# Supplementary materials

## Supplementary figure legend

**Supplement figure 1**: (A) Schematic for RVF model establishing that intraperitoneal injection of LPS (1mg/kg) in rats with pulmonary hypertension. (B) Schematic for NLRP3 inhibition that intravenous administration of MCC950 (10mg/kg) one hour before LPS injection. (C) The right ventrical pressure-volum loop obtained by right catheterization among four group of rats' right ventricle were shown. (E) The mRNA level of SERCA2a among four group of rats' right ventricle were shown. The significance of the difference was analysed by one-way ANOVA (n = 6). (F) The mRNA level of RYR2 among four group of rats' right ventricle were shown. The significance of the difference was analysed by one-way ANOVA (n = 6).

**Supplement figure 2**: (A) The protein band of NLRP3, cleaved-casp1, GSDMD, GSDMD-N and GAPDH in PAH+LPS rats (SD rats were fed for 28 days after intraperitoneal injection of MCT, intravenous injection of saline was performed 1 hour before LPS injection and the samples were collected 6 hours after intraperitoneal injection of LPS) and PAH+MCC950+LPS rats (SD rats were fed for 28 days after intraperitoneal injection of MCT, intravenous injection of MCC950 was performed 1 hour before LPS injection and the samples were collected 6 hours after intraperitoneal injection of LPS). (B) The protein level of NLRP3 among above-mentioned two group of rats' right ventricle were shown. The significance of the difference was analysed by unpaired Welch's t test (n = 3). (C) The protein level of cleaved-casp1 among above-mentioned two group of rats' right ventricle were shown. The significance of the

difference was analysed by unpaired Welch's t test (n = 3). (D) The protein level of GSDMD-N among above-mentioned two group of rats' right ventricle were shown. The significance of the difference was analysed by unpaired Welch's t test (n = 3). (E) Survival analysis shows the application of MCC950 could reduce the mortality within 6 hours of intraperitoneal injection of LPS in PAH rats (n = 18-21). (F) The IL-1β immunofluorescence in ventricular tissue of the Normal+LPS rats and Normal+MCC950+LPS rats 6h after LPS injection were shown. (G) The ratio of IL-1β area% in right ventricle to left ventricle of above mentioned two groups was shown. The significance of the difference was analysed by unpaired Welch's t test (n = 3). (H) The mRNA level of RYR2 in PAH+LPS rats and PAH+MCC950+LPS rats' right ventricle were shown. The significance of the difference was analysed by unpaired Welch's t test (n = 6). (I) The mRNA level of SERCA2a among above-mentioned two group of rats' right ventricle were shown. The significance of the difference was analysed by unpaired Welch's t test (n = 6). *p<0.05, *p<0.01, ***p<0.001.

**Supplement figure 3**: (A) The Venn diagram showed there were five cytokines (MCP-1, CINC1, CINC2, CINC3, b-NGF) that are significantly elevated in RVF rats' heart, and stayed at low level after pharmacological inhibition of NLRP3 pathway. (B)(C)(D)(E) We further verified the array results of MCP-1, CINC1, CINC2, CINC3 in the right ventricular myocardium of Normal rats, Normal + LPS rats, PAH rats, PAH+LPS rats and PAH+MCC950+LPS rats by q-PCR. The significance of the difference was analysed by one-way ANOVA (n = 4-6). (F)The process for the segregation of CD45 positive cells, neutrophils. (G)The process for the segregation of macrophages and the M1 phenotype. (H)(I) Enrichment

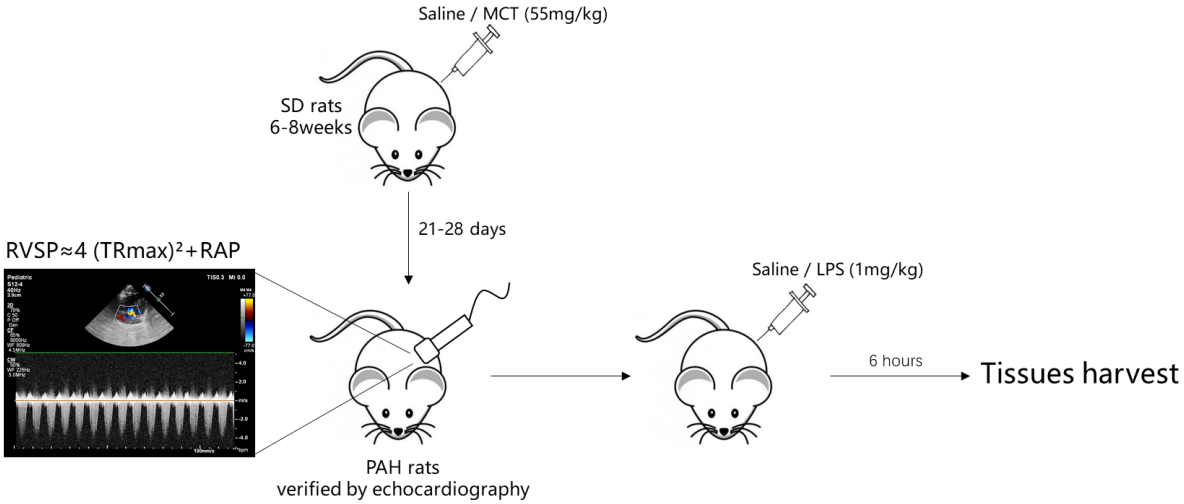
of CD45 positive cells, the significance of the difference was analysed by unpaired Welch's t test (n = 16). *p<0.05, *p<0.01, ***p<0.001.

**Supplement figure 4**: (A) The protein bands of NLRP3, cleaved-casp1, GSDMD-N and GAPDH in H9C2, H9C2+LPS, H9C2+AVP, H9C2+AVP+LPS, H9C2+AVP+MCC950+LPS groups of cells were shown. (B) The protein level of NLRP3 among above-mentioned five groups of cells were shown. The significance of the difference was analysed by one-way ANOVA (n = 3). (C) The protein level of cleaved-casp1 among above-mentioned five groups of cells were shown. The significance of the difference was analysed by one-way ANOVA (n = 3). (D) The protein level of GSDMD-N among above-mentioned five groups of cells were shown. The significance of the difference was analysed by one-way ANOVA (n = 3). (E) We exposed H9C2 cells to AVP (1 μmol/ml) for 72h to simulate the hypertrophy of right ventricular myocardium in rats with pulmonary hypertension, to MCC950(100mM) for 1h to inhibit the NLRP3 pathway, to LPS (100ug/ml) for 6h to mimic the inflammation state in vivo RVF model. The primary macrophage cells were exposed to LPS (100ug/ml) for 6h to mimic the inflammation state in vivo RVF model, to MCC950(100mM) for 1h to inhibit the NLRP3 pathway. The mRNA level of IL-1β in H9C2, H9C2+LPS, H9C2+AVP, H9C2+AVP+LPS, H9C2+AVP+MCC950+LPS, macrophage, macrophage + LPS, macrophage+MCC950+LPS groups of cells was shown. The significance of the difference between two groups was analysed by unpaired Welch's t test (n = 3). p<0.05, *p<0.01, ***p<0.001.(F) The arg1 mRNA level in the macrophage+H9C2+PBS, macrophage+H9C2+LPS, macrophage+AVP-conditioned H9C2+PBS and macrophage+AVP-conditioned H9C2+LPS cell groups is shown. The

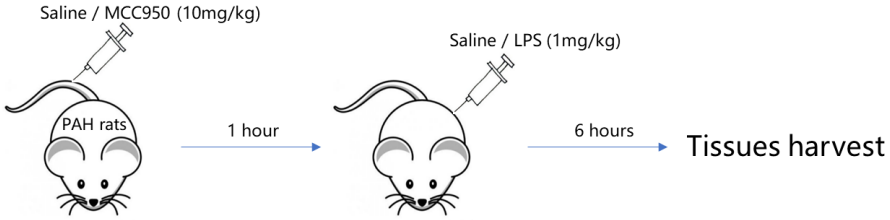
significance of differences between two groups was determined with unpaired Welch's t test (n = 3). (G) The IL-10 mRNA level in the macrophage+H9C2+PBS, macrophage+H9C2+LPS, macrophage+AVP-conditioned H9C2+PBS and macrophage+AVP-conditioned H9C2+LPS cell groups is shown. The significance of differences between two groups was determined with an unpaired Welch's t test (n = 3). (H) The arg1 mRNA level in the macrophage+AVP-conditioned H9C2+LPS and macrophage+AVP-conditioned H9C2+MCC950+LPS cell groups is shown. (I) The IL-10 mRNA level in the macrophage+AVP-conditioned H9C2+LPS and macrophage+AVP-conditioned H9C2+MCC950+LPS cell groups is shown.The significance of differences was analysed with unpaired Welch's t test (n = 3). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

*Supplementary figure 1*

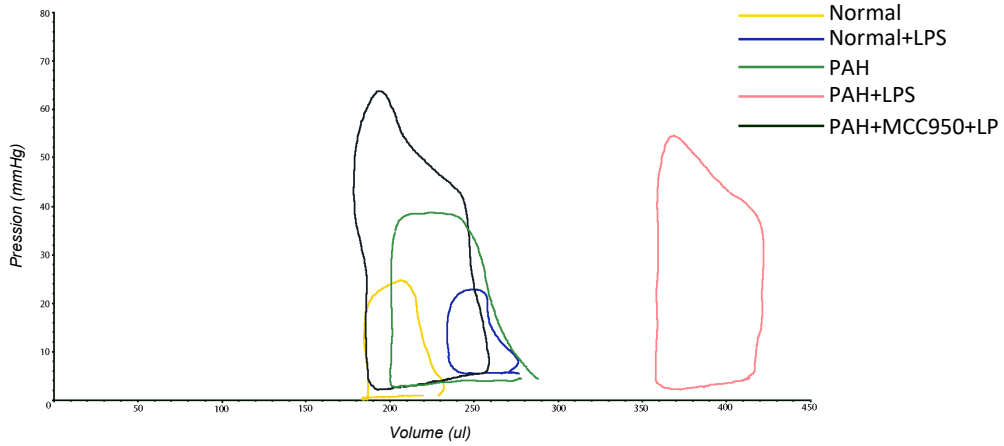
A



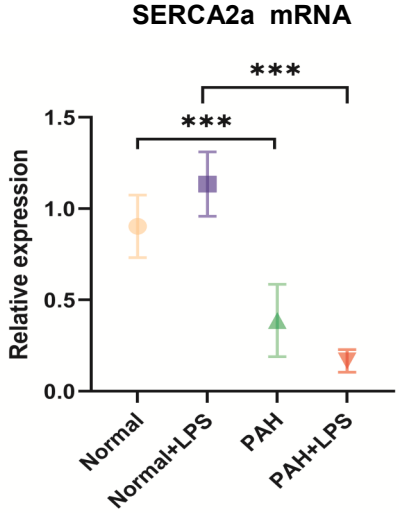

B



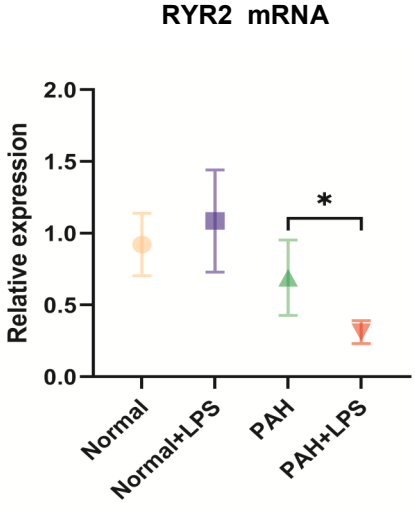

C



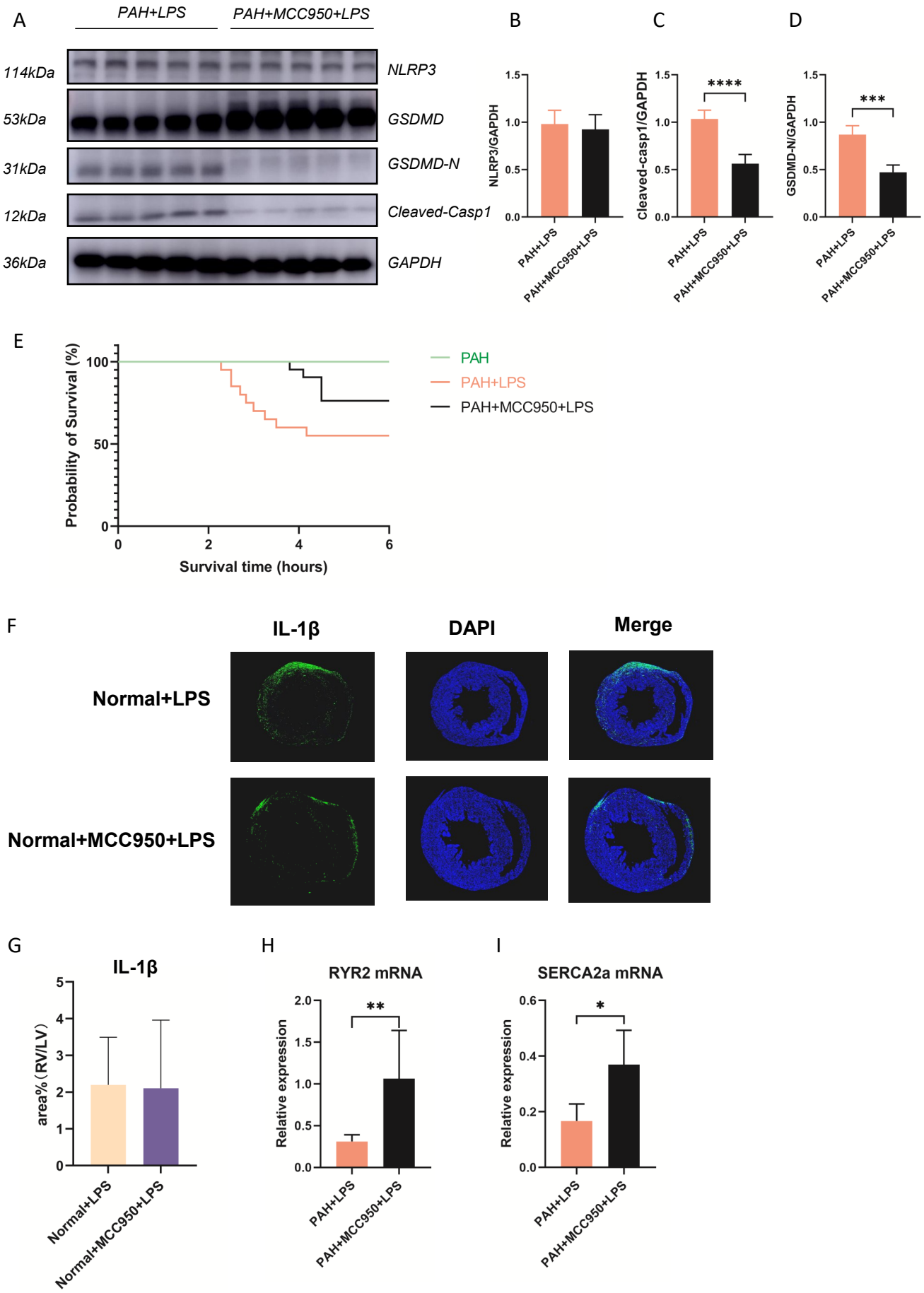

D



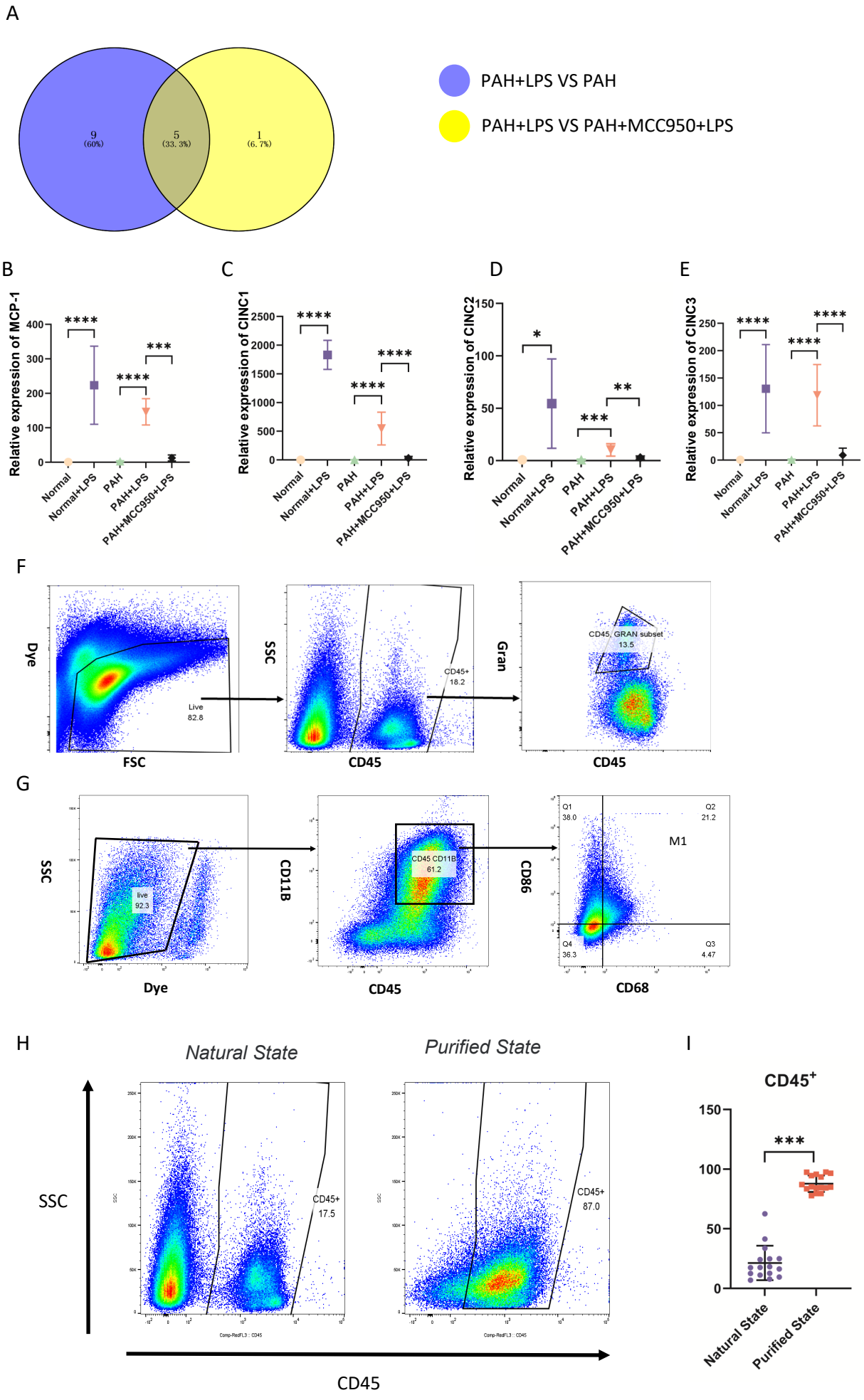

E



*Supplementary figure 2*



*Supplementary figure 3*



*Supplementary figure 4*