

Supplementary Material

Supplementary Figures

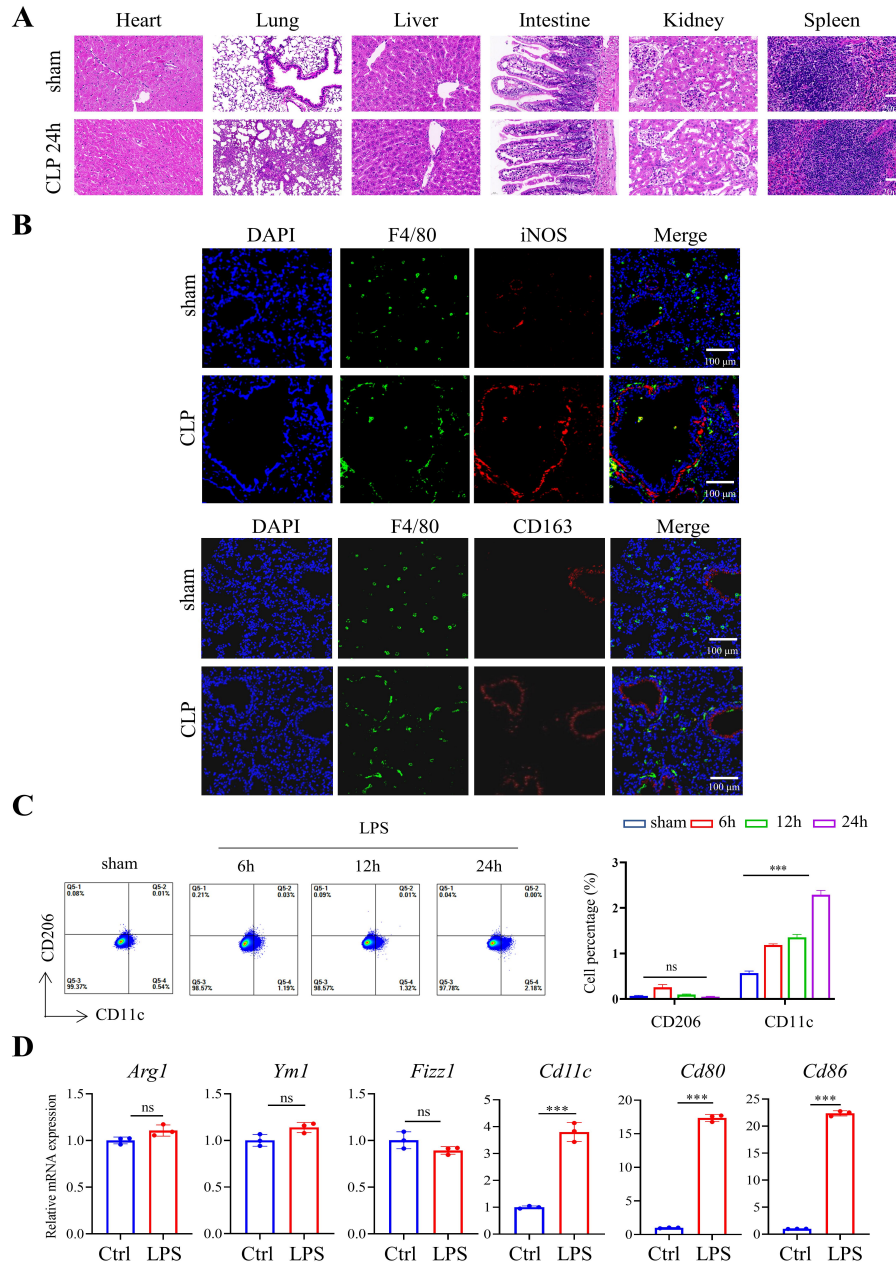
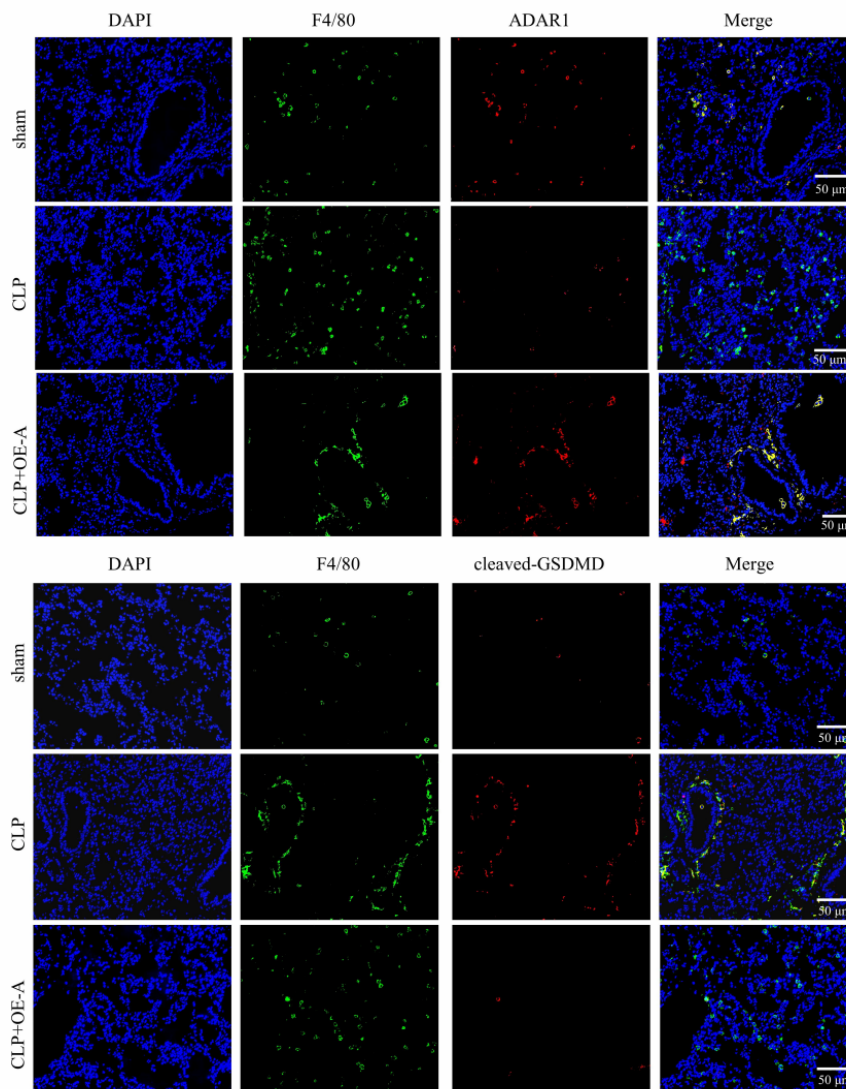
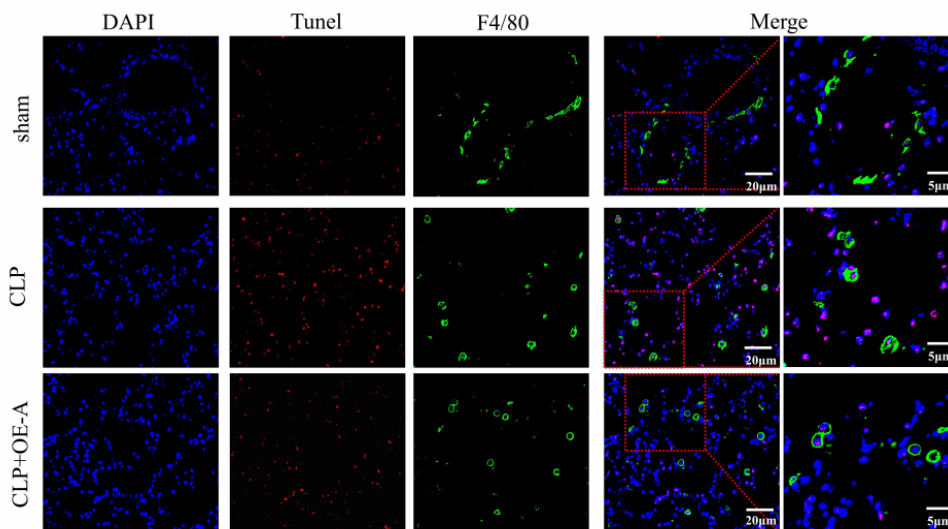
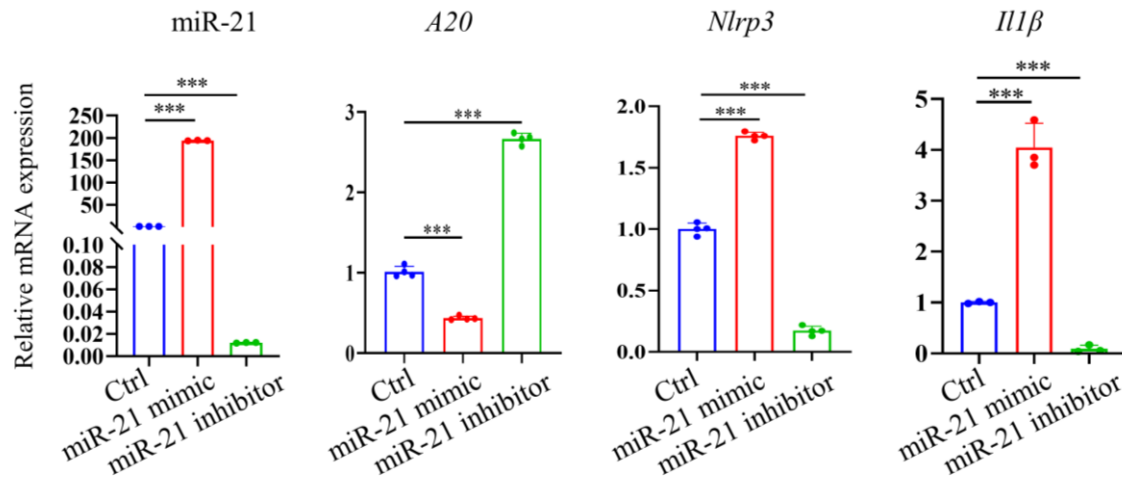


Fig.S1

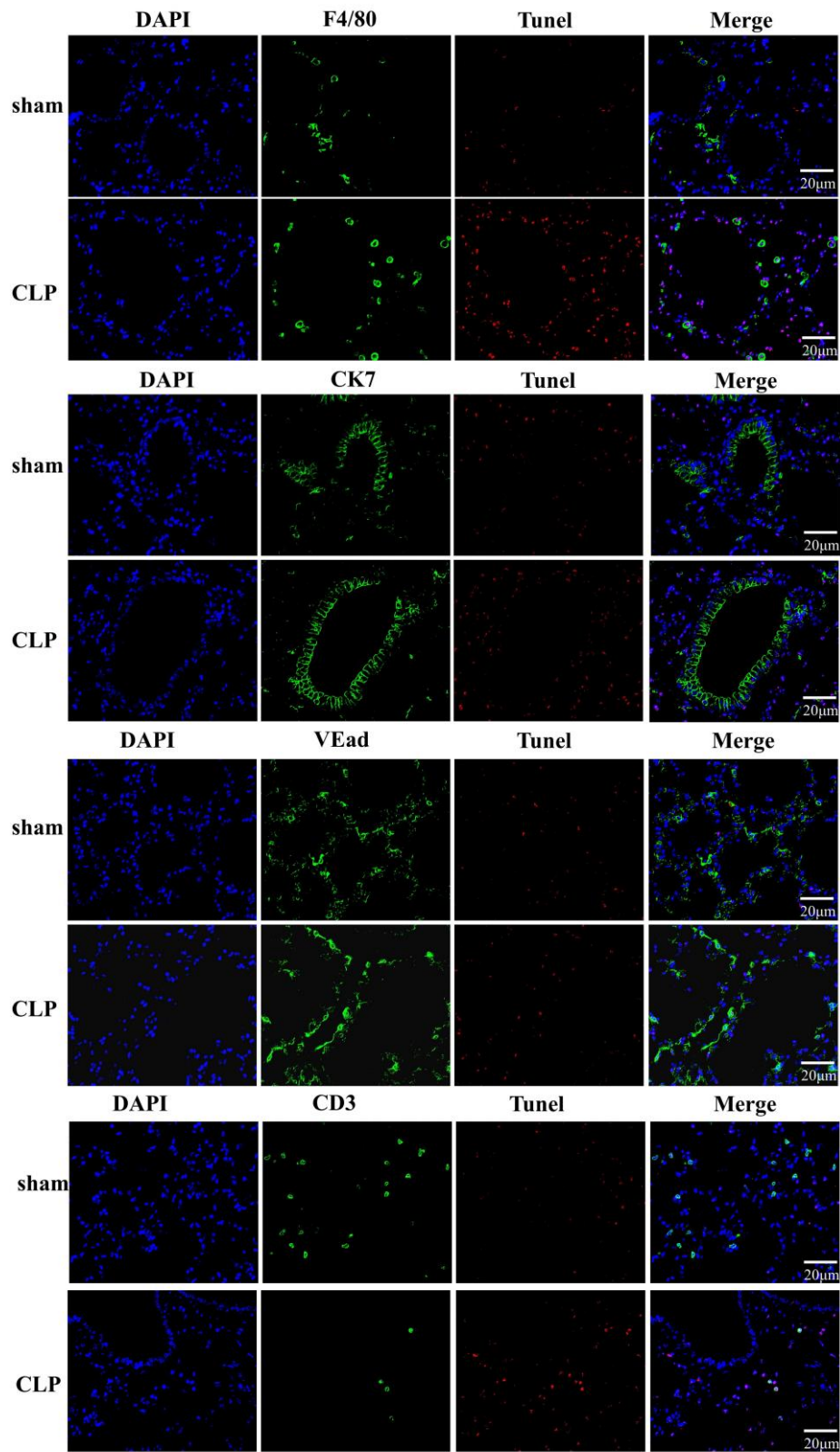
Supplementary Figure 1. CLP-induced organ pathological injuries in mice and macrophage polarization in lung tissues of CLP mice and RAW264.7 cells after LPS. (A), Representative HE images of mice heart, lung, liver, intestine, kidney, and spleen tissues after CLP treatment for 24 h. N=6. Scale bar means 20 μ m. (B), Representative immunofluorescence images of double staining of F4/80 and iNOS (M1 marker) or CD163 (M2 marker) in murine lung tissues after CLP. N=6. Scale bar means 100 μ m. (C), Flow cytometry of RAW264.7 cells with LPS stimulation over time showing cell percentage of CD11c (M1 marker) and CD206 (M2 marker) positive cells. N=3. (D), qRT-PCR was used to assess the expression of M1 and M2 polarization in Raw 264.7 cells stimulated by LPS. N=3. Data were shown as mean \pm SD. *** P < 0.001, ns=no statistical significance (sham versus LPS-24h).

A**B**

Supplementary Figure 2. Overexpression of ADAR1 alleviated CLP-induced pyroptosis and cell death in mice. (A), Double staining of F4/80 (green) and ADAR1 (red), as well as F4/80 (green) and cleaved-GSDMD (red) in murine lung tissues after CLP with or without ADAR1-overexpressing adenovirus infection. DAPI is blue. N=3. Scale bar means 50 μm. (B), Immunofluorescence staining of tunel (red) and F4/80 (green) in the three groups. DAPI is blue. N=3. Scale bar means 20 μm.



Supplementary Figure 3. ADAR1/miR-21/A20 signaling in RAW264.7 cells. RAW264.7 cells were transfected with miR-21 mimic or inhibitors, and relative mRNA levels of miR-21, A20, NLRP3, and IL-1β were detected via RT-qPCR. N=3. Data were shown as mean ± SD. *P< 0.05, **P< 0.01, ***P< 0.001.



Supplementary Figure 4 Cell death of different cells in mice septic model. Double staining of F4/80 (green, macrophages), CK7 (green, epithelial cells), CD3 (green, T lymphocytes), VEad (green, endotheliocytes), and tunel (red) in the mice lung tissues of sham and CLP mice models (24 h). DAPI is blue. N=6. Scale bar means 20 μm.

Supplementary Table 1. Primer sequences used in RT-qPCR.

Gene	Forward (5'-3')	Reverse (5'-3')
<i>ADAR1</i>	CTGAGACCAAAGAAACGCAGA	GCCATTGTAATGAACAGGTGGTT
<i>A20</i>	CACACAAAGCACCTCAAGGC	GTTGGGATGCTGACACTCCA
<i>NLRP3</i>	GATCTTCGCTGCGATCAACAG	CGTGCATTATCTGAACCCAC
<i>IL1</i>	TGGCATTGATCTGGTTCATC	GTTTAGGAATCTTCCCCTT
<i>IL4</i>	AACGGCTCGACAGGAACCT	CTCTGGTTGGCTTCCTTCACA
<i>IL6</i>	GACAGCCACTCACCTCTTCA	TTCACCAGGCAAGTCTCCTC
<i>IL10</i>	AGGGCACCCAGTCTGAGAACA	CGGCCTTGCTCTTGTTTTAC
<i>GADPH</i>	AGAAGGCTGGGGCTCATTG	AGGGGCCATCCACAGTCTTC
<i>Adar1</i>	CCGTACCATGTCCTGTAGTGACA	GCCCTTGGCTGAAAAGGTAAC
<i>A20</i>	GAACAGCGATCAGGCCAGG	GGACAGTTGGGTGTCTCACATT
<i>Nlrp3</i>	TGGTGACTTTGTATATGCGTG	CTTAGGTCCACACAGAAAGT
<i>Il1β</i>	CAGGATGAGGACATGAGCACC	CTCTGCAGACTCAAACCTCCAC
<i>Il6</i>	TGCTGGTGACAACCACGGC	GTACTCCAGAAGACCAGAGG
<i>Il10</i>	GCCAGAGCCACATGCTCCTA	GATAAGGCTTGGCAACCCAAGTAA
<i>Tnf</i>	CGTCAGCCGATTTGCTATCT	CGGACTCCGCAAAGTCTAAG
<i>Caspase1</i>	AGGCACGGGACCTATGTGAT	AGGGCAAACTTGAGGGTCC
<i>Gsdmd</i>	GATCAAGGAGGTAAGCGGCA	AACACTCCGGTTCTGGTTCT
<i>Smad7</i>	AGGCTGTGTTGCTGTGAATCTTA	TGGGTATCTGGAGTAAGGAGGAG
<i>Pten</i>	CATTGCCTGTGTGTGGTGATATC	TCCTCTGGTCCTGGTATGAAGAA
<i>Bax</i>	ACCAGGGTGGCTGGGAAG	CCTTCCCCTTCCCCCATTC
<i>Pcd4</i>	TCTGAAGCTGAACACTGCCTTAA	TGCACTTTCTCCAGTTGACTCTAA
<i>Ccr7</i>	CAGGTGTGCTTCTGCCAAGAT	GGTAGGTATCCGTCATGGTCT
<i>Gapdh</i>	GGTGAAGGTCGGTGTGAACG	CTCGCTCCTGGAAGATGGTG