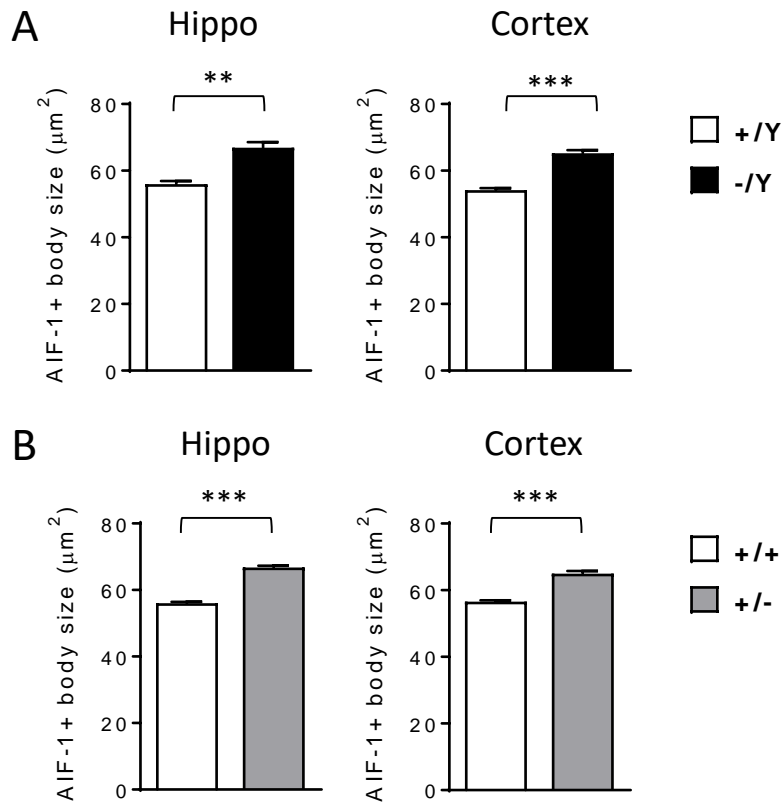


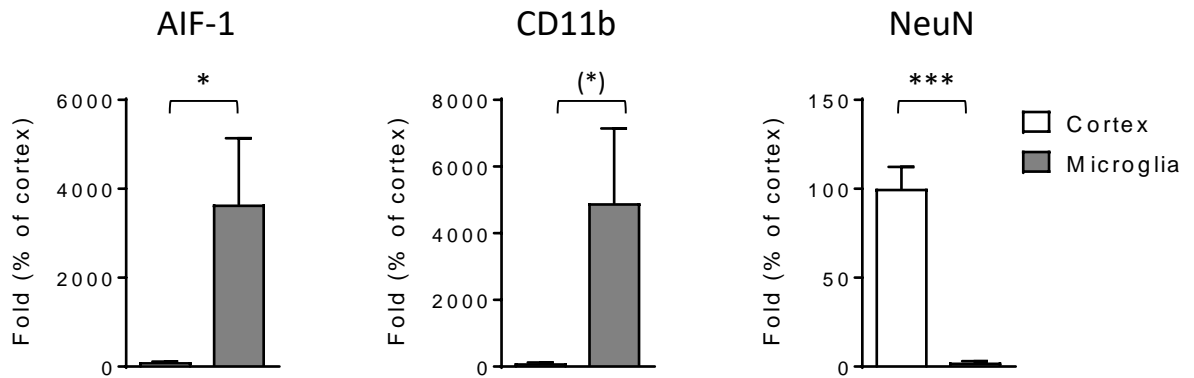
| Gene | | Primer sequence (5'-3') |
|-------------------------------|----------------|--------------------------------|
| <i>IL-1β</i> | <i>Forward</i> | TGCCACCTTTTGACAGTGATG |
| | <i>Reverse</i> | TGATGTGCTGCTGCGAGATT |
| <i>IL-6</i> | <i>Forward</i> | CTCTGCAAGAGACTTCCATCCA |
| | <i>Reverse</i> | GACAGGTCTGTTGGGAGTGG |
| <i>TNFα</i> | <i>Forward</i> | TAGCCCACGTCGTAGCAAAC |
| | <i>Reverse</i> | GCAGCCTTGTCCCTTGAAGA |
| <i>CX3CR1</i> | <i>Forward</i> | TGCTTGACATTGGGGAGACTGGA |
| | <i>Reverse</i> | AGGGAACGCTAAAGTCCTGGCTGA |
| <i>AIF-1</i> | <i>Forward</i> | GTCCTTGAAGCGAATGCTGG |
| | <i>Reverse</i> | CATTCTCAAGATGGCAGATC |
| <i>mCdk15</i> | <i>Forward</i> | TGCAGACACAAGGAAACACATGA |
| | <i>Reverse</i> | TTTCCTGCTTGAGAGTGC GAA |
| <i>CD11b</i> | <i>Forward</i> | CCTTGTTCTCTTTGATGCAG |
| | <i>Reverse</i> | GTGATGACA ACTAGGATCTT |
| <i>NeuN</i> | <i>Forward</i> | ACACACACACTCCATACTGAGG |
| | <i>Reverse</i> | GCTCTGGGCTCTCTGTTTGC |

Supplementary Table 1. List of primers used for quantitative RT-PCR.



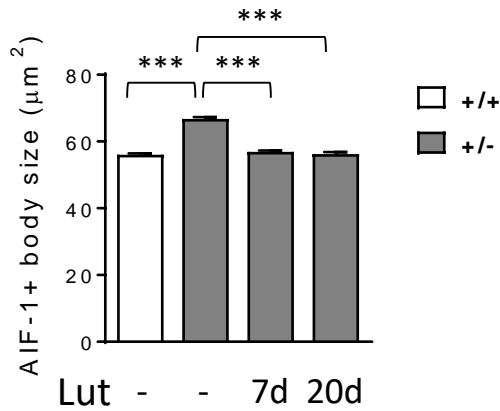
Supplementary Figure 1

Mean AIF-1-cell body size of microglial cells in hippocampal (Hippo) and somatosensory cortex (Cortex) sections from 3-month-old male (+/Y n=4, -/Y n=4; A), and female (+/+ n=5, +/- n=6; B) *Cdkl5* KO mice. The results in A and B are presented as means \pm SEM. ** p<0.01; ***p<0.001 (two-tailed Student's t-test).



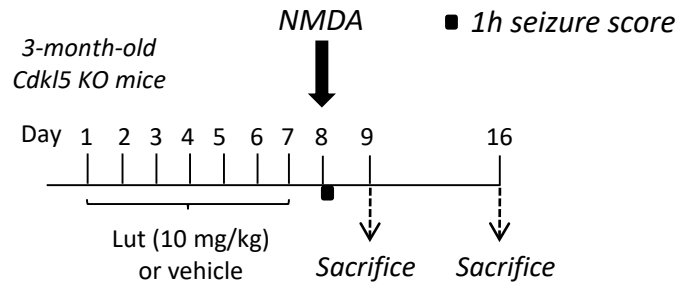
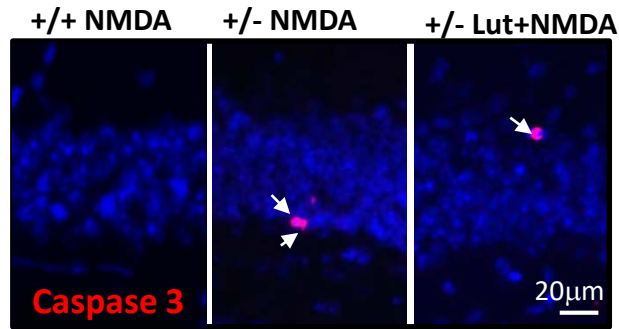
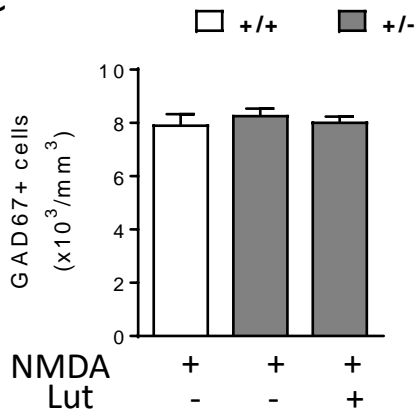
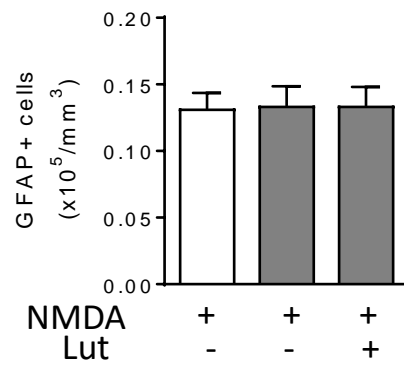
Supplementary Figure 2

Real-time qPCR analysis of Allograft inflammatory factor 1 (AIF-1), CD11b, and NeuN gene expression in the cortex of 3-month-old *Cdk15* $+/+$ mice (n=6) and microglial cells purified from 3-month-old *Cdk15* $+/+$ mice (n=6). Data are given as a percentage of *Cdk15* $+/+$ mice cortical expression. The results are presented as means \pm SEM. (*) $p=0.057$; * $p<0.05$; *** $p<0.001$ (two-tailed Student's t-test).



Supplementary Figure 3

Mean AIF-1-cell body size of microglial cells in the hippocampus of 3-month-old *Cdk15* +/+ (n=5) and *Cdk15* +/- (n=6) mice, and *Cdk15* +/- mice daily treated with luteolin intraperitoneal injections (i.p. 10 mg/kg) for 7 (Lut 7d, n=4) or 20 days (Lut 20d, n=4). Values are represented as mean \pm SEM. ***p<0.001 (Fisher's LSD test after one-way ANOVA).

A**B****C****D**

Supplementary Figure 4

A: Schematic view of *in vivo* treatments in 3-month-old *Cdkl5* KO female mice. Mice received a single intraperitoneal injection of NMDA (60 mg/kg) after 7 days of vehicle or luteolin treatment. Seizure grades were scored in a 60-minute observation period after NMDA injection (black square). Animals were sacrificed 1 day or 8 days after NMDA administration. **B:** Examples of cleaved caspase-3 positive cells (white arrows) in the hippocampus of a *Cdkl5* *+/+* and a *Cdkl5* *+/-* mouse treated with vehicle and NMDA, and in a *Cdkl5* *+/-* mouse pre-treated for 7 days with luteolin before NMDA injection. Mice were sacrificed 24 h after NMDA treatment. **C,D:** Quantification of GAD67 (C) and GFAP (D) positive cells in CA1 layer of hippocampal sections from mice treated as in A and sacrificed 8 days after NMDA administration. Values in C,D are represented as means \pm SEM. (Fisher's LSD test after one-way ANOVA).