP
17966	Nbr1	0.000	1.29	UP
52589	Ncald	0.006	1.51	UP
17970	Ncf2	0.025	11.86	UP
380969	Nckap5l	0.009	1.29	UP
17977	Ncoa1	0.002	1.36	UP
14299	Ncs1	0.000	0.69	Down
67052	Ndc80	0.001	0.66	Down
17988	Ndrg1	0.002	1.59	UP
15531	Ndst1	0.000	1.25	UP
66706	Ndufaf3	0.025	1.90	UP
66218	Ndufb9	0.045	0.80	Down
75406	Ndufs7	0.012	0.74	Down
72900	Ndufv2	0.012	0.82	Down
66961	Neat1	0.000	1.85	UP
234258	Neil3	0.018	0.60	Down
66244	Nemf	0.000	0.79	Down
18010	Neu1	0.000	1.50	UP
68810	Nexn	0.037	0.76	Down
18023	Nfe2l1	0.000	1.26	UP
80859	Nfkbiz	0.000	1.58	UP
52530	Nhp2	0.004	0.74	Down
18080	Nin	0.015	1.29	UP
18087	Nktr	0.000	1.36	UP
216856	Nlgn2	0.000	1.37	UP
18102	Nme1	0.000	0.81	Down
57741	Noc2l	0.000	0.76	Down
28126	Nop16	0.000	0.58	Down
110109	Nop2	0.000	0.69	Down
55989	Nop58	0.000	0.71	Down
18127	Nos3	0.003	2.03	UP
18132	Notch4	0.000	2.07	UP
18148	Npm1	0.000	0.83	Down
114249	Npnt	0.049	0.75	Down

18160	Npr1	0.029	1.72	UP
18162	Npr3	0.033	0.78	Down
18166	Npy1r	0.043	2.88	UP
223649	Nrbp2	0.022	1.56	UP
268903	Nrip1	0.005	1.52	UP
18187	Nrp2	0.004	1.20	UP
18193	Nsd1	0.000	1.21	UP
18194	Nsdhl	0.000	1.56	UP
67872	Nsmce4a	0.000	0.73	Down
70021	Nt5dc2	0.040	0.81	Down
18208	Ntn1	0.000	1.34	UP
98415	Nucks1	0.000	0.80	Down
18221	Nudc	0.000	0.77	Down
66977	Nuf2	0.005	0.78	Down
69482	Nup35	0.001	0.65	Down
445007	Nup85	0.000	0.66	Down
269966	Nup98	0.000	1.32	UP
108907	Nusap1	0.000	0.62	Down
246728	Oas2	0.008	1.65	UP
231655	Oasl1	0.013	1.78	UP
23962	Oasl2	0.001	1.23	UP
320634	Ocrl	0.002	1.39	UP
23965	Odz3	0.009	1.20	UP
108155	Ogt	0.005	1.25	UP
99543	Olfml3	0.000	1.25	UP
71648	Optn	0.036	1.32	UP
18438	P2rx4	0.005	1.29	UP
18813	Pa2g4	0.000	0.73	Down
381404	Pabpc1l	0.029	593.63	UP
211347	Pank3	0.000	1.31	UP
74229	Paqr8	0.038	1.57	UP
381038	Parl	0.018	0.74	Down
547253	Parp14	0.004	1.28	UP
80285	Parp9	0.015	1.20	UP
170736	Parvb	0.001	1.67	UP
52033	Pbk	0.035	0.75	Down
75599	Pcdh1	0.002	1.52	UP
93887	Pcdhb16	0.010	2.12	UP
93888	Pcdhb17	0.009	1.76	UP
93706	Pcdhgc3	0.000	1.21	UP
319263	Pcmtd1	0.048	1.28	UP
245867	Pcmtd2	0.034	1.54	UP
18538	Pcna	0.000	0.71	Down
100102	Pcsk9	0.000	4.58	UP

66881	Pcyox1	0.000	1.25	UP
68671	Pcyt2	0.000	1.39	UP
207728	Pde2a	0.000	2.01	UP
54611	Pde3a	0.022	1.43	UP
18576	Pde3b	0.029	1.39	UP
18591	Pdgfb	0.000	2.22	UP
54635	Pdgfc	0.003	0.00	Down
228026	Pdk1	0.000	1.47	UP
213019	Pdlim2	0.000	0.79	Down
68070	Pdzd2	0.000	1.41	UP
18613	Pecam1	0.000	1.89	UP
170676	Peg10	0.000	1.22	UP
27412	Peg12	0.025	0.54	Down
18616	Peg3	0.008	1.78	UP
18628	Per3	0.005	1.60	UP
67199	Pfdn1	0.020	0.74	Down
170768	Pfkfb3	0.032	1.29	UP
18641	Pfkl	0.000	1.23	UP
18645	Pfn2	0.005	0.75	Down
18654	Pgf	0.000	2.07	UP
53328	Pgrmc1	0.001	0.81	Down
18676	Phf2	0.007	1.25	UP
236539	Phgdh	0.000	0.77	Down
21664	Phlda1	0.018	0.75	Down
18693	Pick1	0.002	2.72	UP
27392	Pign	0.021	1.33	UP
216505	Pik3ip1	0.002	2.62	UP
18711	Pikfyve	0.000	1.53	UP
18763	Pkd1	0.000	1.35	UP
231507	Plac8	0.000	0.68	Down
211623	Plac9	0.000	2.18	UP
18792	Plau	0.000	1.88	UP
18803	Plcg1	0.001	1.39	UP
18806	Pld2	0.023	1.37	UP
213783	Plekhg1	0.013	1.55	UP
18817	Plk1	0.000	0.77	Down
20620	Plk2	0.002	0.76	Down
18822	Plod1	0.000	1.24	UP
84094	Plvap	0.001	2.06	UP
18845	Plxna2	0.001	1.30	UP
67784	Plxnd1	0.000	1.53	UP
68603	Pmvk	0.016	1.33	UP
116939	Pnpla3	0.040	10.78	UP
108767	Pnrc1	0.002	1.26	UP

18968	Pola1	0.001	0.68	Down
18973	Pole	0.002	0.72	Down
66420	Polr2e	0.021	0.81	Down
20022	Polr2j	0.016	0.76	Down
269823	Pon3	0.043	1.28	UP
67895	Ppa1	0.003	0.80	Down
19024	Ppfibp2	0.041	1.50	UP
67738	Ppid	0.006	0.69	Down
70225	Ppil3	0.025	0.73	Down
14208	Ppm1g	0.000	0.79	Down
52040	Ppp1r10	0.030	1.22	UP
18938	Ppp1r14b	0.000	0.72	Down
228852	Ppp1r16b	0.000	3.11	UP
54646	Ppp1r3f	0.016	4.31	UP
235542	Ppp2r3a	0.039	1.24	UP
243819	Ppp6r1	0.001	1.24	UP
233406	Prc1	0.000	0.76	Down
18477	Prdx1	0.000	0.83	Down
54683	Prdx5	0.000	0.82	Down
109294	Prex2	0.001	1.37	UP
19076	Prim2	0.024	0.74	Down
19092	Prkg2	0.007	0.26	Down
15469	Prmt1	0.000	0.76	Down
26434	Prnd	0.000	1.79	UP
328099	Prps1l3	0.049	0.77	Down
110639	Prps2	0.001	0.63	Down
226562	Prrc2c	0.000	1.22	UP
69017	Prrt2	0.042	2.22	UP
107272	Psat1	0.000	0.81	Down
234353	Psd3	0.000	1.37	UP
19166	Psma2	0.000	0.81	Down
26444	Psma7	0.015	0.82	Down
19172	Psmb4	0.003	0.82	Down
19173	Psmb5	0.018	0.78	Down
19175	Psmb6	0.003	0.79	Down
19184	Psmc5	0.001	0.80	Down
59029	Psmd14	0.002	0.79	Down
19206	Ptch1	0.005	2.09	UP
56351	Ptges3	0.000	0.75	Down
19242	Ptn	0.030	1.79	UP
19243	Ptp4a1	0.006	0.73	Down
24000	Ptpn21	0.038	0.81	Down
19275	Ptprn	0.045	1.33	UP
19288	Ptx3	0.000	0.70	Down

19290	Pura	0.046	0.79	Down
52118	Pvr	0.049	0.79	Down
66194	Pycrl	0.046	0.66	Down
53869	Rab11a	0.000	0.74	Down
76877	Rab36	0.025	4.10	UP
74760	Rab3il1	0.035	1.30	UP
216363	Rab3ip	0.021	0.75	Down
19344	Rab5b	0.000	1.30	UP
19352	Rabggtb	0.024	0.78	Down
19362	Rad51ap1	0.001	0.56	Down
66679	Rae1	0.004	0.72	Down
228850	Ralgapb	0.011	1.24	UP
19730	Ralgds	0.011	1.33	UP
19384	Ran	0.000	0.77	Down
19385	Ranbp1	0.000	0.79	Down
19387	Rangap1	0.000	0.79	Down
217944	Rapgef5	0.019	1.96	UP
77300	Raph1	0.007	1.25	UP
69903	Rasip1	0.002	1.84	UP
215653	Rassf2	0.015	1.40	UP
245688	Rbbp7	0.000	0.81	Down
19650	Rbl1	0.029	0.73	Down
56275	Rbm14	0.021	1.28	UP
209003	Rbmx2	0.036	0.62	Down
98711	Rdh10	0.007	1.42	UP
68703	Rere	0.000	1.24	UP
19718	Rfc2	0.006	0.75	Down
53970	Rfx5	0.003	1.60	UP
19727	Rfxank	0.041	1.58	UP
242406	Rgp1	0.032	1.32	UP
19734	Rgs16	0.015	1.29	UP
78757	Rictor	0.006	1.42	UP
225870	Rin1	0.038	0.62	Down
74030	Rin2	0.002	1.39	UP
74194	Rnd3	0.013	0.77	Down
81018	Rnf114	0.029	1.28	UP
24018	Rngtt	0.037	0.68	Down
74144	Robo4	0.000	1.92	UP
68275	Rpa1	0.001	0.83	Down
67025	Rpl11	0.000	0.81	Down
65019	Rpl23	0.000	0.77	Down
57808	Rpl35a	0.000	0.79	Down
67248	Rpl39	0.000	0.78	Down
20005	Rpl9	0.000	0.83	Down

56040	Rplp1	0.000	0.80	Down
67186	Rplp2	0.000	0.70	Down
67097	Rps10	0.000	0.78	Down
267019	Rps15a	0.000	0.82	Down
20068	Rps17	0.000	0.82	Down
66481	Rps21	0.000	0.82	Down
75617	Rps25	0.000	0.83	Down
78294	Rps27a	0.000	0.81	Down
67941	Rps27l	0.000	0.76	Down
20090	Rps29	0.000	0.79	Down
20116	Rps8	0.000	0.77	Down
66922	Rras2	0.000	0.68	Down
20133	Rrm1	0.000	0.81	Down
20135	Rrm2	0.000	0.62	Down
59014	Rrs1	0.003	0.77	Down
58185	Rsad2	0.000	2.92	UP
225215	Rsl24d1	0.014	0.71	Down
70432	Rufy2	0.022	1.39	UP
66521	Rwdd1	0.008	0.81	Down
20194	S100a10	0.000	0.71	Down
20198	S100a4	0.000	0.77	Down
20200	S100a6	0.000	0.73	Down
13609	S1pr1	0.018	1.30	UP
56459	Sae1	0.000	0.80	Down
217125	Samd14	0.016	1.51	UP
209086	Samd9l	0.002	1.25	UP
66234	Sc4mol	0.000	1.38	UP
235293	Sc5d	0.000	1.51	UP
20778	Scarb1	0.000	1.38	UP
380713	Scarf1	0.037	2.80	UP
20249	Scd1	0.000	1.69	UP
20250	Scd2	0.000	1.55	UP
64929	Scel	0.001	0.71	Down
20266	Scn1b	0.021	1.31	UP
20272	Scn7a	0.000	1.43	UP
56367	Scoc	0.001	0.70	Down
20289	Scx	0.041	0.29	Down
20970	Sdc3	0.000	1.34	UP
67680	Sdhb	0.005	0.79	Down
20324	Sdpr	0.002	0.80	Down
227648	Sec16a	0.000	1.23	UP
20335	Sec61g	0.015	0.83	Down
114679	Selm	0.012	0.79	Down
20344	Selp	0.001	1.47	UP

20350	Sema3f	0.002	1.65	UP
20359	Sema6b	0.014	1.64	UP
214968	Sema6d	0.000	1.41	UP
20361	Sema7a	0.008	1.85	UP
75826	Senp2	0.028	0.78	Down
20363	Sepp1	0.000	1.42	UP
20715	Serpina3g	0.000	1.69	UP
546546	Serpina3h	0.001	3.50	UP
20716	Serpina3n	0.000	1.42	UP
20706	Serpinb9b	0.000	0.76	Down
18787	Serpine1	0.000	0.76	Down
12258	Serping1	0.000	1.23	UP
56086	Set	0.000	0.79	Down
269254	Setx	0.000	1.28	UP
20319	Sfrp2	0.000	1.28	UP
20393	Sgk1	0.000	0.82	Down
27387	Sh2d3c	0.030	1.79	UP
230863	Sh2d5	0.034	2.36	UP
231147	Sh3tc1	0.003	2.59	UP
58234	Shank3	0.001	1.91	UP
20419	Shcbp1	0.029	0.73	Down
214547	She	0.007	2.48	UP
75991	Slain2	0.012	1.27	UP
20492	Slbp	0.019	0.76	Down
75750	Slc10a6	0.037	1.58	UP
20502	Slc16a2	0.000	1.23	UP
80879	Slc16a3	0.000	1.37	UP
20514	Slc1a5	0.000	1.24	UP
20513	Slc1a6	0.001	0.57	Down
20516	Slc20a2	0.003	0.81	Down
13358	Slc25a1	0.000	1.21	UP
63959	Slc29a1	0.014	0.81	Down
71279	Slc29a3	0.040	1.31	UP
227659	Slc2a6	0.000	2.75	UP
227059	Slc39a10	0.000	1.45	UP
100434	Slc44a1	0.030	1.21	UP
20536	Slc4a3	0.002	1.89	UP
20541	Slc8a1	0.039	1.27	UP
327978	Slfn5	0.000	1.44	UP
276950	Slfn8	0.002	1.51	UP
17130	Smad6	0.015	0.83	Down
93762	Smarca5	0.014	0.82	Down
64074	Smoc2	0.000	1.25	UP
67847	Sncaip	0.004	2.05	UP

208777	Sned1	0.028	1.54	UP
319317	Snhg11	0.040	4.31	UP
20623	Snrk	0.001	1.43	UP
68981	Snrpa1	0.000	0.69	Down
20638	Snrpb	0.000	0.78	Down
20641	Snrpd1	0.000	0.64	Down
20643	Snrpe	0.000	0.57	Down
12702	Socs3	0.000	1.24	UP
20657	Sod3	0.000	1.24	UP
20411	Sorbs1	0.011	0.69	Down
234214	Sorbs2	0.017	1.53	UP
20672	Sox18	0.000	2.50	UP
20680	Sox7	0.003	1.82	UP
20684	Sp100	0.000	1.40	UP
13602	Sparcl1	0.000	1.52	UP
219140	Spata13	0.000	2.39	UP
66442	Spc25	0.016	0.72	Down
74392	Specc1l	0.014	1.23	UP
216892	Spns2	0.001	1.98	UP
233744	Spon1	0.000	1.31	UP
20751	Spr	0.048	0.76	Down
20775	Sqle	0.000	1.41	UP
20788	Srebf2	0.000	1.29	UP
117600	Srgap1	0.000	1.53	UP
19073	Srgn	0.028	1.92	UP
20810	Srm	0.000	0.81	Down
68792	Srpx2	0.000	1.22	UP
110809	Srsf1	0.000	0.81	Down
20383	Srsf3	0.000	0.77	Down
76650	Srxn1	0.000	0.78	Down
237860	Ssh2	0.004	1.71	UP
20833	Ssrp1	0.000	0.79	Down
20452	St8sia4	0.045	2.29	UP
192187	Stab1	0.000	1.89	UP
170459	Stard4	0.000	1.45	UP
20846	Stat1	0.000	1.31	UP
20847	Stat2	0.000	1.44	UP
70358	Steap1	0.010	0.77	Down
68428	Steap3	0.000	1.28	UP
117167	Steap4	0.000	1.65	UP
106504	Stk38	0.000	1.29	UP
16765	Stmn1	0.000	0.72	Down
74732	Stx11	0.003	1.79	UP
20910	Stxbp1	0.006	1.21	UP

56451	Suclg1	0.002	0.76	Down
22218	Sumo1	0.004	0.81	Down
225115	Svil	0.007	1.27	UP
319565	Syne2	0.002	1.24	UP
118449	Synpo2	0.015	1.49	UP
57752	Tacc2	0.005	0.75	Down
21335	Tacc3	0.000	0.72	Down
270627	Taf1	0.004	1.24	UP
108143	Taf9	0.011	0.83	Down
21345	Tagln	0.000	0.70	Down
21351	Taldo1	0.000	0.81	Down
66860	Tanc1	0.003	1.32	UP
21356	Tapbp	0.000	1.28	UP
230908	Tardbp	0.000	0.79	Down
381801	Tatdn2	0.011	0.77	Down
381085	Tbc1d22b	0.036	1.33	UP
67016	Tbc1d2b	0.000	1.25	UP
272589	Tbcel	0.042	1.31	UP
21372	Tbl1x	0.010	1.23	UP
67923	Tceb1	0.015	0.74	Down
106795	Tcf19	0.026	0.78	Down
21411	Tcf20	0.036	1.22	UP
27060	Tcirg1	0.000	1.35	UP
21453	Tcof1	0.000	0.71	Down
70381	Tecpr1	0.042	1.37	UP
21687	Tek	0.001	1.33	UP
214133	Tet2	0.006	1.85	UP
21810	Tgfbi	0.000	1.84	UP
21817	Tgm2	0.000	1.53	UP
21824	Thbd	0.000	0.66	Down
21826	Thbs2	0.000	1.28	UP
21827	Thbs3	0.002	1.43	UP
330267	Thsd7a	0.037	1.26	UP
21846	Tie1	0.004	1.81	UP
21854	Timm17a	0.005	0.73	Down
30058	Timm8a1	0.032	0.69	Down
66131	Tipin	0.032	0.73	Down
21877	Tk1	0.019	0.77	Down
68385	Tlcd1	0.006	1.68	UP
380712	Tlcd2	0.037	1.41	UP
17112	Tm4sf1	0.000	0.82	Down
68212	Tmbim4	0.042	0.75	Down
320534	Tmem104	0.027	1.30	UP
215210	Tmem120a	0.047	0.79	Down

232086	Tmem150a	0.001	1.46	UP
621976	Tmem170b	0.049	1.43	UP
66058	Tmem176a	0.000	1.32	UP
65963	Tmem176b	0.000	1.21	UP
170706	Tmem37	0.011	0.44	Down
100201	Tmem64	0.033	1.25	UP
67020	Tmem88	0.042	2.22	UP
19241	Tmsb4x	0.000	0.75	Down
387314	Tmtc1	0.006	1.57	UP
18383	Tnfrsf11b	0.007	1.57	UP
27279	Tnfrsf12a	0.000	0.69	Down
665113	Tnik	0.025	2.04	UP
57783	Tnip1	0.000	1.33	UP
21951	Tnks	0.000	1.53	UP
67952	Tomm20	0.000	0.71	Down
66169	Tomm7	0.049	0.69	Down
106021	Topors	0.011	0.82	Down
30935	Tor3a	0.020	1.27	UP
22004	Tpm2	0.000	0.69	Down
217410	Trib2	0.042	0.76	Down
20128	Trim30a	0.000	1.95	UP
384309	Trim56	0.038	1.54	UP
66949	Trim59	0.001	0.72	Down
101700	Trim68	0.021	2.21	UP
109181	Trip11	0.013	1.35	UP
69716	Trip13	0.000	0.63	Down
277414	Trp53i11	0.000	1.90	UP
60599	Trp53inp1	0.001	1.43	UP
68728	Trp53inp2	0.000	1.39	UP
83925	Trps1	0.037	1.28	UP
64930	Tsc1	0.001	1.38	UP
66637	Tsen15	0.020	0.64	Down
22099	Tsn	0.018	0.83	Down
241556	Tspan18	0.041	1.58	UP
52808	Tspyl2	0.010	1.23	UP
74569	Ttc17	0.008	1.35	UP
218343	Ttc37	0.018	1.31	UP
22143	Tuba1b	0.000	0.71	Down
22146	Tuba1c	0.000	0.67	Down
22152	Tubb3	0.004	0.81	Down
227613	Tubb4b	0.000	0.74	Down
22154	Tubb5	0.000	0.74	Down
67951	Tubb6	0.000	0.74	Down
233870	Tufm	0.009	0.82	Down

22166	Txn1	0.000	0.78	Down
50493	Txnrd1	0.000	0.70	Down
232223	Txnrd3	0.011	1.66	UP
22171	Tyms	0.018	0.81	Down
108121	U2af1	0.001	0.74	Down
50995	Uba2	0.002	0.81	Down
74153	Uba7	0.003	1.41	UP
68612	Ube2c	0.004	0.78	Down
56550	Ube2d2	0.001	0.83	Down
77891	Ube2s	0.000	0.76	Down
140630	Ube4a	0.002	1.28	UP
68795	Ubr3	0.017	1.24	UP
224111	Ubxn7	0.022	1.30	UP
56207	Uchl5	0.013	0.71	Down
18140	Uhrf1	0.000	0.75	Down
107448	Unc5a	0.032	1.44	UP
54445	Unc93b1	0.000	1.52	UP
22224	Usp10	0.024	0.78	Down
59025	Usp14	0.000	0.73	Down
338362	Ust	0.001	1.63	UP
195434	Utp14b	0.013	1.68	UP
22288	Utrn	0.015	1.23	UP
238328	Vash1	0.000	2.18	UP
22335	Vdac3	0.000	0.81	Down
22339	Vegfa	0.000	1.33	UP
666173	Vps13b	0.013	1.36	UP
320528	Vps13c	0.019	1.25	UP
230895	Vps13d	0.010	1.26	UP
69091	Vps26b	0.010	0.81	Down
67776	Vwa5a	0.001	1.23	UP
22378	Wbp2	0.000	1.27	UP
75410	Wbp7	0.001	1.39	UP
79565	Wbscr27	0.001	1.99	UP
268752	Wdfy2	0.004	2.27	UP
22388	Wdr1	0.000	0.83	Down
216156	Wdr18	0.005	0.74	Down
104082	Wdr7	0.004	1.32	UP
73674	Wdr75	0.026	0.81	Down
107823	Whsc1	0.001	0.77	Down
234135	Whsc1l1	0.025	1.22	UP
78428	Wibg	0.034	0.69	Down
69847	Wnk4	0.025	4.10	UP
321003	Xpnpep3	0.027	2.27	UP
24127	Xrn1	0.033	1.47	UP

77864	Ypel2	0.021	1.77	UP
229096	Ythdf3	0.020	1.22	UP
667118	Zbed6	0.002	1.45	UP
58203	Zbp1	0.001	1.31	UP
56805	Zbtb33	0.007	1.53	UP
245007	Zbtb38	0.000	1.39	UP
241322	Zbtb6	0.036	1.58	UP
244871	Zc3h12c	0.013	1.74	UP
78781	Zc3hav1	0.000	1.35	UP
71918	Zcchc24	0.000	1.31	UP
214290	Zcchc6	0.000	1.33	UP
24136	Zeb2	0.000	1.21	UP
30046	Zfp292	0.000	1.50	UP
22695	Zfp36	0.000	1.30	UP
12192	Zfp36l1	0.000	1.26	UP
235682	Zfp445	0.003	1.28	UP
225207	Zfp521	0.020	1.27	UP
434377	Zfp560	0.035	2.03	UP
269023	Zfp608	0.004	1.59	UP
70227	Zfp619	0.027	2.70	UP
78266	Zfp687	0.005	1.34	UP
235050	Zfp810	0.000	1.97	UP
211978	Zfyve26	0.001	1.39	UP
22401	Zmat3	0.022	0.81	Down
328365	Zmiz1	0.000	1.23	UP
98999	Znfx1	0.000	1.34	UP
229937	Znhit6	0.030	0.66	Down
66136	Znrd1	0.036	0.65	Down
414872	Zyg11b	0.049	1.21	UP
22793	Zyx	0.000	0.83	Down

Supplemental Table 3. Significant different genes in cardiac fibroblasts of ATF3KO mice compared to cardiac fibroblasts of WT mice after Ang II infusion.

Gene symbol	Gene name	WT CF	ATF3KO -CF	Fold-Change
Fibrotic genes:				
Col14a1	collagen, type XIV, alpha 1	31.67	40.85	1.29
Col18a1	collagen, type XVIII, alpha 1	6.52	10.15	1.56
Col27a1	collagen, type XXVII, alpha 1	0.95	1.81	1.89
Col3a1	collagen, type III, alpha 1	1511.39	1928.46	1.28
Col6a1	collagen, type VI, alpha 1	91.88	112.86	1.23
Ctgf	connective tissue growth factor	306.50	252.91	0.83
Fbl	fibrillarin	115.73	91.33	0.79
Fndc1	fibronectin type III domain containing 1	64.84	87.91	1.36
Fndc3a	fibronectin type III domain containing 3A	24.31	33.31	1.37
Fndc3b	fibronectin type III domain containing 3B	40.27	50.15	1.25
Fgf23	fibroblast growth factor 23	2.77	5.68	2.05
Thbs2	thrombospondin 2	96.81	124.36	1.28
Thbs3	thrombospondin 3	10.77	15.37	1.43
Tgfbi	transforming growth factor, beta induced	17.78	32.81	1.84
Hypertropic genes:				
Itga1	integrin alpha 1	5.98	8.26	1.38
Itga11	integrin alpha 11	6.63	9.02	1.36
Itga3	integrin alpha 3	3.56	5.49	1.54
Itga6	integrin alpha 6	2.00	3.66	1.82
Itgb2	integrin beta 2	3.74	6.84	1.83
Itgb3	integrin beta 3	4.14	5.94	1.44
Itgb5	integrin beta 5	141.30	173.46	1.23
Dag1	dystroglycan 1	48.25	63.34	1.31
Agrn	agrin	6.13	8.22	1.34
Lama5	laminin, alpha 5	1.79	2.71	1.51
Il6st	interleukin 6 signal transducer	199.52	256.85	1.29
Igf1	insulin-like growth factor 1	11.97	15.99	1.34
Igfbp3	insulin-like growth factor binding protein 3	70.77	99.29	1.40
Igfbp5	insulin-like growth factor binding protein 5	4.23	11.91	2.81
Edn1	endothelin-1	25.99	34.58	1.33
Ace	angiotensin I converting enzyme (peptidyl-dipeptidase A) 1	4.16	7.19	1.73
Inflammatory genes:				
Ccl11	chemokine (C-C motif) ligand 11	16.61	24.26	1.46
Ccl6	chemokine (C-C motif) ligand 6	5.08	9.00	1.77
Ccl8	chemokine (C-C motif) ligand 8	57.65	104.74	1.82
Ccl9	chemokine (C-C motif) ligand 9	14.33	22.24	1.55

Cxcl10	chemokine (C-X-C motif) ligand 10	0.46	4.27	9.35
Cxcl12	chemokine (C-X-C motif) ligand 12	143.91	190.23	1.32
Il2rg	interleukin 2 receptor, gamma chain	4.72	8.13	1.72
Il33	interleukin 33	23.08	31.31	1.36
Irf1	interferon regulatory factor 1	14.01	18.76	1.34
Irf7	interferon regulatory factor 7	29.39	43.43	1.48
C1qtnf1	C1q and tumor necrosis factor related protein 1	8.11	11.25	1.39
C1qtnf6	C1q and tumor necrosis factor related protein 6	36.27	48.19	1.33
C1rl	complement component 1, r subcomponent-like	7.10	10.97	1.54
C1s	complement component 1, s subcomponent	14.51	25.55	1.76
C3	complement component 3	107.32	159.17	1.48
C4b	complement component 4B (Childo blood group)	7.91	10.81	1.37
Tnfrsf11b	tumor necrosis factor receptor superfamily, member 11b	5.81	9.11	1.57

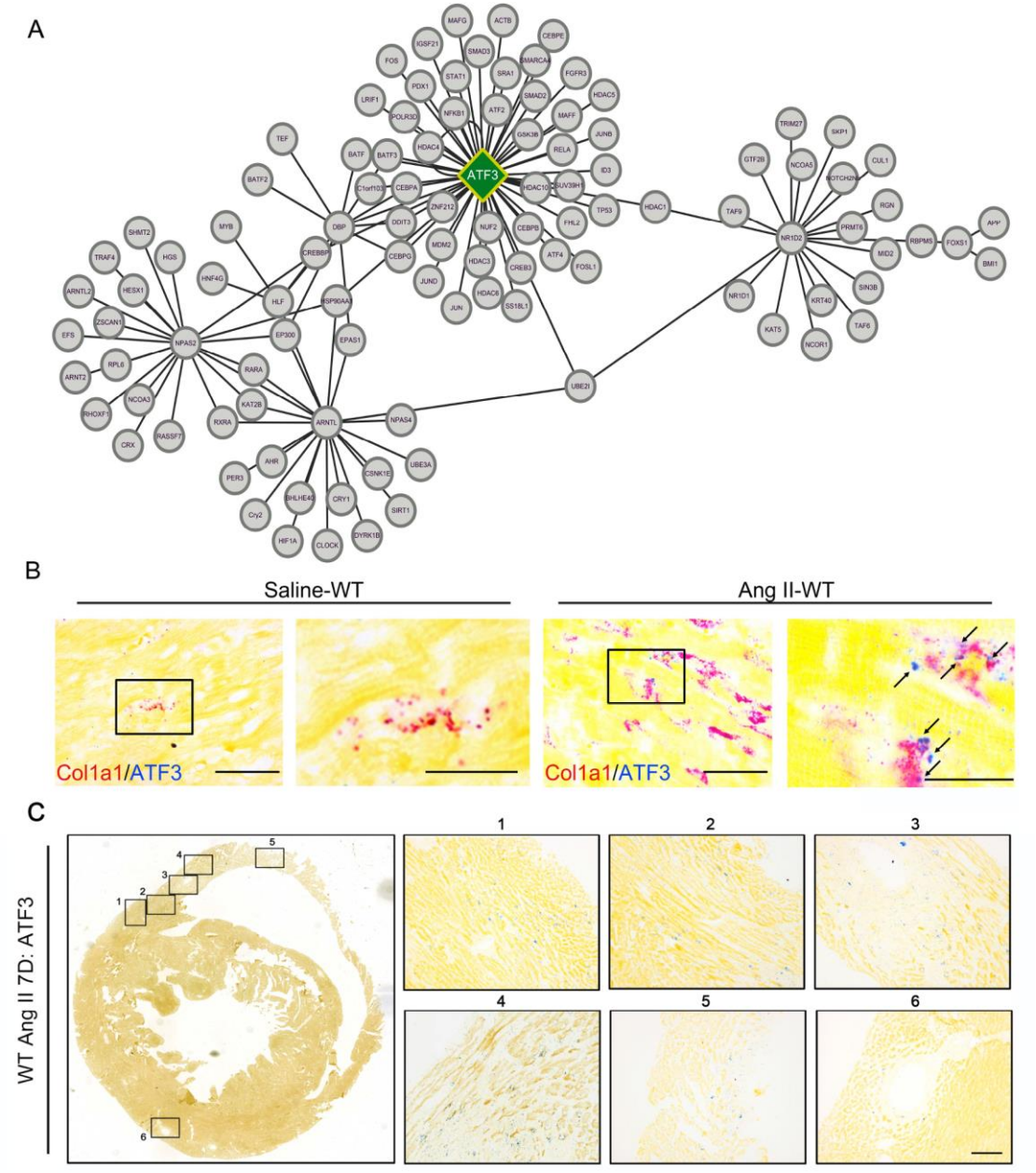
Supplemental Table 4. The list of 31 genes identified by overlay of the transcriptome in ATF3 depleted fibroblast and Chip sequencing for ATF3 binding sites

	RNA-seq Data				CHIP-seq Data			
Symbol	WT-CF -RPKM	ATF3KO-CF- RPKM	FC	FDR	Adcon- count	ATF3- count	FC	FDR
Npy1r	0.5	1.4	2.9	4.3E-02	0.0	4.2	30.8	1.6E-73
Map2k3	**26.0**	**54.5**	**2.1**	**0.0E+00**	**0.0**	**3.7**	**26.8**	**1.0E-60**
Mttp	1.0	2.0	2.0	3.2E-02	0.0	3.0	21.5	1.5E-44
Dnm3os	1.9	3.7	2.0	0.0E+00	0.0	2.8	20.2	1.1E-40
Col27a1	1.0	1.8	1.9	7.0E-03	0.0	2.6	18.9	6.4E-37
Elk4	2.3	3.9	1.7	2.5E-02	0.0	2.4	17.6	3.0E-33
Serpina3g	14.3	24.2	1.7	0.0E+00	0.0	2.3	17.1	4.7E-32
Steap4	8.2	13.5	1.7	0.0E+00	0.0	2.2	16.3	1.1E-29
Dock4	2.0	3.2	1.6	2.0E-03	0.0	2.1	15.4	2.3E-27
Dhcr24	58.0	90.5	1.6	0.0E+00	0.0	2.0	14.9	3.1E-26
Gfra1	5.7	8.8	1.5	5.0E-03	0.0	2.0	14.5	4.1E-25
Itga3	3.6	5.5	1.5	8.0E-03	0.0	1.8	13.6	6.5E-23
Ifit3	24.2	36.9	1.5	0.0E+00	0.0	1.8	13.6	6.5E-23
Ccl11	16.6	24.3	1.5	2.6E-02	0.0	1.8	13.2	7.9E-22
Arrdc3	5.0	7.2	1.4	2.0E-02	0.0	1.8	13.2	7.9E-22
Rdh10	12.3	17.4	1.4	7.0E-03	0.0	1.7	12.8	8.9E-21
Bcl9	5.1	7.0	1.4	3.3E-02	0.0	1.7	12.8	8.9E-21
Calcoco1	14.8	20.5	1.4	2.0E-03	0.0	1.7	12.3	1.0E-19
Atrx	9.8	13.3	1.4	0.0E+00	0.0	1.7	12.3	1.0E-19
Nktr	15.0	20.4	1.4	0.0E+00	0.0	1.5	11.4	1.1E-17
Zfp687	9.8	13.1	1.3	5.0E-03	0.0	1.5	11.4	1.1E-17
Nbr1	33.1	42.8	1.3	0.0E+00	0.0	1.5	11.4	1.1E-17
Cp	62.4	80.1	1.3	0.0E+00	0.0	1.5	11.0	1.1E-16
Rnf114	15.0	19.2	1.3	2.9E-02	0.0	1.5	11.0	1.1E-16
Trps1	3.9	5.0	1.3	3.7E-02	0.0	1.5	11.0	1.1E-16
Junb	185.0	233.4	1.3	0.0E+00	0.0	1.5	11.0	1.1E-16
Camta2	10.3	12.9	1.3	4.1E-02	0.0	1.5	11.0	1.1E-16
Syne2	4.8	5.9	1.2	2.0E-03	0.0	1.4	10.6	9.9E-16
Utrn	6.1	7.5	1.2	1.5E-02	0.0	1.4	10.6	9.9E-16
Prrc2c	24.4	29.7	1.2	0.0E+00	0.0	1.4	10.1	9.0E-15
Kcnq1ot1	1.3	1.5	1.2	9.0E-03	0.0	1.4	10.1	9.0E-15

Supplemental Table 5. Demographic information of five enrolled HCM patients.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Clinical/demographic features					
Male	YES	YES	YES	YES	NO
Age at presentation, years	52	54	59	51	48
Family history of HCM	NO	NO	NO	NO	NO
Syncope	YES	NO	NO	NO	NO
Hypertension	YES	YES	YES	YES	YES
Systolic blood pressure, mmHg	160	140	180	140	168
Diastolic blood pressure, mmHg	102	100	110	100	105
NYHA	3	3	3	3	3
Echocardiography data					
Left ventricular ejection fraction,%	57	60	58	69	59
Left atrial diameter,mm	41	36	47	43	44
Maximum interventricular septum Thickness,mm	24	15	17.8	17	22
LV end-diastolic diameter, mm	48	51	52	41	44
Durg treatment					
β-Blockers	NO	YES	NO	NO	YES
Calcium channel blockers	NO	NO	NO	YES	YES
ACEI or ARB	NO	NO	YES	NO	NO

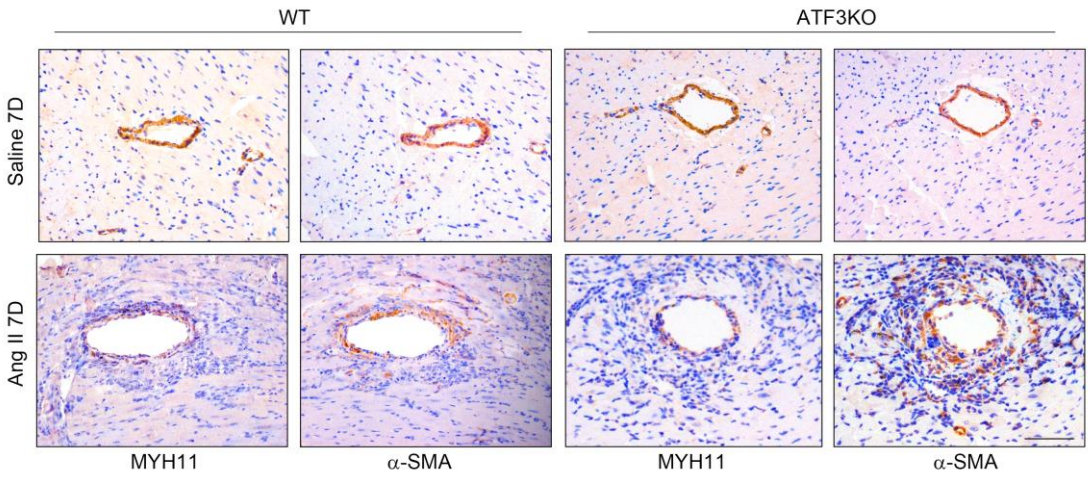
Supplemental Figures and supplemental Figure legends



Supplemental Figure 1. The protein-protein interactions analysis of 7 overlapped transcription factors and ATF3 mRNA localization

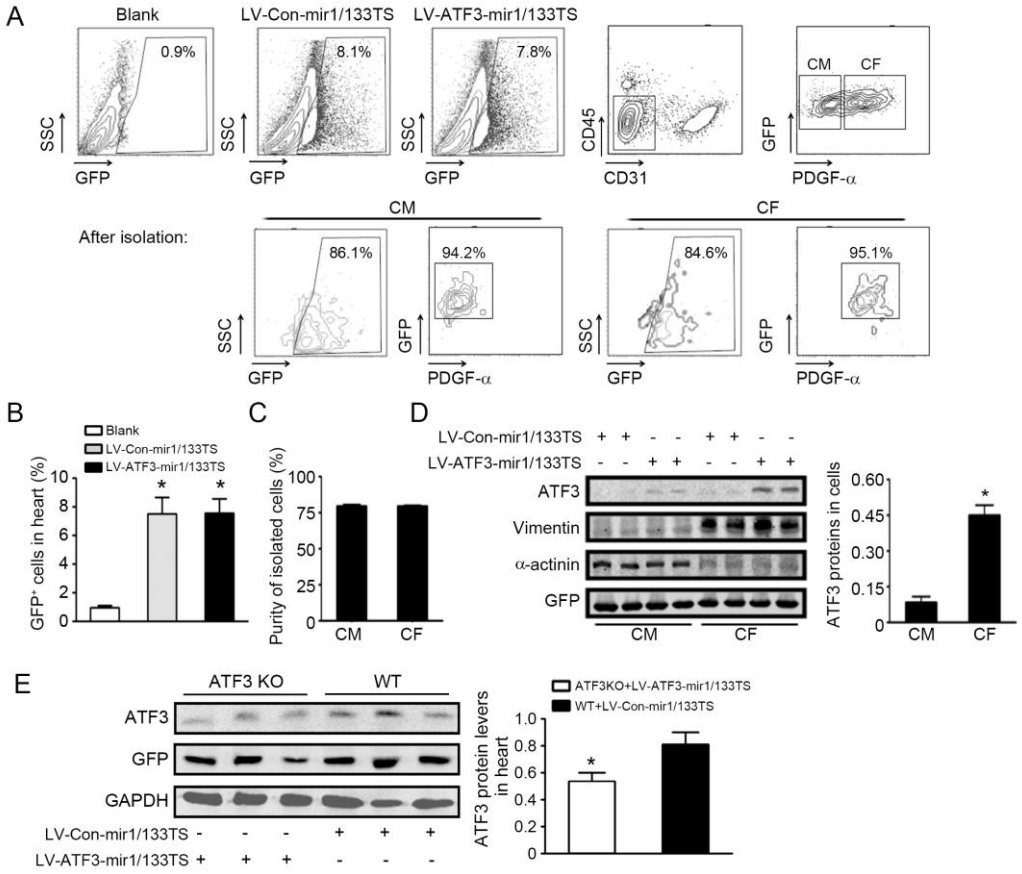
(A) We identified 7 TFs (ATF3, Arntl, Foxs1, Npas2, Dbp, Hlf and Nr1d2), that were commonly regulated in heart in both Ang II infusion and TAC models. We used both Human Protein Reference Database (HPRD, www.hprd.org) and BioGRID (www.thebiogrid.org) database to query interested 7 transcription factors, and got the PPI network structure from query results. The visulization of the PPI was performed using Cytoscape software (http://cytoscape.org/) **(B)** In situ hybridization analysis

demonstrates ATF3 signal was markedly detected in Col1a1^{+} cardiac fibroblasts after Ang II infusion (black arrows). Bars=50 μm. In enlarged image, Bars=25 μm. (C) *In situ* hybridization upon Ang II infused hearts using a probe against ATF3 (blue) alone. A stitched version of a whole heart section was presented on the left. High magnification (200 x) images from the rectangular boxed area were presented on the right. Bars=100 μm (right).



Supplemental Figure 2. Expression of SM22 positive cells in WT and ATF3KO heart section

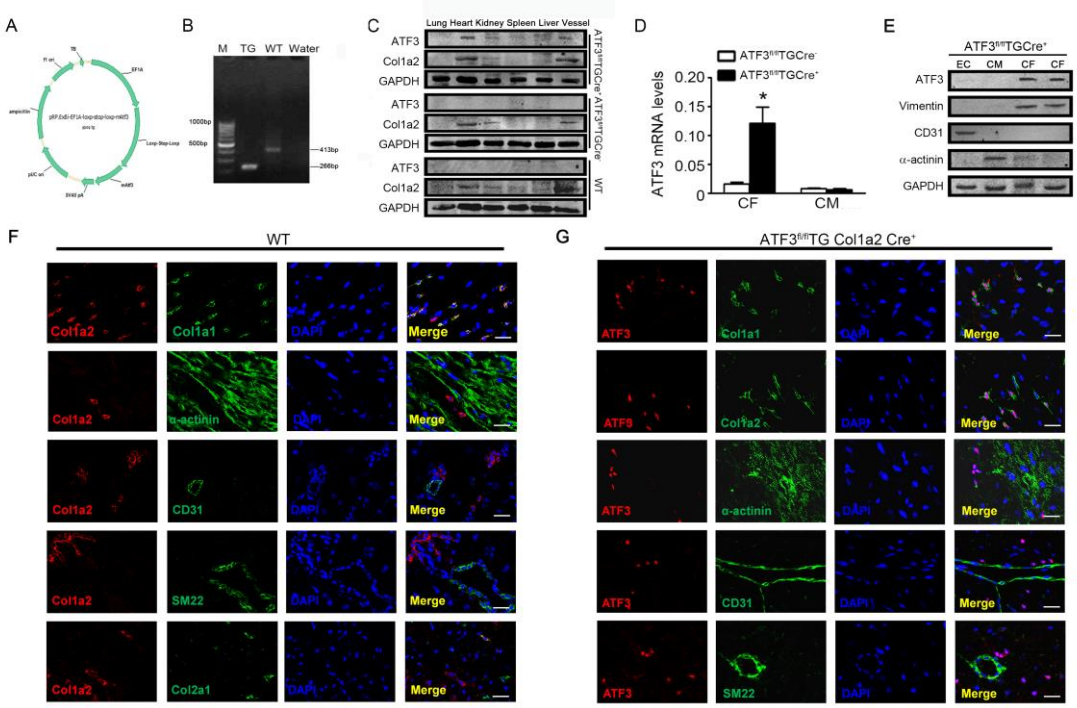
MYH11 or α-SMA expressions were assessed by immunohistochemistry on the serial sections from WT and ATF3KO heart tissue after saline or Ang II infusion for 7 days. Bars=50 μm.



Supplemental Figure 3. ATF3 expression in mice transduced with LV-ATF3/con-mir1/133TS

(A) ATF3 KO mice were injected with saline, LV-Con-mir1/133TS, LV-ATF3-mir1/133TS (3×10^8PFU/mice) followed by Ang II infusion for 7 days, respectively. The efficiency of viral transduction in heart and the purity of isolated cardiomyocytes (CM) and cardiac fibroblasts (CF) were evaluated by flow cytometry. **(B)** GFP^+ cells accounted for about 5-10% of total cells in mouse heart with viral transduction. *p<0.05 compared to ATF3KO+saline (n=6-8 mouse/per group). **(C)** Gated on $GFP^+CD45^-CD31^-$ cardiac cells from ATF3KO mice injected with LV-Con-mir1/133TS or LV-ATF3-mir1/133TS, we isolated $PDGFR\alpha^+$ CF and $PDGFR\alpha^-$ CM. The purity of GFP^+ CF and GFP^+ CM were over 75%. **(D)** ATF3 proteins expression was evaluated in the cardiomyocytes and cardiac fibroblasts isolated from ATF3 mice transducted with LV-Con-mir1/133TS or LV-ATF3-mir1/133TS. *p<0.05 compared to ATF3KO CM+LV-ATF3-mir1/133TS (n=6-8 mouse/per group). **(E)** ATF3KO and WT mice were injected

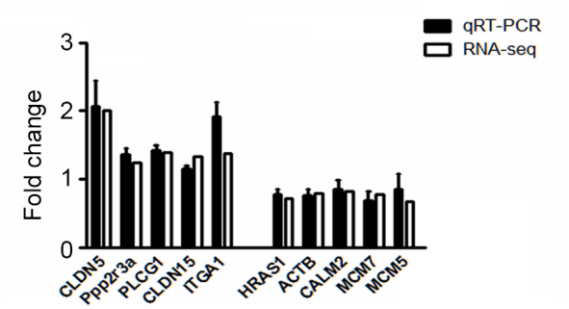
with LV-ATF3-mir1/133TS or LV-Con-mir1/133TS (3×10^8PFU/mice), followed by Ang II infusion for 7 days, respectively. Cardiac ATF3 expression was assessed by western-blot. LV-ATF3-mir1/133TS transduction restored ATF3 expression in ATF3KO mice, reached 68% of WT mouse ATF3 expression. *p<0.05 compared to WT+ LV-Con-mir1/133TS. Statistical significance was determined by the unpaired t test. Statistical significance was determined by the unpaired t test (B, D).



Supplemental Figure 4. Identification of cardiac fibroblast-specific ATF3 overexpression

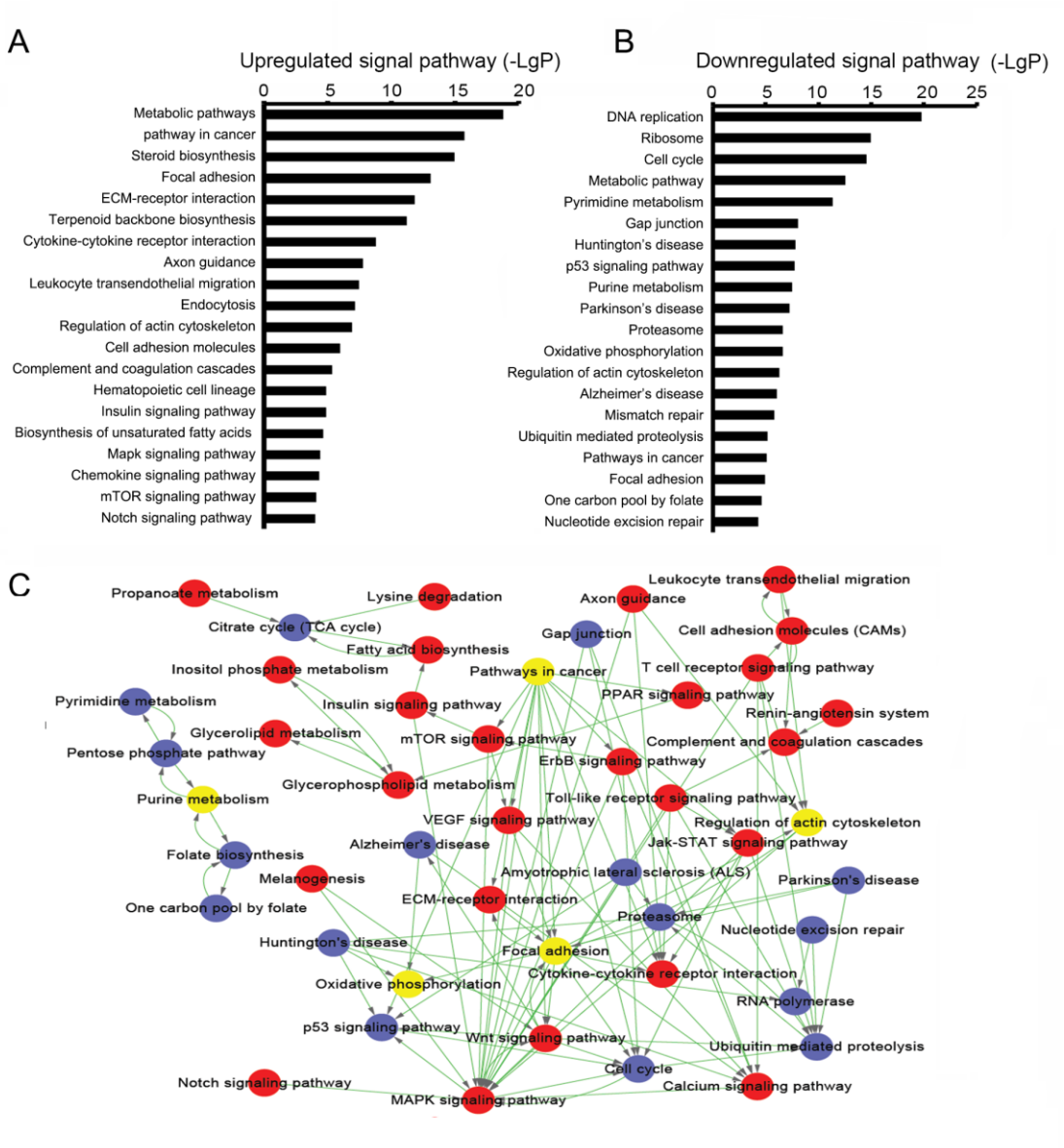
(A) The scheme for construction of the pRP.ExBi-EF1A-loxp-stop-loxp-mAtf3 vectors. **(B)** ATF3 transgene was confirmed by genotyping. PCR of genomic DNA from wild type (WT) and ATF3 fl/fl TG mice was performed using specific primers for ATF3 over-expression (216 bp) and internal reference (IR; 413 bp). **(C)** ATF3 protein expression was assessed in the different tissues (lung, heart, kidney, spleen, liver, and vessel) isolated from ATF3 $^{fl/fl}$ TG Cre^{+} mice with tamoxifen administration using western-blot. **(C)** Col1a2 and ATF3 expression was evaluated in heart, liver, lung, kidney, spleen, and vessels from ATF3$^{fl/fl}$TGCol1a2 Cre^{+}, ATF3$^{fl/fl}$TGCol1a2 Cre^{-} and WT mice. **(D)** ATF3 expression was measured in cardiac fibroblast or cardiomyocyte isolated from ATF3$^{fl/fl}$ TG Cre^{-} and ATF3 $^{fl/fl}$ TG Cre^{+} mice with tamoxifen administration using qRT-PCR. Data represent the average of 3 independent experiments. **(E)** We isolated the cardiac fibroblasts (PDGFRα^{+}CD31^{-}CD45^{-}), cardiomyocytes (PDGFRα^{-}CD31^{-}CD45^{-}) and endothelial cells (PDGFRα^{-}CD31^{+}CD45^{-}) from ATF3$^{fl/fl}$TG Col1a2 Cre^{+} mice and tested the ATF3 proteins expression. **(F)** Hearts of sham WT mice were immunofluorescent stained to determine expression of Col1a2 (red) in Col1a1 (cardiac

fibroblasts), α-actinin (cardiomyocytes), CD31 (endothelial cells), SM22 (smooth muscle cells) and Col2a1 (valve cells)-positive cells. Scale bar=10 μm. All Col1a2^{+} expressing cells are Col1a1^{+} positive cardiac fibroblasts (First row). Col1a2^{+} cells are negative for cardiomyocyte, endothelial, and smooth muscle marker staining (rows 2-4). A small portion of Col1a2^{+} cells are co-stained with Col2a1 (valve cell marker, last row). **(G)** Immunofluorescent staining of hearts from sham ATF3$^{fl/fl}$TG Col1a2Cre^{+} mice after tamoxifen injection, assessing ATF3 (red) expression in Col1a2, CD31, SM22, and Col1a2-positive cells. All cells expressing ATF are Col1a1^{+} or Col1a2^{+} positive cardiac fibroblasts. Scale bar=10μm. *p<0.05 compared to CF in ATF3$^{fl/fl}$TG Cre^{-}. Statistical significance was determined by the unpaired t test (D).



Supplemental Figure 5. Comparison of DEGs expression using RNA-seq and qRT-PCR

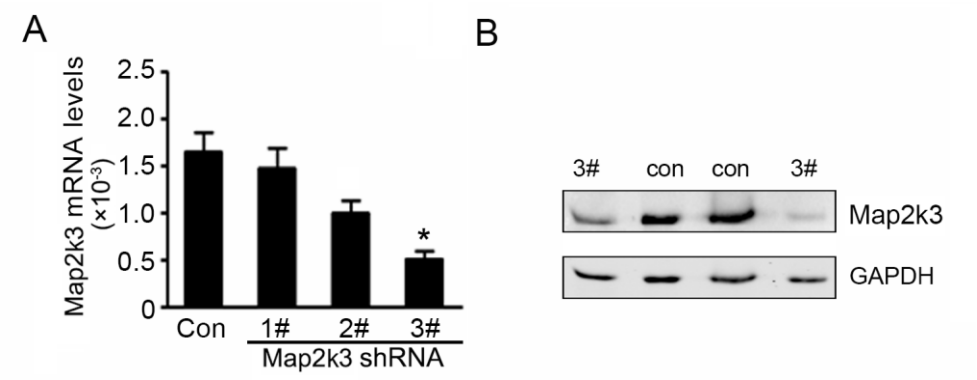
The expression of DEGs identified from the comparison between WT and ATFKO CF were confirmed by qRT-PCR. X-axis represents 10 randomly selected genes for qRT-PCR assays and Y-axis represents the fold change derived from RNA-Seq and qRT-PCR. Data represent the average of 3 independent experiments.



Supplemental Figure 6: MAPK is an important down-stream pathway of ATF3, as determined by RNA-seq analysis

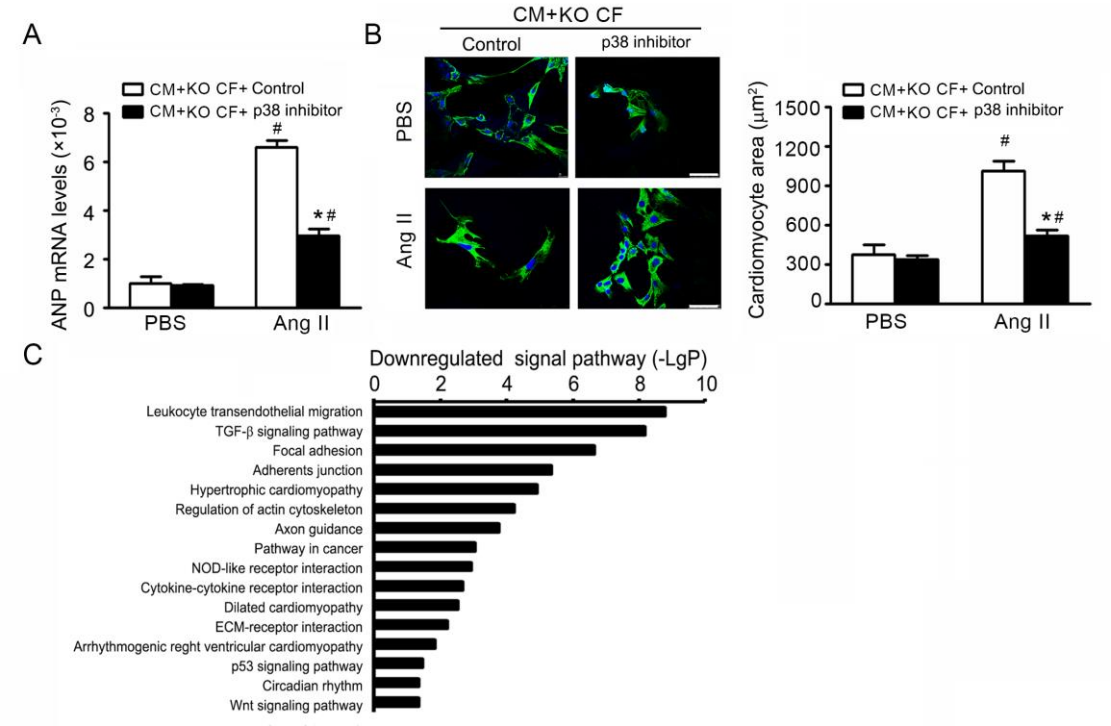
Cardiac fibroblasts were isolated from WT and ATF3 KO mice after Ang II infusion for 7 days. Genome-wide RNA-Seq in cardiac fibroblasts was performed and analyzed with the KEGG pathway database. **(A, B)** Pathway analysis commenced, based upon DEGs identified from comparison of ATF3KO and WT cardiac fibroblasts. Significant pathways were targeted by upregulated and downregulated DEGs. The vertical axis is the pathway category, and the horizontal axis is the enrichment of pathways. **(C)** The Path-Net of significant pathways in the ATF3KO versus WT cardiac fibroblasts is shown ($P<0.05$). 47 of 107 significant pathways were chosen to build the Path-Net;

potential interactions between the pathways were evaluated using Degree. Red dots represent significantly upregulated pathways, blue dots represent significantly downregulated pathways, and yellow dots represent other relevant pathways. Lines represent pathway interactions.



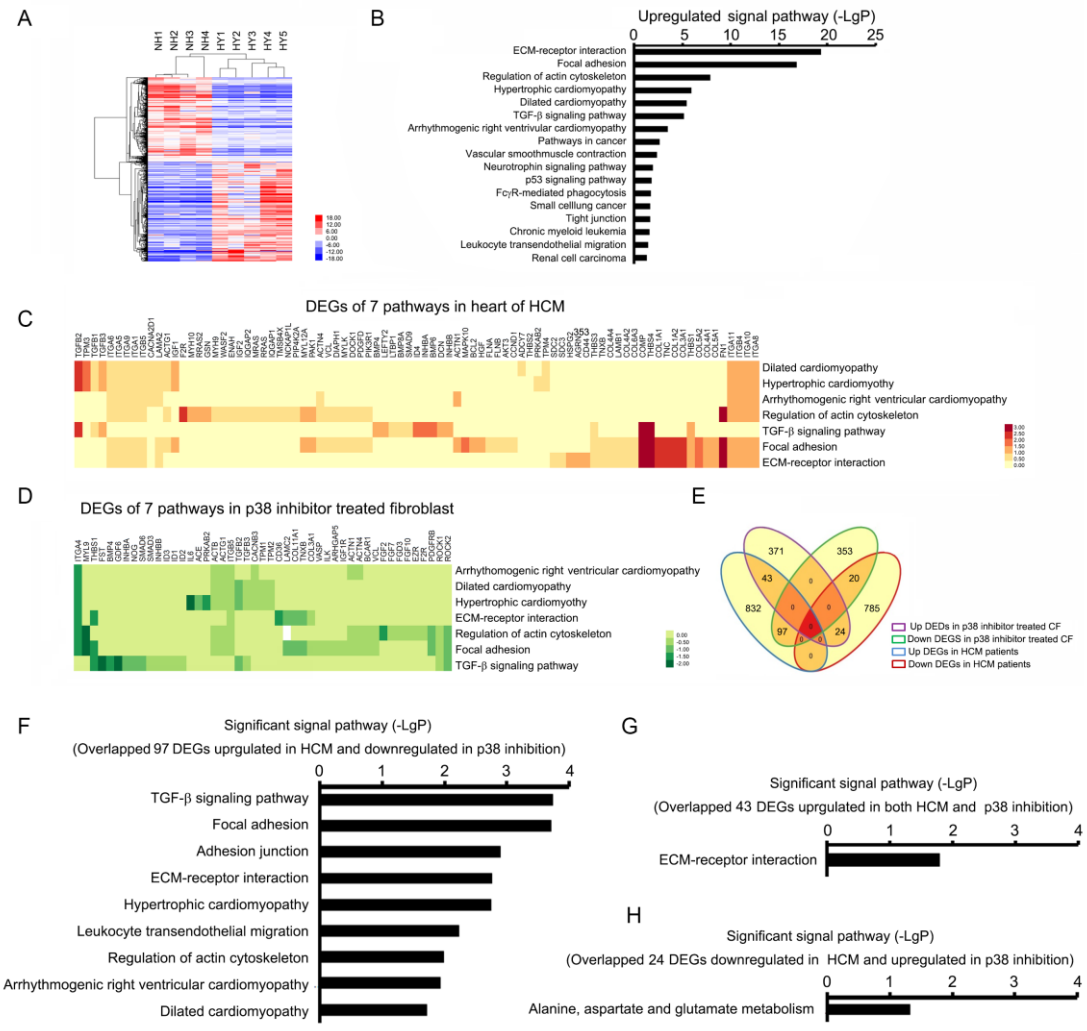
Supplemental Figure 7. Inhibited efficiency of Map2K3 shRNA

(A,B) Cardiac fibroblast was transfected the lentivirus expressing a Map2K3 shRNA (LV-Map2K3-shRNA) or empty (LV-con-shRNA) for 72 hours, then the Map2K3 mRNA and protein expression was determined by qRT-PCR and western blot analysis. Data represent the average of 3 independent experiments. *p<0.05 compared to Control shRNA. Statistical significance was determined by 1-way ANOVA test (A).



Supplemental Figure 8. Pathway analysis and TGF-β signaling-related DEGs in fibroblast treated with p38 inhibitor

(A-B) CMs were treated with supernatant from ATF3 KO cardiac fibroblasts pretreated with p38 inhibitor or control, with or without Ang II. ANP mRNA expression and cardiomyocyte area were evaluated. *p<0.05 compared with CM+KO CF + Ang II. #P<0.05 vs CM+KO CF+PBS. All data represent the average of 3 independent experiments. **(C)** Cardiac fibroblasts were treated with or without a p38 inhibitor. We completed RNA-seq analysis, and 438 upregulated and 470 downregulated DEGs (p<0.05, fold change>1.2) were detected. Pathway analysis commenced, based upon downregulated DEGs identified from comparisons between Ang II stimulated-CF pretreated with or without p38 inhibitor. The vertical axis is the pathway category, and the horizontal axis is the enrichment of pathways. Statistical significance was determined by 1-way ANOVA test (A and B).



Supplemental Figure 9. Pathway analysis in overlapped DEGs between heart from HCM and cardiac fibroblast treated with p38 inhibitor

We performed cross-species transcriptome analysis HCM patient and normal hearts, and of Ang II-stimulated CF pretreated with or without a p38 inhibitor. **(A)** Hierarchical clustering of DEGs in heart tissue from HCM patient (n=5) or normal heart (n=4). **(B)** Pathway analysis of DEGs in HCM heart classified and arranged per statistical significance. **(C,D)** Heat map of the TGF-β signaling pathway, ECM-receptor interaction, focal adhesion, hypertrophic cardiomyopathy pathway, arrhythomogenic right ventricular cardiomyopathy, regulation of actin cytoskeleton, and dilated cardiomyopathy genes identified by KEGG analysis, as differentially expressed by p38-regulated cardiac fibroblasts and the HCM heart. Each point reveals the calculated Log2 ratio (HCM/control, p38 inhibitor treatment/control) of the transcription of a gene.

Genes with enhanced transcription are shown in red, and genes with repressed transcription are green. **(E)** Overlap between p38-regulated DEGs identified in cardiac fibroblasts after p38 inhibitor treatment, and HCM-regulated DEGs in HCM. **(F-H)** The KEGG pathway analysis was performed based on the 4 groups of overlapped DEGs. Significant pathways was shown, based 97 DEGs upregulated in heart of HCM but downregulated in p38 inhibitor treated cardiac fibroblast **(F)**; based 43 DEGs upregulated in both heart of HCM and p38 inhibitor treated cardiac fibroblast **(G)**; based 24 DEGs downregulated in heart of HCM but upregulated in p38 inhibitor treated cardiac fibroblast **(H)**. There is no significant pathway in 20 DEGs downregulated in both heart of HCM and p38 inhibitor treated cardiac fibroblast.

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