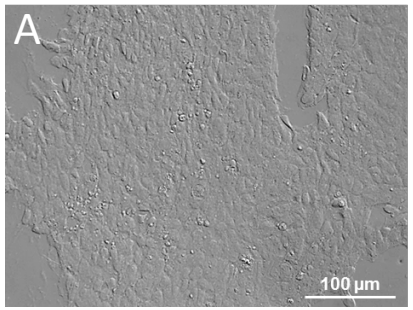
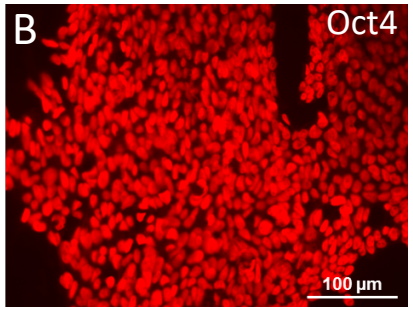
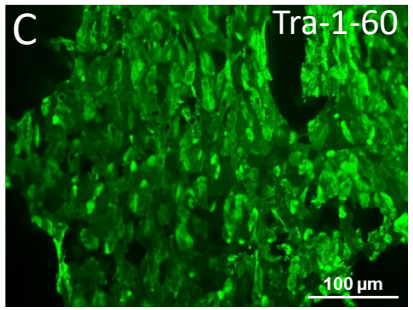
Appendix Figure S1-9

Appendix Figure S1







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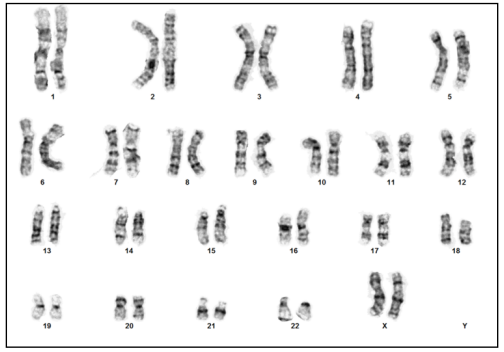
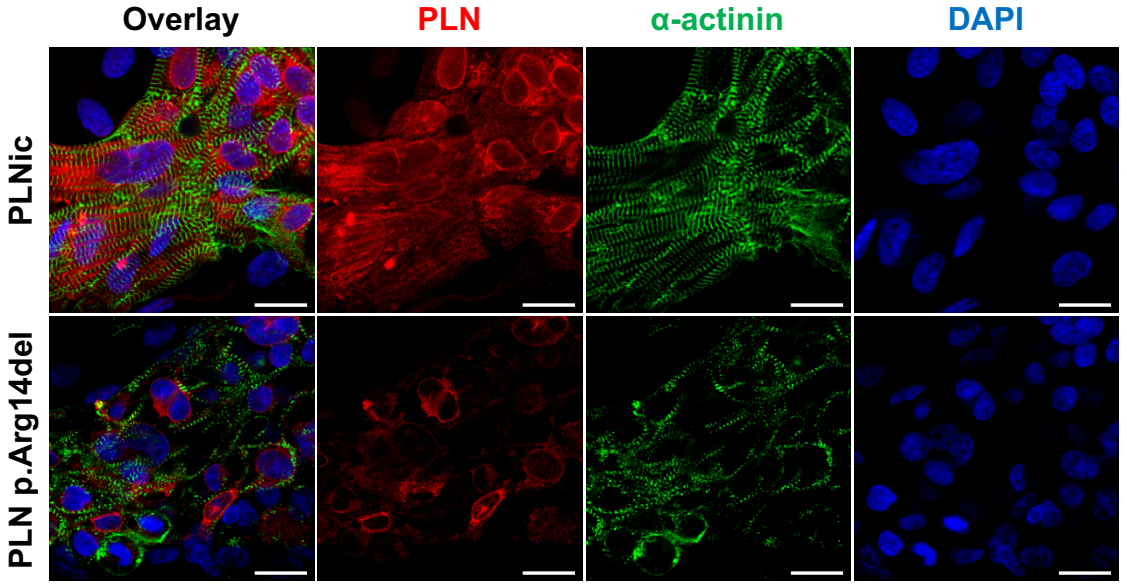


E

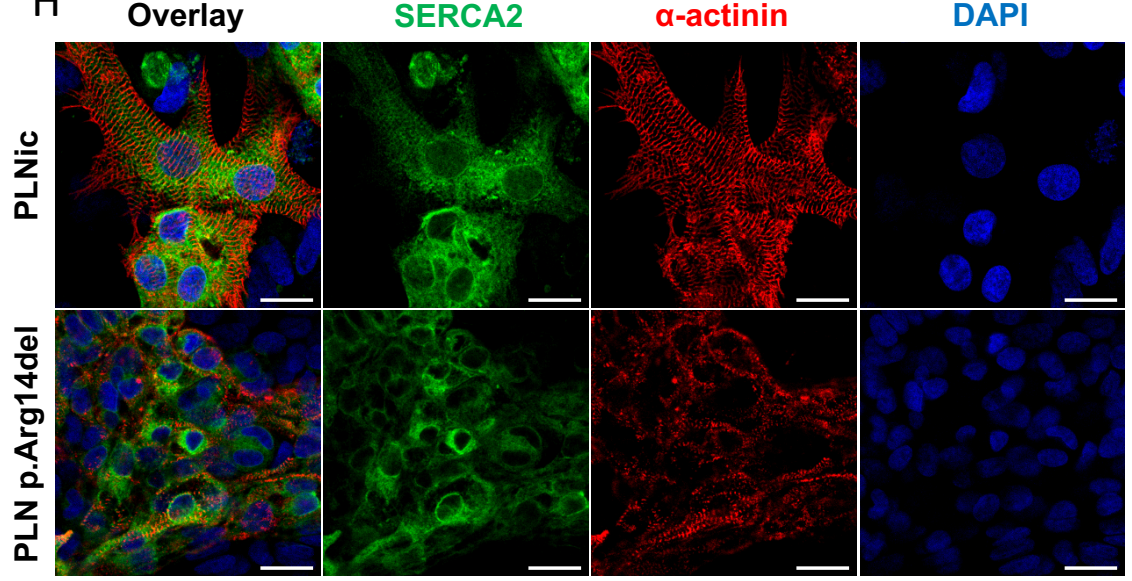
F

Name	Sequence forward (5'-3')	Sequence reverse (5'-3')	PCR product size
OT1	AGCAGGCAGCCCTATTTTCAT	AGAGAGGAGCAAGACAGACTCA	555 bp
OT2	GACATGGCTGATTATATTCTTGCTG	GATCCAGGCTGGCTAAGGTAG	508 bp
OT3	GGGAGCCCACTGATGTGAAG	ACAATCTCAACGTGGAATAGGGA	530 bp
OT4	GGGTGGGCTGAGCCAATAAT	TGAGTATACATTGCTTTGGAGTACA	657 bp
OT5	AGGCACTCGCAAGCTTCTTT	CAGCAGAAGTGTACTACAAAGACC	530 bp
OT6	CCTCATGTATCTGCAGGTGTGT	TGCCACAATGGCTAGTGTATGT	720 bp
OT7	TGTCTCACTCAACATACGTGGT	CTGAGGAAGCAGGAGAGGAGTA	815 bp
OT8	TTGTTCTGCCAGGACCCTAAG	TGAGCACCACAAAATGGGACT	501 bp
OT9	AGGGTGGGTGACTGAGTGTT	ACTTGTCATGGGAGTCGCTTT	587 bp
OT10	AAGTCTGTGACAGGTTCAGGG	ATTGGCAAAAGCAACTGCGAG	502 bp

G

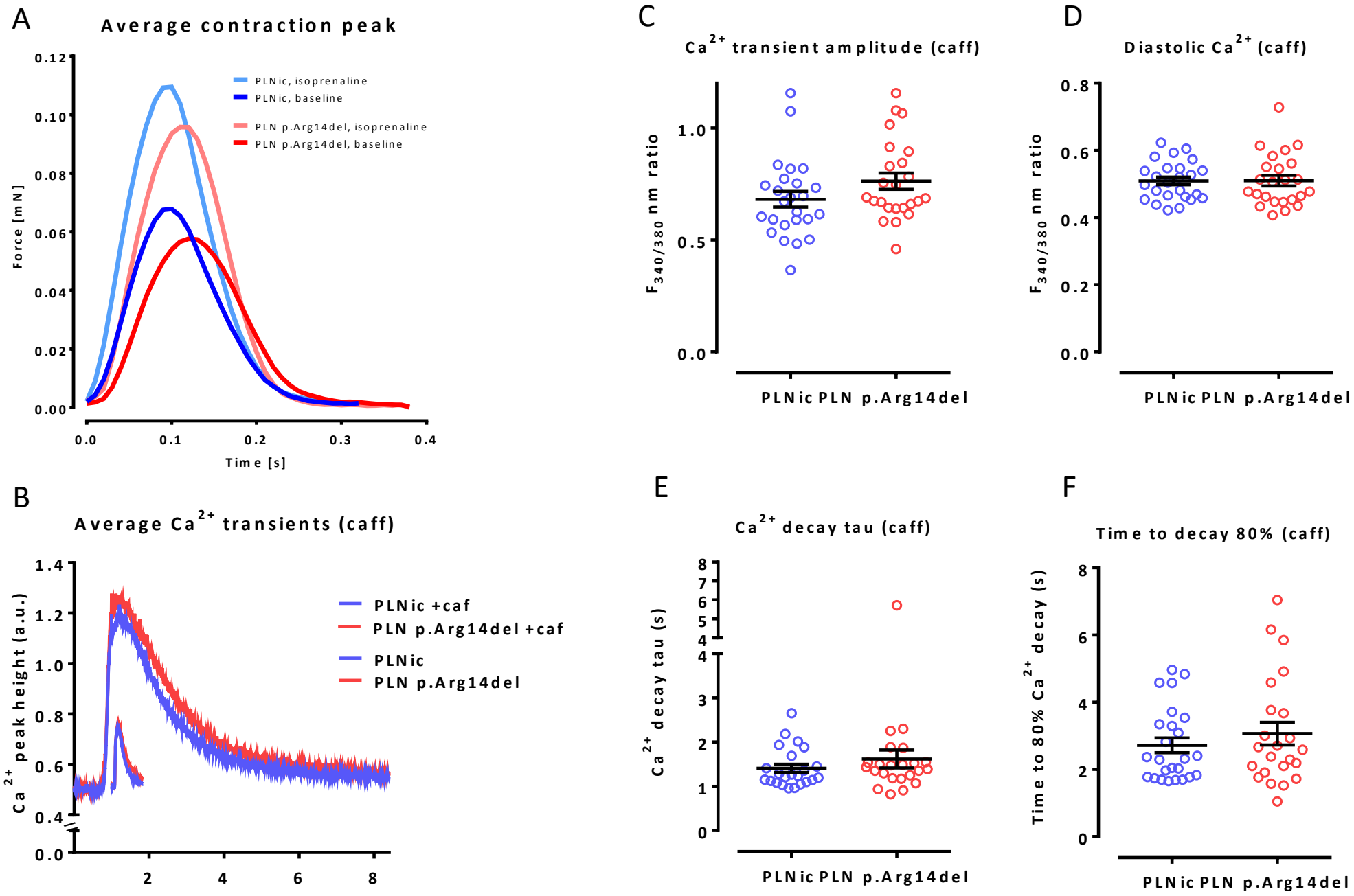


H



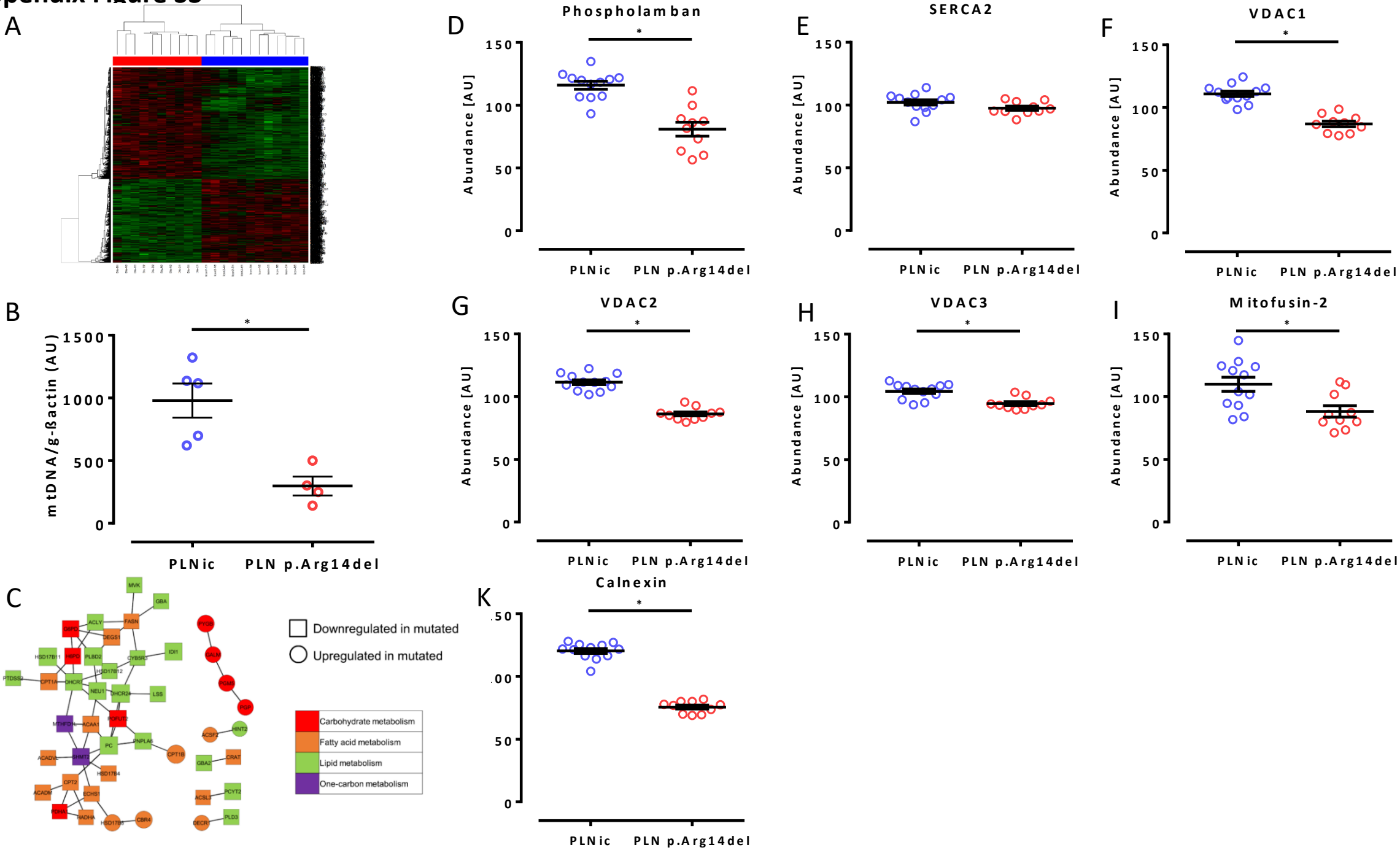
Appendix Figure S1. Characterization of hiPSC and hiPSC-CM. **A**: Bright field microscopy and immunofluorescence for pluripotency markers: **B:** Oct4 (red) and **C**: Tra-1-60 (green). G-banding chromosome analysis for **D:** PLN p.Arg14del hiPSC and **E:** isogenic control hiPSC demonstrating normal karyotype (46, XX). **F**: PCR primer sequences and estimated product size for off target (OT) sequencing. **G, H:** Immunofluorescence of 2D hiPSC-CM from PLNic and PLN p.Arg14del with antibodies against PLN (red), α-actinin (green and red), SERCA2 (green); DAPI staining for nuclei (blue); scale bar 20 µm.

Appendix Figure S2



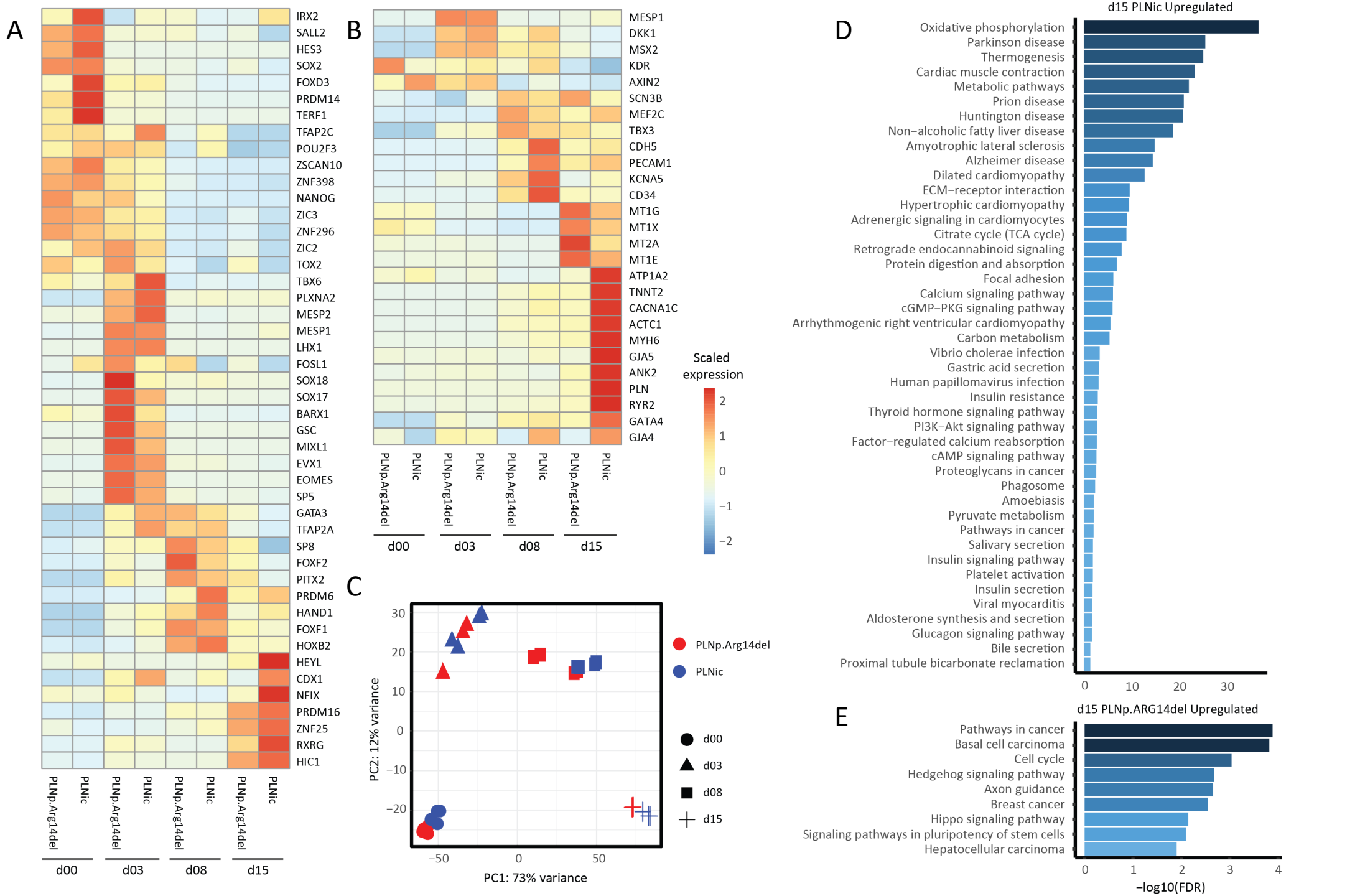
Appendix Figure S2. A: Average force contraction peak for PLNic and PLN p.Arg14del at baseline (EC50 [Ca^{2+}]) and in response to isoprenaline (ISO; 100 nM), data are related to Figure 2E, F. Ca^{2+} transient analysis in FURA 2-loaded 2D hiPSC-CM after caffeine puff (20 mM). **B:** Average Ca^{2+} transient peak, **C:** Ca^{2+} transient amplitude, **D:** Diastolic Ca^{2+}, **E:** Time to decay 80% and **F:** Ca^{2+} decay tau; PLNic: n=25 hiPSC-CM from 2 batches and PLN p.Arg14del: n=24 hiPSC-CM from 2 batches, mean ± SEM, Mann–Whitney U test, *$p<0.05$. The data are representative of n= 2 independent experiments.

Appendix Figure S3



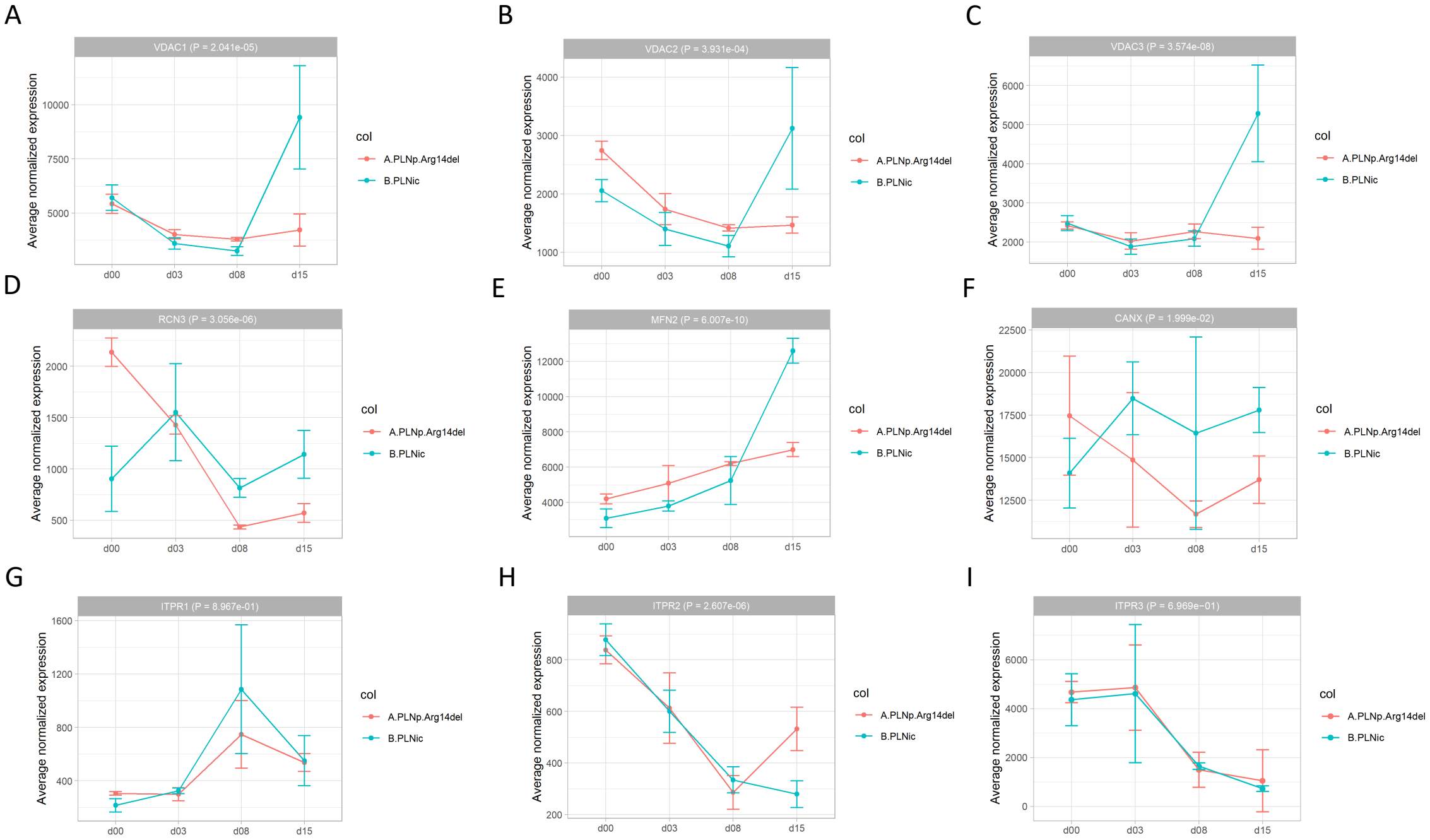
Appendix Figure S3. A: Heat map representation of differentially abundant proteins after unsupervised hierarchical clustering (ANOVA, FDR<0.05). **B:** PCR amplification of genomic DNA for the mitochondrial encoded NADH dehydrogenase (Mt-ND1/2), normalized to the nuclear-encoded gene actin; PLNic: n=5 EHTs, PLN p.Arg14del n=4 EHTs, mean±SEM, Mann–Whitney U test, *p< 0.05. **C:** Co-expression network of differentially abundant proteins, which are related to metabolism (according to Uniprot characterization). **D-K:** Protein abundance of selected candidate proteins in the proteome screen, data extracted from **Table EV1**, PLNic: n=12, PLN p.Arg14del n=10, mean ± SEM, false discovery rate, * p<0.05.

Appendix Figure S4



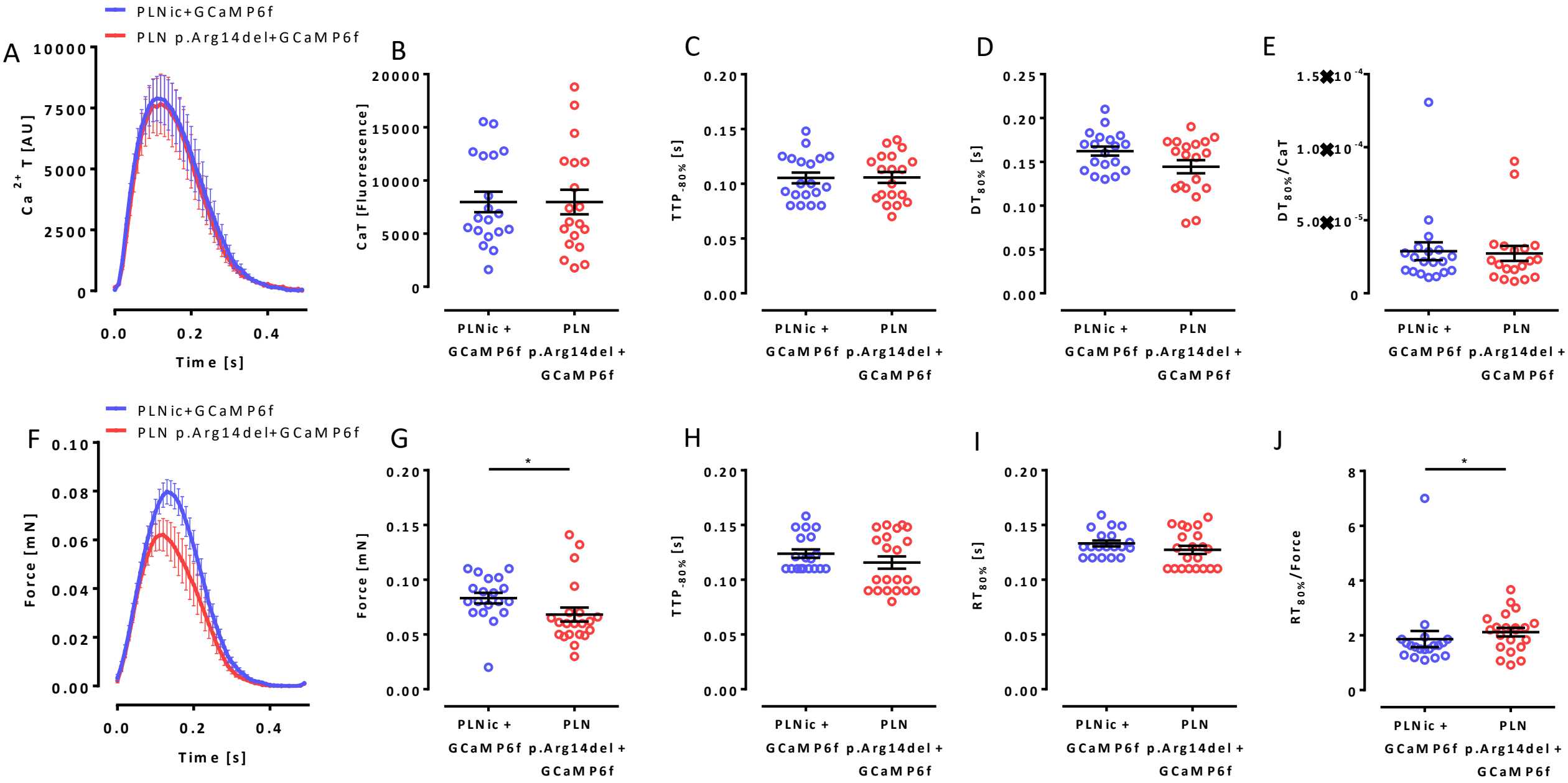
Appendix Figure S4. RNA sequencing analysis at different time points of cardiac differentiation of PLNic and PLN p.Arg14del hiPSC on day 0 (d00; hiPSC), day 3 (d03; mesodermal progenitors), day 8 (d08; cardiac progenitors) and day 15 (d15; early cardiomyocytes). **A, B** Heatmap of stage-specific markers of cardiac differentiation**.** The heatmap is scaled by row (gene) and the selected genes correctly define different stages of differentiation for both, PLNic and PLN p.Arg14del. **C:** Principal component analysis of PLNic and PLN p.Arg14del, n= 3-4 replicates, The data are representative of n= 2 independent differentiation rounds. **D, E:** Analysis of KEGG pathways of d15 samples that were significantly upregulated in PLNic (**D**) and PLN p.Arg14del (**E)**.

Appendix Figure S5



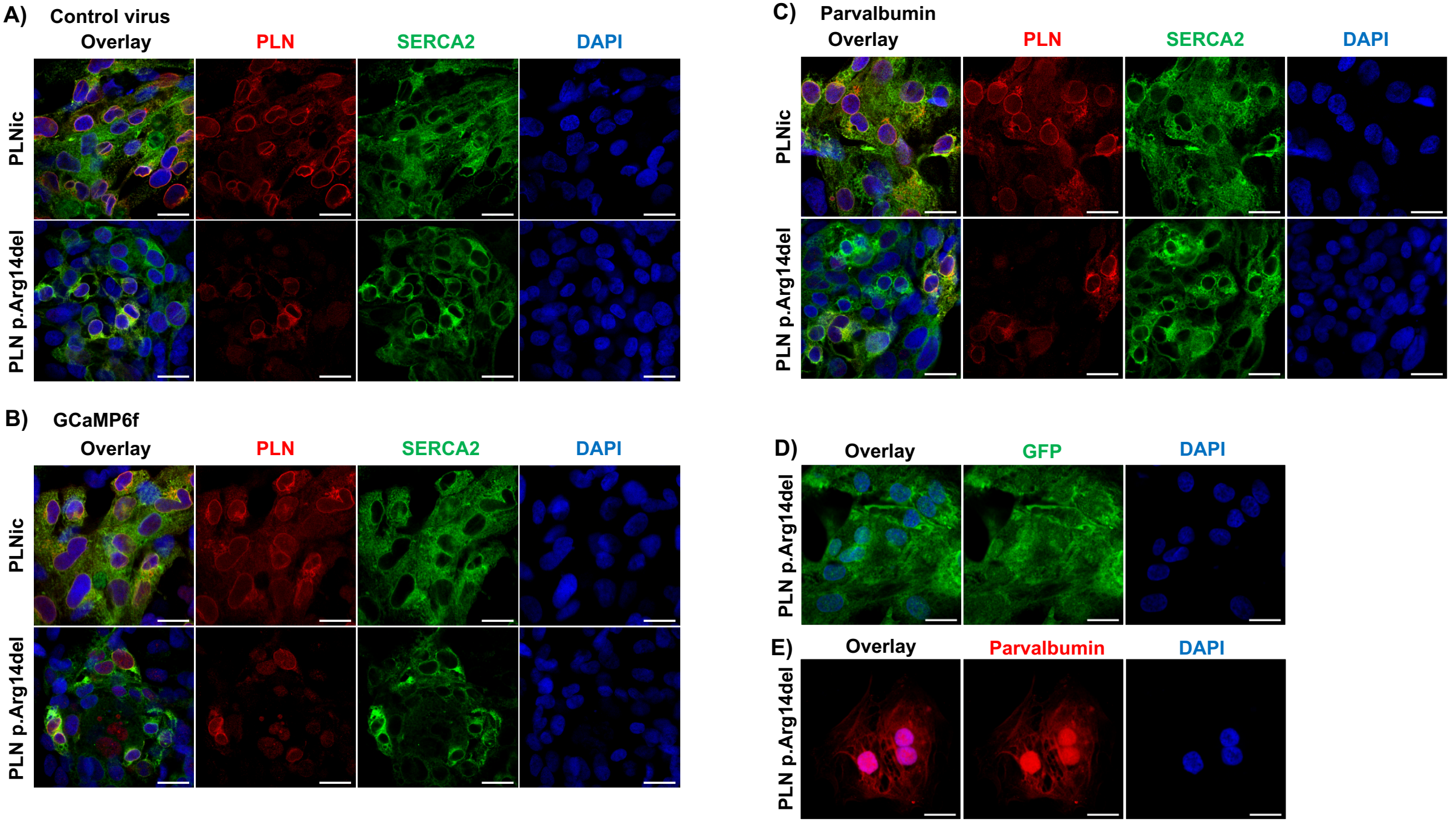
Appendix Figure S5. RNA sequencing analysis. **A-I:** Transcriptional expression profile of *VDAC1*, *VDAC2*, *VDAC3*, *MFN2*, *CANX, RCN3, ITPR1, ITPR2, ITPR3* at day 0, 3, 8, 15 of cardiac differentiation of PLNic and PLN p.Arg14del. 'P' indicates the adjusted p value of the difference in gene expression between PLNic and PLN p.Arg14del calculated by DESeq2 at day 15 of cardiac differentiation.

Appendix Figure S6



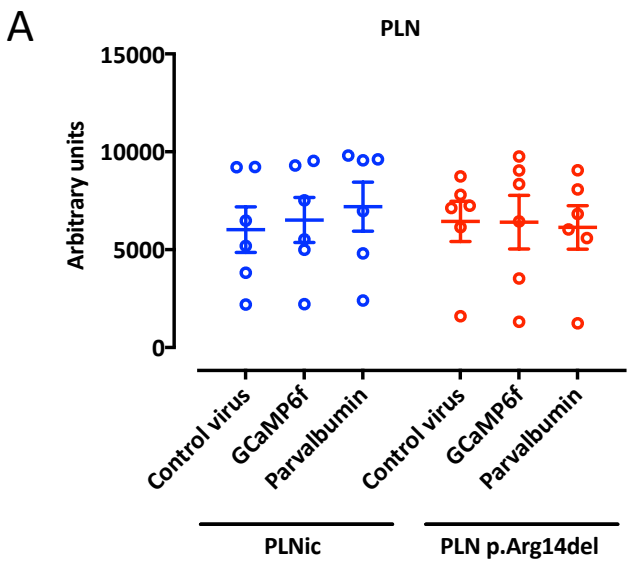
Appendix Figure S6. Ca^{2+} transient and force analysis of GCaMP6f-transduced EHTs. **A**: Average Ca^{2+} transient peak, **B:** Fluorescence amplitude, **C:** Ca^{2+} time to peak ($TTP_{80\%}$), **D:** Ca^{2+} decay time ($DT_{80\%}$), **E:** $DT_{80\%}$/fluorescence amplitude ratio, **F**: Average force peak, **G:** force amplitude, **H: f**orce time to peak ($TTP_{80\%}$), **I: f**orce relaxation time ($RT_{80\%}$), **J:** $RT_{80\%}$/force amplitude ratio. Mean ± SEM, PLNic: n=19 EHTs; PLN p.Arg14del: n=21 EHTs. Mann–Whitney U test, * $p<0.05$. The data are representative of 3 different batches.

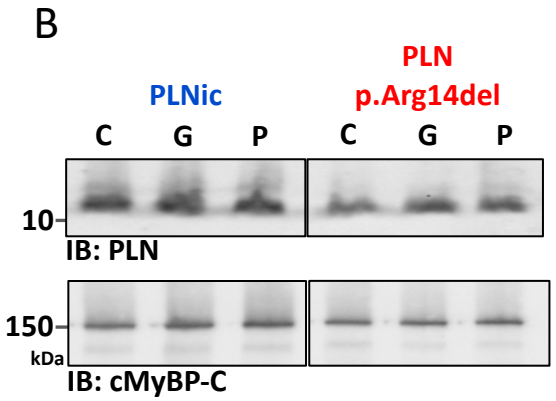
Appendix Figure S7

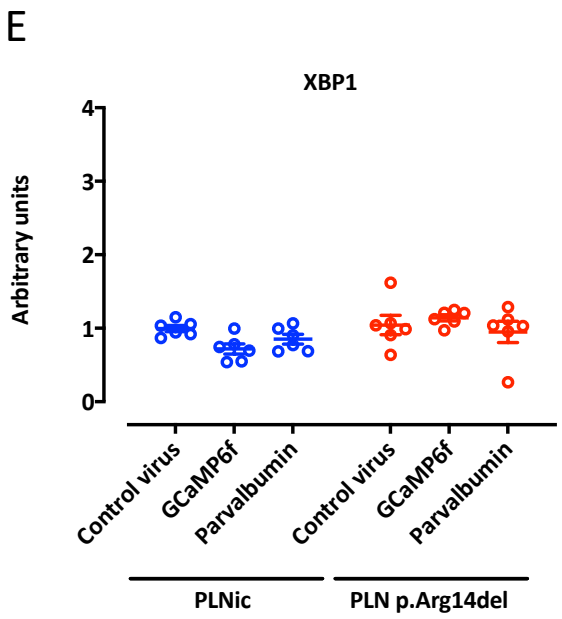


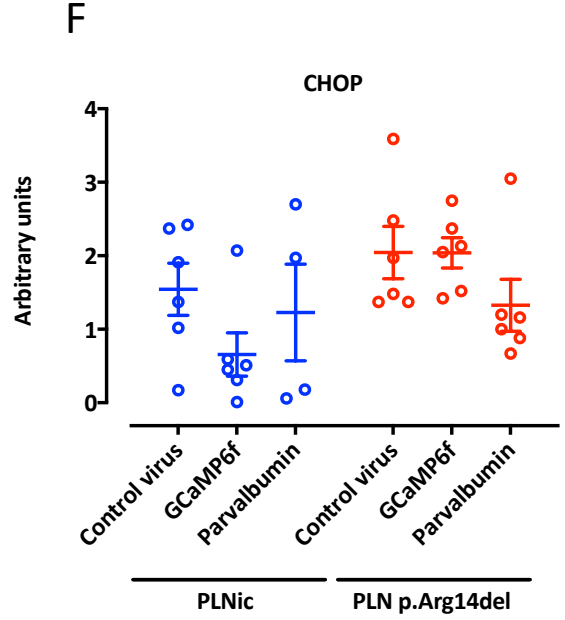
Appendix Figure S7. Immunofluorescence of 2D hiPSC-CM from PLNic and PLN p.Arg14del after transduction with a control virus **A**., a virus encoding for GCaMP6f **B**. or parvalbumin **C**. with antibodies recognizing PLN (red), SERCA2 (green), DAPI staining for nuclei (blue), **D**. PLN p.Arg14del hiPSC-CM after transduction with a virus encoding for GCaMP6f using an antibody detecting GFP, **E**. PLN p.Arg14del hiPSC-CM after transduction with a virus encoding for parvalbumin with an antibody detecting parvalbumin; scale bar 20 µm.

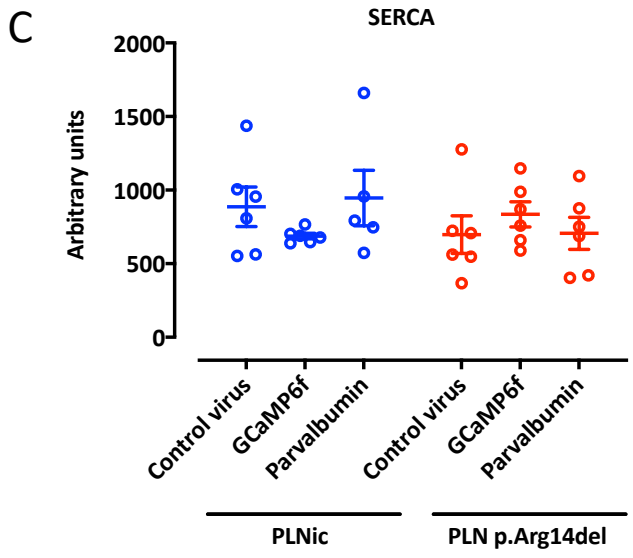
Appendix Figure S8

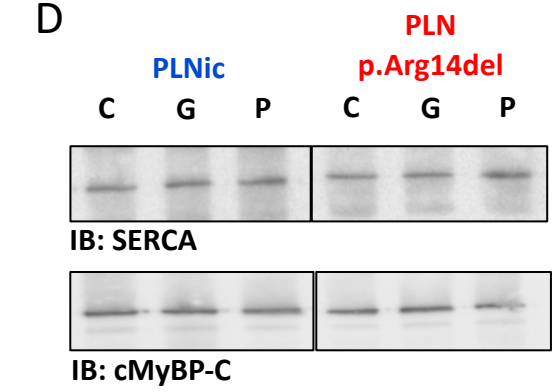


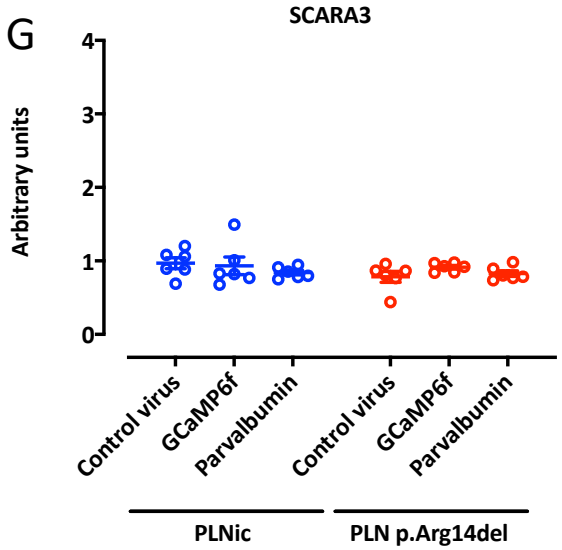






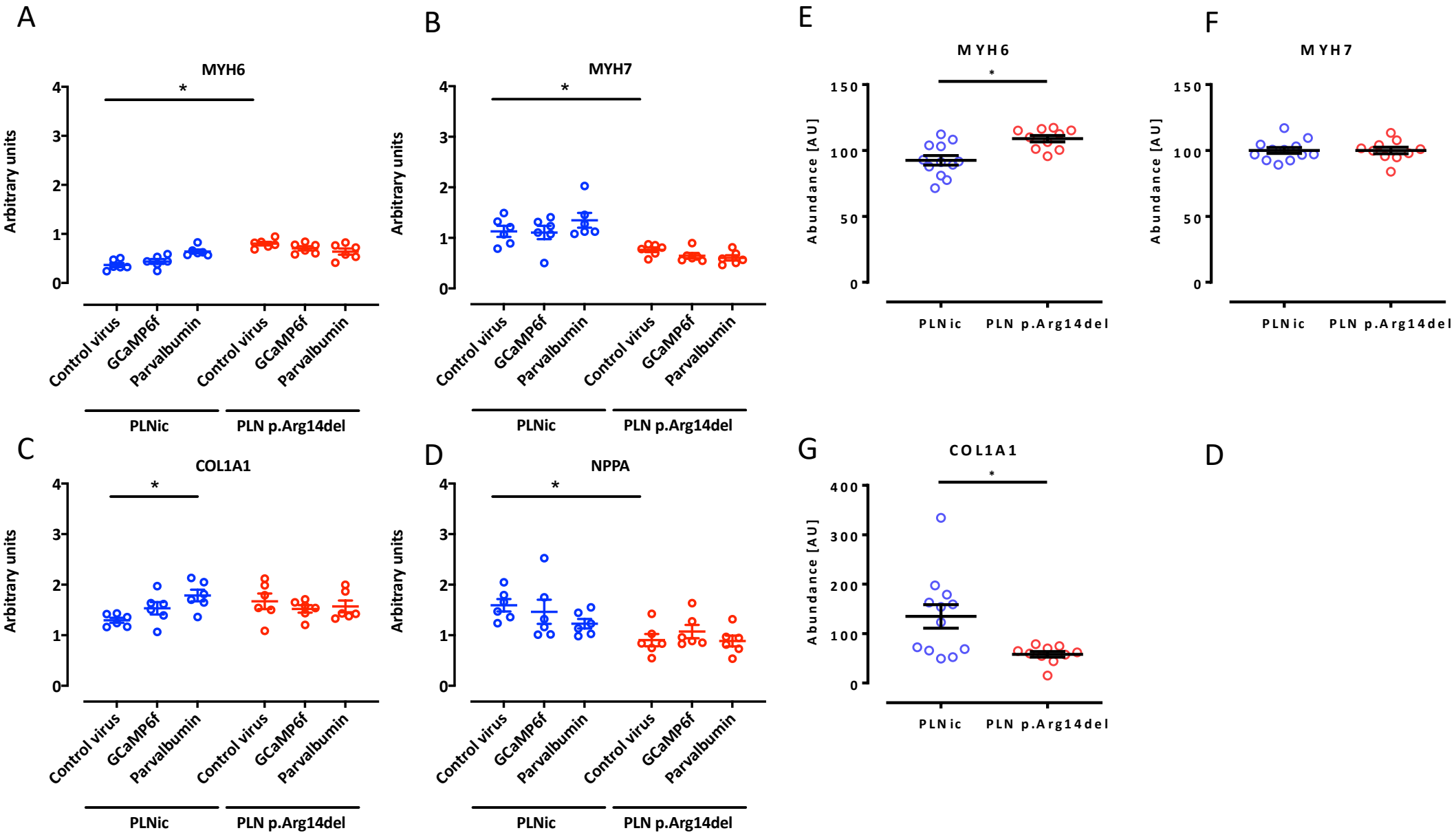






Appendix Figure S8. A-D. Western immunoblots for PLN and SERCA2 for PLNic and PLN p.Arg14del hiPSC-CM after transduction with control-, GCaMP6f- or parvalbumin-virus, n= 6-9, each replicate consists of a pool of 2-3 EHTs. Two-way ANOVA (comparing genotypes and virus conditions with Šidák`s post-test, mean ± SEM, *p<0.05. C: control virus, G: GCaMP6f virus. P: parvalbumin virus. **E-G.** Quantitative PCR of ER stress marker genes**.** PLNic and PLN p.Arg14del EHT after transduction with control-, GCaMP6f- or parvalbumin-virus; n= 6; each replicate consists of a pool of 2-3 EHTs. Two-way ANOVA (comparing genotypes and virus conditions) with Šidák`s post-test, mean ± SEM , *p<0.05.

Appendix Figure S9



Appendix Figure S9. Fetal gene program markers. **A.** Quantitative PCR for *MYH6*, *MYH7*, *COL1A1* and *NPPA* of PLNic and PLN p.Arg14del EHTs after transduction with control- , GCaMP6f- or parvalbumin-virus; n= 6; each replicate consists of a pool of 2-3 EHTs. Two-way ANOVA (comparing genotypes and virus conditions) with Šidák`s post-test, mean ± SEM, *p<0.05. B. Protein abundance of MYH6, MYH7 and COL1A1 in the proteomic screen, data extracted from **Table EV1**, PLNic: n=12, PLN p.Arg14del n=10, mean±SEM, false discovery rate, * p<0.05. NPPA not detected.

Figure	Sample	Replicate number	p value	Statistical test
2B	NFH left ventricle	5	0,0002	1way ANOVA
	PLNic, EHT	8		
	PLN p.Arg14del, EHT	8		
2D	PLNic, EHT, baseline	8	0,0417	2way ANOVA
	PLNic, EHT, ISO	8	PM vs. PM + Iso	
	PLN p.Arg14del, EHT baseline	8		
	PLN p.Arg14del, EHT, ISO	8		
2E	PLNic, EHT, baseline	27, 6 experiments	<0.0001	1way ANOVA
	PLNic, EHT, ISO	27, 6 experiments		
	PLN p.Arg14del, EHT baseline	19, 6 experiments	<0.0001	1way ANOVA
	PLN p.Arg14del, EHT, ISO	19, 6 experiments		
2F	PLNic, EHT, baseline	27, 6 experiments	<0.0001	1way ANOVA
	PLNic, EHT, ISO	27, 6 experiments		
	PLN p.Arg14del, EHT baseline	19, 6 experiments	<0.0001	1way ANOVA
	PLN p.Arg14del, EHT, ISO	19, 6 experiments		
3A	PLNic, EHT	70, 10 experiments	<0.0001	Mann-Whitney U
	PLN p.Arg14del, EHT	77, 10 experiments		
3B	PLNic, EHT	70, 10 experiments	<0.0001	Mann-Whitney U
	PLN p.Arg14del, EHT	77, 10 experiments		
3C	PLNic, EHT	67, 9 experiments	<0.0001	Mann-Whitney U
	PLN p.Arg14del, EHT	65, 9 experiments		
3D	PLNic, EHT	67, 9 experiments	0,0106	Mann-Whitney U
	PLN p.Arg14del, EHT	65, 9 experiments		
3G	PLNic, EHT	21, 8 experiments	<0.0001	Unpaired two-sided Student's t-test
	PLN p.Arg14del, EHT	35, 8 experiments		
3H	PLNic, EHT	67, 9 experiments	0,1287	Unpaired two-sided Student's t-test
	PLN p.Arg14del, EHT	65, 9 experiments		
3I	PLNic, EHT	67, 9 experiments	0,1604	Unpaired two-sided Student's t-test
	PLN p.Arg14del, EHT	65, 9 experiments		
3J	PLNic, EHT	67, 9 experiments	<0.0001	Unpaired two-sided Student's t-test
	PLN p.Arg14del, EHT	65, 9 experiments		
4B	PLNic, 2D hiPSC-CM	25, 2 experiments	0,6519	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	24, 2 experiments		
4C	PLNic, 2D hiPSC-CM	25, 2 experiments	0,8313	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	24, 2 experiments		
4D	PLNic, 2D hiPSC-CM	25, 2 experiments	0,0011	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	24, 2 experiments		
4E	PLNic, 2D hiPSC-CM	25, 2 experiments	0,0646	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	24, 2 experiments		
4G	PLNic, EHT	24, 32, 41, 5 experiments	0.6537 (interaction)	2way ANOVA, Tukey's post test
	PLN p.Arg14del, EHT	15, 24, 23, 5 experiments	0.0187 (row factor)	
			<0,0001 (column factor)	
5C	PLNic, EHT	12, 2 batches	<0.05	Benjamini-Hochberg, Multiple testing
	PLN p.Arg14del, EHT	10, 1 batch		

Figure	Sample	Replicate number	p value	Statistical test
6B	PLNic, 2D hiPSC-CM	6	0,0022	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	6		
6C	PLNic, 2D hiPSC-CM	6	0,0152	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	6		
6D	PLNic, 2D hiPSC-CM	6	0,0022	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	6		
6E	PLNic, EHT	8	0,0002	Mann-Whitney U
	PLN p.Arg14del, EHT	8		
7B	NFH	3, 15	<0.0001	1way ANOVA, Tukey's post test
	FH ICM	2, 10		
	FH PLN CM	3, 14		
7C	NFH	3, 15	<0.0001	1way ANOVA, Tukey's post test
	FH ICM	3, 15		
	FH PLN CM	3, 15		
8A	PLNic, EHT, control virus	6	0.0005 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	6	0.0007 (row factor)	
	PLNic, EHT, parvalbumin	6	0.0001 (column factor)	
	PLN p.Arg14del, EHT, control virus	6		
	PLN p.Arg14del, EHT, GCaMP6f	6		
	PLN p.Arg14del, EHT, parvalbumin	6		
8C	PLNic, EHT, control virus	9	0.6280 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	9	0.0186 (row factor)	
	PLNic, EHT, parvalbumin	9	<0.0001 (column factor)	
	PLN p.Arg14del, EHT, control virus	9		
	PLN p.Arg14del, EHT, GCaMP6f	9		
	PLN p.Arg14del, EHT, parvalbumin	9		
8E	PLNic, EHT, control virus	24	0.0001 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	23	0.0003 (row factor)	
	PLNic, EHT, parvalbumin	24	<0.0001 (column factor)	
	PLN p.Arg14del, EHT, control virus	22		
	PLN p.Arg14del, EHT, GCaMP6f	24		
	PLN p.Arg14del, EHT, parvalbumin	22		
8F	PLNic, EHT, control virus	6	0.0002 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	6	0.0664 (row factor)	
	PLNic, EHT, parvalbumin	6	0.0010 (column factor)	
	PLN p.Arg14del, EHT, control virus	6		
	PLN p.Arg14del, EHT, GCaMP6f	6		
	PLN p.Arg14del, EHT, parvalbumin	6		
8G	PLNic, EHT, control virus	6	0.0007 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	6	<0.0001 (row factor)	
	PLNic, EHT, parvalbumin	6	<0.0001 (column factor)	
	PLN p.Arg14del, EHT, control virus	6		
	PLN p.Arg14del, EHT, GCaMP6f	6		
	PLN p.Arg14del, EHT, parvalbumin	6		
8H	PLNic, EHT, control virus	6	0.0693 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	6	0.0387 (row factor)	
	PLNic, EHT, parvalbumin	6	0.8969 (column factor)	
	PLN p.Arg14del, EHT, control virus	6		
	PLN p.Arg14del, EHT, GCaMP6f	6		
	PLN p.Arg14del, EHT, parvalbumin	6		

Figure	Sample	Replicate number	p value	Statistical test
6B	PLNic, 2D hiPSC-CM	6	0,0022	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	6		
6C	PLNic, 2D hiPSC-CM	6	0,0152	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	6		
6D	PLNic, 2D hiPSC-CM	6	0,0022	Mann-Whitney U
	PLN p.Arg14del, 2D hiPSC-CM	6		
6E	PLNic, EHT	8	0,0002	Mann-Whitney U
	PLN p.Arg14del, EHT	8		
7B	NFH	3, 15	<0.0001	1way ANOVA, Tukey's post test
	FH ICM	2, 10		
	FH PLN CM	3, 14		
7C	NFH	3, 15	<0.0001	1way ANOVA, Tukey's post test
	FH ICM	3, 15		
	FH PLN CM	3, 15		
8A	PLNic, EHT, control virus	6	0.0005 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	6	0.0007 (row factor)	
	PLNic, EHT, parvalbumin	6	0.0001 (column factor)	
	PLN p.Arg14del, EHT, control virus	6		
	PLN p.Arg14del, EHT, GCaMP6f	6		
	PLN p.Arg14del, EHT, parvalbumin	6		
8C	PLNic, EHT, control virus	9	0.6280 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	9	0.0186 (row factor)	
	PLNic, EHT, parvalbumin	9	<0.0001 (column factor)	
	PLN p.Arg14del, EHT, control virus	9		
	PLN p.Arg14del, EHT, GCaMP6f	9		
	PLN p.Arg14del, EHT, parvalbumin	9		
8E	PLNic, EHT, control virus	24	0.0001 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	23	0.0003 (row factor)	
	PLNic, EHT, parvalbumin	24	<0.0001 (column factor)	
	PLN p.Arg14del, EHT, control virus	22		
	PLN p.Arg14del, EHT, GCaMP6f	24		
	PLN p.Arg14del, EHT, parvalbumin	22		
8F	PLNic, EHT, control virus	6	0.0002 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	6	0.0664 (row factor)	
	PLNic, EHT, parvalbumin	6	0.0010 (column factor)	
	PLN p.Arg14del, EHT, control virus	6		
	PLN p.Arg14del, EHT, GCaMP6f	6		
	PLN p.Arg14del, EHT, parvalbumin	6		
8G	PLNic, EHT, control virus	6	0.0007 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	6	<0.0001 (row factor)	
	PLNic, EHT, parvalbumin	6	<0.0001 (column factor)	
	PLN p.Arg14del, EHT, control virus	6		
	PLN p.Arg14del, EHT, GCaMP6f	6		
	PLN p.Arg14del, EHT, parvalbumin	6		
8H	PLNic, EHT, control virus	6	0.0693 (interaction)	2way ANOVA, Sidak's post test
	PLNic, EHT, GCaMP6f	6	0.0387 (row factor)	
	PLNic, EHT, parvalbumin	6	0.8969 (column factor)	
	PLN p.Arg14del, EHT, control virus	6		
	PLN p.Arg14del, EHT, GCaMP6f	6		
	PLN p.Arg14del, EHT, parvalbumin	6		

Figure	Sample	Replicate number	p value	Statistical test	
EV1B	PLNic, EHT, pPDH	6	0,0013	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, EHT, pPDH	6			
EV1B	PLNic, EHT, pAMPK	6	0,0072	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, EHT, pAMPK	6			
EV1B	PLNic, EHT, galectin-3	3	0,0252	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, EHT, galectin-3	3			
EV1B	PLNic, EHT, SLTM	3	0,0006	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, EHT, SLTM	3			
EV1B	PLNic, EHT, LMCD1	3	0,0006	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, EHT, LMCD1	3			
EV1B	PLNic, EHT, calnexin	6	0,0009	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, EHT, calnexin	6			
EV1B	PLNic, EHT, reticulocalbin-3	3	0,1592	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, EHT, reticulocalbin-3	3			
Appendix Figure S2 C	PLNic, 2D hiPSC-CM	25, 2 experiments	0,1158	Mann-Whitney U	
	PLN p.Arg14del, 2D hiPSC-CM	24, 2 experiments			
Appendix Figure S2 D	PLNic, 2D hiPSC-CM	25, 2 experiments	0,7249	Mann-Whitney U	
	PLN p.Arg14del, 2D hiPSC-CM	24, 2 experiments			
Appendix Figure S2 E	PLNic, 2D hiPSC-CM	25, 2 experiments	0,2926	Mann-Whitney U	
	PLN p.Arg14del, 2D hiPSC-CM	24, 2 experiments			
Appendix Figure S2 F	PLNic, 2D hiPSC-CM	25, 2 experiments	0,5632	Mann-Whitney U	
	PLN p.Arg14del, 2D hiPSC-CM	24, 2 experiments			
Appendix Figure S3B	PLNic, EHT	5	0,0159	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, EHT	4			
Appendix Figure S3D-K	PLNic, EHT	12, 2 batches	< 0.05	Benjamini-Hochberg, Multiple testi	
	PLN p.Arg14del, EHT	10, 1 batch			
Appendix Figure S5A	PLNic, hiPSC EBs	3-4/time point	$2.04x10^{-5}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			
Appendix Figure S5B	PLNic, hiPSC EBs	3-4/time point	$3.031x10^{-4}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			
Appendix Figure S5C	PLNic, hiPSC EBs	3-4/time point	$3.574x10^{-8}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			
Appendix Figure S5D	PLNic, hiPSC EBs	3-4/time point	$3.056x10^{-6}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			
Appendix Figure S5E	PLNic, hiPSC EBs	3-4/time point	$6.007x10^{-10}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			
Appendix Figure S5F	PLNic, hiPSC EBs	3-4/time point	$1.999x10^{-2}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			
Appendix Figure S5G	PLNic, hiPSC EBs	3-4/time point	$8.967x10^{-1}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			
Appendix Figure S5H	PLNic, hiPSC EBs	3-4/time point	$2.607x10^{-6}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			
Appendix Figure S5I	PLNic, hiPSC EBs	3-4/time point	$6.969x10^{-1}$	Unpaired two-sided Student's t-test	
	PLN p.Arg14del, hiPSC EBs	3-4/time point			

Figure	Sample	Replicate number	p value	Statistical test	
Appendix Figure S6B	PLNic, EHT	19	0,8326	Mann-Whitney U	
	PLN p.Arg14del, EHT	21			
Appendix Figure S6C	PLNic, EHT	19	0,9827	Mann-Whitney U	
	PLN p.Arg14del, EHT	21			
Appendix Figure S6D	PLNic, EHT	19	0,1069	Mann-Whitney U	
	PLN p.Arg14del, EHT	21			
Appendix Figure S6E	PLNic, EHT	19	0,8326	Mann-Whitney U	
	PLN p.Arg14del, EHT	21			
Appendix Figure S6G	PLNic, EHT	19	0,004	Mann-Whitney U	
	PLN p.Arg14del, EHT	21			
Appendix Figure S6H	PLNic, EHT	19	0,1849	Mann-Whitney U	
	PLN p.Arg14del, EHT	21			
Appendix Figure S6I	PLNic, EHT	19	0,154	Mann-Whitney U	
	PLN p.Arg14del, EHT	21			
Appendix Figure S6J	PLNic, EHT	19	0,0379	Mann-Whitney U	
	PLN p.Arg14del, EHT	21			
Appendix Figure S8A	PLNic, EHT	6	0.8190 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.9350 (row factor)		
			0.8009 (column factor)		
Appendix Figure S8C	PLNic, EHT	6	0.2136 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.8621 (row factor)		
			0.3368 (column factor)		
Appendix Figure S8E	PLNic, EHT	6	0.1022 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.4141 (row factor)		
			0.0168 (column factor)		
Appendix Figure S8F	PLNic, EHT	6	0.2124 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.3100 (row factor)		
			0.0338 (column factor)		
Appendix Figure S8G	PLNic, EHT	6	0.3794 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.4426 (row factor)		
			0.2064 (column factor)		
Appendix Figure S9A	PLNic, EHT	6	0.0002 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.2981 (row factor)		
			< 0.0001 (column factor)		
Appendix Figure S9B	PLNic, EHT	6	0.1527 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.5926 (row factor)		
			< 0.0001 (column factor)		
Appendix Figure S9C	PLNic, EHT	6	0.0374 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.1990 (row factor)		
			0.5857 (column factor)		
Appendix Figure S9D	PLNic, EHT	6	0.4352 (interaction)	2way ANOVA, Sidak's post test	
	PLN p.Arg14del, EHT	6	0.2850 (row factor)		
			0.0003 (column factor)		
Appendix Figure S9E	PLNic, EHT	12, 2 batches	< 0.05	Benjamini-Hochberg, Multiple testi	
	PLN p.Arg14del, EHT	10, 1 batch			
Appendix Figure S9F	PLNic, EHT	12, 2 batches	< 0.05	Benjamini-Hochberg, Multiple testi	
	PLN p.Arg14del, EHT	10, 1 batch			
Appendix Figure S9G	PLNic, EHT	12, 2 batches	< 0.05	Benjamini-Hochberg, Multiple testi	
	PLN p.Arg14del, EHT	10, 1 batch			

Appendix Figure S10. Statistical details