Supplementary material

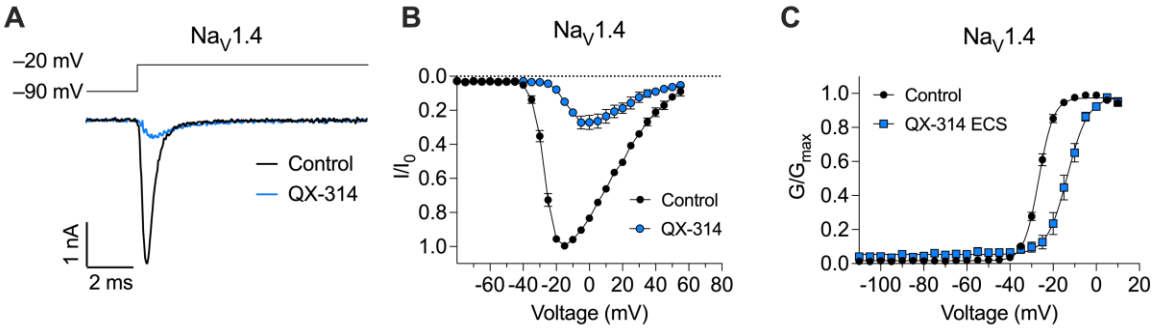

Figure S1. Effect of external QX-314 on electrophysiological properties of $Na_V1.4$. (**A**) Representative traces of sodium current at $Na_V1.4$ before (black) and after addition of 5 mM QX-314 (blue). (**B**) Current-voltage relationship in absence (black, n = 5) and presence of external QX-314 (blue, n = 5). Current in presence of QX-314 was normalized to buffer control. (**C**) Voltage-dependence of activation of $Na_V1.4$ at absence (black) and presence of 5 mM external QX-314 (blue). External QX-314 shifted activation to more depolarizing potentials (V50: control, –26.7 ± 0.4 mV, n = 5; QX-314 ECS, –13.6 ± 1.4 mV, n = 5; $p < 0.0001$, unpaired t-test). Data are represented as mean ± SEM.

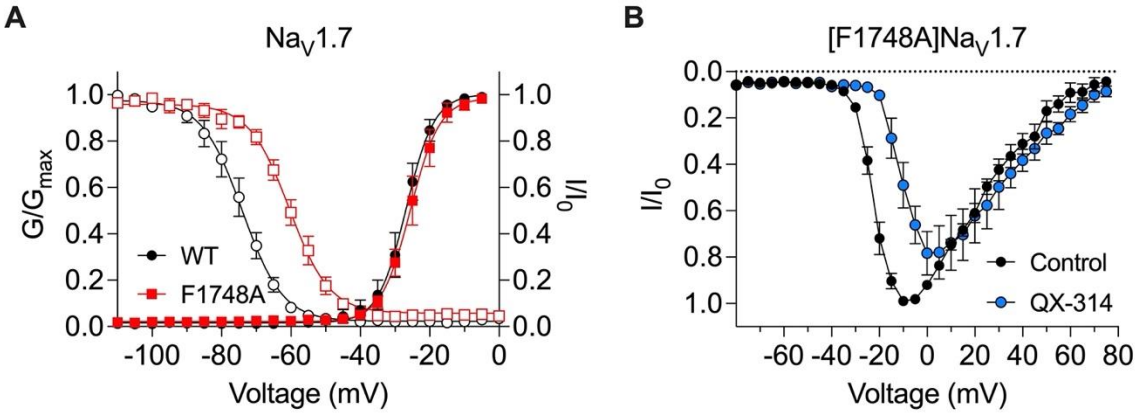

Figure S2. (**A**) Voltage-dependence of activation (filled symbols) and fast inactivation (clear symbols) of HEK293 cells transfected with WT $Na_V1.7$ (black) or [F1748A]$Na_V1.7$ (red). The F1748A mutation did not affect activation (V_{50}: WT, –27.2 ± 1.7 mV, n = 6; F1748A, –25.2 ± 1.7 mV, n = 7) but shifted fast inactivation to more depolarized potentials (V_{50}: WT, –74.3 ± 1.9 mV, n = 6; F1748A, –60.2 ± 1.4 mV, n = 6; $p < 0.01$, unpaired t-test) (**B**) Current-voltage relationship in absence (black, n = 5) and presence of 5 mM QX-314 (blue, n = 4). Current in presence of QX-314 was normalized to buffer control. Data are presented as mean ± SEM.

	V_{50} of voltage-dependence of activation	*V_{50} of voltage-dependence of fast inactivation*
WT $Na_V1.7$	–27.2 ± 1.7 mV	–74.3 ± 1.9 mV
[F1748A]$Na_V1.7$	–25.2 ± 1.7 mV	–60.2 ± 1.4 mV*

Table S1: V_{50} values of voltage-dependent activation and fast inactivation in WT $Na_V1.7$ and [F1748A]$Na_V1.7$. Data reported as mean ± SEM. * indicates statistically significant shifts tested with unpaired t-test.