Supplementary methods

1 Characterization of COS

The compositions of COS were determined with liquid chromatography-mass spectrometry (LC-MS). In brief, high performance liquid chromatography (HPLC) (DIONEX, USA) was performed on a Dionex UltiMate3000 HPLC system equipped with an evaporation light scattering detector (ELSD) and a μ-Bondapack NH_2 column (3.9*300 mm, 10 μm, Waters, USA). The chromatographic conditions are as follows: mobile phase acetonitrile-water (7:3) at 1.0 mL/min, column temperature 30ºC, evaporation chamber temperature 90ºC, detection wavelength 254 nm. The mass spectrometer (WATERS MALDI SYNAPT Q-TOF MS, Waters Corporation, USA) was conducted in positive ion mode, with MS scans run over a range of m/z 100 to 1100. The detailed conditions as follows: capillary voltage 3.5 kV, TOF detector voltage 1800 V, source block temperature 120℃, desolvation temperature 280℃, desolvation gas flow 700 L/h, cone gas flow 50 L/h.

2 Histopathological and immunohistochemistry analysis

Hematoxylin-eosin staining: Tissues were carefully soaked for 24 h in 4% formalin solution (pH 7.0) and embedded in paraffin, then the paraffin was sliced at the center of the tissue to produce 5 μm paraffin tissue flakes, which were dewaxed in xylene for 5-10 min, replaced with fresh xylene and dewaxed for another 5-10 min, immersed in absolute ethanol for 5 min, then separately immersed in 90%, 80% and 70% ethanol for 2 min in proper order. Then slides were rinsed with distilled water for 2 min. After that, slides were stained with hematoxylin solution for 5-10 min, washed with water to remove the excess staining solution for 10 min, successively washed again quickly with distilled water, and then stained with eosin staining solution for 1 min. Then slides were immersed in 70%, 80%, 90% and absolute ethanol for 10 sec in proper order, and then submerged in xylene for 5 min. Finally, after the slides were sealed, they were observed under the microscope that the nucleus was blue and the cytoplasm was pink or red (Nikon, Japan).

Masson's trichrome staining: After being deparaffinized, the slides were placed into the slide holder containing the Bouin's solution for 1 h at 60°C. Then slides were washed in running tap water for 5 min to ensure complete removal of the Bouin's solution and transferred into a coplin jar. Next, tissue sections were stained with Weigert's iron hematoxylin for 10 min. After being washed in running tap water for 5 min and rinsed twice in distilled water, slides were incubated in Biebrich scarlet-acid fuchsin solution for 5 min. Slides were placed in phosphotungstic/phosphomolybdic acid solution for 10 min after being washed, and then transferred to aniline blue for 5 min. Rinsed with distilled water for three times, slides were incubated in 1% acetic acid for 1 min to differentiate the colors of the dyed tissue structures. Then the slides were first rinsed in distilled water and then sequentially dehydrated in 95%, 100% ethanol for 2 min each. After that, slides were cleared in xylene for 2 min and mounted with Cytoseal XYL mounting medium. Finally, image sections were presented by using a light microscope (Nikon, Japan). To visualize the collagen deposition/distribution in different affected

organs/tissues and compare it to the corresponding healthy tissues, the fibrotic areas stained with Masson's Trichrome were showed blue staining.

Immunohistochemistry: Tissue slides were dewaxed in xylene for 5-10 min, replaced with fresh xylene and dewaxed for another 5-10 min, immersed in absolute ethanol for 5 min, and then separately immersed in 90%, 80% and 70% ethanol for 2 min in proper order. Slides were Then rinsed with distilled water for 2 min. After that, tissue slides are blocked in 10% (v/v) normal serum in PBS for 20 min. Blocked tissue slides were incubated with primary antibody diluted in PBS with antibody dilution buffer at room temperature for the time indicated for each antibody. The volume of primary antibody solution should be enough to cover the tissue on the slide. After being incubated with the primary antibody, the tissue slides were washed twice with PBS for 5 min. After being washed, the tissues were incubated with HRP-polymer secondary antibody for 30 min at 37°C. Slides were washed twice with PBS for 5 min and incubated in freshly prepared ABC reagent for 30 min, then washed twice with PBS. After that, slides were incubated with 0.1% diaminobenzidine (DAB) for 5 min, rinsed in tap water for 2 min, rinsed with deionized water successively. For counterstaining, slides were incubated in Mayer's hematoxylin for 30 s and rinsed with tap water for 5 min. Dehydrated in 70%, 95%, and 100 % ethanol for 2 min each, slides were immersed in xylene for 5 min. After three cycles repeated, slides were mounted with cover glass and analyzed under an optical microscope (Nikon, Japan). Positive areas were indicated and demonstrated with brown/dark color, which were quantified by the percentage of total area (n = 10 random, visual fields per group) by ImageJ software (NIH, USA).

Western blot: Total proteins were extracted from liver by protein extraction buffer. Proteins were separated by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and then transferred to polyvinylidene fluoride membranes. Next, the membranes were soaked in the blocking solution with continuous gentle shaking or rocking at room temperature for 1 h and then probed with primary antibodies overnight at 4°C. After being washed for three times with TBST solution for 15 min each, the membranes were incubated in TBST solution with secondary antibodies for 1-2 h at room temperature. Then the membranes were continued to be washed with TBST three times for 15 min each, the target protein blots were visualized by ECL reagents (Thermofisher Scientific, MA, USA). The levels of target protein were analyzed quantitatively by ImageJ software (NIH, USA).

Supplementary results

Species	Gene	Forward (5′–3′)	Reverse (5′–3′)	Accession NO.
Mouse	α-SMA	CCCAGACATCAGGGAGTA	TCTATCGGATACTTCAGCGT	AK002886
Mouse	COL1a1	GCTCCTCTTAGGGGCCAC	CCACGTCTCACCATTGGGG	NM_007742
Mouse	COL4a1	CTGGCACAAAAGGGAC	ACGTGGCCGAGAATTTCACC	NM_009931
Mouse	TGF-β1	CTCCCGTGGCTTCTAGTGC	GCCTTAGTTTGGACAGGATC	NM_011577
Mouse	TNF-α	ACCACGCTCTTCTGTCTAC	TCCACTTGGTGGTTTGCTAC	NM_013693
Mouse	IL-6	CAAAGCCAGAGTCCTTCA	GTCCTTAGCCACTCCTTCTG	NM_031168
Mouse	IL-4	GGTCTCAACCCCCAGCTAGT	GCCGATGATCTCTCTCAAGTGAT	NM_021283
Mouse	IL-1β	GCAACTGTTCCTGAACTC	ATCTTTTGGGGTCCGTCAAC	NM_008361
Mouse	MCP-1	GAGGACAGATGTGGTGGG	AGGAGTCAACTCAGCTTTCT	NM_008570
Mouse	ARG-1	CTCCAAGCCAAAGTCCTTAG	AGGAGCTGTCATTAGGGACATC	NM_007482
Mouse	MRC-1	CTCTGTTCAGCTATTGGACGC	CGGAATTTCTGGGATTCAGCTTC	NM_008625
Mouse	MRC-2	TCTCCCGGAACCGACTCTTC	GGTCGAGCACATAGGTCTTCT	NM_008626
Mouse	GAPDH	AGGTCGGTGTGAACGGAT	TGTAGACCATGTAGTTGAGG	NM_008084
Human	α-SMA	CTATGAGGGCTATGCCTTGCC	GCTCAGCAGTAGTAACGAAGGA	NM_001613
Human	COL1a1	ATCAACCGGAGGAATTTCCG	CACCAGGACGACCAGGTTTTC	NM_000088
Human	COL4a1	CCAGGGGTCGGAGAGAAAG	GGTCCTGTGCCTATAACAATTCC	NM_001845
Human	TGF-β1	GGCCAGATCCTGTCCAAGC	GTGGGTTTCCACCATTAGCAC	NM_000660
Human	TIMP-1	AGAGTGTCTGCGGATACTTCC	CCAACAGTGTAGGTCTTGGTG	NM_003254
Human	TIMP-2	GCTGCGAGTGCAAGATCAC	TGGTGCCCGTTGATGTTCTTC	NM_003255
Human	GAPDH	CTGGGCTACACTGAGCACC	AAGTGGTCGTTGAGGGCAATG	NM_001256799

Table. S1. Specific primers used for qRT-PCR analysis.

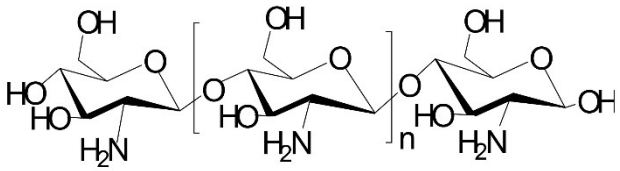

Fig. S1. The structure of COS (n=0, 1, 2).

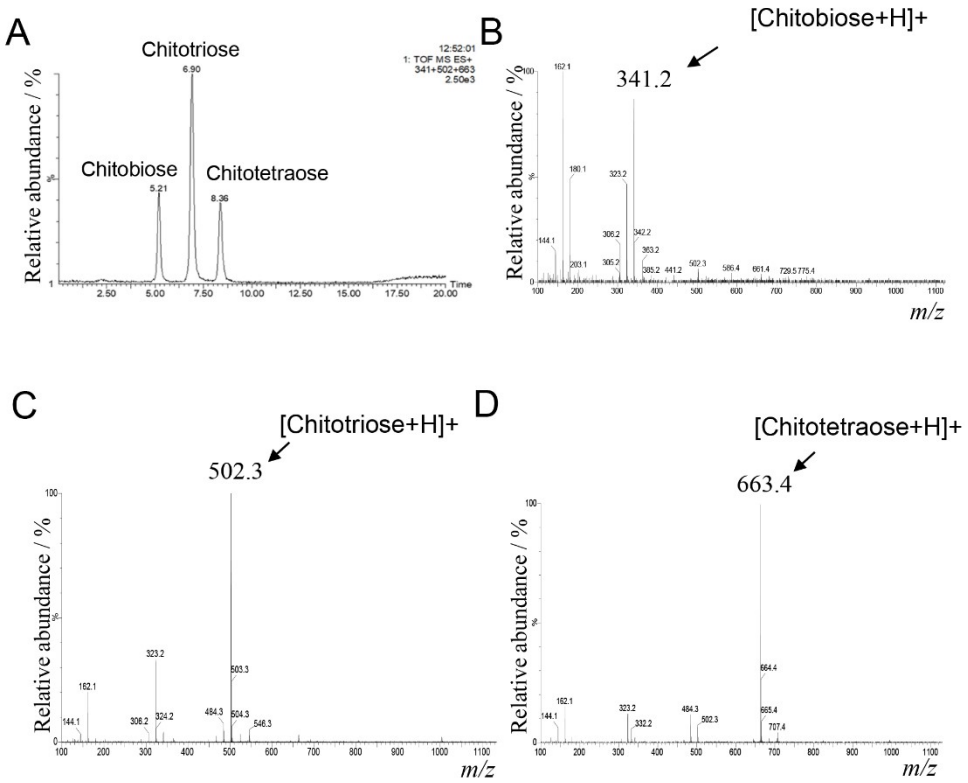

Fig. S2. Characterization of COS by LC-MS in positive ion mode. (A) The LC chromatogram of COS. The mass/charge ratio and intensities (%) of mass spectrum peaks of chitobiose (B), chitotriose (C) and chitotetraose (D).

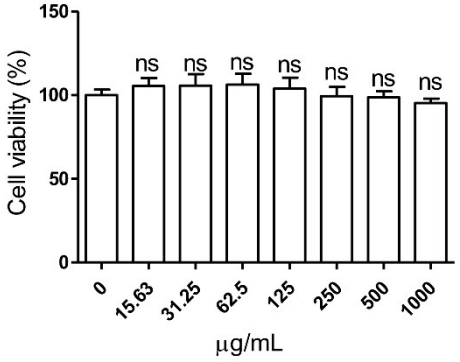

Fig.S3. Evaluation of COS toxicity on KCs. COS was added to stimulate KCs proliferation for 24 h, the proliferation of KCs was measured by CCK-8 assay. All values are means ± S.D (n=6). No statistical difference (ns P >0.05) in COS group compared with CTL group.

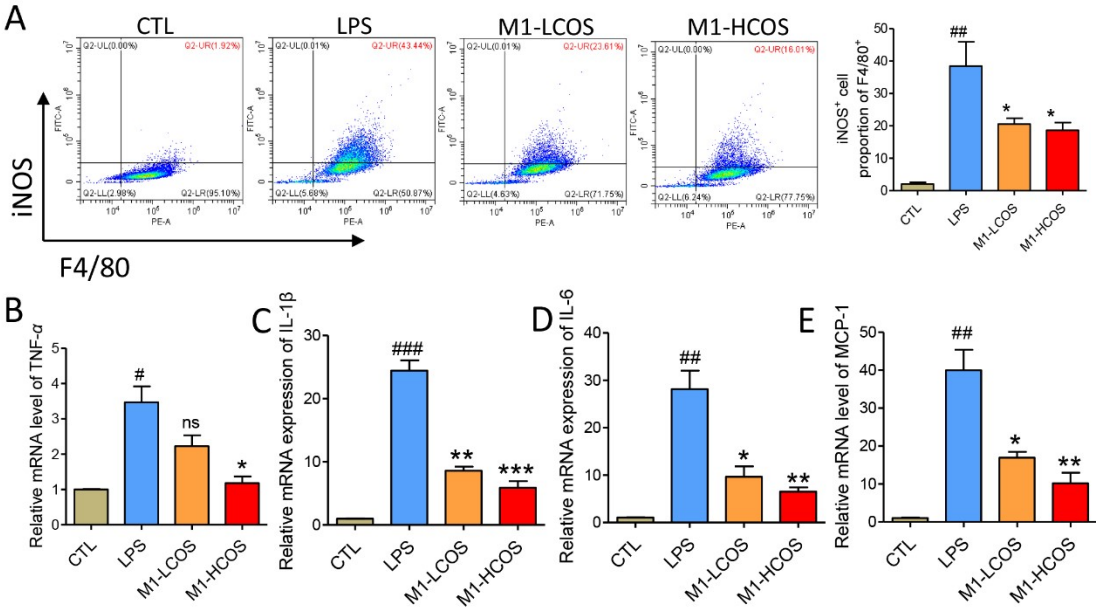

Fig. S4. M1 polarization was suppressed by COS *in vitro*. (A) The quantification of F4/80 and iNOS positive cell number was analyzed by flow cytometry. (B) The mRNA level of TNF-α. (D) The mRNA level of IL-1β. (E) The mRNA level of IL-6. (F) The mRNA level of MCP-1. All values were expressed as means ± S.D (n=3) and the results were analyzed by a one-way analysis of variance (ANOVA). Significantly different ($^{\#}P < 0.05$, $^{\#\#}P < 0.01$, $^{\#\#\#}P < 0.001$) versus CTL group. Significantly different ($^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$) versus LPS group. No statistical difference (ns P >0.05) compared with LPS group.

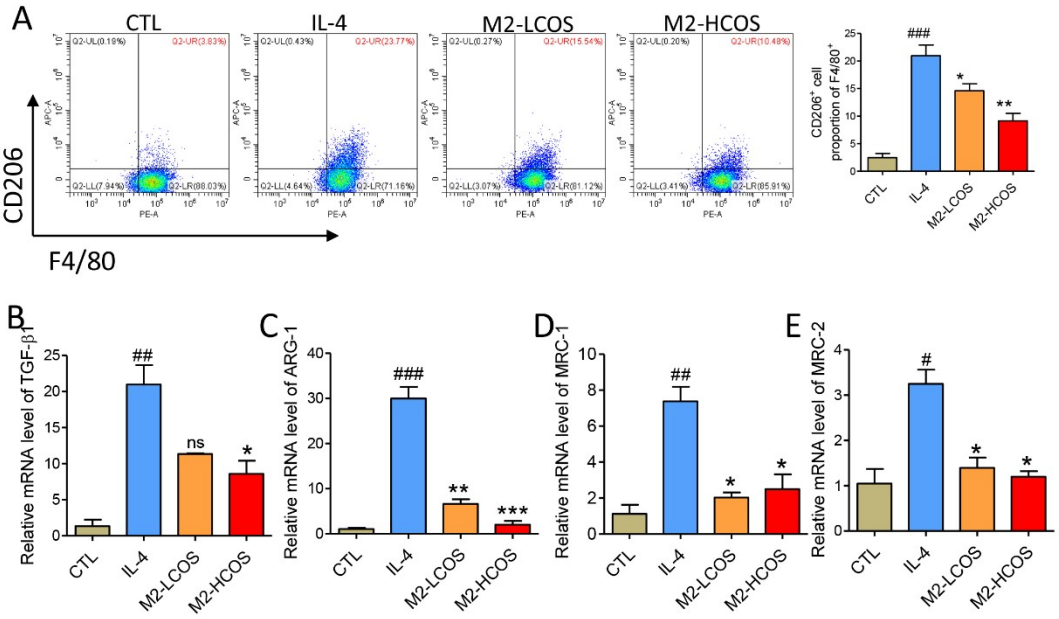

Fig. S5. M2 polarization was suppressed by COS *in vitro.* (A) The quantification of F4/80 and CD206 positive cell number was analyzed by flow cytometry. (B) The mRNA level of TGF-β1. (D) The mRNA level of ARG-1. (E) The mRNA level of MRC-1. (F) The mRNA level of MRC-2. All values were expressed as means ± S.D (n=3) and the results were analyzed by a one-way analysis of variance (ANOVA). Significantly different ($^{\#}P < 0.05$, $^{\#\#}P < 0.01$, $^{\#\#\#}P < 0.001$) versus CTL group. Significantly different ($^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$) versus IL-4 group. No statistical difference (ns $P > 0.05$) compared with IL-4 group.

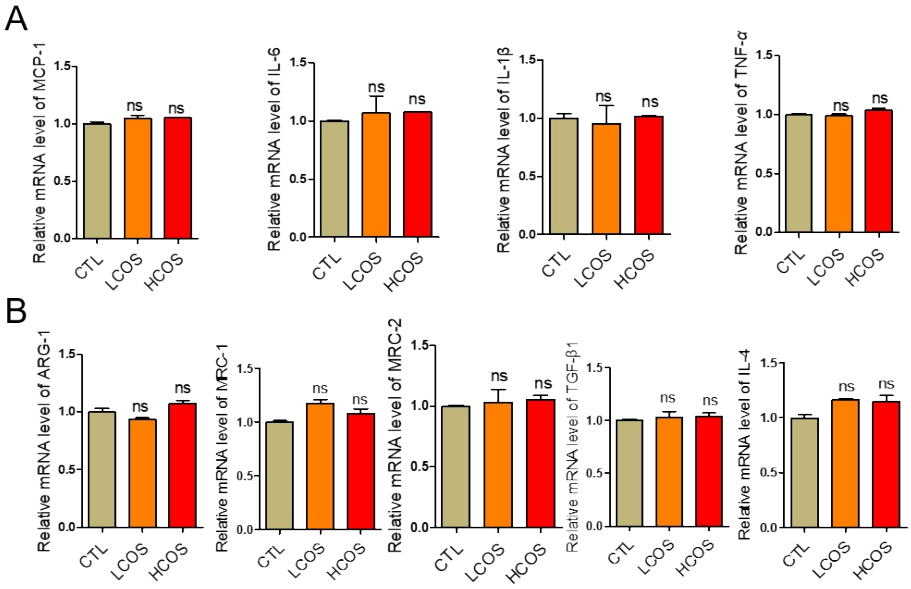

Fig.S6. Evaluation the effects of COS on KCs polarization *in vitro*. (A) The markers of M1 macrophages in KCs were supplemented with COS and cultured for 24 h. (B) The markers of M2 macrophages in KCs were supplemented with COS and cultured for 24 h. All values are means ± S.D (n=3). No statistical difference (ns $P > 0.05$) in LCOS and HCOS groups compared with CTL group.

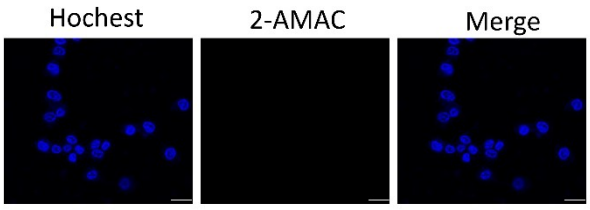

Fig.S7. Cellular uptake of control antibody 2-AMAC depicted by CLSM. Scale bars: 25 μm.

Western blots images

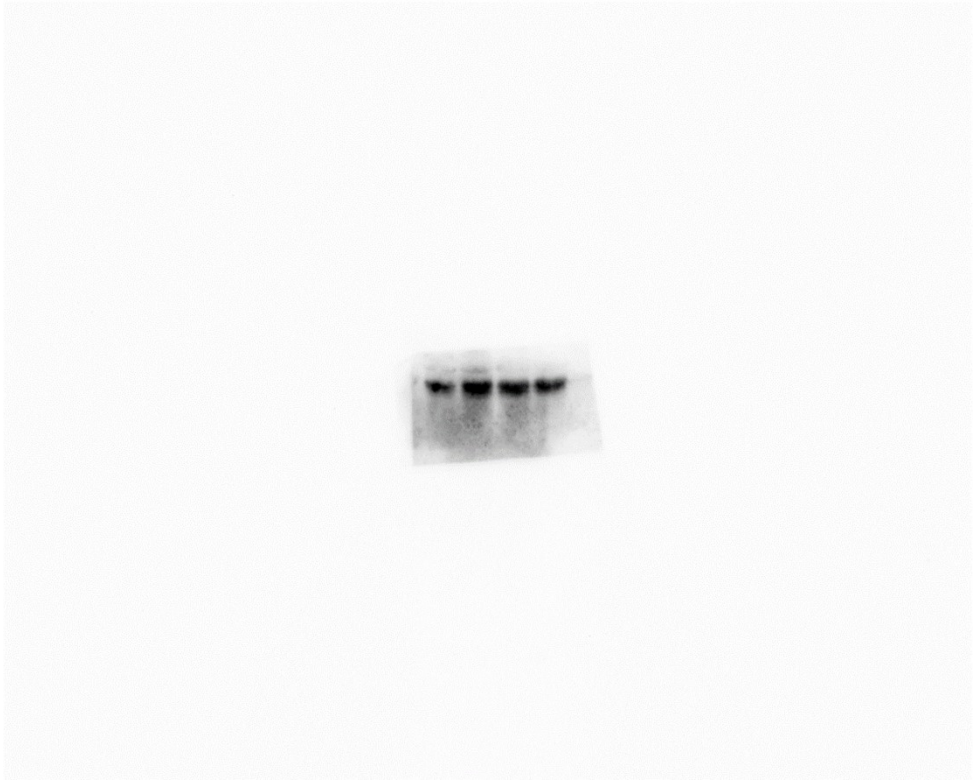

Fig.S8. Western blots image of TGF-β1 in Fig. 3A.

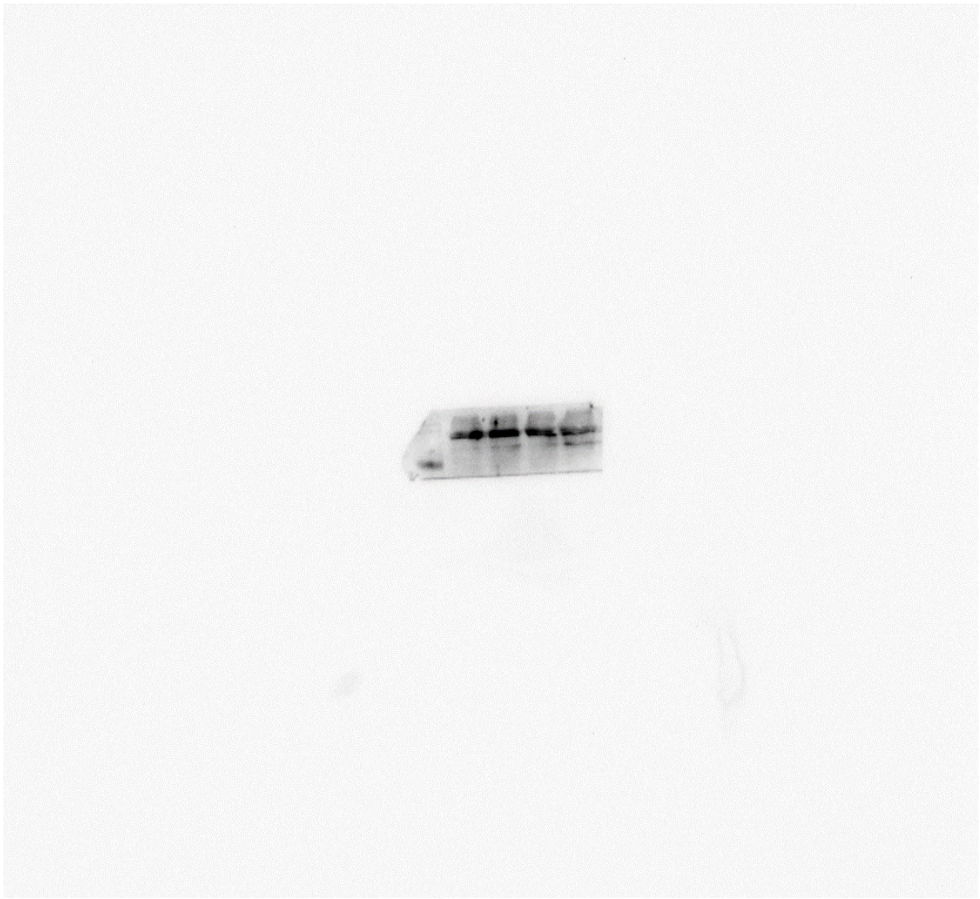

Fig.S9. Western blots image of TNF-α in Fig. 3A.

Fig.S10. Western blots image of ARG-1 in Fig. 3A.

Fig.S11. Western blots image of iNOS in Fig. 3A.

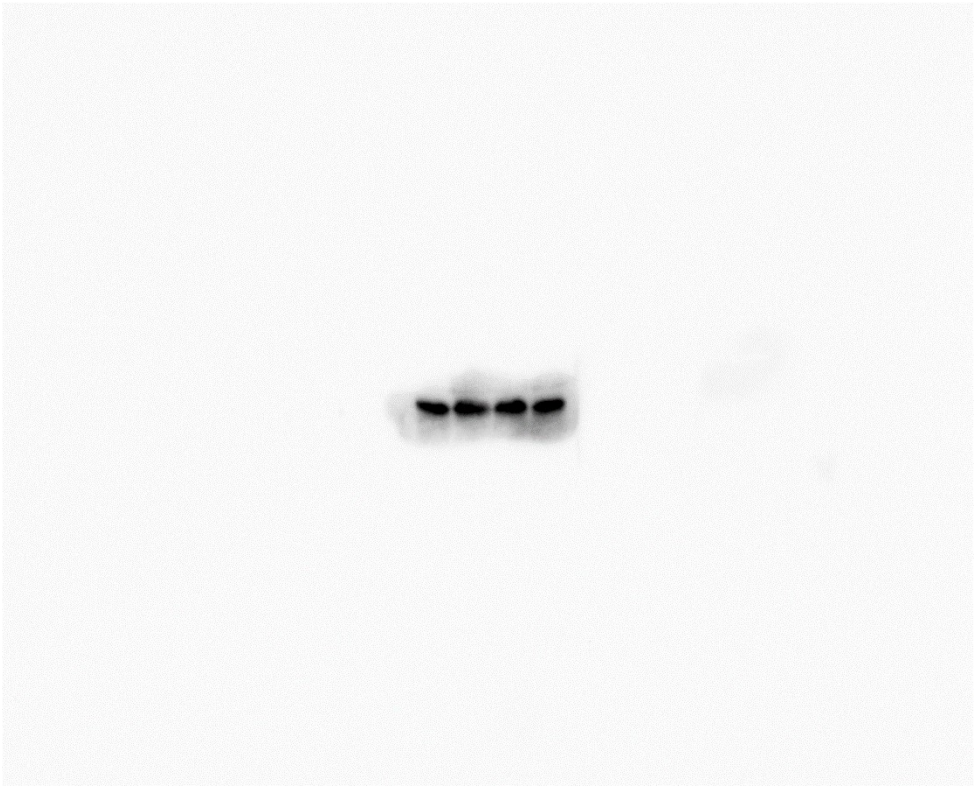

Fig.S12. Western blots image of GAPDH in Fig. 3A.

Fig.S13. Western blots image of α-SMA in Fig. 4H.

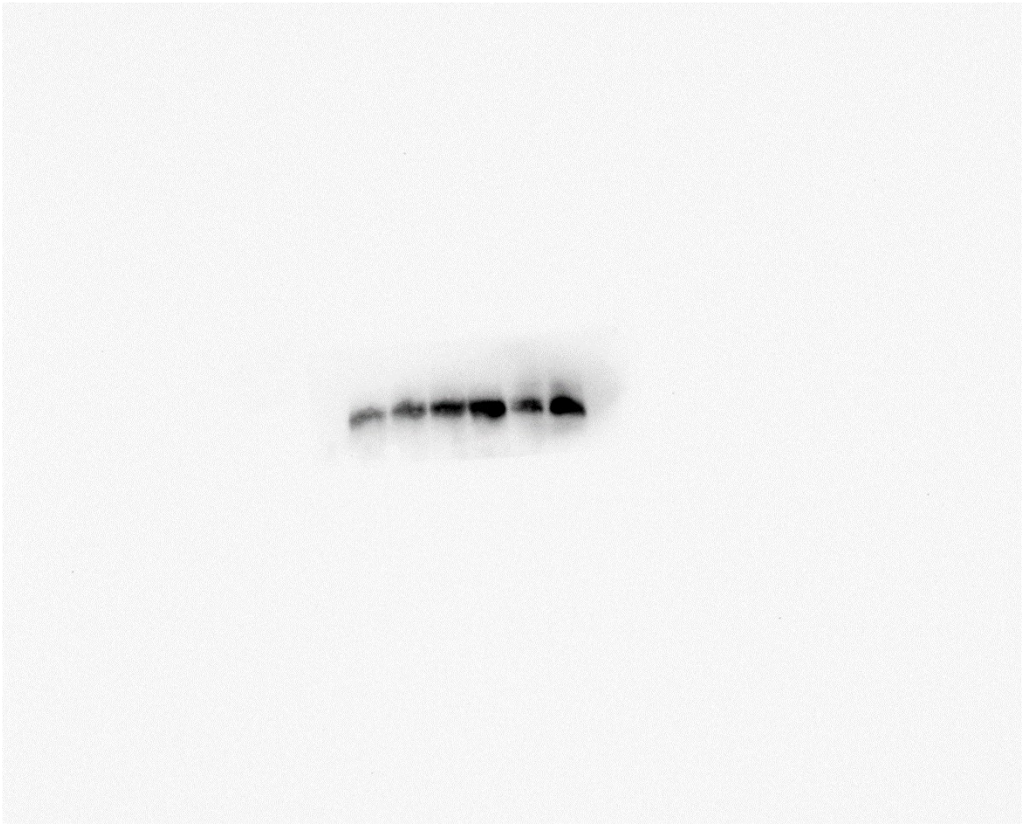

Fig.S14. Western blots image of COL1 in Fig. 4H.

Fig.S15. Western blots image of GAPDH in Fig. 4H.

Fig.S16. Western blots image of IL-1β in Fig. 7A.

Fig.S17. Western blots image of iNOS in Fig. 7A.

Fig.S18. Western blots image of P-JAK2 in Fig. 7A.

Fig.S19. Western blots image of JAK2 in Fig. 7A.

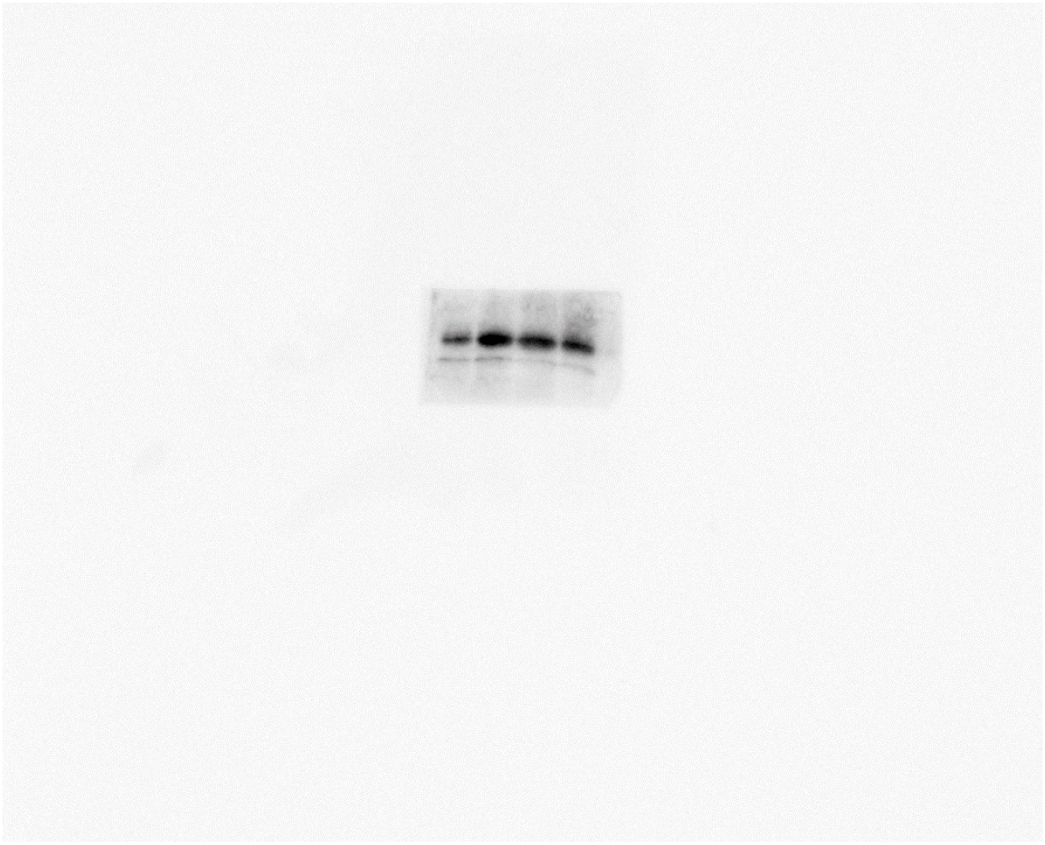

Fig.S20. Western blots image of P-STAT1 in Fig. 7A.

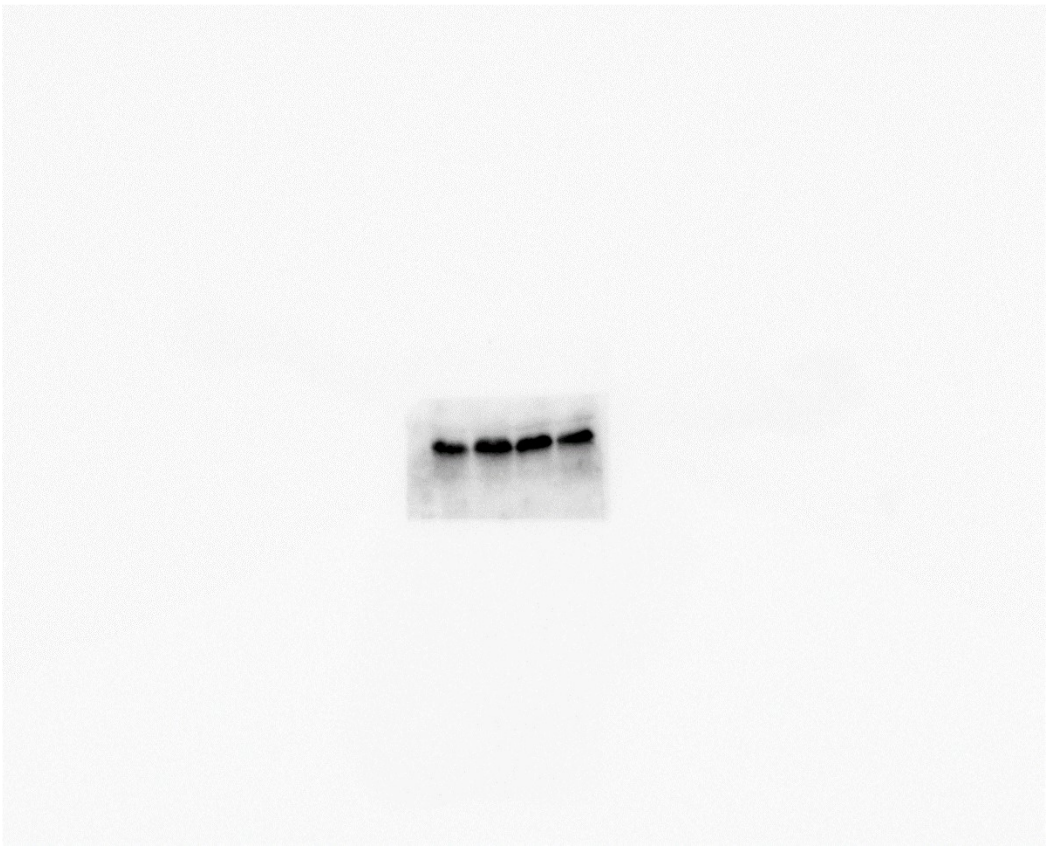

Fig.S21. Western blots image of STAT1 in Fig. 7A.

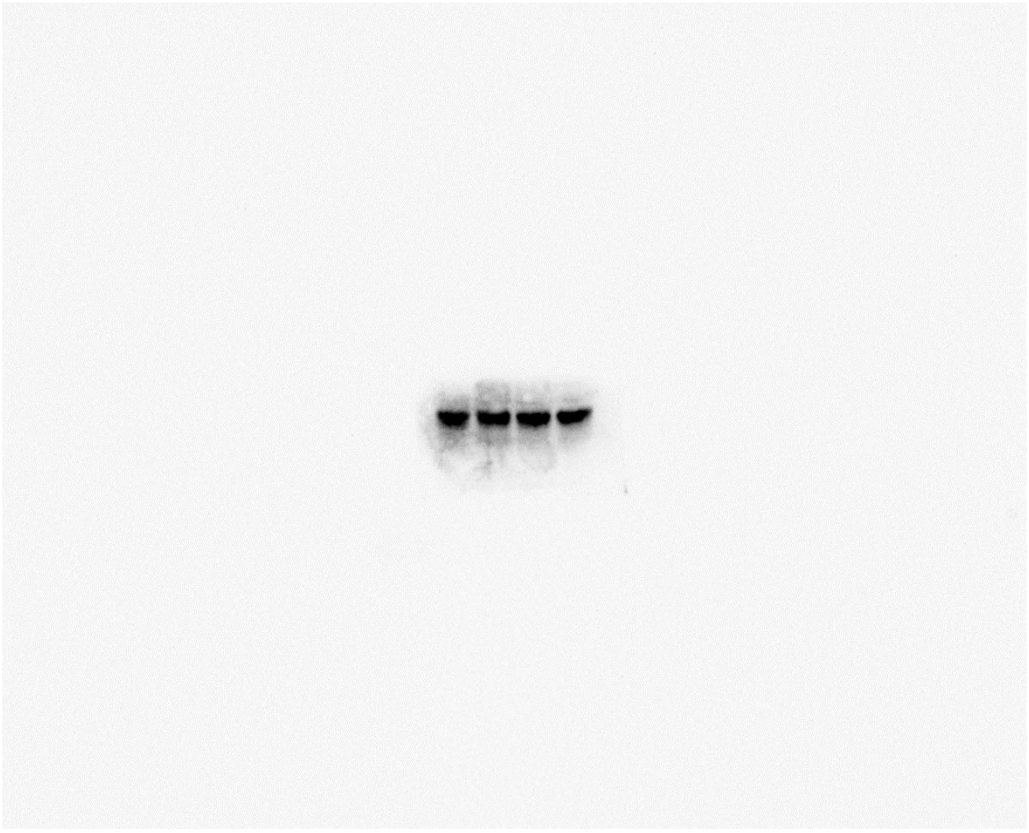

Fig.S22. Western blots image of GAPDH in Fig. 7A.

Fig.S23. Western blots image of TGF-β1 in Fig. 7F.

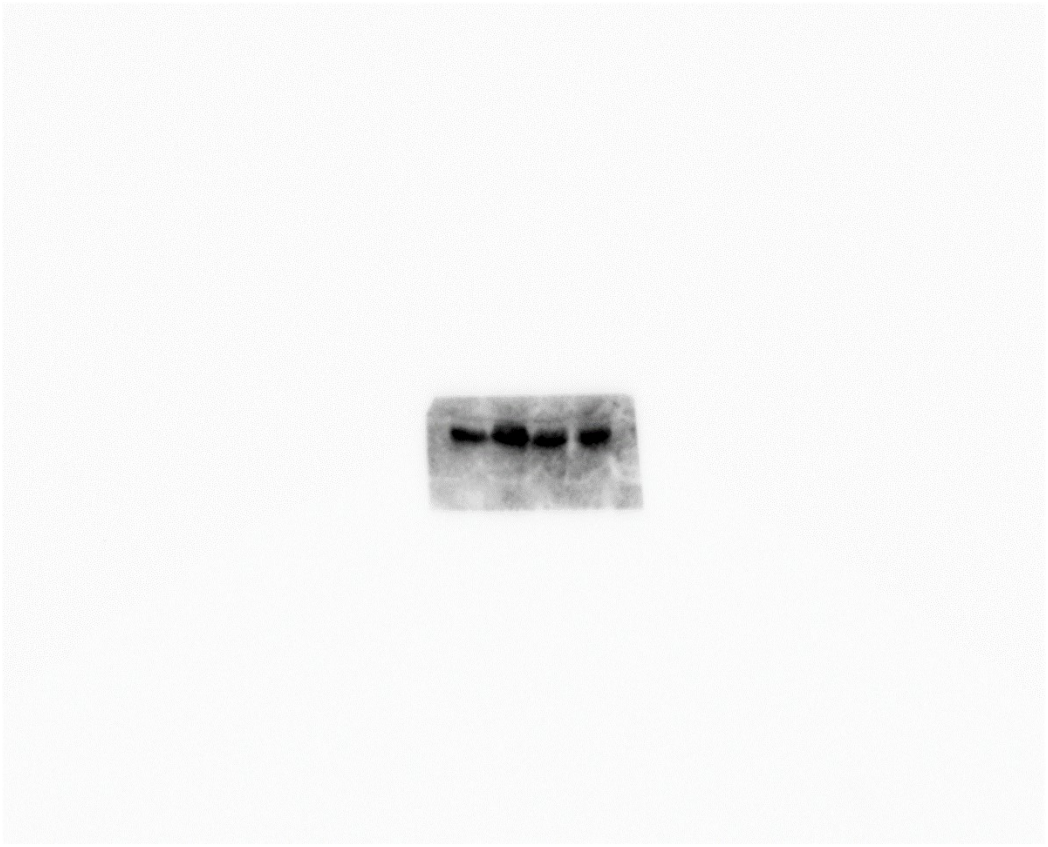

Fig.S24. Western blots image of ARG-1 in Fig. 7F.

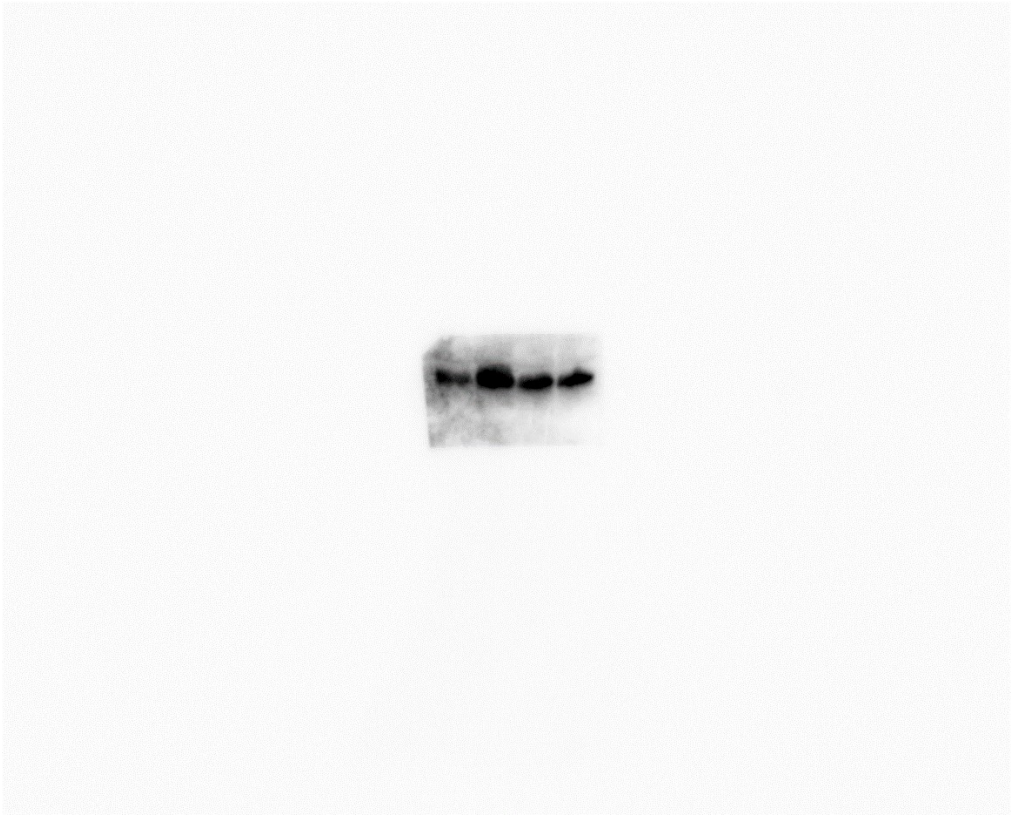

Fig.S25. Western blots image of P-JAK1 in Fig. 7F.

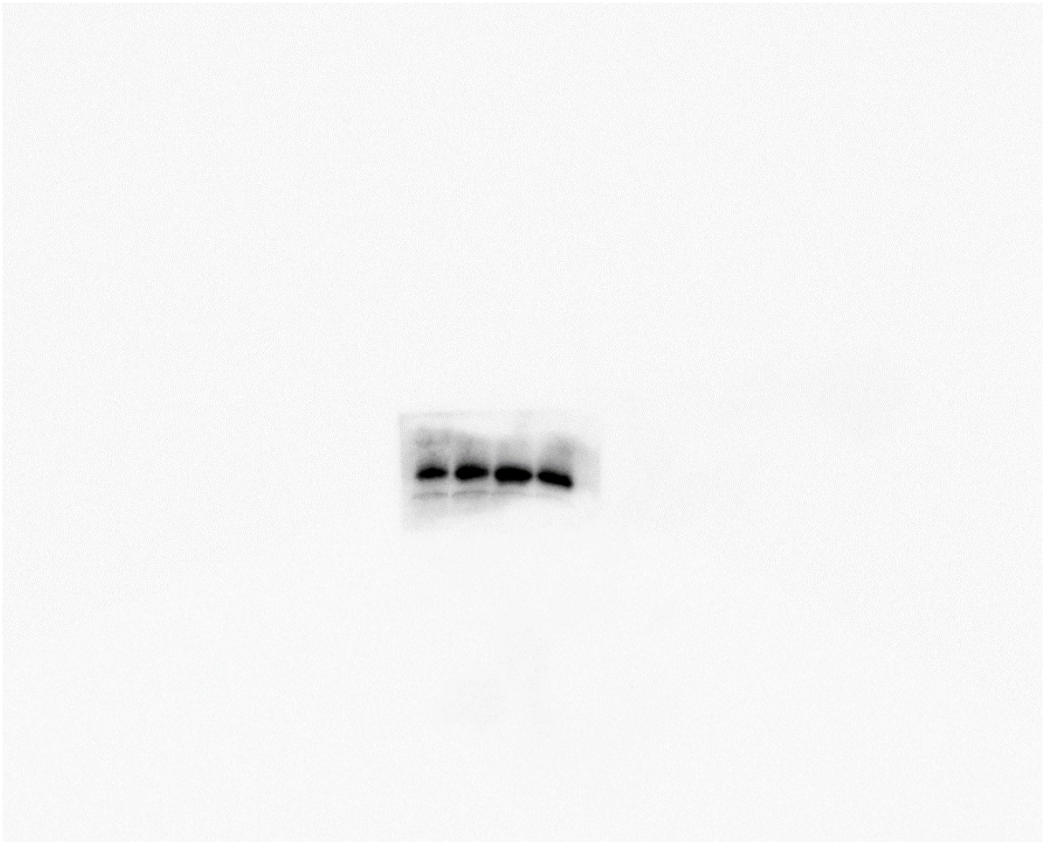

Fig.S26. Western blots image of JAK1 in Fig. 7F.

Fig.S27. Western blots image of P-STAT6 in Fig. 7F.

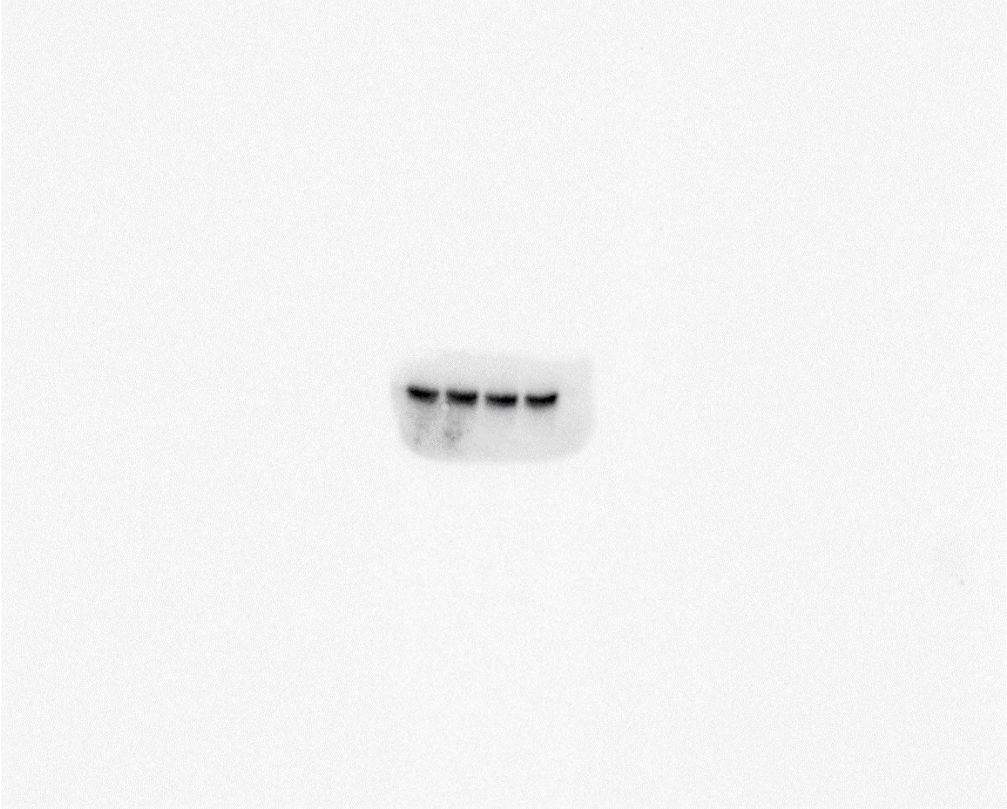

Fig.S28. Western blots image of STAT6 in Fig. 7F.

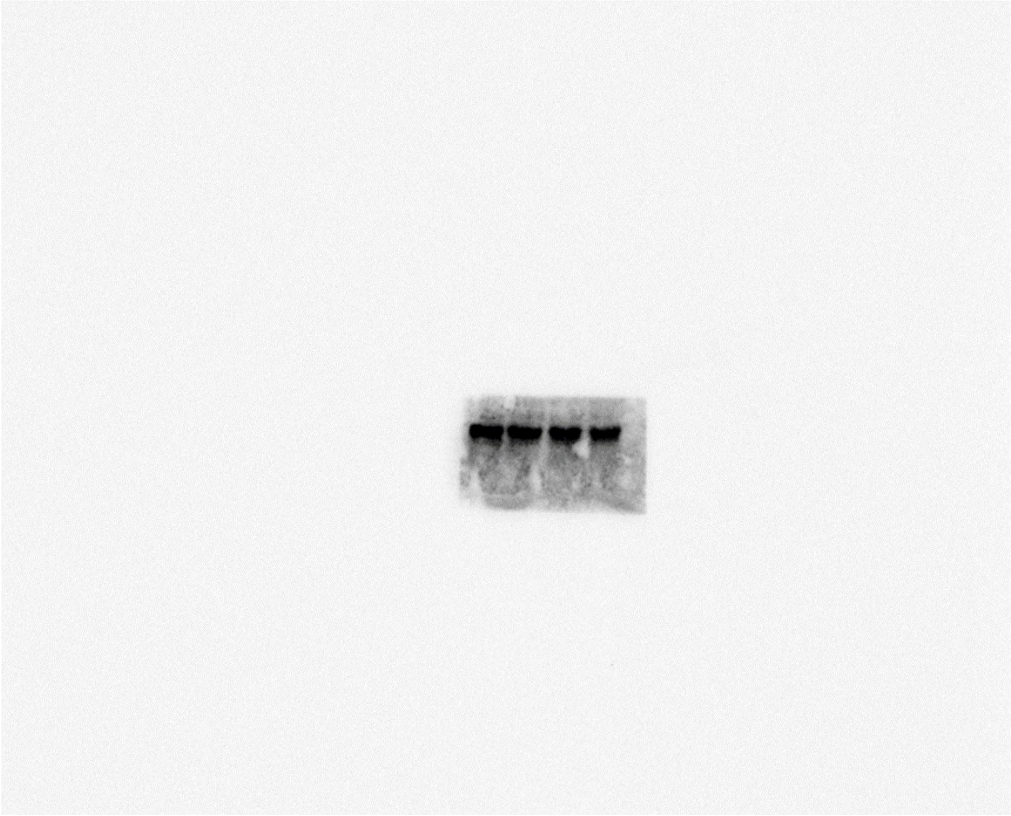

Fig.S29. Western blots image of GAPDH in Fig. 7F.