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| --- | --- | --- | --- |
| **Supplementary File 1** |  | Displacement threshold  (µm) | Inactivation time constant, τ (ms) |
| HEK293 cells | **Piezo2 + mock** | 3.47 ± 0.30  (n=17) | 3.29 ± 0.54  (n=11) |
| **Piezo2 + Mtmr2** | 4.92 ± 0.38  (n=12); p=0.0098; Mann-Whitney test | 3.57 ± 0.60  (n=11) |
|  |  |  |
| **Piezo2 + mock** | 4.59 ± 0.26  (n=17) | 2.56 ± 0.36  (n=14) |
| **Piezo2 + Mtmr2 C417S** | 3.84 ± 0.38  (n=18) | 2.89 ± 0.68  (n=14) |
|  |  |  |
| **Piezo1 + mock** | 3.64 ± 0.20  (n=25) | 12.00 ± 1.19  (n=19) |
| **Piezo1 + Mtmr2** | 3.85 ± 0.32  (n=20) | 17.16 ± 2.81  (n=12); p = 0.3011; Mann-Whitney test |
|  |  |  |  |
| HEK293 cells | **Piezo2-P1 mutant + mock** | 3.54 ± 0.39  (n=13) | 3.17 ± 0.40  (n=13) |
| **Piezo2-P1 mutant + Mtmr2** | 4.00 ± 0.4  (n=10) | 3.46 ± 0.88  (n=10) |
|  |  |  |  |
| DRG neurons | **CTRL**  **(Allstar negative control)** | 3.17 ± 0.18  (n=66) | 4.21 ± 0.28  (n=57) |
| **Mtmr2 siRNA** | 2.87 ± 0.17  (n=77) | 4.63 ± 0.27  (n=63) |
|  |  |  |
| **mock plasmid** | 3.71 ± 0.28  (n=28) | 3.67 ± 0.49  (n=23) |
| **Mtmr2 cDNA** | 3.90 ± 0.24  (n=30) | 3.59 ± 0.40  (n=27) |
|  |  |  |  |
| DRG neurons  DRG neurons  DRG neurons | **Mtmr2 siRNA + DMSO** | 2.15 ± 0.21  (n=27) | 4.75 ± 0.52  (n=22) |
| **Mtmr2 siRNA + Apilimod** | 3.10 ± 0.23  (n=30); p=0.005 (vs. Mtmr2 siRNA + DMSO); Kruskal Wallis trst followed by Dunn’s multiple comparison | 3.57 ± 0.39  (n=25); ns; Kruskal Wallis trst followed by Dunn’s multiple comparison |
| **Mtmr2 siRNA + Wortmannin** | 2.68 ± 0.21  (n=28) | 4.94 ± 0.70  (n=27) |
|  |  |  |
| **+ DMSO** | 2.81 ± 0.41  (n=16) | 5.44 ± 0.76  (n=14) |
| **+ Apilimod** | 2.08 ± 0.52  (n=12) | 6.47 ± 1.09  (n=8) |
|  |  |  |
| **Isotonic extra** | 3.59 ± 0.20  (n=53) | 3.13 ± 0.34  (n=35) |
| **Hypotonic extra** | 2.84 ± 0.14  (n=81); p=0.0021; Mann-Whitney test | 3.18 ± 0.24  (n=61) |
| DRG neurons | **Mtmr2 siRNA + Isotonic intra** | 3.59 ± 0.25  (n=29) | 2.96 ± 0.43  (n=23) |
| **Mtmr2 siRNA + Hypotonic intra** | 4.52 ± 0.21  (n=25); p=0.0131;  Mann-Whitney test | 3.05 ± 0.47  (n=21) |
|  |  |  |
| **Mtmr2 cDNA + Isotonic extra** | 3.50 ± 0.33  (n=14) | 4.43 ± 0.86  (n=9) |
| **Mtmr2 cDNA + Hypotonic extra** | 2.79 ± 0.27  (n=19) | 3.89 ± 0.56  (n=14) |
|  |  |  |
| **CTRL** | 3.74 ± 0.29  (n=27) | 3.49 ± 0.42  (n=20) |
| **+ 1µM PI(3)P** | 3.65 ± 0.32  (n=17) | 2.65 ± 0.36  (n=14); ns; Kruskal Wallis trst followed by Dunn’s multiple comparison |
| **+ 1µM PI(3,5)P2** | 3.52 ± 0.31  (n=21) | 2.32 ± 0.50  (n=9); ns; Kruskal Wallis trst followed by Dunn’s multiple comparison |
|  |  |  |  |
| DRG neurons | **CTRL (IA-MA)** | 3.17 ± 0.33  (n=23) | 16.28 ± 1.10  (n=23) |
| **Mtmr2 siRNA (IA-MA)** | 3.40 ± 0.53  (n=10) | 16.87 ± 2.94  (n=9) |
|  |  |  |
| **CTRL (SA-MA)** | 2.50 ± 0.32  (n=12) | 55.43 ± 5.18  (n=5) |
| **Mtmr2 siRNA (SA-MA)** | 2.36 ± 0.52  (n=11) | 48.60 ± 4.93  (n=3) |