

Online Table 1
Electrocardiographic Data

Genotype	Wild type	<i>Myh6-Mcm^{Tam}</i>	<i>Mb21dl^{-/-}</i>	<i>Myh6-Mcm^{Tam}:Dsp^{F/F}</i>	<i>Myh6-Mcm^{Tam}:Dsp^{F/F}:Mb21dl^{-/-}</i>	<i>p</i> (ANOVA)
Number of mice	7	8	11	19	19	NA
Heart rate (bpm)	467.3±36.6	470.8±36.1	477.6± 24.8	480.9±33.7	498.6±33.9	0.1363
P duration (msec)	14.3±2.1	14.5±1.9	14.1±1.5	13.9±2.2	14.9±1.9	0.6080
PR Interval (msec)	40.8±8.8	38.4±4.0	39.3±5.4	35.6±5.1	39.5±4.5	0.1330
QRS duration (msec)	16.6±3.8	17.3±2.9	16.1±1.0	15.6±2.5	17.4±3.6	0.4763*
2 nd degree AVB (N, %)	0 (0, 0%)	0.1±0.4 (1, 13%)	0 (0, 0%)	0.6±1.5 (13, 16%)	0.3± 0.7 (5, 16%)	0.3893*
3 rd degree AVB (N, %)	0 (0, 0%)	0 (0, 0%)	0 (0, 0%)	0.4±1.2 (3, 16%)	0.1±0.2 (1, 5%)	0.3201*
PACs (N, %)	1.6±3.7 (11, 29%)	0.3±0.5 (2, 25%)	5.0±3.9 (55, 73%)	1.5±3.2 (28, 42%)	1.8±5.5 (35, 26.3%)	0.0223*
PVCs (N, %)	0 (0, 0%)	0 (0, 0%)	0 (0, 0%)	137.0±556.1 (2,466, 65%)	211.2±521.7 (4,103, 79%)	0.5679
SVT (N, %)	0 (0, 0%)	0 (0, 0%)	0 (0, 0%)	0 (0, 0%)	0.2±0.7 (3, 5%)	0.6810
VT (N, %)	0 (0, 0%)	0 (0, 0%)	0 (0, 0%)	0.2±0.3 (2, 11%)	0.2±0.3 (2, 11%)	1.0000
Other rhythms	None	None	None	Isorhythmic atrial rhythm, lasting up to 360 sec. Isorhythmic ventricular rhythm lasting 30 min.	Isorhythmic atrial rhythm lasting up to 250 sec. Frequent runs of ventricular bigeminy.	NA

Abbreviations: *Myh6*: Myosin heavy chain; *Mcm^{Tam}*: MerCreMer mice injected with tamoxifen; *Mb21dl*: Gene encoding CGAS; *Dsp^{F/F}*: Gene encoding Dsp with floxed alleles; NA: Non-applicable; AVB: atrioventricular block; N: number per events; %: Percent of mice with the event; PACs: Premature atrial contractions; PVCs: Premature ventricular contractions; SVT: supraventricular tachycardia; VT: Ventricular tachycardia.

* By the Kruskal-Wallis because of unequal variations

Online Table 2

Oligonucleotide Primers, Antibodies

Genotyping Primers

Gene	Forward sequence	Reverse sequence
<i>Cre recombinase</i>	TCTATTGCACACAGCAATCCA	WT: GTAGGAAGTTCAAAGGATGC Mutant: CCAGCATTGTGAGAACAAAGG
<i>Mb21d1(Ex2)</i>	ATATTTCCCCCTGTGTTGGA	WT: GTGCCAGGTGACACAACATC Mutant: CGGATGGATGAACAAACAGA
<i>Dsp</i>	GTTGGGCCTCTCGAATCAT	TCTTTGTCTGTTGCCATGTGA

List of antibodies

Antibodies	Concentration	Supplier	Catalog number
Anti-mouse IgG HRP linked antibody	1:3000 (IB)	Cell Signaling Technology	7076
Anti-Rabbit IgG HRP linked antibody	1:3000 (IB)	Cell Signaling Technology	7074
ASC	1:1000(IB)	Cell Signaling Technology	67824
ATM	1:1000(IB)	Cell Signaling Technology	2873S
ATP5F1A	1:100 (IF)	Proteintech	66037-1-Ig
BAD	1:1000(IB)	Cell Signaling Technology	9292
BAX	1:2000(IB)	Proteintech	50599-2-Ig
CASP3	1:1000(IB)	Cell Signaling Technology	14220
CASP8	1:1000(IB)	Cell Signaling Technology	4927
CDKN1A	1:250 (IB)	BD Pharmingen	556431
CGAS	1:1000(IB)	Cell Signaling Technology	31659
COL1A1	1:100 (IF)	Abcam	Ab21286
GAPDH	1:1000(IB)	Abcam	Ab8245
Goat anti Mouse Alexa Fluor 647	1:500 (IF)	Invitrogen	A32728
Goat anti Rabbit Alexa Fluor 594	1:1000 (IF)	Invitrogen	A11012
GSDMD	1:1000(IB)	Cell Signaling Technology	39754
H3K9ac	1:500 (IF)	Active Motif	39917
IRF3	1:1000(IB)	Cell Signaling Technology	4302

MLKL	1:1000(IB)	Cell Signaling Technology	37705
MMP9	1:1000(IB)	Proteintech	10375-2-AP
P50	1:1000(IB)	Cell Signaling Technology	13586
P52 (RELB)	1:1000(IB)	Cell Signaling Technology	4882S
P60	1:1000(IB)	Cell Signaling Technology	8242
Phospho-Histone H2A.X (Ser139)	1:100 (IF) 1:1000(IB)	Cell Signaling Technology	2577S
Phospho-IRF3-386	1:1000(IB)	Cell Signaling Technology	37829
Phospho-IRF3-396	1:1000(IB)	Cell Signaling Technology	4947
RIPK1	1:1000(IB)	Cell Signaling Technology	3493
RIPK3	1:1000(IB)	Cell Signaling Technology	15828
SFRP3	1:500(IB)	Santa Cruz	sc-514350
SPP1	1:1000(IB)	Proteintech	30200-1-AP
STING1	1:1000(IB)	Abcam	ab92605
TBK	1:1000(IB)	Cell Signaling Technology	3504
TGFβ	1:1000(IB)	Bio-Techne	mab1835
TP53	1:1000(IB)	Cell Signaling Technology	32532S
TP53BP1	1:100 (IF)	Novus	NB100-304
TUBA1A	1:1000(IB)	Cell Signaling Technology	2125S
VCL	1:10000 (IB)	Abcam	Ab129002
VIM	1:5000(IB)	Proteintech	10366-1-AP

Oligonucleotide primers used in qPCR reactions

Name	Sequence
<i>12s</i>	Forward: AAGGTTTGGTCCTGGCCTTA Reverse: GTGGCTAGGCAAGGTGTCTT
<i>16s</i>	Forward: CACTGCCTGCCAGTGA Reverse: ATACCGCGGCCGTAAA
<i>18s</i>	Forward: GGCTCTTCCGTGTCTACGAG Reverse: CCAGCCAACGTAGAAAAGCC
<i>Actb</i>	Forward: CTTGTTTGCCTTCCTGCTG Reverse: ACCGGCCGCATTATTACCAT
<i>Apob</i>	Forward: CGTGGGCTCCAGCATTCTA Reverse: TCACCAGTCATTCTGCCTTTG
<i>Ccl7</i>	Forward: CCACATGCTGCTATGTCAAGA

	Reverse: ACACCGACTACTGGTGATCCT
<i>Cd44</i>	Forward: GGCTCTGATTCTTGCCGTCT Reverse: TCCTGTCTTCCACTGTCCCA
<i>Cd83</i>	Forward: CGCAGCTCTCCTATGCAGTG Reverse: GTGTTTTGGATCGTCAGGGAAT
<i>Cox1</i>	Forward: TCGGAGCCCCAGATATAGCA Reverse: TTTCCGGCTAGAGGTGGGTA
<i>Cytb</i>	Forward: GCTTTCCACTTCATCTTACCATTTA Reverse: TGTGGGTTGTTTGATCCTG
<i>Gapdh</i>	Forward: GCCTCCTCCAATTCAACCCT Reverse: CATAGGTCAGGATGCCCTGC
<i>Hk2</i>	Forward: GCCAGCCTCTCCTGATTTTAGTGT Reverse: GGGAACACAAAAGACCTCTTCTGG
<i>Irf7</i>	Forward: GAGACTGGCTATTGGGGGAG Reverse: GACCGAAATGCTTCCAGGG
<i>Mmp9</i>	Forward: GGACCCGAAGCGGACATTG Reverse: CGTCGTCGAAATGGGCATCT
<i>Nd1</i>	Forward: CTAGCAGAAACAAACCGGGC Reverse: CCGGCTGCGTATTCTACGTT
<i>Nd4</i>	Forward: AACGGATCCACAGCCGTA Reverse: AGTCCTCGGGCCATGATT
<i>Nr4a2</i>	Forward: GTGTTCAGGCGCAGTATGG Reverse: TGTATTCTCCCGAAGAGTGGTAA
<i>Rps18</i>	Forward: TGTGTTAGGGGACTGGTGGACA Reverse: CATCACCCACTTACCCCCAAAA
<i>Sfrp1</i>	Forward: TACTGGCCCGAGATGCTCAA Reverse: GAGGCTTCCGTGGTATTGGG
<i>Sfrp2</i>	Forward: CCCTTTGTAAAAATGACTTCGCAC Reverse: CAGGATGATCTTGGTGTCTCTGT
<i>Spp1</i>	Forward: AGCAAGAAACTCTTCCAAGCAA Reverse: GTGAGATTTCGTCAGATTCATCCG
<i>Tnc</i>	Forward: TTTGCCCTCACTCCCGAAG Reverse: AGGGTCATGTTTAGCCCCACTC
<i>Tnfrsf1a</i>	Forward: GGCAGTGCATACCTGTTTTTG Reverse: AACCGCAACTGGACGATGAG
<i>Vcl</i>	Forward: CAGCCCAGATGCTTCAGTCA Reverse: CGAACCTCAGCCTCATCGAA
<i>Vim</i>	Forward: TGCACGATGAAGAGATCCAGG Reverse: CTTTCATACTGCTGGCGCAC