Supplemental Data

Figure S1

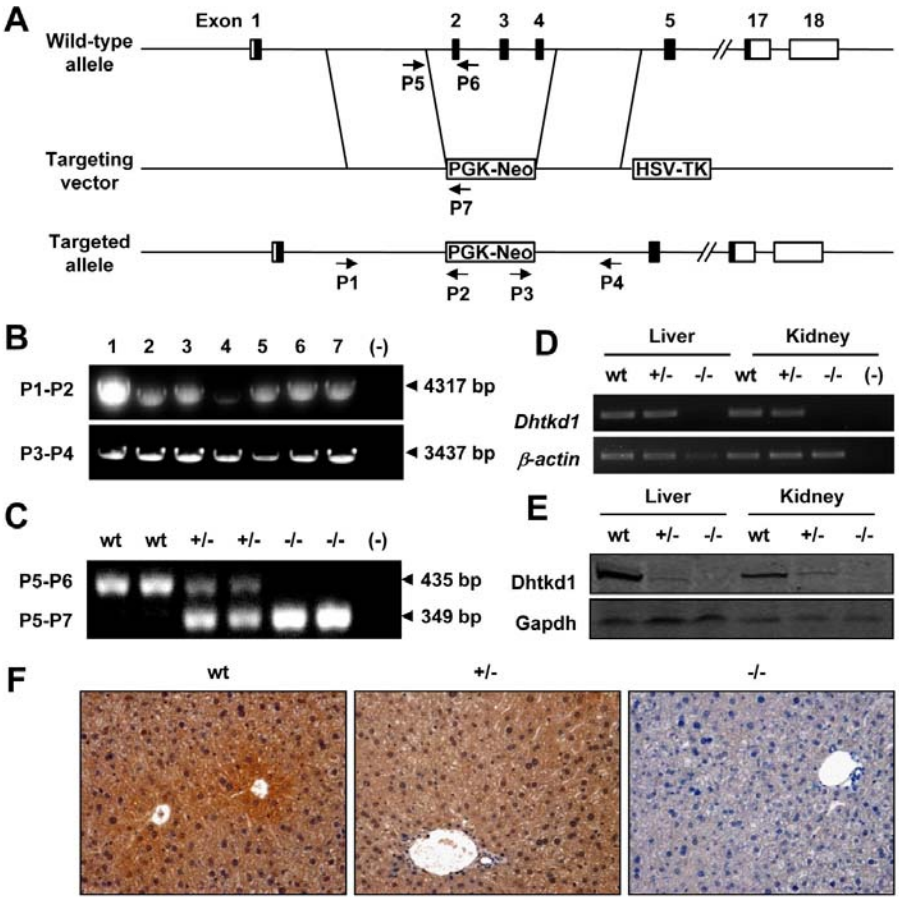

Figure S1. Targeted deletion of *Dhtkd1* in mice. (A) Schematic representation of *Dhtkd1* gene knock-out strategy. The targeting vector was designed to delete the genomic region from exon 2 to exon 4. Exons and introns are represented by boxes and horizontal lines, respectively. The coding region is shown in black. Fragments amplified by PCR for genotyping are indicated by arrows. (B) PCR analysis of recombinant ES cell clones. Genomic DNA extracted from ES cell clones was amplified using 5'-external and 3'-external primers as shown in panel. Homologous recombination events yielded a 4.3-kb or 3.4-kb fragments, respectively. (C) PCR genotyping of progenies from heterozygous matings. Wild-type (wt), heterozygous (*Dhtkd1*$^{+/-}$) and homozygous (*Dhtkd1*$^{-/-}$) mice were identified by PCR amplification of the fragments specific for either *Dhtkd1* wild-type allele (435 bp) or the targeted allele

(349 bp). (D) RT-PCR analysis for *Dhtkd1* mRNA in liver and kidney with primer e1/e3. The 418-bp *Dhtkd1*-specific fragment is absent only in *Dhtkd1*$^{-/-}$ mice. *Actb* is used as a loading control. (E) Western blot analysis shows that Dhtkd1 protein is disappeared in liver and kidney of *Dhtkd1*$^{-/-}$ mice. (F) Immunohistochemical staining for Dhtkd1 in liver. Magnification, 200×.

Figure S2

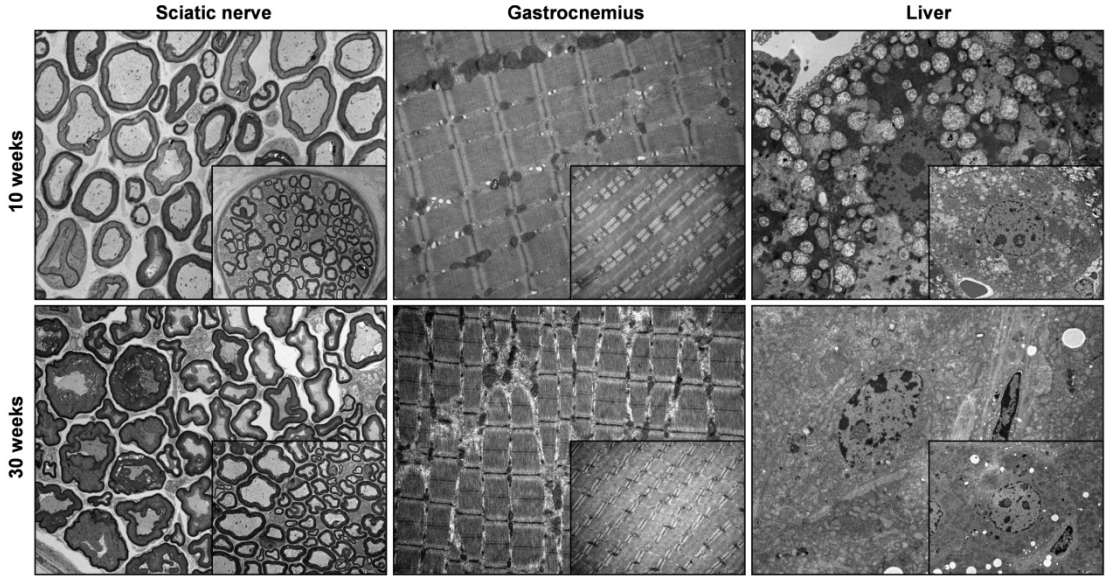

Figure S2. Aggravation of peripheral nerve, muscle and liver changes with the age of mice lacking *Dhtkd1*. Electron micrographs of cross-sections of sciatic nerves, gastrocnemius muscle and liver in the young adulthood (10 weeks old) and middle age (30 weeks old) of *Dhtkd1*$^{-/-}$ mice are shown. The inserts indicate morphology of wt tissues.

Figure S3

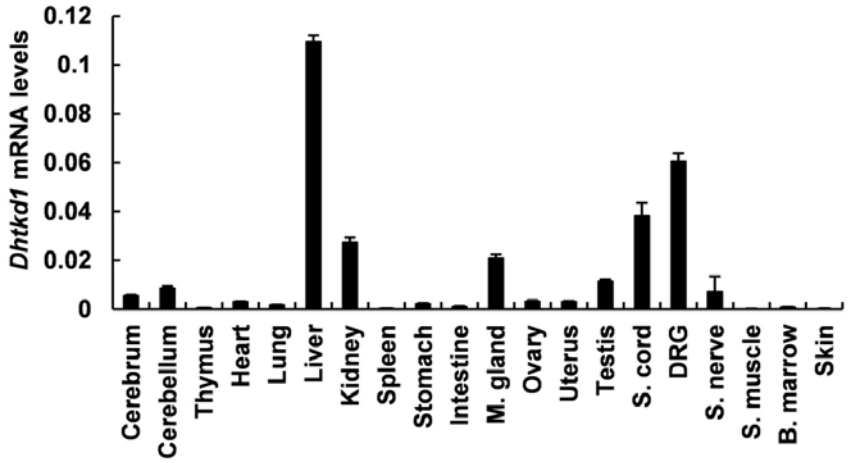

Figure S3. *Dhtkd1* expression profile in mice. Real-time PCR analysis for *Dhtkd1* mRNA expression. Values are shown as means ± S.D. M. gland, mammary gland; S. cord, spinal cord; DRG, dorsal root ganglion; S. nerve, sciatic nerve; S. muscle, skeletal muscle; B. marrow, bone marrow.

Figure S4

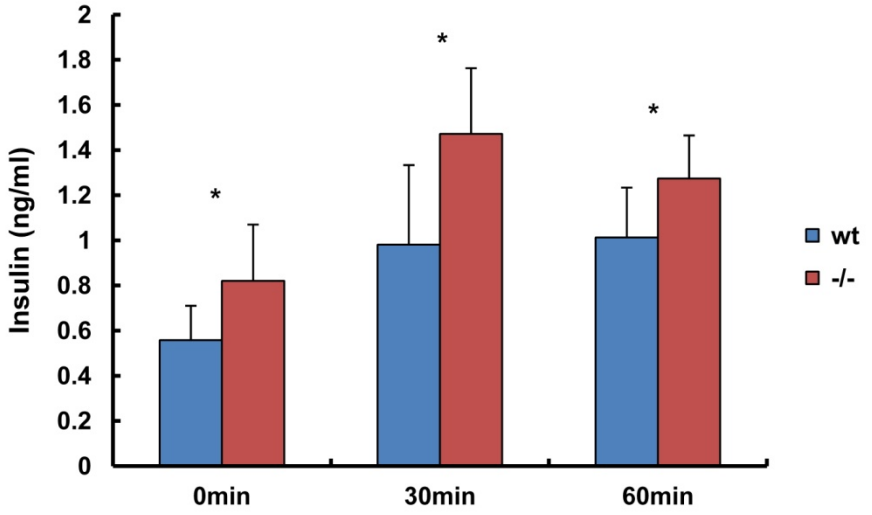

Figure S4. Insulin levels during GTT, related to Fig3G. During the GTT, insulin levels of different time points were determined by ELISA. Values are shown as means ± S.D.

Figure S5

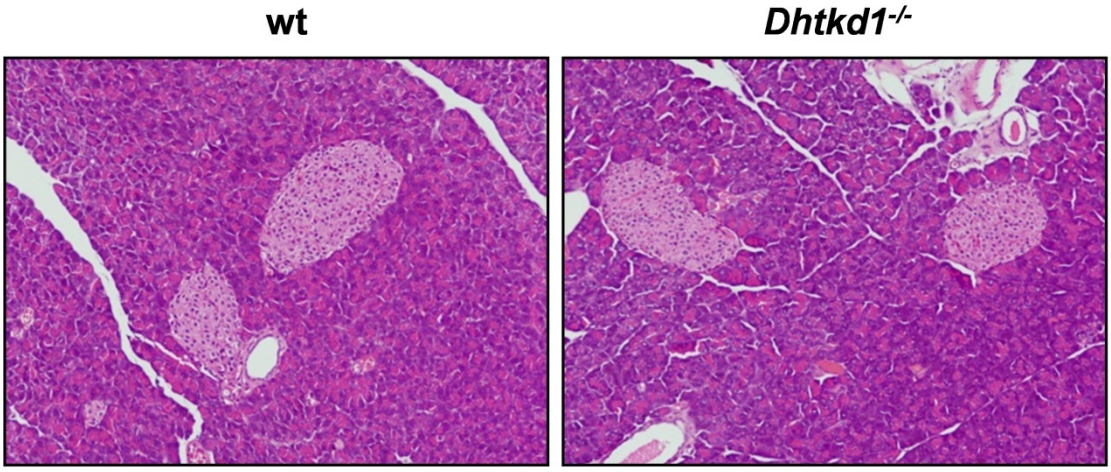

Figure S5. Comparison of islet structure between wt and *Dhtkd1*$^{-/-}$ mice. H&E staining of tissue and cellular morphology in wt and *Dhtkd1*$^{-/-}$ pancreas and islets, showing no significant structural difference between two genotypes.

Figure S6

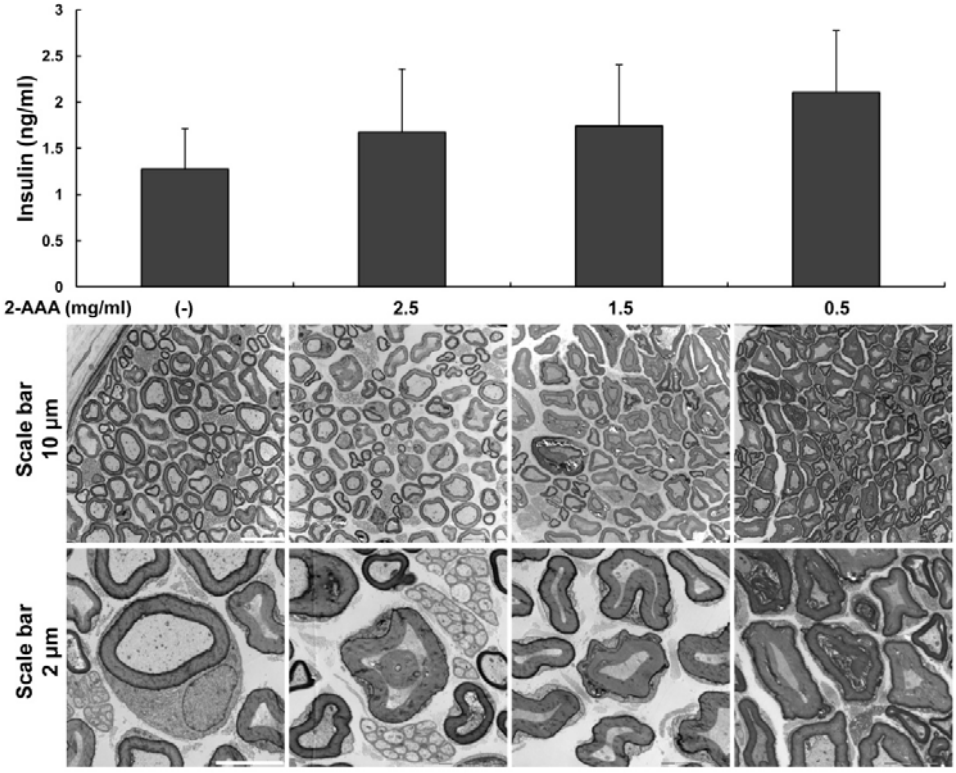

Figure S6. Insulin levels and pathological changes (TEM) of sciatic nerve.

Table S1. The primers used in this study

P1	GAAAAATGGCGATCCTCAAG
P2	GGGGAACTTCCTGACTAGGG
P3	TCGCCTTCTTGACGAGTTCT
P4	CTCTGAGCAGACCTGGGAAC
P5	GTTGGCTTTGGTGTTGCGTC
P6	AAGGCTCTTCCTGCCAGTTC
P7	GGTAGAATTTCGACGACCTGC
Dhtkd1-e1	ATTCTTCCACGGCGTCTT
Dhtkd1-e3	CTCTCTCTTCCTGGCTCTGAA
Dhtkd1	GCTGCTGCGGTTTATTGGTG
	CAAGGCAAGTGTCTCTGCG
Gjb1	GCACGTAGCTCACCAACAG
	TGATGACATAGGTCCACCACA
Mpz	TACAGTGACAACGGCACTTTC
	GCAGTACCGAATCAGGTAGAAGA
Mbp	GGCCAGTAAGGATGGAGAGAT
	CCTCTGAGGCCGTCTGAGA
Pmp22	ATGGACACACGACTGATCTCT
	CAGCCATTCGCTCACTGATGA
Prx	GGCGGCAAAGAAGGAATC
	CAAAGAACACACGGGCACT

Srebp2	CAGGTGCAGACGGTACAGG
	CGTGGTCAACACAAGGGAATC
Fbxo32	CAGCTTCGTGAGCGACCTC
	GGCAGTCGAGAAGTCCAGTC
MuRF1	GTGTGAGGTGCCTACTTGCTC
	GCTCAGTCTTCTGTCCTTGGA
Glut2	TCAGAAGACAAGATCACCGGA
	GCTGGTGTGACTGTAAGTGGG
Gck	AGACGAAACACCAGATGTATTCC
	GAAGCCCTTGGTCCAGTTGAG
Pcx	AATGTCCGGCGTCTGGAGTA
	ACGCACGAAACACTCGGAT
Ins1	CACTTCCTACCCCTGCTGG
	ACCACAAAGATGCTGTTTGACA
Ins2	GCTTCTTCTACACACCCATGTC
	AGCACTGATCTACAATGCCAC
Sytl4	TGAGAAAAGGATTCGGCGACT
	CTGGCACAGGTTCGATCACT
Ucn3	AAGCCTCTCCCACAAGTTCTA
	GAGGTGCGTTTGGTTGTCATC
Glp1r	ACGGTGTCCCTCTCAGAGAC
	ATCAAAGGTCCGGTTGCAGAA

Abcc8	TGAGCATTGGAAGACCCTCAT
	CAGCACCGAAGATAAGTTGTCA
Kcnj11	AAGGGCATTATCCCTGAGGAA
	TTGCCTTTCTTGGACACGAAG
Pclo	AAGAGTTGGATAGTAGTCAGGCT
	ACCTAAACGTGTCCGTAGTTCT
Noc2	AGCAGAGAGGCTAGACATCCT
	AGACACTGGGAGAGACCGTT
Pcsk1	CTTTCGCCTTCTTTTGCGTTT
	TCCGCCGCCCATTCATTAAC
Ero1lb	ACCCTGAGCTTCCTCTCAAGT
	AAAGGACATGGTCGTTTCAGATT
Slc30a8	AGCCACCAAGATGTACGCC
	CTTGCTTGCTCGACCTGTT
Egr2	GCCAAGGCCGTAGACAAAATC
	CCACTCCGTTCATCTGGTCA
S100b	TGGTTGCCCTCATTGATGTCT
	CCCATCCCCATCTTCGTCC
Bdnf	TTACCTGGATGCCGCAAACAT
	TGACCCACTCGCTAATACTGTC
Ngf	TGATCGGCGTACAGGCAGA
	GCTGAAGTTTAGTCCAGTGGG

β-actin	GGCTGTATTCCCCTCCATCG
	CCAGTTGGTAACAATGCCATGT