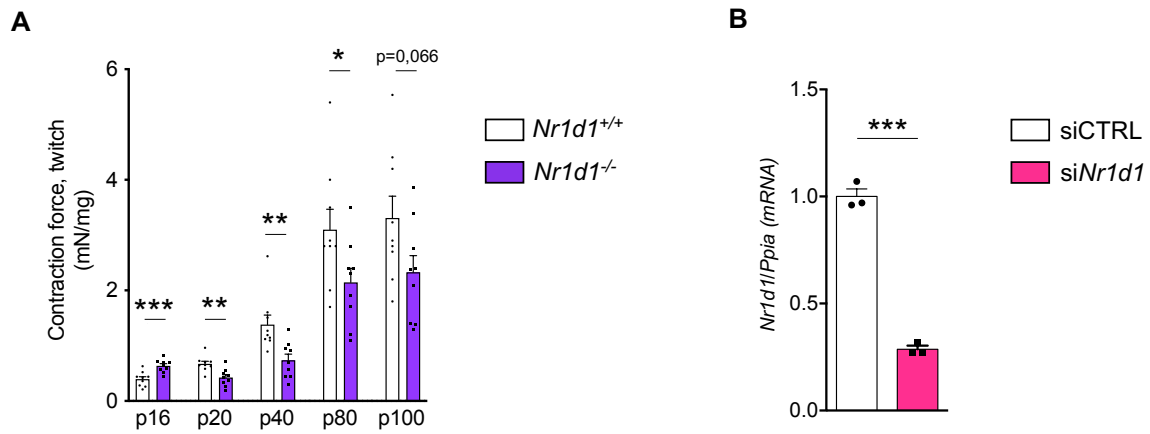
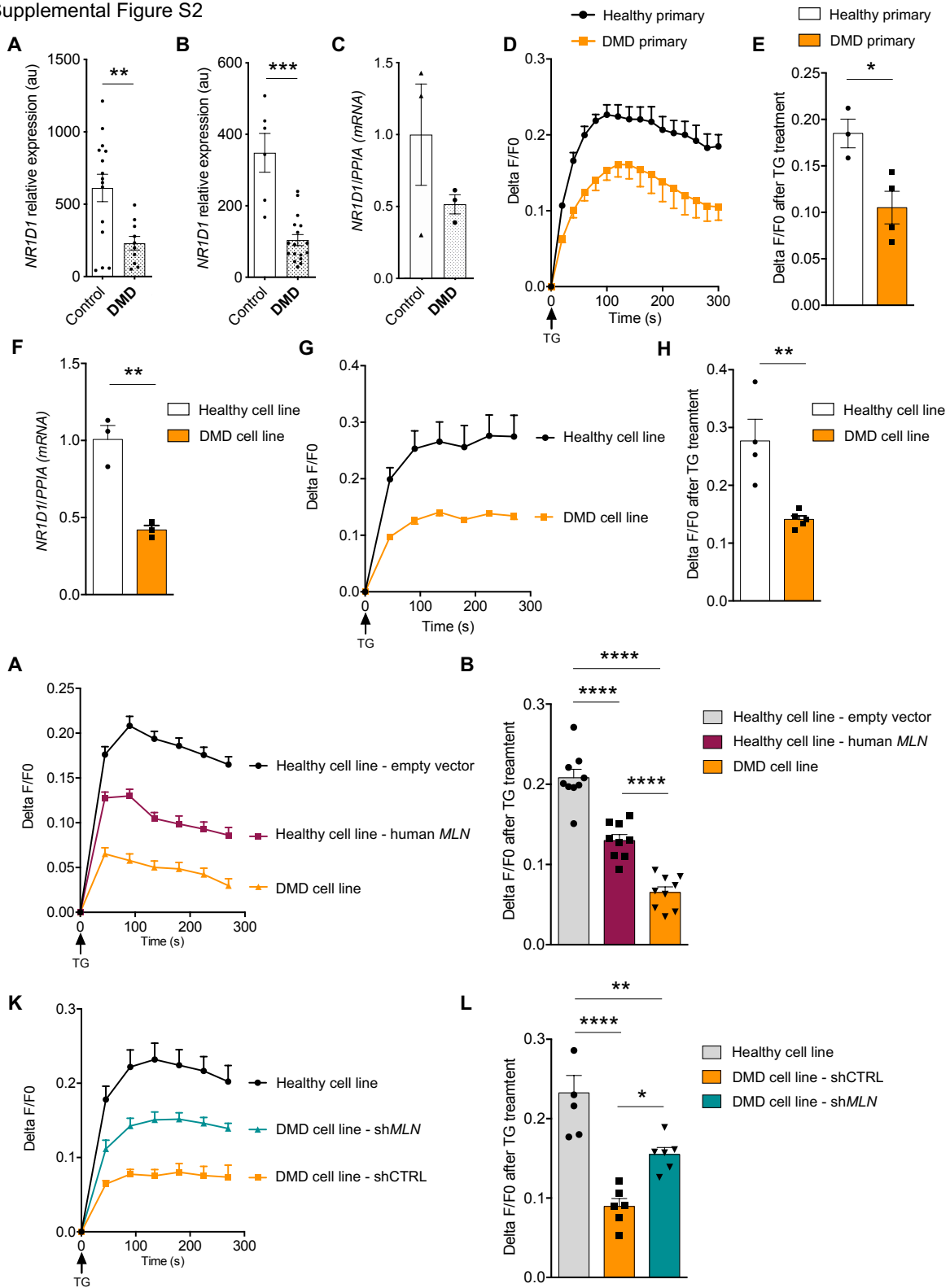


Supplemental Figure S1



Supplemental Figure S1. *NR1D1* modulates mouse muscle contraction. (A) Tetanic contraction of *tibialis anterior* muscle obtained with incremental frequency stimulation (from 16Hz to 100Hz) in *Nr1d1*^{+/+} and *Nr1d1*^{-/-} mice (n=9). * p<0,05, ** p<0,01 and *** p<0,001. (B) *Nr1d1* expression in C2C12 transfected with si*Nr1d1* (n=3).

Supplemental Figure S2

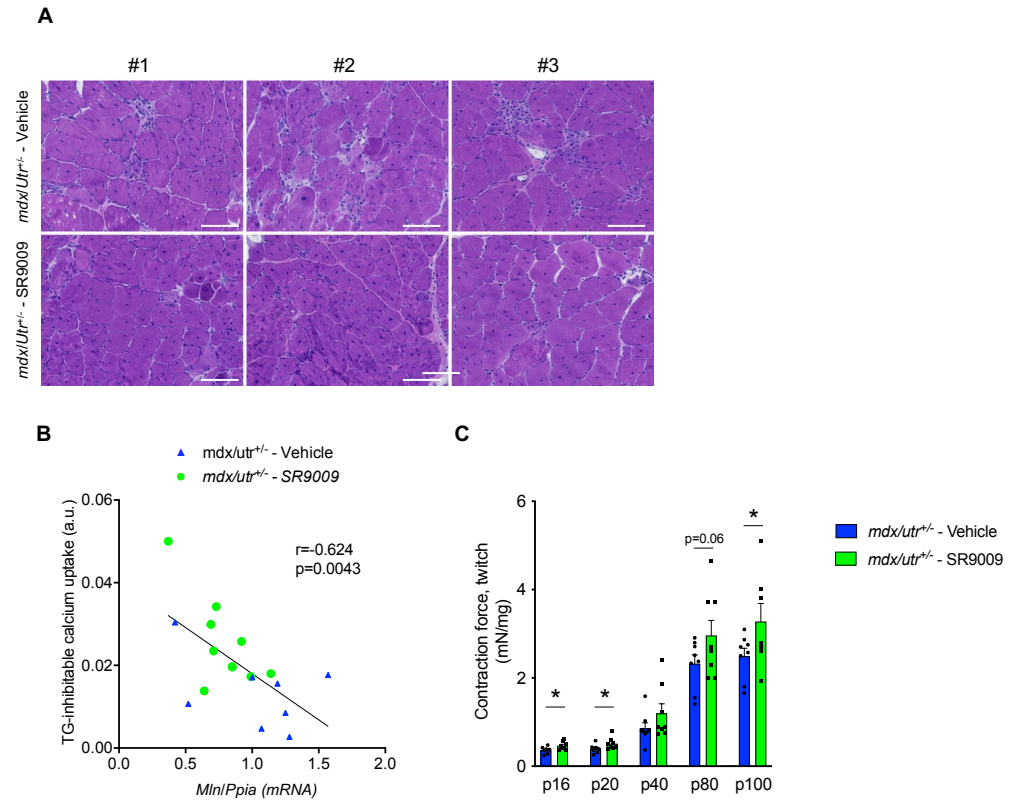


Supplemental Figure S2. *MLN* downregulation in myotubes from patients suffering from Duchenne muscular dystrophy (DMD) restores ER calcium content. Data from (A) GSE3307

probe 204769, **(B)** GSE109178 probe 31637. ** $p < 0.01$, *** $p < 0.001$ vs. control, unpaired t-test. **(C)** RTqPCR results obtained in dorsal muscles from control and DMD patients provided by the French Myobank, $n=3$ independent samples in each group. **(D)** Representative curves and **(E)** peak fluorescence intensity of thapsigargin (TG)-induced Sarcoplasmic Reticulum (SR) Ca^{2+} release in primary myotubes from healthy controls or patients suffering from Duchenne Muscular Dystrophy (DMD). Cells are loaded with Fluo4-AM and SR Ca^{2+} release is induced by the addition of $1\mu\text{M}$ TG. Results are expressed as means $\pm$ SEM of the Delta F/F0 ratio, $n=3$ healthy controls, $n=4$ in DMD groups. * $p=0.0110$ vs. control cells, unpaired t-test. **(F)** Representative curves and **(G)** peak fluorescence intensity of TG-induced SR Ca^{2+} release in immortalized myotubes from healthy controls or patients suffering from DMD. Cells are loaded with Fluo4-AM and SR Ca^{2+} release is induced by the addition of $1\mu\text{M}$ TG. Results are expressed as means $\pm$ SEM of the Delta F/F0 ratio, $n=4$ healthy controls, $n=5$ in DMD groups. ** $p=0.005$ vs. control cells, unpaired t-test. **(H)** *NR1D1* expression in healthy control or DMD immortalized myotubes, $n=5-7$. * $p=0.0035$ vs. control cells in panel B, unpaired t-test. **(I)** Representative curves and **(J)** peak fluorescence intensity of TG-induced Sarcoplasmic Reticulum (SR) Ca^{2+} release in immortalized myotubes from healthy controls or patients suffering from DMD with overexpression of the human MLN or the corresponding empty vector. Cells are loaded with Fluo4-AM and SR Ca^{2+} release is induced by the addition of $1\mu\text{M}$ TG. Results are expressed as means $\pm$ SEM of the Delta F/F0 ratio, $n=9$ replicates for each group. **** $p < 0.0001$ healthy control + human MLN vs. healthy control + empty vector, **** $p < 0.0001$ healthy control + human MLN vs. DMD, **** $p < 0.0001$ healthy control + empty vector vs. DMD 1-way ANOVA, Tukey's multiple comparison test. **(K)** Representative curves and **(L)** peak fluorescence intensity of TG-induced Sarcoplasmic Reticulum (SR) Ca^{2+} release in immortalized myotubes from healthy controls or patients suffering from DMD with shCTRL or shMLN. Cells are loaded with Fluo4-AM and SR Ca^{2+} release is induced by the

addition of 1 μ M TG. Results are expressed as means $\pm$ SEM of the Delta F/F0 ratio, n=9 replicates for each group. ****p<0.0001 healthy control *vs.* DMD + shCTRL, **p<0.0055 healthy control *vs.* DMD + shMLN, *p<0.0174 DMD + shCTRL *vs.* DMD + shMLN, 1-way ANOVA, Tukey's multiple comparison test.

Supplemental Figure S3



Supplemental Figure 3. Effects of SR9009 on muscles from *mdx/Utr*^{+/-} mice. (A) H&E staining on *tibialis anterior* sections from three different (#1, #2, #3) *mdx/Utr*^{+/-} mice treated with SR9009 or vehicle for 20 days. Scale bars indicate 100µm. (B) Pearson correlation analysis between *Mln* expression and SERCA activity in muscle from vehicle- or SR9009-treated *mdx/Utr*^{+/-} mice. (C) Tetanic contraction of *tibialis anterior* muscle obtained with incremental frequency stimulation (from 16Hz to 100Hz) in vehicle- and SR9009-injected *mdx/Utr*^{+/-} mice, n=8-9, * p<0,05.

Supplemental Table S1: Mouse RTqPCR primers

target	Accession number	forward 5'-3'	reverse 3'-5'
<i>Serca1</i>	NM_007504	AAGGAGCCCAGATCAACAGGCA	ACTCCCACAGAGACTGCCTTCCTC
<i>Serca2</i>	NM_009722	GCCATCAGCCAAGTCTCCACAT	AGCTGGCTGCACACCTAAACAA
<i>Ryr1</i>	NM_009109	ACGTACAGTCAGGTGGCTCAGA	CCAGCACAATGAGGTCCTGGTC
<i>Mln</i>	NM_001304739	GTTGCACCCCTGAACAGAACCA	CCTCAGGAGGTAGCAGGTAGCA
<i>Pdgfra</i>	NM_001083316.2	TGCTAGCGCGGAACCTCAGA	ATAGCTCCTGAGACCCGCTG
<i>Colla2</i>	NM_007743.2	CTGCTGGTGTTCTGTGGTTC	CGGCTGTATGAGTTCTTC
<i>Ppia</i>	NM_008907	GCATACGGGTCCTGGCATCTTGTC	ATGGTGATCTTCTTGCTGGTCTTGC

Supplemental Table S2: Human RTqPCR primers

target	Accession number	forward 5'-3'	reverse 3'-5'
<i>MLN</i>	NM_001304732	TCCCTTGACTTTGGACTTCGCT	TCAGCACAGGTGGTCTCTTAGC
<i>NR1D1</i>	NM_021724	ATCAATCGCAACCGCTGCCAGC	TTGGGGATGCGCCCAAACGC
<i>PPIA</i>	NM_001123068	GCATACGGGTCCTGGCATCTTGTC	ATGGTGATCTTCTTGCTGGTCTTGC

Supplemental Table S3: ChIP qPCR primers

target	forward 5'-3'	reverse 3'-5'
<i>Site -1.4kb</i>	TATCTGATACGCAGGTTATCTG	GGGAGAGGGTGTGCAAGTTA
<i>Site -5.4kb</i>	GGCCAGATCTGCTTTAGTATG	CAGGGTGGCTACATTACTCA
<i>Site -6.7kb</i>	GCAGGACATCTCTGACACC	TCAGAGTTCTCTGGCTTTCAG
<i>negative control region</i>	CTGCAGCCCCTTCAGAGGT	CAACCTTGCTAGTGCTAAAAC