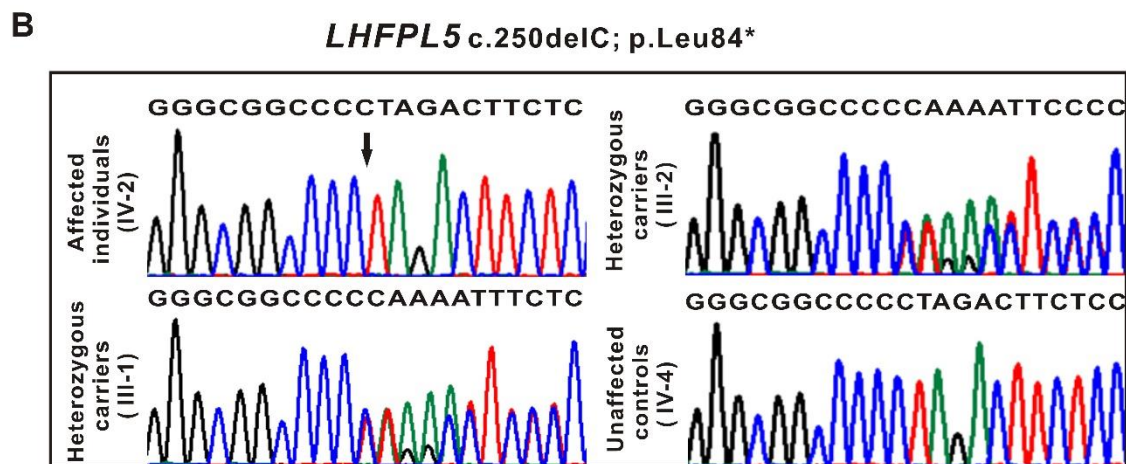
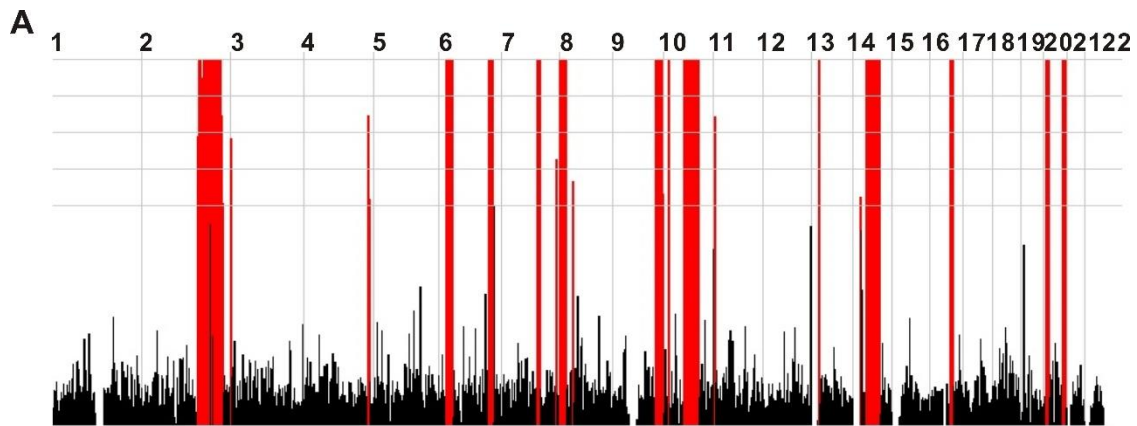


Table S1. Offspring of crosses between *Tmem141*^{WT/p. Trp90*} mice

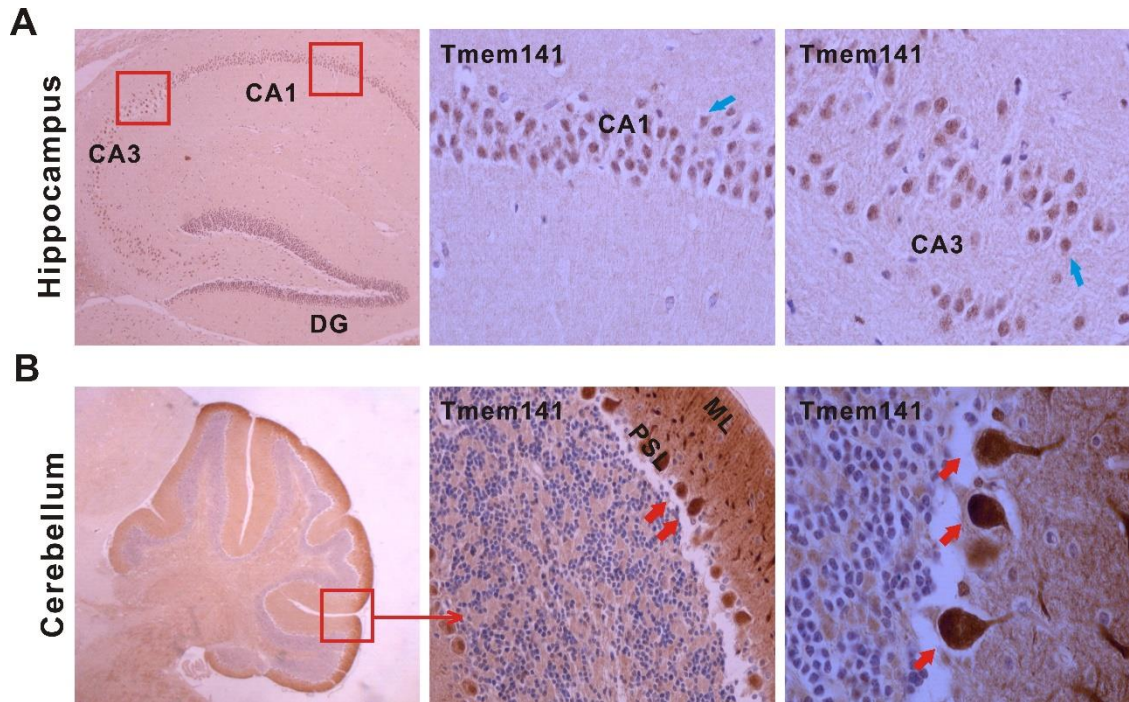
Genotype	<i>Tmem141</i> WT/WT	<i>Tmem141</i> WT/ p. Trp90*	<i>Tmem141</i> p. Trp90*/p. Trp90*
Number of mice	37	23	11
Actual ratio	52%	33%	15%
Expected ratio according to Mendel's law	50%	25%	25%

Fig. S1. Homozygosity mapping and a frameshift variant in *LHFPL5*



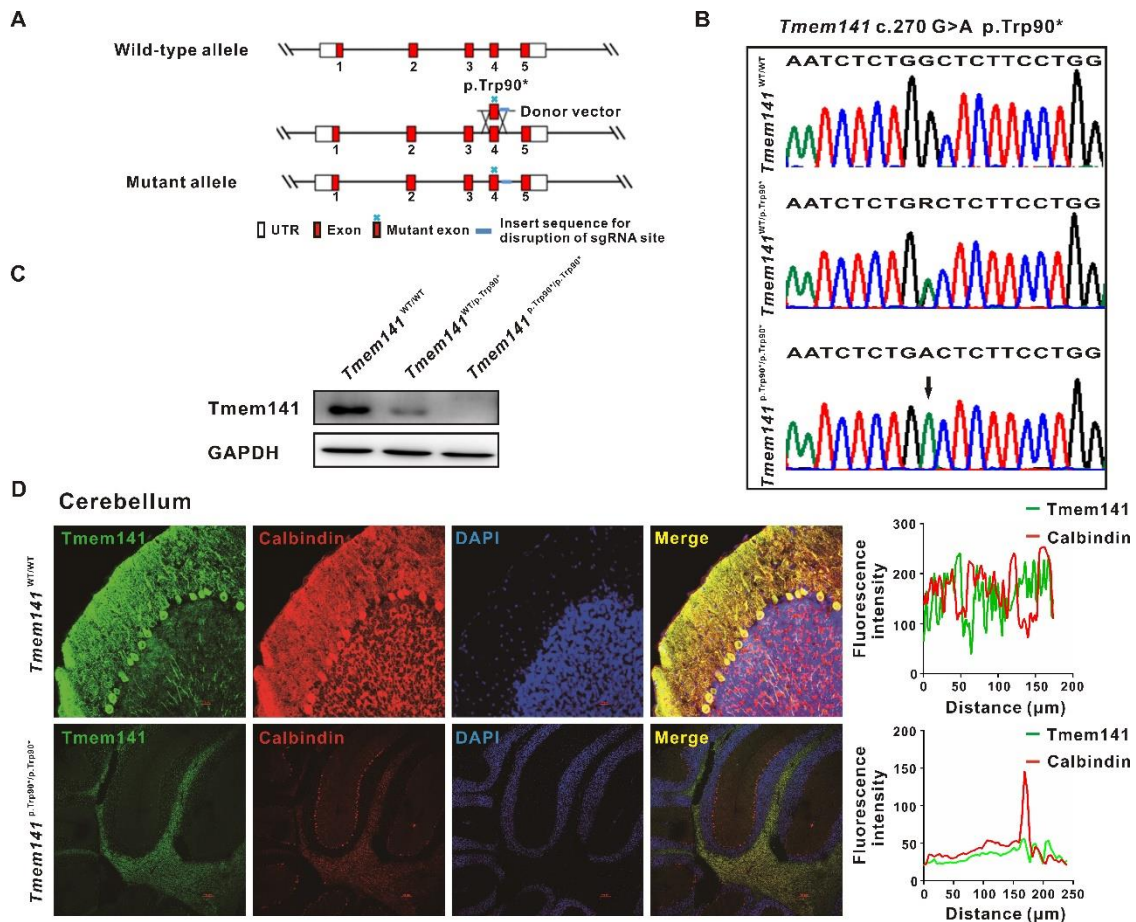
(A) Genome-wide homozygosity in the patient showing a large number of homozygosity blocks (red). Numbers at the top represent the chromosome numbers. (B) Sequencing chromatograms of affected individuals, heterozygous carriers of the *LHFPL5* c.250delC variant. An unaffected control is also shown and the variant site is denoted by a black arrow.

Fig. S2. Immunohistochemical staining for Tmem141 in hippocampus and cerebellum



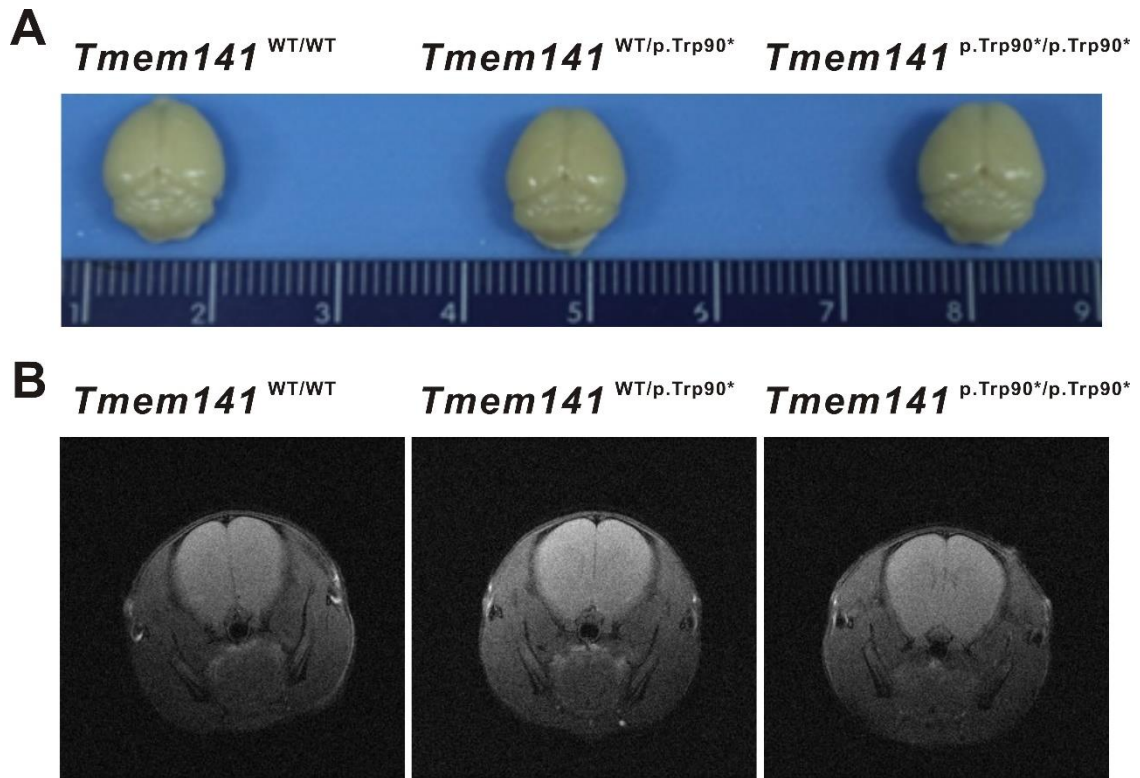
(A) Tmem141 ubiquitously expressed in the hippocampal neurons of hippocampal subregions CA1, CA3 and DG (dentate gyrus). **(B)** Tmem141 mainly expressed in Purkinje cells of the cerebellum. ML: molecular layer; PSL: Purkinje neurons soma layer.

Fig. S3. Establishment of the *Tmem141* KI mouse model



(A) Schematic map of *Tmem141* with the p. Trp90* nonsense variant in exon 4. (B) Sanger Sequence chromatograms of *Tmem141* in mice to identify the genotype. (C) Immunoblotting results of Tmem141 protein in brain tissues of mice. Loss of Tmem141 was confirmed in *Tmem141* p. Trp90*/p. Trp90* mice. (D) IF staining for Tmem141 and calbindin (marker of cerebellar Purkinje cells) in cerebellum. The fluorescence integrated density was measured by Plot Profile tool of ImageJ software, showing reduced expression of Tmem141 in *Tmem141* p. Trp90*/p. Trp90* mice.

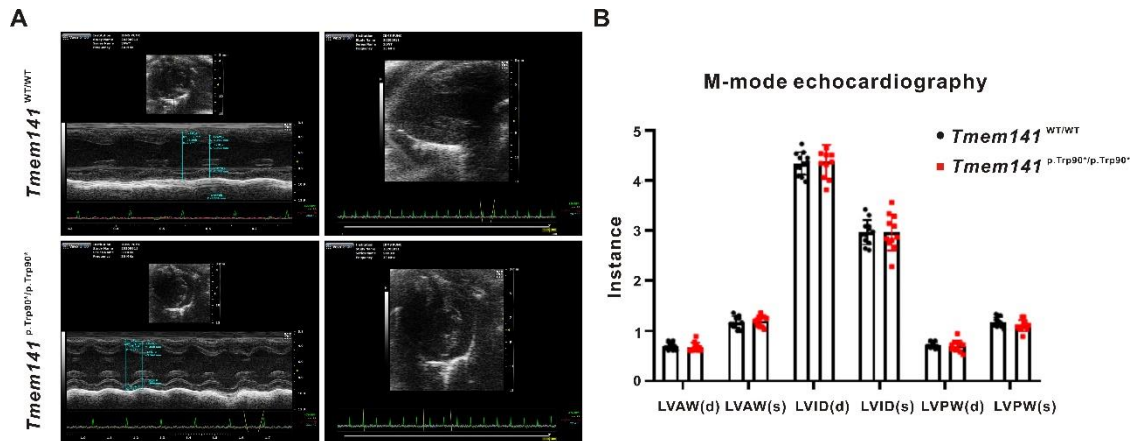
Fig. S4. Images of gross brains and cerebral MRI testing



Images of gross brains (A) and cerebral MRI testing (B) showed no visible defects in the size and structure between *Tmem141*^{p.Trp90*/p.Trp90*} and WT littermates.

Fig. S5. M-mode echocardiography of the *Tmem141*^{WT/WT} and *Tmem141*^{p.Trp90*/p.} mice

Trp90* mice



(A) Imaging of mouse heart obtained using M-mode ultrasonic testing. **(B)** M-mode echocardiographic results indicating no significant difference in LVAW(d), LVAW(s), LVID(d), LVID(s), LVPW(d), and LVPW(s) between WT and mutant littermates. LVAW(d), end-diastolic left ventricular anterior wall; LVAW(s), end-systolic left ventricular anterior wall; LVID(d), end-diastolic left ventricular internal dimension; LVID(s), end-systolic left ventricular internal dimension; LVPW(d), end-diastolic left ventricular posterior wall; and LVPW(s), end-systolic left ventricular posterior wall.