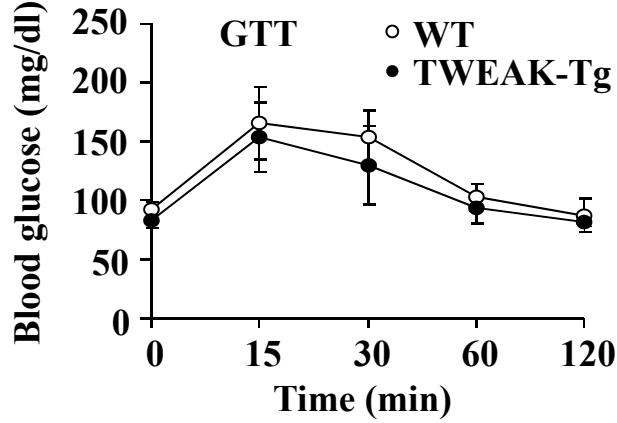
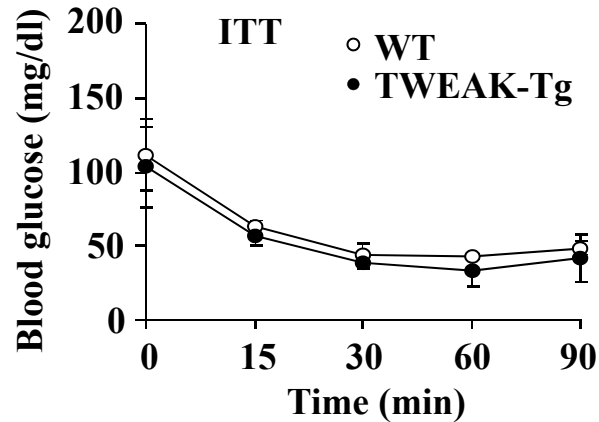


FIGURE S1

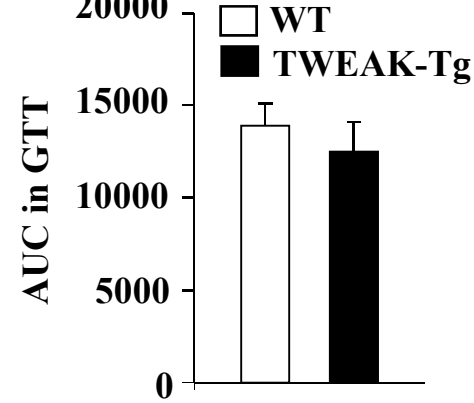
A.



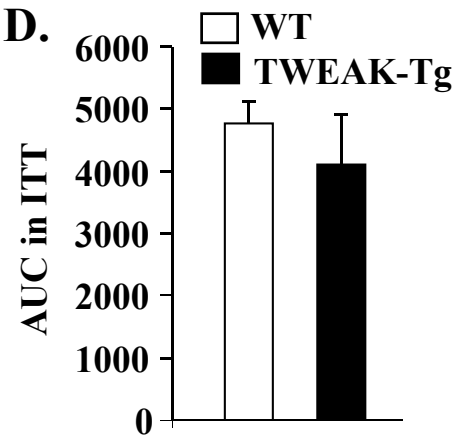
C.



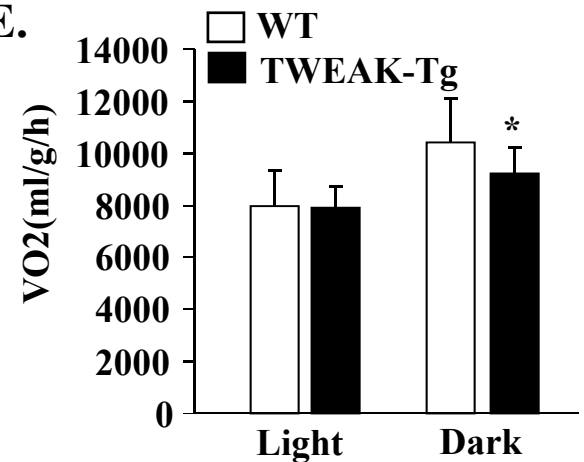
B.



D.



E.



F.

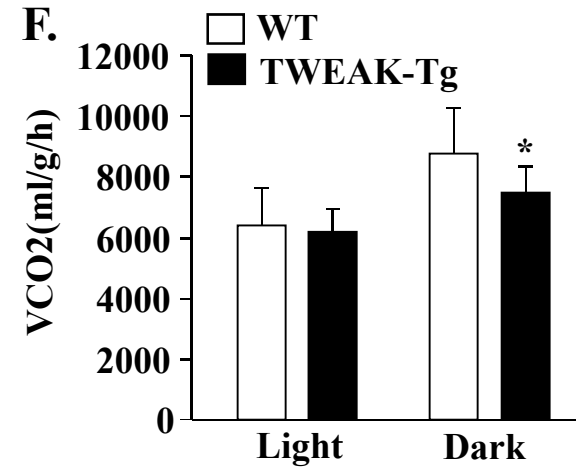


FIGURE S1. GTT and ITT in 4-month old WT and TWEAK-Tg mice. (A) Glucose tolerance test (GTT). Glucose (1g/kg i.p.) was given to 4-month-old WT (○) and TWEAK-Tg (●) mice and plasma glucose levels were measured at 0, 15, 30, 60, 90 and 120 min. (B) Area under the curve (AUC) for intraperitoneal GTT. (C) Insulin tolerance test (ITT). Insulin (0.75 U/Kg, i.p.) was given to 4-month-old WT (○) and TWEAK-Tg (●) mice and plasma glucose levels were measured at 0, 15, 30, 60 and 90 min. (D) AUC for intraperitoneal ITT. N = 4 or 5 in each group for both GTT and ITT. 18-month old TWEAK-Tg and littermate WT mice were placed in metabolic cage and monitored over 24 hours in 12-h light (6am-6pm), 12-h dark (6pm-6am) conditions. Data presented here demonstrate differences in (E) Oxygen consumption rate (VO₂); (F) Carbon dioxide production rate (VCO₂) normalized to their lean body mass. N=3 in each group. Error bars represent SD. *P < 0.05, values significantly different from littermate WT mice.

FIGURE S2

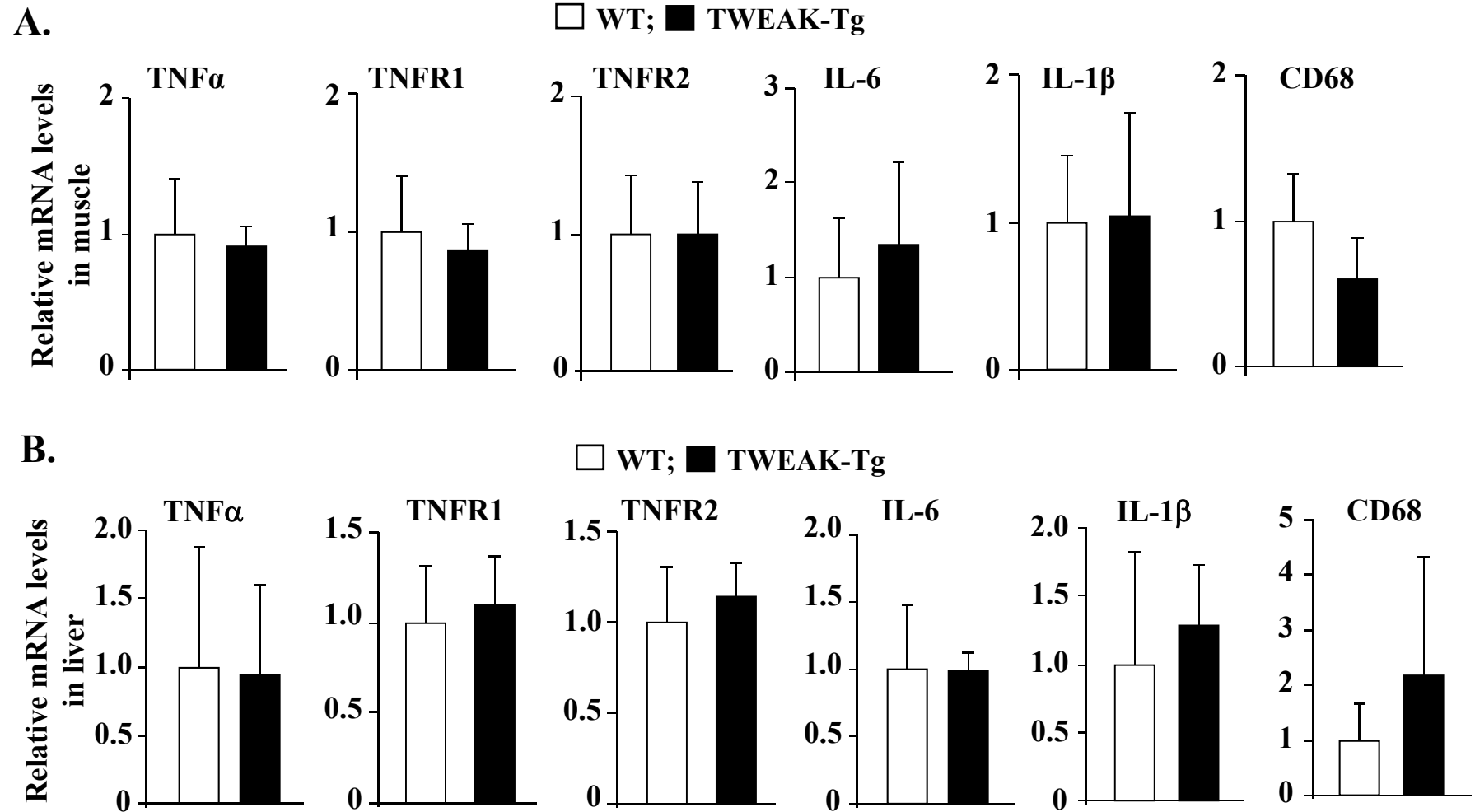


FIGURE S2. Transcript levels of inflammatory molecules in skeletal muscle and liver of WT and TWEAK-Tg mice. Total RNA was isolated from gastrocnemius muscle and liver of 18-months old littermate WT and TWEAK-Tg and analyzed for mRNA levels of TNF- α , TNFR1, TNFR2, IL-1 β , IL-6, and CD68. Data presented here demonstrate that there was no significant difference in mRNA levels of these molecules in (A) gastrocnemius muscle and (B) liver of WT and TWEAK-Tg mice. N=4 in each group.

FIGURE S3

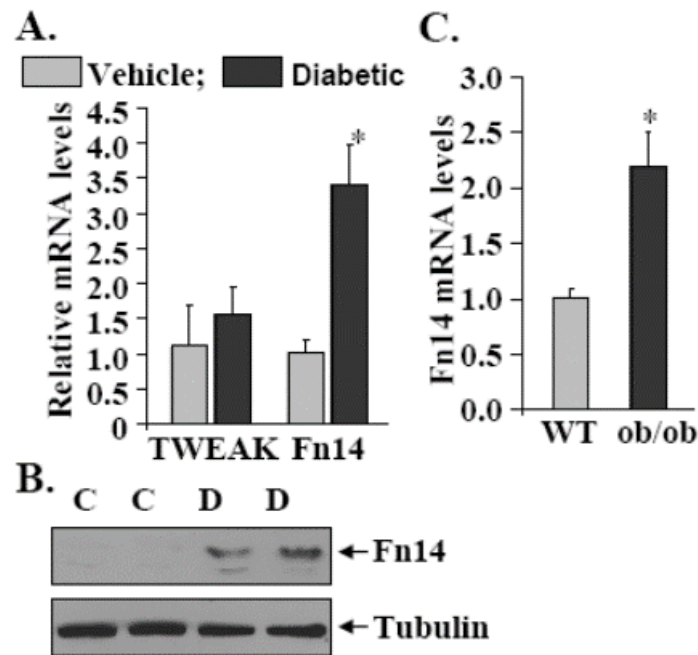


FIGURE S3. Levels of Fn14 are increased in skeletal muscle of diabetic mice. (A) mRNA and (B) protein levels of Fn14 in gastrocnemius (GA) muscle of control and diabetic (induced by intraperitoneal injection of streptozotocin) mice. N=6 in each group. (C) mRNA levels of Fn14 in GA muscle of 8-week old wild-type (WT) and ob/ob mice. N=4. *p<0.01, values significantly different from control mice. C, Control (vehicle); D, Diabetic (streptozotocin).

FIGURE S4

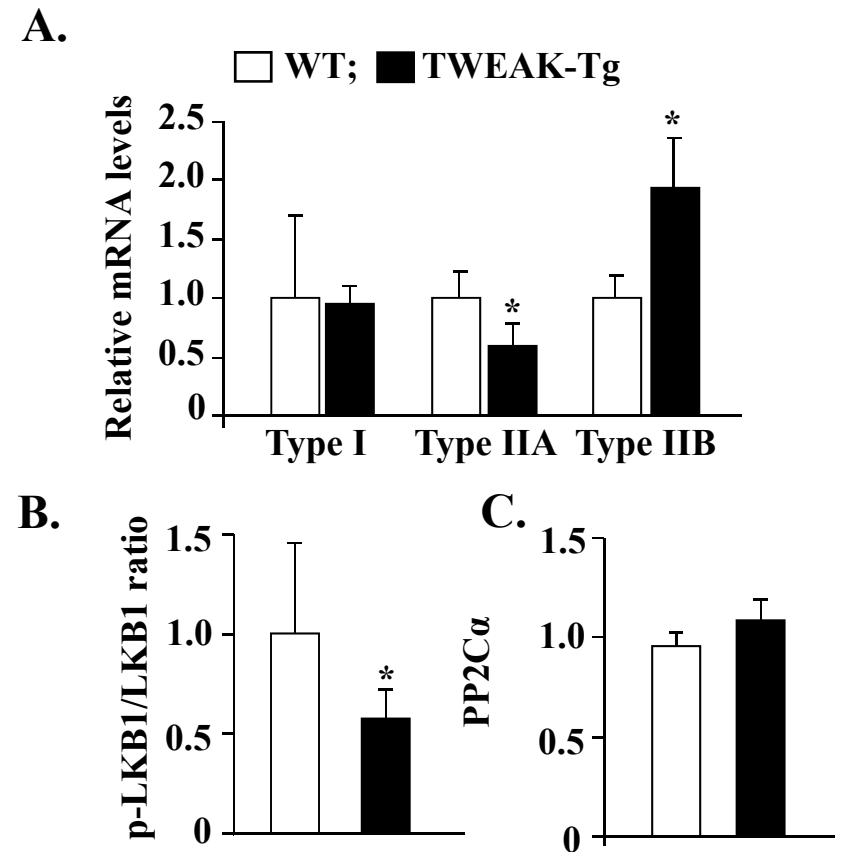


FIGURE S4. Transcript levels of various MyHC isoforms and quantification of pLKB1/LKB1 ration and total PPC2α levels in skeletal muscle of WT and TWEAK-Tg mice. (A) Total RNA was isolated from gastrocnemius muscle of 18-months old littermate WT and TWEAK-Tg and analyzed for mRNA levels of MyHC IA, IIA, and IIB. Data presented here demonstrate that mRNA levels of MyHC IIA is significantly decreased whereas mRNA levels of MyHC IIB increased in gastrocnemius muscle of TWEAK-Tg mice compared with WT mice. N=4 in each group. (B) Ratios of phosphorylated and total LKB1 and (C) total levels of PPC2α in gastrocnemius muscle of WT and TWEAK-Tg mice measured by densitometry analysis of immunoblots. Error bars represent SD. *P < 0.05, values significantly different from littermate WT mice.

Table S1: Primer sequence used for QRT-PCR assays.

| Gene name | Forward primer (5'-3') | Reverse primer (5'-3') |
|----------------|---------------------------|---------------------------|
| TWEAK | GCTACGACCGCCAGATTGGG | GCCAGCACACCGTTCACCAG |
| Fn14 | AAGTGCATGGACTGCGCTTCTT | GGAAACTAGAAACCAGCGCCAA |
| TNF- α | GCATGATCCGCGACGTGGAA | AGATCCATGCCGTTGGCCAG |
| TNFR1 | AACCAGTTCCAACGCTACCTGA | AGAAAGAACCCTGCATGGCA |
| TNFR2 | TAAGTGCCATCCCAAGGACACTCT | CCCAGTGATGTCACTCCAACAATC |
| IL-1 β | CTCCATGAGCTTTGTACAAGG | TGCTGATGTACCAGTTGGGG |
| IL-6 | CCTTCTTGGGACTGATGCTGG | GCCTCCGACTTGTGAAGTGGT |
| CD-68 | TTACTCTCTGCCATCCTTCACGA | CCATTTGTGGTGGGAGAACTGTG |
| MAC-1 | AGGGTTGTCCAGCCGATGATAT | CCCAGCTTCTTGACGTTGTTGA |
| PGC-1 α | TGGAGTGACATAGAGTGTGCTGC | CTCAAATATGTTCCGAGGCTCA |
| HKII | GAAGGGGCTAGGAGCTACCA | CTCGGAGCACACGGAAGTT |
| Glut4 | GACGGACTIONCCATCTGTTG | CATAGCTCATGGCTGGAACC |
| Mef2A | GTGTACTCAGCAATGCCGAC | AACCCTGAGATAACTGCCCTC |
| Mef2B | GACCGTGTGCTGCTGAAGTA | AGCGTCTCGAGGATGTCAGT |
| Mef2C | AGATACCCACAACACACCACGCGCC | ATCCTTCAGAGAGTCGCATGCGCTT |
| Mef2D | GCTCCATGCAGTTCAGCAATCCAA | AGGCTCCATTAGCACTGTTGAGGT |
| KLF15 | TGCGTCGGCACACAGGCGAGAA | CCGGTGCC TTGACAACCTCATCT |
| MyoD | GGAAGTGGGATATGGAGCTT | GCAGTCGATCTCTCAAAGCA |
| Ppar δ | TCCATCGTCAACAAAGACGGG | ACTTGGGCTCAATGATGTCAC |
| mCPT1 | GCACACCAGGCAGTAGCTTT | CAGGAGTTGATTCCAGACAGGTA |
| MHCI | AGTCCCAGGTCAACAAGCTG | TTCCACCTAAAGGGCTGTTG |
| MHCIIA | AGTCCCAGGTCAACAAGCTG | GCATGACCAAAGGTTTCACA |
| MHCIIIB | AGTCCCAGGTCAACAAGCTG | TTTCTCCTGTCACCTCTCAACA |
| β -actin | CAGGCATTGCTGACAGGATG | TGCTGATCCACATCTGCTGG |