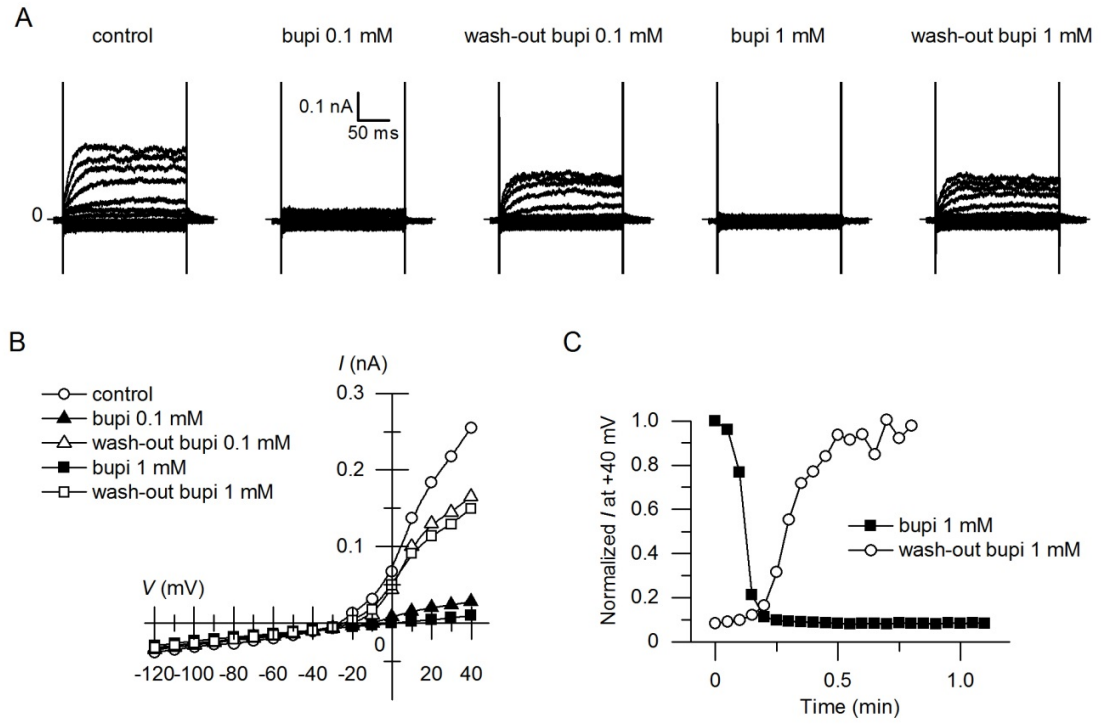
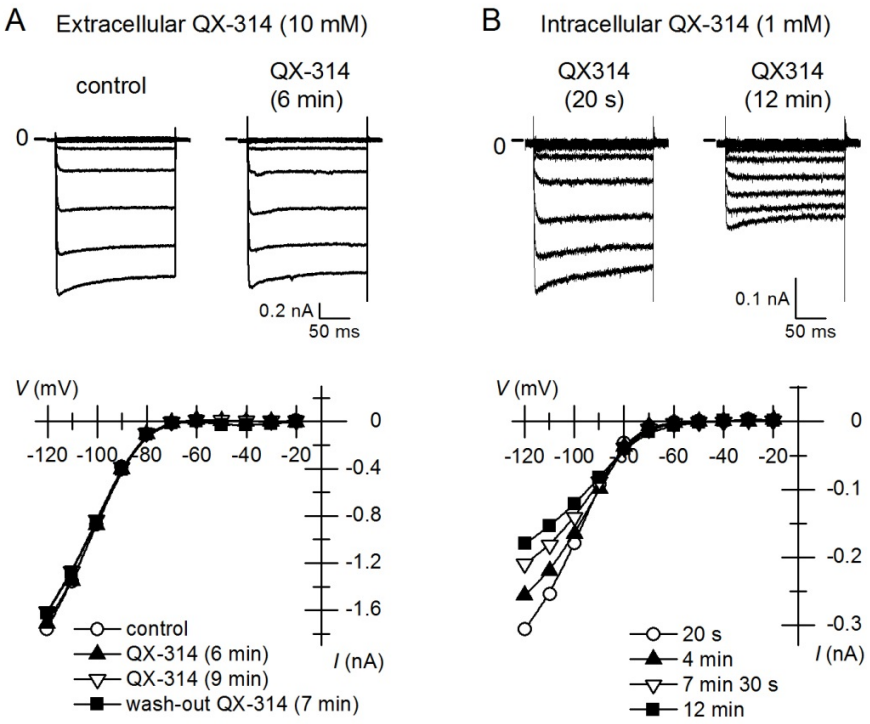
Supplementary Fig. 1



Effects of bupivacaine on endogenous currents of HEK 293 cells.

(A) Currents sequentially obtained before, during, and after the application 0.1 and 1 mM bupivacaine. Families of currents were obtained using voltage steps ranging from −120 to +40 mV in 10-mV increments from a holding potential of −40 mV. (B) *I-V* relationships obtained from currents shown in A. (C) Time courses of changes in outward currents at +40 mV observed upon application (■) and removal (○) of 1 mM bupivacaine. Current amplitudes are normalized to the value at the time of application of bupivacaine.

Supplementary Fig. 2



Effects of QX-314, a membrane impermeable derivative of lidocaine added to extracellular (A) and intracellular (B) solutions on Kir2 channels. (A) Kir2.2 currents and their *I-V* relationships obtained before and after applying 10 mM QX-314 to the extracellular (bath) solution. *I-V* relationships obtained ~9 min after application of QX-314, and ~7 min after washout of QX-314, are also presented to show the stability of currents during the experiment. (B) Kir2.1 currents and their *I-V* relationships obtained using the intracellular (pipette) solution containing 1 mM QX-314. Times after rupturing the patch membrane are indicated. Note that the currents may be already inhibited at 20 s. Shown in A and B are results representative of five and four different experiments, respectively.

Supplementary Table 1

Inhibition of mouse Kir2.1 channels by lidocaine and bupivacaine extracellularly applied during the whole-cell recordings

	Mouse Kir2.1		Human Kir2.1	
1 mM lidocaine	0.78 ± 0.11	(*n*=3)	0.70 ± 0.08	(*n*=7)
10 mM lidocaine	0.22	(*n*=2)	0.08 ±0.02	(*n*=6)
1 mM bupivacaine	0.88 ± 0.09	(*n*=3)	0.92 ± 0.07	(*n*=7)

Data are I/I_0 values obtained at -110 mV. The data for 1 mM bupivacaine were obtained at ~5 min after its application. For comparison, the data for human Kir2.1 (Fig. 5) are also presented.