

Gene	log ₂ FC	StdErr	p-adj	Direction	Biological function
Interferon / immune signaling					
<i>Trim12a</i>	-1.437	0.229	3.70×10 ⁻⁶	↓	Interferon-stimulated gene (ISG), innate immune response
<i>Trim30d</i>	-2.222	0.36	5.01×10 ⁻⁶	↓	ISG, innate immune response
<i>Trim34a</i>	-1.522	0.311	3.69×10 ⁻³	↓	ISG, antiviral response
<i>Trim30a</i>	-1.542	0.38	4.91×10 ⁻²	↓	ISG, immune regulation
<i>Usp18</i>	-2.441	0.552	1.99×10 ⁻²	↓	Negative regulator of IFN signaling
<i>Bst2</i>	-1.516	0.342	1.99×10 ⁻²	↓	Interferon-induced antiviral protein
<i>Ifi2712a</i>	-3.261	0.743	2.01×10 ⁻²	↓	ISG, interferon response
<i>Ifi204</i>	-4.053	0.941	2.49×10 ⁻²	↓	Immune sensor, interferon pathway
<i>Nlrc5</i>	-1.781	0.411	2.38×10 ⁻²	↓	Regulator of MHC-I expression
<i>Gzmk</i>	-3.542	0.839	3.27×10 ⁻²	↓	Immune effector protease
<i>Tgtp1</i>	-1.701	0.419	4.91×10 ⁻²	↓	IFN-induced GTPase
<i>Parp12</i>	-0.627	0.153	4.70×10 ⁻²	↓	Stress response / interferon pathway
<i>H2-Q6</i>	-2.855	0.638	1.94×10 ⁻²	↓	MHC-I molecule
<i>H2-Q7</i>	-2.511	0.572	2.01×10 ⁻²	↓	MHC-I molecule
ECM and structural					
<i>Hspg2</i>	-0.506	0.122	4.14×10 ⁻²	↓	Extracellular matrix, synaptic stability (perlecan)
<i>Myo7a</i>	-0.823	0.183	1.94×10 ⁻²	↓	Cytoskeletal organization
Oxidative stress and metabolism					
<i>Pon2</i>	-0.424	0.103	4.16×10 ⁻²	↓	Oxidative stress regulation, mitochondrial protection
Epilepsy / neurodevelopment					
<i>Cdkl5</i>	0.762	0.103	2.91×10 ⁻⁹	↑	CDD causal gene
Other / limited annotation					
<i>Fibin</i>	1.232	0.291	3.22×10 ⁻²	↑	Secreted signaling molecule, embryonic development, limited CNS annotation
<i>Ndfip2</i>	0.283	0.062	1.59×10 ⁻²	↑	E3 ubiquitin ligase adaptor, protein ubiquitination, trafficking and degradation
<i>Ddx4</i>	1.728	0.353	3.69×10 ⁻³	↑	ATP-dependent RNA helicase
<i>Gm43720</i>	5.776	1.392	4.14×10 ⁻²	↑	Predicted gene, unknown function
<i>Ttc34</i>	-1.227	0.245	3.15×10 ⁻³	↓	Tetratricopeptide repeat (TPR)-domain-containing scaffold protein; poorly characterized

Table S3. Functional classification of genes differentially expressed in the hippocampus of heterozygous *Cdkl5* +/- female mice at 3 months. Genes were identified through RNA sequencing of hippocampal tissue from wild-type and *Cdkl5* +/- female mice at 3 months of age, followed by differential expression analysis using DESeq2. Log₂ fold change (log₂FC) values and their standard error (StdErr) represent differential expression between genotypes at 3 months. Direction indicates upregulation (↑) or downregulation (↓) in heterozygous mice relative to wild-type controls. Genes are grouped by biological function. All genes with an adjusted *p*-value (*p*-adj) < 0.05 are shown. This classification highlights a dominant interferon-related transcriptional signature, with a coordinated downregulation of interferon-stimulated genes and MHC-I-related genes.