**Supporting data**

**Figure s1. Expression of PON1 protein in microglial cell lines.**

The expression of PON1 protein in human microglia HM1900, mouse microglia BV2 and rat primary microglia was determined by western blot. GAPDH was used as loading control. MG, microglia

**Figure s2.** **Changes in body weight and brain weight of WT and PON1-/- rats.**

A. Body weights of PON1-/- ratswere lower than WT rats (*n* =7 for WT male and PON1-/- male, *n* =4 for WT female and PON1-/- female) although the difference was not statistically significant; B. Brain weights of PON1-/- ratswere lower than for WT rats (*p*<0.05, *n* =7 for WT male and PON1-/- male, *n* =4 for WT female and PON1-/- female). \**p*<0.05. NS, no significance.

**Figure s3.** **Cytokines regulated by PON1 knockout in primary rat microglia.**

IL-4 (A) and IL-5 (B) were decreased in culture supernatants of LPS-treated PON1-/- microglia compared with WT (*p*<0.05, *n* = 3 per group). For IL-7 (C), IL-12 (D), MCP-1 (E), VEGF (F) and G-CSF (G), there was no significant difference between the two groups (*n* = 3 per group). \**p*<0.05. NS, no significance

**Figure s4.** **Effect of PON1 KO on LPS/TLR4/NFκB signaling pathway.**

Total protein lysates of WT, PON1-/-, WT LPS and PON1-/- LPS microglia were prepared and the level of TLR4 was determined by western blot. The nuclear and cytoplasmic proteins of WT, PON1-/-, WT LPS and PON1-/- LPS microglia were extracted and the level of P65 was detected by western blot (*n*  = 3 per group). Nucleolin and GAPDH were used as the markers of nucleus and cytosol, respectively.

**Figure s5. Effects of PON1 KO on P38 and JNK signaling pathways.**

Total protein lysates of WT, PON1-/-, WT LPS and PON1-/- LPS microglia were prepared and the levels of p-P38, p-JNK, t-P38 and t-JNK were determined by western blot (*n* = 3 per group).

**Figure s6. The microglia cells and phagocytosis 24h post-injection**

Representative images (A) of Aβ oligomers (red) and quantitation analysis of microglia cells (B) at the injection sites of WT and PON1-/- rat brains (n= 5 WT, n= 4 KO) 24h post-injection. DAPI (blue) stained the nucleus. Scale bar, 750 or 250 or 50 μm; A yellow circles indicate microglia hyperplastic focus. Representative confocal images of microglia cells labelled with Iba1 (green) merged with Aβ (red) at the injection sites of WT and PON1-/- rats 24h post-injection (C). (WT, ①-⑧; KO, ①’-⑧’ ). Scale bar=25μm. \* p<0.05 indicate significance. ① indicates resting microglia cells with long branches, ②’ indicates phagocytizing microglia cells with open mouth, others were microglia cells with uptake of Aβ.

**Figure s7. Aβ injection and TREM2 expression**

The transcription of TREM2 mRNA in the hippocampus from WT and PON1-/- rats 0-, 1- and 3- day post-injection was detected using real time PCR (A). n= 5 for WT and PON1-/- rats 0-day post-injection; n= 4 for WT and PON1-/- rats 1-day and 3-day post-injection. \* p<0.05 indicate significance, WT versus PON1-/- rats 3-day post-injection. The expression of TREM2 proteins in the hippocampus from WT and PON1-/- rats 14- day post-injection was detected using western blot (B). n=3- 4 for WT and PON1-/- rats 14-day post-injection.