Molecular Pharmacology

Supplemental Data

Pore polarity and charge determine differential block of Kir1.1 and Kir7.1 potassium channels by the small-molecule inhibitor VU590

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Figure S1

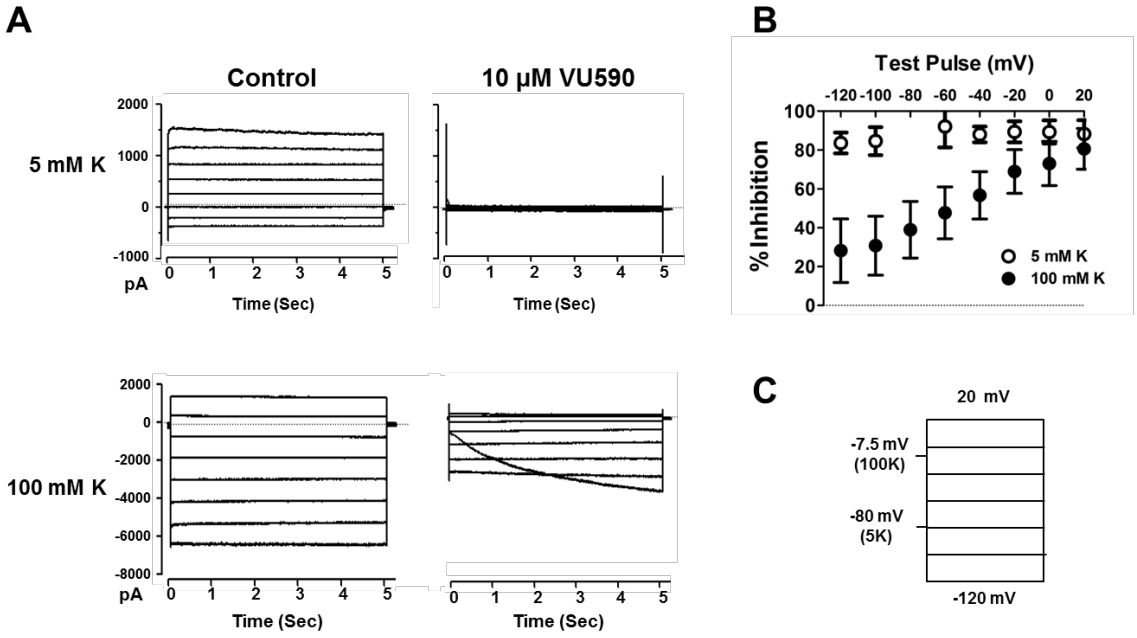

Figure S1. Voltage- and K^+-dependence of Kir1.1 block by VU590. A) Representative whole-cell Kir1.1 currents evoked from holding potential of -80 mV (5 mM bath K) or -7.5 mV (100 mM bath) to -120 mV to 120 mV in 20-mV increments. Currents were measured before control) or after bath addition of 10 µM VU590. B) Mean ± SD percent Kir1.1 inhibition calculated at each test potential in the presence of 5 mM or 100 mM bath K^+ (n=4 each). C) Voltage clamp protocol used to evoke currents. Step duration was 5 sec.

Figure S2

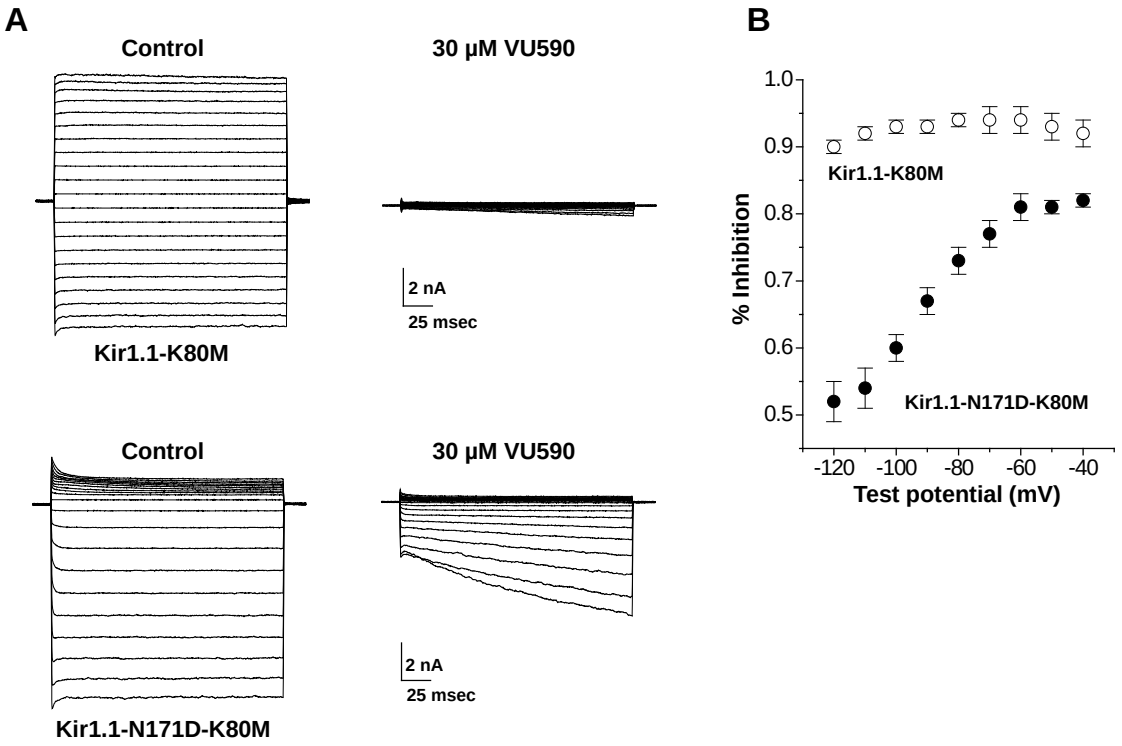

Figure S2. The N171D mutation increases the voltage- and K-dependence of Kir1.1-K80M block by VU590. A) Whole-cell Kir1.1-K80M (top) or Kir1.1-K80M-N171D (bottom) current traces evoked by voltage steps between -120 mV and 80 mV in 10 mV increments from a holding potential of -25 mV. Currents were recorded in the presence of 50 mM bath K^+ before (control) or after bath addition of 30 μM VU590. C) Mean ± SEM fraction of Kir1.1-K80M (open circles) or Kir1.1-K80M-N171D (closed circles) current blocked at the indicated test potentials (n=5 each).

Figure S3

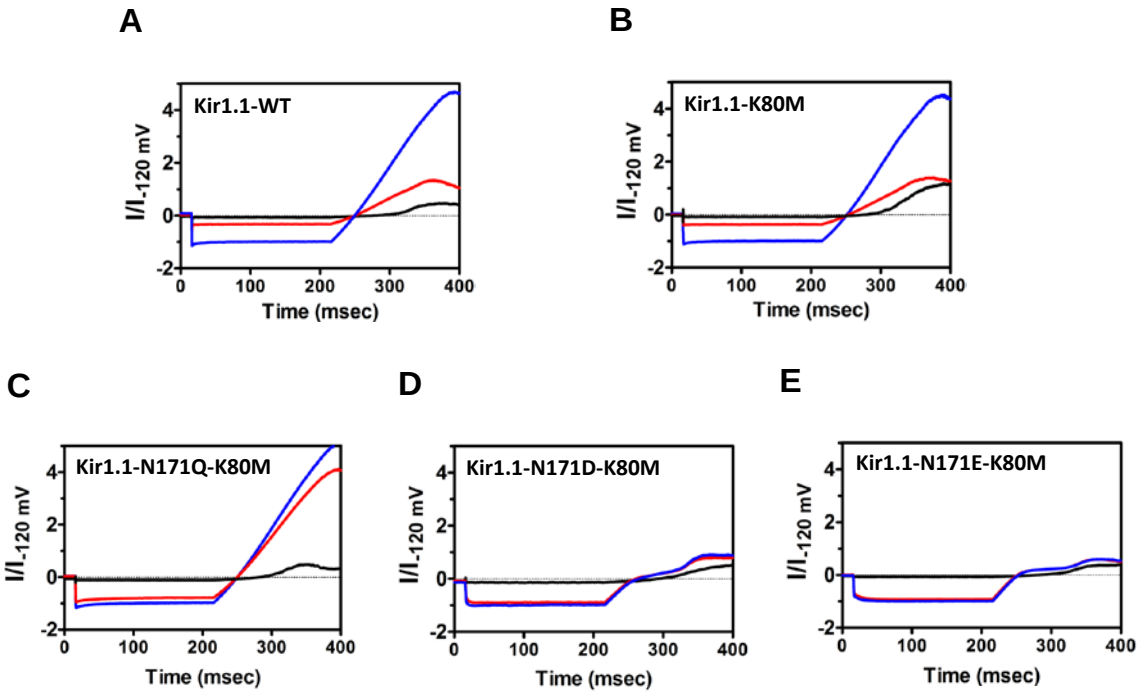

Figure S3. Representative whole-cell Kir1.1 current traces. A) Kir1.1-WT, B) Kir1.1-K80M, C) Kir1.1-N171Q-K80M, D) Kir1.1-N171D-K80M, and E) Kir1.1-N171E-K80M. Currents were evoked from a holding potential of -75 mV by stepping to -120 mV for 200 msec and then ramping to 120 mV (see Methods), in the absence (blue) or presence (red) of 300 nM VU590 and 2 mM barium chloride (black).

Figure S4

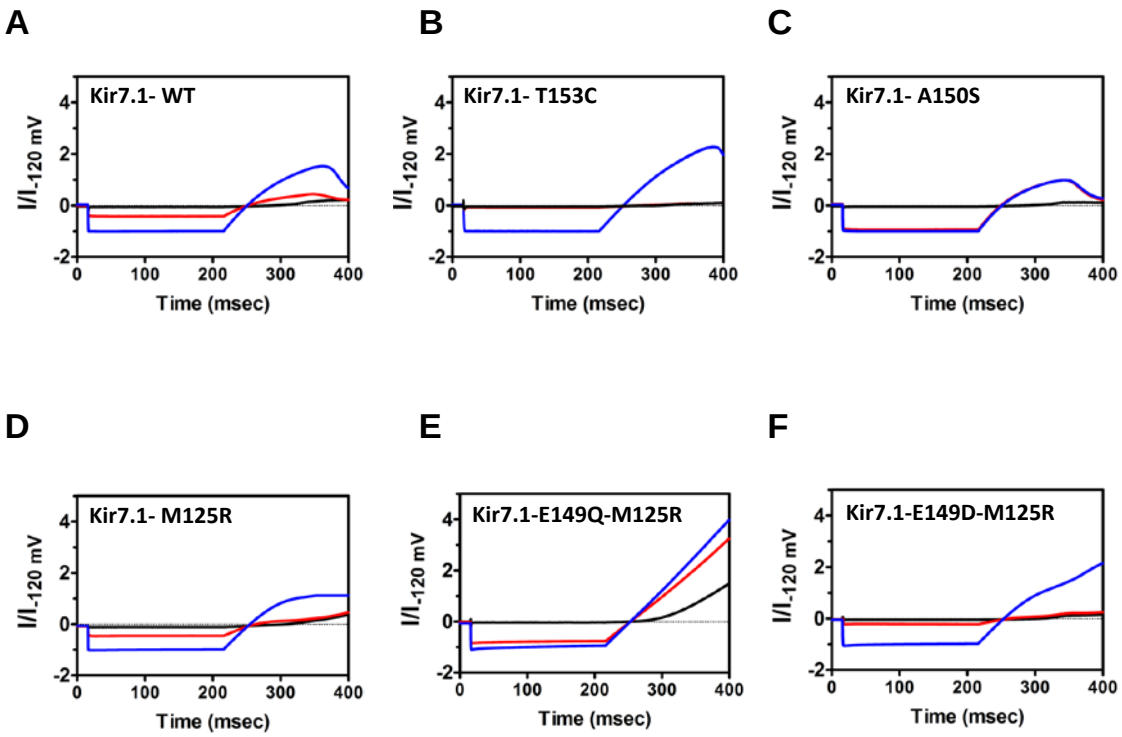

Figure S4. Representative whole-cell Kir7.1 current traces. A) Kir7.1-WT, B) Kir7.1-T153C, C) Kir7.1-A150S, D) Kir7.1-M125R, E) Kir7.1-E149Q-M125R, and F) Kir7.1-E149D-M125R. Currents were evoked from a holding potential of -75 mV by stepping to -120 mV for 200 msec and then ramping to 120 mV (see Methods), in the absence (blue) or presence (red) of 10 µM VU590 and 2 mM barium chloride (black).