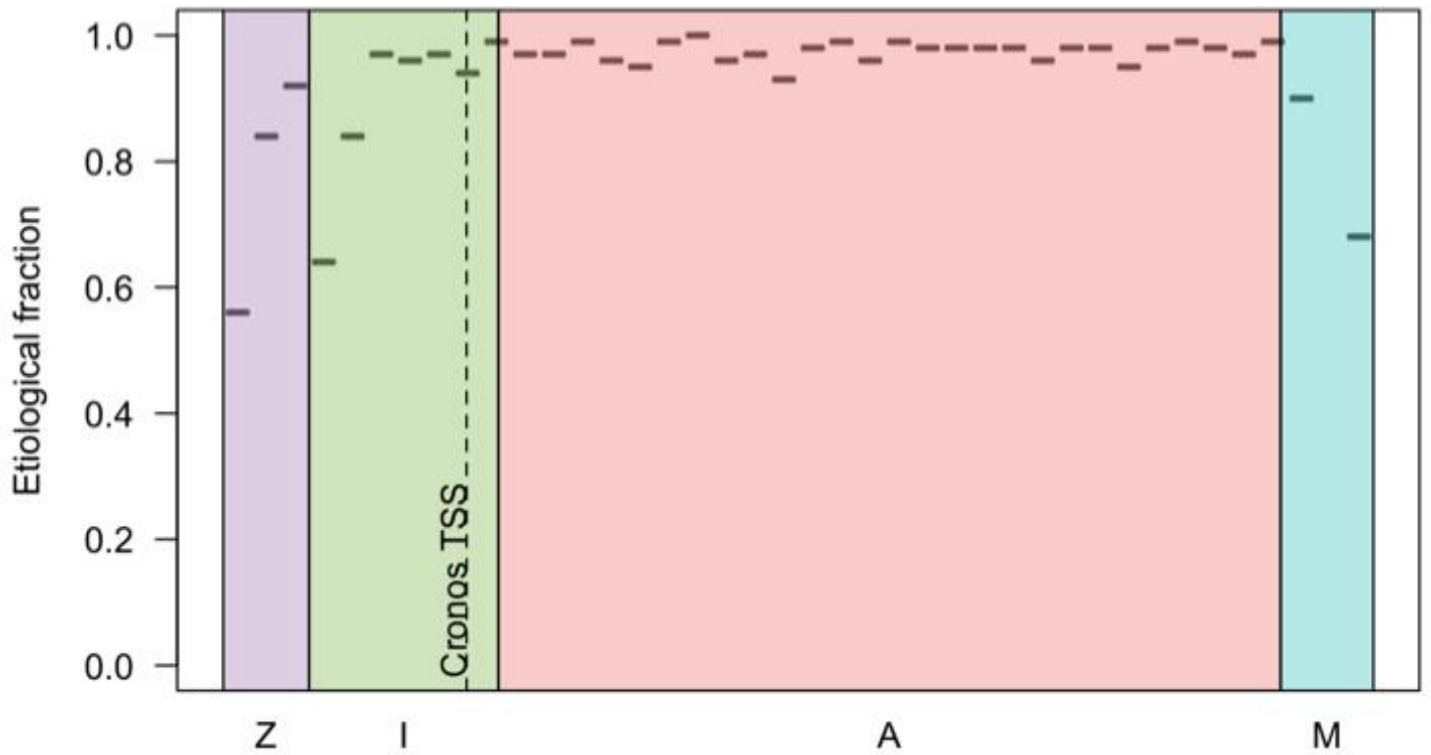


**Supplementary Figure 1**

**Identification of an alternative, distal transcription start site in Titin.**

From outside to inside, track 1 shows the location of the subunits of titin; the gene is on the antisense strand and so is transcribed counterclockwise in this view. Track 2 shows the gene structure of titin with the exons shown as orange rectangles and the introns shown as black lines. Track 3 shows the location of transcription start sites identified by the analysis of CAGE data taken from human heart samples in the FANTOM5 consortium as identified using CAGEr. Track 4 shows the location of H3K4me3 ChIP-seq narrow peaks (a mark of active promoters) from fetal heart samples in the Epigenomics Roadmap data set. Track 5 shows H3K4me3 ChIP-seq peaks from adult heart (left ventricle) taken from the Epigenomics Roadmap data set. Track 6 shows H3K9ac (also a mark of active promoters) taken from the fetal heart samples in the Epigenomics Roadmap data set. Together these data show that in the heart there are likely two transcription start sites, the canonical transcription start site at the beginning of the gene and another transcription start site found close to the start A-band, which appears to be most strongly used in fetal heart but is still present in adult human heart.



**Supplementary Figure 2**

**Etiological fraction of TTNtv in 40 bins across the titin locus.**

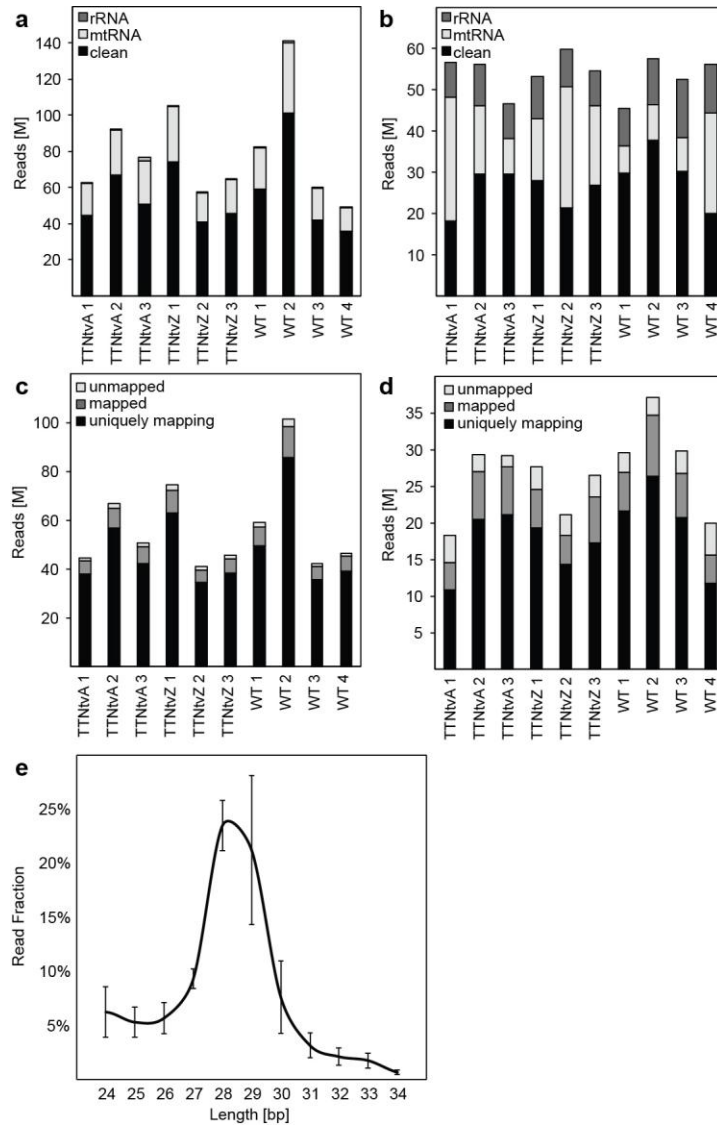
The constitutive (PSI > 90%) regions of titin are split into 40 bins ranging from the N terminus to the C terminus, and the etiological fraction of TTNtv for each individual region is plotted. The dashed line marks the position of the internal *Cronos* promoter. Purple, Z-disc; green, I-band; pink, A-band; blue, M-line.



### Supplementary Figure 3

#### Truncating mutations introduced to F344 rats.

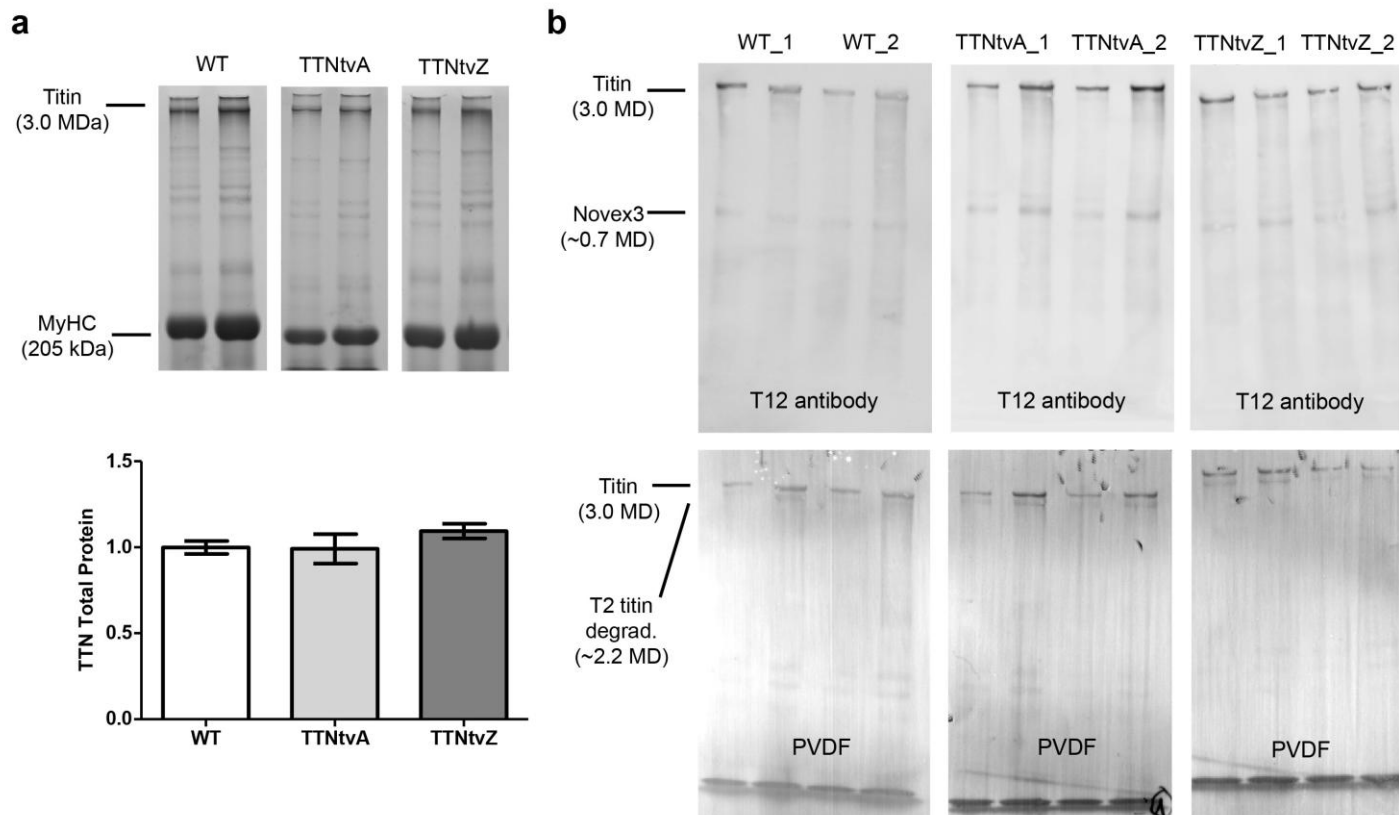
(a) The proximal truncating variant in titin is a large deletion located near the Z-disc at the N terminus of the meta transcript (TTNvZ). It spans from exon 2 (b) to exon 6 (c). Exons 3–5 are not present in TTNvZ rats and can thus be used to assess transcription and translation from the wild-type allele in heterozygous animals. (d) The deletion causes a frameshift that results in a premature stop codon located in exon 7. (e) The truncating variant in the A-band is located in the large exon 312 and an indel that also causes a frameshift and introduces a stop codon shortly after.



**Supplementary Figure 4**

**RNA sequencing and ribosome profiling data for TTNvA, TTNvZ and wild-type rats.**

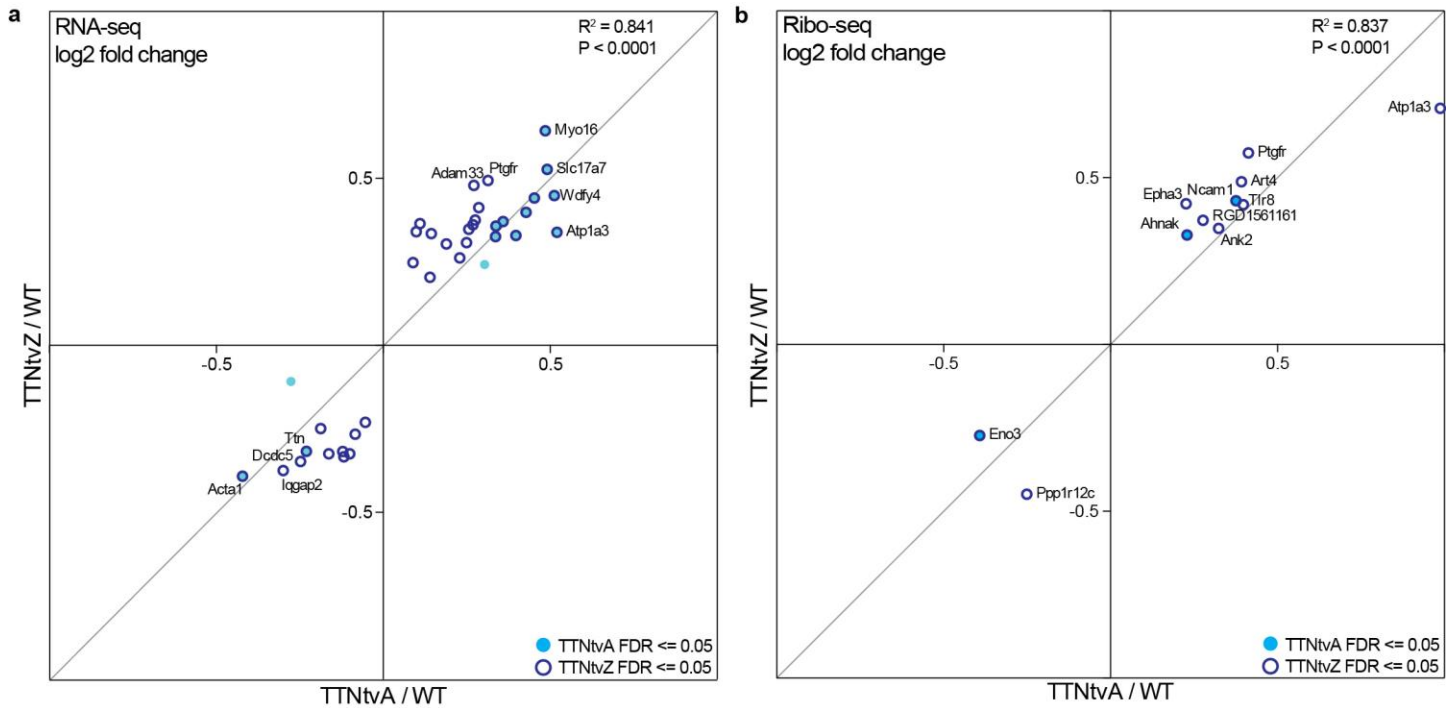
(a,b) RNA-seq reads (a) and Ribo-seq reads (b) mapping to mitochondrial and ribosomal sequences were filtered out, and the remaining sequences were mapped to the genome. (c,d) Uniquely mapping RNA-seq (c) and Ribo-seq (d) reads were counted and used in later analyses to assess gene expression on the transcriptional and translational levels. (e) After adaptor trimming, Ribo-seq libraries displayed a size distribution typical for ribosome profiling experiments: ribosomes mostly protected RNA fragments of 28 and 29 bp in size.



### Supplementary Figure 5

#### Absence of truncated Ttn protein in TTNtvA and TTNtvZ rat hearts.

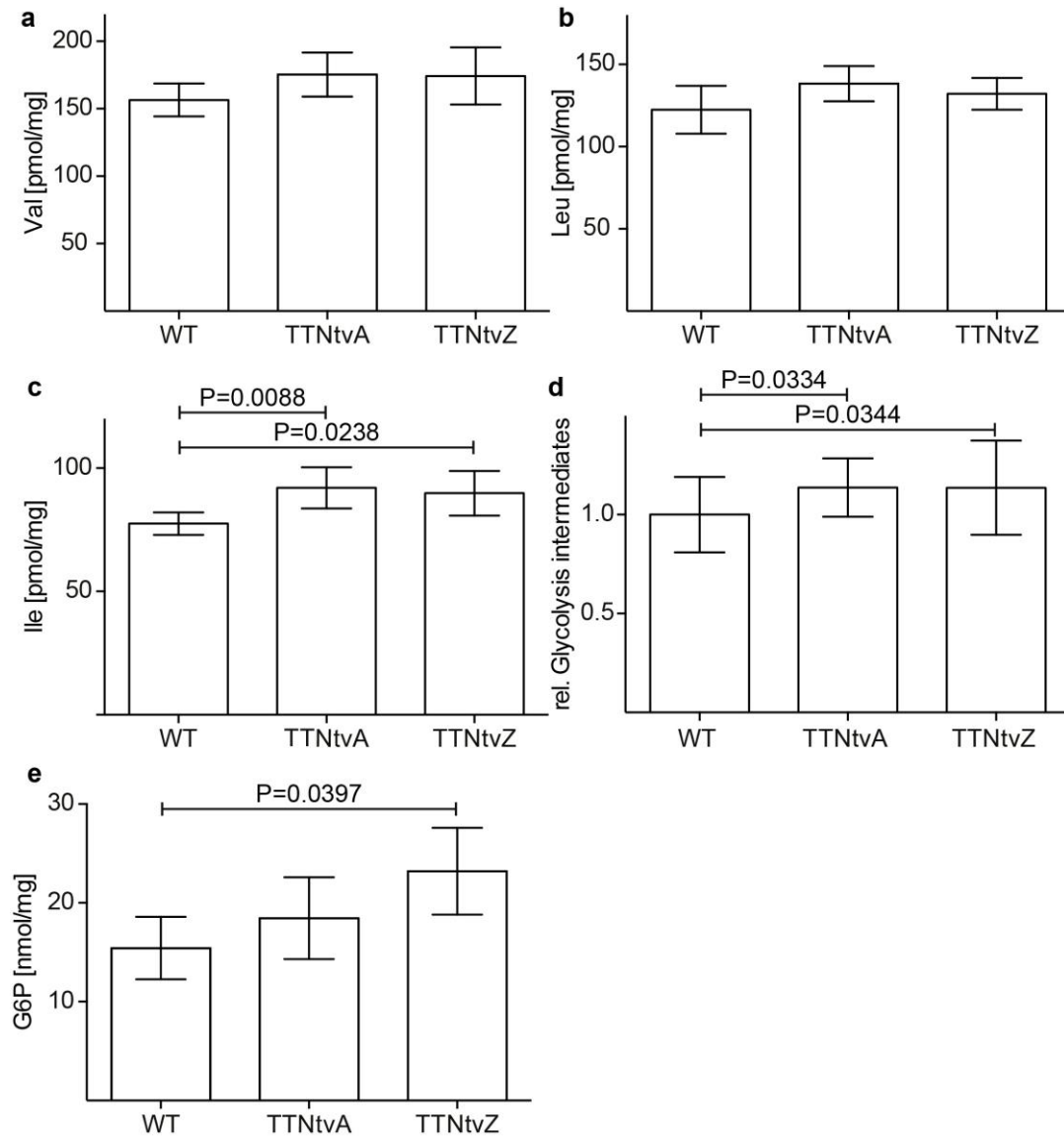
Representative titin gels and immunoblots from 3-month-old wild-type, TTNtvA and TTNtvZ rat hearts. **(a)** SDS-PAGE was performed on 2.5% polyacrylamide/1% agarose gels, and total protein was visualized by Coomassie blue staining. Each sample was analyzed in duplicate at lower (left) and higher (right) protein concentration. Mhc was used as a loading control. The relative Ttn/Mhc ratio was determined (below). Data are shown as means  $\pm$  s.e.m. ( $n = 4$ /group). **(b)** Immunoblotting analysis on 1.8% polyacrylamide/1% agarose gel transferred to PVDF and blotted with T12 antibody against titin and Novex3 (top). The corresponding PVDF blot was used as loading control (bottom).



**Supplementary Figure 6**

**Transcriptional and translational gene expression differences between wild-type and TTNtv rats.**

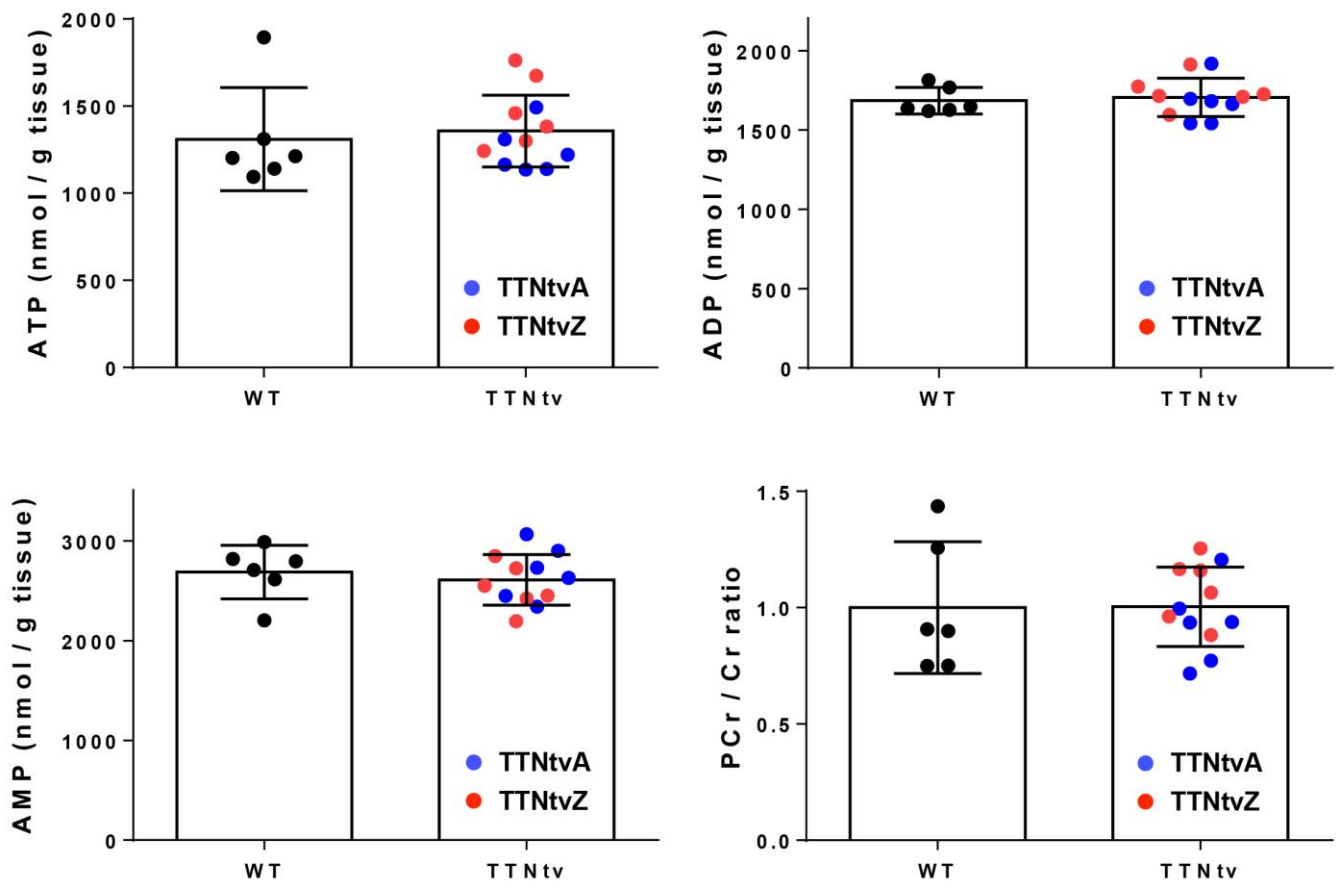
(a,b) Differential gene transcription (a) and translation (b) is compared between TTNtv and wild-type rats. Both TTNtvA and TTNtvZ show highly correlated fold changes in differentially expressed genes (DEseq2 FDR ≤ 0.05) when compared to control rats (Pearson correlation). Genes that were not differentially expressed in any comparison were not considered.



**Supplementary Figure 7**

**Differences in cardiac metabolism between wild-type, TTNtvA and TTNtvZ rats.**

(a–c) Metabolite profiles showing branched-chain amino acids, including valine (a), leucine (b) and isoleucine (c). (d) Sum of measured glycolytic intermediates (metabolites are detailed in **Supplementary Table 3**). (e) Glucose-6-phosphate (G6P) levels in cardiac tissue from wild-type ( $n = 6$ ) and TTNtv (TTNtvA,  $n = 6$ ; TTNtvZ,  $n = 6$ ) rats. Data are shown as mean  $\pm$  s.d. (Dunnett).

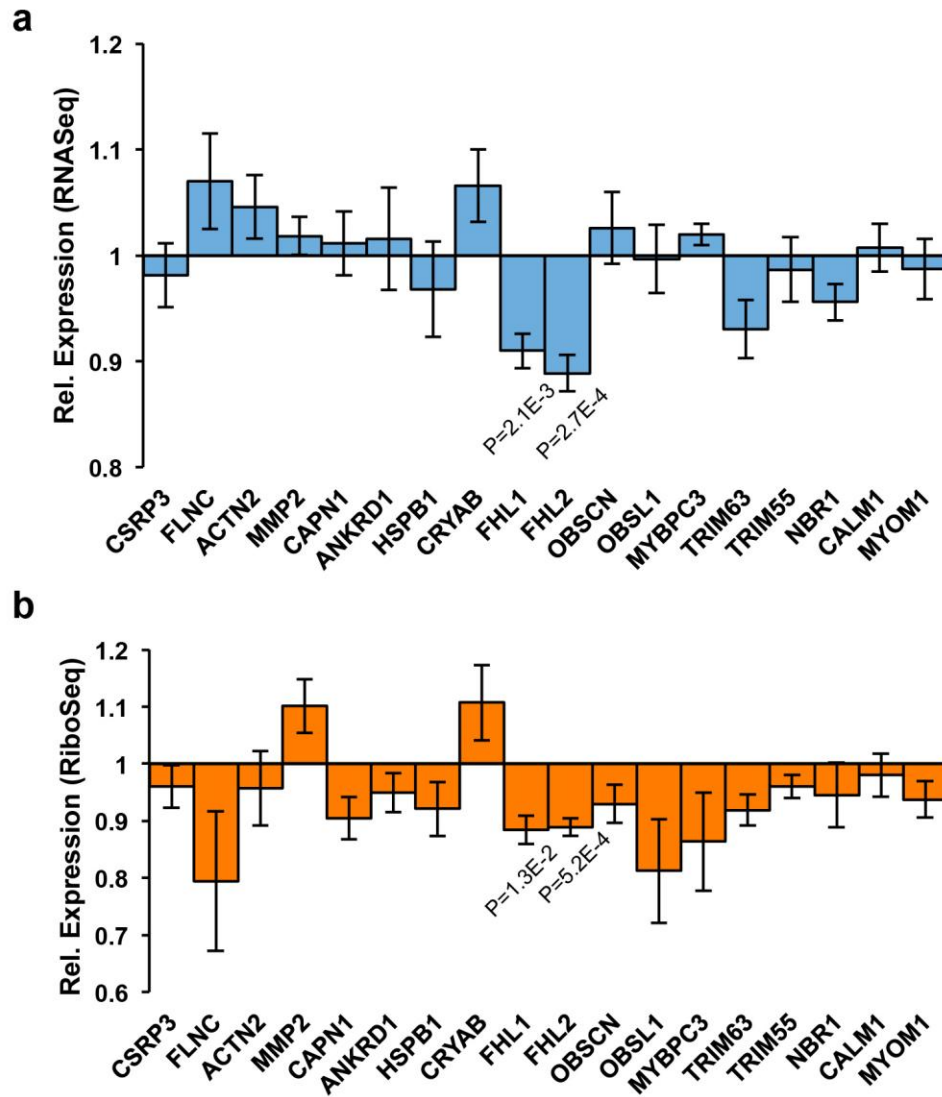


**Supplementary Figure 8**

**TTNtv rat hearts have normal energy substrate abundance.**

Metabolite levels of ATP, ADP, AMP and ratio of phosphocreatine (PCr) to creatine (Cr) in 4-month-old wild-type ( $n = 6$ ) and TTNtv (TTNtvA,  $n = 6$ ; TTNtvZ,  $n = 6$ ) rat hearts.

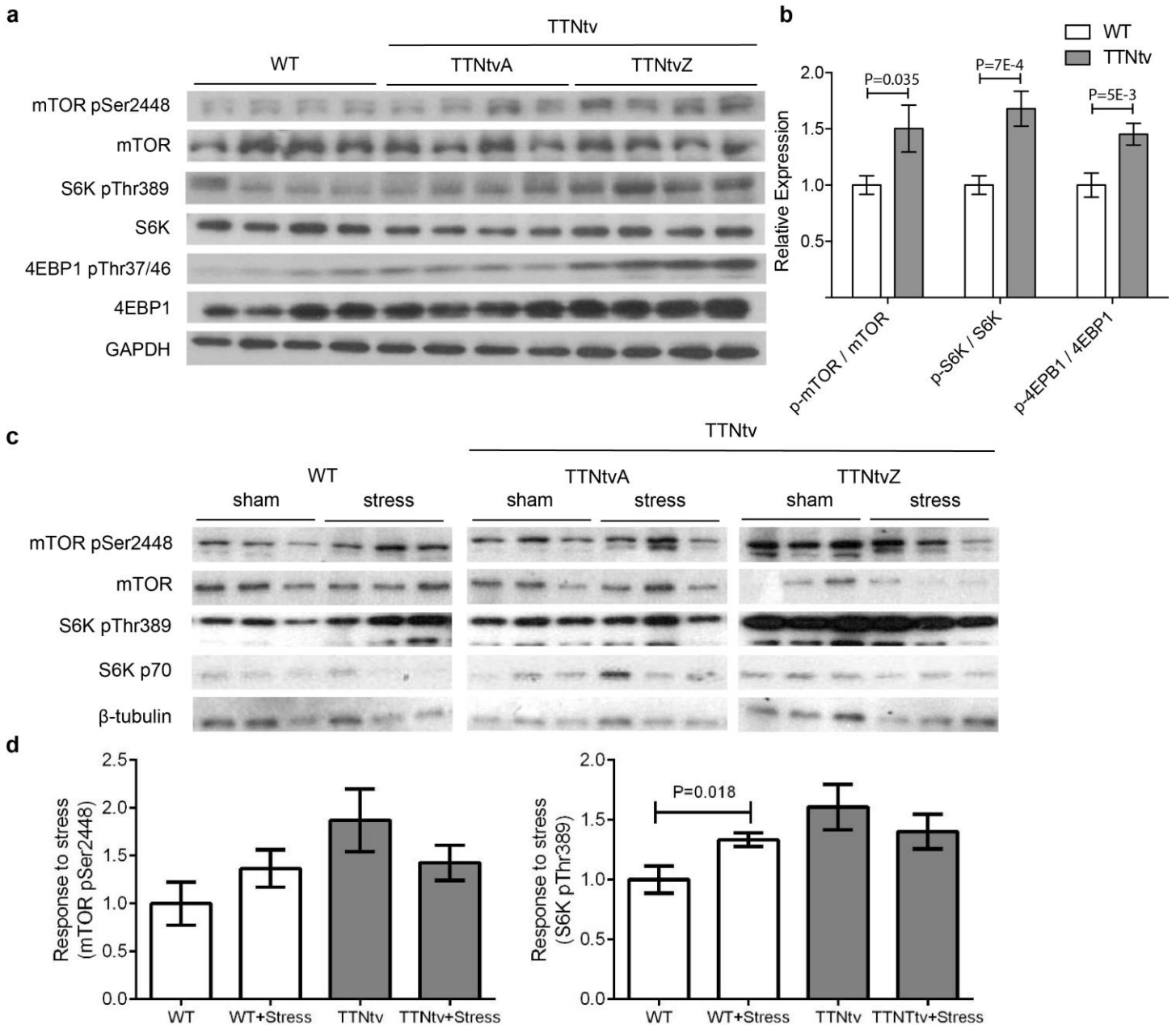




Supplementary Figure 9

Relative expression of titin-associated proteins in wild-type and TTNtv rats.

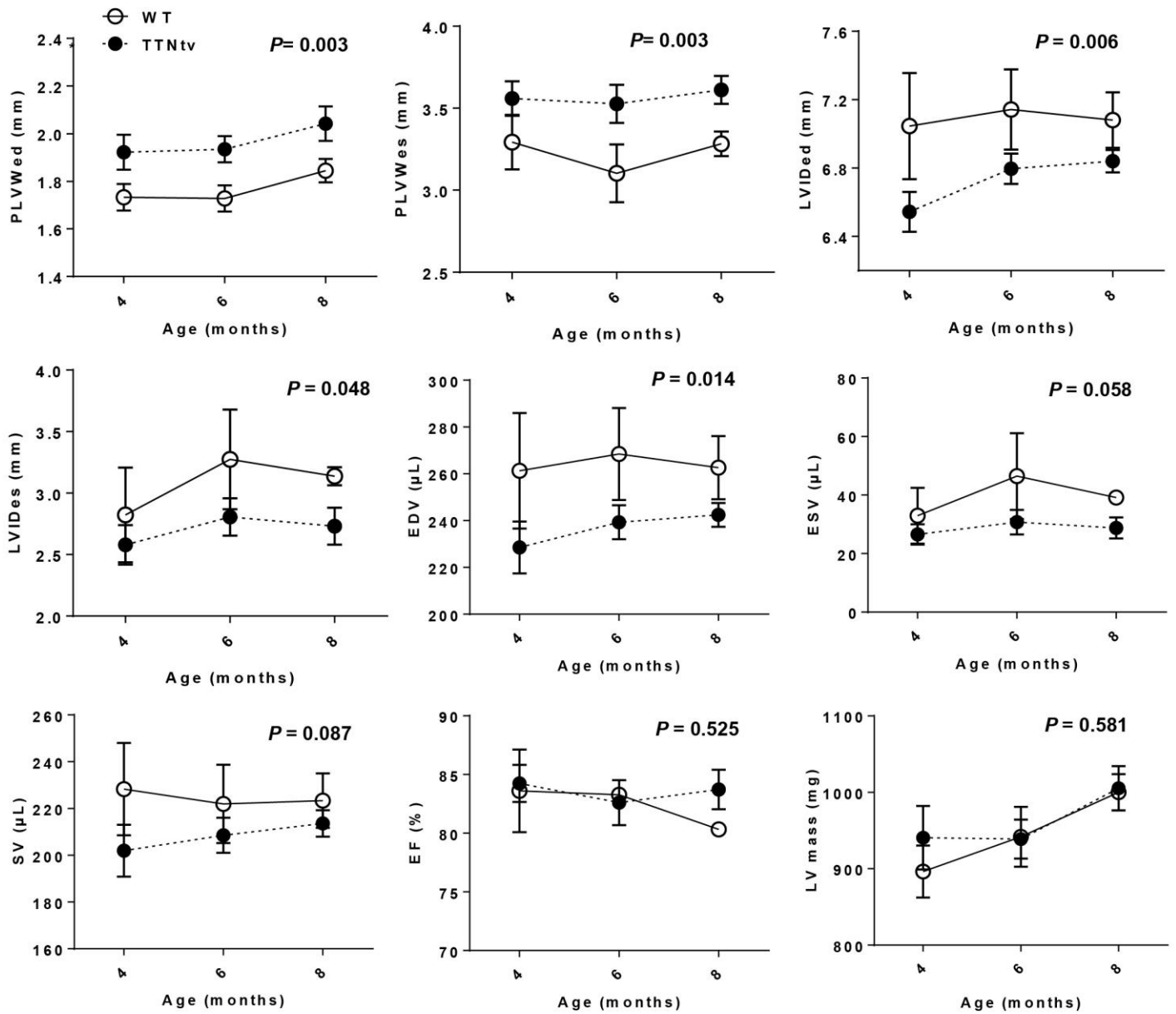
(a,b) Relative difference (TTNtv/WT) in transcription (a) and translation (b) of titin-associated proteins showing a significant decrease in FHL1 and FHL2 expression in 8-week-old TTNtv (TTNtvA,  $n = 3$ ; TTNtvZ,  $n = 3$ ) as compared to wild-type ( $n = 4$ ) rats. Data are shown as mean fold change  $\pm$  s.e.m. \* $P < 0.05$  (DEseq2  $P$  value, not corrected for genome-wide testing).



**Supplementary Figure 10**

**mTORC1 signaling is altered in TTNtv rat hearts.**

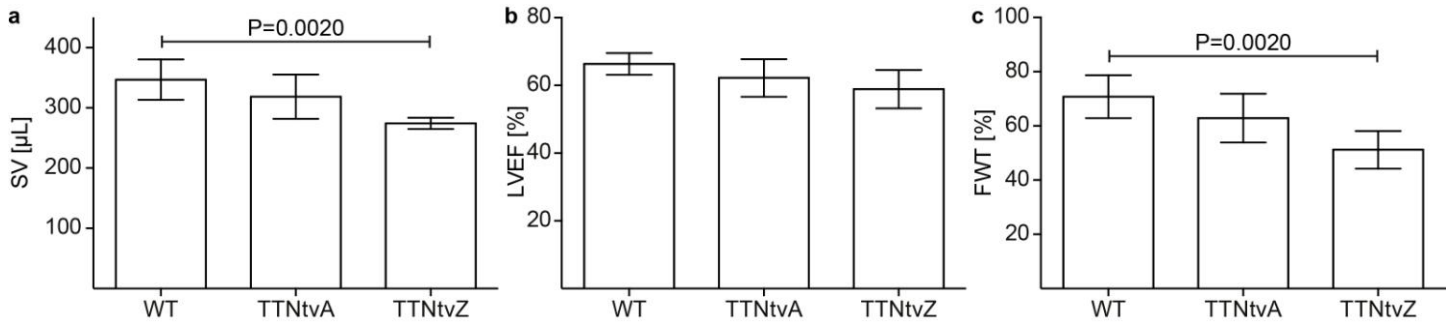
(a) Immunoblot analysis showing increased phosphorylation of mTOR (Ser2448), S6 kinase (Thr389) and 4EBP1 (Thr37/46) in TTNtv as compared to wild-type hearts in extracts from rats immediately after sacrifice. (b) Semiquantitative densitometry of band intensities from several immunoblots across separate experiments and shown as means  $\pm$  s.e.m. (Student's *t* test, Welsh correction). (c) Immunoblot analysis of phosphorylated mTOR (Ser2448) and S6 kinase (Thr389) in myocardial tissue following sham treatment or volume overload in wild-type and TTNtv rat hearts on the Langendorff apparatus perfused for the same duration. (d) Semiquantitative densitometry representation of band intensities from the blot in c and other experiments showing mTOR and S6K response to acute stress relative to wild-type unstressed hearts of the respective genotypes. Data are shown as means  $\pm$  s.d. (versus unstressed wild-type hearts, Student's *t* test, Welsh correction).



Supplementary Figure 11

**Young TTNtv rats display concentric remodeling.**

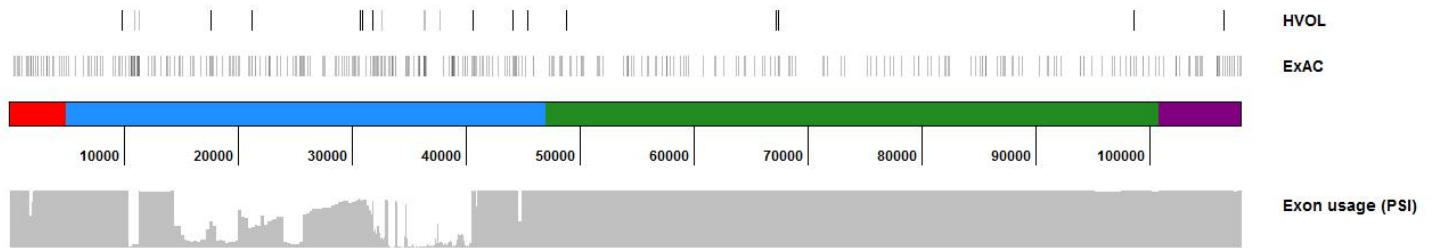
Echocardiographic measurements of 4- to 8-month-old male wild-type ( $n = 4$ ) and TTNtv (TTNtvA,  $n = 4$ ; TTNtvZ,  $n = 4$ ) rats. PLVWed (mm), posterior left ventricular wall thickness end diastole; PLVWes (mm), posterior left ventricular wall thickness end diastole; LVIDed (mm), left ventricular internal diameter end diastole; LVIDes (mm), left ventricular internal diameter end systole; EDV ( $\mu$ L), end-diastolic volume; ESV ( $\mu$ L), end-systolic volume; SV ( $\mu$ L), stroke volume. EF (%), ejection fraction.  $P$  values indicate statistical analysis by two-way analysis of variance (ANOVA).



## Supplementary Figure 12

### CMR in TTNtvA and TTNtvZ rats.

(a–c) SV (stroke volume) (a), LVEF (left ventricular ejection fraction) (b) and FWT (fractional wall thickening) (c) measured with CMR in 13- to 16-month-old male wild-type ( $n = 5$ ) and TTNtv (TTNtvA,  $n = 8$ ; TTNtvZ,  $n = 6$ ) rats. Data are shown as means  $\pm$  s.d. (Dunnett).



### Supplementary Figure 13

#### Distribution of TTNtv detected in the general population for MRI.

The top track shows the distribution of TTNtv in healthy volunteers (HVOL) who were phenotyped using cardiac magnetic resonance imaging. The track below depicts the distribution of TTNtv from ExAC data. Only truncations located in exons with PSI >15% are shown.

## Supplementary Tables

**Supplementary Table 1. Differential gene expression on the transcriptional and translational level as assessed by DESeq2 (FDR = 0.05). Green depicts down- and blue indicates up-regulated genes in TTNtv animals.**

Ensembl ID	Gene Symbol	log 2 Fold Change TTNtv / WT				Adj. P-value TTNtv vs WT			
		RNA-seq		Ribo-seq		RNA-seq		Ribo-seq	
		TTNtvA	TTNtvZ	TTNtvA	TTNtvZ	TTNtvA	TTNtvZ	TTNtvA	TTNtvZ
ENSRNOG00000000164	Lamp2	0.01	0.03	0.18	0.18	0.028	n.s.	n.s.	n.s.
ENSRNOG000000001522	Metap1d	-0.08	-0.06	-0.03	0.04	n.s.	1.2E-06	n.s.	n.s.
ENSRNOG000000003189	Cited1	0.14	0.33	0.11	0.19	n.s.	0.011	n.s.	n.s.
ENSRNOG000000003284	Epn3	0.29	0.41	0.04	0.06	n.s.	0.002	n.s.	n.s.
ENSRNOG000000003626	Atp5h	-0.01	0.03	-0.08	0.05	0.002	0.001	n.s.	n.s.
ENSRNOG000000004078	Eno3	-0.23	-0.18	-0.39	-0.27	n.s.	n.s.	5.3E-06	0.024
ENSRNOG000000005670	Art4	0.43	0.40	0.39	0.49	5.6E-04	2.2E-03	n.s.	0.003
ENSRNOG000000006509	Srgap3	0.25	0.31	-0.02	0.20	n.s.	0.028	n.s.	n.s.
ENSRNOG000000007545	Angptl4	0.09	0.25	0.03	0.30	n.s.	0.016	n.s.	n.s.
ENSRNOG000000007674	Nacad	0.27	0.36	0.18	0.35	n.s.	0.013	n.s.	n.s.
ENSRNOG000000009691	Lrrn2	0.45	0.44	0.21	0.17	1.7E-04	3.1E-04	n.s.	n.s.
ENSRNOG000000011076	Ank2	-0.02	-0.08	0.23	0.33	n.s.	n.s.	n.s.	0.016
ENSRNOG000000011491	Dnajc13	-0.04	-0.04	0.08	0.17	n.s.	0.008	n.s.	n.s.
ENSRNOG000000014933	Dnttip1	0.03	-0.03	0.01	-0.01	3.3E-03	0.000	n.s.	n.s.
ENSRNOG000000015852	Arhgap35	0.02	-0.04	0.14	0.08	n.s.	0.016	n.s.	n.s.
ENSRNOG000000015912	Ptdss2	-0.06	-0.10	0.06	0.06	n.s.	0.003	n.s.	n.s.
ENSRNOG000000016483	Myo16	0.49	0.64	0.37	0.45	3.4E-05	5.8E-10	n.s.	n.s.
ENSRNOG000000016892	Nr2f6	-0.05	-0.23	-0.10	-0.03	n.s.	0.028	n.s.	n.s.
ENSRNOG000000017460	Imp3	0.00	-0.12	0.01	0.01	n.s.	0.003	n.s.	n.s.
ENSRNOG000000017503	Ppargc1b	-0.14	-0.24	-0.17	-0.22	0.001	0.001	n.s.	n.s.
ENSRNOG000000017786	Acta1	-0.42	-0.39	-0.53	-0.41	n.s.	n.s.	0.003	n.s.
ENSRNOG000000018610	Pde6d	0.05	-0.04	0.05	0.02	1.8E-08	0.003	n.s.	n.s.
ENSRNOG000000019028	Znrf2	-0.06	-0.13	-0.04	0.00	n.s.	0.003	n.s.	n.s.
ENSRNOG000000019094	Gstm2	0.06	0.04	0.03	-0.03	n.s.	0.016	n.s.	n.s.
ENSRNOG000000020263	Atp1a3	0.52	0.34	0.99	0.71	n.s.	n.s.	n.s.	1.8E-06
ENSRNOG000000020373	Dap3	-0.04	-0.01	-0.14	-0.12	n.s.	0.008	n.s.	n.s.
ENSRNOG000000020417	Gsk3a	-0.03	-0.07	-0.09	0.00	0.001	0.003	n.s.	n.s.
ENSRNOG000000020641	RGD1560789	-0.16	-0.32	-0.21	-0.08	n.s.	0.034	n.s.	n.s.
ENSRNOG000000020650	Slc17a7	0.49	0.53	0.31	0.34	3.4E-05	2.5E-06	n.s.	n.s.
ENSRNOG000000020915	Setd2	-0.05	-0.12	-0.11	-0.10	n.s.	0.001	n.s.	n.s.
ENSRNOG000000021095	Fxyd3	0.40	0.33	0.25	0.26	6.5E-04	1.6E-02	n.s.	n.s.
ENSRNOG000000021242	Adam33	0.27	0.48	0.09	0.18	n.s.	0.000	n.s.	n.s.
ENSRNOG000000022178	Dcdc5	-0.25	-0.35	-0.19	-0.28	n.s.	0.015	n.s.	n.s.
ENSRNOG000000025518	Lrrc16b	0.19	0.30	-0.05	0.16	n.s.	0.001	n.s.	n.s.
ENSRNOG000000027959	Ppp1r12c	-0.13	-0.13	-0.25	-0.45	n.s.	n.s.	n.s.	0.001
ENSRNOG000000028498	Wdr1	-0.05	-0.02	-0.05	-0.04	n.s.	0.016	n.s.	n.s.
ENSRNOG000000029662	Wdfy4	0.51	0.45	0.32	0.39	1.5E-07	1.4E-05	n.s.	n.s.
ENSRNOG000000030285	Epha3	-0.01	0.16	0.23	0.42	n.s.	n.s.	n.s.	0.016
ENSRNOG000000031890	Ncam1	0.36	0.37	0.38	0.43	n.s.	n.s.	0.014	0.001
ENSRNOG000000033893	Cacna1h	0.34	0.36	0.24	0.30	0.034	0.008	n.s.	n.s.
ENSRNOG000000039582	RGD1561161	0.19	0.15	0.28	0.37	n.s.	n.s.	n.s.	0.039
ENSRNOG000000040201	Atp6ap1l	0.28	0.38	0.22	0.34	n.s.	0.001	n.s.	n.s.
ENSRNOG000000042245	Dcaf7	-0.06	-0.12	0.03	-0.03	0.034	n.s.	n.s.	n.s.
ENSRNOG000000045992	Tlr8	-0.02	-0.06	0.40	0.42	n.s.	n.s.	n.s.	0.029
ENSRNOG000000046468	Ptgr	0.31	0.49	0.41	0.57	n.s.	n.s.	n.s.	0.001
ENSRNOG000000046772	Fam83c	0.26	0.35	0.11	0.08	n.s.	0.016	n.s.	n.s.
ENSRNOG000000050145	Ahnak	0.08	0.01	0.32	0.35	n.s.	n.s.	n.s.	0.030
ENSRNOG000000050841	Ache	0.11	0.36	0.13	0.28	n.s.	0.003	n.s.	n.s.

**Supplementary Table 2. Metabolite measurements of acylcarnitines from WT and TTNtv rat hearts.**

Acylcarnitine	Concentration (pmol/mg tissue)								TTNtv/WT Ratio	TTNtv/WT P value
	WT (n=5)		TTNtvA (n=5)		TTNtvZ (n=5)		TTNtv			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
C2	394.91	43.55	528.12	104.03	297.18	86.89	412.65	137.78	1.04	0.717
C3	4.36	0.99	5.76	1.68	4.84	1.84	5.30	1.80	1.22	0.213
C4	8.99	1.78	11.11	1.26	7.79	1.65	9.45	2.23	1.05	0.693
C5:1	0.56	0.11	0.50	0.08	0.61	0.18	0.55	0.14	0.99	0.966
C5	1.26	0.43	1.24	0.42	1.78	0.90	1.51	0.69	1.20	0.404
C4-OH	8.02	2.43	9.98	2.85	8.20	5.40	9.09	4.21	1.13	0.544
C6	3.16	0.92	2.45	0.80	1.40	0.58	1.93	0.71	0.61	0.036
C5-OH/C3-DC	3.67	0.51	4.23	0.66	3.08	0.53	3.66	0.82	1.00	0.971
C4-DCC6-OH	10.77	1.78	13.32	2.02	9.63	2.12	11.47	2.63	1.07	0.553
C8	1.14	0.43	0.87	0.36	0.53	0.23	0.70	0.25	0.61	0.081
C5-DC	0.49	0.05	0.50	0.05	0.41	0.05	0.45	0.07	0.92	0.226
C8-OH/C6-DC	0.38	0.08	0.41	0.14	0.20	0.10	0.30	0.16	0.80	0.235
C12:1	0.54	0.20	0.49	0.17	0.33	0.09	0.41	0.11	0.76	0.235
C12	1.91	0.71	1.54	0.61	0.95	0.49	1.25	0.46	0.66	0.110
C12:1-OH	0.09	0.02	0.08	0.03	0.05	0.02	0.06	0.02	0.68	<b>0.041</b>
C12-OH/C10-DC	0.12	0.03	0.12	0.03	0.07	0.04	0.10	0.04	0.78	0.139
C14:2	0.70	0.32	0.55	0.30	0.47	0.22	0.51	0.19	0.73	0.270
C14:1	2.93	0.97	2.68	0.79	1.95	0.80	2.31	0.68	0.79	0.251
C14	7.54	2.77	5.97	2.56	4.61	1.68	5.29	1.36	0.70	0.147
C14:2-OH	0.41	0.16	0.30	0.18	0.33	0.21	0.31	0.15	0.75	0.271
C14:1-OH	1.48	0.47	1.20	0.54	0.81	0.31	1.00	0.34	0.68	0.090
C14-OH/C12-DC	0.80	0.13	0.74	0.13	0.63	0.28	0.69	0.20	0.86	0.219
C16:2	1.42	0.61	1.24	0.50	1.11	0.39	1.17	0.29	0.83	0.431
C16:1	7.94	2.46	6.81	1.84	4.85	2.55	5.83	2.02	0.73	0.142
C16	39.33	12.07	29.09	11.32	21.63	9.28	25.36	7.62	0.64	0.059
C16:2-OH	0.50	0.13	0.38	0.15	0.32	0.12	0.35	0.10	0.70	0.069
C16:1-OH/C14:1-DC	1.71	0.46	1.48	0.46	1.28	0.59	1.38	0.42	0.81	0.213
C16-OH	2.11	0.35	2.11	0.22	1.94	0.93	2.03	0.65	0.96	0.760
C18:3	2.29	1.04	1.35	1.05	1.05	0.24	1.20	0.31	0.52	0.077
C18:2	17.85	8.08	11.51	7.94	9.49	2.42	10.50	2.42	0.59	0.111
C18:1	39.98	13.59	29.46	12.27	20.50	10.26	24.98	8.64	0.62	0.068
C18	12.03	3.78	6.56	4.63	6.02	1.85	6.29	1.55	0.52	<b>0.025</b>
C18:2-OH/C16:2-DC	0.94	0.32	0.85	0.25	1.02	0.57	0.93	0.39	1.00	0.993
C18:1-OH/C16:1-DC	2.62	0.59	2.58	0.37	2.27	1.20	2.43	0.84	0.93	0.618
C18-OH/C16-DC	0.71	0.20	0.60	0.19	0.58	0.25	0.59	0.17	0.83	0.265
C20:4	1.72	0.64	0.92	0.82	0.85	0.36	0.89	0.35	0.51	<b>0.040</b>
C20:3	0.51	0.17	0.32	0.20	0.31	0.13	0.32	0.10	0.62	0.067
C20:2	0.71	0.19	0.65	0.13	0.70	0.48	0.68	0.33	0.95	0.794
C20:1	1.37	0.37	1.20	0.29	1.19	0.71	1.20	0.49	0.88	0.468
C20	0.31	0.09	0.24	0.08	0.20	0.11	0.22	0.08	0.71	0.098
C20:1-OH/C18:1-DC	0.32	0.08	0.34	0.03	0.29	0.16	0.32	0.11	1.00	0.985
C20-OH/C18-DC	0.15	0.06	0.11	0.06	0.08	0.02	0.09	0.03	0.60	0.094
C22:4	0.12	0.04	0.07	0.06	0.07	0.05	0.07	0.05	0.59	0.076
C22:1	0.13	0.04	0.14	0.03	0.12	0.05	0.13	0.04	1.04	0.798
C22	0.11	0.03	0.15	0.02	0.07	0.01	0.11	0.05	1.04	0.825

**Supplementary Table 3. Metabolite measurements of glycolysis intermediates from WT and TTNtv hearts.**  
Concentration (nmol/g tissue)

Metabolite	WT (n=6)		TTNtvA (n=6)		TTNtvZ (n=6)		TTNtv		TTNtv/WT	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Ratio	P value
Dihydroxyacetone phosphate	176	64	183	49	172	46	177	46	1	0.96
Fructose 1,6-diphosphate	271	129	297	138	299	127	298	126	1.1	0.68
Fructose 6-phosphate	349	156	380	152	409	167	394	153	1.1	0.57
Glucose 1-phosphate	117	50	125	49	132	54	129	49	1.1	0.63
Glucose 6-phosphate	1460	715	1605	709	1773	805	1689	728	1.2	0.54
Lactic acid	13744	2540	15430	2501	14835	3163	15132	2736	1.1	0.31
Phosphoenolpyruvic acid	10	2	10	2	11	1	11	2	1.1	0.43



**Supplementary Table 4. TTNtvs in expressed exons (PSI>15%) in healthy individuals who underwent cardiac MRI in the Digital Heart Project.**

Sample identification	Hg19 genomic start position	LRG genomic start position	Transcript effect	Protein effect	Exon number	Median exon PSI	Present in NZBA	Present in NZB	Band	Variant type	ExAC frequency
14AB03203	179629515	71015	c.9727C>T	p.Q3243X	42	100	Y	Y	I-band	Nonsense	0
14ZN01340	179595884	104646	c.17508dupA	NA	61	35	Y		I-band	Frameshift	0
14JD01896	179588844	111686	c.21142C>T	p.R7048X	74	25	Y		I-band	Nonsense	0.00002
14AL03036	179563642	136888	c.30683-1G>T	NA	113	80	Y		I-band	Splice acceptor variant	0
14EC01433	179560998	139532	c.30803-2A>G	NA	115	74	Y		I-band	Splice acceptor variant	0
14MS02961	179554624	145906	c.31763-1G>A	NA	123	78	Y		I-band	Splice acceptor variant	0.00027
14RH03039	179554624	145906	c.31763-1G>A	NA	123	78	Y		I-band	Splice acceptor variant	0.00027
14CB02200	179506963	193567	c.40558+1G>A	NA	220	100	Y	Y	I-band	Splice donor variant	0.00012
14HB02599	179495671	204859	c.44015-1G>T	NA	239	100	Y	Y	I-band	Splice acceptor variant	0
14MC001427	179486054	214476	c.45391delA	NA	247	100	Y	Y	I-band	Frameshift	0
14RS02105	179479631	220899	c.48703C>T	p.Q16235X	261	100	Y	Y	A-band	Nonsense	0
14JM01448	179444855	255675	c.67159delA	p.I22387X	319	100	Y	Y	A-band	Frameshift	0
14SM01546	179444666	255864	c.67348C>T	p.Q22450X	319	100	Y	Y	A-band	Nonsense	0
14JC01930	179404286	296244	c.98506C>T	p.R32836X	353	100	Y	Y	A-band	Nonsense	0
14TW02859	179394786	305744	c.106432G>T	p.E35478X	360	100	Y	Y	M-band	Nonsense	0

**Supplementary Table 5: For each cardiac phenotype two linear regression models were built to adjust for the known contribution of clinical variables. The first model was optimized to minimize the Bayesian Information Criterion. To the optimized first model, the *ttt* genotype was then added to create a second model and details of this presented here. The two models were then compared using ANOVA. BSA = body surface area; LVEDV = left ventricular end diastolic volume; LVESV = left ventricular end systolic volume; LVEF = left ventricular ejection fraction; LVM = left ventricular mass; SBP = systolic blood pressure; TTNtv = titin truncating variants.**

Phenotype	Model Terms	Unstandardized Coefficient	Standardized Coefficient	Standard Error	Component P value	Full model		P value for comparison between models
						Adjusted R <sup>2</sup>	P value	
<b>LVEDV (ml)</b>	(Intercept)	-3.99	0	7.46	0.59	0.58	4.57 x10 <sup>-261</sup>	0.03
	Age (years)	-0.54	-0.23	0.04	1.13 x10 <sup>-31</sup>			
	Gender (male)	13.8	0.21	1.44	3.52 x10 <sup>-21</sup>			
	SBP (mmHg)	0.15	0.07	0.04	0.001			
	Race	-4.64	-0.12	0.65	2.05 x10 <sup>-12</sup>			
	BSA (kg/m <sup>2</sup> )	75.3	0.48	3.53	9.08 x10 <sup>-88</sup>			
	Activity Score	8.06	0.22	0.66	3.23 x10 <sup>-32</sup>			
	Heart Rate (bpm)	-0.13	-0.07	0.03	1.47 x10 <sup>-05</sup>			
TTNtv	11.9	0.04	5.39	0.03				
<b>LVESV (ml)</b>	(Intercept)	4.58	0	4	0.25	0.43	5.4 x10 <sup>-170</sup>	0.015
	Age (years)	-0.29	-0.24	0.02	2.25 x10 <sup>-30</sup>			
	Gender (male)	9.06	0.28	0.83	1.33 x10 <sup>-26</sup>			
	Race	-1.8	-0.09	0.38	3.21 x10 <sup>-06</sup>			
	BSA (kg/m <sup>2</sup> )	26.2	0.33	2.03	7.29 x10 <sup>-36</sup>			
	Activity Score	3.73	0.19	0.39	4.25 x10 <sup>-21</sup>			
	Heart Rate (bpm)	-0.04	-0.05	0.02	0.008			
	TTNtv	7.69	0.05	3.17	0.015			
<b>LVEF (%)</b>	(Intercept)	60.5	0	1.18	<1x10 <sup>-100</sup>	0.14	3.05 x10 <sup>-43</sup>	0.03
	Age (years)	0.07	0.18	0.01	4.79 x10 <sup>-11</sup>			
	Gender (male)	-2.95	0.27	0.28	7.93 x10 <sup>-24</sup>			
	SBP (mmHg)	0.04	0.12	0.01	2.12 x10 <sup>-05</sup>			
	Activity Score	-0.65	-0.11	0.16	3.32 x10 <sup>-05</sup>			
	TTNtv	-2.81	-0.05	1.29	0.03			