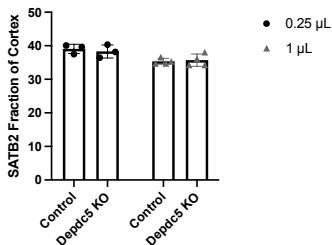
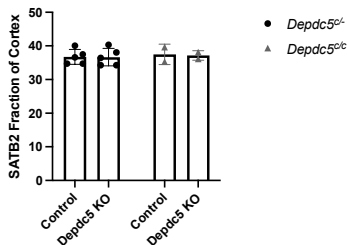


Video 1. Spontaneous seizure in postnatal focal *Depdc5* knockout mouse. Seizure shows focal phenotype with unilateral repetitive jerking on one side of the body and unidirectional rolling/spinning.

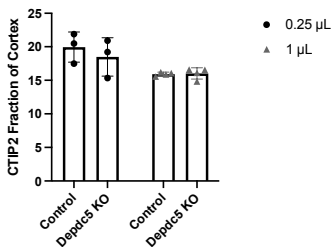
SATB2



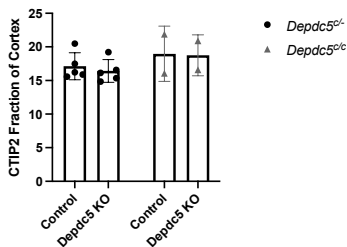
SATB2



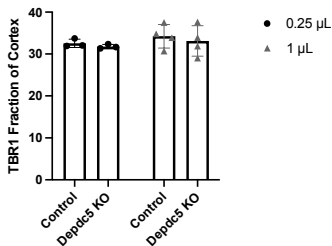
CTIP2



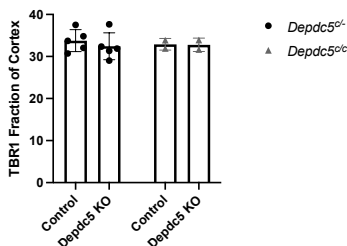
CTIP2



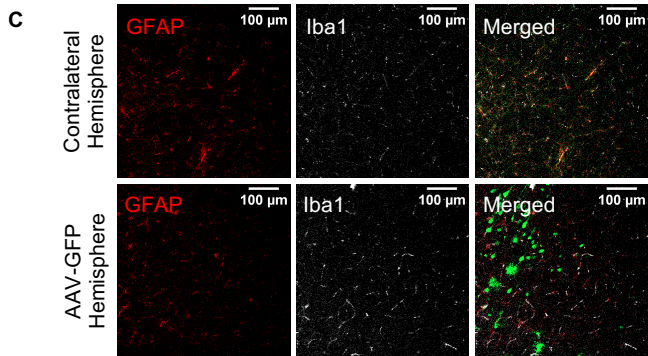
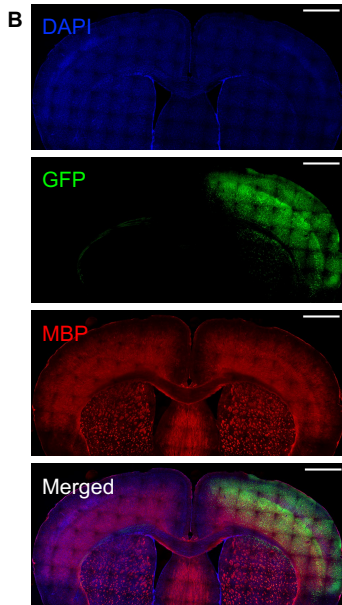
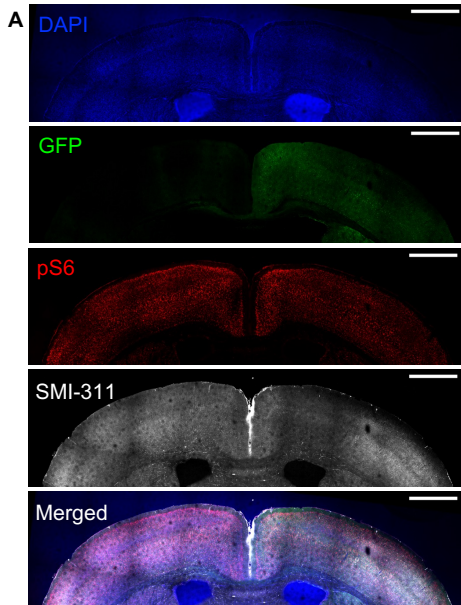
TBR1



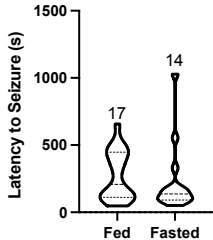
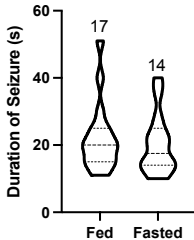
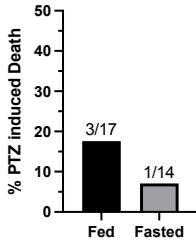
TBR1



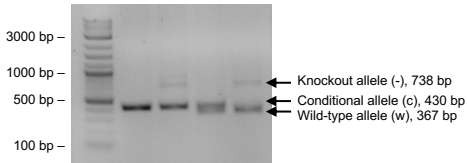
Supplemental Figure 1. Normal cortical architecture is maintained across genotype and injection volumes. Cortical layer thickness measurements at 4 paired sites in at least 3 sections per brain from each cortical layer marker (SATB2, CTIP2, and TBR1) at different injections volumes (0.25 μ L or 1 μ L) and in different genotypes (*Depdc5^{c/c}* or *Depdc5^{c/-}*) (Two-way ANOVA).



Supplemental Figure 2. No mTOR hyperactivation, neuropathological defects, or glial pathology are observed in control AAV-GFP injected mice. (A) Immunohistochemistry shows cortical uptake of AAV-GFP in the injected hemisphere of adult *Depdc5^{c/-}* mice (n=5), but no change in the intensity of pS6 or SMI-311 staining between the two hemispheres, indicating no evidence of mTORC1 hyperactivity (pS6) or dysplastic neurons (SMI-311). DAPI, blue; GFP, green; pS6, red; SMI-311, white; Merged with DAPI, GFP, pS6, and SMI-311. Scale bar: 1000 μ m. (B) Immunohistochemistry shows cortical uptake of AAV-GFP in the injected hemisphere of adult *Depdc5^{c/-}* mice (n=3), but no change in the intensity of MBP staining between the two hemispheres, indicating no evidence of hypomyelination. DAPI, blue; GFP, green; MBP, red; Merged with DAPI, GFP, and MBP. Scale bar: 1000 μ m. (C) Immunohistochemistry shows no difference in reactive astrogliosis (GFAP) or microglial activation (Iba1) between the AAV-GFP injected hemisphere and the contralateral hemisphere of adult *Depdc5^{c/-}* mice (n=3). GFAP, red; Iba1, white; Merged with GFAP, Iba1, and GFP. Scale bar: 1000 μ m.

A**B****C**

Supplemental Figure 3. Fasting has no impact on seizure latency, seizure duration, or seizure-induced death in focal *Depdc5* knockout mice. (A) Seizure latency was not significantly different between fed and fasted focal *Depdc5^{c/c}* knockout mice. (Dashed lines show median, dotted lines show IQR) (Student's t-test) (B) Seizure duration was not significantly different between fed and fasted focal *Depdc5^{c/c}* knockout mice. (Dashed lines show median, dotted lines show IQR) (Student's t-test) (C) Seizure-induced death was not significantly different between fed and fasted focal *Depdc5^{c/c}* knockout mice. (Fisher's exact test)

A***Depdc5* DNA***c/c* *c/-* *c/w* *w/-***B*****Depdc5* DNA***c/c* *c/-* *c/w* *w/-*

Supplemental Figure 4. PCR product confirms the presence of knockout, conditional, and wild-type alleles. (A) PCR product delineates presence of knockout allele (-), conditional allele (c) or wild-type allele (w) in *Depdc5* DNA samples of various genotypes. **(B)** A secondary primer pair provides confirmation of the presence of a knockout allele (-) in *Depdc5*^{c/-} and *Depdc5*^{w/-} mice.