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 siNr1d1 (n=3).
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 1µM TG. Results are expressed as means ± 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 µM TG. Results are expressed as means ± 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 1µM TG. Results are expressed as means ± 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 µM TG. Results are expressed as means ± 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 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’ |
|--------|-----------------|---------------|---------------|
| Serca1 | NM_007504       | AAGGAGCCCAGATCAACAGGCA | ACTCCCAAGAGACTTGCTTCTC |
| Serca2 | NM_009722       | GCCATCAGCCAAGTCTCCACAT | AGCTGGCTGACACCTAAACAA |
| Ryr1   | NM_009109       | ACGTACAGTCAGGGCTCAGA | CCAGCACAATGAGGGTCTGGTC |
| Mln    | NM_001304739    | GTTGCAACCCTGAACAGAAACCA | CCTCAGGAGGATGCAGGTAGCA |
| Pdgfra | NM_001083316.2  | TGCTAGCGCGGAACCTCAGA | ATAGCTCTTGAGACCCGCTG |
| Col1a2 | NM_007743.2     | CTGCTGGTGTTCCGGTTC | CGGCTGTATGAGTCTTTC |
| Ppia   | NM_008907       | GCATACGGGTCTGGCATCTGTCC | ATGGTGATCTTCTTGCTGGTCTTG |

### Supplemental Table S2: Human RTqPCR primers

| target | Accession number | forward 5’-3’ | reverse 3’-5’ |
|--------|-----------------|---------------|---------------|
| MLN    | NM_001304732    | TCCCTTGACTTGGACTCGCT | TCAGCACAGGTTGCTCTTACG |
| NR1D1  | NM_021724       | ATCAATCGGACTCGGCTGACG | TGGGGATGCGCCCAAGC |
| PPIA   | NM_001123068    | GCATACGGGTCTGGCATCTTTCC | ATGGTGATCTTCTTGCTGGTCTTG |
**Supplemental Table S3: ChIP qPCR primers**

| target              | forward 5'-3'                  | reverse 3'-5'                  |
|---------------------|--------------------------------|--------------------------------|
| Site -1.4kb         | TATCTGATACGCAGGTTATCTG         | GGGAGAGGGTGTCAGGAAGTA          |
| Site -5.4kb         | GCCAGATCTGCTTGTATG             | CAGGGTGCTACATTACCTCA           |
| Site -6.7kb         | GCAGGACATCTCTGACACC            | TCAGAGTTCTCTGGCTTTCAG          |
| negative control region | CTGCAGCCCCTTCAGAGG           | CAACCTTGCTAGTGCTAAAAAC         |