Supplemental Material

Figure S1. Most inwardly rectifying potassium channels display low halothane sensitivity.

Kir2.1, 2.2, 2.3, 2.4, 3.2, 3.4(S143T), 4.1 and 7.1 were expressed in oocytes and inwardly rectifying currents were recorded as described in the methods. Effects of 0.5 mM halothane on channel activity were determined for each one and summery data is presented (n=4-6). Kir3.2 is by far the most sensitive, the homomeric active Kir3.4 was also inhibited but to a lesser extent. The G protein-insensitive channels were either slightly activated or inhibited with Kir7.1 being most sensitive to the effect of halothane.

Figure S2. Co-expression of cβARK reverses halothane inhibition in Kir3.1/3.2 expressing oocytes.

- **A.** Two-electrode voltage-clamp recordings from an oocyte expressing Kir3.1/3.2, where halothane inhibits channel activity.
- **B.** Two-electrode voltage-clamp recordings from an oocyte expressing Kir3.2 and the membrane targeted PH-domain of β Adrenergic Receptor Kinase (cβARK), which strongly binds and scavenges Gβγ. Currents were significantly smaller in the presence of cβARK (note different scale from **A**) indicating effectiveness of cβARK and halothane activated the channel similar to findings for Kir3.2 in Figure 2.
- **C.** Summary data showing the effectiveness of cβARK co-expression in reducing Kir3.1/3.2 currents (control n=5, cβARK co-expressed n=5).
- **D.** Summary data comparing effects of halothane on Kir3.2 alone and Kir3.1/3.2 co-expressed with cβARK. Scavenging Gβγ reversed the effects of halothane (control n=5, cβARK co-expressed n=5).

Figure S3. Sample TEVC recordings from an oocyte expressing Kir3.1/3.2(F192M) showing that reversing the order of halothane and ACh application preserved the synergy shown in Figure 7.

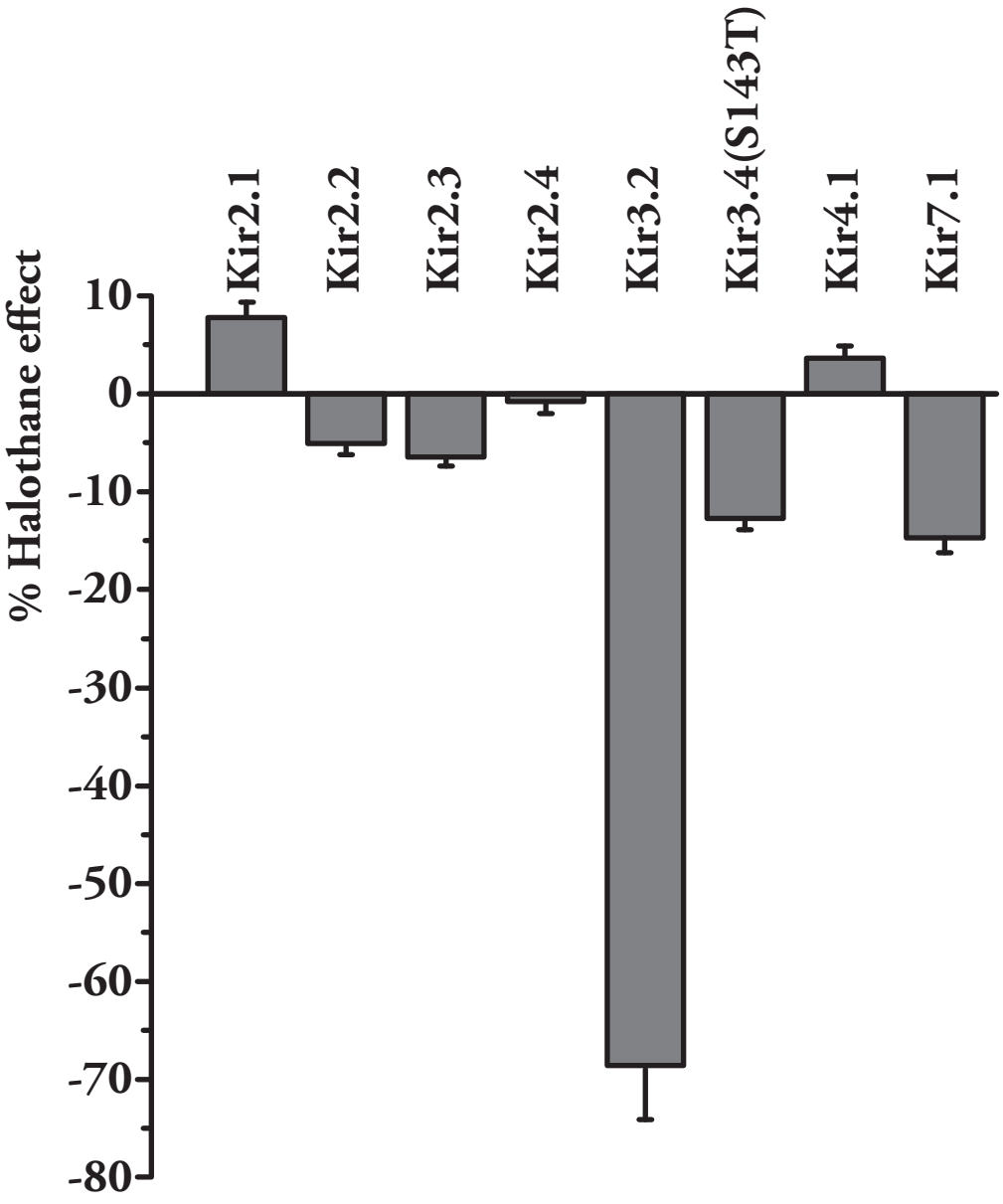
Figure S4. The constitutively active mutant Kir3.2(S177T) is activated by halothane.

Sample TEVC recording from an oocytes expressing Kir3.2(S177T) and its response to halothane. Bar graph on the right shows average data from 8 similar recordings

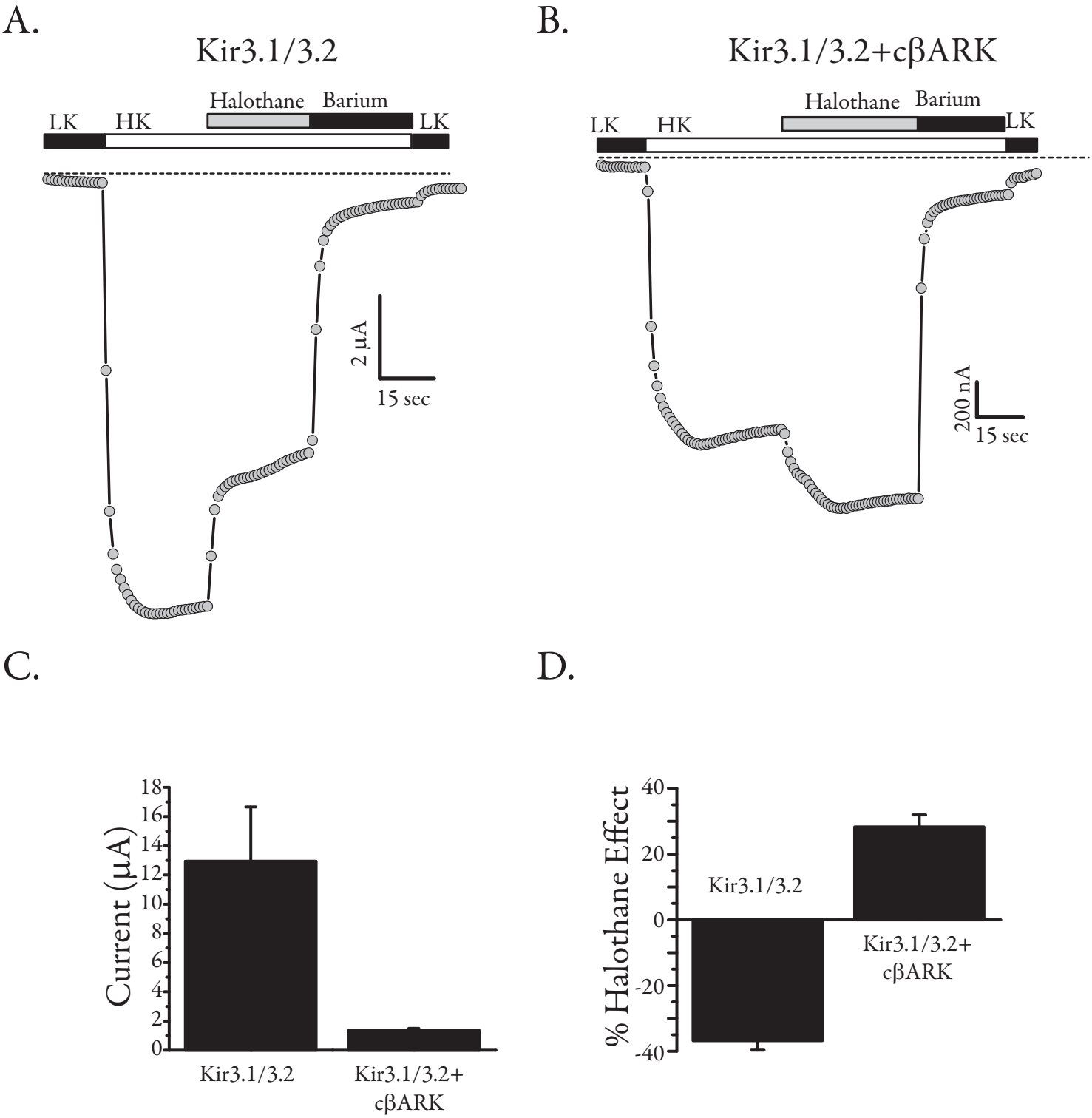
Figure S5. Enflurane and halothane similarly modulate Kir3.1/3.2 activity.

Recordings from oocytes expressing **A**. Kir3.1/3.2(F192M) **B.** Kir3.1/3.2(F192Y) and **C**. Kir3.1/3.2(F192L). The mutants responded similarly to halothane and enflurane. Similar effects were observed for isoflurane (data not shown).

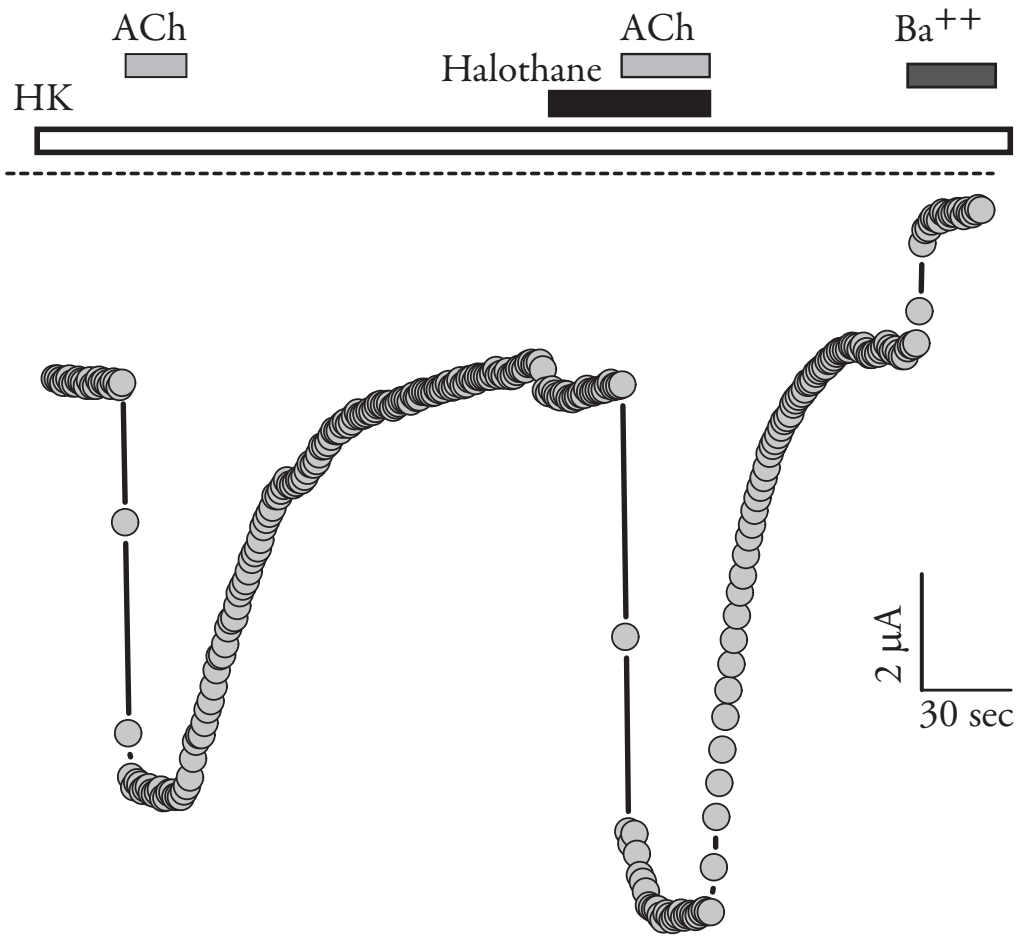
Styer et al., Figure S1



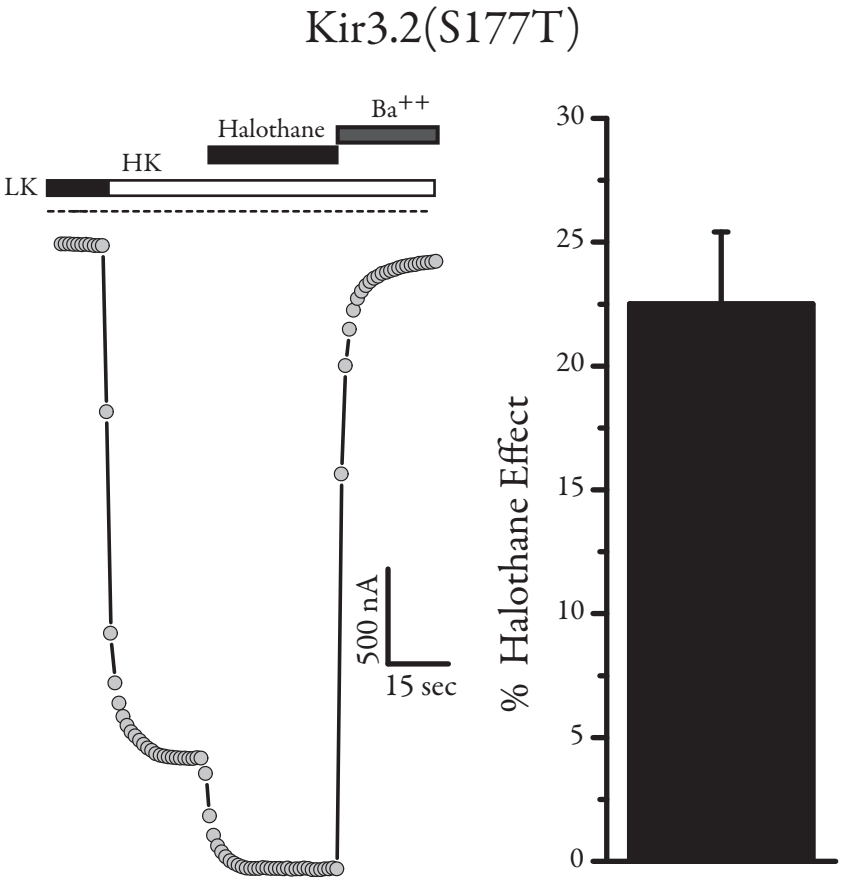
Styer et al., Figure S2



Styer et al., Figure S3



Styer et al., Figure S4



Styer et al., Figure S5