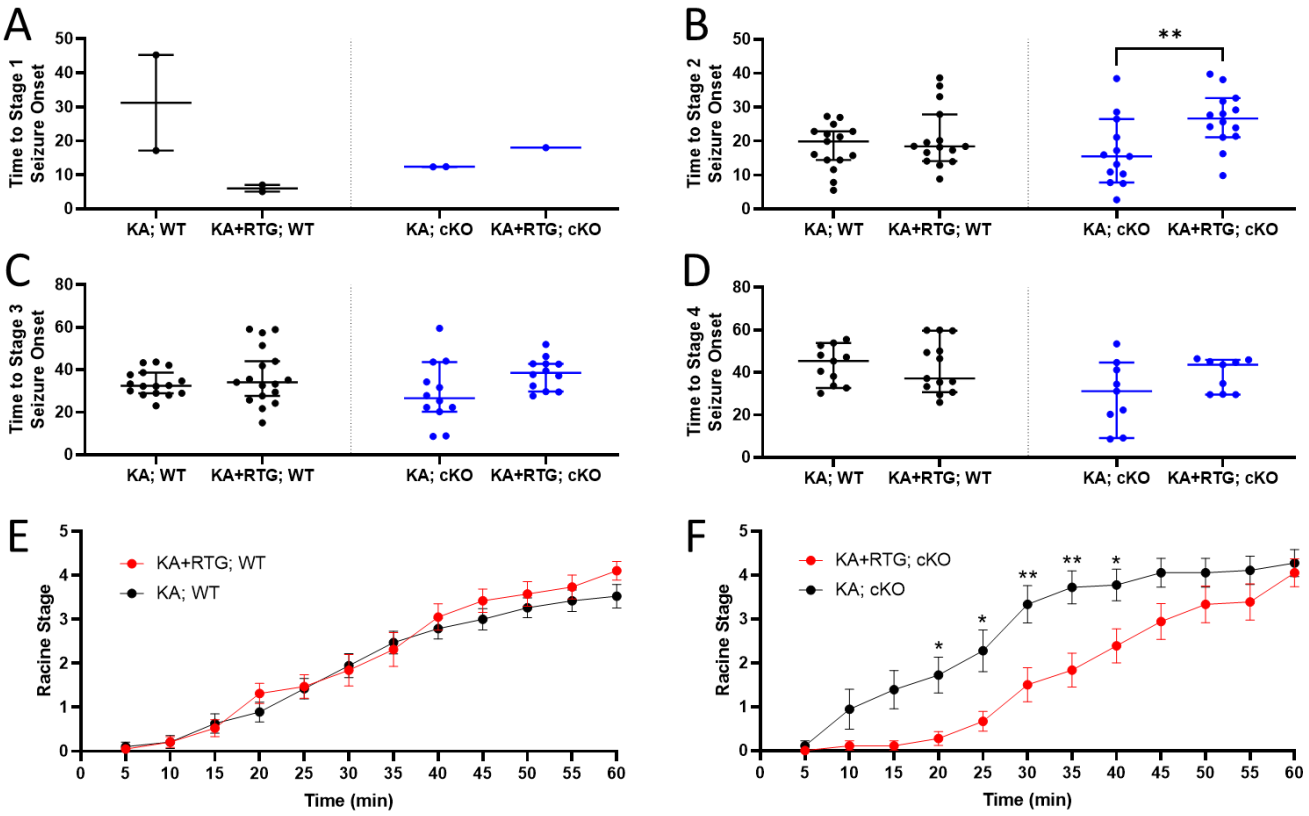

Figure S1. Progression through Racine Scale Stages with Kainic Acid administration in WT vs cKO. (A-D) Comparison between KA with and without RTG across Racine Stage 1-4. cKO but not WT mice had an increased latency to Stage 2 onset after RTG administration (**p<0.01, Kruskal-Wallis test with Dunn's post-hoc testing); (E) No difference in Racine Stage at any time point between RTG and saline; (F) Significantly reduced Racine Stage between 20-40 minutes after KA administration in cKO mice pre-treated with RTG (*p<0.05, **p<0.01, 2-way ANOVA with post-hoc Holm-Sidak tests).

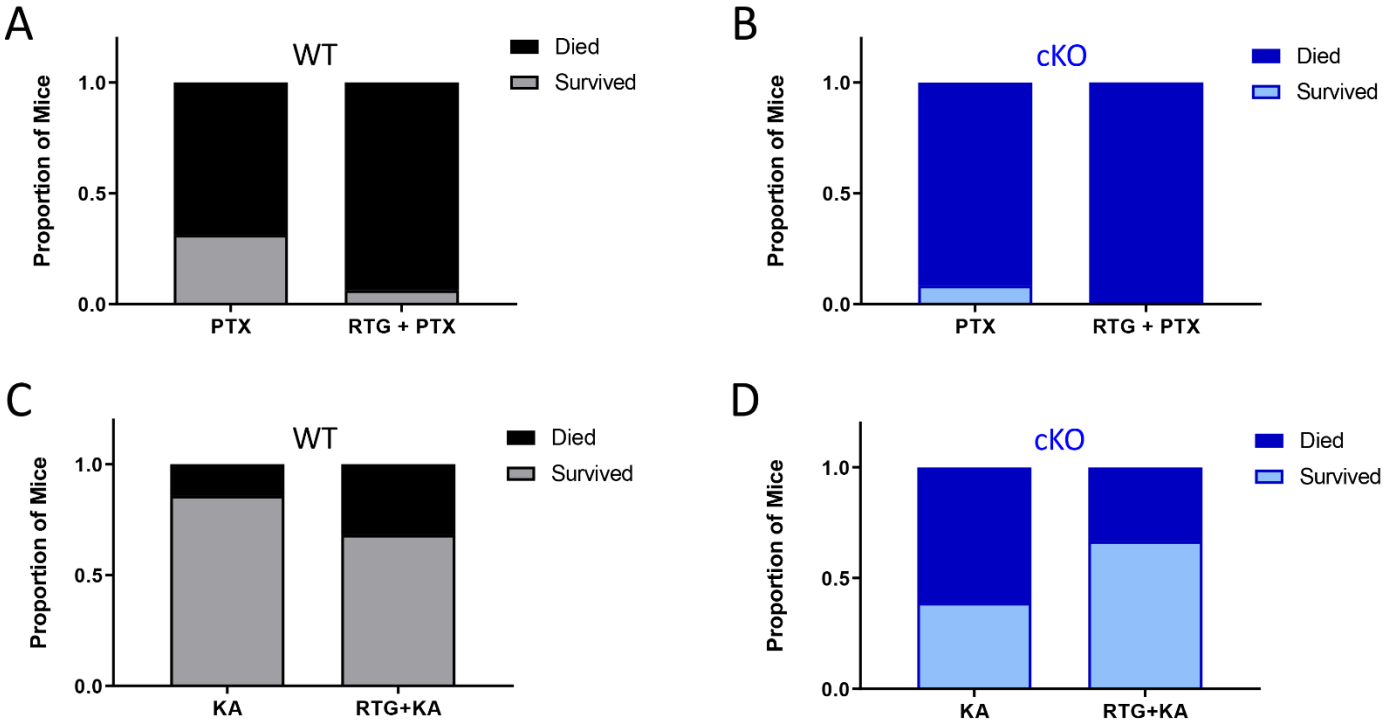

Figure S2. No change in seizure-induced mortality with RTG for cKO mice. Mortality following PTX-induced seizures was not significantly altered with RTG treatment in either (A) WT (n=16, 16) or (B) cKO (n=12, 14) mice. Mortality following KA-induced seizures was not significantly altered with RTG treatment in either (C) WT (n=21, 22) or (D) cKO (n=18, 18) mice (Chi-square test, $p>0.05$).

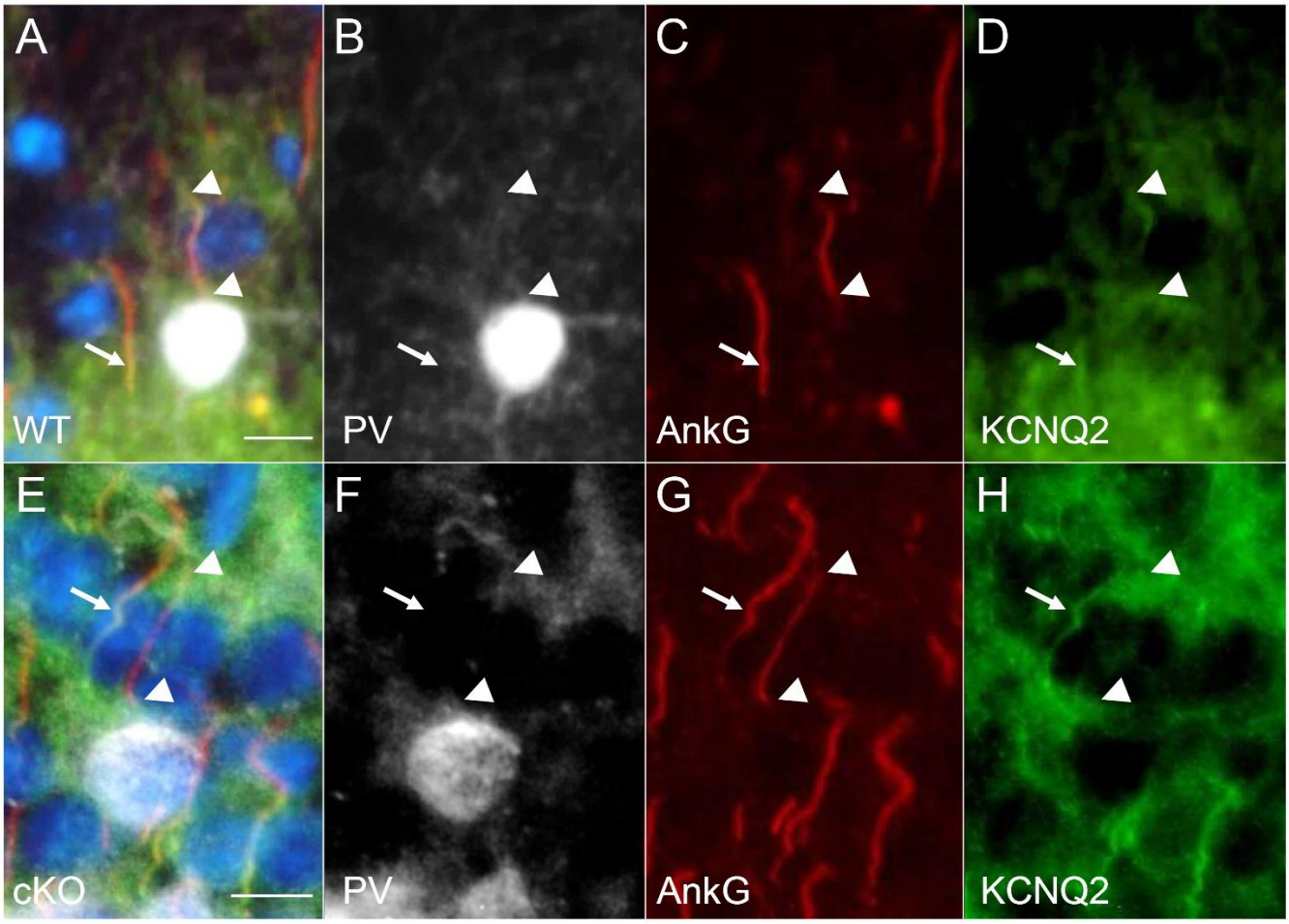

Figure S3. Selective deletion of KCNQ2 from cortical PV-IN in cKO mice. (A-D) In WT mice, KCNQ2 (green) was co-expressed with anti-AnkG (red) at the distal axon initial segment (AIS) of PV-IN (TdTomato – pseudocolored in white), seen here in Layer 2 of the neocortex (arrowheads) as well as non-PV-IN (arrow). (E-H) In cKO mice, KCNQ2 was no longer co-expressed with AnkG in PV-INs (arrowheads) but remained evident in the AIS of non-PV-INs (arrow); bar=10 μm.

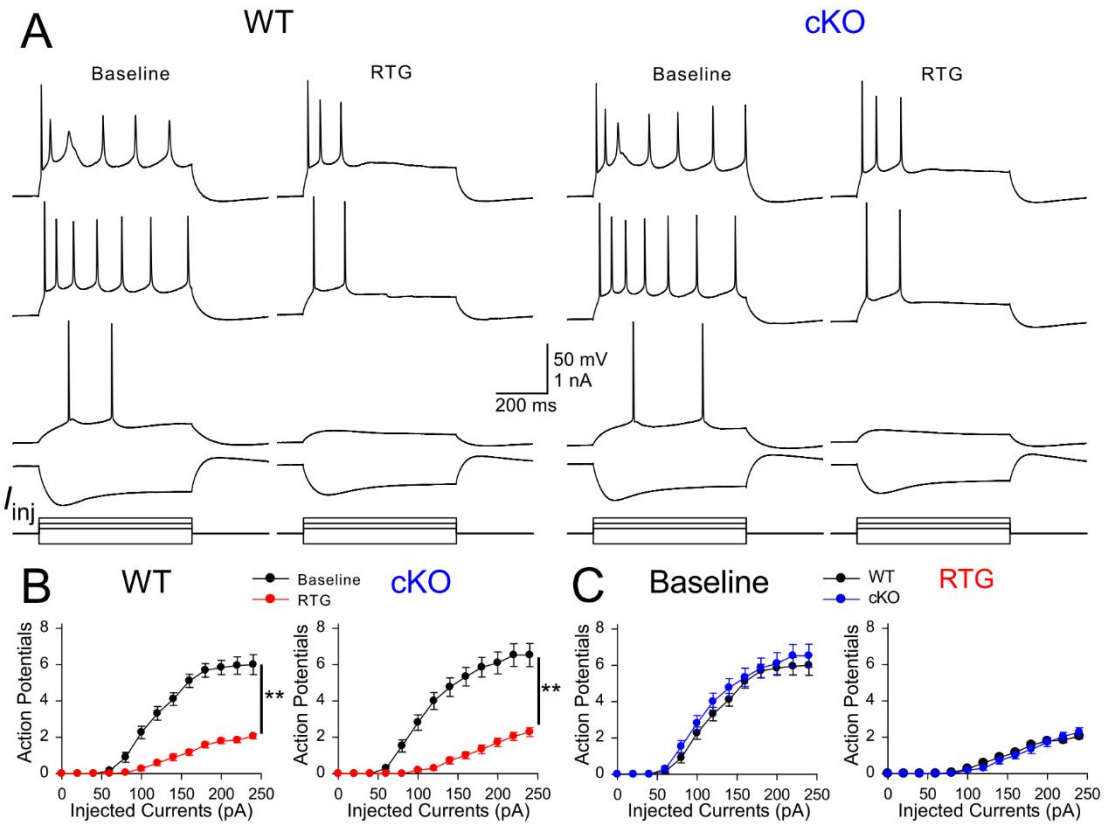

Figure S4. Effects of RTG on the excitability of hippocampal CA1-PCs *in vitro*. (A) Representative membrane voltage responses to different current steps in CA1-PCs from WT (left) and cKO (right) before and after 10 μM RTG treatment. (B) RTG was effective in suppressing APs in WT PCs (left, n=19, $^{**}p<0.01$ with two-way ANOVA) and in cKO PCs (right, n=21, $^{**}p<0.01$ with two-way ANOVA). (C) *Kcnq2* conditional knock-out from PV-INs did not significantly change AP-I curve of CA1-PCs at baseline (left). RTG induced a similar degree of suppression on the excitability of CA1-PCs from WT and cKO mice (right).

Table: Active and Passive Membrane Properties of CA1 PV-INs and CA1-PCs in WT and cKO.

Cell Type	WT PV-INs		cKO PV-INs		CA1-PC in WT		cKO CA1-PC in cKO	
Treatment	Baseline	RTG	Baseline	RTG	Baseline	RTG	Baseline	RTG
Rheobase (pA)	135.79 ± 19.68	216.84 ± 24.00 **	134.44 ± 16.31	177.78 ± 17.10 **	90.53 ± 4.15	133.68 ± 7.18 **	88.57 ± 5.08	152.38 ± 8.34 **
Input Resistance (MΩ)	159.36 ± 19.90	119.25 ± 14.35 **	162.54 ± 14.97	121.35 ± 10.48 **	144.85 ± 5.73	114.95 ± 5.02 **	143.80 ± 6.71	108.74 ± 5.56 **
RMP (mV)	-60.36 ± 1.04	-66.11 ± 1.07 **	-60.21 ± 0.89	-63.22 ± 0.96 **	-70.34 ± 0.74	-69.15 ± 0.56	-69.44 ± 0.70	-69.31 ± 0.76
AP Threshold (mV)	-36.69 ± 0.86	-37.80 ± 0.96	-35.93 ± 0.80	-35.86 ± 0.99	-37.01 ± 1.73	-36.34 ± 1.93	-39.56 ± 1.83	-38.89 ± 1.81
AP Amplitude (mV)	66.62 ± 1.45	69.70 ± 1.50 **	66.16 ± 1.14	65.66 ± 1.15	88.12 ± 2.43	85.43 ± 2.81 **	90.75 ± 1.80	88.65 ± 1.71 **
AHP (mV)	24.06 ± 0.83	21.83 ± 0.87 **	24.24 ± 0.60	22.08 ± 0.67 **	10.05 ± 1.66	10.09 ± 1.60	10.01 ± 1.21	9.94 ± 1.23
AP Half width (ms)	0.61 ± 0.02	0.57 ± 0.02 **	0.58 ± 0.02	0.56 ± 0.02	2.07 ± 0.04	1.99 ± 0.04 **	2.00 ± 0.05	1.93 ± 0.04 **

AHP: afterhyperpolarization, AP: action potential, RMP: resting membrane potential. ** $p<0.01$ RTG vs Baseline with Two-way Repeated Measures ANOVA. Genotype X Treatment interaction on rheobase of PV-INs: F=4.30, $p<0.05$; interaction on RMP of PV-INs: F=4.3, $p<0.05$; interaction on AP amplitude of PV-INs: F=5.2, $p<0.05$; interaction on AP half width of PV-INs: F=4.7, $p<0.05$; interaction on rheobase of CA1-PCs, F=4.5, $p<0.05$.