



Supplemental figure 1. Additional results from model simulations. **A)** Simulated currents are shown for 4-sec voltage steps to -20 and +20 mV for control (gray traces) and 30 μ M Rosc (black traces). Note the smaller Rosc-induced inhibition at -20 mV. **B)** Simulated currents measured at the end of the 4 sec step ranging from -60 to +40 mV (20 mV increments) are plotted vs. the step voltage. Relative currents (normalized to 0 mV in control) are shown for control (upward triangles) and 30 μ M Rosc (solid circle). **C)** Inactivated channels are relatively less sensitive to Rosc block. Simulated current was

elicited by an 8-sec step to +60 mV and tail currents were elicited at -40 mV. 30 μ M Rosc was applied during the +60 mV step and was continued into the tail (*). Rosc decreased current during the step by 33% (cf. $14 \pm 7\%$ for HERG current), but strongly blocked the tail current (55% compared with $29\% \pm 7\%$ for HERG current). **D)** Peak simulated tail currents were measured at voltages ranging from 20 to -100 mV (20 mV increments) following a 1 sec step to 60 mV (Tail I-V), and are plotted vs. tail voltage for control (upward triangle) and 30 μ M Rosc (solid circle). **E)** Percent inhibition by 30 μ M Rosc was calculated from simulated tail currents in panel D and plotted vs. tail voltage. **F)** Rosc decreases inactivation kinetics primarily at intermediate voltages. The recovery from inactivation τ (circles) was measured (single exponential equation) from the raising phase of simulated tail currents upon hyperpolarization from +60 mV to the indicated voltage (x-axis). The development of inactivation τ (squares) was measured from a triple pulse protocol where voltage was stepped to +60 (500 ms), -100 (5 ms) and the indicated voltage (x-axis) for 250 ms. A single exponential equation was used to fit inactivation during the third voltage step. Data are shown for control and during the application of 30 μ M Rosc (open and closed symbols, respectively).