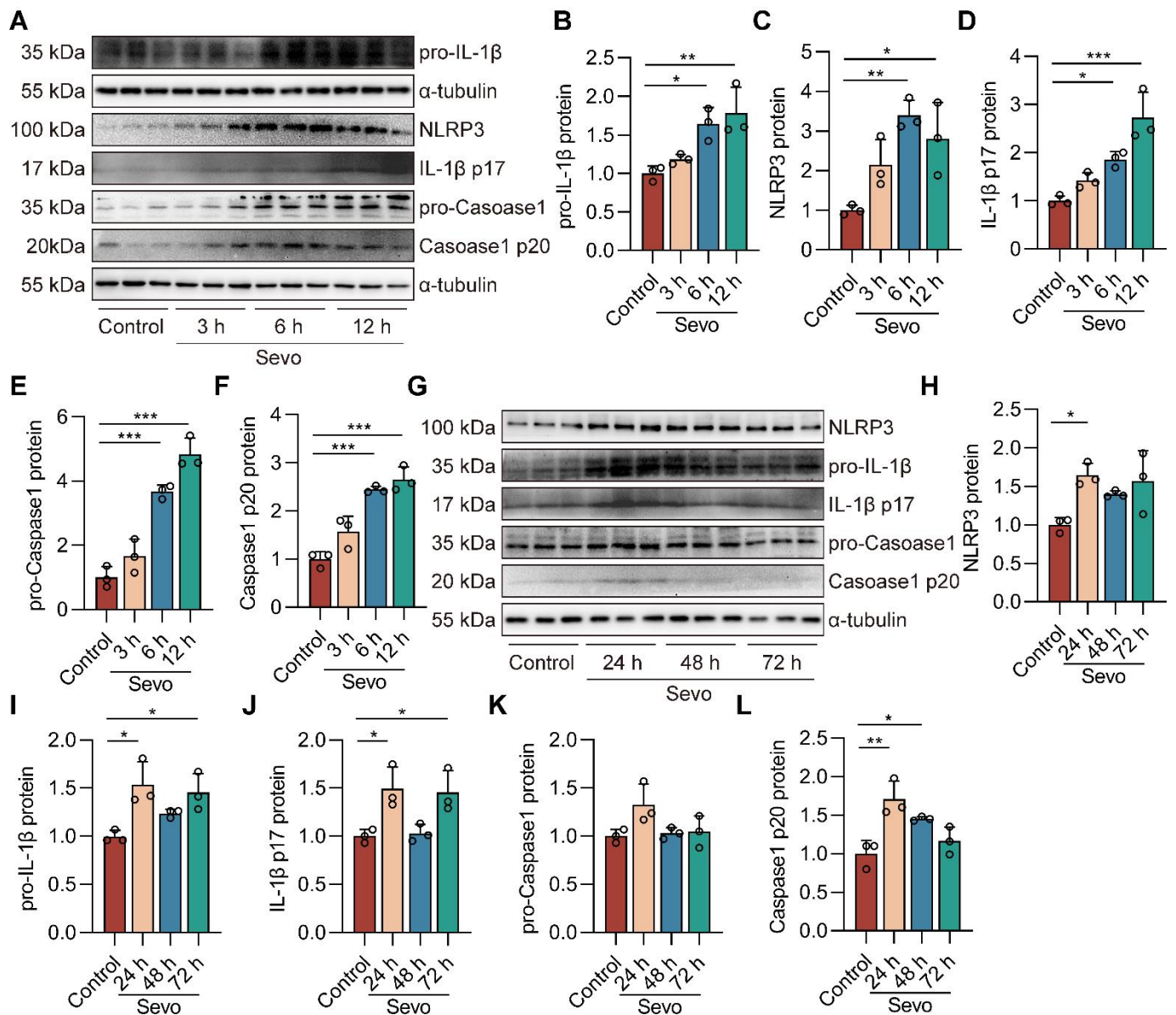
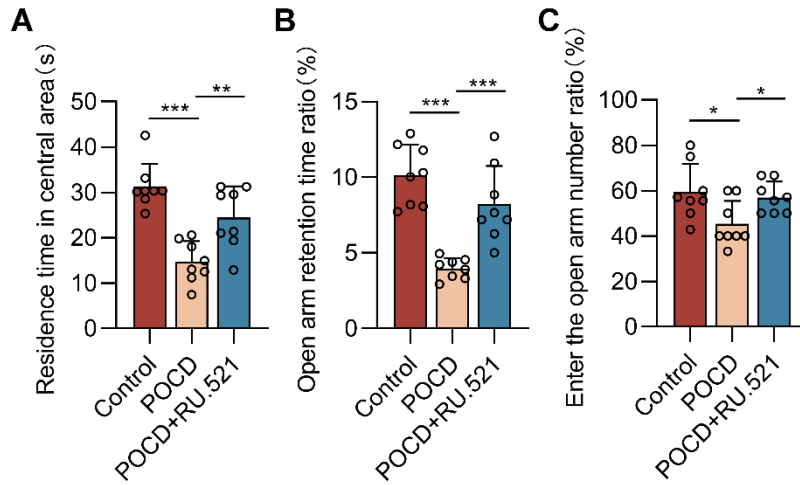


## Supplementary Figure and Figure legend

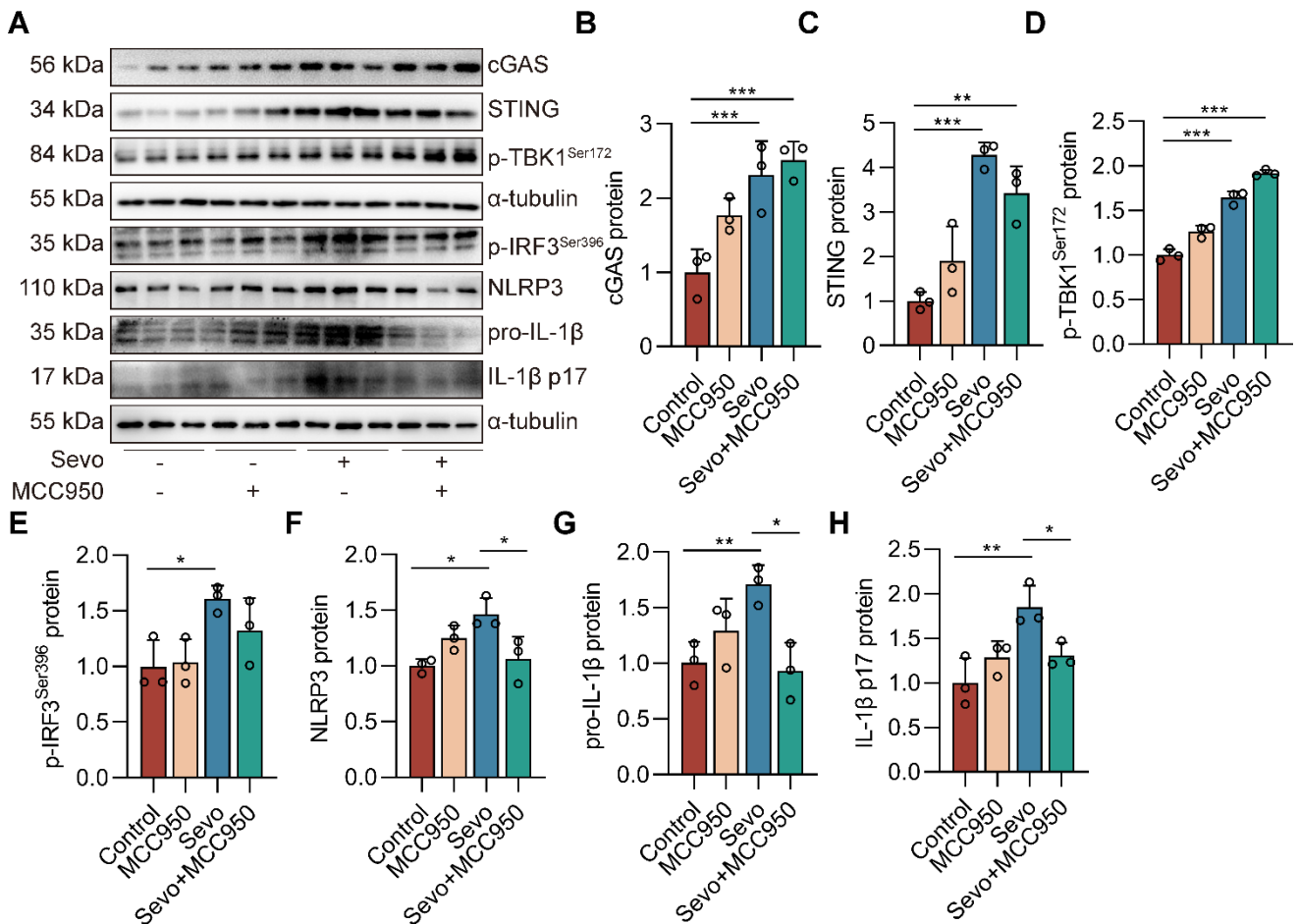


**Figure S1. Sevoflurane led to the activation of the NLRP3 inflammasome in microglia at different times.**

**A-F** BV2 cells were treated with 1 mM Sevoflurane for 3, 6, and 12 h, and the pro-IL-1β, NLRP3, IL-1β p17, pro-Caspase1, and Caspase1 p20 levels were measured by Western Blot ( $n=3$ ). **G-L** BV2 cells were treated with 1 mM Sevoflurane for 24, 48, and 72 h. The protein expression of NLRP3, pro-IL-1β, IL-1β p17, pro-Caspase1, and Caspase1 p20 were detected by western blot ( $n=3$ ). Data are expressed as the Mean  $\pm$  SD. Differences among multiple groups were performed using ANOVA. \* $P < 0.05$ , \*\* $P < 0.01$ , and \*\*\* $P < 0.001$ .

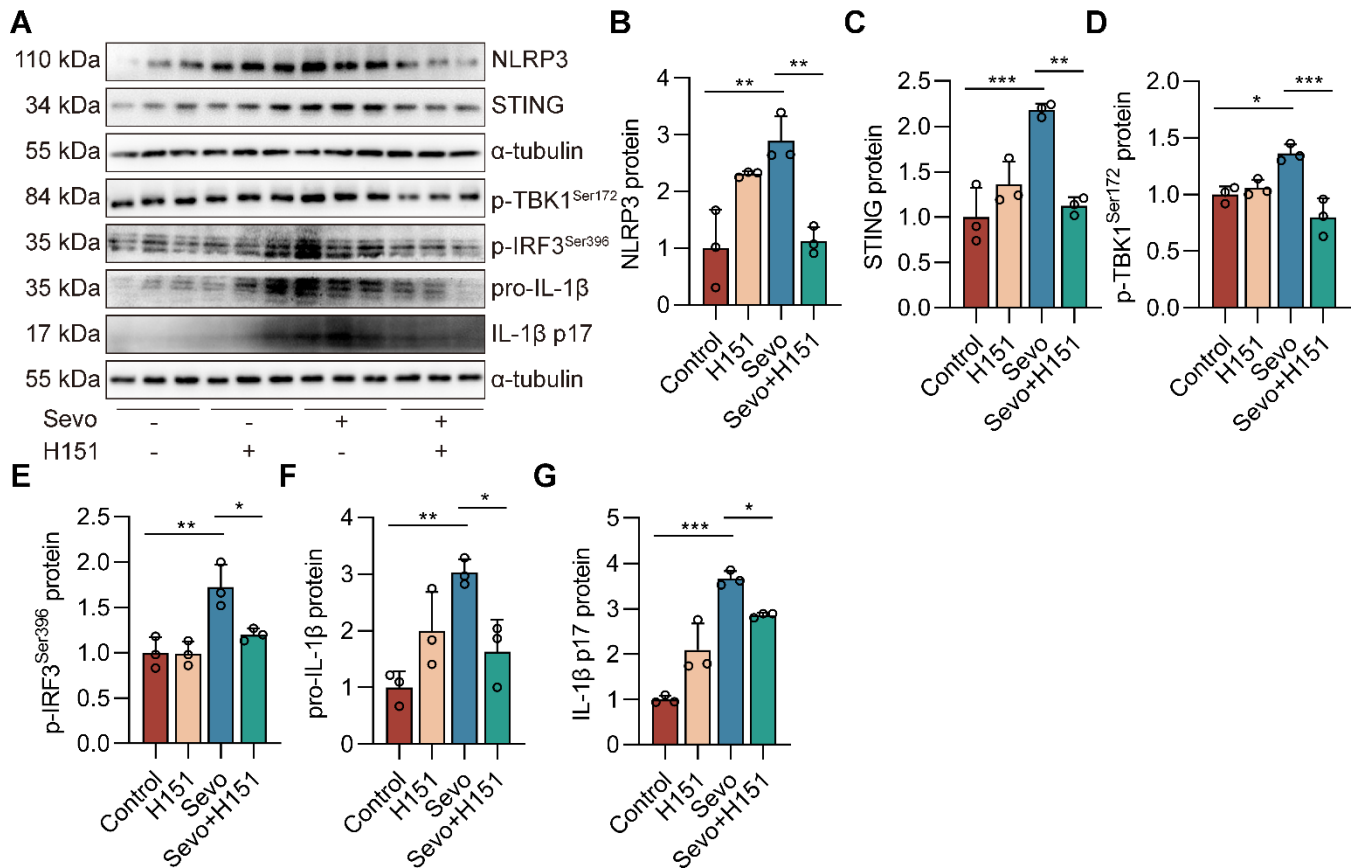


**Figure S2. Inhibition of cGAS reduces cognitive impairment in POCD mice.** **A** The Open Field Test was conducted to assess the residence time in the central area ( $n=8$ ). **B-C** The Elevated Plus Maze was conducted to assess the ratio of time spent in the open arm and the ratio of times entering the open arm ( $n=8$ ). Data are expressed as the Mean  $\pm$  SD. Differences among multiple groups were performed using ANOVA.  $*P < 0.05$ ,  $**P < 0.01$ , and  $***P < 0.001$ .

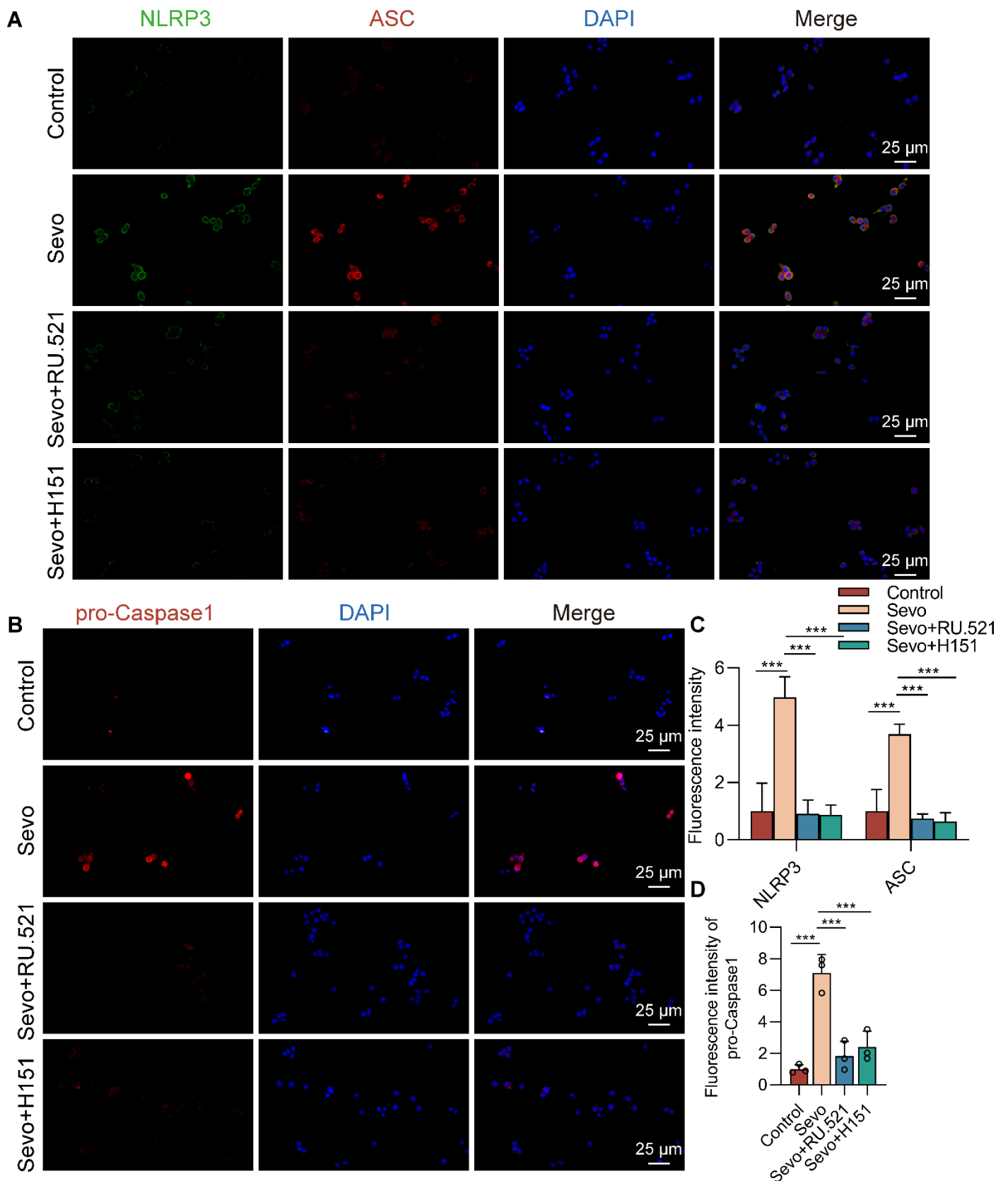


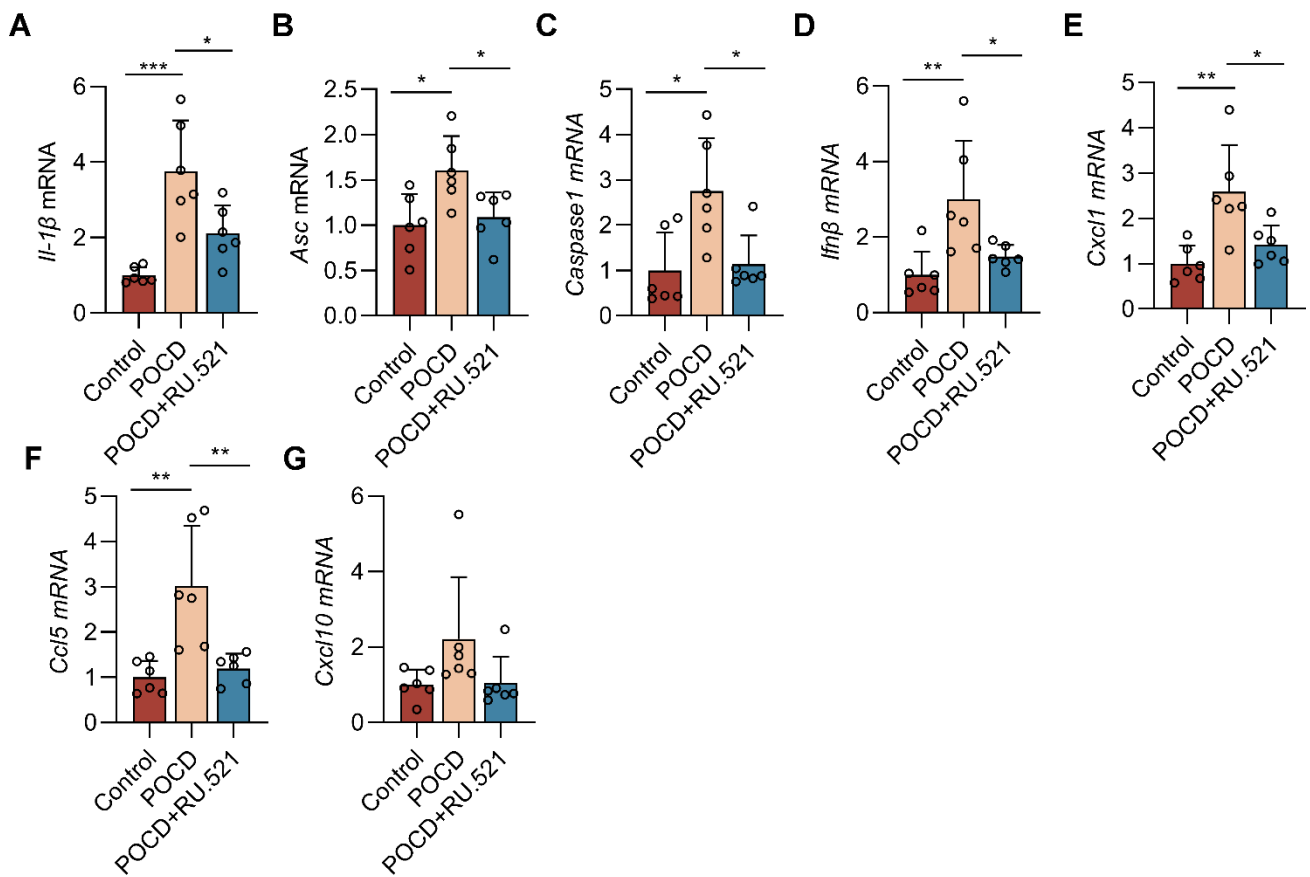
**Figure S3. Inhibition of NLRP3 inflammasome has no effect on sevoflurane-induced cGAS-STING pathway activation in microglia.** **A-H** BV2 cells were treated with 1 mM sevoflurane for 12 h after 10  $\mu$ M

MCC950 intervention for 30 min. The protein expression of cGAS, STING, p-TBK1<sup>Ser172</sup>, p-IRF3<sup>Ser396</sup>, NLRP3, pro-IL-1 $\beta$ , and IL-1 $\beta$  p17 levels were measured by Western Blot ( $n=3$ ). Data are expressed as the Mean  $\pm$  SD. Differences among multiple groups were performed using ANOVA.  $*P < 0.05$ ,  $**P < 0.01$ , and  $***P < 0.001$ .



**Figure S4. Inhibition of STING suppresses the sevoflurane-induced NLRP3 inflammasome activation in microglia.** A-G BV2 cells were treated with 1 mM sevoflurane for 12 h after 5  $\mu$ M H151 intervention for 30 min. The protein expression of NLRP3, STING, p-TBK1<sup>Ser172</sup>, p-IRF3<sup>Ser396</sup>, pro-IL-1 $\beta$ , and IL-1 $\beta$  p17 levels were measured by Western Blot ( $n=3$ ). Data are expressed as the Mean  $\pm$  SD. Differences among multiple groups were performed using ANOVA.  $*P < 0.05$ ,  $**P < 0.01$ , and  $***P < 0.001$ .





**Figure S6. RU.521 inhibits the activation of cGAS-STING pathway downstream genes in POCD mice.**

**A-G** *Il-1β*, *ASC*, *Caspase1*, *Ifnβ*, *Cxcl10*, *Ccl5*, and *Cxcl10* mRNA expression in the hippocampus were detected by real-time PCR ( $n=6$ ). Data are expressed as the Mean  $\pm$  SD. Differences among multiple groups were performed using ANOVA. \* $P < 0.05$ , \*\* $P < 0.01$ , and \*\*\* $P < 0.001$ .