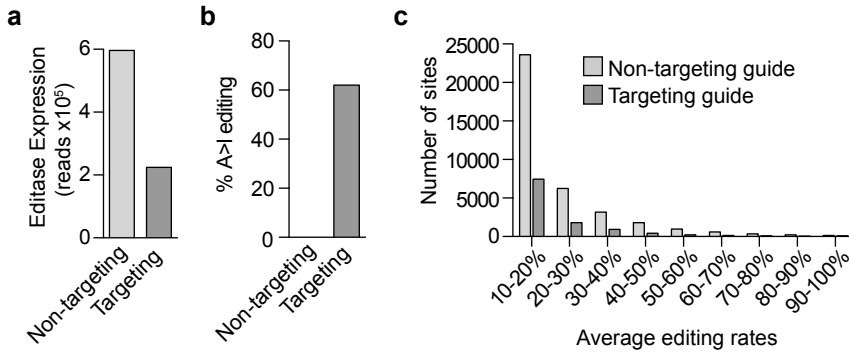


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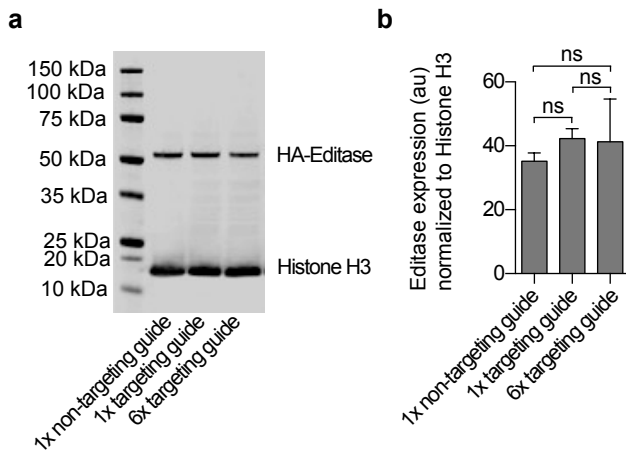
## Supplemental Information

### ***In Vivo* Repair of a Protein Underlying a Neurological Disorder by Programmable RNA Editing**

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Supplementary Figure 1. Whole transcriptomic RNA-seq analysis of the same RNA used in our published study (Sinnamon et al., 2017) of *Mecp2*<sup>317G>A</sup> hippocampal neurons (DIV14), 7 days following transduction with AAV1/2 virus. Related to Figure 3. Promoters, Editase and guide sequences are identical to that shown in Figure 1a in this study. a) The number of RNA-seq reads that aligned to the Editase coding sequence for each viral condition. b) Histogram showing that on-target editing is guide-dependent. One sample each condition. c) Histogram showing the number of off-target editing sites, binned according to the editing rates.



Supplementary Figure 2. The number of copies of the human U6 promoter driving guide expression does not influence Editase protein expression. Related to Figure 3. a), Representative immunoblot of whole cell lysates prepared from Neuro-2A neuroblastoma cells 72 hours after transfection with plasmids containing the Editase cDNA expressed from the human *Synapsin I* promoter and indicated guides. Blots were probed with anti-HA antibody for Editase detection and anti-Histone H3 for loading control. b) Quantification of Editase expression from immunoblots (mean  $\pm$  SD, n = 3 biological replicates), each condition normalized to Histone H3. au, arbitrary units. ns, not significant by One-way ANOVA and Tukey's multiple comparisons test.

Supplementary Table 1. Guide and primer sequences. Related to STAR Methods

**Guide sequences**

mouse *Mecp2*<sup>317G>A</sup> 2xBoxB Targeting guide  
Non-targeting guide

**Sequence, 5'→ 3'**

cagactctctggccctgaaaaagggccttaagcttccgggtccaaccttcaggcaggccctgaaaaagggcctggggtcac  
gaagagcgagctcttctgttttagagctagaaatagcaagtaaaataaggctagtcggttatcaactgaaaaagtggcaccgagtcggtgc

**Amplification of endogenous *Mecp2* cDNA**

mouse *Mecp2*-14 ATG Fwd  
mouse *Mecp2*-3'UTR+92 Rev

aaccggtccggaaaatggcc  
ggaagctttgtcagagccctaccataag

**Sequencing primers for *Mecp2* RT-PCR**

mouse *Mecp2* 554 Rev  
mouse *Mecp2* 914 Rev  
mouse *Mecp2* 1122 Rev  
mouse *Mecp2*-3'UTR+92 Rev

ctcctggaggggctcccttc  
gaccgatggaagactcctca  
actgctgctgcgccctt  
ggaagctttgtcagagccctaccataag

**Cloning primers**

Human U6 NdeI Fwd  
mouse *Mecp2* 2xBoxB Targeting guide Rev

gtgtcatatgcttaccgtaactgaaag  
cacagggcccaaaaagatgacccaggccct

