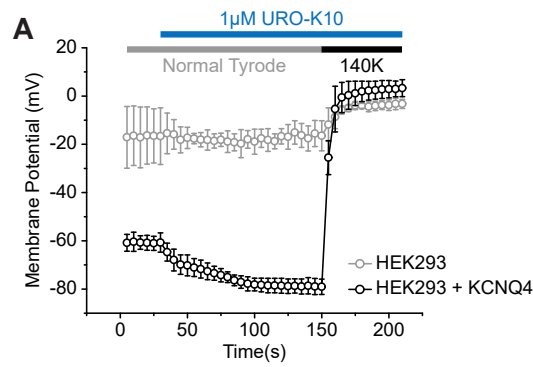
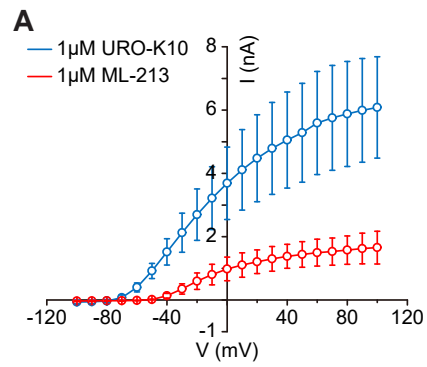


**Supplementary Fig. 1. Electrophysiologic characteristics of overexpressed Kv7.4 and Kv7.5 channels in the presence of XE991.** Current-voltage (I-V) relationships of 1  $\mu\text{M}$  URO-K10 induced Kv channels (*blue*) and 1  $\mu\text{M}$  URO-K10 induced Kv channels with 10  $\mu\text{M}$  XE-991 (*gray*) are shown. Note that the blue I-V curves are identical to the curves in Fig. 2. (A) Corresponding I-V curve is plotted with steady-state currents measured from -100 mV to +100 mV at 10 mV step intervals. At +100 mV, URO-K10 induced Kv7.4-expressing cells showed  $2.48 \pm 1.38$  nA ( $n = 6$ ) whole-cell current in the presence of 10  $\mu\text{M}$  XE-991. (B) I-V curve of Kv7.5 expressing cells is shown. At +100 mV, Kv7.5-expressing cells showed  $2.40 \pm 1.38$  nA ( $n = 8$ ) whole-cell current in the presence of 10  $\mu\text{M}$  XE-991.



**Supplementary Fig. 2. Change of membrane potential in response to URO-K10 in HEK293 cells expressing either KCNQ4 channel or an empty vector.** (A) Membrane potential of HEK293 cells expressing either empty vector (HEK293, gray line) or KCNQ4 channels (HEK293 + KCNQ4, black line). Resting membrane potential of normal HEK293 cells under normal Tyrode solution showed  $-17.11 \pm 12.78$  mV ( $n = 3$ ) while expression of KCNQ4 channel shifted the resting membrane potential to  $-60.83 \pm 3.51$  mV ( $n = 3$ ). The administration of  $1 \mu\text{M}$  URO-K10 over normal Tyrode solution (NT +  $1 \mu\text{M}$  URO-K10) showed no significant effect onto normal HEK293 cells but induced further hyperpolarization in KCNQ4-expressing HEK293 cells ( $-79.04 \pm 2.19$  mV,  $n = 3$ ). Exchanging the bath solution from normal Tyrode to high-K solution with  $1 \mu\text{M}$  URO-K10 ( $140 \text{ K} + 1 \mu\text{M}$  URO-K10) shifted the membrane potential of KCNQ4-expressing HEK293 cells towards 0 mV, suggesting that the given membrane potential is highly dependent on potassium ion concentration gradient, hence potassium permeability.



**Supplementary Fig. 3. Electrophysiologic characteristics of overexpressed Kv7.4 channels in the presence of ML-213.** (A) Application of 1  $\mu$ M ML-213 did not activate currents of Kv7.4 channels as much as 1  $\mu$ M URO-K10. Corresponding I-V curves are shown for 1  $\mu$ M URO-K10 induced Kv7.4 channels (*blue*), and 1  $\mu$ M ML-213 induced Kv7.4 channels (*red*). At +100 mV, Kv7.4 channel showed  $1.66 \pm 0.52$  nA ( $n = 6$ ) whole-cell current in the presence of 1  $\mu$ M ML-213. Note that the blue I-V curves are identical to the curves in Fig. 2.