Jeng et al., http://dx.doi.org/10.1085/jgp.201611651

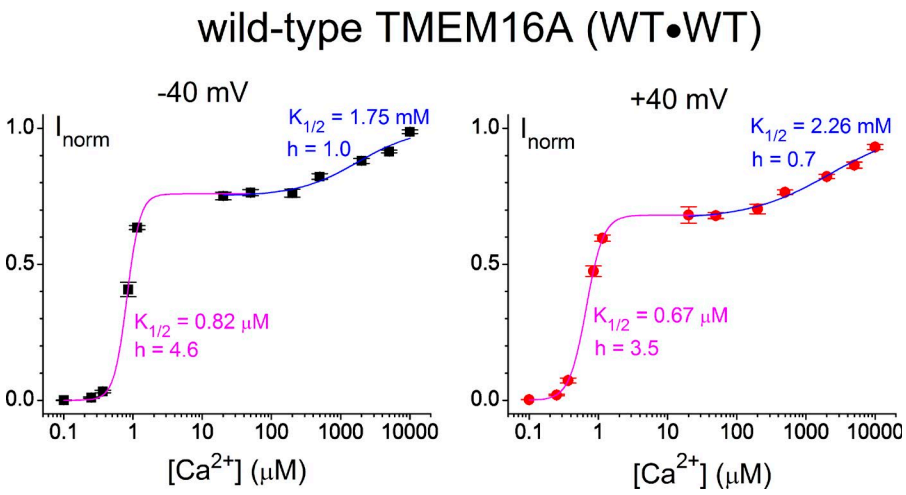

Figure S1. **Dose–response curves of the wild-type TMEM16A channel (WT•WT) from 0.1 µM to 10 mM [Ca^{2+}].** Left and right panels show data obtained at −40 and 40 mV, respectively. Data points (mean ± SEM) were obtained by normalizing the Ca^{2+}-activated currents at each [Ca^{2+}] to those obtained at 20 mM. Solid curves are drawn according to the curve fitting of data points to the Hill equation in two concentration ranges: high-affinity range (0.1–50 µM, magenta curves) and low-affinity range (20 µM to 20 mM, blue curves). In fitting data points from 0.1 to 50 µM (the high-affinity range), the maximal I_{norm} was set as a free parameter for curve fitting while the minimal value of I_{norm} was 0. The fitted saturated I_{norm} values at −40 and 40 mV in this high-affinity region were 0.759 and 0.681, respectively. For the curve fitting in the low-affinity region, the minimal I_{norm} was set as a free parameter while the saturated I_{norm} was 1. The fitted minimal I_{norm} values for data at −40 and 40 mV were 0.751 and 0.666, respectively. The $K_{1/2}$ and the Hill coefficient, h, of each dose–response curve are depicted next to the curve.

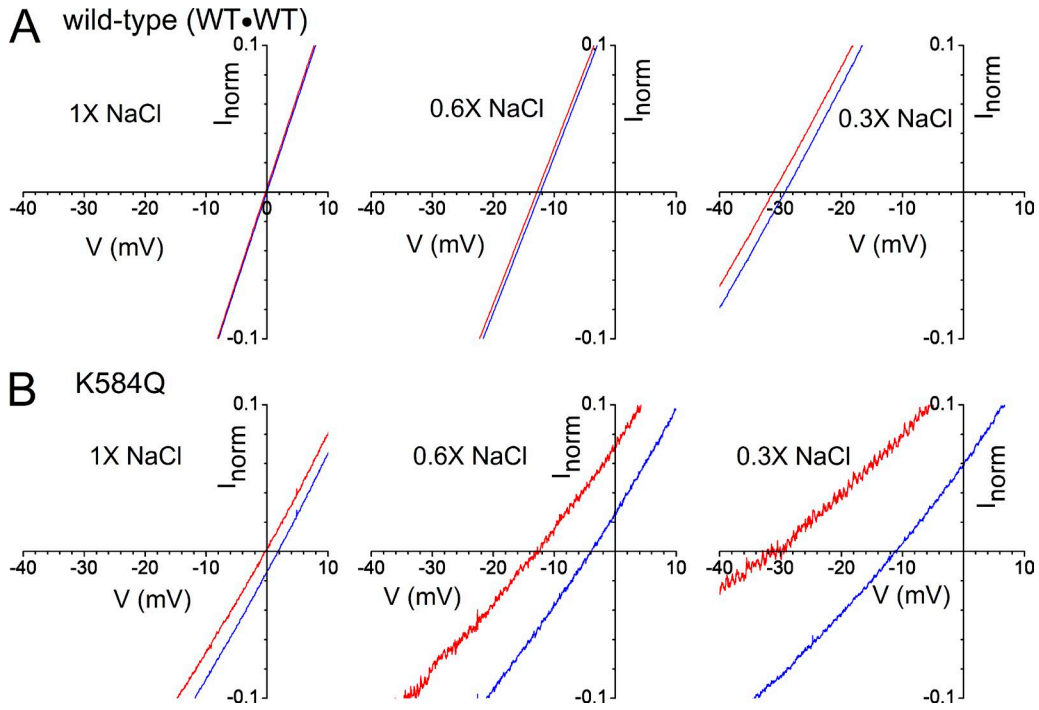

Figure S2. **Precisions of E_{rev} measurements are affected by leak current subtraction.** (A) Wild-type TMEM16A (WT•WT). (B) K584Q mutant. In both panels, current traces with and without leak subtraction are colored in red and blue, respectively. Recording traces were obtained with 1× $[NaCl]_o$ (140 mM) and indicated $[NaCl]_i$ in each panel. Four and seven normalized I-V curves of the wild-type channel and the K584Q mutant, respectively, were averaged. The SEM for each averaged I-V curve is not shown. The leak-subtracted traces in 1× $[NaCl]_i$ are the same as those shown in Fig. 7 C (left). Notice that E_{rev} is shifted to more depolarized voltage without subtraction of the I-V curve obtained in 0 $[Ca^{2+}]$. The effect of the endogenous current on the E_{rev} of the wild-type channel was small (only ~2 mV in the worst case of 0.3× $[NaCl]_i$). In contrast, the shift of E_{rev} was significant in the K584Q mutant because the expression of this mutant was much worse than that of the wild-type channel. Furthermore, the I-V curve of K584Q is outwardly rectified, and the rectification effect was further amplified by reducing $[NaCl]_i$ (see Fig. 6 A), leading to a small ratio of channel conductance/leak conductance. Thus, without leak subtraction, the more reduction of $[NaCl]_i$, the greater the error of E_{rev}.

Table S1. **Reversal potentials in millivolts (mean ± SEM) for the wild-type TMEM16A channel and various channel constructs harboring the K584Q mutation**

Channel constructs	$[NaCl]_i$ = 140 mM (1×)	$[NaCl]_i$ = 84 mM (0.6×)	$[NaCl]_i$ = 42 mM (0.3×)
WT•WT (n = 4)	−0.5 ± 0.5	−13.0 ± 0.4	−31.5 ± 0.3
K584Q (n = 7)	−0.4 ± 0.4	−13.1 ± 0.5	−31.4 ± 0.5
E698C(K584Q)-WT (n = 4)	−0.3 ± 0.3	−12.0 ± 0.4	−30.8 ± 0.5
E698C-WT (n = 4)	−1.2 ± 0.5	−13.3 ± 0.5	−31.0 ± 0.9
E698C-WT(K584Q) (n = 4)	−0.8 ± 0.3	−13.0 ± 1.0	−32.5 ± 0.3

$[NaCl]_o$ = 140 mM. $[Ca^{2+}]_i$ = 20 μM.