**Supplementary Figure Legends**

**Fig. S1** Expression of pro-inflammatory (M1) markers in the gastrocnemius muscle from notexin-treated mice.

iNOS, IL-1β, NFκB, CXCL1, and CXCL2 are all upregulated in the muscle of notexin- treated mice compared with control mice. Gastrocnemius muscle injury was induced by a single intramuscular injection of 20 μl notexin (12.5 μg/ml) in PBS. All qPCR results show that gene expression was normalized to that of GAPDH. Data are shown as the mean ± standard error of the mean (n = 6). Statistical significance was determined using Student’s t-test. Data are denoted by asterisks where \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

**Fig. S2** Histological features of control and notexin-treated muscle in WT and Nogo KO mice.

Myofibers have appeared normal in control WT and Nogo KO mice in H&E staining. Injured myofibers with infiltration of inflammatory cells have appeared three days post notexin (12.5 μg/ml, 20 μl), a single intramuscular injection in WT and Nogo KO mice in H&E staining. Scale bar represents 200 µm in control and 500 µm in notexin treated groups respectively.

**Fig. S3** Tunicamycin-induced ER stress was mediated by the Nogo-A-CHOP pathway.

**a** TheNogo-A expression level is up-regulated in the skeletal muscle of tunicamycin-treated WT mice compared with Nogo-KO mice. **b** CHOP is highly expressed in tunicamycin-treated skeletal muscle of WT mice compared with Nogo-KO mice. **c**, **d** IL-6 and TNF-α are highly expressed in skeletal muscle of tunicamycin-treated WT mice compared with skeletal muscle of Nogo-KO mice. Data are shown as the mean ± standard error of the mean (n = 3). Statistical significance was determined using Student’s t-test. Data are denoted by asterisks where \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

**Fig. S4** Isolation of bone marrow-derived macrophages (BMDM) from WT and Nogo-KO mice.

**a** Macrophages obtained from WT and Nogo-KO mice were cultured for seven days (n = 3). After culture, BMDM were stimulated with pro-inflammatory mediators, lipopolysaccharide (LPS), and the anti-inflammatory mediator IL-4 for 24 h. **b** IF staining for the ER protein Nogo-A (red) and the macrophage marker CD68 (green). After 7 days of culture of LPS-treated (100 ng/ml) and IL-4-treated (20 ng/ml) BMDM, a molecular analysis was performed. Alexa Fluor (AF)-488 and AF-555 were used as secondary antibodies. DAPI was used for nuclear staining. Scale bar, 5 µm, ×1000 magnification.

**Fig. S5** Expression of anti-inflammatory (M2) factors in BMDM.

**a-c** mRNA levels of M2 factors including arginase-1, CD206, and IL-10 in WT and Nogo- KO BMDM after LPS treatment (100 ng/ml) for 24 h. **d** IF analysis of Nogo-A and the M2 macrophage marker CD206 in WT and Nogo-KO BMDM. **e** IF analysis of Nogo-A and CD206 in WT and Nogo-KO BMDM after IL-4 treatment (20 ng/ml) for 24 h. Nogo-KO BMDM exhibit increased expression of CD206 compared with IL-4-treated WT BMDM. **f** FACS analysis of CD206 in WT BMDM and Nogo-KO BMDM after IL-4 treatment. BMDM were isolated from WT and Nogo-KO mice and cultured for seven days. qPCR results show that gene expression was normalized to that of GAPDH. The results are presented as the mean ± standard error of the mean (n = 3). Statistical significance was determined using Student’s t-test. Alexa Fluor (AF)-488 (green) and AF-555 (red) were used as secondary antibodies. Scale bar, 5 µm, ×1000 magnification.

**Fig. S6** Nogo-A co-localized with calnexin, an endoplasmic reticulum (ER) marker in BMDM.

**a** IF co-staining for Nogo-A and calnexin, an endoplasmic reticulum marker, in WT BMDM (n = 3). IF staining showed that Nogo-A and calnexin colocalized in the cytoplasm. **b** IF staining for calnexin in Nogo-KO BMDM (n = 3). AF-488 (green) and AF-555 (red) were used as secondary antibodies. Scale bar, 10 µm, ×400 magnification.