Supplementary Materials

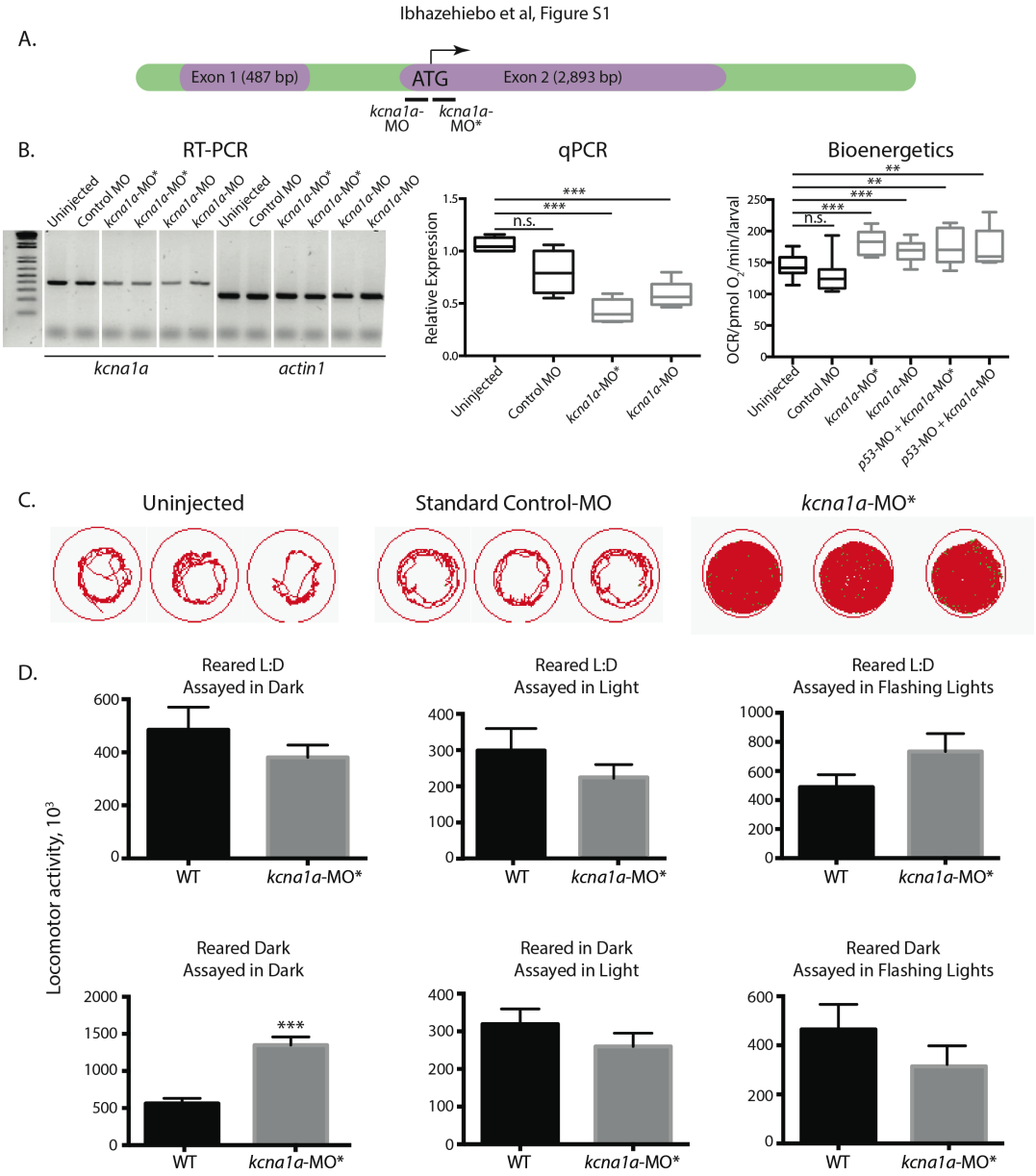

Fig. S1. ***Kcna1*-MO zebrafish display hyperexcitable phenotypes.** (A) Cartoon representation of the *kcna1a* gene, with the location of the two ATG-blocking morpholinos depicted. *Kcna1a*-MO* is the MO used throughout this paper. (B) The effects of two, non-overlapping *kcna1a*-MOs on endogenous *kcna1a* transcript levels are shown first by RT-PCR and then quantitatively by qPCR. Additionally, the specificity of these two *kcna1a*-MOs +/- co-injection of p53-MO is tested in the bioenergetic assay on 3 dpf injected larvae. Both *kcna1a*-MOs when co-injected with a p53-MO display the same phenotype as when injected alone, suggesting that the phenotype of the *kcna1a*-MOs are not due to off target effects on apoptosis. (C) Representative scribes showing hyperactivity of larval (5 dpf) *kcna1a*-MO* epileptic fish relative to WT. (C) Representative data showing *kcna1a*-MO* zebrafish exhibit hyperactivity only compared to WT when reared in dark and assayed in dark, compared to other conditions of rearing and assay. Data in (D) is shown as mean ± SEM; ****P* <0.0001 (unpaired t test); n = 24 fish per group.

Ibhazehiebo et al, Figure S2

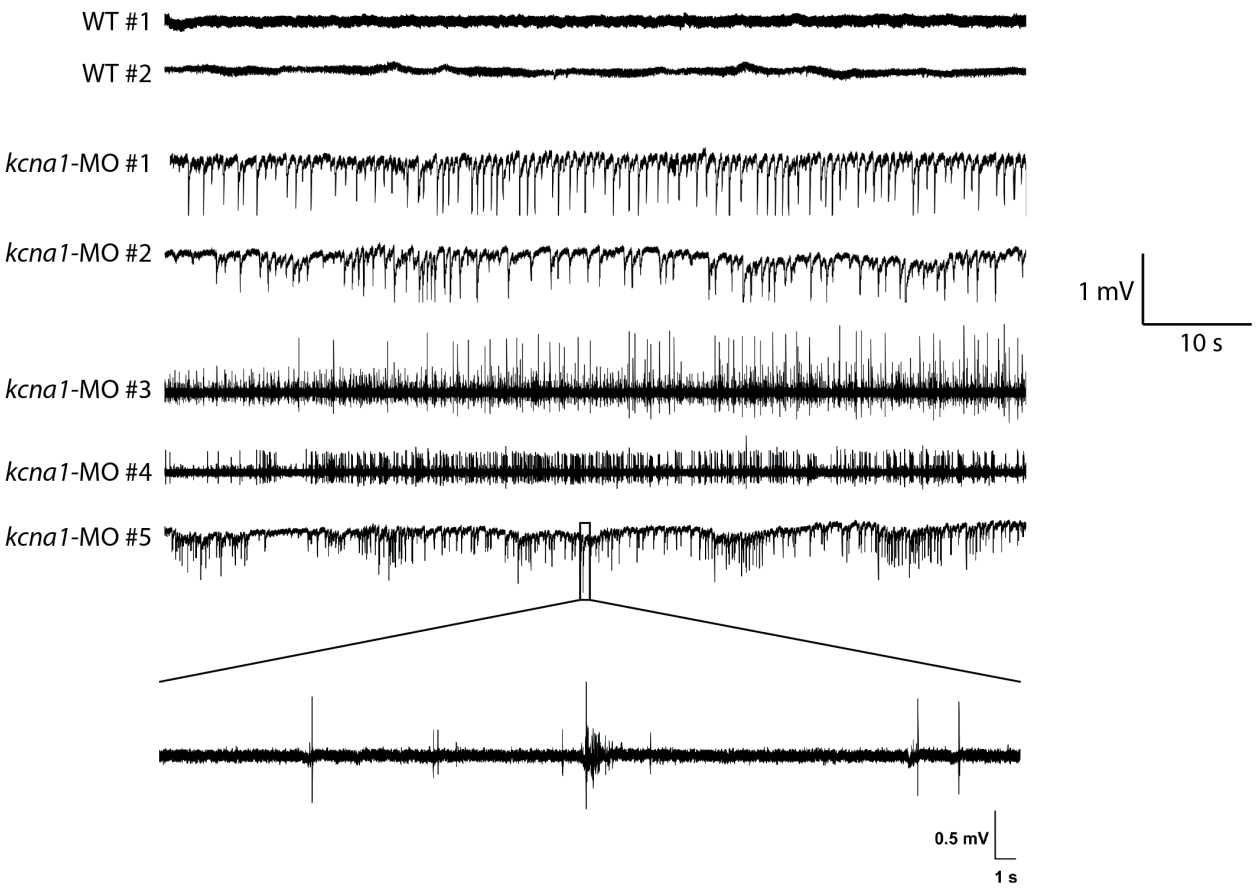

Fig. S2. ***Kcna1*-MO zebrafish display hyperexcitable phenotypes based on EEG.** Representative extracellular field recording obtained from the tectum of 6 dpf zebrafish larvae in current clamp mode. The presence of high frequency, large amplitude spikes indicative of hyperexcitability in *kcna1*-MO animals is shown. Here, we define epileptiform events as upward or downward deflections greater than 2x baseline levels. A zoomed in view shows ictal- (>1000 ms in duration) and inter-ictal (<300 ms duration) like activity, consistent with epileptiform events.

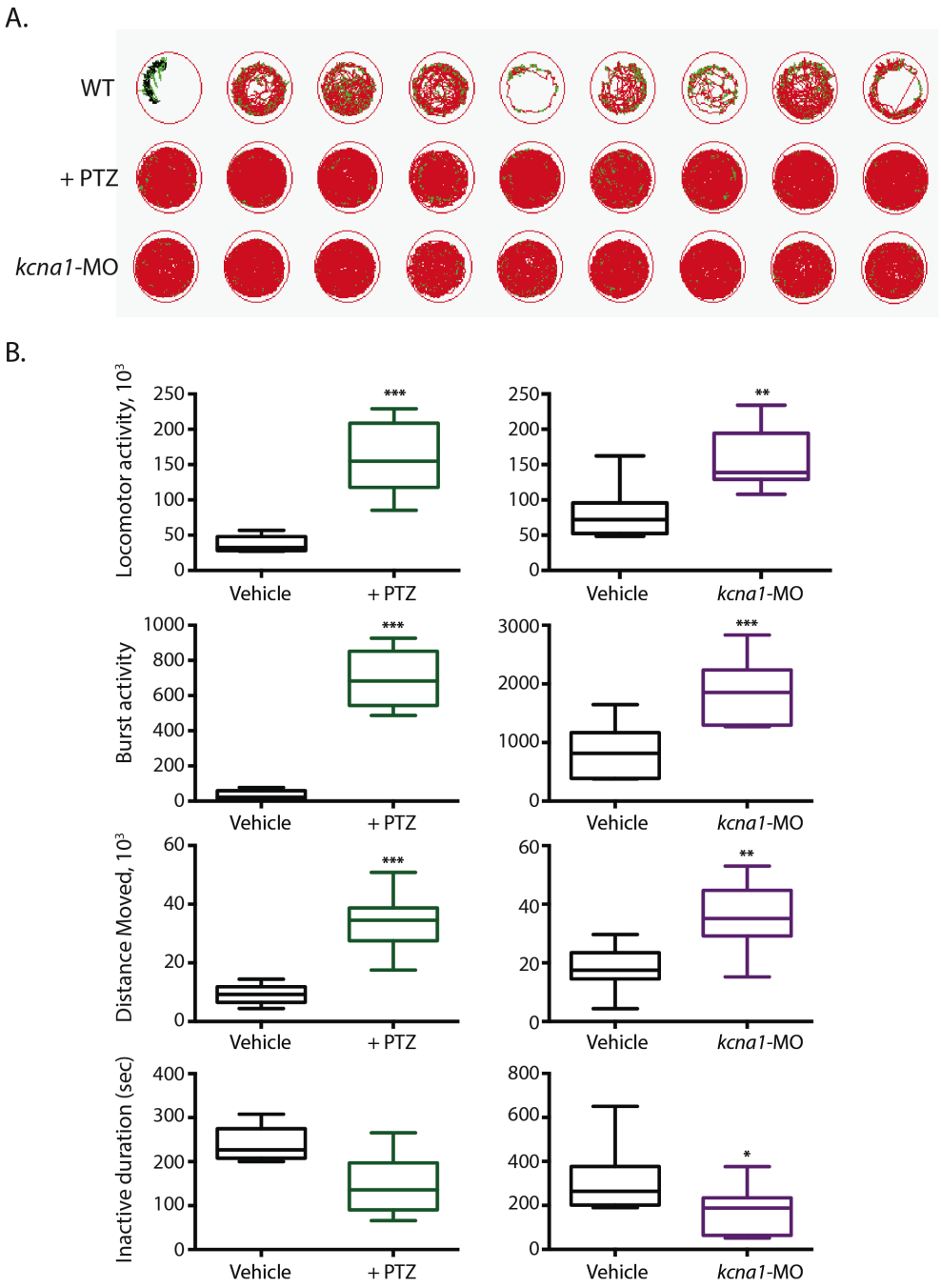

Fig. S3. ***kcna1*-MO zebrafish behavioral analyses.** (A) Representative scribes showing equal levels of hyperexcitability in larval 5pdf *kcna1*-MO and PTZ induction models of epilepsy compared to WT. (B) PTZ-induction and *kcna1*-MO models of epilepsy exhibit comparable behavioral phenotypes. In both models, total locomotor activity, burst activity, distance moved and inactive duration are comparatively similar. Data in (C) is shown as mean ± SEM; **P* <0.05, ***P* <0.001, ****P* <0.0001 (unpaired t test); n = 24 fish per group.

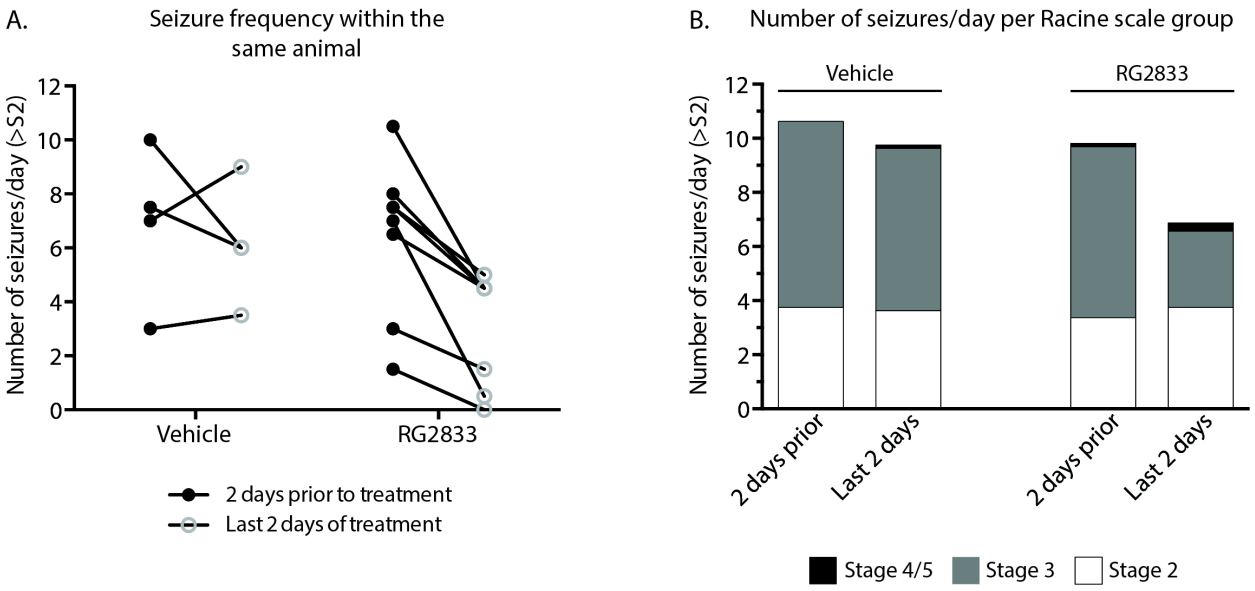

Fig. S4. **Inhibition of HDAC 1, 3 decreases seizures in *Kcna1*-null mice.** (A) Seizure frequency is decreased within the same animal from baseline levels (2 days prior to treatment) to the last 2 days of treatment in RG2833-treated (100 mg/kg/bw/day) animals. No overall change in seizure frequency is observed in vehicle-treated animals. (B) Treatment with RG2833 (100 mg/kg/bw/day) specifically decreased Stage 3 seizures, as per a modified Racine scale scoring (*21*). n = 4-8 animals per group.