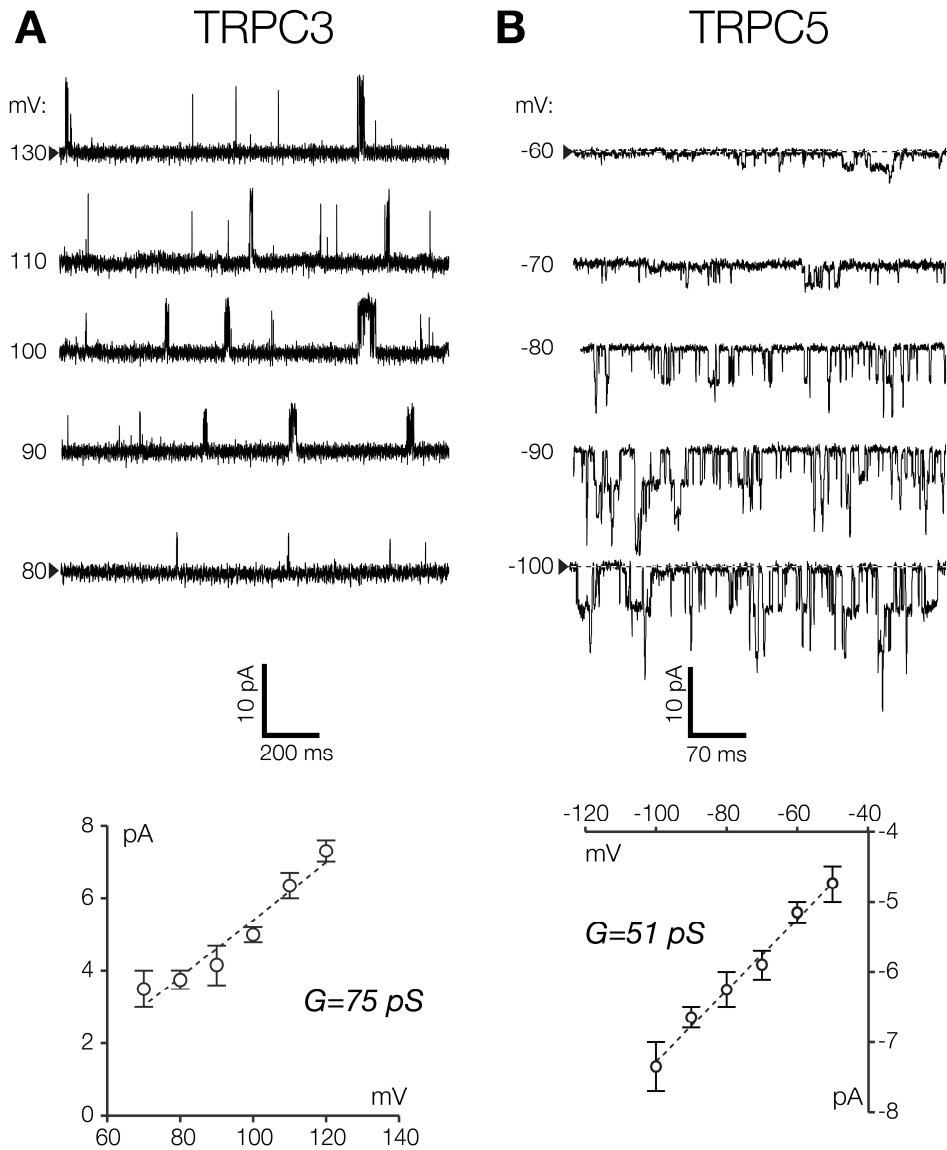


**Table s1. Key resources**

| <i>Recombinant DNA</i>              | <i>Source</i>   |
|-------------------------------------|---|
| <i>Human Piezo1- pIRES2-EGFP</i>    | Philip Gottlieb, SUNY Buffalo                         |
| <i>Mouse TRPA1- pcDNA5/FRT/TO</i>   | Alexander Staruschenko, Medical College of Wisconsin, |
| <i>Human TRPC3- pcDNA3.1</i>        | Philip Gottlieb, SUNY Buffalo                         |
| <i>Mouse TRPC5- pcDNA6</i>          | Xiaoqiang Yao, The Chinese University of Hong Kong    |
| <i>Human TRPC6- pIRES2-EGFP</i>     | Eric Honoré, IPMC                                     |
| <i>Human TRPV1- pEYFP-N3</i>        | Linlin Ma, The University of Queensland               |
| <i>Human TRPV3- pcDNA5/FRT/TO</i>   | Sara Baratchi, RMIT University                        |
| <i>Human TRPV4- pcDNA 5/FRT/TO</i>  | Peter McIntyre, RMIT University                       |
| <i>Human TRPM4- pCAGGS/IRES GFP</i> | Veit Flockerzi, Saarland University                   |
| <i>Human TRPM8- pEF5/FRT/V5</i>     | Sara Baratchi, RMIT University                        |
| <i>Human PKD2L1- pIRES2-EGFP</i>    | Paul DeCaen, Northwestern University                  |
| <i>Mouse TRPML1(4A)- pEGFP/C2</i>   | Youxing Jiang, University of Texas                    |

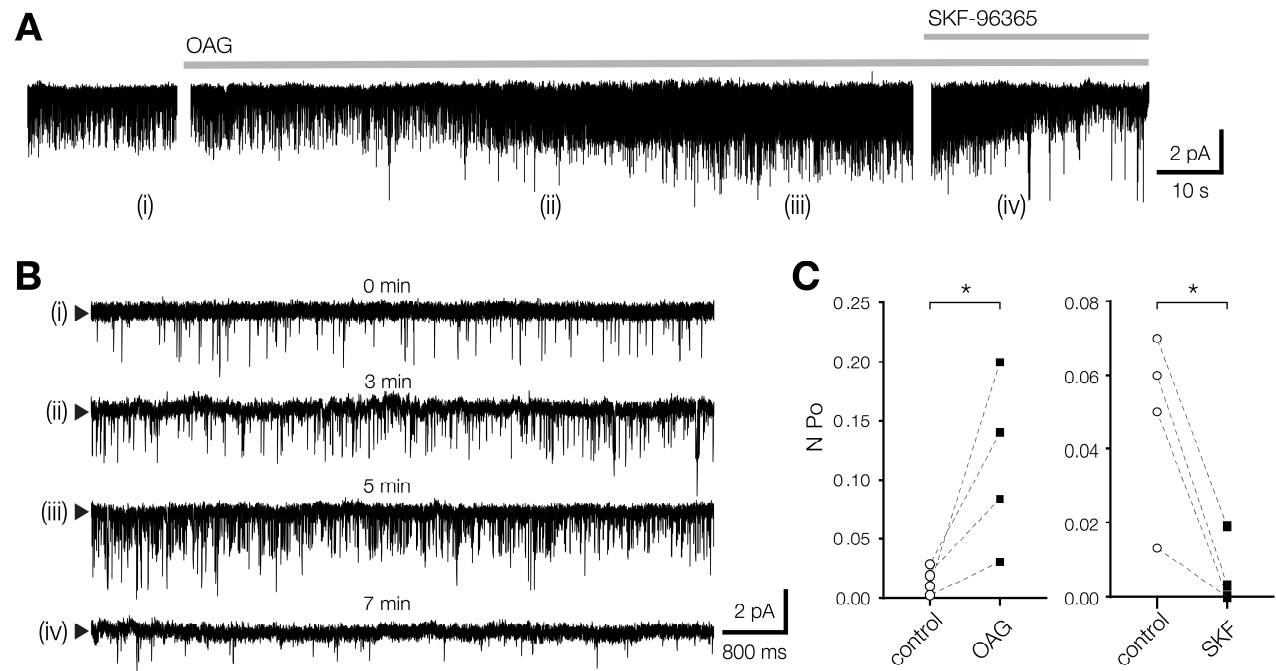
**Table s2. List of *C. elegans* strains**

| <i>Strain</i>    | <i>Genotype</i>   |
|------------------|---|
| <i>Wild type</i> | N2  |
| <i>GN132</i>     | <i>osm-10(rtIs27) III; osm-9(ky10) IV; rtIs27 (Posm-10::GFP X)</i>  |
| <i>COP1493</i>   | <i>knuSi749 [ pnu1336 (osm10p::rtrpv1-wt-optimized::tbb-2u, unc-119(+)) ] II; unc-119(ed3) III; osm-9(ky10) IV; rtIs27 (Posm-10::GFP X)</i> |
| <i>COP1830</i>   | <i>knuSi791 [ pnu1668 (osm10p::mTRPC6-wt-optimized::tbb-2u, unc-119(+)) ] II; unc-119(ed3) III; osm-9(ky10) IV; rtIs27 (Posm-10::GFP X)</i> |



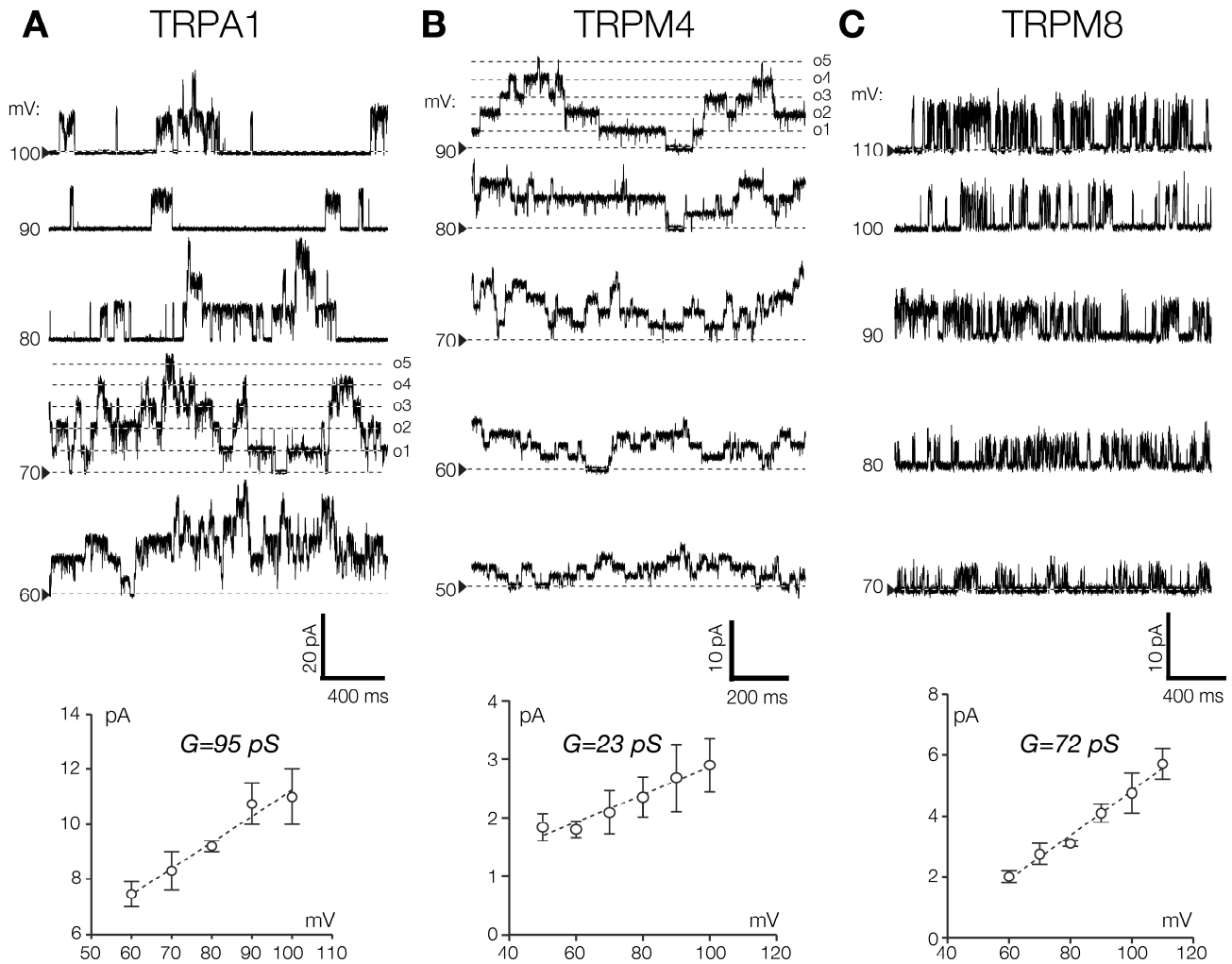
**Figure s1. Single channel properties of TRPC3 and TRPC5 ion channels in HEK293T cells**

(A) (B) Representative hTRPC3 and mTRPC5 single channel recording at different voltages in cell-attached patch from HEK293T cells. Black arrows indicate the position of the baseline current. Downward single channel deflections represent inward current. At the bottom: current-voltage relationship for single channels of TRPC3 (N=4) and TRPC5 (N=3), with indicated single channel conductance (mean  $\pm$  s.e.m.):  $75.3 \pm 9.1 \text{ pS}$  and  $51 \pm 2.6 \text{ pS}$ .



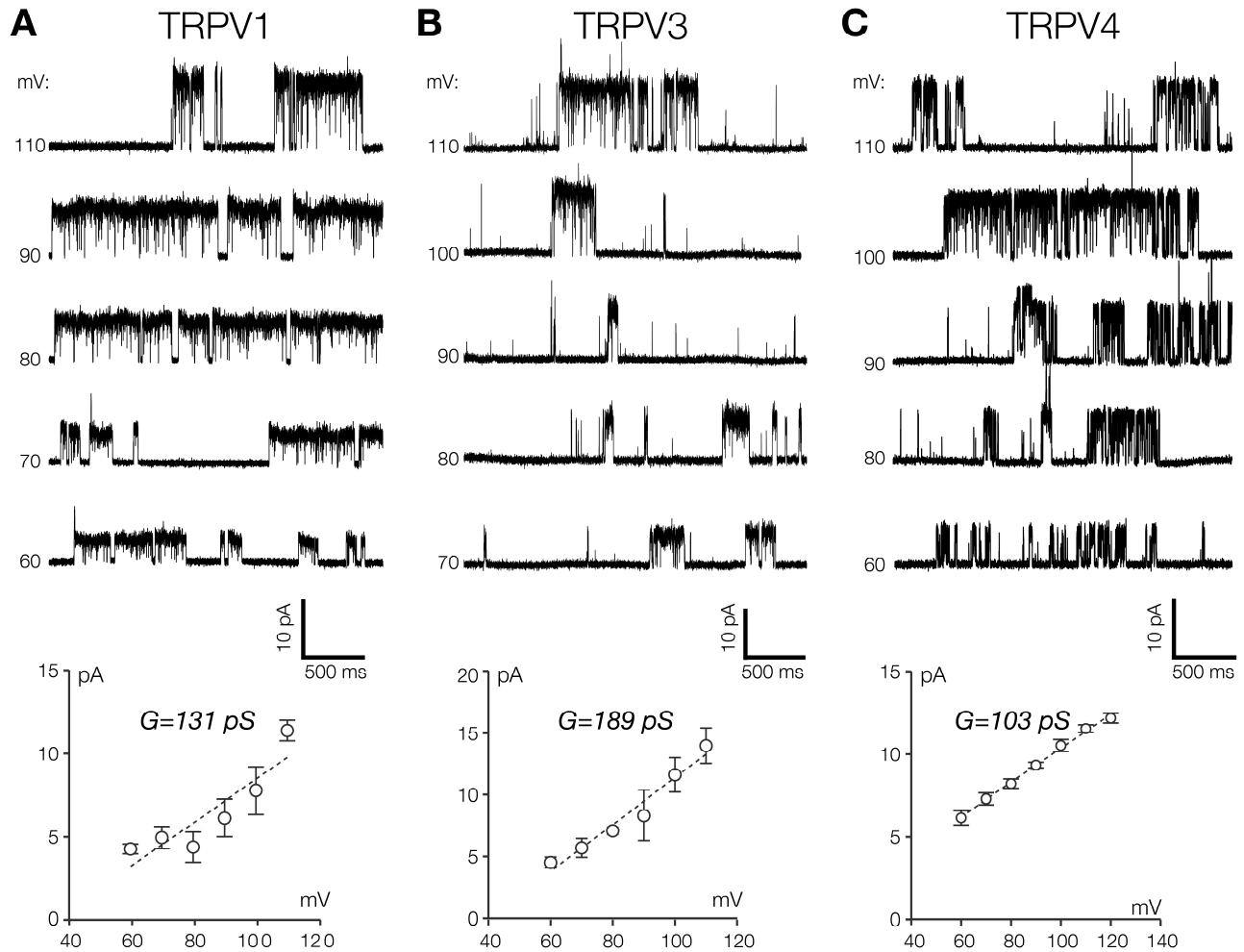
### Figure s2. Pharmacology of TRPC6 ion channels

(A) Application of agonist OAG (30  $\mu$ M) and antagonist SKF-96365 (10  $\mu$ M) to TRPC6 single channel activity in inside-out mode at -50 mV. (B) Enlarged segments of TRPC6 channel activity from (A) (C) Graph summarizing the channel open probability (N Po) before and after application of OAG and SKF-96365. \*P < 0.05, paired t-test



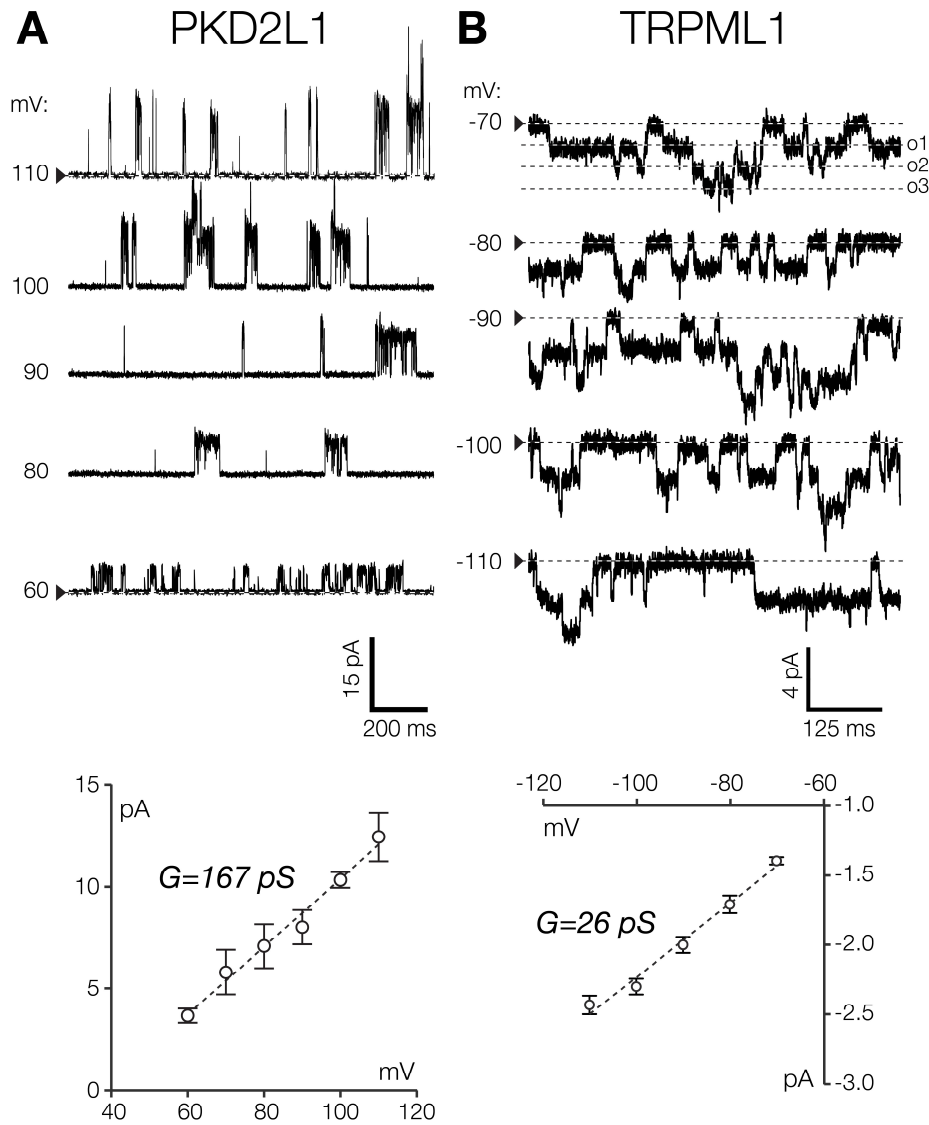
**Figure s3. Single channel properties of TRPA1, TRPM4, and TRPM8 ion channels in HEK293T cells**

(A) (B) (C) Representative mTRPA1, hTRPM4, and hTRPM8 single channel recording at different voltages in cell-attached patch recorded at room temperature. Black arrows indicate the closed state of the channels. Upward single channel deflections represent outward current. At the bottom: single conductance values (mean±s.e.m.) with current-voltage relationships for single channels of TRPA1 (N=3), TRPM4 (N=4) and TRPM8 (N=3): 95.5±11 pS, 23.3±2.5 pS, and 72.8±4.1 pS respectively.



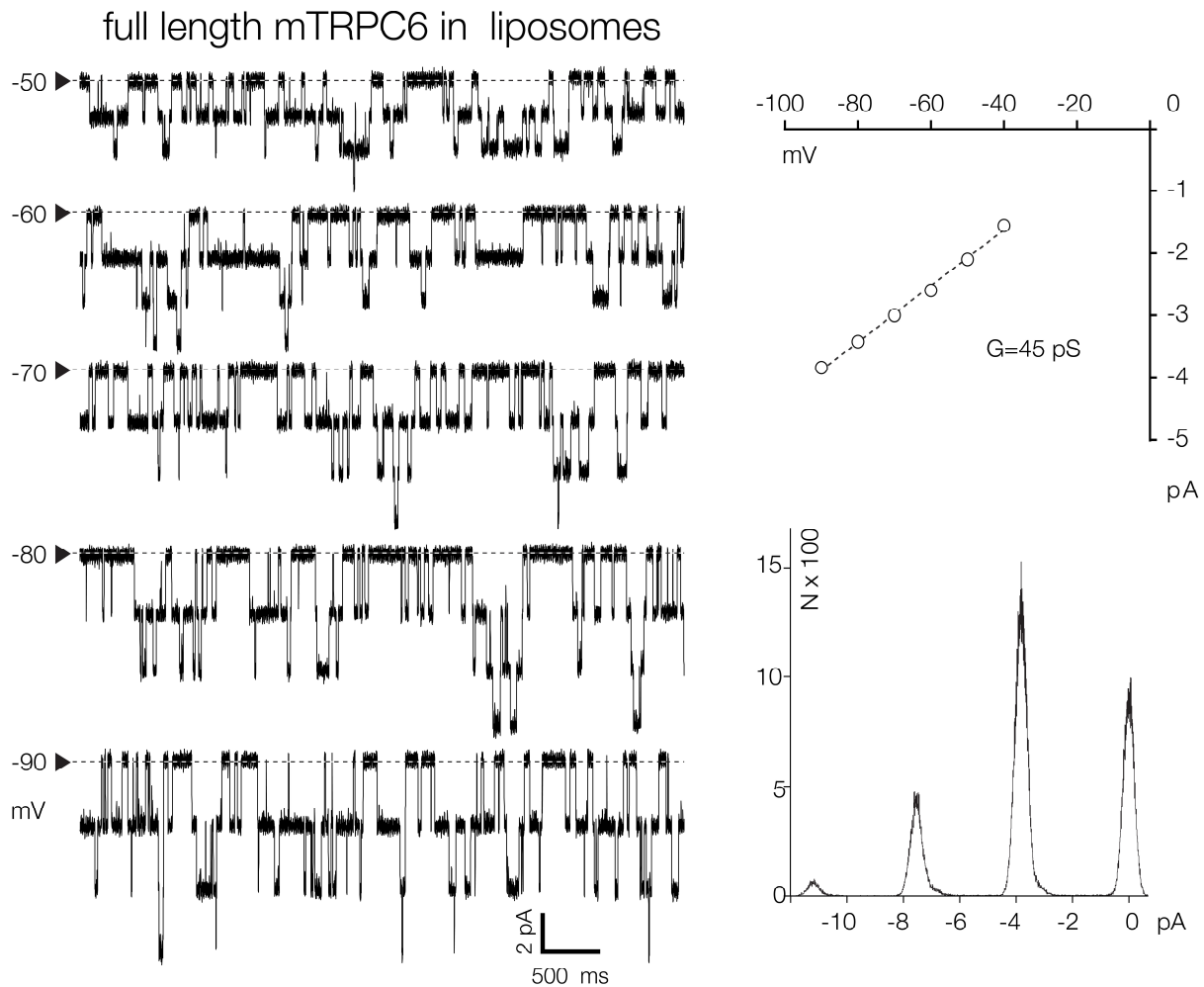
**Figure s4. Single channel properties of TRPV subfamily channel members in HEK293T cells**

(A) (B) (C) Single channel recordings of hTRPV1, hTRPV3, and hTRPV4 at different voltages in cell-attach patch recorded at room temperature. Upward single channel deflections represent outward current. At the bottom: fittings with single conductance values (mean $\pm$ s.e.m.) of TRPV1 (N=4), TRPV3 (N=3), and TRPV4 (N=3): 131.1 $\pm$ 32.9 pS, 189.4 $\pm$ 19 pS, and 103.5 $\pm$ 2.9 pS respectively.



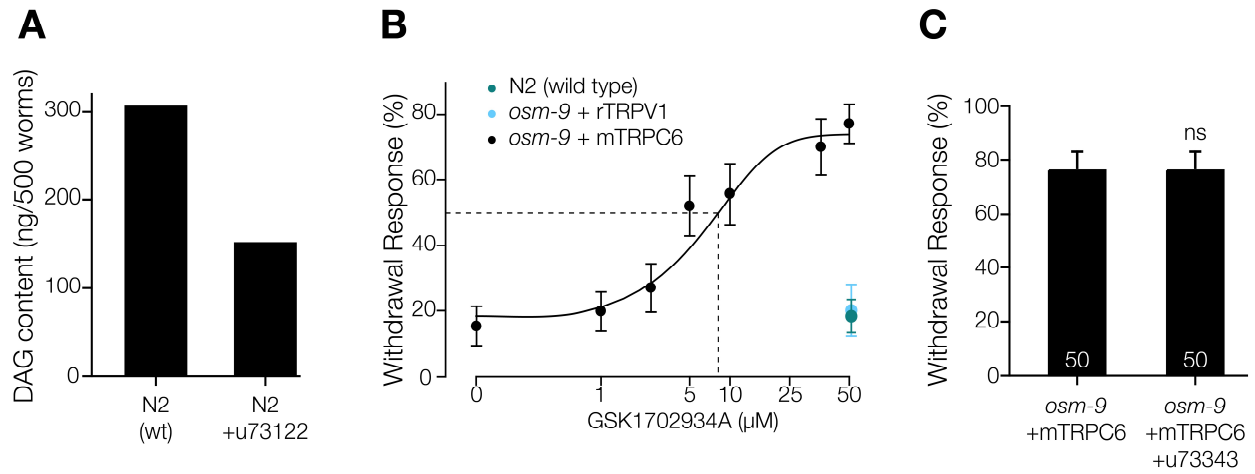
**Figure s5. Single channel properties of PKD2L1 and TRPML1 channels in HEK293T cells**

(A) (B) Single channel recordings of hPKD2L1 and mTRPML1 (4A), surface expressing mutant, at different voltages. PKD2L1 was recorded in cell-attached configuration, TRMPL1 was recorded in inside-out configuration. At the bottom: fittings with single conductance values (mean $\pm$ s.e.m.) of PKD2L1 (N=4) and TRPML1 (N=4): 167.0 $\pm$ 10 and 45 $\pm$ 2 pS.



**Figure s6. Single channel properties of full length TRPC6 recorded in liposomes**

Spontaneous activity of the full length mTRPC6 channel in the liposomes recorded at a range of voltages in excised patch. On the right: current-voltage relationship with the linear fitting and amplitude histogram corresponding to the channel activity at -90 mV. N=1.



**Figure s7. Related to Figure 6**

(A) Diacylglycerol (DAG) content in control vs. PLC inhibitor (u73122) treated worms as determined by LC-MS. (B) Dose-response profile of TRPC6 agonist GSK1702934A for wild type (N2), TRPC6, and TRPV1 expressing *osm-9* worms. For each value (mean  $\pm$  s.e.m.)  $n \geq 25$ .  $EC_{50} = 7.01 \pm 9.7 \mu$ M. (C) Worms (*osm-9* strain) expressing mTRPC6 were fed with an inactive PLC inhibitor analog (u73343) and then subjected to touch response test.