SUPPLEMENTARY MATERIALS

Supplementary table 1. List of antibodies used in the study. Dilution used in Western blots and immunohistochemistry (denoted by asterisks) were stated.

Supplementary Figure 1. Screening of FKRP mice and embryos. A. Southern blot of genomic DNA from ES cells digested with EcoRV. When probed with
PB3/4, the wild-type FKRP allele generates a 12kb fragment whereas the P448L targeted allele generates a 7.5kb fragment due to the creation of a new EcoRV site in the Neo'. Clone 134, 163 and 311 were examples of positive ES cells.  

B. PCR genotyping of wild-type (WT), heterozygous FKRP-neo-P448L/wt (het) and homozygous FKRP-neo-P448L/ FKRP-neo-P448L (P448L) mutant mice. The wild-type FKRP allele can only be amplified by the allele-specific primer set W (8010/PT5), generating a 1606bp fragment. On the other hand, the P448L targeted allele can only be amplified by primer set M (F3/PT5), generating a 1638bp fragment. C. Homologous recombination of the P448L targeting vector to the correct FKRP locus was confirmed by PCR using primer set (A1/UNI).  

D. PCR genotyping of wild-type (WT), heterozygous E310del/wt (het) and homozygous E310del/E310del mutant embryos of E7.5 day. Two allele-specific primer sets, 4714/rN374 and 4714/neo1 were used to amplify wild-type FKRP allele (1206bp) and E310del targeted allele (1401bp), respectively. Both primer sets were combined in one single PCR reaction.
Supplementary figure 2. Summary of body weight of wild-type (wt), heterozygous (het) and homozygous FKRP-neo-P448L mice. A. Body weight of the male and female mice over a period of 5-7 weeks. The number of mice analyzed is denoted by n in the parenthesis. Mutant mice have a $p$-value = 0.0002 compared to wild-type and heterozygous mice. B. Body weight of mice at 5 week, n=3.
5 weeks old. Error bar represents mean±SEM. Mutant mice have a $p$-value = 0.014 compared to wild-type and heterozygous mice.
Supplementary figure 3. Levels of serum CK, ALT, BUN, ALP and cholesterol of wild-type (wt), heterozygous (het) and homozygous (P448L) mice from 5 to 15 weeks of age. The number of mice analyzed is denoted by n in the parenthesis. The mean CK levels in the FKRP-neo-P448L mutant mice were elevated ~10X (p=0.0244) compared to the wild-type controls. Error bar represents mean±SEM.
Supplementary figure 4. A. Relative expression of FKRP in different tissues of wild-type (WT), heterozygous (het) and homozygous FKRP-neo-P448L mutant. The amount of qRT-PCR product with WT tissue as 100% (1). B. Relative expression of FKRP between skeletal muscle and heart in wild-type (WT) and heterozygous (het) mice. The amount of qRT-PCR product with gastronemius as 100% (1)
**Supplementary figure 5.** H&E staining of quadriceps of newborn homozygous FKRP-neo-P448L mouse died at 2 days old. No obvious pathology was observed in the muscles of the mutant mouse. Wt, age-matched wild-type control.
Supplementary figure 6. Masson’s trichrome staining of diaphragm and quadriceps muscles of 10-week-old male wild-type (wt) and homozygous FKRP-neo-P448L mutant mice. Note the marked replacement by connective tissues (blue staining) in the diaphragm of the FKRP-neo-P448L mutant mice. Bar, 50µm.
**Supplementary Figure 7.** Control immunofluorescence images of heterozygous (left column) and FKRP-neo-P448L mutant muscle (right column). Sections were stained with secondary Alexa 594-tagged goat-anti-mouse IgM only as negative controls. Blue spots, DAPI staining.
Supplementary Figure 8. Immunofluorescence images with antibody to beta 1 integrin of quadriceps from wild type (wt) (left panel) and FKRP-neo-P448L mutant (right panel) mice. Upper panel, sections were stained with rabbit polyclonal antibody Integrin beta-1/CD29 (1:50 dilution, #1798-1, Epitomics, CA) and the primary antibody was detected by Alexa 594-tagged goat-anti-rabbit IgG.
Lower panel images are the controls stained with secondary Alexa 594-tagged goat-anti-rabbit IgG only. Blue spots, DAPI staining for nuclei.