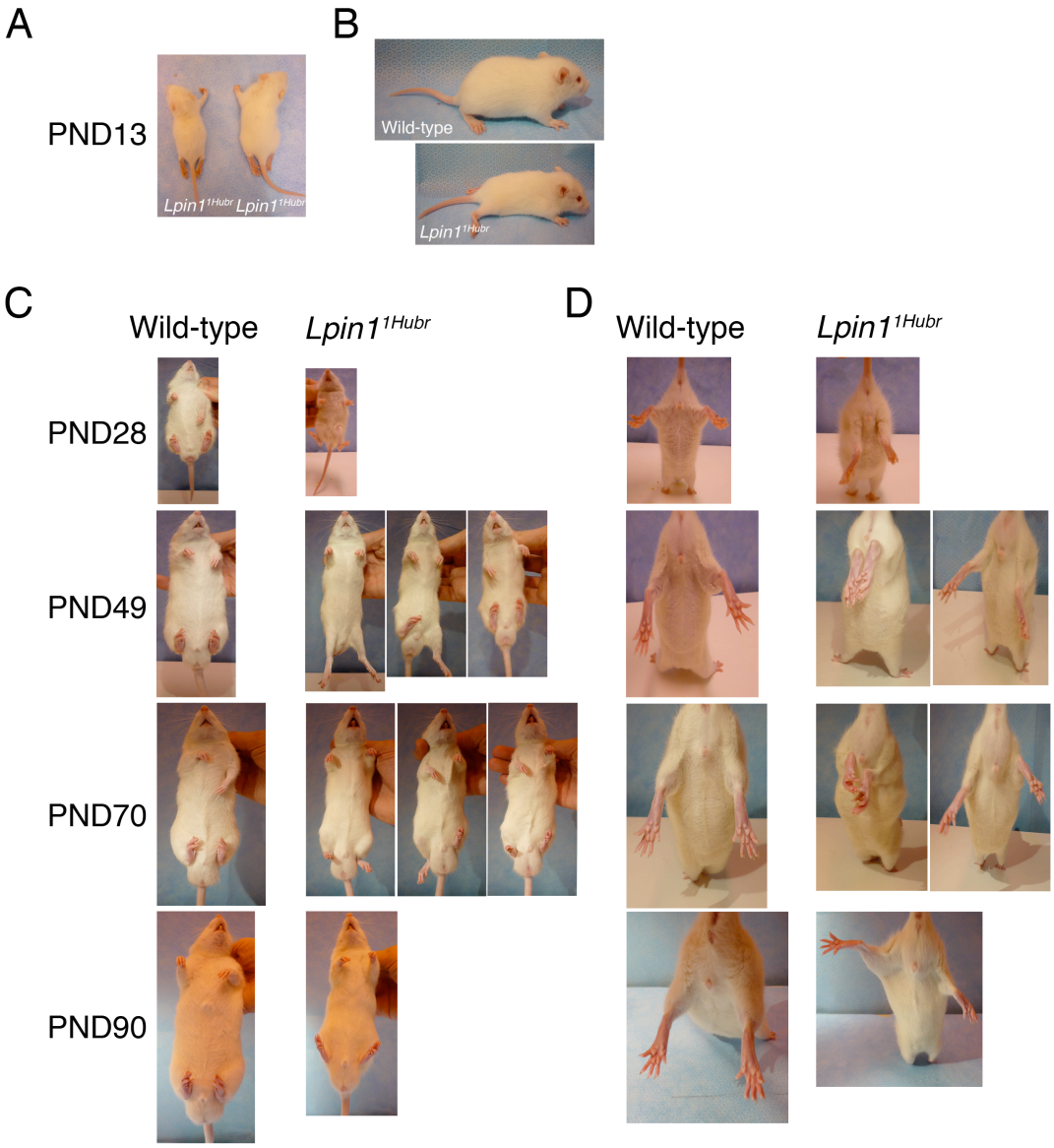
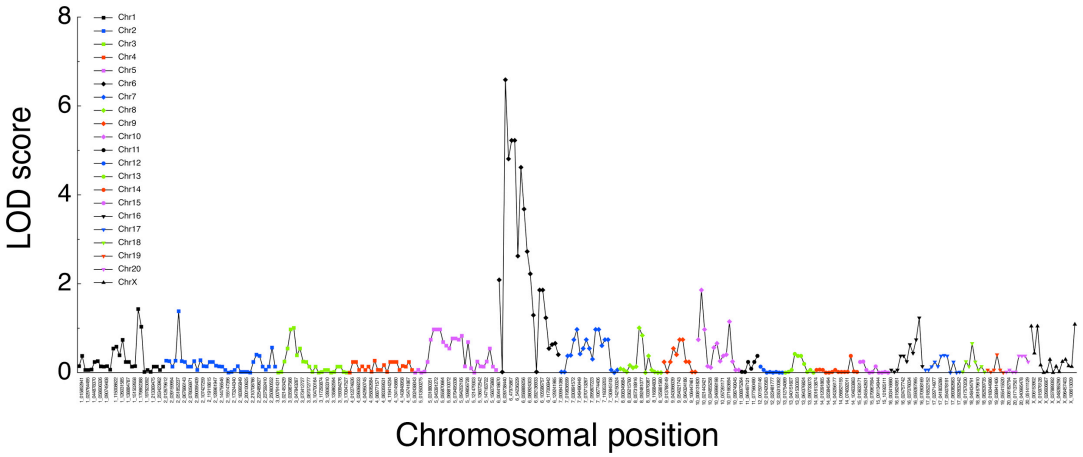


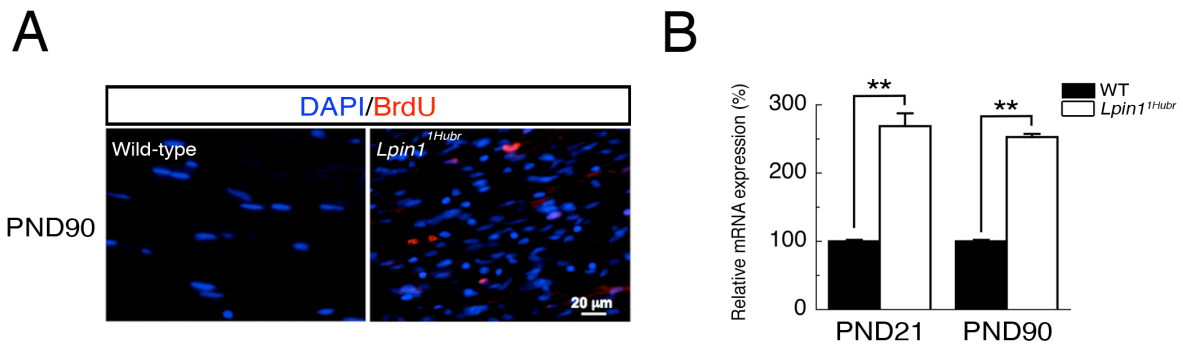
Supplemental Figure S1. Progression of neuropathy, lipodystrophy and muscle wasting phenotypes in *Lpin1^{1Hubr}* rats

A. The onset of the *Lpin1^{1Hubr}* phenotype occurred approximately between PND 7 and PND 14. Early onset (left male pup) resulted in a more severe phenotype compared to later onset (right male pup) due to decreased mobility, and possibly decreased suckling behavior. ***B***. At PND 13, *Lpin1^{1Hubr}* pups showed severe lipodystrophy, hindquarter muscle wasting, and decreased body length as compared to wild-type pups. ***C***. At PND 28, *Lpin1^{1Hubr}* rats showed severe lipodystrophy, hindquarter muscle wasting, a decreased body length, and no characteristic retraction of the hindlimbs as compared to wild-type rats. However, at PND 49 and onwards, some *Lpin1^{1Hubr}* rats gain the ability to retract their hindlimbs when picked up. Moreover, the severe lipodystrophy and hindquarter muscle wasting in *Lpin1^{1Hubr}* rats became less pronounced. At PND 90, almost all *Lpin1^{1Hubr}* rats regain the ability to retract their hindlimbs. ***D***. Wild-type rats splayed their hindlimbs and toes when picked up by the tail, whereas *Lpin1^{1Hubr}* rats clenched their hindlimbs to their body. However, at PND 49 and onwards, *Lpin1^{1Hubr}* rats splayed their hindlimbs and toes, or clenched their hindlimbs to their body when picked up by the tail. At PND 90, almost all *Lpin1^{1Hubr}* rats regained the ability to splay their hindlimbs.



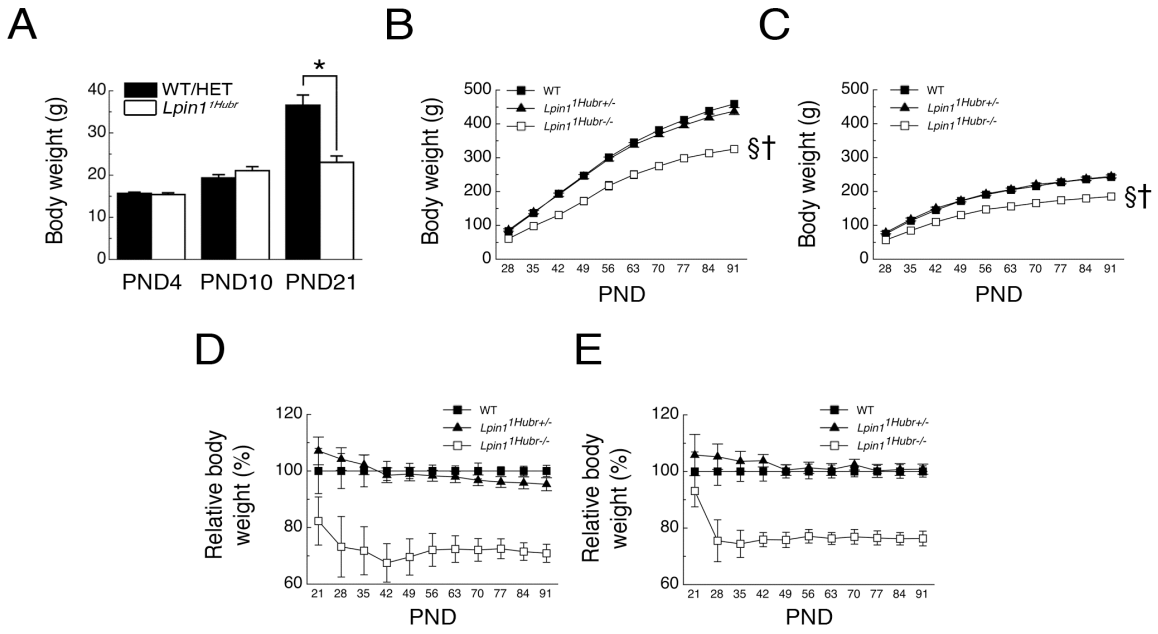
Supplemental Figure S2. Linkage analysis

Linkage analysis based on the genotyping results in the Wistar/BN F_5 population using 321 informative markers revealed a significant LOD score for the *Lpin1*^{1Hubr} mutation in a region on chromosome 6 between 37.1Mb and 40.7Mb. Rat *Lpin1* is located on chromosome 6 at 40.3Mb.



Supplemental Figure S3. Increased DNA replication and cell proliferation in *Lpin1*^{1Hubr} sciatic nerves.

A. Immunohistochemistry of DAPI and BrdU in medial sciatic nerve tissue at PND 90 revealed increased cellularity and DNA replication in *Lpin1*^{1Hubr} rats as compared to wild-type rats. ***B***. Relative expression of *Cyclin D1* (marker of cell proliferation) was increased in *Lpin1*^{1Hubr} rats at PND 21 and PND 90 as compared to wild-type rats (** $P < 0.001$; n = 2 per group).



Supplemental Figure S4. Decreased body weight in male and female *Lpin1^{1Hubr}* rats

A. No significant difference in body weight between wild-type/heterozygous (WT/HET; mixed gender) and *Lpin1^{1Hubr}* (mixed gender) rats was observed at PND 4 (n = 4-9 per group) and PND 10 (n = 7-18 per group). However, as the *Lpin1^{1Hubr}* phenotype develops, body weight started to diverge and body weight was decreased in *Lpin1^{1Hubr}* rats (mixed gender) as compared to wild-type rats (mixed gender) at PND 21 (n = 8-9 per group; * $P < 0.05$). ***B***. Body weight of male *Lpin1^{1Hubr}* rats (*Lpin1$^{1Hubr-/-}$*) was decreased as compared to male wild-type (WT) and heterozygous (*Lpin1$^{1Hubr+/-}$*) rats between PND 28 and PND 90 (n = 4-11 per group; $^{\S}P<0.001$ *Lpin1^{1Hubr}* vs. WT; $^{\dagger}P<0.001$ *Lpin1$^{1Hubr-/-}$* vs. *Lpin1$^{1Hubr+/-}$*; Bonferroni *post hoc* analysis). ***C***. Body weight of female *Lpin1^{1Hubr}* rats was decreased as compared to female wild-type and heterozygous rats between PND 28 and PND 90 (n = 11-13 per group; $^{\S}P<0.001$ *Lpin1^{1Hubr}* vs. wild-type; $^{\dagger}P<0.001$ *Lpin1^{1Hubr}* vs. heterozygous; Bonferroni *post hoc* analysis). ***D***. Relative body weight of male *Lpin1^{1Hubr}* (*Lpin1$^{1Hubr-/-}$*) rats was decreased as compared to male wild-type (WT) and heterozygous (*Lpin1$^{1Hubr+/-}$*) rats between PND 21 and 90 (n = 4-11 per group). ***E***. Relative body weight of female *Lpin1^{1Hubr}* (*Lpin1$^{1Hubr-/-}$*) rats was decreased as compared to female wild-type (WT) and heterozygous (*Lpin1$^{1Hubr-/-}$*) rats between PND 21 and 90 (n = 11-13 per group). Data are expressed as mean ± S.E.M.

Supplemental Table S1: primer sequences (F, forward; R, reverse; m, mouse; r, rat)

Name	Sequence
mUbiquitin	F: CAGCCACCAAGACTGACCAA R: CATTCACCAGTGCTATGAGGGA
rUbiquitin	F: AGTGCGGAAAACTGGAAGCC R: GGACTGGATTACTTGGTCAGTCTTG
mCds1	F: CTGAGCCTGGTGAAGAAGCACTAC R: CCATGCGAACATATAGAACTGCA
rCds1	F: TTTGAAGGCATGATATGGTTCCT R: CATTGCAGATGACGCTTGATATG
rFabp4	F: GGAGACGAGATGGTGACAAGC R: TCACGCCTTTCATGACACATTC
rPparγ1	F: GCAAGAGATCACAGAGTATGCCAA R: TCAAGGTTAATGAAACCAGGGATAT
rPparγ2	F: TTTTGAAAACAAGGACTACCCTTTAC R: GGCATCTCTGTGTCAACCATG
rLpinEx18-19	F1: GCCTGCCGATGTGTATTCCTAC F2: CAAAGCTGTATCACAAAGTAAGCCA R1: ATTCTATTCAGGGACACTCCCA
rLpin1α	F3: GCCCCAGTCCTTCAGGCTC R3: GCTCAGAATCACTTTTTGGTGTTG
rLpin1β	F4: GTAGATTGTCAGAGGACTCCCCCT R4: CAAGAGCTAGAGAGAACTCCCTCG
rMpz	F: TTCACAAGTCTTCTAAGGACTCCTCG R: GCACTGGCGTCTGCCG
rPmp22	F: GGAGTCTTCCAAATCCTTGCTG R: GATGGCCGCTGCACTCAT
rKrox20	F: GGAGGCCCCTTTGATCAGA R: TGTTGATCATGCCATCTCCAG
rOct6	F: GAGCTTCAAGAACATGTGCAAGCT R: TCCAGCCACTTGTTGAGCAG
rCyclinD1	F: GCACTTTCTTTCCAGAGTCATCAA R: CAGGCACGGAGGCAGTC