Supplemental Material

Table S1. List of the applied primers used for PCR per gene.

Gene	Forward primer 5' to 3'	Reverse primer 5' to 3'
DPPA4	TGGTGTCAGGTGGTGTGTGG	CCAGGCTTGACCAGCATGAA
KLF4 endogenous	ACAGTCTGTTATGCACTGTGGTTTCA	CATTTGTTCTGCTTAAGGCATACTTGG
KLF4 transgene	CCTCGCCTTACACATGAAGAGACA	CACCAGACCAACTGGTAATGGTAGC
MYC endogenous	ACAGAAATGTCCTGAGCAATCACCT	GCCAAGGTTGTGAGGTTGCAT
MYC transgene	GCTACGGAACTCTTGTGCGTGA	CACCAGACCAACTGGTAATGGTAGC
NANOG	AGGTCTCGTATTTGCTGCATCGT	GAAACACTCGGTGAAATCAGGGTAA
OCT4 endogenous	GGAAGGAATTGGGAACACAAAGG	AACTTCACCTTCCCTCCAACCA
OCT4 transgene	GGCTCTCCCATGCATTCAAAC	CATGGCCTGCCCGGTTATTA
RPL37A	GTGGTTCCTGCATGAAGACAGTG	TTCTGATGGCGGACTTTACCG
SCN5A adult specific	TCATGGCATACAAACTGAATT	GCTTCTTCACAGACTGGAT
SCN5A fetal specific	TCATGGCGTATGTATCAGAAAA	GCTTCTTCACAGACTGGAT
SOX2 endogenous	TGGCGAACCATCTCTGTGGT	CCAACGGTGTCAACCTGCAT
SOX2 transgene	GCACACTGCCCCTCTCACAC	CACCAGACCAACTGGTAATGGTAGC
ZNF206	TCACCATGGCCAGAGGAGAG	GCAGGCCACGCCTTATTCTC

Table S2. Average cell capacitance and series resistance in all experimental groups. Values are depicted as mean±SEM.

	Early-stage hiPSC-CMs				**Late-stage hiPSC-CMs**			
	Ctrl1	**Ctrl2**	**I230T^{het}**	**I230T^{homo}**	**Ctrl1**	**Ctrl2**	**I230T^{het}**	**I230T^{homo}**
Cell capacitance (pF)	22.7±2.0	19.8±2.2	21.2±2.0	23.4±1.6	27.5±2.0	20.2±3.0	31.4±2.4	48.8±5.8
Series resistance (MΩ)	6.1±0.3	6.6±0.5	7.0±0.4	6.6±0.4	6.3±0.3	7.4±0.5	6.3±0.5	5.7±0.4

Figure S1. Scheme of experimental approach depicting the different time points during differentiation at which the different steps, i.e. addition of lactate, enzymatic dissociation, collection of RNA and electrophysiological measurements, were performed.

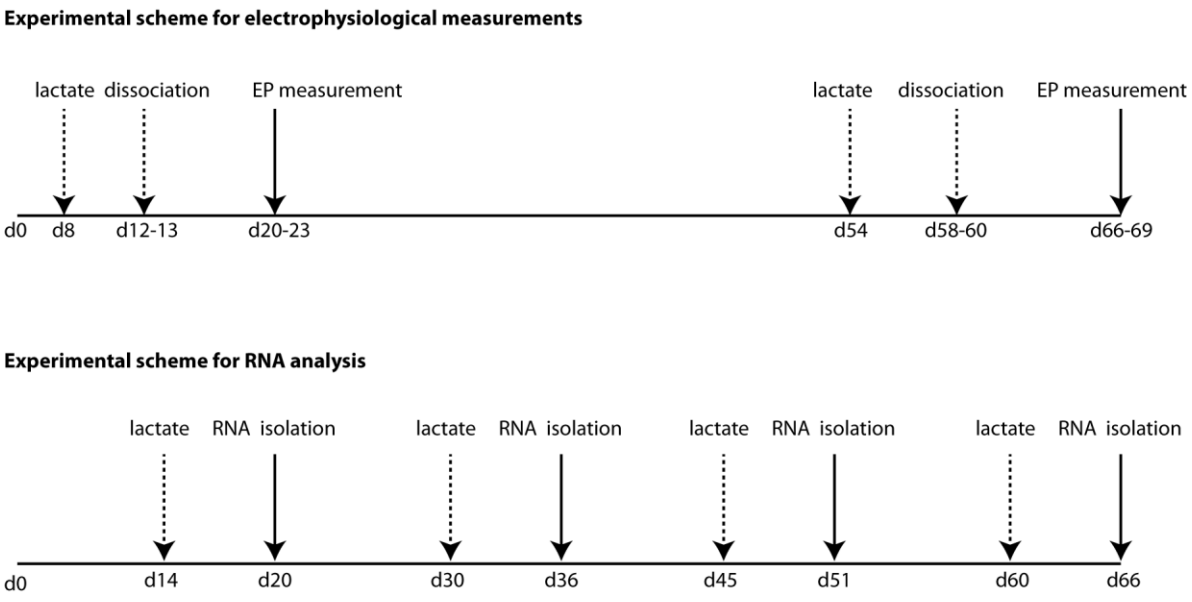

Figure S2. Comparison of I_{Na} properties in control 1 (Ctrl1) hiPSC-CMs measured after a short and extended culture period (early- and late-stage, respectively). Current-voltage relationships (**A)**, voltage dependence of activation (**B**), voltage dependence of inactivation (**C**), recovery from inactivation (**D**) and time dependence of inactivation (**E**) are shown. Inset in **D** depicts the voltage clamp protocol to determine P2/P1 values. In **E**, left and right panel indicate τ_{slow} and τ_{fast}, respectively.
Upon extended time in culture, I_{Na} density, recovery rate and inactivation rate increase. *indicates $p<0.05$ (Mann-Whitley U test).

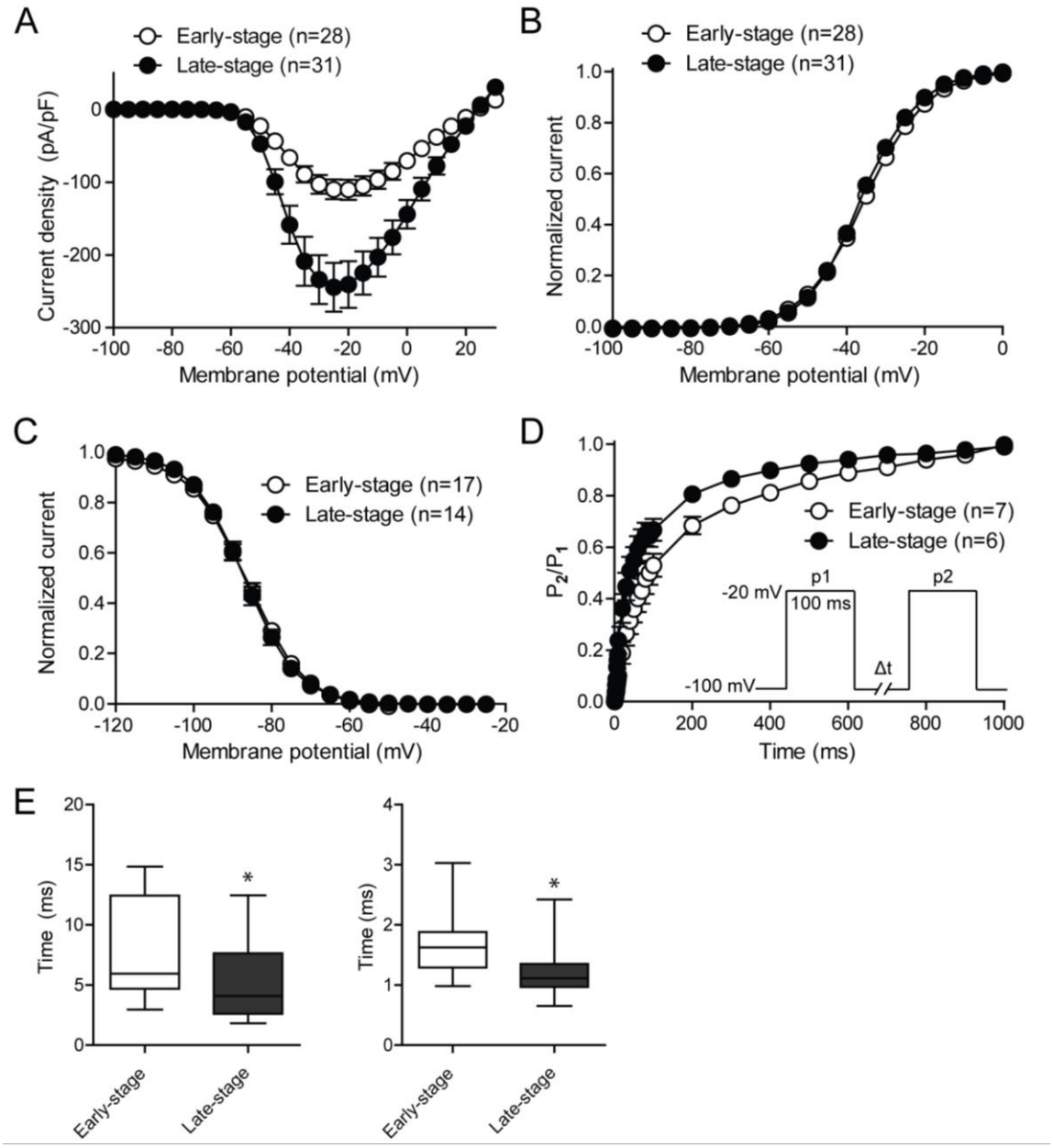

Figure S3. Comparison of I_{Na} properties in control 2 (Ctrl2) hiPSC-CMs measured after a short and extended culture period (early- and late-stage, respectively). Current-voltage relationships (**A)**, voltage dependence of activation (**B**), voltage dependence of inactivation (**C**), recovery from inactivation (**D**) and time dependence of inactivation (**E**) are shown. Inset in **D** depicts the voltage clamp protocol to determine P2/P1 values. In **E**, left and right panel indicate τ_{slow} and τ_{fast}, respectively. Upon extended time in culture, I_{Na} density and the slow component of inactivation rate increase, while voltage dependence of inactivation displays a positive shift of 3 mV . *indicates p<0.05 (Mann-Whitley U test).