



**Supplementary Figure 1. Stereological analysis of neuronal and oligodendrocyte injury and loss in the cerebral cortex in response to intrathecal HSP60.** (A-D) Forty micrograms of HSP60 or 40  $\mu$ g of SA were injected intrathecally into 8-12 week-old C57BL/6J (WT, HSP60  $n=11$ , SA  $n=8$ ), TLR4<sup>-/-</sup> (HSP60  $n=11$ , SA  $n=8$ ), and MyD88<sup>-/-</sup> (HSP60  $n=11$ , SA  $n=8$ ) mice. Naïve mice received no injection (WT  $n=6$ , TLR4<sup>-/-</sup>  $n=4$ , MyD88<sup>-/-</sup>  $n=4$ ). Injection of LPS into WT mice served as a positive control for TLR4 activation ( $n=10$ ). Injection of water into WT mice served as a carrier control ( $n=7$ ). After 3 d, the cerebral cortex was immunostained with NeuN antibody (A, B) or stained by TUNEL assay (C, D). Subsequently, stereological analysis was performed by (A, C) quantification of NeuN<sup>+</sup> or TUNEL<sup>+</sup> objects

and **(B, D)** determination of the percentage of the area of NeuN<sup>+</sup> or TUNEL<sup>+</sup> ROI (region of interest). Results are presented as mean  $\pm$  SD, Mann-Whitney *U* test for indicated groups.

**(E, F)** Three days after intrathecal injection of 40  $\mu$ g HSP60 or 40  $\mu$ g SA (control) coronal brain sections of C57BL/6J (WT, HSP60 *n*=4, SA *n*=4), TLR4<sup>-/-</sup> (HSP60 *n*=4, SA *n*=4), and MyD88<sup>-/-</sup> (HSP60 *n*=4, SA *n*=4) mice were immunostained with an antibody against APC. Subsequently, stereological analysis was performed by **(E)** quantification of APC<sup>+</sup> objects and **(F)** determination of the percentage of the area of APC<sup>+</sup> ROI. Results are presented as mean  $\pm$  SD, Mann-Whitney *U* test for indicated groups.