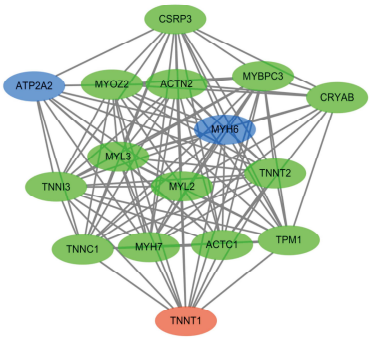
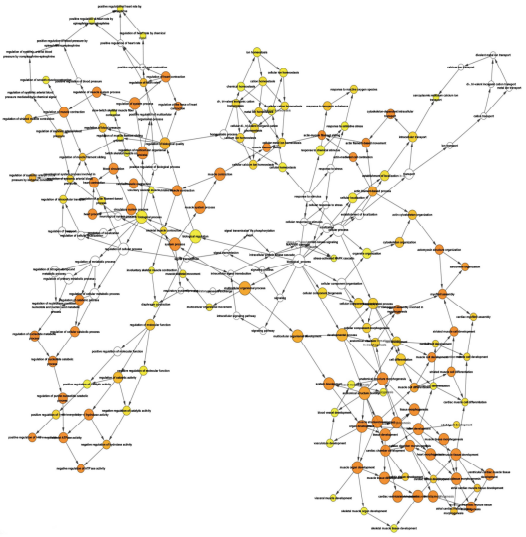
A

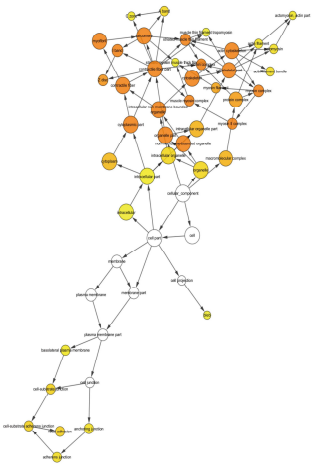


Gene	MCODE Score
TNNT1	12
CSRP3	12
TPM1	11.86813187
TNNT2	11.86813187
TNNI3	11.86813187
TNNC1	11.86813187
MYOZ2	11.86813187
MYL3	11.86813187
MYL2	11.86813187
MYH7	11.86813187
MYH6	11.86813187
MYBPC3	11.86813187
ACTN2	11.86813187
ACTC1	11.86813187
CRYAB	10
ATP2A2	10

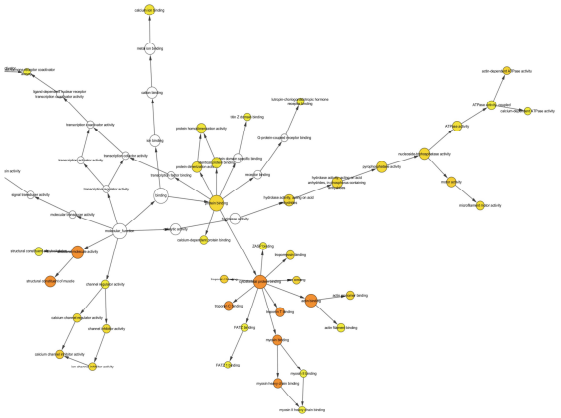
B



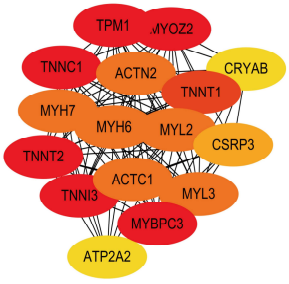
C



D



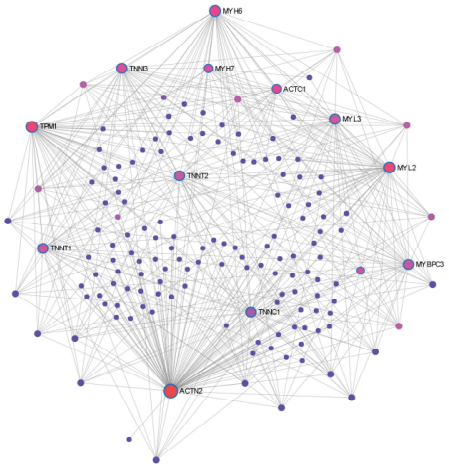
E



Rank	Gene	Score
1	MYOZ2	0.968457999
1	TNNI3	0.968457999
1	TNNC1	0.968457999
1	TNNT2	0.968457999
1	TPM1	0.968457999
1	MYBPC3	0.968457999
7	TNNT1	0.965908121
8	ACTC1	0.95141165
8	ACTN2	0.95141165
8	MYH6	0.95141165
8	MYL3	0.95141165
8	MYH7	0.95141165
8	MYL2	0.95141165
14	CSRP3	0.94593572
15	ATP2A2	0.897868042
15	CRYAB	0.897868042

Fig. S1: Identification of the most significant module and analysis of its gene network. (A) Using MCODE to identify the PPI network with 16 nodes and 110 sides as the essential module (left panel). The MCODE score of genes from the most significant module is listed (right panel). (B) The biological process analysis of the genes involved in the most significant module constructed using BiNGO. The color depth of the node refers to the adjusted p-value of the ontology. The size of the node refers to genes related to ontology. P<0.01 is considered statistically significant. (C) The cellular component analysis of the genes involved in the most significant module constructed using BiNGO. (D) The molecular function analysis of the genes involved in the most significant module constructed using BiNGO. (E) Screening out the 13 most crucial hub genes using the Cytoscape software plugin cytoHubba.

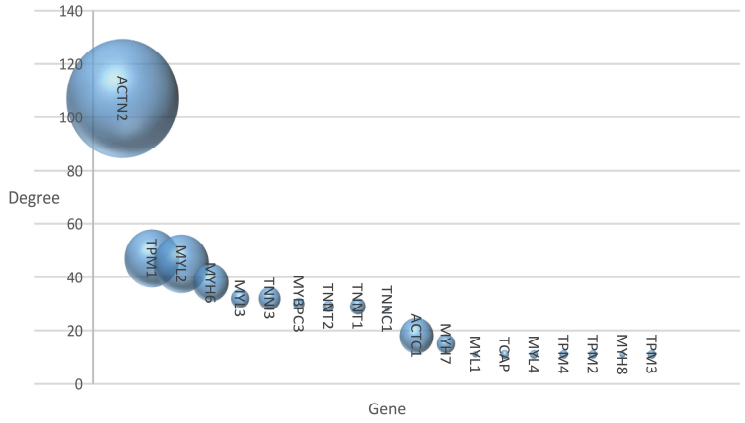
A



B

Gene	Degree	Betweeness
ACTN2	107	8636.113
TPM1	47	2055.698
MYL2	45	2079.56
MYH6	38	879.9598
MYL3	32	222.7265
TNNI3	32	332.3598
MYBPC3	30	89.9334
TNNT2	29	79.9961
TNNT1	29	168.0364
TNNC1	28	17.03636
ACTC1	18	785.4994
MYH7	15	231.6006
MYL1	11	23.52268
TCAP	11	51.03846
MYL4	11	47.49545
TPM4	11	47.49545
TPM2	11	47.49545
MYH8	11	23.52268
TPM3	11	47.49545

C



D

Description	False Discovery Rate (FDR)
Biological Process(GO)	
Actin filament based movement	1.95E-53
Actin filament based process	7.83E-48
Wound healing	2.98E-40
Blood coagulation	1.49E-38
Coagulation	1.76E-38
Cellular Component(GO)	
Contractile fiber	1.23E 58
Myofibril	4.15E-54
Actin cytoskeleton	3.4E-52
Contractile fiber part	3.4E-52
Sarcomere	1.03E-46
Molecular Function(GO)	
Actin binding	8.39E-48
Cytoskeletal protein binding	3.43E-44
Structural constituent of muscle	2.76E-31
Calmodulin binding	2.34E-17
Structural molecule activity	2.32E-16
KEGG Pathway	
Focal adhesion	4.56E-28
Regulation of actin cytoskeleton	6.79E-26
Hypertrophic cardiomyopathy(HCM)	1.86E-22
Dilated cardiomyopathy	8.65E-22
Leukocyte transendothelial migration	1.67F-14
Reactome Pathway	
Muscle contraction	1.53E-70
Platelet degranulation	1.07E-49
Striated Muscle Contraction	1.14E-49
Response to elevated platelet cytosolic Ca2+	1.17E-48
Platelet activation, signaling and aggregation	9.51E-40

E

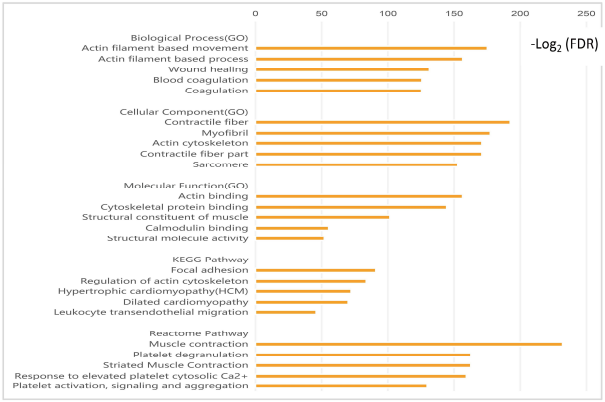
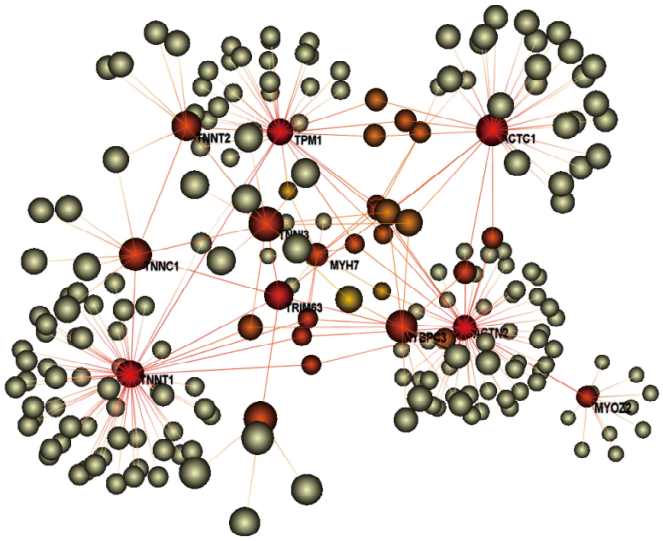


Fig. S2: The 13 most critical hub genes were subjected to co-expression network and enrichment analysis. (A) The hub genes and its co-expressed genes analyzed by STRING. The nodes in the bold blue outline represent the hub genes. Purple nodes represent co-expressed genes. (B) Genes with node degree >10 and their between ness centrality scores in the co-expression network of fig. 5A were listed. (C) The bubble chart showing the degree centrality score and between ness centrality score of genes with node degree >10 in the co-expression network of fig. 5A. The abscissa represents a gene, the ordinate represents degree centrality score and bubble size represents the between ness centrality score. (D) The enrichment analysis of GO, KEGG pathway and Reactome pathway of the 13 hub genes. (E) FDR of the enrichment after negative logarithm transformation.

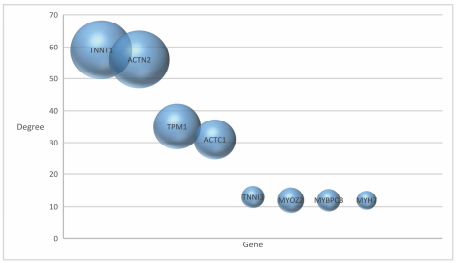
A



B

Gene	Degree	Betweeness
TNNT1	59	11244.32
ACTN2	56	10860.45
TPM1	35	6712.892
ACTC1	31	5269.179
TNNI3	13	1585.341
MYOZ2	12	2105
MYBPC3	12	1648.777
MYH7	12	1161.696

C



D

Description	False Discovery Rate (FDR)
Biological Process(GO)	
Actin filament_based movement	2.4E-22
Actin filament_based process	6.64E-11
Striated muscle contraction	0.000000472
Regulation of muscle contraction	0.00000263
Signal transduction in response to DNA damage	0.0000225
Cellular Component(GO)	
Sarcomere	5.3E-33
Contractile fiber part	5.22E-31
Myofibril	2.05E-30
Contractile fiber	2.05C-30
Actin cytoskeleton	1.74E-19
Molecular Function(GO)	
Cytoskeletal protein binding	1.24E-23
Actin binding	9.72E-16
Structural constituent of muscle	8.82E-14
Protein domain specific binding	0.000000792
Transcription coactivator activity	0.0000324
KEGG Pathway	
Hypertrophic cardiomyopathy(HCM)	1.85E-10
Dilated cardiomyopathy	2.63E-10
Cardiac muscle contraction	0.000000078
Adrenergic signaling in cardiomyocytes	0.00000838
Viral carcinogenesis	0.00000838
Reactome Pathway	
Striated Muscle Contraction	2.48E-24
Muscle contraction	5.15E-19
Nephrin interactions	0.000732
Cell Cycle Checkpoints	0.0811
Regulation of APC/C activators between G1/S and early anaphase	0.0948

E

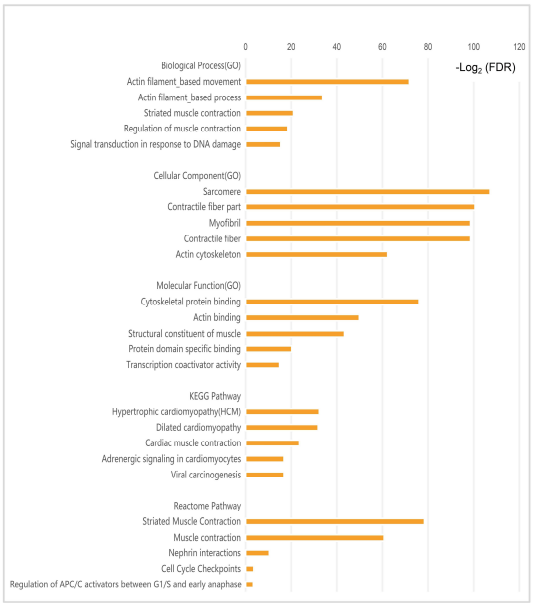
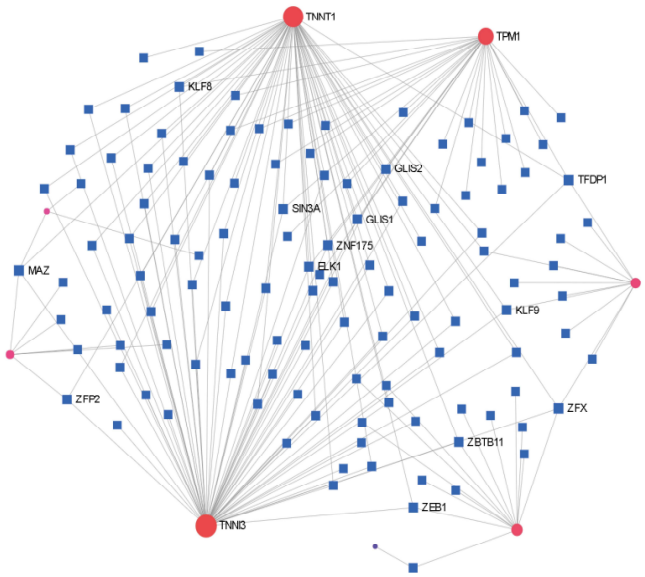


Fig. S3: Tissue-specific (left ventricle) gene co-expression network and enrichment analysis of the 13 most critical hub genes are shown. (A) The 13 hub genes and their co-expression genes analysis based on the Differential NET database. Each sphere represents a gene. The red sphere represents the nuclear gene, and the yellow-brown sphere represents the co-expression gene. (B) List of the genes with node degree >10 and them between ness centrality scores in the co-expression network of fig. 6A. (C) The bubble chart showing the degree centrality score and between ness centrality score of genes with node degree >10 in fig. 6A. The abscissa represents a gene, the ordinate represents degree centrality score, and bubble size represents the between ness centrality score. (D) The tissue-specific enrichment analysis of GO, KEGG pathway and Reactome pathway of the 13 hub genes. (E) FDR of the tissue-specific enrichment after negative logarithm transformation.

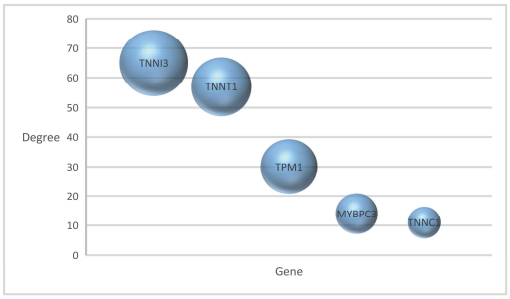
A



B

Gene	Degree	Betweeness
TNNI3	65	3787.677
TNNT1	57	2912.306
TPM1	30	2612
MYBPC3	14	1424
TNNC1	11	870.6837

C



D

Description	False Discovery Rate (FDR)
Biological Process(GO)	
Regulation of nucleobase_containing compound metabolic process	1.95E-42
Regulation of transcription,DNA_dependent	1.95E-42
Regulation of RNA metabolic process	1.95E-42
Transcription, DNA_dependent	1.95E-42
RNA biosynthetic process	3.03E-42
Cellular Component(GO)	
Nucleus	8.88E-29
Nuclear chromatin	2.09E-14
Nuclear lumen	4.52E-14
Nucleoplasm	7.35E-14
Nuclear chromosome part	7.78E-13
Molecular Function(GO)	
DNA binding	8.46E-57
Transcription from RNA polymerase II promoter	6.83E-34
Sequence_specific DNA binding	4.35E-30
Negative regulation of transcription,DNA_dependent	3.92E-24
Positive regulation of transcription,DNA_dependent	4.78E-23
KEGG Pathway	
Transcriptional misregulation in cancer	2.77E-08
Adrenergic signaling in cardiomyocytes	0.00162
Huntington's disease	0.00162
Hypertrophic cardiomyopathy(HCM)	0.00364
Dilated cardiomyopathy	0.0038
Reactome Pathway	
Striated Muscle Contraction	4.51E-08
Generic Transcription Pathway	3.76E-07
Muscle contraction	0.00000128
Transcriptional activity of SMAD2/SMAD3:SMAD4 heterotrimer	0.000198
SMAD2/SMAD3:SMAD4 heterotrimer regulates transcription	0.000419

E

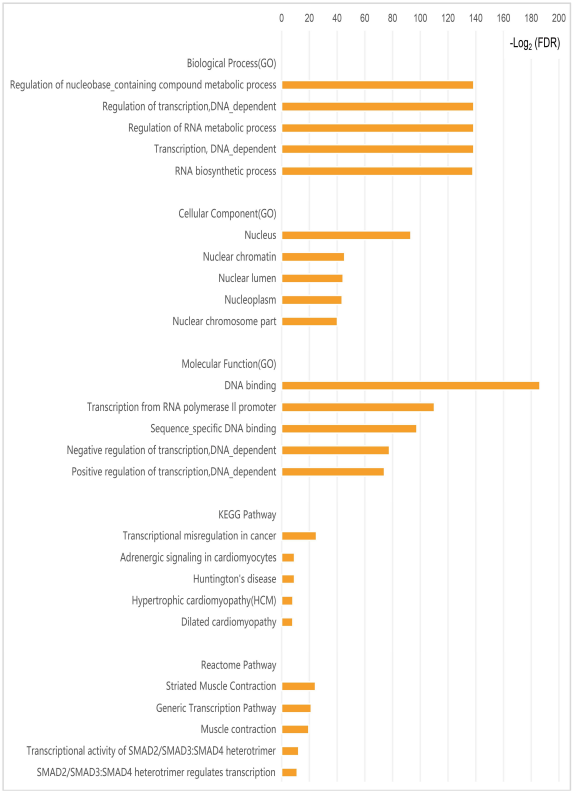


Fig. S4: Transcription-factor gene interaction of the 13 hub genes were analyzed. (A) The transcription-factor gene interaction of the 13 hub genes based on ENCODE ChIP-seq data. (B) List of the genes with node degree >10 and their between ness centrality scores in the interaction network of fig. 7A. (C) The bubble chart showing the degree centrality score and between ness centrality score of genes with node degree >10 in fig. 7A. The abscissa represents a gene, the ordinate represents degree centrality score, and bubble size represents the between ness centrality score. (D) The TF-gene enrichment analysis of GO, KEGG pathway and Reactome pathway of the 13 hub genes. (E) FDR of the TF-gene interaction network after negative logarithm transformation.