Supplementary Information

Scapuloperoneal spinal muscular atrophy and hereditary motor and sensory neuropathy type IIC are allelic disorders caused by mutations in TRPV4

Han-Xiang Deng*, Christopher J. Klein, Jianhua Yan, Yong Shi, Yanhong Wu, Faisal Fecto, Hau-Jie Yau, Yi Yang, Hong Zhai, Nailah Siddique, E. Tessa Hedley-Whyte, Robert DeLong, Marco Martina, Peter J. Dyck, Teepu Siddique*

*Correspondence should be addressed to H.-X.D (h-deng@northwestern.edu) or T.S (t-siddique@northwestern.edu)
Supplementary Figures

Supplementary Figure 1. Pathology of autopsy samples from a patient with SPSMA.

(a) Muscle autopsy samples showing extensive fatty replacement, increased endomysial fibrosis, severe muscle type grouping and atrophy, marked variability of fiber size, and many fibers with multiple internal nuclei, fiber splitting, and multiple nuclear bags. (b) Luxol fast blue/H&E staining of spinal cord sections from the autopsy sample revealed a normal number of motor neurons in the motor cortex and spinal cord. The lateral corticospinal tracts were well preserved.
Supplementary Figure 2. Schematic model of TRPV4. The channel’s core consists of six -helical transmembrane domains and a pore loop (PL) flanked by TM5 and TM6 in the C-terminal part \(^1\)\(^-\)\(^3\). Six ankyrin-repeat domains that have been shown to be a common structural feature in TRPV family \(^4\)\(^,\)\(^5\) near the N-terminus are individually labeled (ARD1-6). Mutations identified in the ARD-containing region are shown by red ovals.
Supplementary Figure 3. Effect of mutations on TRPV4 activity when stimulated with moderate heat. Effect of stimulation with a moderate thermal stimulus (37 °C) on internal fluorescence ratio in WT-TRPV4 (a), R269H (b) and R316C (c) transfected HEK293 cells. (d) Application of thermal stimulus induced an increase in [Ca²⁺]. Average increases, basal and maximum values are given. For each condition, n>10 in at least three independent recordings. * indicates significant differences when compared with WT-TRPV4 (two-tailed Student’s t-test, p<0.0001). Error bars represent means ± S.E.M.
Supplementary Figure 4. Effect of mutations on TRPV4 activity when stimulated with arachidonic acid. Effect of stimulation with arachidonic acid (AA, 10 μM) on internal fluorescence ratio in WT-TRPV4 (a), R269H (b) and R316C (c) transfected HEK293 cells. (d) Application of 10 μM AA induced an increase in [Ca^{2+}]. Average increases, basal and maximum values are given. For each condition, n>10 in at least three independent recordings. * indicates significant differences when compared with WT- TRPV4 (two-tailed Student’s t-test, p<0.05). Error bars represent means ± S.E.M.

References

**Supplementary Table 1. Primers used for PCR amplification and site-directed mutagenesis**

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