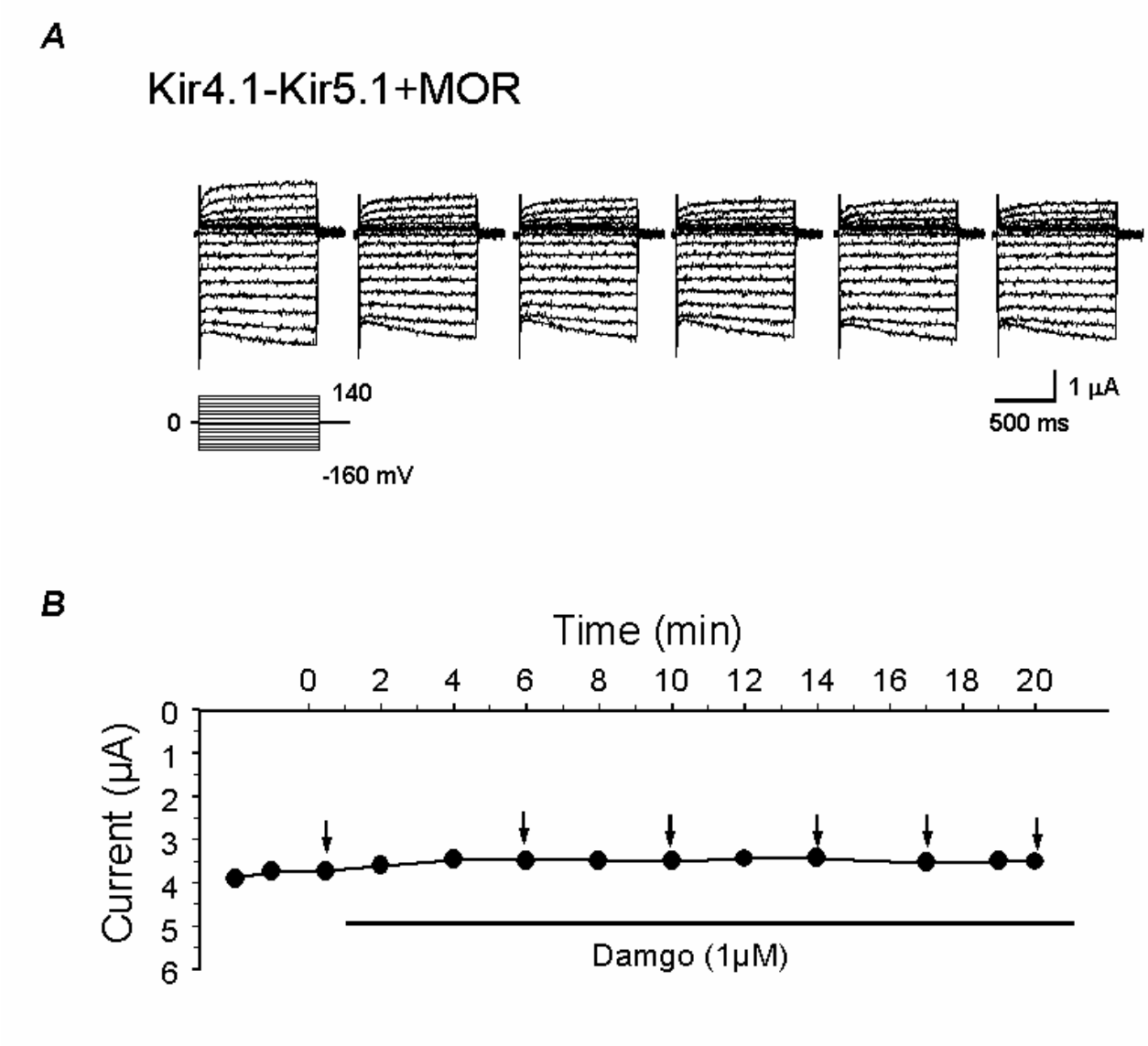
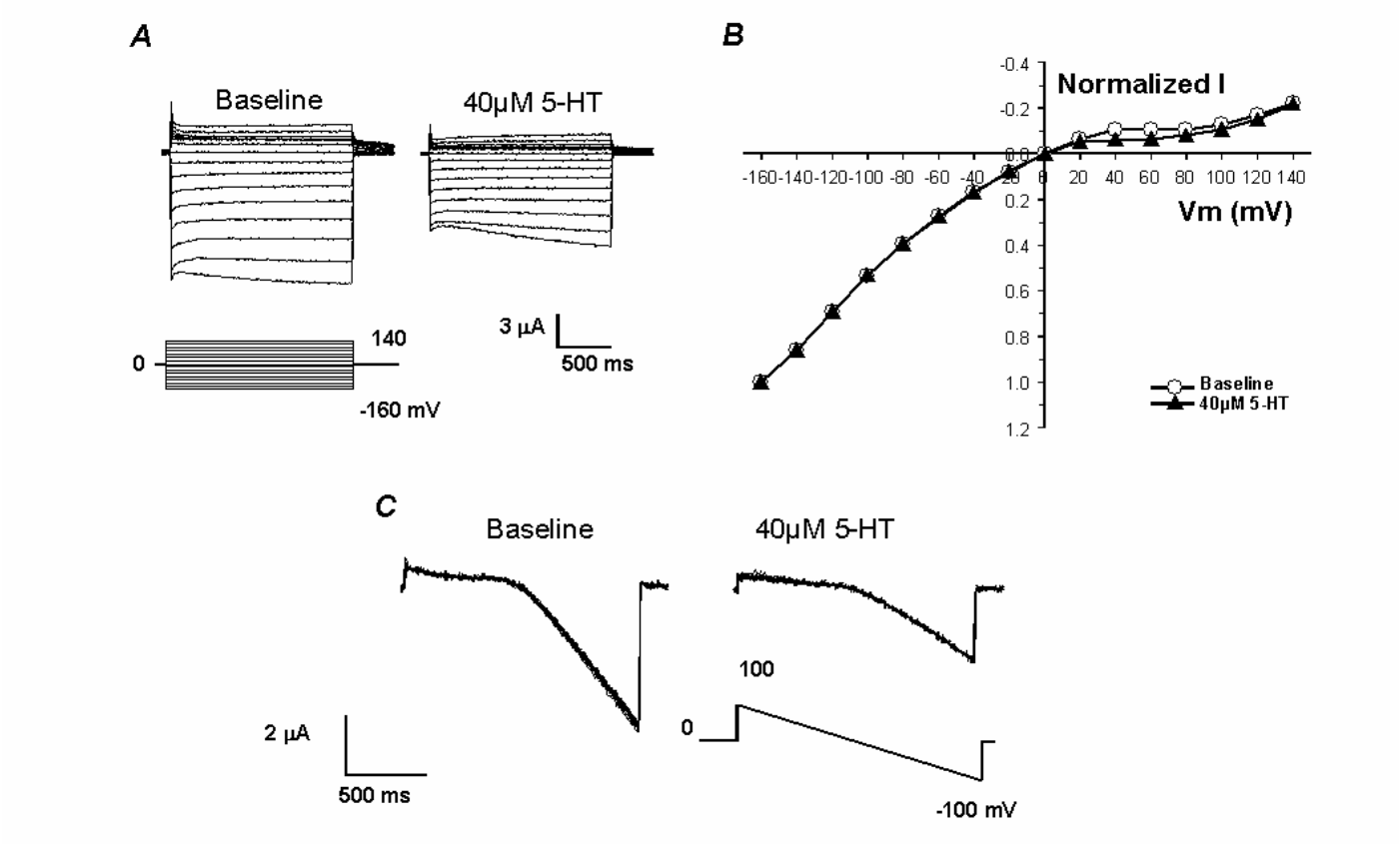
Online-Figure 1. ***A***. Using TEVC whole-cell Kir4.1-Kir5.1 currents were recorded from an oocyte 3 days post-injection of the Kir4.1-Kir5.1 dimer cDNA along with the mu-opioid receptor (MOR) cDNA. With 90 mM K^+ in the extracellular solution inward rectifying currents were recorded at baseline. Membrane potential (V_m) was held at 0 mV. A series of command pulse potentials from –160 mV to 140 mV with a 20-mV increment was applied to the cell. Exposure to 1 μM DAMGO failed to affect the channel currents, suggesting that the Kir4.1-Kir5.1 channel is modulated by $G_{\alpha q}$ receptors and not G_s receptors. ***B***. The time profile shows that the current amplitude did not change when DAMGO was present in the bath solution.

Online-Figure 2. ***A***. Whole-cell currents were recorded from an oocyte 3 days post-injection of the Kir4.1-Kir5.1 tandem-dimer cDNA along with the 5-HT2A receptor cDNA using TEVC. Currents were recorded in the presence of high K^+ (90 mM). Exposure to 40 μM 5-HT (serotonin) inhibited the currents by 35%. ***B***. When baseline and affected currents were scaled to the same magnitude at -160 mV, the I/V relationship of the currents recorded in these two conditions were superimposed, suggesting that the effects are voltage-independent. ***C*.** TEVC recording from an oocyte using a ramp protocol, clearly shows inhibition of the inward currents by 5-HT.

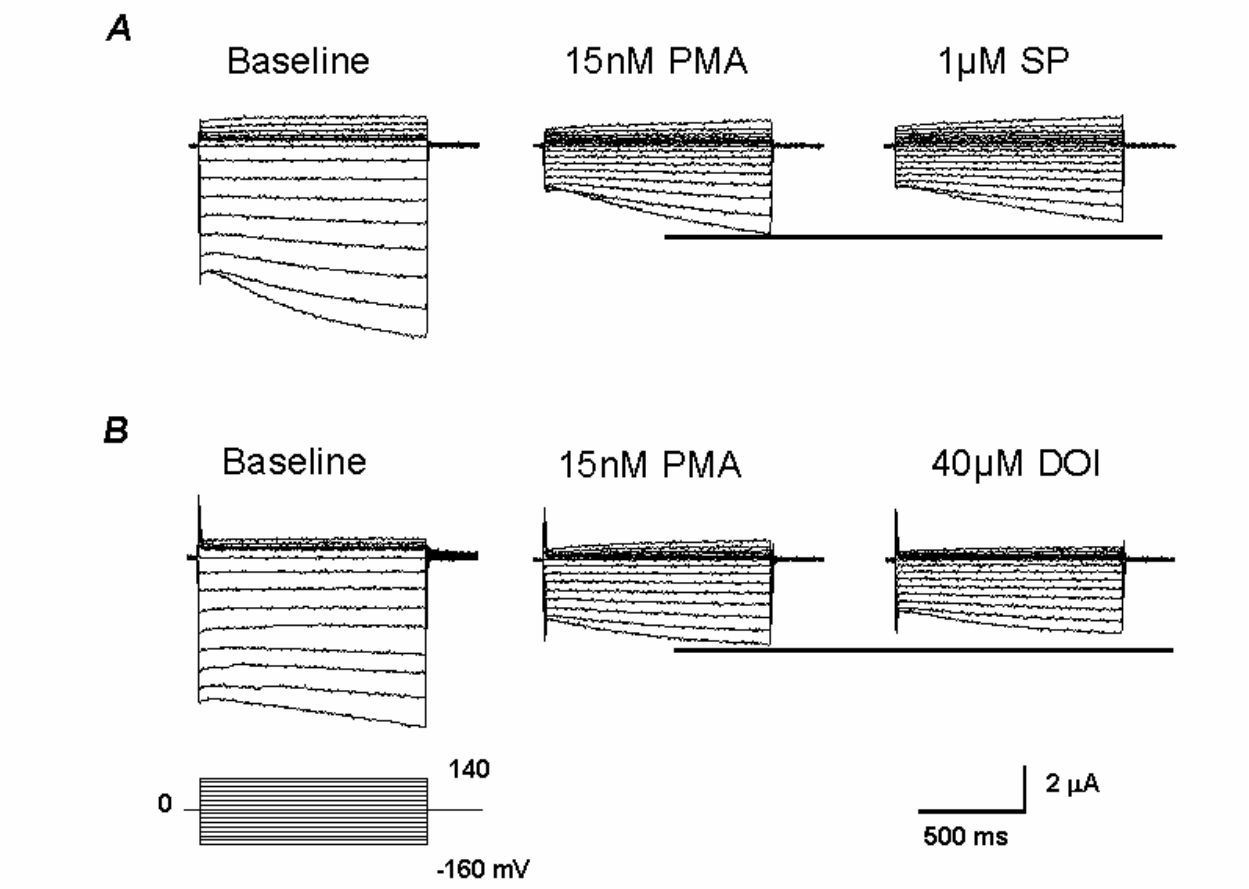
Online-Figure 3. ***A, B***. Currents were recorded from an oocyte in the same condition as in Figure 4A. Following exposure to 15 nM PMA the cells were subsequently treated with 1 μM SP or 40 μM DOI. Prior exposure to PMA resulted in a much lower channel response to the neurotransmitters. Instead of 36% current inhibition for SP and 43% current inhibition for DOI, the Kir4.1-Kir5.1 currents were barely inhibited (>10%).


A
Kir4.1-Kir5.1+MOR
140
0
-160 mV
1 µA
500 ms
B
Time (min)
0 2 4 6 8 10 12 14 16 18 20
Current (µA)
0 1 2 3 4 5 6
Damgo (1µM)

Online Fig. 1


A
Baseline
40µM 5-HT
140
0
-160 mV
3 µA
500 ms
B
Normalized I
-0.4
-0.2
0.2
0.4
0.6
0.8
1.0
1.2
-160 -140 -120 -100 -80 -60 -40 20 40 60 80 100 120 140
Vm (mV)
Baseline
40µM 5-HT
C
Baseline
40µM 5-HT
100
0
2 µA
500 ms
-100 mV

Online Fig. 2


A
Baseline
15nM PMA
1μM SP
B
Baseline
15nM PMA
40μM DOI
140
0
-160 mV
2 μA
500 ms

Online Fig. 3