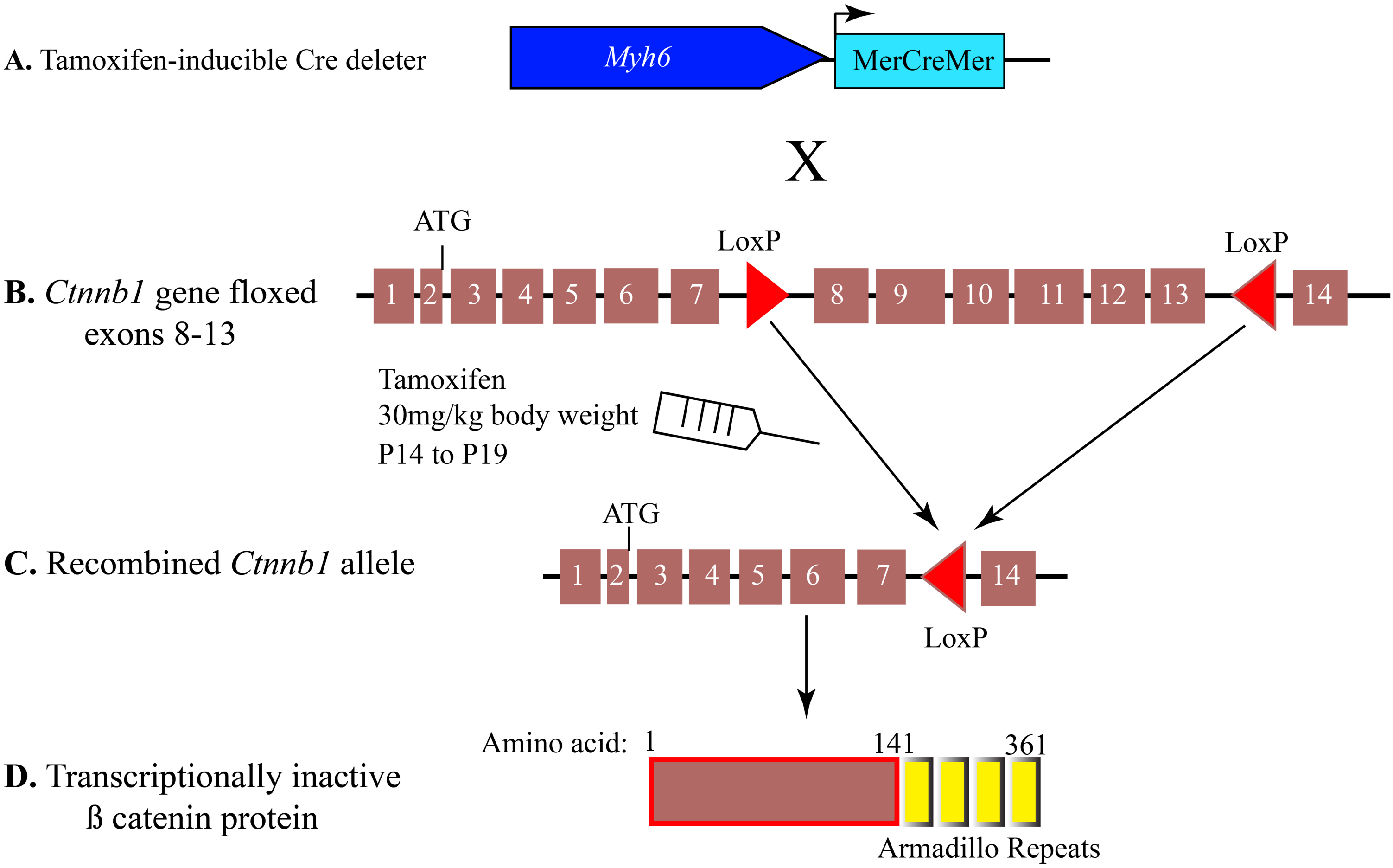
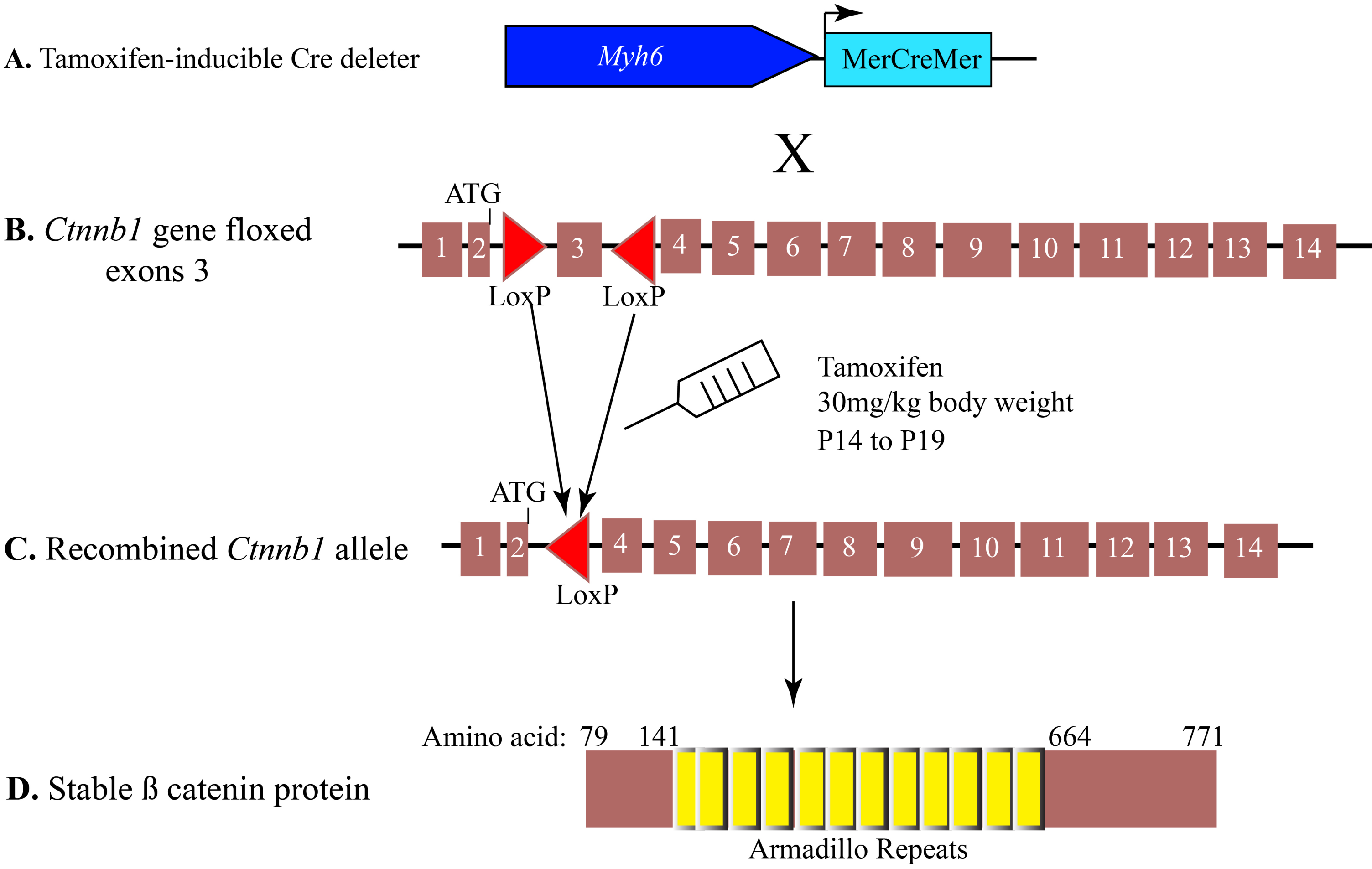
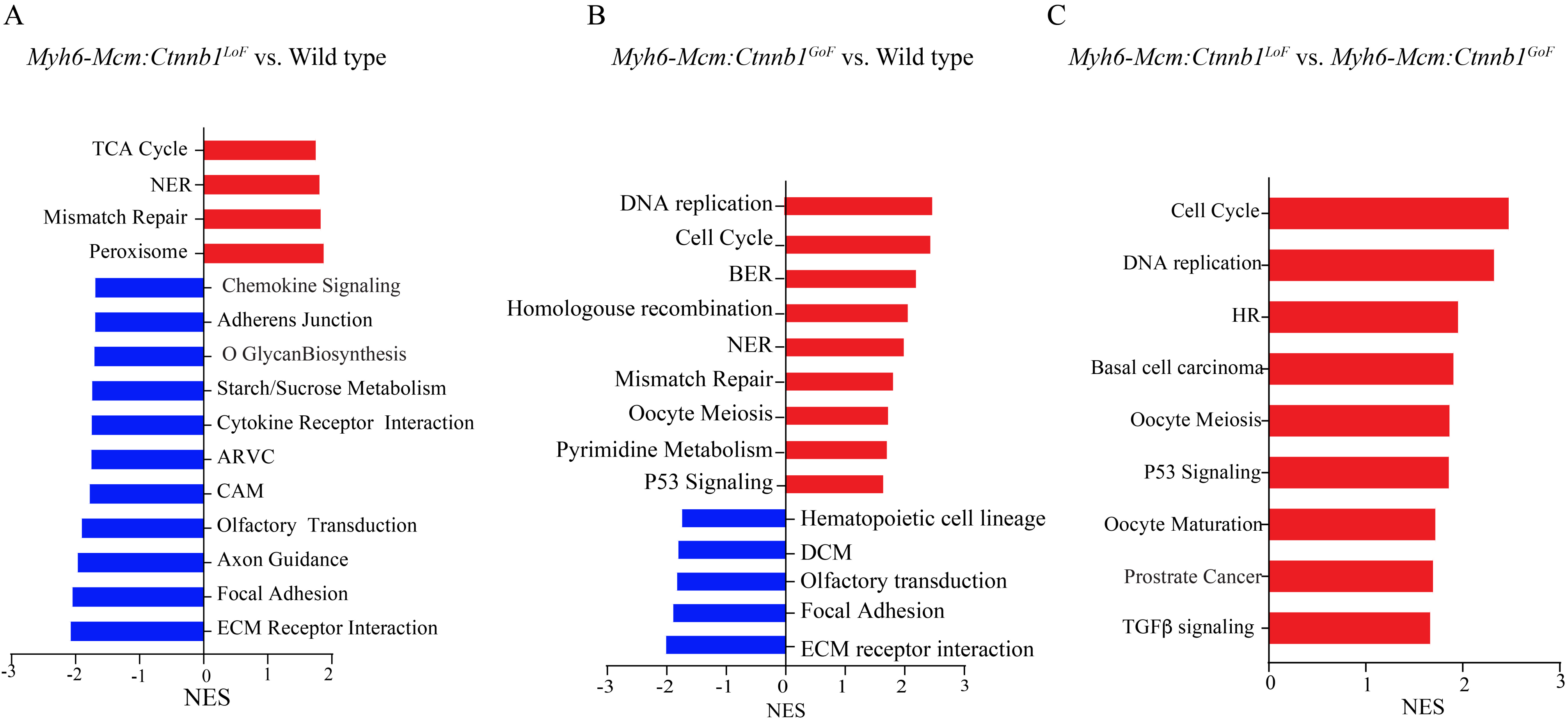
A. CTNNB1 loss of function



B. CTNNB1 gain of function

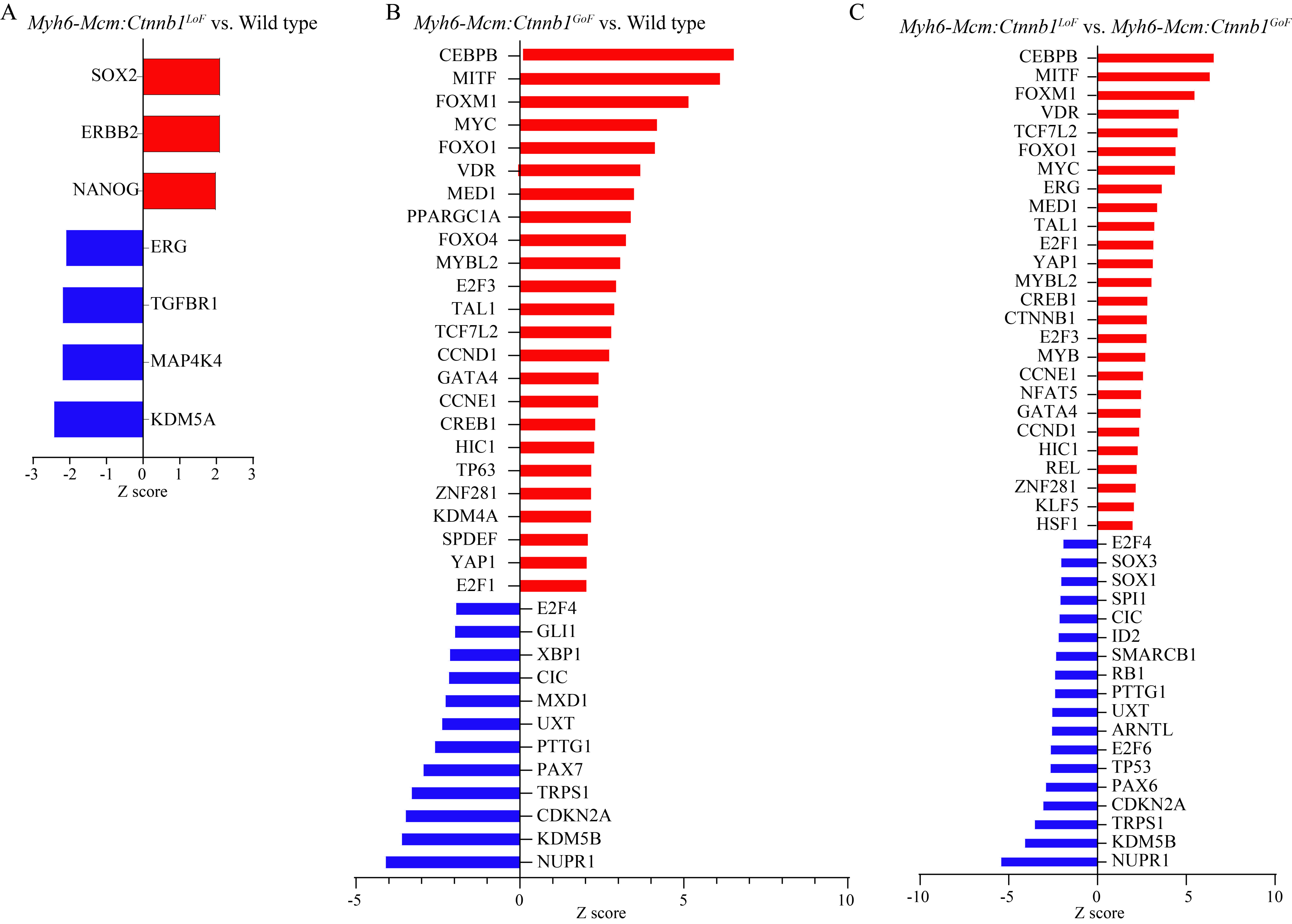


Online Figure 1. Schematic illustration of loss of function and gain of function ß catenin mice using *Myh6-MerCreMer* and *Ctnnb1* floxed alleles



Online Figure 2. Biological pathways predicted to be dsyregulated in the myocytes isolated from the *Myh6-Mcm:Ctnnb1*^{LoF} (A), *Myh6-Mcm:Ctnnb1*^{GoF} (B) compared to myocytes isolated from the wild type mice. Panel C depicts the predicted biological pathways dysregulated when comparing the DEGs in the myocytes from the *Myh6-Mcm:Ctnnb1*^{LoF} and *Myh6-Mcm:Ctnnb1*^{GoF} mice. The NES values are depicted only for pathways that had a q-value of <0.05.

Abbreviations:
NES: Normalized enrichment score.
TCA: tricarboxylic acid
NER: Nucleotide excision repair
ARVC: Arrhythmogenic right ventricular cardiomyopathy
CAM: Crassulacean acid metabolism
ECM: Extracellular matrix
BER: Base excision repair
DCM: Dilated cardiomyopathy
HR: Homologous recombination
TGFβ: Transforming growth factor beta



Online Figure 3. Transcriptional regulators of gene expression predicted to be dsyregulated in the myocytes isolated from the *Myh6-Mcm:Ctnnb1*^{LoF} (A) *Myh6-Mcm:Ctnnb1*^{GoF} (B) compared to myocytes isolated from the wild type mice. Panel C depicts predicted transcriptional regulators of the DEGs the myocytes from the *Myh6-Mcm:Ctnnb1*^{LoF} and *Myh6-Mcm:Ctnnb1*^{GoF} mice.

Online Table 1: Oligonucleotide Primers, Antibodies, and TaqMan probes

Genotyping primers:

Gene	Forward sequence	Reverse sequence
Cre recombinase	TCTATTGCACACAGCAATCCA	CCAGCATTGTGAGAACAAGG
Ctnnb1(Ex3)	AGACTGCCTTGGGAAAAGCGC	TGGATGGGATCTGCATGCCCTCATCTA
Ctnnb1(Ex8-13)	TGCAGCTTACCTGACTCCTG	CCTGTTAGCCCTCATGGTGT

List of antibodies

Antibodies	Concentration	Supplier	Catalog number
Anti-mouse IgG HRP linked antibody	1:4000 (IB)	Cell Signaling Technology	7076
Anti-Rabbit IgG HRP linked antibody	1:2000 (IB)	Cell Signaling Technology	7074
Donkey anti Rat Alexa Fluor 594	1:1000 (IF)	Invitrogen	A11007
Goat anti Mouse Alexa Fluor594	1:1000 (IF)	Invitrogen	A11005
Goat anti Rabbit Alexa Fluor 488	1:1000 (IF)	Invitrogen	A11012
GAPDH	1:1000 (IB)	Cell Signaling Technology	2118
Vinculin	1:10000 (IB)	Abcam	Ab129002
CTNNB1 (C-terminal)	1:1000 (IB) 1:100 (IF)	Cell Signaling Technology	8480S
CTNNB1 (N-terminal)	1:1000 (IB)	Cell Signaling Technology	9562S
CTNNB1	1:50 (IF)	Cell Signaling Technology	9561S
Ki-67	1:250 (IF)	Abcam	ab15580
Phospho Histone H3	1:1000 (IF)	Abcam	ab10543
PCM1	1:1000 (IF)	Sigma	HPA023370
PCM1	1:50 (IF)	Santa Cruz	Sc-398365
PLIN	1:100 (IF)	Cell signaling	9349

Oligonucleotide primers used in qPCR reactions

Name	Sequence
Gapdh	Forward: AACTTTGGCATTGTGGAAGG Reverse: GGATGCAGGGATGATGTTCT
Ctnnb1 GOF (ex3)	Forward: AGTCCTTCACGCAAGAGCAA Reverse: CAAACTGCGTGGATGGGATC
Ctnnb1 GOF (ex3-4)	Forward: TTCCCAGTCCTTCACGCAAG Reverse: TGCCCTCATCTAGCGTCTCA

Ctnnb1 LOF (ex9)	Forward: TCTTGTACGCACCGTCCTTC Reverse: CCATAATGAAGGCGAACGGC
Ctnnb1 LOF (ex12-13)	Forward: ACTCCAGGAATGAAGGCGTG Reverse: TGGTCAGCTCGACTGAAAGC
Ccnb1	Forward: GTGCCGCCTGTACATAGGAT Reverse: TCGACAACTTCCGTTAGCCT
E2f1	Forward: CCACGAGGCCCTTGACTATC Reverse: ACACCCTGAATCCCTAGGCT
Aurka	Forward: GAGCTACCGGGATCGCTTG Reverse: CCGAAGGGAACAGTGGTCTT
Ccnb2	Forward: CTATCCGGCGGGCAGTTTTA Reverse: GGCAGAGCTGGTACTTTGGT
Cenpe	Forward: AAGTTCGGAGAGAGTGCAGC Reverse: TTCCTCGCTTAGGAGCGTTG
Mcm5	Forward: CGCCGCTGTGAGGTACA Reverse: TCAGGAACTCCTTGAATCGCC
Smc4	Forward: CAGTCGTAACTTGGCCCTCG Reverse: TTCTGGGACCCGCGAATTT
Mcm2	Forward: CTCCAAGGCTGGCATCGTTA Reverse: CAAAGCGGGAAATGATGGGC
Mcm3	Forward: GGGCACAGTAGTGCTGGATG Reverse: TCCCGAACCTTGTTCTGGTAA
Ccnd2	Forward: ATTCAGCCAAAGGAAGGAGGTAAG Reverse: ACCACTCGGTCCCGACTGTAA
Cox7a1	Forward: TGCCAGGATCCGGAGTCTTAGAA Reverse: GGTCATTGTCGGCCTGGAAG
Atp5e	Forward: TGGACTCAGCTACATCCGGT Reverse: CGTTCGCTTTGAACTCGGTC
Cox6a2	Forward: GCCCAGAGTTCATCCCGTAT Reverse: AGGATTGACGTGGGGATTGT
Atp5g1	Forward: CGCTCAGACCAAGGGCTAAA Reverse: CCCTGGTACAGGAGCGAATC
Cox7a2	Forward: AGAGGACCATCAGCACCACT Reverse: CATCAGATGCCCCGCCTTTC
Cox8b	Forward: GCCAGCCAAAACTCCCACTTC Reverse: GCTCTCCAAGTGGGCTAAGA
Cox6c	Forward: GGCTGGTATCTTTCAGAGTGC Reverse: TAGTTCAGGAGCGCAGGTCA
Ndufa5	Forward: AAGCTGGATATGGTCAAGGCG Reverse: CTCTTCCACTTCACCACCCT
Ndufs6	Forward: TTTCGGGGTTCAAGTGTCGC Reverse: CGAACCCTCCTGTAGTCTTT
Uqcr10	Forward: CGCAGAACTTCCACCTTTGC Reverse: CCACAGTTTCCCCTCGTTGA
Uqcrq	Forward: GCCTTCCCAAGCTATTTCAGCA Reverse: ACCTGGTTGCCCCATGTGTAG
Vcl	Forward: GGTCTAGCAAGGGCAATGAC Reverse: TGAATAAGTGCCCGCTTGGT
Mmp12	Forward: TCTGCTGAAAGGAGTCTGCAC Reverse: AGGTTTCTGCTGGGAACCTTCA

Lgals3	Forward: TACTAGAAGCGGCCGAGC Reverse: TGTCTGCCATTTTCCTGGGTA
Lrp1	Forward: CAAAGCTGAAGGCTCCGAGT Reverse: TATGCGGACACTCTCATCGC
Tgfb1	Forward: TGGAGCAACATGTGGAACTC Reverse: GTCAGCAGCCGGTTACCA
Tgfb2	Forward: AGGAGTGGCTTCACCACAAAGACA Reverse: ATTAGACGGCACGAAGGTACAGCA
Tgfb3	Forward: AGCTCTTCCAGATACTTCGACC Reverse: AAAGACAGCCATTCAGCGGT
Timp1	Forward: CATGGAAAGCCTCTGTGGATA Reverse: CTCAGAGTACGCCAGGGAAC
Postn	Forward: AGAGAAATCCCTGCACGACA Reverse: GTTGGTGCAAACAAGGTCCA
Bcl2	Forward: CACCCCTGGTGGACAACATC Reverse: GTTCCACAAAGGCATCCCAGC
Col1a1	Forward: TGACTGGAAGAGCGGAGAGTA Reverse: GAGTAGGGAACACACAGGTCT
Col3a1	Forward: CTGTAACATGGAAACTGGGGAAA Reverse: CCATAGCTGAACTGAAAACCACC
Casp3	Forward: AGCTTGGAACGGTACGCTAA Reverse: GAGTCCACTGACTTGCTCCC
Casp8	Forward: GCGTGGAACAGGAAGTGAGTA Reverse: GAAGAGCTGTAACCTGTGGC
Bok	Forward: CAGCGTATACCGGAACGTGG Reverse: TTGCCCCATGTGATACCTGC
Bak	Forward: CAAGATCGCCTCCAGCCTATT Reverse: CCCAGGAAGCCGGTCAAAC
Bid	Forward: CCGCAAACCTTTGCCTTAGC Reverse: AACCGTTGCTGACCTCAGAGT
Bad	Forward: AAATGGGAACCCCAAAGCAG Reverse: GAACATACTCTGGGCTGCTGG
Puma (Bbc3)	Forward: GAGACAAGAAGAGCAGCATCG Reverse: TAGTTGGGCTCCATTTCTGG
Bax	Forward: ACAGGGGCCTTTTTGCTACA Reverse: CACTCGCTCAGCTTCTTGGT
Noxa (Pmaip1)	Forward: ATAACTGTGGTTCTGGCGCA Reverse: CAATCCTCCGGAGTTGAGCA
Apoa5	Forward: AACCGAGCAGGGGCCAT Reverse: TAGTCCCAGAGGCTCTTCCG
Pnpla2	Forward: AATCTCTACCGCCTCTCGAA Reverse: AGGGTTGGGTTGGTTCAGTA
Angptl3	Forward: TTTGGGAGGCTCGATGGAGAA Reverse: TGCTTGCTGTCTTTCCAGTCT
Angptl4	Forward: GACTGCCAGGAACTCTTCCAA Reverse: GTCCAGCCTCCATCTGAAGT
Lpl	Forward: TACCCCCTAGACAACGTCCA Reverse: CCAGCTGGATCCAAACCAGT
Gpihbp1	Forward: CACAGCGGAACCGACAAAG Reverse: GACTGGCAACAGGTCTGAGT

Agpat1	Forward: AACCTTTGTCGGTTCCGCT Reverse: GACAGAGATACAGCCAGCCG

TaqMan probes

Gene	**TaqMan Assay ID**
Gapdh	Mm99999915_g1
Vcl	Mm00447745_m1
Myh7	Mm0060555_m1
Nppb	Mm01255770_g1
Nppa	Mm01255748_g1
Acta1	Mm00808218_g1
Acta2	Mm00725412_s1
Atp2a2	Mm00437634_m1
Myh6	Mm00440354_m1
Myh7b	Mm01249977_m1

Online Table 2

Summary of STAR Alignment

Genotypes	Total number of reads	Uniquely mapped reads (N)	Uniquely mapped reads (%)
WT	56,986,661	44,080,962	77.35
WT	58,592,357	45,042,018	76.87
WT	57,741,248	43,997,161	76.2
WT	47,657,324	36,515,508	76.62
WT	51,350,429	36,020,507	70.15
Myh6-Mcm	49,365,176	38,120,087	77.22
Myh6-Mcm	55,698,208	42,618,724	76.52
Myh6-Mcm	52,784,899	37,604,823	71.24
Myh6-Mcm	54,496,135	41,523,760	76.2
Myh6-Mcm	62,083,142	46,430,324	74.79
Myh6-Mcm:*Ctnnb1*$^{\mathrm{LoF}}$	49,258,626	37,285,368	75.69
Myh6-Mcm:Ctnnb1$^{\mathrm{LoF}}$	55,434,509	43,330,362	78.16
Myh6-Mcm:*Ctnnb1*$^{\mathrm{LoF}}$	56,104,421	43,793,695	78.06
Myh6-Mcm:*Ctnnb1*$^{\mathrm{LoF}}$	66,455,498	51,492,977	77.48
Myh6-Mcm:*Ctnnb1*$^{\mathrm{LoF}}$	51,960,626	41,176,883	79.25
Myh6-Mcm:*Ctnnb1*$^{\mathrm{GoF}}$	57,822,245	46,206,202	79.91
Myh6-Mcm:*Ctnnb1*$^{\mathrm{GoF}}$	52,708,415	41,106,319	77.99
Myh6-Mcm:*Ctnnb1*$^{\mathrm{GoF}}$	48,100,763	37,181,898	77.3
Myh6-Mcm:*Ctnnb1*$^{\mathrm{GoF}}$	48,171,139	37,186,377	77.2
Myh6-Mcm:*Ctnnb1*$^{\mathrm{GoF}}$	53,481,970	40,409,473	75.56

Abbreviations: WT: wild type; *Myh6:Mcm*: Myosin heavy chain 6:MerCreMer; Ctnnb1: β-catenin; LoF: Loss-of-function; GoF: Gain-of-function.

Data in the WT and *Myh6-Mcm* groups are from Rouhi et al. [33]