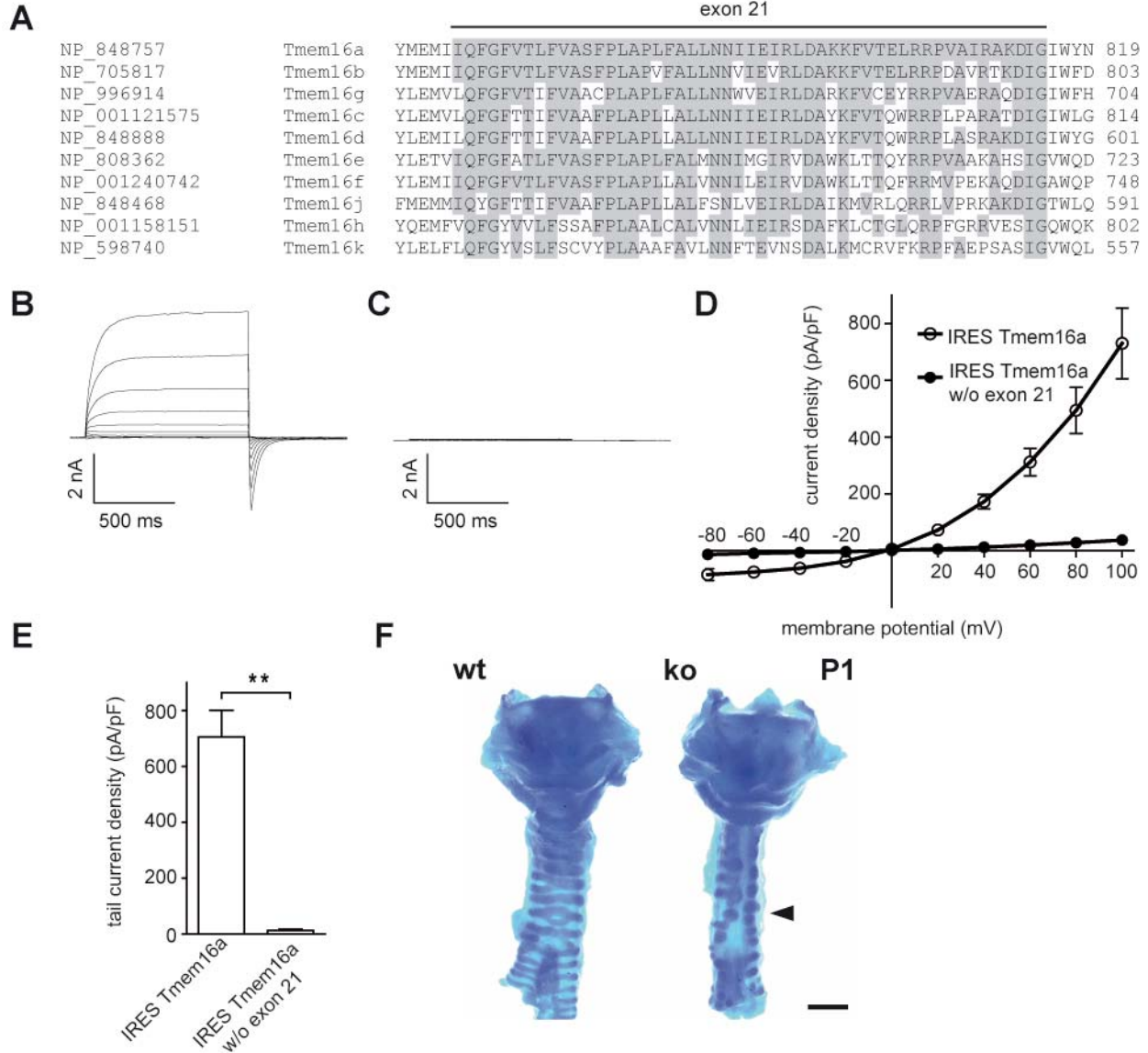


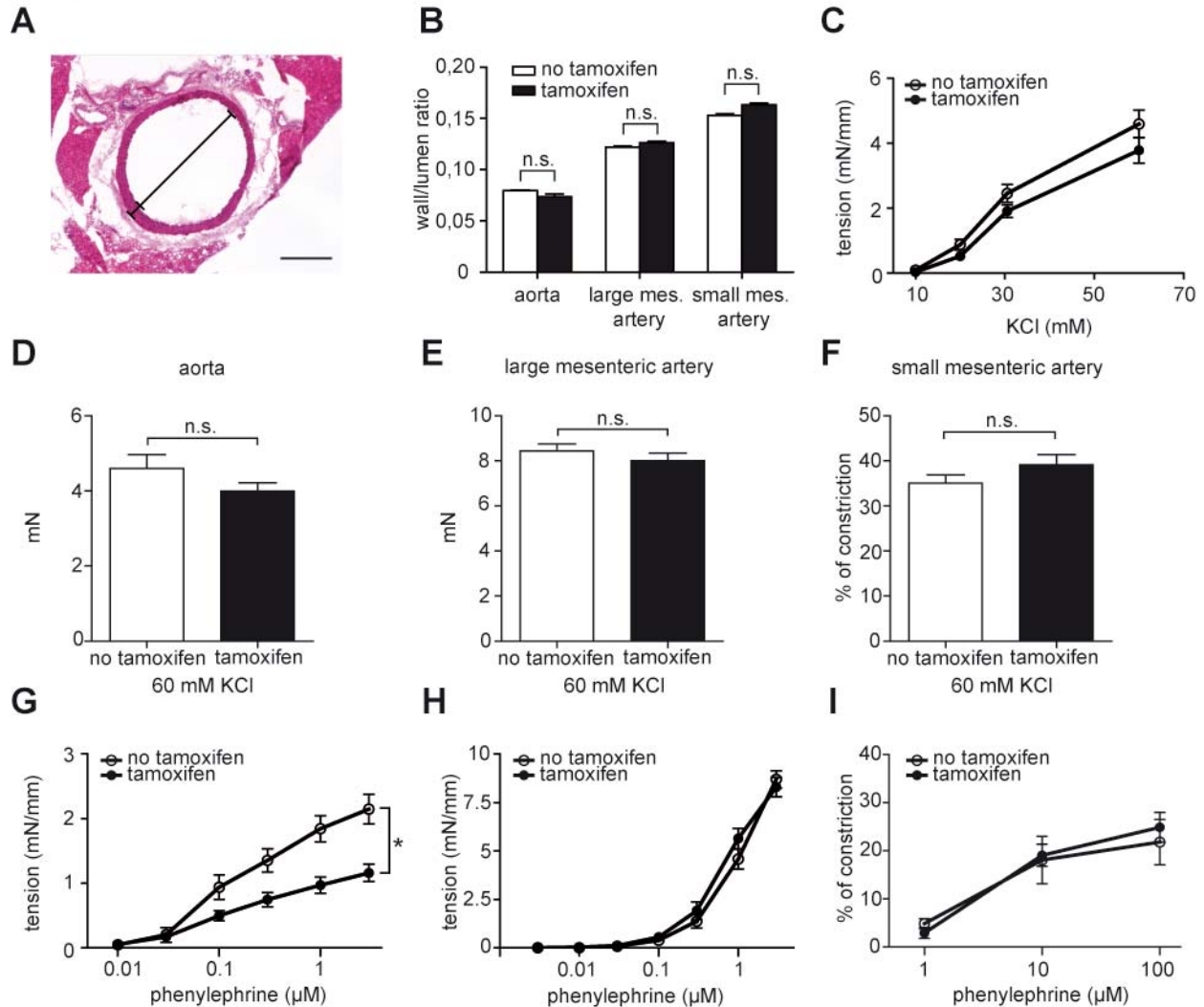
Supplemental information 1



Supplemental information 1

(**A**) Alignment for the amino acid sequence encoded by *Tmem16a* exon 21 with the family of TMEM16 proteins generated with Clustal alignment program (55). (**B,C**) Typical patch-clamp recordings of HEK293 cells transfected with either a cDNA encoding wild-type TMEM16A (**B**) or a variant devoid of exon 21 (**C**). Cells were clamped to voltages between -80 mV and +100 mV in 20 mV steps, followed by a voltage jump to -80 mV. (**D**) Current densities for TMEM16A and TMEM16A without exon 21 measured in transfected HEK293 cells 1 s after depolarization steps to the indicated voltage as described for (**B**). (**E**) Tail current densities for TMEM16A wild-type and TMEM16A without exon 21 in transfected HEK293 cells ($n = 12$ in each group). (**F**) In contrast to wild-type, the cervical situs of a 2-days-old knockout mouse (right) revealed abnormal tracheal cartilages (arrowhead).

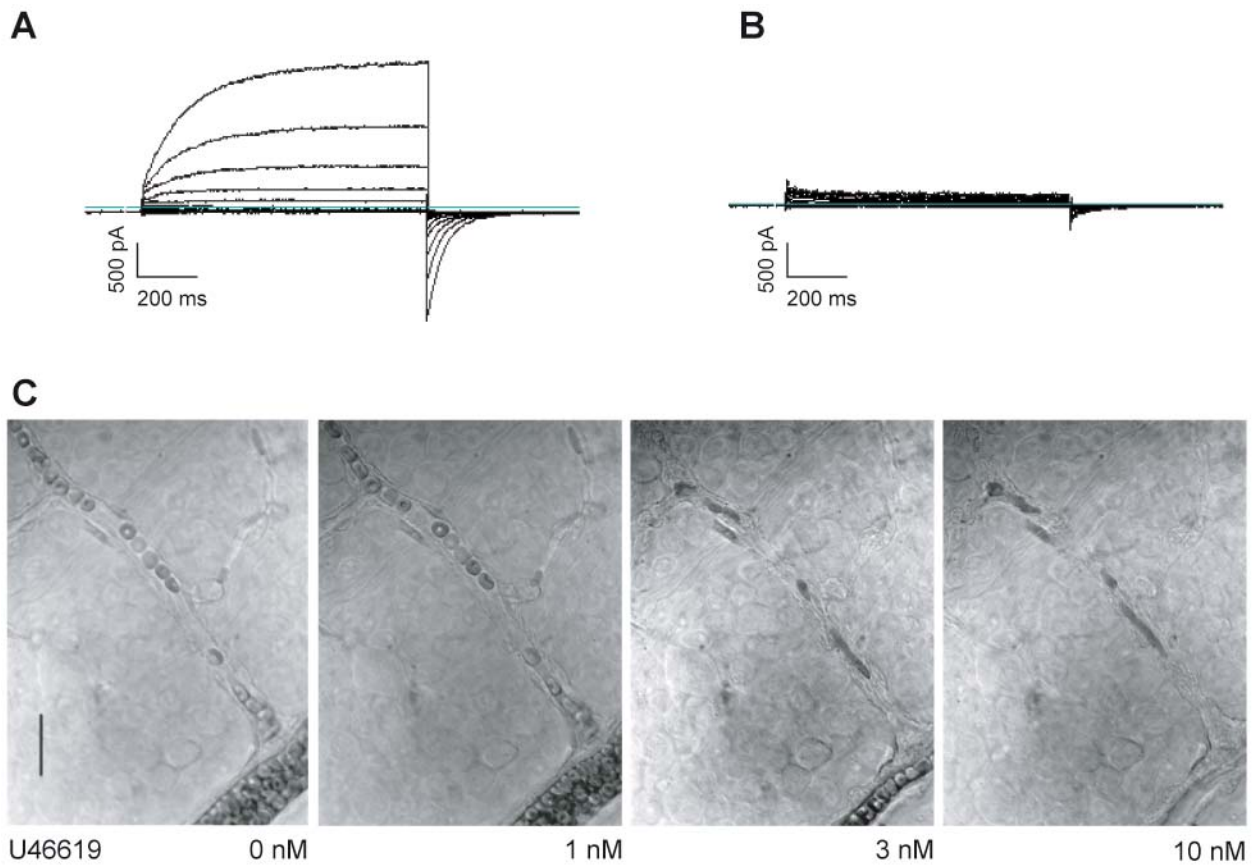
Supplemental information 2



Supplemental information 2

(A,B) Wall-to-lumen ratio determined in transversal sections of HE stained blood vessels ($n = 3$ mice per group). Scale bar 500 μm . n.s.: not significant; Student's t-test; $p > 0.05$. (C) Contractile effects of different extracellular KCl concentrations on aortic rings. (D,E) Contractile effects of 60 mM KCl on aortic (D) and 1st/2nd order mesenteric artery rings (E) determined by wire myography. (F) Changes in diameter of pressurized 3rd/4th order mesenteric arteries at 60 mM KCl determined by videomicroscopy. (G,H) Dose-response curves for the contractile effects of phenylephrine for aortic rings (G; $n = 6$ in each group) and for 1st and 2nd order mesenteric artery rings (H; $n = 16$ to 24 in each group) determined by wire myography. 2-way-ANOVA; *: $p < 0.05$; **: $p < 0.01$. (I) Change in diameter of pressurized 3rd and 4th order mesenteric arteries by phenylephrine determined by videomicroscopy ($n = 4$ to 6 in each group).

Supplemental information 3



Supplemental information 3

(**A,B**) Typical currents recorded from pericytes isolated from brain of non-induced control mice (**A**) and induced conditional TMEM16A knockout mice (**B**). (**C**) Representative time lapse images showing a constriction of a primary and higher order retinal arteriole of non-induced control mice taken 20 min after application of the indicated concentration of the vasoconstrictor U46619. Scale bar: 20 μ m.