

Supplemental figure 1

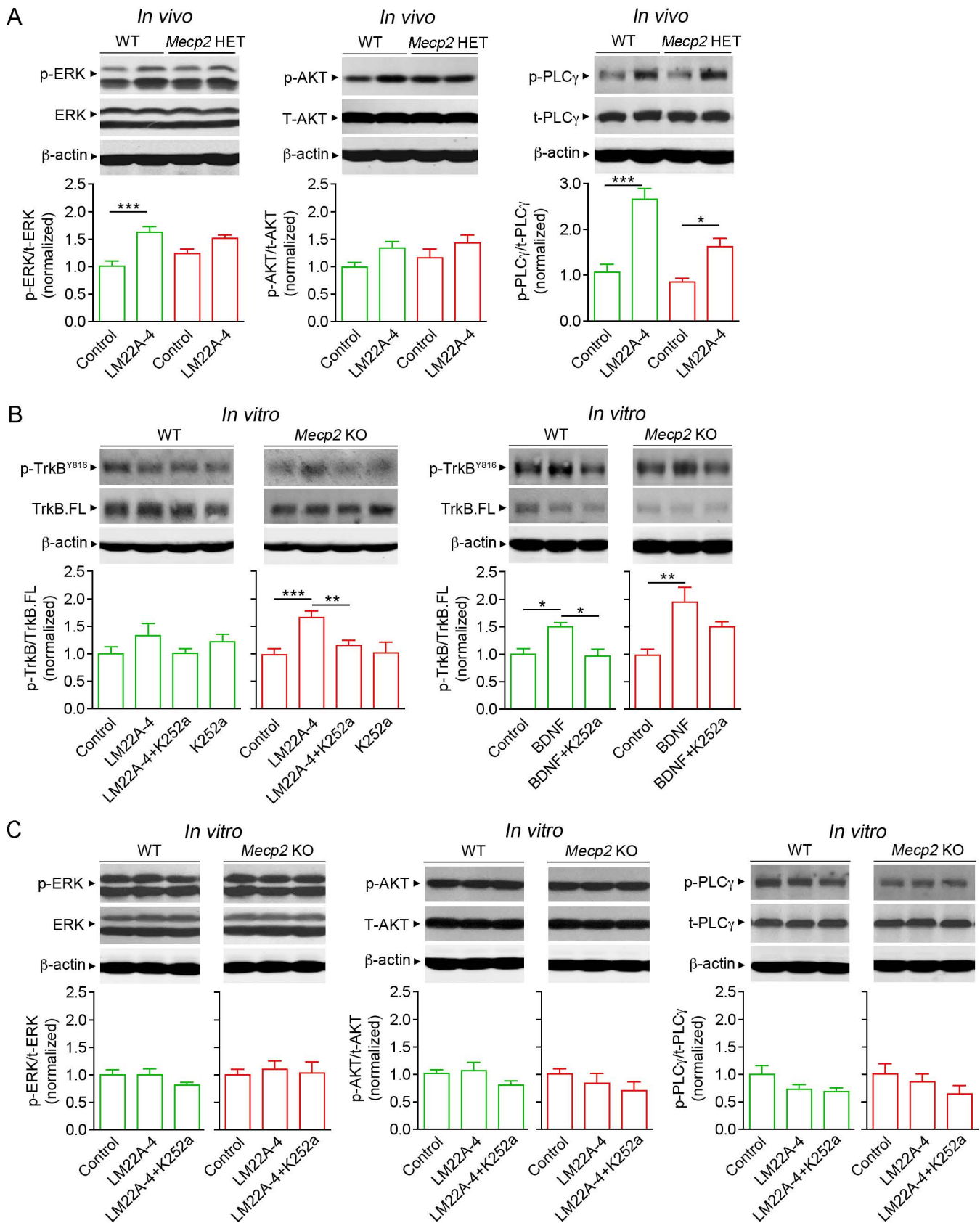


Figure S1. *In vivo* and *in vitro* treatments with LM22A-4 activate TrkB signaling in *Mecp2* HET or KO mice

(A) Quantitative analyses of the levels of phosphorylated ERK/total ERK (*left*), phosphorylated AKT/total AKT (*middle*), and phosphorylated PLC γ /total PLC γ (*right*). Insets show corresponding representative examples of Western immunoblots. Hippocampal homogenates were prepared from female WT or *Mecp2* HET mice treated with vehicle or LM22A-4 for 2 months. (B) Quantitative analyses of the levels of phosphorylated TrkB/TrkB.FL in male WT and *Mecp2* KO mice. Insets show corresponding representative examples of Western immunoblots. Hippocampal homogenates were prepared from acute hippocampal slices treated for 30 min with aCSF, LM22A-4, LM22A-4+K252a, K252a, BDNF, and BDNF+K252a. (C) Quantitative analyses of the levels of phosphorylated ERK/total ERK (*left*), phosphorylated AKT/total AKT (*middle*), and phosphorylated PLC γ /total PLC γ (*right*). Insets show corresponding representative examples of Western immunoblots. Hippocampal homogenates were prepared from acute hippocampal slices treated for 30 min with control aCSF, LM22A-4, LM22A-4+K252a. Data are mean \pm SEM. * P <0.05, ** P <0.01, *** P <0.001.

Supplemental figure 2

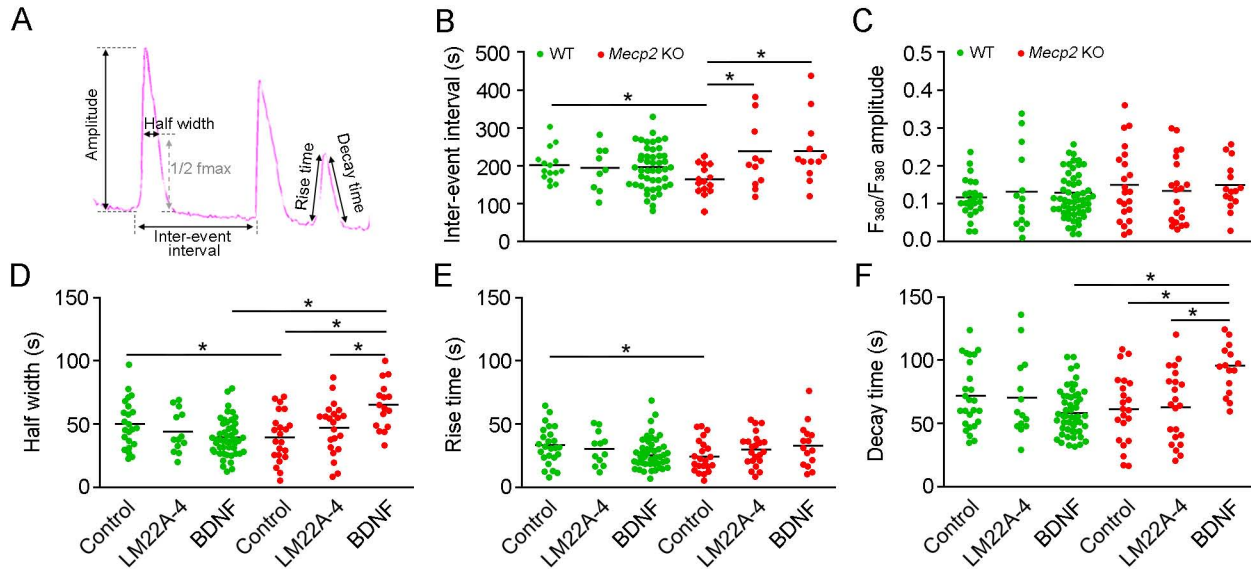


Figure S2. LM22A-4 alters features of SCTs in cultured hippocampal neurons from male *Mecp2* KO mice

(A) Schematic of measurement of SCTs. The inter-event interval (IEI) is the time from the beginning of a SCT to the beginning of the next SCT; SCT amplitude is the difference between the baseline and the peak of the SCT; SCT half width is the time duration at the half maximal SCT amplitude; SCT rise time is the time from the SCT start time to the time of its peak; and SCT decay time is the time from the time of SCT peak to the time of its returning to the baseline. (B-F) Average SCT IEI

LM22A-4 improves hippocampal function in Rett mice

(B), amplitude (C), half width (D), rise time (E), and decay time (F) in WT and *Mecp2* KO neurons treated with aCSF, LM22A-4 (500 nM), and BDNF (250 ng/mL). Data are means. * $P < 0.05$.