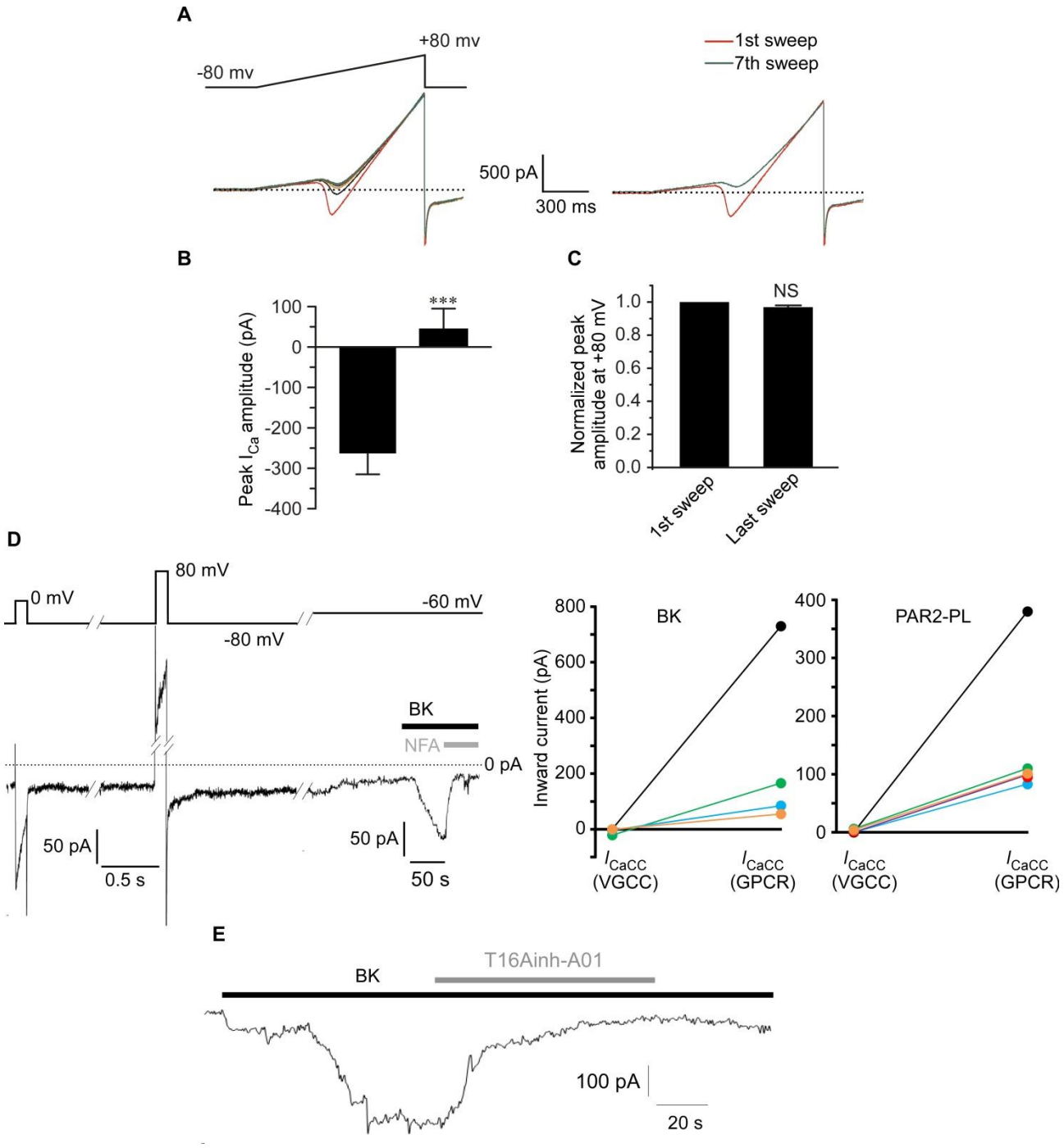

Fig. S1. CaCC in small DRG neurons is not activated by VGCC. (**A**) Voltage ramps (depicted above current traces on the left) from -80 to +80 mV were used to activate VGCC (downward 'hump' in current traces) and to test if outward current at +80 mV is CaCC. The interval between the sweeps was set at 1 s to cause rapid use-dependent inactivation of VGCC. At these recording conditions VGCC current was inhibited by 5^{th}-7^{th} sweep (green trace) but this did not affect the amplitude of outward current at +80 mV. (**B, C**) Summary of the difference in the amplitude of peak VGCC current (B) and the outward current at +80 mV (C) between the first and the last sweeps (n = 10). (**D**) **L**eft: Representative current trace testing the CaCC stimulation by VGCC and GPCR ligand on the same DRG neuron. Right: Scatter plots of experiments as on the left. Amplitudes of VGCC-coupled tail currents [I_{CaCC}(VGCC)] and GPCR-induced inward currents [I_{CaCC}(GPCR)] recorded form the same neuron are connected. PAR2-PL (10 μM) and BK (1 μM) induced inward current of 145 ± 47 pA (n=6) and 259 ± 158 pA (n=4), respectively. (**E**) Inhibition of the BK-induced inward current in a small DRG neuron by the selective TMEM16A inhibitor, T16Ainh-A01 (50 μM). Example represents 6 experiments in which T16Ainh-A01 inhibited BK-induced CaCC by 88 ± 6%.

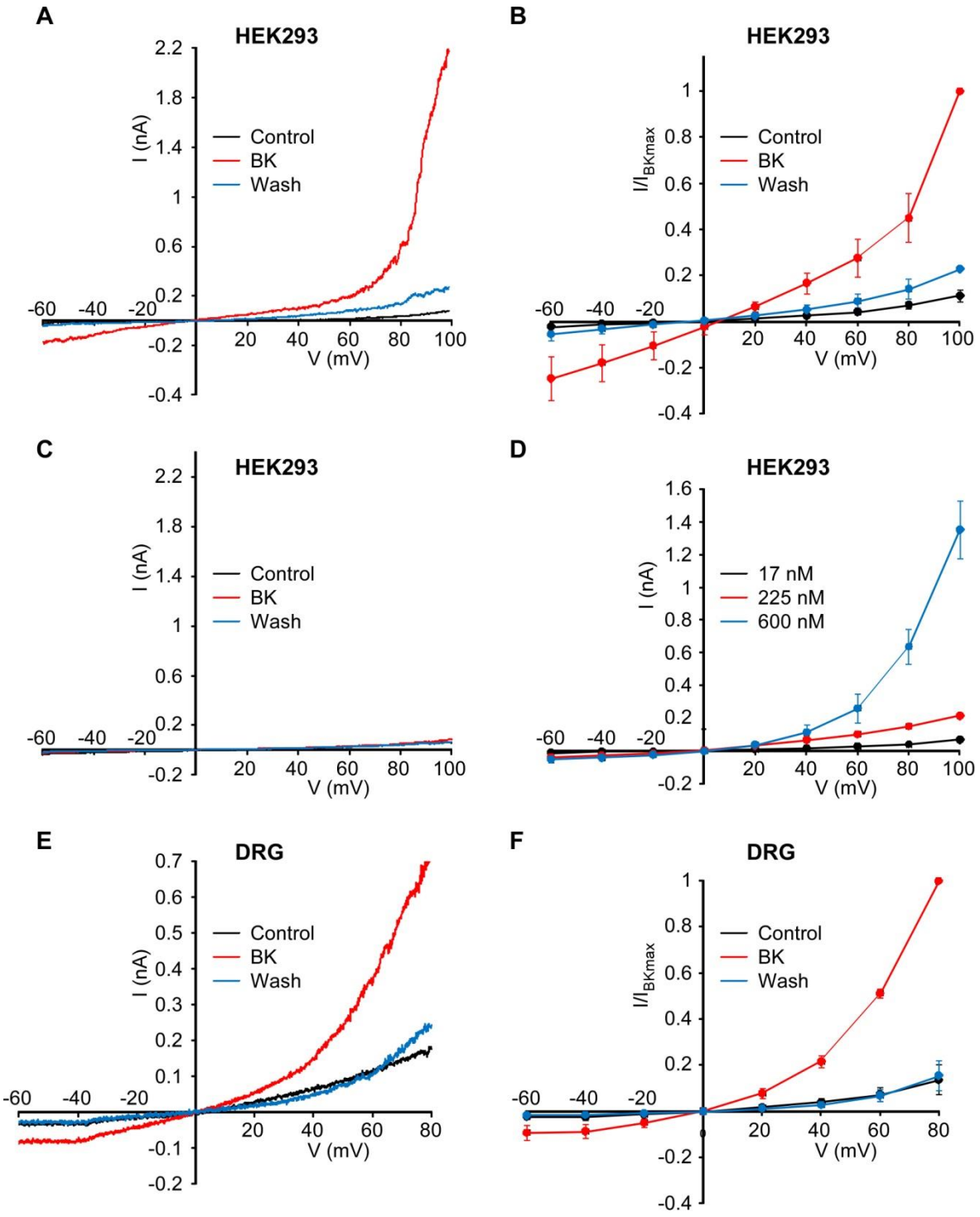

Fig. S2. Properties of BK-induced CaCC in HEK293 cells overexpressing ANO1 and B2R and in cultured small DRG neurons. (**A**) Exemplary current traces recorded in whole cell patch clamp by the voltage ramps from -60 to 100 mV in HEK293 cell line stably expressing ANO1 and transiently transfected with the B_2R. (**B**) Average current-voltage relationships for 5 experiments as (A). (**C**) Exemplary current traces recorded from HEK293 cells overexpressing B_2R only. (**C**) Average current-voltage relationships for 5 experiments as in (A). (**D**) Activation of ANO1 in HEK293 cells by dialysis of Ca^{2+} through the whole-cell patch pipette (concentrations of free Ca^{2+} are as indicated, n=4). (**E-F**) Recordings of BK-induced CaCC from cultured DRG neurons; similar to (A) and (B) but recorded by a voltage ramps from -60 to 80 mV from cultured small DRG neurons, n=5. Exemplary traces are shown in (E) and average current-voltage relationships are shown in (F). 1 μM of BK was used throughout.

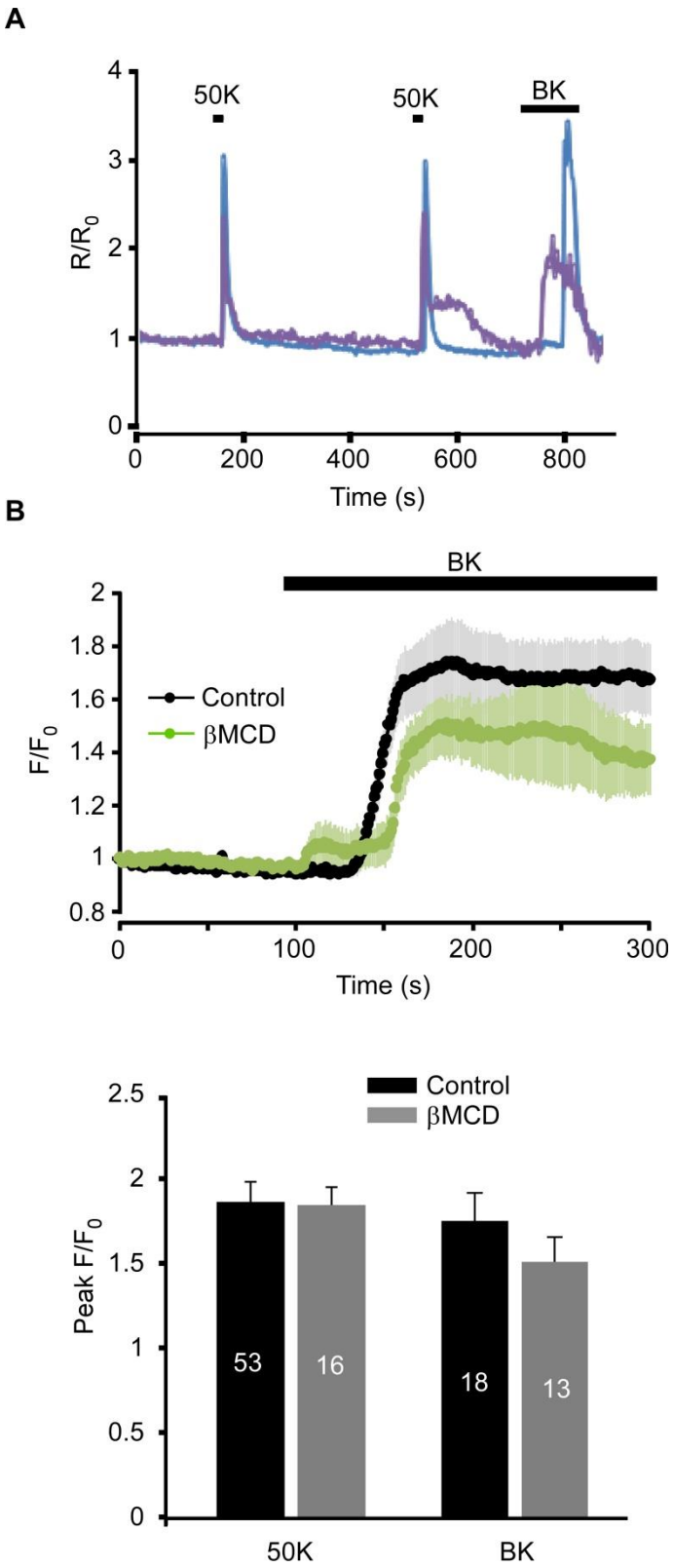

Fig. S3. Lipid raft disruption with βMCD does not significantly affect BK- or depolarization-induced Ca^{2+} transients in DRG. (**A**) Examples of BK- and depolarization- (50 mM KCl) induced Ca^{2+} transients in small DRG neurons measured with fura-2 ratiometric Ca^{2+} imaging. (**B**) Fluo-4 Ca^{2+} imaging was performed to evaluate the effect of βMCD (10 mM, 45 minutes incubation during the loading with fluo-4 AM) on the BK-induced Ca^{2+} responses. Shown are mean values (sphere symbols) ± standard error of mean (shaded area) for the pulled time-courses of the fluo-4 fluorescence of 18/31 control and 13/31 βMCD-treated neurons that responded to 250 nM BK. The bar graph below is a summary of the βMCD effect on peak Ca^{2+} transients induced by 50 mM KCl and BK (number of neurons is indicated within the bars).

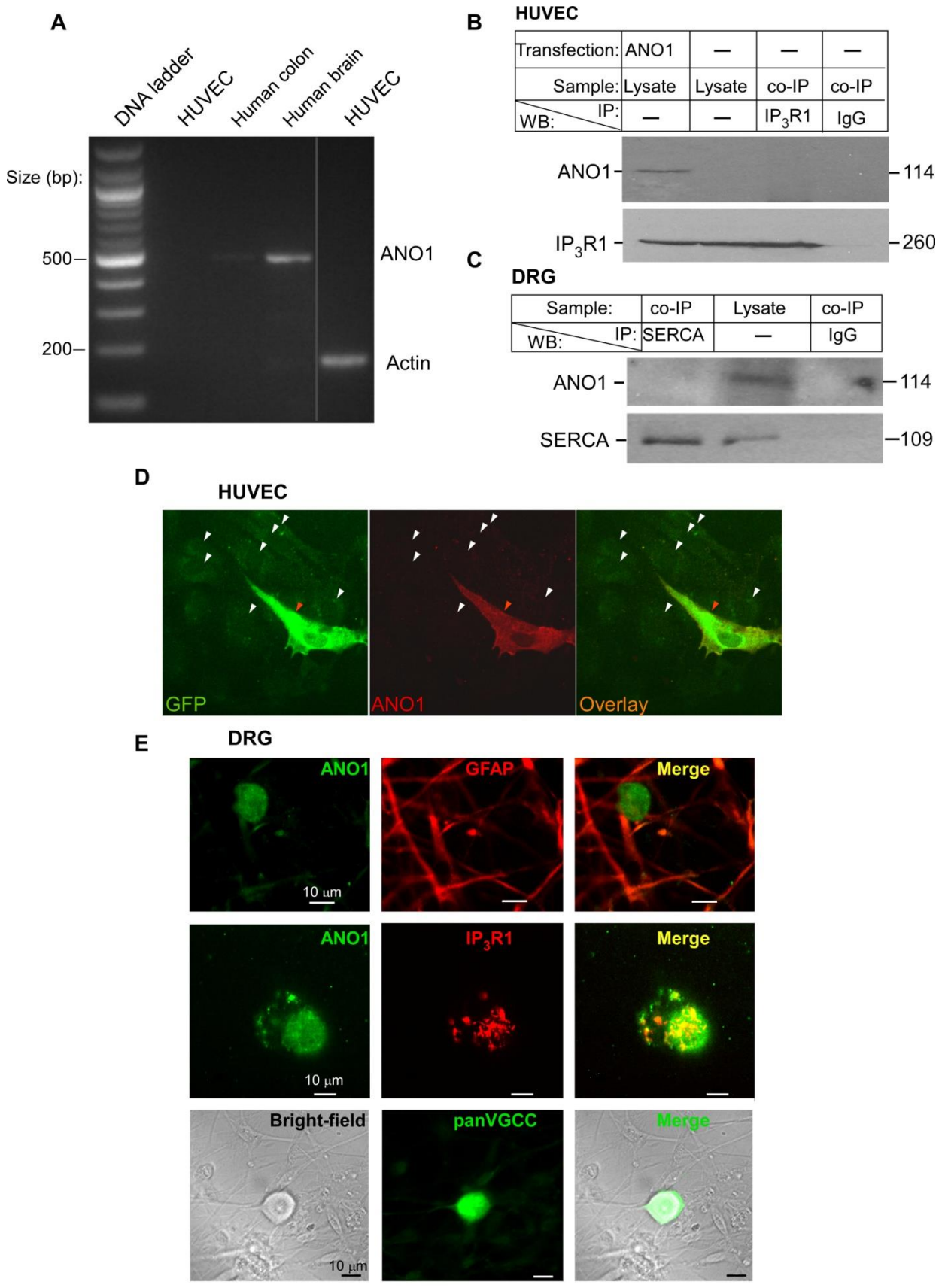

Fig. S4. Antibody specificity experiments. (**A**) RT-PCR revealed no detectable expression of ANO1 in HUVECs while ANO1 specific products were detected in human colon and brain. Forward primer: GTAATACGGCAATAAGGTAGC; reverse primer: ACAACTCTGAGGTCGG. Beta-actin was detected in the HUVEC sample as a positive control. (**B**) Detection of ANO1 immunoreactivity in HUVECs transfected with *Ano1* cDNA (left lane) by Western blot. No immunoreactivity was detected in nontransfected HUVECs (middle-left); no immunoprecipitation of ANO1 by the IP_3R1 antibody or IgG is detected in nontransfected HUVECs. (**C**) Antibody against sarco-endoplasmic calcium ATPase (SERCA) failed to immunoprecipitate

ANO1 from DRG. (**D**) ANO1 antibody specifically labelled cultured HUVECs co-transfected with ANO1 and GFP (orange arrow) but not the nontransfected cells (white arrows). (**E**) Top row: ANO1 antibody specifically labelled small DRG neuron but not glia (as labelled with antibody against GFAP). Middle row: IP_3R1 antibody labelled reticular structures in the ANO1-positive DRG neuron cell body. Bottom row: pan-VGCC antibody labelled DRG neuron but not glia (visible using bright-field illumination).