Figure S1. The transfection efficiency of Raw264.7 cells. (A) The transfection efficiency of Raw246.7 cells transfected with Cy3-miR-21a-5p mimic for 24 h at 37˚C. (B) The transfection efficiency of Raw264.7 cells transfected with Cy3-SOCS1 siRNA for 24 h at 37˚C. (C) The transfection efficiency of Raw246.7 cells transfected with Cy3-miR-21a-5p inhibitor for 24 h at 37˚C. Scale bar, 50 μm.

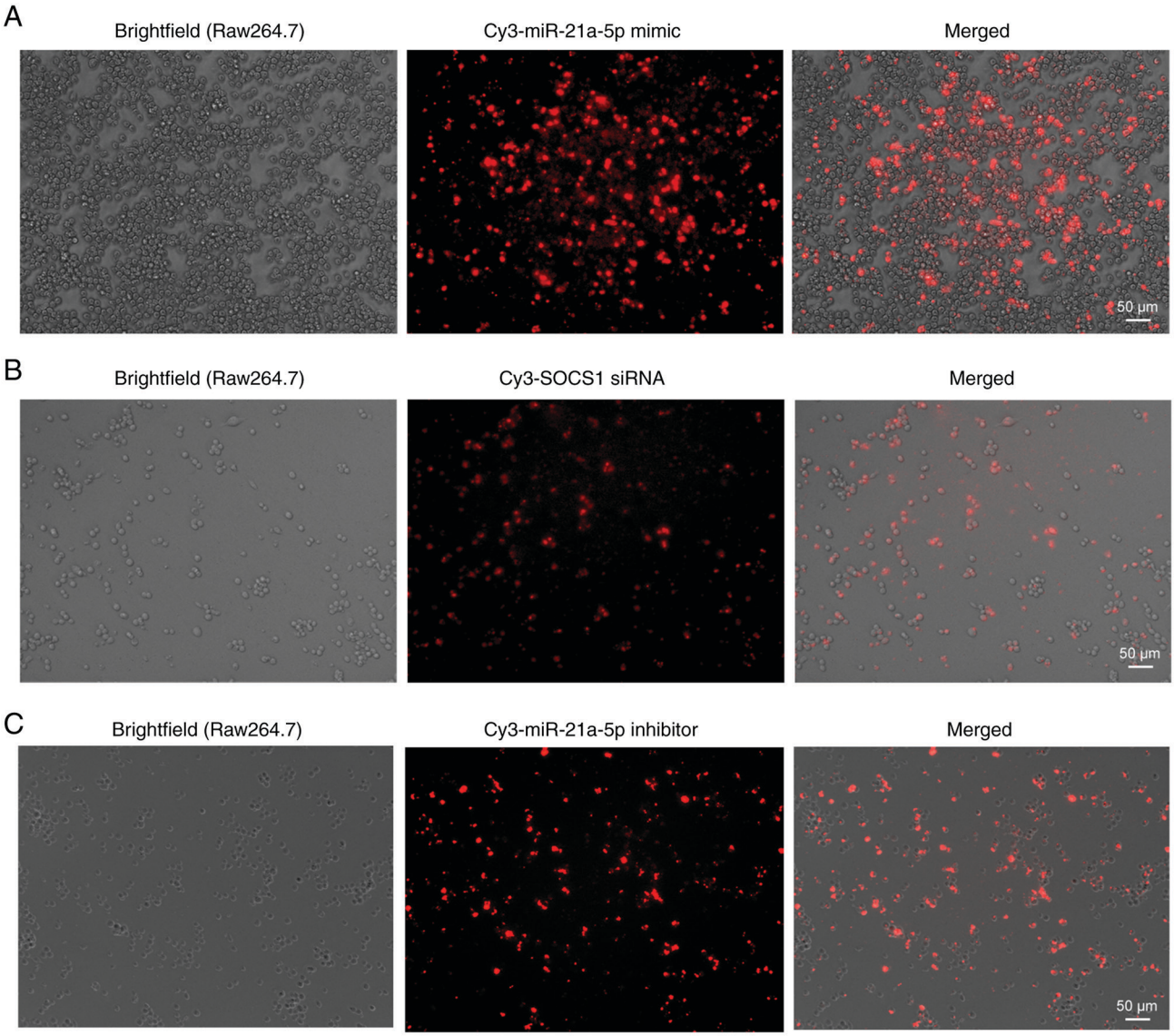

Figure S2. The transfection efficiency of MLE-12, THP1 and 293T cells. (A) The transfection efficiency of MLE-12 cells transfected with FAM-miR-21a-5p mimic for 24 h at 37˚C. (B) The transfection efficiency of THP1 cells transfected with Cy3-miR-21a-5p mimic for 48 h at 37˚C. (C) The transfection efficiency of 293T cells transfected with Cy3-miR-21a-5p mimic for 48 h at 37˚C. Scalebar, 50 μm. FAM, fluorescein amidite.

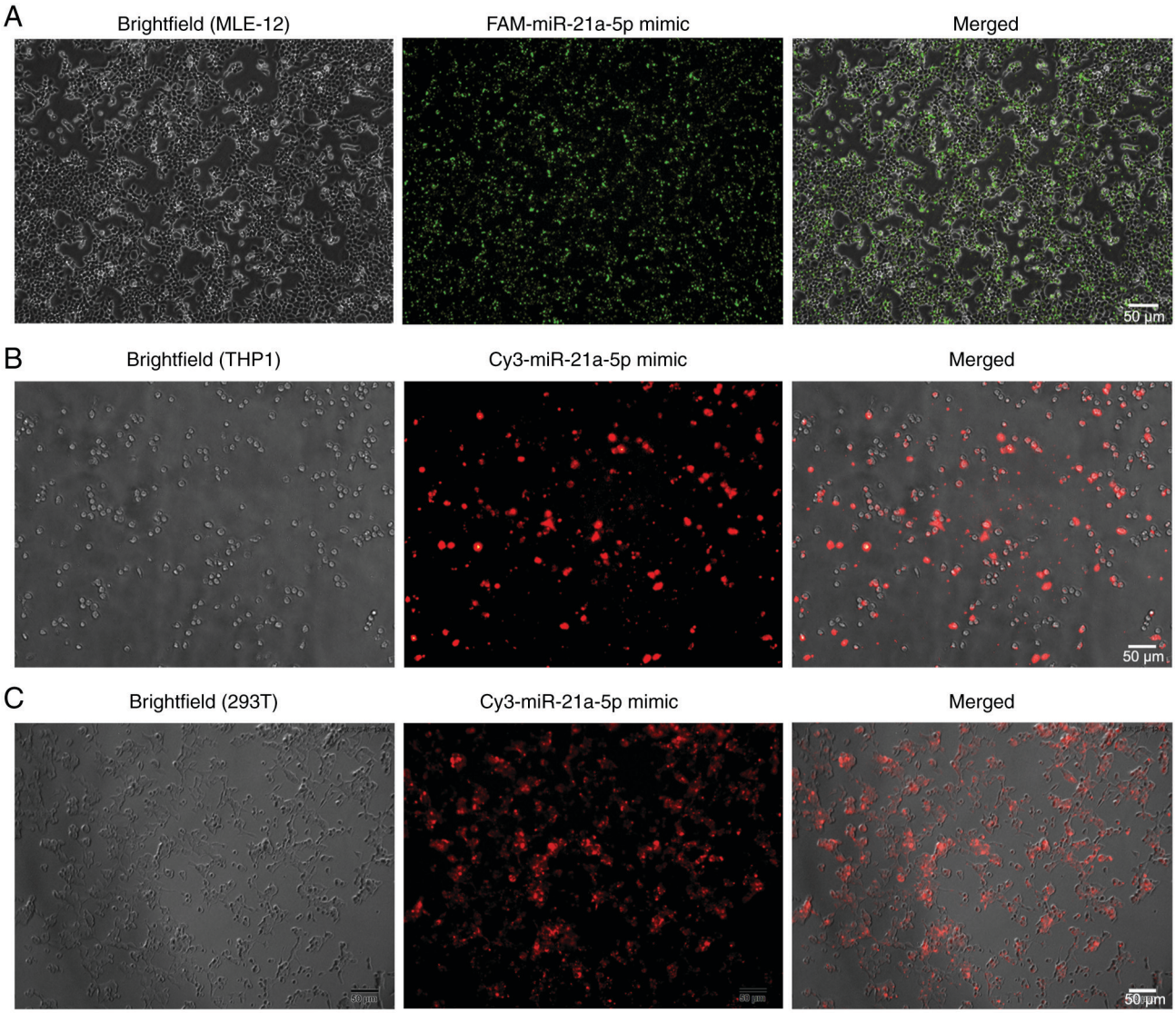

Figure S3. CS doesnot induce inflammation in MLE-12 cells. (A-C) TNF-α, IL-6 and IL-1β levels in the medium of MLE-12 cells subjected to CS, assessed using ELISA (n=4). (D) LDH activity in the medium was assessed usingan assay kit (n=4). Data are expressed as the mean ± SEM. CS, cyclic stretching; ns, not significant.

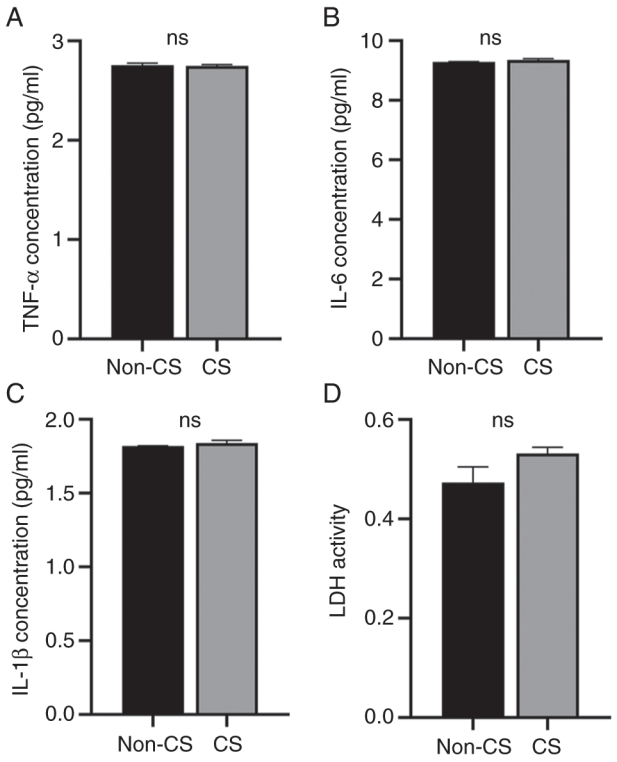

Figure S4. CS upregulates miR-21a-5p expression in MLE-12 cells. miR-21a-5p expression in MLE-12 cells subjected to CS, assessed usingreverse transcription-quantitative PCR (n=6). Data are expressed as the mean ± SEM. **P<0.01, vs. non-CS group. CS, cyclic stretching.

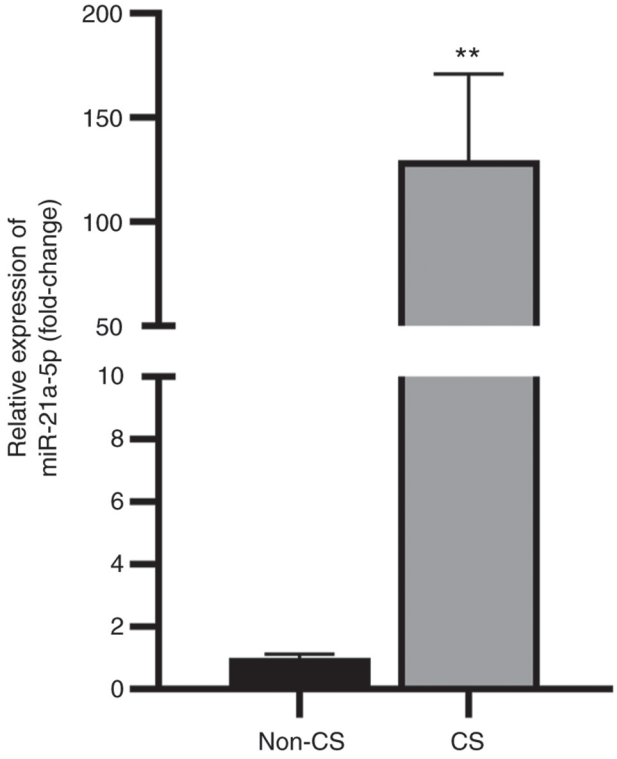

Figure S5. Exosomal FAM-miR-21a-5p uptake by macrophages. Macrophages were co-cultured with PKH26-labeled exosomes from MLE-12 cells transfected with FAM-miR-21a-5p mimic and subjected to CS for 6 h. FAM-miR-21a-5p signals (green) colocalized in the cytoplasm of macrophages with PKH26 (red); nuclei were stained with DAPI (blue), which was verified usingconfocal microscopy. Scale bar, 20 μm. FAM, fluorescein amidite.

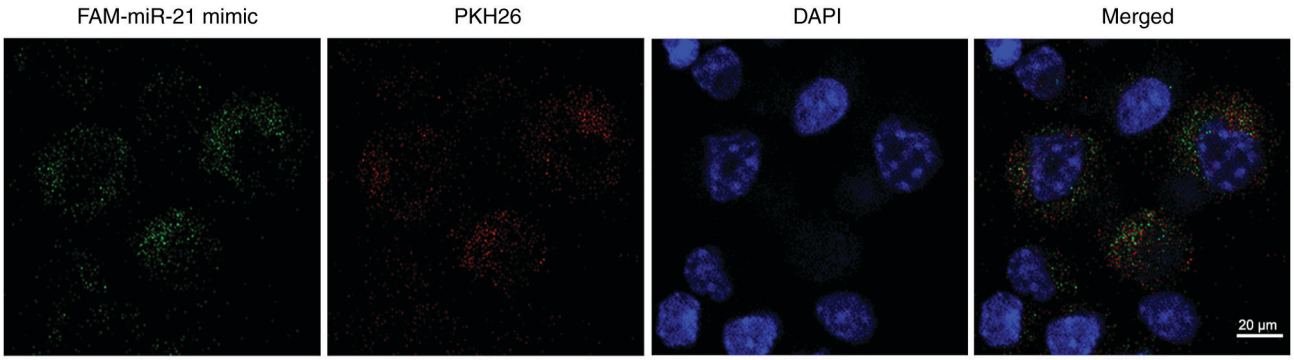

Figure S6. Notch2/SOCS1 axis regulateshuman THP1 cell polarization. (A-C) Notch2/SOCS1 protein expression were assessed usingwestern blot analysis following transfection with miR-21a-5p mimic or NC for 48 h (n=4). (D and E) Macrophage markers, assessed usingreverse transcription-quantitative PCR (n=4). Data are expressed as the mean ± SEM. *P<0.05 and ***P<0.001, vs. NC. NC, negative control; SOCS1, suppressor of cytokine signaling 1; Arg1, arginase 1; HLA-DR, major histocompatibility complex, class II, DR beta 1; CCL22, C-C motif chemokine ligand 22; MRC-1, mannose receptor C-type 1.

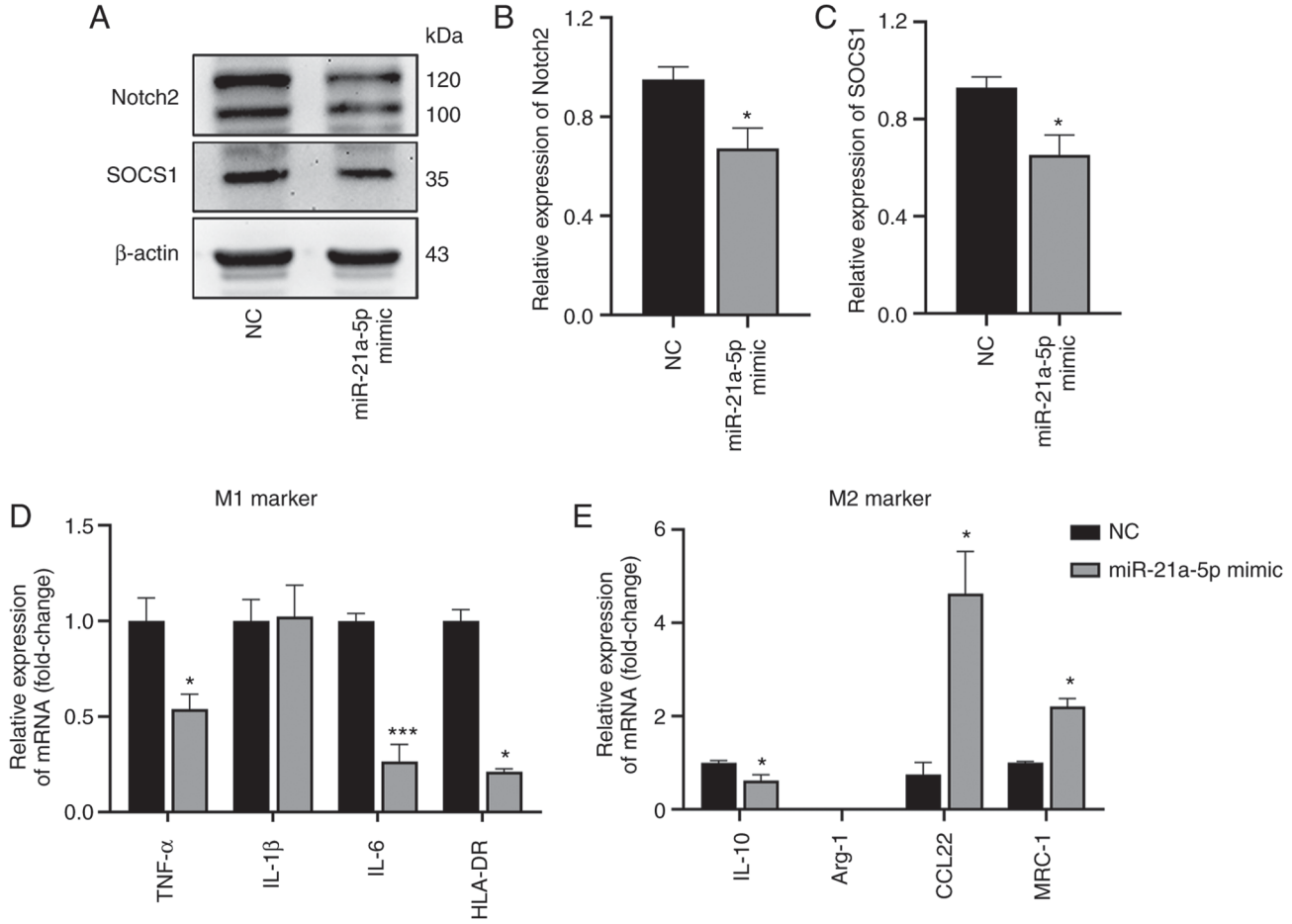

Figure S7. Notch2/SOCS1 is involved in M2 polarization induced by mechanical ventilation *in vivo*. Mice were challenged CS-exo through a tracheal cannula or subjected to mechanical ventilation. Mice were administered miR-21a-5p antagomir or NC 24 h prior to treatment with CS-exo. (A and B) The expression of Notch2 in lung tissues of mice-treated with CS-exo was detected using western blot analysis (n=6). (C and D) Mice were administered miR-21a-5p antagomir or NC 24 h prior to treatment with CS-exo. The expression levels of Notch2 and SOCS1 were measured using western blot analysis (n=6). (E and F) Expression of Notch2 and SOCS1 in lung tissues of mice subjected to LtVt or HtVt or the ctrl procedure for 2 h (n=6). (G and H) Mice were treated with miR-21a-5p agomir or NC 23 h prior to the challenge with JAG. Protein expression of Notch2 and SOCS1 in lung tissues (n=6). (I and J) Mice were treated with miR-21a-5p agomir or NC for 24 h. The expression of CD11c and CD206 of cells in BALF was detected using flow cytometry (n=9). (K and L) miR-21a-5p agomir or NC were administered for 23 h and followed by treatment with JAG for 1 h. The expression CD11c and CD206 of cells in BALF was detected using flow cytometry (n=9). Data are expressed as the mean ± SEM. *P<0.05, vs. control; $^{\#}$P<0.05, vs. agomir + PBS. SOCS1, suppressor of cytokine signaling 1; NC, negative control; LtVt, low-tidal-volume ventilation; HtVt, high-tidal-volume ventilation; JAG, Jagged-1; CS, cyclic stretching; non-CS-exo, incubated with exosomes isolated from medium of cells not subjected to CS; CS-exo, incubated with exosomes isolated from medium of cells subjected to CS.