**Supplementary information**

**Additional file 1: Fig. S1 LPS treatment induces expression of CD38 and non-canonical PARP isozymes. (a)** Differential expression of NAD-related genes in primary murine microglia treated with 100 ng/mL LPS versus equivalent volume of PBS for 4 h. n=3. GSE49329. **(b)** Differential expression of NAD-related genes in adult microglia from C57BL/6 male mice 20 h after treatment with 100 ng/mL LPS or vehicle for 4 h. GSE102482. **(c, d)** Differential expression of NAD-related genes from the ipsilaterial brain samples obtained from C57Bl/6J mice either (c) one day or (d) 4 d after intrastriatal injection of 1 µL of LPS (*E. coli* 0127:B8, 5 mg/mL) or PBS. n = 3, each replicate comprised a pooled RNA sample derived from 3 different mice. GSE122815.

**Additional file 2: Fig. S2. Administration of NR and apigenin did not ameliorate LPS-induced neuroinflammation in CD38 KO mice.**

**(a)** Treatment scheme and timeline of biochemical analysis. **(b)** Evaluation of NAD+ levels in the HPC of WT and CD38 KO mice after treatment with saline (-), apigenin 40 mg/kg, or NR 400 mg/kg via i.p. injection for 7 d followed by LPS injection. *n* = 5. Data represent mean ± SEM. *P* values were determined by one-way ANOVA followed by Scheffe’s *F* test. \*\**p* < 0.01 between WT and CD38 KO mice and +*p* < 0.05 compared WT control. **(c-h)** RT-qPCR analysis for the expression of inflammatory genes in the HPC of control- or LPS-injected WT and CD38 KO mice pretreated with saline, apigenin, or NR for 7 d in WT and CD38 KO mice. *n* = 5. Data represent mean ± SEM. *P* values were determined by two-way ANOVA followed by Scheffe’s *F* test. \**p* < 0.05 and \*\**p* < 0.01 between WT and CD38 KO mice. +*p* < 0.05, ++*p* < 0.01 vs. WT LPS-injected mice.

**Additional file 3: Fig. S3 NR and apigenin attenuated LPS-induced neurodegeneration.**

 **(a)** Representative immunofluorescence images ofMAP2 in the HPC (CA1 and CA3) of control- or LPS-injected WT mice pretreated with saline, apigenin, or NR for 7 d. Nuclei were counterstained with DAPI. Scale bars: 100 µm. **(b)** Thegraphs represent the intensity of MAP2 in the hippocampus (CA1 and CA3). *n* = 6. Data represent mean ± SEM. *P* values were determined by two-way ANOVA followed by Scheffe’s *F* test. \**p* < 0.05 and \*\**p* < 0.01 vs LPS injected control mice. #*p* < 0.05, ##*p* < 0.01 between control- and LPS-injected mice. \**p* < 0.05 and \*\**p* < 0.01 vs LPS-injected mice.