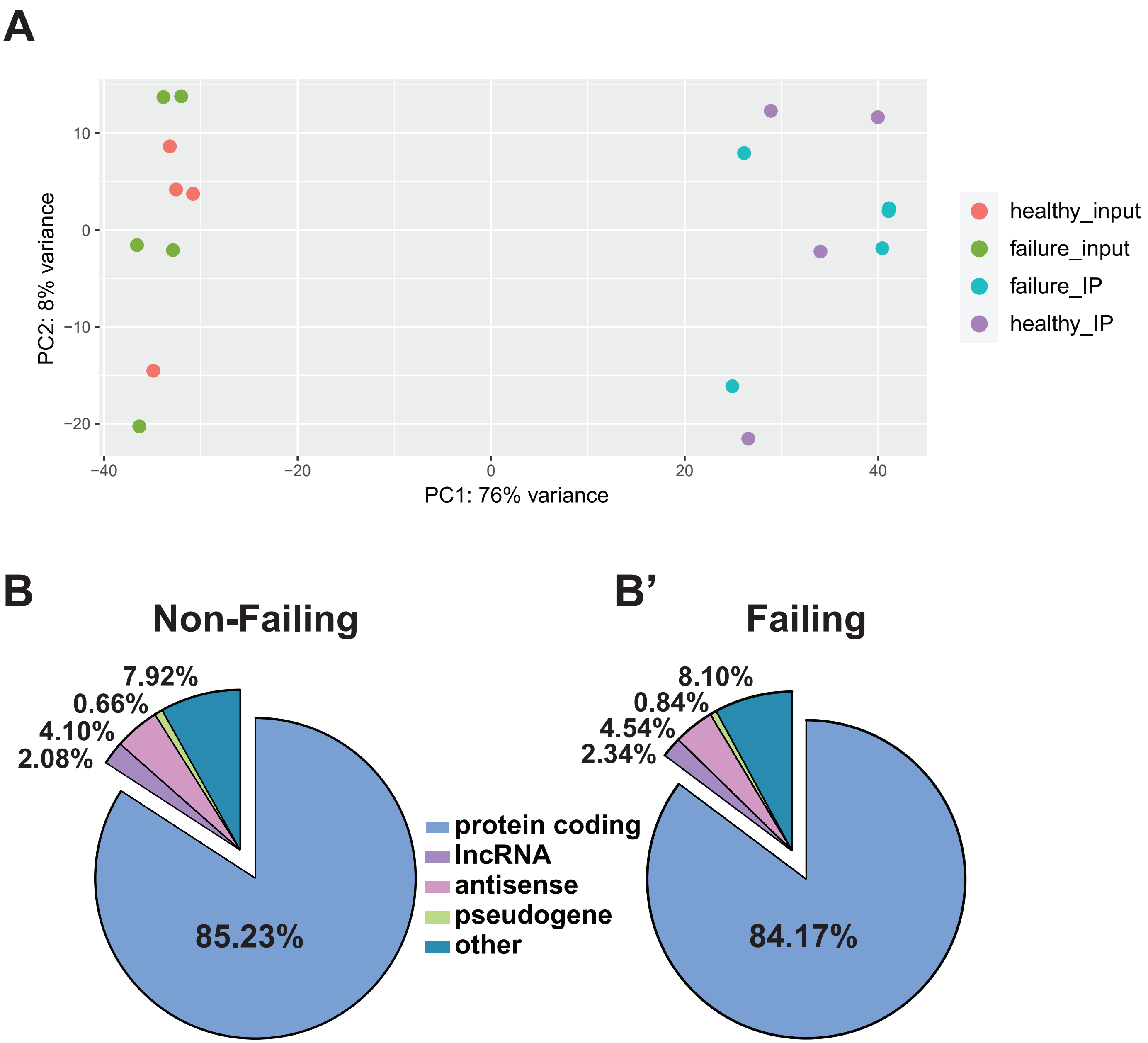
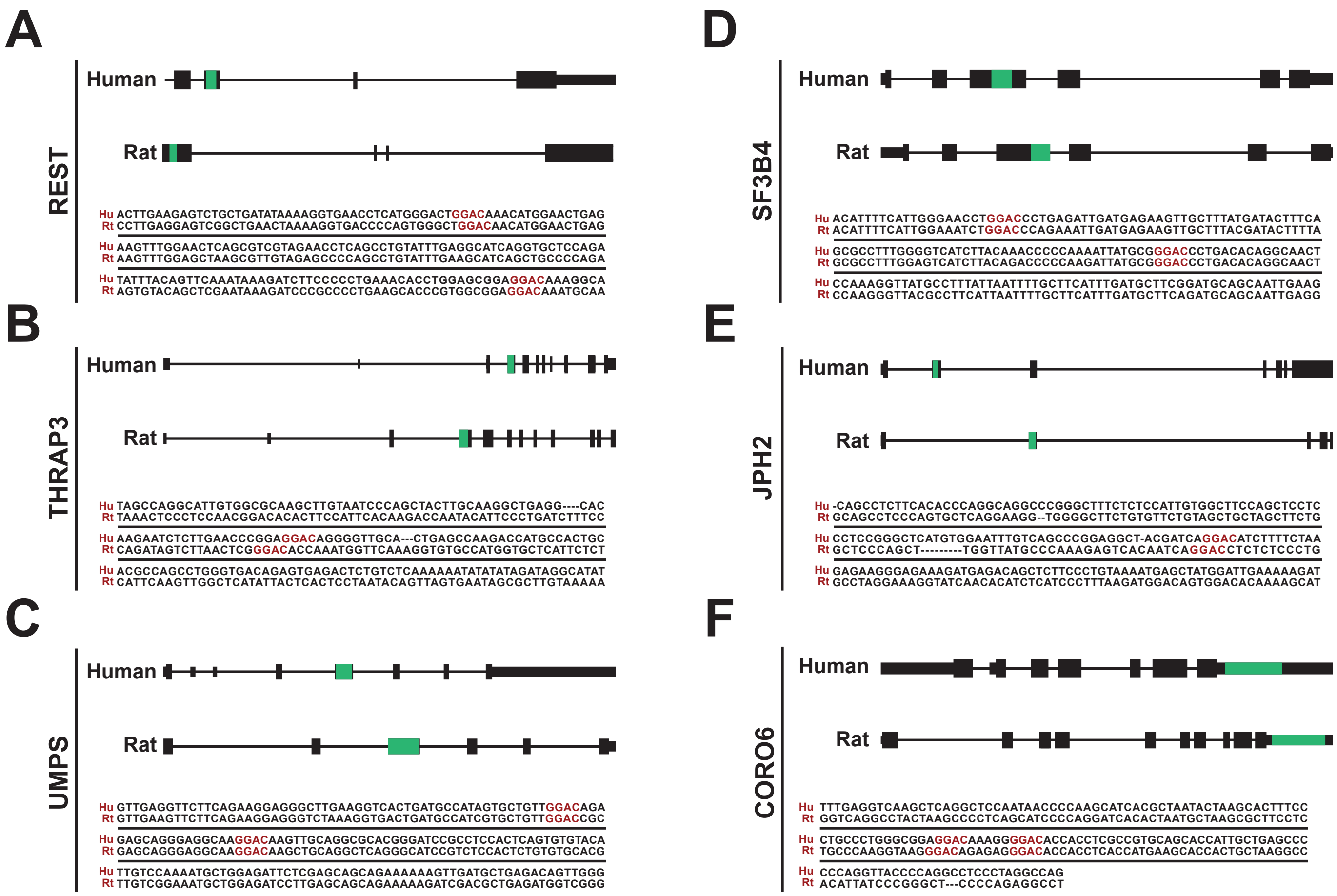
Supplemental Figure 1



Supplemental Figure 1. Principal component analysis of human heart RNA-seq samples and RNA subtype of predicted m^6A peaks. (**A**) Principal component analysis of top 500 enriched transcripts from non-failing and failing human heart RNA samples, including both input RNA and m^6A-IP RNA samples. (**B**) Pie charts outlining RNA subtypes found to have detected m^6A peaks and their percent make-up in regard to total detected peaks in either (**B**) non-failing or (**B’**) failing human heart RNA samples.

Supplemental Figure 2



Supplemental Figure 2. Sequence of m⁶A peaks differentially regulated with stress and conserved between human heart and rat cardiomyocytes. (A-F) Human and rat gene schematic (top) are shown to display the location of the m⁶A peaks in each gene (green) for transcripts that have GGAC motifs (m⁶A consensus sequence, red) in conserved gene locations. Human sequence is labeled as 'Hu', while rat sequence is labeled as 'Rt'.

Supplemental Table 1

Gene ontology (GO) analysis of transcripts with m^6A peak enrichment determined by exomePeak analysis in human failing or non-failing RNA samples. Red indicates an overlap in GO category when using either total transcriptome (left) or heart-specific transcriptome (right) as background.

Failing

Molecular Function

Total Background

Description	Enrichment	FDR
histone methyltransferase activity (H3-K4 specific)	11.17158177	0.025194751
microtubule plus-end binding	10.5144299	0.025194751
alpha-actinin binding	7.207472109	0.001616646
ubiquitin conjugating enzyme binding	7.207472109	0.018755669
histone-lysine N-methyltransferase activity	6.951206434	0.011722831
protein kinase A binding	6.516756032	0.011263632
N-methyltransferase activity	5.644588684	0.027336317
histone methyltransferase activity	5.487794553	0.027336317
protein-lysine N-methyltransferase activity	5.127939173	0.025194751
lysine N-methyltransferase activity	5.045230477	0.02396898

Heart Background

Description	Enrichment	FDR
histone methyltransferase activity (H3-K4 specific)	10.20824479	0.056103994
histone-lysine N-methyltransferase activity	5.954809463	0.036162688
protein kinase A binding	5.27812657	0.053706088
N-methyltransferase activity	4.683782905	0.008617622
histone methyltransferase activity	4.644751381	0.056103994
protein methyltransferase activity	3.828091798	0.056103994
ubiquitin-like protein ligase activity	2.900703439	0.036162688
ubiquitin protein ligase activity	2.79579738	0.053706088
methyltransferase activity	2.675548031	0.056103994
actin binding	2.390259048	0.025695811

Cellular Component

Total Background

Description	**Enrichment**	**FDR**
nuclear cyclin-dependent protein kinase holoenzyme complex	13.3280303	8.40E-05
nucleotide-excision repair complex	11.42402597	0.002434402
TOR complex	10.66242424	4.37E-04
intercalated disc	7.31734997	0.00388701
A band	6.834887335	0.024715785
sarcoplasmic reticulum membrane	6.834887335	0.024715785
transcription elongation factor complex	6.547102605	0.002108201
histone methyltransferase complex	6.058195592	0.045184833
cell-cell contact zone	6.006999573	0.040413143
Z disc	5.544460606	0.030608911

Heart Background

Description	**Enrichment**	**FDR**
histone methyltransferase complex	5.133592522	0.00202423
intercalated disc	4.941082803	0.042315325
transcription elongation factor complex	4.941082803	0.042315325
intermediate filament cytoskeleton	4.74343949	0.006477863
methyltransferase complex	4.56099951	0.001702185
Z disc	4.468457491	0.001158629
I band	4.462913499	0.001037425
cell-cell contact zone	4.256932876	0.042315325
fibrillar center	4.124729992	0.002632505
sarcomere	3.720344698	0.001158629

Non-Failing

Molecular Function

Total Background

Description	Enrichment	FDR
GDP-dissociation inhibitor activity	11.07508306	0.019856925
mitogen-activated protein kinase kinase binding	11.07508306	0.063499893
phosphatase regulator activity	3.964376321	0.063499893
unfolded protein binding	3.613480489	0.056685902
ubiquitin protein ligase binding	2.739419837	0.019856925
ubiquitin-like protein ligase binding	2.731606056	0.019856925
DNA-binding transcription repressor activity, RNA polymerase II-specific	-2.46804285	0.056685902
cadherin binding	2.461129568	0.063499893

Heart Background

Description	Enrichment	FDR
GDP-dissociation inhibitor activity	9.331779332	0.142363324
mitogen-activated protein kinase kinase binding	7.998667999	0.142363324
protein phosphatase regulator activity	3.612301677	0.142363324
phosphatase regulator activity	3.315237394	0.142363324
inorganic anion transmembrane transporter activity	3.25527186	0.142363324
unfolded protein binding	3.142333857	0.142363324
anion transmembrane transporter activity	2.321564614	0.142363324
ubiquitin protein ligase binding	2.128923041	0.142363324

transcription coactivator activity	2.330674124	0.060469616
cell adhesion molecule binding	2.270623723	0.060469616

ubiquitin-like protein ligase binding	2.122390245	0.142363324
cell adhesion molecule binding	1.893404502	0.142363324

Cellular Component

Total Background

Description	Enrichment	FDR
ribbon synapse	14.46	0.003830351
septin ring	13.77142857	0.045335623
septin complex	13.77142857	0.026744475
septin filament array	13.77142857	0.029053498
septin cytoskeleton	12.85333333	0.032081556
cytoplasmic ubiquitin ligase complex	12.05	0.006608115
podosome	6.426666667	0.005565724
sarcoplasmic reticulum membrane	6.179487179	0.005565724
cell cortex region	6.025	0.005565724
sarcoplasmic reticulum	5.670588235	0.023749091

Heart Background

Description	Enrichment	FDR
sarcoplasmic reticulum	4.82558196	0.014526763
sarcoplasm	4.688491564	0.011209474
ruffle	3.1460902	0.011209474
cell cortex	2.677308024	0.01116406
focal adhesion	2.644790113	5.46E-04
cell-substrate adherens junction	2.623910191	5.46E-04
cell-substrate junction	2.610172441	5.46E-04
myofibril	2.560381918	0.047166377
ubiquitin ligase complex	2.465660902	0.023420444
coated vesicle	2.434143113	0.04185038

Supplemental Table 2

Gene ontology (GO) analysis of transcripts with enrichment determined by DESeq2 analysis in human failing or non-failing RNA samples. Red indicates an overlap in GO category when using either total transcriptome (left) or heart-specific transcriptome (right) as background.

Failing

Molecular Function

Total Background

Description	Enrichment	FDR
IgG binding	13.85075619	0.00383095
retinol dehydrogenase activity	10.15722121	0.00383095
calcium-dependent phospholipase A2 activity	8.125776965	0.044059228
immunoglobulin binding	7.94912964	0.010061398
C-C chemokine receptor activity	6.6242747	0.031563072
C-C chemokine binding	6.348263254	0.037510266
G protein-coupled chemoattractant receptor activity	5.859935311	0.047137946
chemokine receptor activity	5.859935311	0.047137946
chemokine binding	5.713436929	0.026354439
CCR chemokine receptor binding	5.613201193	0.013335332
lipopolysaccharide binding	5.540302476	0.028918353
chemokine activity	5.186666148	0.011076498
chemokine receptor binding	4.995354692	0.005287033
monocarboxylic acid binding	4.232175503	0.011076498
hormone activity	4.16706511	8.13E-04
phospholipase activity	3.550096732	0.011076498
protease binding	3.440349118	0.009279644
G protein-coupled peptide receptor activity	2.983239795	0.014772073
cytokine activity	2.948870673	0.00383095
receptor ligand activity	2.864857263	4.15E-07
peptide receptor activity	2.863109333	0.020604491
serine-type endopeptidase activity	2.846254294	0.011076498
peptidase inhibitor activity	2.818188543	0.013214652
lipase activity	2.81276895	0.044059228
endopeptidase inhibitor activity	2.75346358	0.020604491
carboxylic acid binding	2.728805697	0.011076498
serine-type peptidase activity	2.688676202	0.011076498
endopeptidase regulator activity	2.642051759	0.028115968
serine hydrolase activity	2.63697089	0.013214652
peptidase regulator activity	2.599478413	0.013335332
organic acid binding	2.587216722	0.013432331
carbohydrate binding	2.539305302	0.009279644
cytokine receptor binding	2.224209023	0.031563072
G protein-coupled receptor binding	2.176547401	0.046601778
metal ion transmembrane transporter activity	1.939105867	0.029715598

Heart Background

Description	Enrichment	FDR
CCR chemokine receptor binding	12.20528455	5.14E-04
immunoglobulin binding	12.20528455	0.002106891
chemokine activity	10.84914182	1.36E-04
signaling pattern recognition receptor activity	9.764227642	0.018934778
pattern recognition receptor activity	9.764227642	0.018934778
chemokine receptor binding	9.415505226	1.36E-04
C-C chemokine receptor activity	9.153963415	0.022856009
C-C chemokine binding	9.153963415	0.022856009
steroid dehydrogenase activity	8.615494978	0.027625132
G protein-coupled chemoattractant receptor activity	8.136856369	0.032086133
chemokine receptor activity	8.136856369	0.032086133
chemokine binding	7.959968187	0.013410131
lipopolysaccharide binding	7.70860077	0.038781422
oxidoreductase activity, acting on paired donors	7.323170732	0.046286896
cysteine-type endopeptidase inhibitor activity	6.538545296	0.025013249
neurotransmitter transporter activity	6.313078217	0.02795871
monocarboxylic acid binding	5.695799458	0.009196299
peptidase inhibitor activity	5.424570912	3.10E-04
cytokine activity	5.230836237	5.97E-05
endopeptidase inhibitor activity	5.163774234	6.84E-04
G protein-coupled peptide receptor activity	5.015870364	0.001836075
peptide receptor activity	4.882113821	0.002106891
protease binding	4.857205077	3.57E-04
endopeptidase regulator activity	4.738522238	0.001356562
phospholipase activity	4.641446238	0.006782431
peptidase regulator activity	4.344253824	4.88E-04
lipase activity	3.87697274	0.01821811
serine-type endopeptidase activity	3.78784693	0.018934778
heparin binding	3.692354991	0.005492297
cytokine receptor binding	3.446197991	0.001293049
G protein-coupled receptor activity	3.406125922	3.10E-04
extracellular matrix structural constituent	3.356453252	0.016391357
carboxylic acid binding	3.254742547	0.013410131
glycosaminoglycan binding	3.164333032	0.007129216
organic acid binding	3.161080891	0.016391357
receptor ligand activity	3.100535995	4.88E-04
receptor regulator activity	2.983514002	4.88E-04
carbohydrate binding	2.946103168	0.013092774
sulfur compound binding	2.921477686	0.009196299

transmembrane signaling receptor activity	2.50995771	1.81E-04
metal ion transmembrane transporter activity	2.405421043	0.018575744

Cellular Component

Total Background

Description	Enrichment	FDR
Schmidt-Lanterman incisure	15.99363636	0.002569004
condensed chromosome outer kinetochore	14.66083333	0.003223793
compact myelin	12.56642857	0.00484363
paranode region of axon	10.995625	0.030366378
pronucleus	10.34882353	0.008136334
mitotic spindle midzone	10.14980769	0.036841175
endolysosome membrane	9.424821429	0.042502114
condensed nuclear chromosome kinetochore	9.424821429	0.042502114
spindle midzone	9.055220588	4.86E-04
sperm midpiece	7.996818182	0.020660226
Flemming body	7.854017857	0.006790793
condensed nuclear chromosome, centromeric region	7.330416667	0.027375611
DNA packaging complex	7.0372	9.97E-06
spindle microtubule	6.766538462	8.48E-04
nucleosome	6.564552239	1.42E-04
extracellular matrix component	6.283214286	0.003223793
mitotic spindle	6.219747475	6.38E-06
kinesin complex	5.809009434	0.004362119
condensed chromosome, centromeric region	5.638782051	6.38E-06
condensed chromosome kinetochore	5.4978125	4.72E-05
tertiary granule membrane	5.4978125	0.001375344
kinetochore	5.29112782	6.38E-06
intercellular bridge	5.218262712	0.006749471
specific granule membrane	4.833241758	0.001444025
collagen trimer	4.549913793	0.004095973
chromosome, centromeric region	4.534278351	2.99E-06
specific granule	4.39825	5.00E-05
condensed chromosome	4.339080717	2.18E-06
specific granule lumen	4.256370968	0.036841175
calcium channel complex	4.123359375	0.040882808
external side of plasma membrane	4.109091696	4.36E-07
condensed nuclear chromosome	3.958425	0.00764899
platelet alpha granule	3.866593407	0.016543166
spindle	3.754603659	8.07E-07
microvillus	3.70936747	0.036841175
midbody	3.600906433	0.001380374
microtubule associated complex	3.566148649	0.0038969
filopodium	3.554141414	0.026908679
tertiary granule	3.507806748	0.00285657
protein-DNA complex	3.507806748	0.00285657
primary lysosome	3.405096774	0.00484363

Heart Background

Description	Enrichment	FDR
pronucleus	11.78727445	0.037133909
extracellular matrix component	8.51303155	8.97E-04
protein complex involved in cell adhesion	7.567139156	0.036800462
spindle midzone	7.296884186	0.039371251
collagen trimer	6.925856176	9.12E-04
DNA packaging complex	6.662372517	0.008278658
mitotic spindle	6.610118615	1.36E-04
nucleosome	6.548485808	0.022561192
tertiary granule membrane	5.959122085	0.005447902
condensed chromosome, centromeric region	5.618600823	3.49E-04
specific granule membrane	5.53859884	0.001504147
intercellular bridge	5.433849926	0.039371251
spindle microtubule	5.433849926	0.039371251
condensed chromosome kinetochore	5.223905724	0.002022683
kinetochore	4.885739846	8.97E-04
external side of plasma membrane	4.852427984	9.39E-06
platelet alpha granule	4.831720609	0.01509913
specific granule	4.709336602	3.49E-04
condensed chromosome	4.35325477	2.65E-04
filopodium	4.157527036	0.031379919
chromosome, centromeric region	3.929091485	0.001307216
anchored component of membrane	3.929091485	0.023250231
tertiary granule	3.811805172	0.008859895
secretory granule membrane	3.588137265	4.33E-04
side of membrane	3.563594602	2.42E-05
collagen-containing extracellular matrix	3.429277727	3.49E-04
extracellular matrix	3.386399291	4.18E-05
spindle	3.331186259	5.79E-04
membrane region	3.301632008	8.97E-04
membrane raft	3.192386831	0.001817495
membrane microdomain	3.179965093	0.001817495
midbody	3.12723608	0.042743857
chromosomal region	2.898053294	0.004885586
secretory granule lumen	2.848226169	0.008278658
cytoplasmic vesicle lumen	2.73633157	0.011217674
vesicle lumen	2.726593735	0.011217674
neuronal cell body	2.451753086	0.011217674
dendrite	2.146142408	0.024958818
dendritic tree	2.141643157	0.024958818
cell body	2.133195841	0.039371251

azurophil granule	3.405096774	0.00484363
blood microparticle	3.257962963	0.040882808
chromosomal region	3.189063444	4.72E-05
spindle pole	3.182944079	0.011380729
anchored component of membrane	3.160419162	0.00764899
actin-based cell projection	3.125659898	0.004154251
side of membrane	3.017510395	2.99E-06
secretory granule membrane	3.00221843	6.08E-04
cation channel complex	2.811666667	0.008165178
collagen-containing extracellular matrix	2.763927596	5.69E-04
extracellular matrix	2.660231855	7.21E-05
microtubule	2.625820896	7.65E-04
secretory granule lumen	2.611460938	0.0038969
membrane region	2.579220679	0.004154251
membrane raft	2.545610932	0.005730886
membrane microdomain	2.537451923	0.005808637
cytoplasmic vesicle lumen	2.487105655	0.005541565
vesicle lumen	2.479725519	0.005601161
apical plasma membrane	2.404188103	0.012448612
apical part of cell	2.345733333	0.006920883
ion channel complex	2.345733333	0.021387383
neuronal cell body	2.171975309	0.006289736
transmembrane transporter complex	2.171975309	0.040857813
transporter complex	2.119638554	0.047039298
presynapse	1.912282609	0.043087311

Non-Failing

Molecular Function

Total Background

Description	**Enrichment**	**FDR**
oxygen carrier activity	22.33717502	8.07E-04
oxygen binding	13.27466401	1.31E-04
peroxidase activity	6.832547653	0.034533573
oxidoreductase activity, acting on peroxide as acceptor	6.335635097	0.046651127
hormone activity	5.460198338	0.001334793
heme binding	4.537238676	0.014736548
tetrapyrrole binding	4.208453265	0.023679562
organic acid binding	4.109197291	0.001241668
receptor ligand activity	2.978290003	8.07E-04

Heart Background

Description	**Enrichment**	**FDR**
neurotransmitter binding	18.83921569	0.013710203
hormone activity	13.08278867	0.012625751
receptor ligand activity	5.697343454	0.001218168
receptor regulator activity	5.233115468	0.001480638

Cellular Component

Total Background

Description	**Enrichment**	**FDR**
haptoglobin-hemoglobin complex	41.10514019	2.29E-05
hemoglobin complex	37.36830926	2.29E-05

Heart Background

Description	**Enrichment**	**FDR**
excitatory synapse	17.95587703	0.016190821
collagen-containing extracellular matrix	5.551728765	0.004129374

chylomicron	20.55257009	0.012085148
endocytic vesicle lumen	18.26895119	0.007331136
axolemma	16.44205607	0.019984942
MHC class II protein complex	16.44205607	0.019984942
MHC protein complex	15.65910102	0.008360439
integral component of lumenal side of endoplasmic reticulum membrane	13.15364486	0.010980077
lumenal side of endoplasmic reticulum membrane	13.15364486	0.010980077
very-low-density lipoprotein particle	12.98057059	0.029604438
triglyceride-rich plasma lipoprotein particle	12.98057059	0.029604438
connexin complex	12.33154206	0.032025322
high-density lipoprotein particle	9.485801582	0.049115497
excitatory synapse	8.38880412	0.011759288
clathrin-coated endocytic vesicle membrane	7.473661852	0.032429239
brush border membrane	6.57682243	0.042864891
main axon	5.957266694	0.029604438
Golgi lumen	5.872162884	0.010980077
voltage-gated potassium channel complex	5.542266093	0.020182481
blood microparticle	5.328444098	0.012085148
axoneme	5.047999672	0.015106419
potassium channel complex	5.033282472	0.027678093
ciliary plasm	5.004104023	0.015309846
clathrin-coated vesicle membrane	4.609922264	0.032429239
perikaryon	4.567237799	0.021428273
collagen-containing extracellular matrix	4.267746795	2.29E-05
presynaptic membrane	4.084982876	0.020706282
extrinsic component of plasma membrane	4.059766932	0.020863208
cluster of actin-based cell projections	4.024279459	0.032429239
extracellular matrix	3.977916792	7.09E-06
anchored component of membrane	3.938217024	0.023699673
integral component of synaptic membrane	3.736830926	0.040920057
motile cilium	3.694844062	0.029604438
endocytic vesicle membrane	3.596699766	0.046223496
endoplasmic reticulum lumen	3.492593611	0.008360439
endocytic vesicle	3.413575656	0.010980077
cation channel complex	3.378504673	0.029604438
plasma membrane bounded cell projection cytoplasm	3.355521648	0.040920057
exocytic vesicle	3.338488543	0.041251013
transmembrane transporter complex	3.298560632	0.010980077
ion channel complex	3.288411215	0.011759288
transporter complex	3.219077244	0.010980077
cell projection membrane	3.190249686	0.011033765
ciliary part	3.176306287	0.004421696
apical plasma membrane	3.17210085	0.014223692
side of membrane	2.905560845	0.008360439
neuronal cell body	2.875668244	0.008360439
synaptic membrane	2.867800478	0.011147619
extrinsic component of membrane	2.864469699	0.040920057
postsynaptic density	2.861750266	0.032025322
asymmetric synapse	2.825978388	0.032429239

extracellular matrix	5.208196377	0.001972475

postsynaptic membrane	2.817174717	0.032429239
presynapse	2.723321917	0.011759288
postsynaptic specialization	2.659744365	0.042864891
neuron to neuron synapse	2.651944528	0.042864891
transport vesicle	2.637763007	0.034711754
apical part of cell	2.630728972	0.03475938
cell-cell junction	2.609850171	0.023699673
glutamatergic synapse	2.583751669	0.049150762
cytoplasmic region	2.402805689	0.034832686

Supplemental Table 3

m6A peaks and transcript location determined by exomePeak analysis that are found to overlap between human failing and rat hypertrophic RNA samples.

gene name	peak	description	hu_ensembl	hu_chromosome	hu_start	hu_end	hu_location	rt_ensembl	rt_chromosome	rt_start	rt_end	rt_location
ACIN1	**1**	apoptotic chromatin condensation inducer 1 [Source:HGNC Symbol;Acc:HGNC:17066]	ENSG00000100813.14	chr14	23068102	23068552	UTR3	ENSRNOG00000013533.7	chr15	33288731	33290445	CDS
	2			chr14	23067443	23067773	UTR3					
ANKRD17	**1**	ankyrin repeat domain 17 [Source:HGNC Symbol;Acc:HGNC:23575]	ENSG00000132466.19	chr4	73091752	73091963	CDS	ENSRNOG00000002940.7	chr14	19377778	19378049	CDS
ATRX	**1**	ATRX chromatin remodeler [Source:HGNC Symbol;Acc:HGNC:886]	ENSG00000085224.22	chrX	77682855	77683066	CDS	ENSRNOG00000056703.1	chrX	76821797	76821858	CDS
BAZ1B	**1**	bromodomain adjacent to zinc finger domain 1B [Source:HGNC Symbol;Acc:HGNC:961]	ENSG00000009954.11	chr7	73476948	73477008	CDS	ENSRNOG00000001453.7	chr12	24482167	24486602	CDS
	2			chr7	73477277	73477487	CDS		chr12	24479826	24480666	CDS
	3			chr7	73477785	73478354	CDS					
CLIP1	**1**	CAP-Gly domain containing linker protein 1 [Source:HGNC Symbol;Acc:HGNC:10461]	ENSG00000130779.20	chr12	122322259	122322620	CDS	ENSRNOG00000001247.7	chr12	38450296	38451602	CDS
	2			chr12	122377689	122377840	CDS					
CRYBG3	**1**	crystallin beta-gamma domain containing 3 [Source:HGNC Symbol;Acc:HGNC:34427]	ENSG00000080200.10	chr3	97876157	97876338	CDS	ENSRNOG00000001687.7	chr11	42946275	42946485	CDS
	2			chr3	97876577	97877058	CDS					
CTNND1	**1**	catenin delta 1 [Source:HGNC Symbol;Acc:HGNC:2515]	ENSG00000198561.14	chr11	57801979	57802159	CDS	ENSRNOG00000030790.5	chr3	72052839	72053049	UTR5
DDI2	**1**	DNA damage inducible 1 homolog 2 [Source:HGNC Symbol;Acc:HGNC:24578]	ENSG00000197312.12	chr1	15661605	15661876	UTR3	ENSRNOG00000012274.8	chr5	160236524	160236944	UTR3
EFCAB14	**1**	ELKS/RAB6-interacting/CAST family member 1 [Source:HGNC Symbol;Acc:HGNC:17072]	ENSG00000159658.12	chr1	46718665	46719114	UTR5	ENSRNOG00000010091.7	chr5	134593546	134594293	UTR5
ERC1	**1**	FAT atypical cadherin 1 [Source:HGNC Symbol;Acc:HGNC:3595]	ENSG00000082805.20	chr12	1028109	1028290	CDS	ENSRNOG00000009264.6	chr4	152089175	152089566	UTR3
FAT1	**1**	filamin binding LIM protein 1 [Source:HGNC Symbol;Acc:HGNC:24686]	ENSG00000083857.14	chr4	186708786	186709717	CDS	ENSRNOG00000030954.5	chr16	50400788	50400819	CDS
	2								chr16	50383594	50383895	CDS
FBLIM1	**1**	FRY like transcription coactivator [Source:HGNC Symbol;Acc:HGNC:29127]	ENSG00000162458.13	chr1	15784656	15784777	CDS	ENSRNOG00000011774.6	chr5	160123973	160124182	CDS
FRYL	**1**	FRY like transcription coactivator [Source:HGNC Symbol;Acc:HGNC:29127]	ENSG00000075539.15	chr4	48498945	48499036	UTR3	ENSRNOG00000002248.8	chr14	37717250	37717520	CDS
H6PD	**1**	hexose-6-phosphate dehydrogenase/glucose 1-dehydrogenase [Source:HGNC Symbol;Acc:HGNC:4795]	ENSG00000049239.12	chr1	9270017	9270288	UTR3	ENSRNOG00000017523.5	chr5	167016512	167016871	CDS
JPH2	**1**	junctophilin 2 [Source:HGNC Symbol;Acc:HGNC:14202]	ENSG00000149596.6	chr20	44177402	44177821	UTR3	ENSRNOG00000008170.5	chr3	159754701	159775643	CDS
KLHL24	**1**	kelch like family member 24 [Source:HGNC Symbol;Acc:HGNC:25947]	ENSG00000114796.16	chr3	183650915	183651215	CDS	ENSRNOG00000033372.5	chr11	84633443	84633504	CDS
	2			chr3	183635609	183636336	UTR5					
LEPROTL1	**1**	leptin receptor overlapping transcript like 1 [Source:HGNC Symbol;Acc:HGNC:6555]	ENSG00000104660.19	chr8	30138272	30177208	CDS	ENSRNOG00000012601.7	chr16	61758916	61769772	CDS
MAP1A	**1**	microtubule associated protein 1A [Source:HGNC Symbol;Acc:HGNC:6835]	ENSG00000166963.13	chr15	43521625	43521955	CDS	ENSRNOG00000014230.6	chr3	113269228	113269558	CDS
	2			chr15	43524743	43525074	CDS					
MFGE8	**1**	milk fat globule-EGF factor 8 protein [Source:HGNC Symbol;Acc:HGNC:7036]	ENSG00000140545.15	chr15	88909943	88910483	Intron	ENSRNOG00000017510.8	chr1	140845464	140845999	CDS
MGA	**1**	MAX dimerization protein MGA [Source:HGNC Symbol;Acc:HGNC:14010]	ENSG00000174197.16	chr15	41750105	41750585	CDS	ENSRNOG00000006378.8	chr3	111714111	111714321	UTR3
	2								chr3	111759760	111759911	CDS
MON2	**1**	MON2 homolog, regulator of endosome-to-Golgi trafficking [Source:HGNC Symbol;Acc:HGNC:29177]	ENSG00000061987.16	chr12	62466936	62467207	UTR5	ENSRNOG00000004185.8	chr7	66771000	66774839	CDS
NIPBL	**1**	NIPBL cohesin loading factor [Source:HGNC Symbol;Acc:HGNC:28862]	ENSG00000164190.19	chr5	36975902	36976323	CDS	ENSRNOG00000056907.1	chr2	57509427	57510457	CDS
PCDHGB1	**1**	protocadherin gamma subfamily B, 1 [Source:HGNC Symbol;Acc:HGNC:8708]	ENSG00000254221.2	chr5	141350250	141350609	CDS	ENSRNOG00000042264.2	chr18	30827160	30827457	CDS
PIGC	**1**	phosphatidylinositol glycan anchor biosynthesis class C [Source:HGNC Symbol;Acc:HGNC:8960]	ENSG00000135845.10	chr1	172394080	172394350	CDS	ENSRNOG00000026497.4	chr13	79886920	79888770	CDS
PLCE1	**1**	phospholipase C epsilon 1 [Source:HGNC Symbol;Acc:HGNC:17175]	ENSG00000138193.15	chr10	94031711	94032252	CDS	ENSRNOG00000014276.6	chr1	257390173	257390474	CDS
RASAL2	**1**	RAS protein activator like 2 [Source:HGNC Symbol;Acc:HGNC:9874]	ENSG00000075391.16	chr1	178341514	178390126	CDS	ENSRNOG00000004917.7	chr13	74812399	74812638	CDS
REST	**1**	RE1 silencing transcription factor [Source:HGNC Symbol;Acc:HGNC:9966]	ENSG00000084093.17	chr4	56931531	56932070	CDS	ENSRNOG00000002074.7	chr14	33150147	33150297	CDS
	2			chr4	56910693	56911172	CDS					
RNF26	**1**	ring finger protein 26 [Source:HGNC Symbol;Acc:HGNC:14646]	ENSG00000173456.5	chr11	119334945	119335454	CDS	ENSRNOG00000007720.6	chr8	48447468	48447885	UTR3
RPRD2	**1**	regulation of nuclear pre-mRNA domain containing 2 [Source:HGNC Symbol;Acc:HGNC:29039]	ENSG00000163125.15	chr1	150472047	150472557	CDS	ENSRNOG00000054294.1	chr2	197887026	197887983	CDS
SACS	**1**	sacsin molecular chaperone [Source:HGNC Symbol;Acc:HGNC:10519]	ENSG00000151835.16	chr13	23330114	23330625	CDS	ENSRNOG00000014509.8	chr15	41458799	41459189	UTR5
	2								chr15	41527489	41527850	CDS
	3								chr15	41528838	41529289	CDS
SEC23IP	**1**	SEC23 interacting protein [Source:HGNC Symbol;Acc:HGNC:17018]	ENSG00000107651.13	chr10	119898485	119898696	CDS	ENSRNOG00000020411.6	chr1	200167168	200175910	CDS
SF3B4	**1**	splicing factor 3b subunit 4 [Source:HGNC Symbol;Acc:HGNC:10771]	ENSG00000143368.10	chr1	149926597	149926777	CDS	ENSRNOG00000021181.5	chr2	198314014	198314417	CDS
SUB1	**1**	SUB1 regulator of transcription [Source:HGNC Symbol;Acc:HGNC:19985]	ENSG00000113387.12	chr5	32591504	32591655	CDS	ENSRNOG00000050563.2	chr2	62029817	62034628	CDS
THRAP3	**1**	thyroid hormone receptor associated protein 3 [Source:HGNC Symbol;Acc:HGNC:22964]	ENSG00000054118.15	chr1	36286644	36286795	CDS	ENSRNOG00000009977.6	chr5	144193441	144193681	CDS
TMF1	**1**	TATA element modulatory factor 1 [Source:HGNC Symbol;Acc:HGNC:11870]	ENSG00000144747.17	chr3	69044588	69047549	CDS	ENSRNOG00000056462.1	chr4	129542166	129544387	CDS
TNIK	**1**	TRAF2 and NCK interacting kinase [Source:HGNC Symbol;Acc:HGNC:30765]	ENSG00000154310.17	chr3	171063507	171063898	CDS	ENSRNOG00000012422.7	chr2	114299772	114317137	CDS
TULP4	**1**	TUB like protein 4 [Source:HGNC Symbol;Acc:HGNC:15530]	ENSG00000130338.13	chr6	158312464	158312705	UTR5	ENSRNOG00000018012.7	chr1	47122864	47123345	CDS
	2			chr6	158312513	158312662	UTR5					
UMPS	**1**	uridine monophosphate synthetase [Source:HGNC Symbol;Acc:HGNC:12563]	ENSG00000114491.14	chr3	124737630	124738199	CDS	ENSRNOG00000001797.6	chr11	70034138	70041367	CDS

Supplemental Table 4

Gene ontology (GO) analysis of transcripts with m^6A peak enrichment determined by exomePeak analysis in rat hypertrophic or control RNA samples. Red indicates an overlap in GO category when using either total transcriptome (left) or heart-specific transcriptome (right) as background.

Hypertrophic

Molecular Function

Total Background

Description	Enrichment	FDR
phosphatidic acid binding	9.917477618	1.30E-05
oxidoreductase activity	5.628838648	0.04658608
transcription factor binding	2.75946553	0.058778444
transcription coregulator activity	2.413690745	0.098134672
actin binding	2.363843231	0.098134672
chromatin binding	2.301801834	0.098134672
ubiquitin-like protein transferase activity	2.161941488	0.14076141
ubiquitin-protein transferase activity	2.107463994	0.222643825
protein serine/threonine kinase activity	2.016857069	0.307623313
protein kinase activity	1.936674814	0.307623313

Heart Background

Description	Enrichment	FDR
phosphatidic acid binding	7.783985102	0.518482093
histone kinase activity	6.368715084	0.797719437
oxidoreductase activity	3.891992551	0.797719437
transcription factor binding	2.133681196	0.01007687
actin binding	1.945996276	0.633831376
chromatin binding	1.858460111	0.627842282
double-stranded DNA binding	1.690639298	0.627842282
sequence-specific double-stranded DNA binding	1.685192651	0.633831376
transcription regulatory region sequence-specific DNA binding	1.667996808	0.797719437
RNA polymerase II regulatory region DNA binding	1.643539376	0.797719437

Cellular Component

Total Background

Description	Enrichment	FDR
lamellipodium	3.77179147	0.011660323
cell leading edge	3.498473248	1.28E-04
mitochondrial membrane part	3.324995235	0.004704933
nuclear speck	3.258204938	0.002706732
endosome membrane	2.963033729	0.009199722
mitochondrial envelope	2.737601711	1.28E-04
axon part	2.595034842	0.003368264
nuclear body	2.593496284	0.001533004
mitochondrial membrane	2.581761006	0.001485982
vesicle membrane	2.558002469	0.011660323

Heart Background

Description	Enrichment	FDR
fibrillar center	3.420223325	0.088890423
cytoplasmic ribonucleoprotein granule	3.228329607	0.088890423
ribonucleoprotein granule	2.964193548	0.088890423
endosome membrane	2.336310186	0.088890423
nuclear speck	2.324857685	0.088890423
cell leading edge	2.309761207	0.088890423
vesicle membrane	2.243811849	0.088890423
cytoplasmic vesicle membrane	2.232447024	0.088890423
cytoplasmic vesicle part	1.89491825	0.088890423
axon	1.817370252	0.088890423

Control

Molecular Function

Total Background

Description	Enrichment	FDR
NADH dehydrogenase (ubiquinone) activity	17.03074866	0.038485532
NADH dehydrogenase (quinone) activity	17.03074866	0.038485532
fatty acid synthase activity	17.03074866	0.574292389
NADH dehydrogenase activity	14.41063348	0.044294978
oxidoreductase activity, acting on NAD(P)H, quinone or similar compound as acceptor	13.87690632	0.044294978
bHLH transcription factor binding	13.38130252	0.19309006
E-box binding	10.40767974	0.095707591
oxidoreductase activity, acting on NAD(P)H	5.947245565	0.496929356
phosphoric ester hydrolase activity	2.968387531	0.418296924
transcription factor binding	2.74344696	0.095707591

Heart Background

Description	Enrichment	FDR
NADH dehydrogenase (ubiquinone) activity	12.94117647	0.089478915
NADH dehydrogenase (quinone) activity	12.94117647	0.089478915
bHLH transcription factor binding	10.84775087	0.336396432
NADH dehydrogenase activity	10.69053708	0.108295035
oxidoreductase activity, acting on NAD(P)H, quinone or similar compound as acceptor	10.24509804	0.108295035
E-box binding	9.835294118	0.108295035
oxidoreductase activity, acting on NAD(P)H	4.639289678	1
transferase activity, transferring acyl groups other than amino-acyl groups	2.711937716	1
phosphatase activity	2.501709986	1
phosphoric ester hydrolase activity	2.415874647	1

Cellular Component

Total Background

Description	Enrichment	FDR
transcriptionally active chromatin	23.57601351	0.042966681

Heart Background

Description	Enrichment	FDR
transcriptionally active chromatin	15.953125	0.116372712

apical dendrite	17.96267696	0.066088586
PML body	9.861861862	0.068577228
RNA polymerase II transcription factor complex	5.715397215	0.122655772
centrosome	4.864891677	0.001758427
nuclear speck	4.392619694	0.0650546
ribosome	4.037482437	0.122655772
nuclear body	4.000778051	0.00339585
microtubule organizing center	3.729538861	0.004967309
mitochondrial membrane	3.01334668	0.089554263

apical dendrite	15.01470588	0.116372712
PML body	7.241134752	0.222263568
mitochondrial respiratory chain complex I	6.898648649	0.388829065
NADH dehydrogenase complex	6.898648649	0.388829065
recycling endosome	4.170751634	0.388829065
centrosome	3.58245614	0.075106605
microtubule organizing center	2.843401885	0.116372712
nuclear body	2.779103853	0.116372712
mitochondrial membrane	2.412156357	0.388829065

Supplemental Table 5

m^{6}A peaks and transcript location determined by exomePeak analysisthat are found to overlap between human non-failing and rat control RNA samples.

gene name	peak	description	hu_ensembl	hu_chromosome	hu_start	hu_end	hu_location	rt_ensembl	rt_chromosome	rt_start	rt_end	rt_location
ASPH	**1**	aspartate beta-hydroxylase [Source:HGNC Symbol;Acc:HGNC:757]	ENSG00000198363.18	chr8	61658846	61659296	UTR3	ENSRNOG00000007445.8	chr5	22746016	22746526	UTR3
CEP85L	**1**	centrosomal protein 85 like [Source:HGNC Symbol;Acc:HGNC:21638]	ENSG00000111860.14	chr6	118465320	118469183	CDS	ENSRNOG00000000414.7	chr20	34616020	34647036	CDS
CORO6	**1**	coronin 6 [Source:HGNC Symbol;Acc:HGNC:21356]	ENSG00000167549.18	chr17	29615351	29615739	UTR3	ENSRNOG00000014496.7	chr10	62691982	62692726	UTR3
DNAAF2	**1**	dynein axonemal assembly factor 2 [Source:HGNC Symbol;Acc:HGNC:20188]	ENSG00000165506.14	chr14	49633703	49633973	CDS	ENSRNOG00000028155.6	chr6	91481953	91489408	CDS
ITGB5	**1**	integrin subunit beta 5 [Source:HGNC Symbol;Acc:HGNC:6160]	ENSG00000082781.12	chr3	124887216	124887690	UTR5	ENSRNOG00000001795.8	chr11	70057127	70062395	CDS
MEDAG	**1**	mesenteric estrogen dependent adipogenesis [Source:HGNC Symbol;Acc:HGNC:25926]	ENSG00000102802.10	chr13	30924410	30924619	CDS	ENSRNOG00000000906.7	chr12	6711746	6712339	UTR3
P3H3	**1**	prolyl 3-hydroxylase 3 [Source:HGNC Symbol;Acc:HGNC:19318]	ENST00000290510.9	chr12	6839309	6839847	CDS	ENSRNOG00000016071.6	chr4	157363026	157363640	CDS
	2			chr12	6839308	6839847	Intron					
PCSK7	**1**	proprotein convertase subtilisin/kexin type 7 [Source:HGNC Symbol;Acc:HGNC:8748]	ENSG00000160613.13	chr11	117205776	117206137	CDS	ENSRNOG00000017478.5	chr8	50221556	50222183	CDS
SON	**1**	SON DNA binding protein [Source:HGNC Symbol;Acc:HGNC:11183]	ENSG00000159140.21	chr21	33553014	33553255	CDS	ENSRNOG00000002021.8	chr11	31812680	31812831	CDS
	2			chr21	33553733	33554123	CDS					
	3			chr21	33551218	33551968	CDS					
UNC13B	**1**	unc-13 homolog B [Source:HGNC Symbol;Acc:HGNC:12566]	ENSG00000198722.14	chr9	35404229	35404319	UTR3	ENSRNOG00000008237.8	chr5	58714855	58715126	UTR3
XPR1	**1**	xenotropic and polytropic retrovirus receptor 1 [Source:HGNC Symbol;Acc:HGNC:12827]	ENSG00000143324.14	chr1	180632021	180632261	CDS	ENSRNOG00000000042.7	chr13	72918489	72920930	CDS