

Supplementary Fig. 1. Identification of the transcription start site in the human *Stabilin-2* gene. (a) The strategy used for 5'-RACE PCR amplification is shown. The locations of the gene-specific primers (GSP) used for 5'-RACE PCR are indicated by arrows. (b) The 5'-RACE PCR product was resolved on 2% agarose gel as a specific band (lane 2). Lane 1, 2: AUAP and antisense GSP-3; Lane 3,4: sense GSP and antisense GSP-3. (c) The transcriptional start site was identified by sequencing the 5'-RACE PCR product.

-1342 АВСТААВСАТ ТАБВССТТТТ ТТТТТТТТТ ТТВАВС<u>ТССС САСС</u>САВЯТТ ТСТВВЕСТВВ ССТСТВАВБВ БССТАТВТ<u>В ВАА</u>АВТТТС MZF1 NFAT -1252 CTAGATTATC GGTCATTATA AATGTTGTTT CAAAAGTTGA AAGGAGTCGG GGGGAGAGAG AGAGAGAGAG AGAGAAAACTT TGTAGAGAAAA CdxA SRY -1162 ТАААББАТС<u>А ТТТААССААА</u> АТТАБТАТСТ <u>СТААБТЕ</u>САТ БААТСТ<u>СССА ТТТААТТТАБ</u> ТБТСАТБАБА САТБСССТББ ТТТБТТААТА C/EBP Nkx-2.5 Oct-1 -1072 AGTCCAAACC TTATCCTTCC TGGTGCTGGG TCTGACACGT TTCCATCATG GTTTCCAATA GAATTGAGAA TACCATCTAT TATTTATTTA GATA HFH, HNF-3b -982 TTCATTAAAT ATTGATTGTT TCAGCAGCAG AGGGCAGTGG TTGACAGTAC TGGCTCTGGA GCCACATAGT TTGAATACTA GATTTACCAC Pbx-1 AML-1a C/FBP -892 CTATTAGCTG TGTGGCCTTG GATAAATTCC TTAACCTCTC TGCCTCAGTT TCCTCCTCTG TAAAATGAGA AGAATCATCC TGTTTTACCA C/EBP c-Ets-1 TAGAATAGTG -802 AGTACTGTGA GAATTAAACA ACTAAATCCA TGGAGAGGCC CAAAAAGTGA TGGCTACTAT ACTAGCATG AGTAAGTTTT GATA-1 SRY CdxA -712 CCTTAACTGT TTTCATTATT TTGAAGTGCA GGTCTCTGCT CTAGGAATCA AGGGGTACAG AGAAGATGAG GCTATATTCT TCTGTCCTCA Nkx-2.5 -622 AGGCATTCAT AGCTGGGCAT GGGAGACAGA CAGATAGATG TGACCTCGGC TTTCATGGCT TTATGTGCAA AATTGTGGGA GCATCTTCAG -532 GETCCTETEG AGEGEGCAGCA CAGEAAGECT TCCTEGAAGE GETEGCTITA GATCTEGAAC TTAAAGEGTA AGATTEAACC TACAGECTCA STAT CdxA c-Ets-1 AP-1 GTCACTTGTT ACTGAAGTGG CATGGAAAAG AAGAAAGAAT AGCATCTGCA TGCAGTA -442 GAGTC CCCACCTGTC NFAT AP-1 deltaE -352 GAGGTTATCC AGGGTGAAGC CACCACCTCC TGCAAGGTTT CTGCAACATT CATTCCATAC CTGGGACCGT GCTCACTTAT GGGCACTCCC C/EBP p300 -262 CCAACCCCGC TCGACAGCAA GCTTGGACCT TTGCATTGGC ACCAAAAGGC CTGCAGTGTT CCATGGCGTG GTTGTGGAAA CATTGACAGG E2F NFAT -172 ассасладавс ласлатладас ладастладла дла<u>давадала лат</u>ладавада ладсла<u>далсс аттст</u>алала сттсасладас л<u>слалалатсс</u> Sp1 HSF1 GATA -82 CGGGCCAAGC CTCTGCCTCA CTGCAG GATATCCTGT CATTCAGCAG GATATATAGA CCATTTACAG TGGCCAATTT CACCAAGACT Transcription initiation site AP-1 GATA-2 TATA box +9 CCTGGATTTG CCATTTTTCC TCTTTCTGAA GGCAGGTCTC ACCTATCTCC TGGTTCGATC TAGGAAAAAG GAAAGGAAGG GATTTAAAAAG NFAT GATA NFAT +99 TAAACAGTGA AATGAGAAAG AATTCACTGG GAGTTTATCA AACTAAGTTA AAATAGCTAA GTCAGCCTGA CAGGTGCTTG GCACAGAGAA +189 GGAGCAAATA TTTCCTC NFAT-binding motif pStab2-1342 K LUC A/TGGAAA pStab2-482 K LUC 1: -1264 TGGAAA -1259 pStab2-414 LUC

pStab2+83 H LUC

pStab2-182

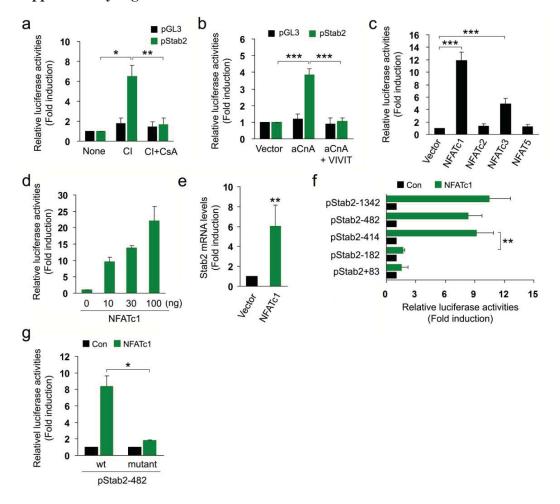
2: -420 <u>TGGAAA</u> -415 3: -188 <u>TGGAAA</u> -183 4,5: +70 <u>AGGAAAAAAGGAAA</u> +82

Supplementary Fig. 2. Characterization of the human stabilin-2 promoter. (a) The human stabilin-2 promoter region. Numbers indicate positions from the transcriptional start site. Putative transcription factor binding sites, which are underlined, were identified using the TFSEARCH program. (b) Schematic representations of the human stabilin-2 promoter construct (nt -1342 to +205) and its deleted constructs. Numbers indicate putative NFAT-responsive elements, which are represented by diamonds.

LUC

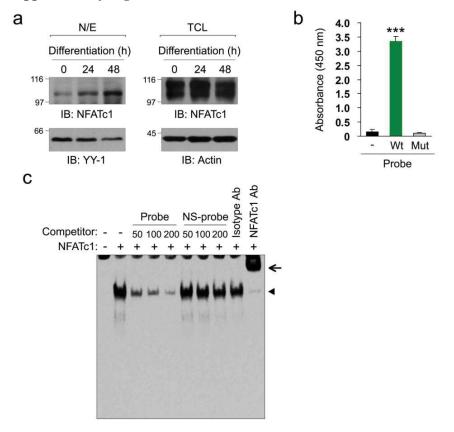
а

b

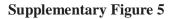


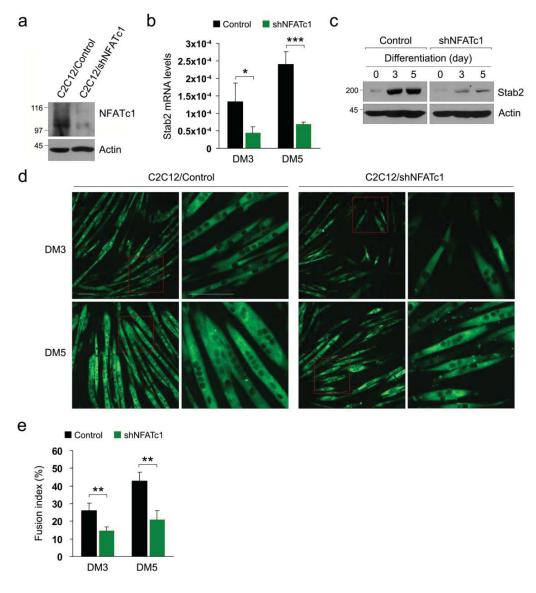
Supplementary Fig. 3. NFATc1 regulates stabilin-2 expression in C2C12 cells. (a) C2C12 cells were transfected with the stabilin-2 promoter construct. At 24 h post-transfection, cells were incubated with vehicle, calcium ionophore A23187 (CI, 1 μ M), or CI plus cyclosporine A (CsA, 1 μ M) for 24 h. Relative luciferase activities were normalized as fold over that of vehicle-treated cells. Data are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (**P* < 0.05, ***P* < 0.01, Student's *t*-test). (b) The stabilin-2 promoter construct (nt -1342 to +205) was co-transfected with plasmid encoding activated calcineurin (aCnA) and/or GFP-VIVIT into C2C12 cells. Relative luciferase activities were normalized as fold over that of the control vector. Data are presented as mean \pm s.d. (n=4). Asterisks indicate statistical significance (****P* < 0.001, Student's *t*-test). (c) C2C12 cells were transfected with stabilin-2 promoter construct and the indicated NFAT expression vector. Relative luciferase activities were normalized as fold over that of pcDNA3.1 vector. Data are presented as mean \pm s.d.

(n=4). Asterisks indicate statistical significance (***P < 0.001, Student's *t*-test). (d) The stabilin-2 promoter construct was cotransfected with the indicated amount of plasmid encoding NFATc1 into C2C12 cells. Relative luciferase activities were normalized as fold over that of the stabilin-2 promoter in the absence of NFATc1. Data are presented as mean \pm s.d. (n=3). (e) C2C12 cells were transfected with plasmid encoding NFATc1 or empty vector. At 48 h post-transfection, total RNAs were isolated, and levels of stabilin-2 mRNA were assessed by quantitative real-time PCR. Expression levels were normalized as fold over that of the cells transfected with pcDNA3.1 vector. Data are presented as mean \pm s.d. (n=4). Asterisks indicate statistical significance (**P < 0.01, Student's *t*-test). (f) The stabilin-2 promoter construct (nt -1342 to +205) and a series of 5' deletion constructs were co-transfected with plasmid encoding NFATc1 into C2C12 cells. Relative luciferase activities were expressed as fold over that of the stabilin-2 promoter in the presence of pcDNA3.1 vector (Con). Data are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (**P < 0.01, Student's *t*-test). (g) The stabilin-2 promoter construct (nt -482 to +205) as well as its NFAT mutant were cotransfected with plasmid encoding NFATc1 into C2C12 cells. Relative luciferase activities were normalized as fold over that of each promoter in the absence of NFATc1. Data are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (*P <0.05, Student's *t*-test).



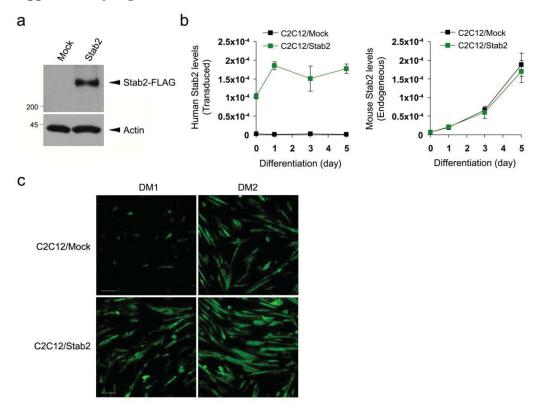
Supplementary Fig. 4. Characterization of the DNA-binding activities of NFATc1 in stabilin-2 promoter. (a) Primary myoblasts were differentiated for the indicated time, and the amounts of NFATc1 protein in total cell lysates (TCL, right panels) and nuclear extracts (N/E, left panels) were analyzed by Western blotting using an anti-NFATc1 antibody. (b) Oligonucleotides containing wild-type (Wt) or mutated (Mut) NFAT-binding site were conjugated onto streptavidin-coated plates, and nuclear extracts from 293FT cells transfected with plasmid encoding NFATc1 were added. After incubation for 2 h, binding between NFATc1 antibody. Data are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (****P* < 0.001, Student's *t*-test). (c) EMSAs were performed with biotin-labelled NFAT-responsive element oligonucleotide in 293FT cells transfected with plasmid encoding NFATc1. For competition experiments, unlabelled oligonucleotides were used at 50-, 100-, or 200-fold molar excesses with respect to the labelled oligonucleotide probe. Closed arrowhead indicates the specific DNA/protein complexes.



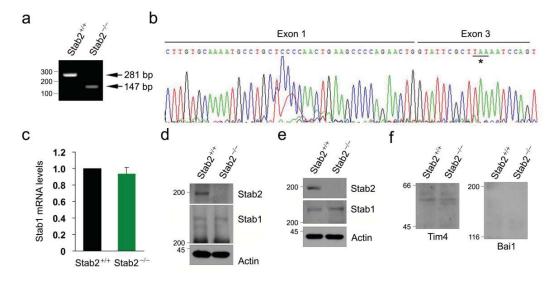


Supplementary Fig. 5. NFATc1 knockdown inhibits myoblast fusion during myogenic differentiation. (a) C2C12 cells infected with retrovirus encoding shRNA against mouse NFATc1 (C2C12/shNFATc1) or retrovirus from pMXs-U6-Puro vector (C2C12/Control) were generated. NFATc1 expression was evaluated by immunoblotting with anti-NFATc1 antibody. A representative result of three independent experiments is shown. (b,c) C2C12/shNFATc1 and C2C12/Control cells were induced to differentiate for the indicated times. Expression of stabilin-2 mRNA (b) and protein (c) were analysed by quantitative real-time PCR and Western blotting, respectively. Data (b) are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (*P < 0.05,

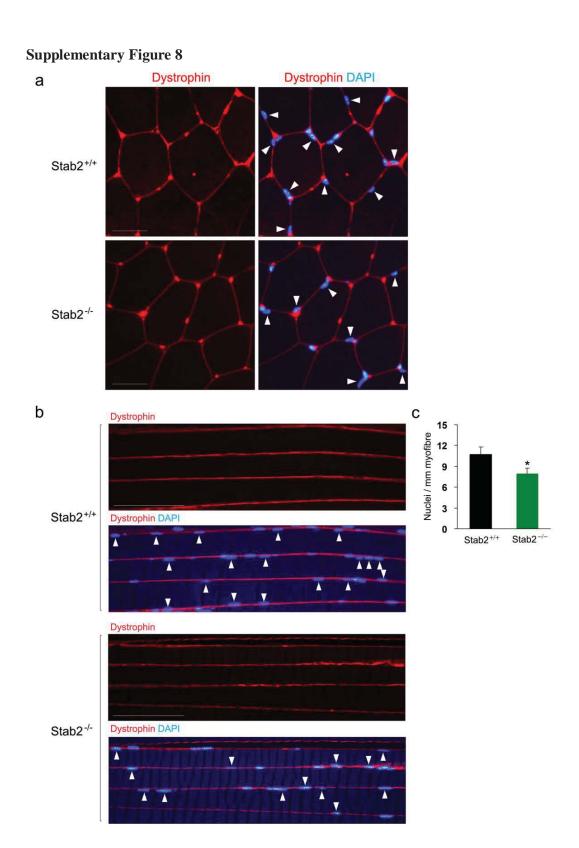
***P < 0.001, Student's *t*-test). (d) C2C12/Control and C2C12/shNFATc1 cells were induced to differentiate for the indicated times. Cells were then fixed and immunostained with anti-MyHC antibody. Representative microscopic fields are shown. Scale bar, 100 µm. Red boxes are shown at higher magnification. (e) C2C12/shNFATc1 and C2C12/Control cells were induced to differentiate for 3 and 5 days, and fusion indices were calculated. Data are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (**P < 0.01, Student's *t*-test).



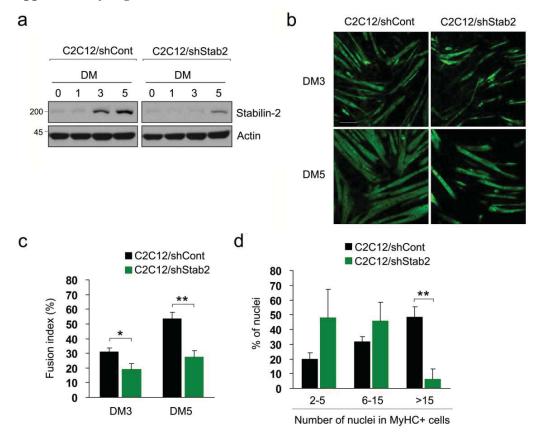
Supplementary Fig. 6. Overexpression of stabilin-2 in C2C12 cells. (a) C2C12 cells stably transfected with plasmid encoding human stabilin-2-FLAG (C2C12/Stab2) or an empty vector (C2C12/Mock) were generated. Stabilin-2 expression was evaluated by immunoblotting with anti-FLAG antibody (1:10,000). A representative result of three independent experiments is shown. (b) Expression levels of transduced human stabilin-2 and endogenous mouse stabilin-2 were determined in C2C12/Mock and C2C12/Stab2 cells using quantitative real-time PCR. Data are presented as mean \pm s.d. (n=3). (c) C2C12/Mock and C2C12/Stab2 cells were induced to differentiate for 24 or 48 h. Cells were then fixed and immunostained with anti-MyHC antibody. Representative microscopic fields are shown. Scale bar, 100 µm.



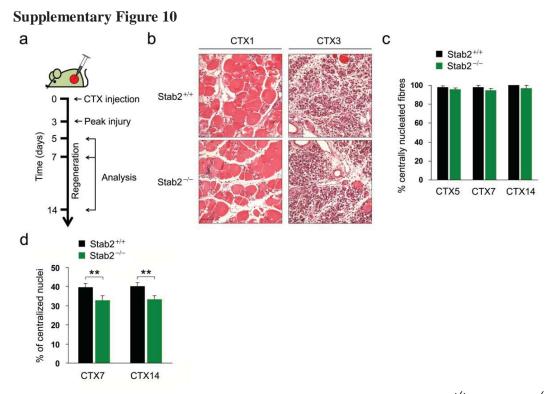
Supplementary Fig. 7. Characterization of Stab2-deficient mice. (**a**,**b**) Deletion of exon 2 in TA muscle of Stab2-deficient mice was confirmed by RT-PCR (a) and DNA sequencing of PCR product (b). Asterisk indicates stop codon. (**c**) Stabilin-1 mRNA levels were analysed in TA muscle of 9-week-old male $Stab2^{+/+}$ and $Stab2^{-/-}$ mice by quantitative real-time PCR (n=3). (**d**,**e**) Expression of stabilin receptors was analysed in TA muscle (d) and primary myoblasts (DM2, e) by immunoblotting. (**f**) Tim4 and Bai1 expression was analysed in TA muscle of 9-week-old male $Stab2^{+/+}$ and $Stab2^{-/-}$ mice by immunoblotting using anti-Tim4 (1:500) and anti-Bai1 (1:500) antibodies, respectively. Representative results are shown.



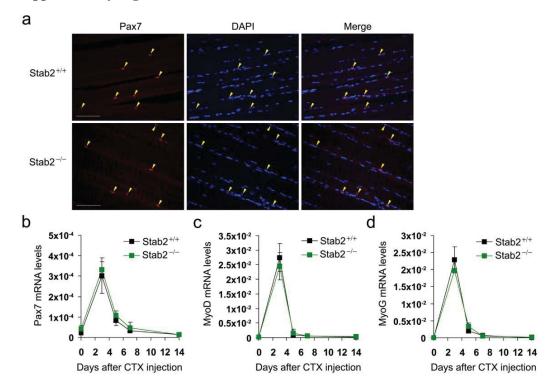
Supplementary Fig. 8. Myonuclear numbers are reduced in $Stab2^{-/-}$ myofibres. (a) Cross-sections of $Stab2^{+/+}$ and $Stab2^{-/-}$ TA muscles were stained with anti-dystrophin antibody (red) and DAPI (blue). Arrowheads indicate myonuclei within myofibres. Scale bar, 25 µm. (b) Longitudinal sections of $Stab2^{+/+}$ and $Stab2^{-/-}$ TA muscles were stained with anti-dystrophin antibody (red) and DAPI (blue). Arrowheads indicate myonuclei within myofibres. Scale bar, 100 µm. (c) The number of nuclei per mm of myofibre (longitudinal sections) was counted for TA muscles of $Stab2^{+/+}$ and $Stab2^{-/-}$ mice. Data are presented as mean ± s.d. (n=5) of each genotype. Asterisks indicate statistical significance (*P < 0.05, Student's *t*-test).



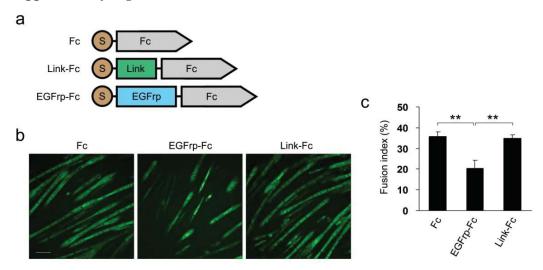
Supplementary Fig. 9. Knockdown of stabilin-2 inhibits myotube formation during myogenic differentiation. (a) C2C12 cells stably transfected with plasmid encoding shRNA against mouse stabilin-2 (C2C12/shStab2) or control shRNA (C2C12/shCont) were generated. Stabilin-2 expression was evaluated by immunoblotting with anti-stabilin-2 antibody. (b) Representative images of myotube formation in C2C12/shCont and C2C12/Stab2 cells after 3 and 5 days of differentiation (DM3 and DM5). Scale bar, 100 μ m. (c) C2C12/shCont and C2C12/shStab2 cells were fixed and immunostained for MyHC after 3 or 5 days of differentiation, and fusion indices were determined. Data are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (**P* < 0.05, ***P* < 0.01, Student's *t*-test). (d) After 5 days of differentiation (DM5), the percentage of nuclei present in MyHC-positive myotubes with the indicated number of nuclei were determined in C2C12/shCont and C2C12/shStab2 cells. Data are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (**P* < 0.01, Student's *t*-test).



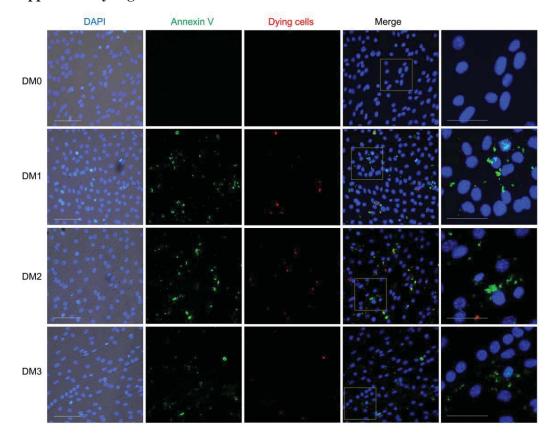
Supplementary Fig. 10. Cardiotoxin injury is comparable for $Stab2^{+/+}$ and $Stab2^{-/-}$ muscles. (a) Schematic diagram of the muscle regeneration experiments. (b) H&E staining of cross sections of $Stab2^{+/+}$ and $Stab2^{-/-}$ TA muscles at CTX1 and CTX3 (days 1 and 3 after CTX injection). Representative sections are shown. Scale bars, 50 µm. (c) The percentage of muscle fibres with centralized nuclei was quantified for $Stab2^{+/+}$ and $Stab2^{-/-}$ TA muscles at CTX5, CTX7, and CTX14. Data are presented as mean \pm s.d. (n=5) of each genotype. (d) The percentage of centralized nuclei was quantified for $Stab2^{+/+}$ and $Stab2^{+/+}$ and $Stab2^{-/-}$ TA muscles at CTX7 and CTX14. Data are presented as mean \pm s.d. (n=5) of each genotype. Asterisks indicate statistical significance (**P < 0.01, Student's *t*-test).



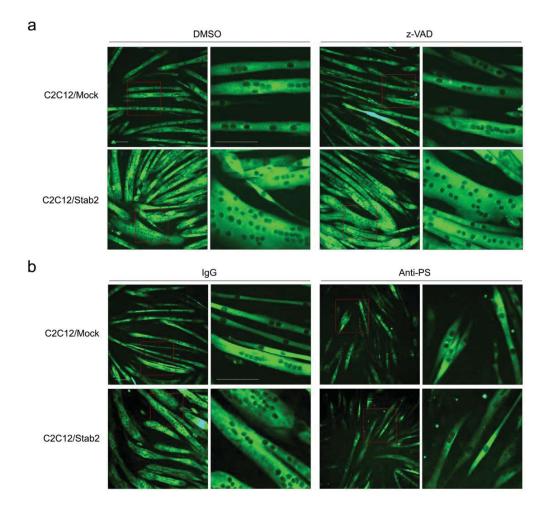
Supplementary Fig. 11. Proliferation and activation of satellite cells is comparable for $Stab2^{+/+}$ and $Stab2^{-/-}$ muscles during muscle regeneration. (a) Longitudinal muscle sections from TA muscle of 9-week-old male $Stab2^{+/+}$ and $Stab2^{-/-}$ mice were co-stained with pax7, a satellite cell specific marker, and DAPI to detect nuclei. Representative microscopic fields are shown. Arrowheads indicate pax7-positive satellite cells. Scale bars, 100 µm. (b-d) Expression levels of pax7, MyoD, and MyoG mRNA in TA muscle of wild type and Stab2-deficient mice were analysed during muscle regeneration after CTX injury. Data are presented as mean ± s.d. (n=3-5).



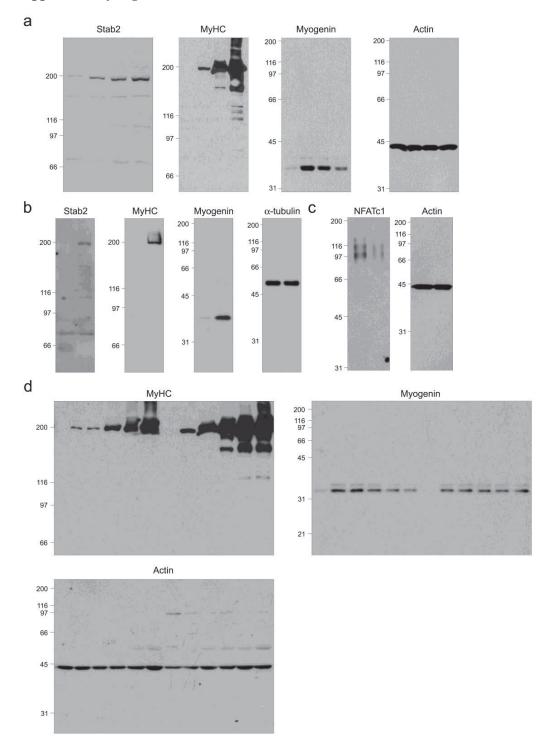
Supplementary Fig. 12. Myoblast fusion was inhibited by masking PS in C2C12 cells using PS-binding domain of stabilin-2. (a) Schematic diagrams of Fc-fusion proteins. (b) C2C12 cells were induced to differentiate in the presence of 20 μ g ml⁻¹ of Fc (control), EGFrp-Fc (PS-binding domain of stabilin-2), or Link-Fc (hyaluronanbinding domain of stabilin-2) protein. After 5 days, cells were then fixed and immunostained with anti-MyHC antibody. Representative microscopic fields are shown. Scale bar, 100 μ m. (c) At DM5, the fusion indices of C2C12 cells in the presence of Fc, EGFrp-Fc, or Link-Fc protein were calculated. Data are presented as mean \pm s.d. (n=3). Asterisks indicate statistical significance (***P* < 0.01, Student's *t*-test).



Supplementary Fig. 13. Phosphatidylserine is expressed on the surface of healthy myoblasts. C2C12 cells were induced to differentiate for the indicated times and stained with Alexa Fluor 488-conjugated Annexin V (for phosphatidylserine) and Fixable Viability Dye eFluor 660 (for dying cells). Cells were then fixed and stained with DAPI. Representative microscopic fields are shown. Scale bar, 100 μ m. Yellow boxes are shown at higher magnification (Scale bar, 50 μ m).



Supplementary Fig. 14. Stabilin-2 mediates myoblast fusion in a PS-dependent manner. (a) C2C12/Mock and C2C12/Stab2 cells were induced to differentiate for the indicated times in the presence of z-VAD-fmk (30 μ M), a pan-caspase inhibitor, or DMSO. Cells were then fixed and immunostained with anti-MyHC antibody. Representative microscopic fields are shown. Scale bar, 100 μ m. Red boxes are shown at higher magnification. (b) C2C12/Mock and C2C12/Stab2 cells were induced to differentiate for the indicated times in the presence of anti-PS antibody (10 μ g ml⁻¹) or mouse IgG (10 μ g ml⁻¹). Cells were then fixed and immunostained with anti-MyHC antibody. Representative microscopic fields are shown. Scale bar, 100 μ m. Red boxes are shown at higher magnification.



Supplementary Fig. 15. Full-size of the blots presented in Fig. 1d (a), Fig. 1e (b), Fig. 2i (c), and Fig. 3f (d).

Primers for RACE-PCR and promoter constructs		
Name	Sequence	
Sense GSP	ATGGAACCTGTGAGTG	CTACTCTGCG
Antisense GSP-1		
Antisense GSP-2		
Antisense GSP-3		
AAP		GTACGGGIIGGGIIGGGIIG
AUAP	GGCCACGCGTCGACTA	
-		
5' pStab2-1342	AAAAGGTACCAGCTAAG	
5' pStab2-482	AAAAGGTACCGATCTGC	
5' pStab2-414	AAAAGCTAGCAGAAGA	
5' pStab2-182	AAAAGCTAGCCATTGAC	
5' pStab2+83	AAAAGCTAGCGGAAGG	
3' pStab2	AAAACTCGAGGAAATAT	
3' pStab2-mNFA		
Primers for quantitative real-time PCR		
Name	Forward	Reverse
	CGCTGTACTCAAGGCTTCCA	CTTCTTGGCACAGGTGTAGGAAC
	TGCTCTGGCTGCCTACTC	GTTGGCTGGCTTCTCACATC
h-Stab2 AC	TGGCTCCTTACCAAACCTGC	GAGCAAACACTGTGTAGGCATCG
Tim-1 CT	GGAATGGCACTGTGACATCC	GCAGATGCCAACATAGAAGCCC
Tim-4 AT	TCTCCCATCCACTTCACAG	CTATCTTCAGTGTTGTCTGGC
Bai1 GC	CAGAACTGGACTTTGAGAAGCTTC	GTCTGGAGGTCAATGATGTC
Myh3 AC	CTCTAGCCGGATGGT	AATTGTCAGGAGCCACGAAAAT
	CATCAAGCCAGGAGACAGC	CCACAGGAAGAAGTCCCAGC
	CTGCTCTGATGGCATGATG	TGGAGATGCGCTCCACTATG
, -	CAAGGTGTGTGTAAGAGGAAG	TGTGGGAGTTGCATTCACTG
	CATCAAATGGGGTGAGGCC	GTTGTCATGGATGACCTTGGC
Primers for Promoter enzyme immunoassay and EMSA		
	Primers for Promoter enzyme imn	hunoassav and EMSA
Name	Primers for Promoter enzyme imn	
Name NFAT-wt (sense)	ř.	Sequence
NFAT-wt (sense)	Biotin-GTGGTTGTGGAA	Sequence ACATTGAC
NFAT-wt (sense) NFAT-wt (antiser	Biotin-GTGGTTGTGGAA Ise) GTCAATGTTTCCACAAC	Sequence ACATTGAC CAC
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense	Biotin-GTGGTTGTGGAA Ise) GTCAATGTTTCCACAAC e) Biotin-GTGGTTGGCTAG	Sequence ACATTGAC CAC CCATTGAC
NFAT-wt (sense) NFAT-wt (antiser	Biotin-GTGGTTGTGGAA Ise) GTCAATGTTTCCACAAC e) Biotin-GTGGTTGGCTAG ense) GTCAATGGCTAGCCAAC	Sequence ACATTGAC CAC CCATTGAC CCAC
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antise	Biotin-GTGGTTGTGGAA se) GTCAATGTTTCCACAAC e) Biotin-GTGGTTGGCTAG ense) GTCAATGGCTAGCCAAC Primers for ChIP	Sequence ACATTGAC CAC CCATTGAC CCAC assay
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense NFAT-mut (antise Name	Biotin-GTGGTTGTGGAA see) GTCAATGTTTCCACAAC e) Biotin-GTGGTTGGCTAG ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward	Sequence ACATTGAC CAC CCATTGAC CCAC assay Reverse
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense NFAT-mut (antise Name Stab2 promoter	Biotin-GTGGTTGTGGAA se) GTCAATGTTTCCACAAC b) Biotin-GTGGTTGGCTAG ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG	Sequence ACATTGAC CCAC CCATTGAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense NFAT-mut (antise Name	Biotin-GTGGTTGTGGAA see) GTCAATGTTTCCACAAC e) Biotin-GTGGTTGGCTAG ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward	Sequence ACATTGAC CCAC CCATTGAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antise Name Stab2 promoter GAPDH	Biotin-GTGGTTGTGGAA se) GTCAATGTTTCCACAAC b) Biotin-GTGGTTGGCTAG ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG	Sequence ACATTGAC CCAC CCATTGAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antise NAME Stab2 promoter GAPDH Name	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot	Sequence ACATTGAC CCAC CCAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antise Name Stab2 promoter GAPDH	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC	Sequence ACATTGAC CCAC CCAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antise Stab2 promoter GAPDH Name Stab2 (sense) Stab2 (antisense	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (snse) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC	Sequence ACATTGAC CCAC CCAC CCAC assay CTCTAGTCCTGCCTACTGCTG CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA IGGA
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antise NFAT-mut (antise Stab2 promoter GAPDH Name Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (snse) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGGCACTCCGTCT	Sequence ACATTGAC CCAC CCAC assay CTCTAGTCCTGCCTACTGCTG CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA TGGA TGAT
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antise Stab2 promoter GAPDH Name Stab2 (sense) Stab2 (antisense	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (snse) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGGCACTCCGTCT	Sequence ACATTGAC CCAC CCAC assay CTCTAGTCCTGCCTACTGCTG CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA TGGA TGAT
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antise NFAT-mut (antise Stab2 promoter GAPDH Name Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (snse) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGCCTTTAATCCTCA	Sequence ACATTGAC CCAC CCAC assay CTCTAGTCCTGCCTACTGCTG CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA TGGA TGAT TCTTC
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antiser Stab2 promoter GAPDH Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise Stab2-Ex1 (sense)	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (snse) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGCCTTTAATCCTCA	Sequence ACATTGAC CCAC CCAC CCAC assay CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA IGGA IGAT TCTTC CAG
NFAT-wt (sense) NFAT-wt (antiser NFAT-mut (sense NFAT-mut (antiser Stab2 promoter GAPDH Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise Stab2-Ex1 (sense)	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGGCACTCCGTCT e) GCTGCCTTTAATCCTCA ense) GCAGGTAATCCTTCCTA	Sequence ACATTGAC CCAC CCATTGAC CCAC assay CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA IGGA IGAT TCTTC CAG
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense NFAT-mut (antisen Stab2 promoter GAPDH Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise Stab2-Ex1 (sense Stab2-Ex3 (antisense Name	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (s) Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGGCACTCCGTCT e) GCTGCCTTTAATCCTCA ense) GCAGGTAATCCTTCCTA	Sequence ACATTGAC CCAC CCAC assay CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA IGGA IGAT TCTTC CAG on vector Sequence
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense) NFAT-mut (antisen Stab2 promoter GAPDH Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise Stab2-Ex1 (sense) Stab2-Ex3 (antisense) Name NFATc1 (sense)	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (se) Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGGCACTCCGTCT e) GCTGCCTTTAATCCTCA Primers for expression AAAAAGGATCCGTCAG/	Sequence ACATTGAC CCAC CCAC CCAC assay CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA TGGA TGAT TCTTC CAG on vector Sequence AGCGAGACTCAGAGG
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense) NFAT-mut (antisen Stab2 promoter GAPDH Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise Stab2-Ex1 (sense) Stab2-Ex3 (antisense) NFATc1 (sense) NFATc1 (sense)	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGGCACTCCGTCT e) GCTGCCTTTAATCCTCA Primers for expression AAAAAGGATCCGTCAG/ e) AAAAACTCGAGCACGC	Sequence ACATTGAC CCAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA TGGA TGAT TCTTC CAG on vector Sequence AGCGAGACTCAGAGG CACGCTGCTTTACGG
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense) NFAT-mut (antisen Stab2 promoter GAPDH Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise Stab2-Ex1 (sense) Stab2-Ex3 (antisense Stab2-Ex3 (antisense) NFATc1 (sense) NFATc1 (sense)	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGGCACTCCGTCT e) GCTGCCTTTAATCCTCA Primers for expression AAAAAGGATCCGTCAG/ AAAAGGATCCGAGAAG	Sequence ACATTGAC CCAC CCATTGAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA TGGA TGAT TCTTC CAG on vector Sequence AGCGAGACTCAGAGG CACGCTGCTTTACGG AGGAGATGC
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense) NFAT-mut (antisen NFAT-mut (antisen Stab2 promoter GAPDH Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise Stab2-Ex1 (sense) Stab2-Ex3 (antisense Stab2-Ex3 (antisense) NFATc1 (sense) EGFrp (sense) EGFrp (antisense)	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC (se) Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC (e) GCTGCCTTTAATCCTCA Primers for expression AAAAAGGATCCGTCAG/ (c) AAAAACTCGAGCCAGAAG (c) AAAACTCGAGGCGCA	Sequence ACATTGAC CCAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA TGGA TGAT TCTTC CAG on vector Sequence AGCGAGACTCAGAGG CACGCTGCTTTACGG AGGAGATGC GGTAAATCCATC
NFAT-wt (sense) NFAT-wt (antisen NFAT-mut (sense) NFAT-mut (antisen Stab2 promoter GAPDH Stab2 (sense) Stab2 (sense) Stab2 (antisense Stab2 (Ex2-antise Stab2-Ex1 (sense) Stab2-Ex3 (antisense Stab2-Ex3 (antisense) NFATc1 (sense) NFATc1 (sense)	Biotin-GTGGTTGTGGAA (se) GTCAATGTTTCCACAAC Biotin-GTGGTTGGCTAG (ense) GTCAATGGCTAGCCAAC Primers for ChIP Forward TGGGACCGTGCTCACTTATG CTCTAGTCCTGCCTACTGCTC Primers for genot GGACACAGGCCATAGC) GGGTTTCTCACTGACC ense) GACTGGCACTCCGTCT e) GCTGCCTTTAATCCTCA Primers for expression AAAAAGGATCCGTCAG/ AAAAGGATCCGAGAAG	Sequence ACATTGAC CCAC CCATGAC CCAC assay Reverse CTCTAGTCCTGCCTACTGCTG ATGTAGGCCATGAGGTCCAC yping Sequence AACTAA TGGA TGAT TCTTC CAG on vector Sequence AGCGAGACTCAGAGG CACGCTGCTTTACGG AGGAGATGC GGTAAATCCATC GGGGTGTTCCATCTAC

Supplementary Table 1. Oligonucleotide sequences used in this study