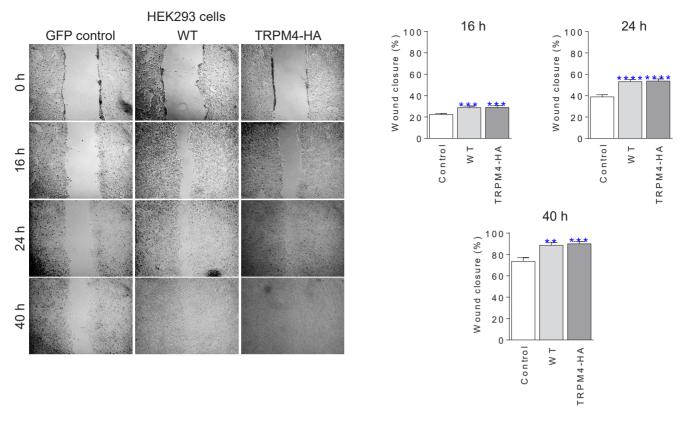
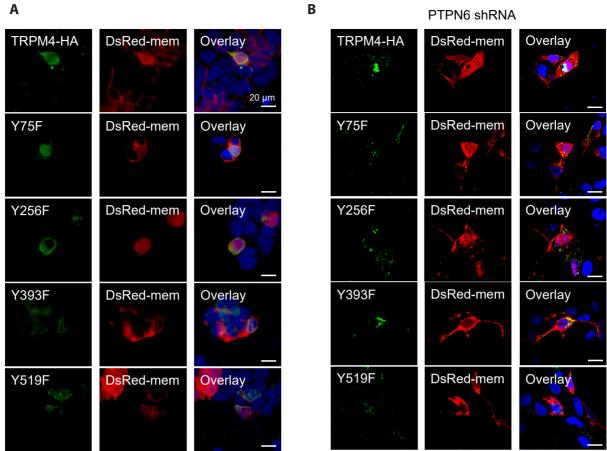


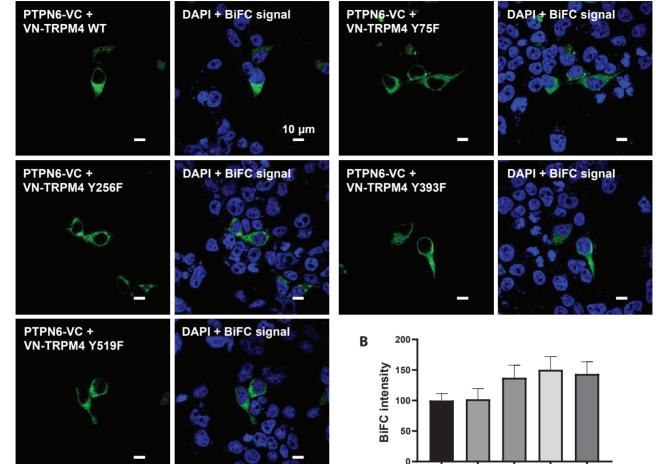
**Supplementary Fig. 1. The basal current densities of both TRPM4 (WT) and TRPM4-HA remain consistent.** (A, B) Variations in current densities inhibited by 9-phenanthrol in cells transfected with WT or TRPM4-HA. (C) Dominant inhibition of channel currents at +100 mV compared with -100 mV by impermeable NMDG in both WT- and TRPM4-HA-transfected cells. Statistical analysis revealed significant differences compared with the control, with \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, \*\*\*\*p < 0.0001. All data are presented as means ± SEM. HA, hemagglutinin; TRPM4, transient receptor potential melastatin 4; NMDG, N-Methyl-D-glucamine; WT, wild-type.



Supplementary Fig. 2. Determination of an hour elapsed time fit to assess wound healing after initiating the scratch assay with HEK293 cells. In the left, images taken elapsed hours after the scratching assay performed on cells overexpressed GFP only (left), wild-type TRPM4 (center), and TRPM4-HA (right) are shown. In the right, quantitative charts represent statistical differences for the wound-closures 16, 24, and 40 h after scratching. \*\*p < 0.01, \*\*\*p < 0.001, \*\*\*p < 0.001. All data are presented as means  $\pm$  SEM. HA, hemagglutinin; TRPM4, transient receptor potential melastatin 4.



Supplementary Fig. 3. Surface expression levels of TRPM4-HA and its YF mutants remain constant. (A) Surface expression changes in cells expressing YF mutants of TRPM4-HA analyzed by confocal microscopy. No significant differences between TRPM4-HA and all YF mutants. (B) Surface expression images of TRPM4-HA and all YF mutants in the presence of PTPN6 shRNA. Scale bar = 20 µm. HA, hemagglutinin; TRPM4, transient receptor potential melastatin 4; PTPN6, protein tyrosine phosphatase, non-receptor type 6.



WT Y75F Y256F Y393F Y519F

**Supplementary Fig. 4. BiFC analysis in cells expressing TRPM4-HA or its YF mutants and PTPN6.** No significant changes were observed in the confocal images (A) or densitometry analysis (B). Scale bar =  $10 \mu$ m. All data are presented as means ± SEM. HA, hemagglutinin; TRPM4, transient receptor potential melastatin 4; PTPN6, protein tyrosine phosphatase, non-receptor type 6; BiFC, bimolecular fluorescence complementation; WT, wild-type.

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