Supporting Information

Molybdenum Nanodots for Acute Lung Injury Therapy

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Supplementary Figures

Supplementary Figure 1. Photographs showing the synthetic procedure of MNDs.
Supplementary Figure 2. Cytotoxicity studies of MNDs in vitro on RAW 264.7 cells. Cell viability of RAW 264.7 incubated with different concentrations of MNDs for 24 (a) and 48 h (b). Data are presented as means ± SD. n = 3 biological replicates per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. MNDs-treated groups were compared to the untreated group (labeled as zero MNDs concentration in the figure) for statistical significance tests.
Supplementary Figure 3. Cytotoxicity studies of MNDs in vitro on MLE-12 cells. Cell viability of MLE-12 incubated with different concentrations of MNDs for 24 (a) and 48 h (b). Data are presented as means ± SD. n = 3 biological replicates per group. One-way ANOVA with Tukey's multiple comparisons test was performed. MNDs-treated groups were compared to the untreated group (labeled as zero MNDs concentration in the figure) for statistical significance tests.
Supplementary Figure 4. Cell proliferation and migration of MLE-12 cells after exposed for 4 passages culture to MNDs, NiCl\(_2\), or BaP. 

a, Cell proliferation of MLE-12 cells after treated with MNDs, NiCl\(_2\), or BaP, and A549 cells. 
b, Representative images of wound healing assay of MLE-12 cells after treated with MNDs, NiCl\(_2\), or BaP, and A549 cells. Scale bar, 100 μm. 
c, Cell migration rate calculated according to b. Data are presented as means ± SD. 

n = 3 biological replicates per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. ****P<0.0001 compared with the MLE-12 group. BaP, benzo(a)pyrene.
Supplementary Figure 5. Tumorigenic potential in C57BL/6 mice of MLE-12 cells after exposed for 4 passages culture to MNDs, NiCl\textsubscript{2}, or BaP. a, Photos of mice with xenograft tumors dissected, as injected with MLE-12 cells exposed to MNDs, NiCl\textsubscript{2}, or BaP, or LLC1 cells. b, c, Tumors growth volume (b) and weight (c) in the MLE-12, MLE-12 + MNDs, MLE-12 + NiCl\textsubscript{2}, MLE-12 + BaP, and LLC1 groups over 14 days. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. ***P<0.001 and ****P<0.0001 compared with the MLE-12 group in b. BaP, benzo(a)pyrene.
Supplementary Figure 6. Gating of flow cytometry data. Gating strategies used to determine the percentage of Annexin V-FITC+ PI+ and Annexin V-FITC+ PI- cells in RAW 264.7 (a) and MLE-12 (b) for final data presented in Figure 2a and 2c.
Supplementary Figure 7. Confocal fluorescence imaging of MLE-12 with ROS staining. 

a, Representative images of MLE-12 stained for ROS (green) and Hoechst (blue) under different treatment conditions. 

b, Relative fluorescence intensity of ROS from quantitative analysis. Scale bar, 100 μm. Data are presented as means ± SD. n = 3 biological replicates per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. ROS, reactive oxygen species.
Supplementary Figure 8. Schematic illustration of the establishment and treatment schedule of PAO1-induced ALI mice. i.t., intratracheal; ALI, acute lung injury; BALF, bronchoalveolar lavage fluid.
Supplementary Figure 9. MNDs present an antioxidative effect on PAO1-induced ALI mice. a, The concentration of MPO in BALF of mice in control, normal saline, 0.1 mg/kg MNDs, and 1 mg/kg MNDs groups. b, c, Concentrations of MDA(b) and SOD (c) in lung homogenates of mice in control, normal saline, 0.1 mg/kg MNDs, and 1 mg/kg MNDs groups. Data are presented as means ± SD. n = 4 animals for the control group and n = 5 animals for the other three treatment groups. One-way ANOVA with Tukey’s multiple comparisons test was performed. ALI, acute lung injury; BALF, bronchoalveolar lavage fluid; MPO, myeloperoxidase; SOD, superoxide dismutase; MDA, malondialdehyde.
Supplementary Figure 10. MNDs ameliorate lung inflammation in PAO1-induced ALI mice. a, Immunofluorescence staining of lungs of mice with F4/80 (green, monocyte/macrophage marker), Ly6G (red, neutrophil marker) and DAPI (blue) in control, normal saline, 0.1 mg/kg MNDs, and 1 mg/kg MNDs groups. Scale bar, 200 μm. b, c, Relative fluorescence intensity of F4/80 (b) and Ly6G (c) from quantitative analysis. Data are presented as means ± SD. n = 4 animals for the control group and n = 5 animals for the other three treatment groups. One-way ANOVA with Tukey’s multiple comparisons test was performed. ALI, acute lung injury.
Supplementary Figure 11. PCA analysis of RNA-seq datasets across ALI-MNDs and ALI groups. Each dot represents each sample, color coded by group. n = 5 animals per group. ALI, acute lung injury; PCA, principal component analysis.
Supplementary Figure 12. KEGG pathway enrichment analysis of specified genes that are differentially expressed. The 20 most significantly enriched pathways except the category of human diseases were shown. n = 5 animals per group. KEGG, Kyoto Encyclopedia of Genes and Genomes; TNF, tumor necrosis factor; IL-17, interleukin 17; JAK-STAT, Janus kinase-signal transducers and activators of transcription.
Supplementary Figure 13. GSEA of ALI-MNDs and ALI groups. GSEA of ALI-MNDs and ALI groups using peroxisome-associated signature (a), tight junction-associated signature (b), and positive regulation of endothelial cells proliferation-associated signature (c). n = 5 animals per group. GSEA, gene set enrichment analysis; ALI, acute lung injury; KEGG, Kyoto Encyclopedia of Genes and Genomes; GO, Gene Ontology; NES, normalized enrichment score; FDR, false discovery rate.
Supplementary Figure 14. Quantitative real-time PCR analysis of genes related to NLRP3-dependent pyroptotic pathway in BMDMs. mRNA levels of Nlrp3 (a), Casp1 (b), Gsdmd (c), and Il1b (d) in BMDMs in control, LPS + ATP, and LPS + ATP + MNDs groups. Data are presented as means ± SD. n = 3 biological replicates per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. LPS, lipopolysaccharide; ATP, adenosine triphosphate; NLRP3, Nod-like receptor protein 3; BMDMs, bone marrow-derived macrophages.
Supplementary Figure 15. Western blot analysis of the indicated proteins related to NLRP3-dependent pyroptotic pathway in BMDMs. a, Western blot analysis of the indicated proteins in BMDMs in control, LPS + ATP, LPS + ATP + MNDs, and LPS + ATP + MCC950 groups. b, Relative quantification of the blots presented in a. Data are presented as means ± SD. n = 3 biological replicates per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. Statistical significance was calculated between the control and LPS group, as well as the LPS and LPS + MNDs group in b. BMDMs, bone marrow-derived macrophage; LPS, lipopolysaccharide; ATP, adenosine triphosphate; NLRP3, Nod-like receptor protein 3; IL-1β, interleukin 1 beta; Sup, supernatant.
Supplementary Figure 16. The concentration of IL-1β in culture supernatants of BMDMs as assessed using ELISA. Data are presented as means ± SD. n = 3 biological replicates per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. BMDMs, bone marrow-derived macrophages; LPS, lipopolysaccharide; ATP, adenosine triphosphate; IL-1β, interleukin 1 beta.
Supplementary Figure 17. The expressions of key genes related to apoptosis and necroptosis in ALI-MNDs and ALI groups according to RNA sequencing analysis. Data are presented as means ± SD. n = 5 animals per group. Unpaired Wilcoxon test was performed. ALI, acute lung injury.
Supplementary Figure 18. Western blot analysis of the indicated proteins related to apoptosis and necroptosis in lung tissues of mice. a, Western blot analysis of the indicated proteins in lung tissues in control, LPS, LPS + MNDs, and LPS + MCC950 groups. b, Relative quantification of the blots presented in a. Data are presented as means ± SD. n = 3 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. Statistical significance was calculated between the control and LPS group, as well as the LPS and LPS + MNDs group in b. LPS, lipopolysaccharide.
Supplementary Figure 19. Relative quantification of the blots presented in Figure 6h. Data are presented as means ± SD. n = 3 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. Statistical significance was calculated between the control and LPS group, the LPS and LPS + MNDs group, respectively. LPS, lipopolysaccharide; NLRP3, Nod-like receptor protein 3; IL-1β, interleukin 1 beta.
Supplementary Figure 20. Positive ratio of caspase-1 within lung tissues presented in Figure 6j. Data are presented as means ± SD. n = 4 animals for the control group and n = 5 animals for the other treatment groups. One-way ANOVA with Tukey’s multiple comparisons test was performed. LPS, lipopolysaccharide.
Supplementary Figure 21. Safety and molybdenum toxicity assessment of intratracheal instillation (i.t.) and intravenous administration (i.v.) of MNDs in healthy mice at 1 day. 

a, Serum levels of ALT, AST, and ALP of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. 
b, Serum levels of BUN, CREA, and UA of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. 
c-g, Blood parameters of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. 
h, Viscera index of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. 
i, ALP levels in liver and kidney tissues of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. 
j, The concentration of copper in liver of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CREA, creatinine; UA, uric acid; WBC, white blood cell; LYM, lymphocyte; MON, monocyte; NEUT, neutrophil; RBC, red blood cell; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; PDW, platelet distribution width; HGB, hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; HCT, hematocrit; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit.
Supplementary Figure 22. H&E staining sections of major organs to assess in vivo safety after intratracheal (i.t.) instillation and intravenous (i.v.) administration of MNDs in healthy mice at 1 day. a, H&E staining sections of lungs of mice from control, MNDs i.t., and MNDs i.v. groups. Scale bar, 100 μm. b, Lung injury scores calculated according to a. c, H&E staining sections of other major organs (liver, spleen, kidney, and heart) of mice from control, MNDs i.t., and MNDs i.v. groups. Scale bar, 50 μm. n = 3 animals per group.
Supplementary Figure 23. Safety and molybdenum toxicity assessment of intratracheal instillation (i.t.) and intravenous (i.v.) administration of MNDs in healthy mice at 7 days. a, Serum levels of ALT, AST, and ALP of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. b, Serum levels of BUN, CREA, and UA of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. c-g, Blood parameters of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. h, Viscera index of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. i, ALP levels in liver and kidney tissues of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. j, The concentration of copper in liver of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey's multiple comparisons test was performed. ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CREA, creatinine; UA, uric acid; WBC, white blood cell; LYM, lymphocyte; MON, monocyte; NEUT, neutrophil; RBC, red blood cell; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; PDW, platelet distribution width; HGB, hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; HCT, hematocrit; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit.
Supplementary Figure 24. Safety and molybdenum toxicity assessment of intratracheal instillation (i.t.) and intravenous (i.v.) administration of MNDs in healthy mice at 14 days. a, Serum levels of ALT, AST, and ALP of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. b, Serum levels of BUN, CREA, and UA of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. c-g, Blood parameters of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. h, Viscera index of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. i, ALP levels in liver and kidney tissues of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. j, The concentration of copper in liver of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey's multiple comparisons test was performed. ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CREA, creatinine; UA, uric acid; WBC, white blood cell; LYM, lymphocyte; MON, monocyte; NEUT, neutrophil; RBC, red blood cell; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; PDW, platelet distribution width; HGB, hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; HCT, hematocrit; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit.
Supplementary Figure 25. Safety and molybdenum toxicity assessment of intratracheal instillation (i.t.) and intravenous administration (i.v.) of MNDs in healthy mice at 28 days. a, Serum levels of ALT, AST, and ALP of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. b, Serum levels of BUN, CREA, and UA of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. c-g, Blood parameters of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. h, Viscera index of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. i, ALP levels in liver and kidney tissues of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. j, The concentration of copper in liver of mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CREA, creatinine; UA, uric acid; WBC, white blood cell; LYM, lymphocyte; MON, monocyte; NEUT, neutrophil; RBC, red blood cell; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; PDW, platelet distribution width; HGB, hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; HCT, hematocrit; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit.
Supplementary Figure 26. Weight and food intake of healthy mice over 28 days. Weight (a) and food intake (b) of the mice in control, MNDs i.t., MNDs i.v., and Mo i.v. groups over 28 days. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. **P<0.01 and ****P<0.0001 compared with the control group. i.t., intratracheal; i.v., intravenous.
Supplementary Figure 27. H&E staining sections of major organs to assess in vivo safety after intratracheal (i.t.) instillation and intravenous (i.v.) administration of MNDs in healthy mice at 30 days. 

a, H&E staining sections of lungs of mice from control, MNDs i.t., and MNDs i.v. groups. Scale bar, 100 μm.

b, Lung injury scores calculated according to a.

c, H&E staining sections of other major organs (liver, spleen, kidney, and heart) of mice from control, MNDs i.t., and MNDs i.v. groups. Scale bar, 50 μm. n = 3 animals per group.
Supplementary Figure 28. Safety and molybdenum toxicity assessment of intratracheal instillation (i.t.) and intravenous (i.v.) administration of MNDs in LPS-induced ALI mice at 14 days. 
a, Serum levels of ALT, AST, and ALP of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. 
b, Serum levels of BUN, CREA, and UA of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. 
c-g, Blood parameters of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. 
h, ALP levels in liver and kidney tissues of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. 
i, Viscera index of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. 
Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. 
ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CREA, creatinine; UA, uric acid; WBC, white blood cell; LYM, lymphocyte; MON, monocyte; NEUT, neutrophil; RBC, red blood cell; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; PDW, platelet distribution width; HGB, hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; HCT, hematocrit; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit; LPS, lipopolysaccharide; ALI, acute lung injury.
Supplementary Figure 29. Safety assessment of whether MNDs could induce lung inflammation or fibrosis in LPS-induced ALI mice at 14 days.

**a**, The concentration of TGF-β1 in lung tissues of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups.

**b**, mRNA levels of Col1a2, Fn1, and Vim in the lung tissues of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups.

**c**, Representative images of H&E stained-lung sections of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. Scale bar of whole lung scan, 1 mm; Scale bar of microscopic image, 100 μm.

**d**, Lung injury scores calculated
according to c. e, Representative images of Masson’s trichrome stained-lung sections of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. Scale bar of whole lung scan, 1 mm; Scale bar of microscopic image, 100 μm. f, Quantification of collagen deposition by image analysis using ImageJ software according to e. Data are presented as means ± SD. n = 4 animals for the control group and n = 5 animals for the other five treatment groups. One-way ANOVA with Tukey’s multiple comparisons test was performed. TGF-β1, transforming growth factor beta 1; LPS, lipopolysaccharide; i.t., intratracheal; i.v., intravenous; ALI, acute lung injury.
Supplementary Figure 30. Safety and molybdenum toxicity assessment of intratracheal instillation (i.t.) and intravenous (i.v.) administration of MNDs in LPS-induced ALI mice at 21 days. a, Serum levels of ALT, AST, and ALP of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. b, Serum levels of BUN, CREA, and UA of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. c-g, Blood parameters of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. h, ALP levels in liver and kidney tissues of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. i, Viscera index of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CREA, creatinine; UA, uric acid; WBC, white blood cell; LYM, lymphocyte; MON, monocyte; NEUT, neutrophil; RBC, red blood cell; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; PDW, platelet distribution width; HGB, hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; HCT, hematocrit; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit; LPS, lipopolysaccharide; ALI, acute lung injury.
Supplementary Figure 31. Safety assessment of whether MNDs could induce lung inflammation or fibrosis in LPS-induced ALI mice at 21 days.

a, The concentration of TGF-β1 in lung tissues of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups.

b, mRNA levels of Col1a2, Fn1, and Vim in the lung tissues of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups.

c, Representative images of H&E stained-lung sections of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. Scale bar of whole lung scan, 1 mm; Scale bar of microscopic image, 100 μm.

d, Lung injury scores calculated.
according to c. e, Representative images of Masson’s trichrome stained-lung sections of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. Scale bar of whole lung scan, 1 mm; Scale bar of microscopic image, 100 μm. f, Quantification of collagen deposition by image analysis using ImageJ software according to e. Data are presented as means ± SD. n = 4 animals for the control group and n = 5 animals for the other five treatment groups. One-way ANOVA with Tukey’s multiple comparisons test was performed. TGF-β1, transforming growth factor beta 1; LPS, lipopolysaccharide; i.t., intratracheal; i.v., intravenous; ALI, acute lung injury.
Supplementary Figure 32. Safety and molybdenum toxicity assessment of intratracheal instillation (i.t.) and intravenous (i.v.) administration of MNDs in LPS-induced ALI mice at 28 days. a, Serum levels of ALT, AST, and ALP of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. b, Serum levels of BUN, CREA, and UA of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. c-g, Blood parameters of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. h, ALP levels in liver and kidney tissues of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. i, Viscera index of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; BUN, blood urea nitrogen; CREA, creatinine; UA, uric acid; WBC, white blood cell; LYM, lymphocyte; MON, monocyte; NEUT, neutrophil; RBC, red blood cell; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; PDW, platelet distribution width; HGB, hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; HCT, hematocrit; MCV, mean corpuscular volume; MPV, mean platelet volume; PCT, plateletcrit; LPS, lipopolysaccharide; ALI, acute lung injury.
Supplementary Figure 33. Safety assessment of whether MNDs could induce lung inflammation or fibrosis in LPS-induced ALI mice at 28 days. 

a, The concentration of TGF-β1 in lung tissues of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. 
b, mRNA levels of Col1a2, Fn1, and Vim in the lung tissues of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. 
c, Representative images of H&E stained-lung sections of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. Scale bar of whole lung scan, 1 mm; Scale bar of microscopic image, 100 μm. 
d, Lung injury scores calculated according to c. 
e, Representative images of Masson’s trichrome stained-lung sections of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. 
f, Collagen deposition (%) in the lung tissues of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups.
sections of mice in control, LPS + normal saline, LPS + 1 mg/kg MNDs i.t., LPS + 1 mg/kg MNDs i.v., LPS + 50 mg/kg MNDs i.v., and bleomycin groups. Scale bar of whole lung scan, 1 mm; Scale bar of microscopic image, 100 μm. 
f. Quantification of collagen deposition by image analysis using ImageJ software according to e. Data are presented as means ± SD. n = 4 animals for the control group and n = 5 animals for the other five treatment groups. One-way ANOVA with Tukey’s multiple comparisons test was performed. TGF-β1, transforming growth factor beta 1; LPS, lipopolysaccharide; i.t., intratracheal; i.v., intravenous; ALI, acute lung injury.
Supplementary Figure 34. Weight and food intake of LPS-induced ALI mice over 28 days. Weight (a) and food intake (b) of ALI mice in normal saline, 1 mg/kg MNDs i.t., 1 mg/kg MNDs i.v., 50 mg/kg MNDs i.v., and 50 mg/kg Mo i.v. groups over 28 days. Data are presented as means ± SD. n = 5 animals per group. One-way ANOVA with Tukey’s multiple comparisons test was performed. i.t., intratracheal; i.v., intravenous; LPS, lipopolysaccharide; ALI, acute lung injury.
Supplementary Figure 35. Biopersistence of MNDs in the mouse lung. n = 5 animals per group.
### Supplementary Table 1. Primers used in this study.

<table>
<thead>
<tr>
<th>Primer sequences for qPCR</th>
<th>Mouse Nlrp3 F</th>
<th>TAAGAACTGTAGGCTAGGGTCAAAACG</th>
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<tr>
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