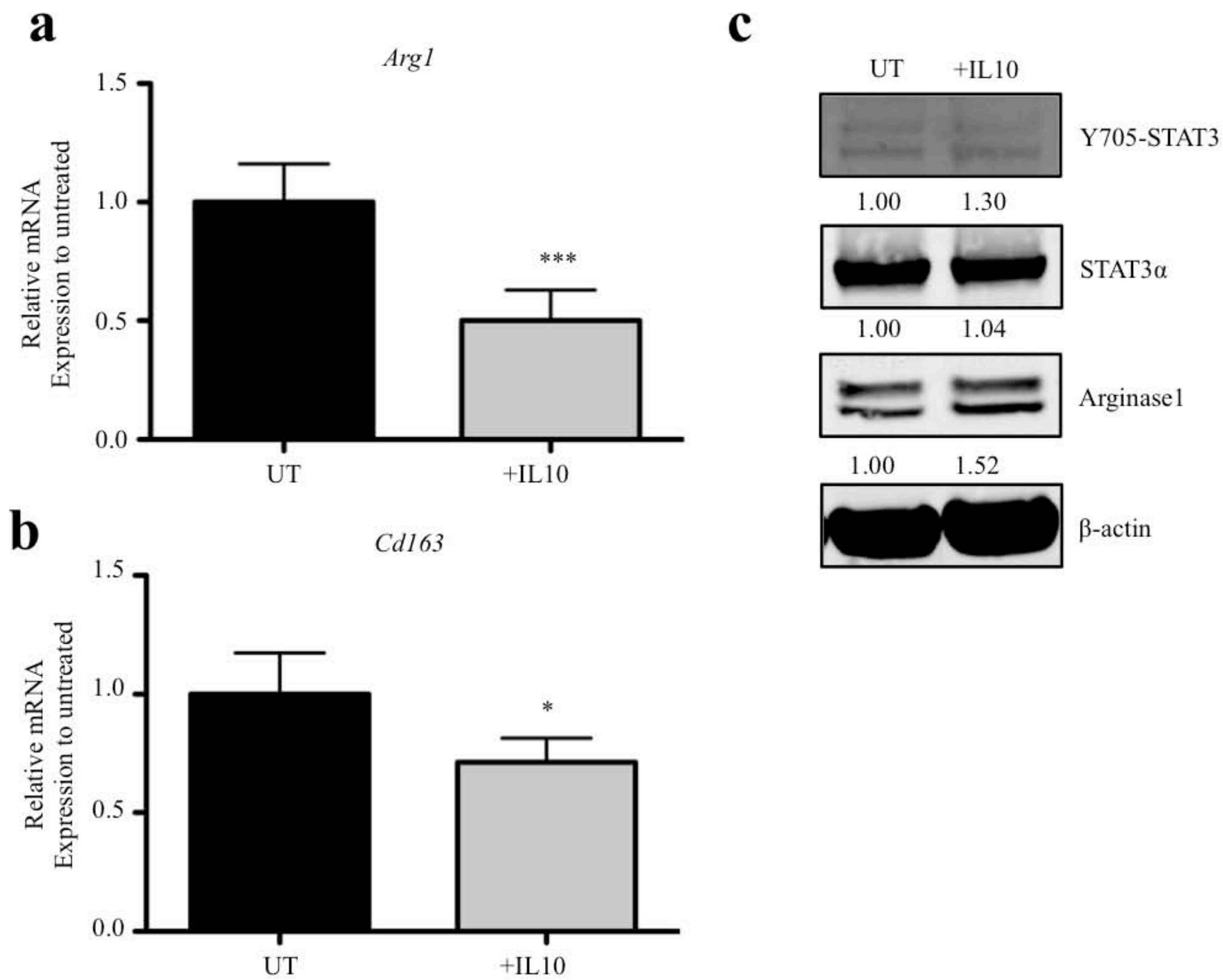
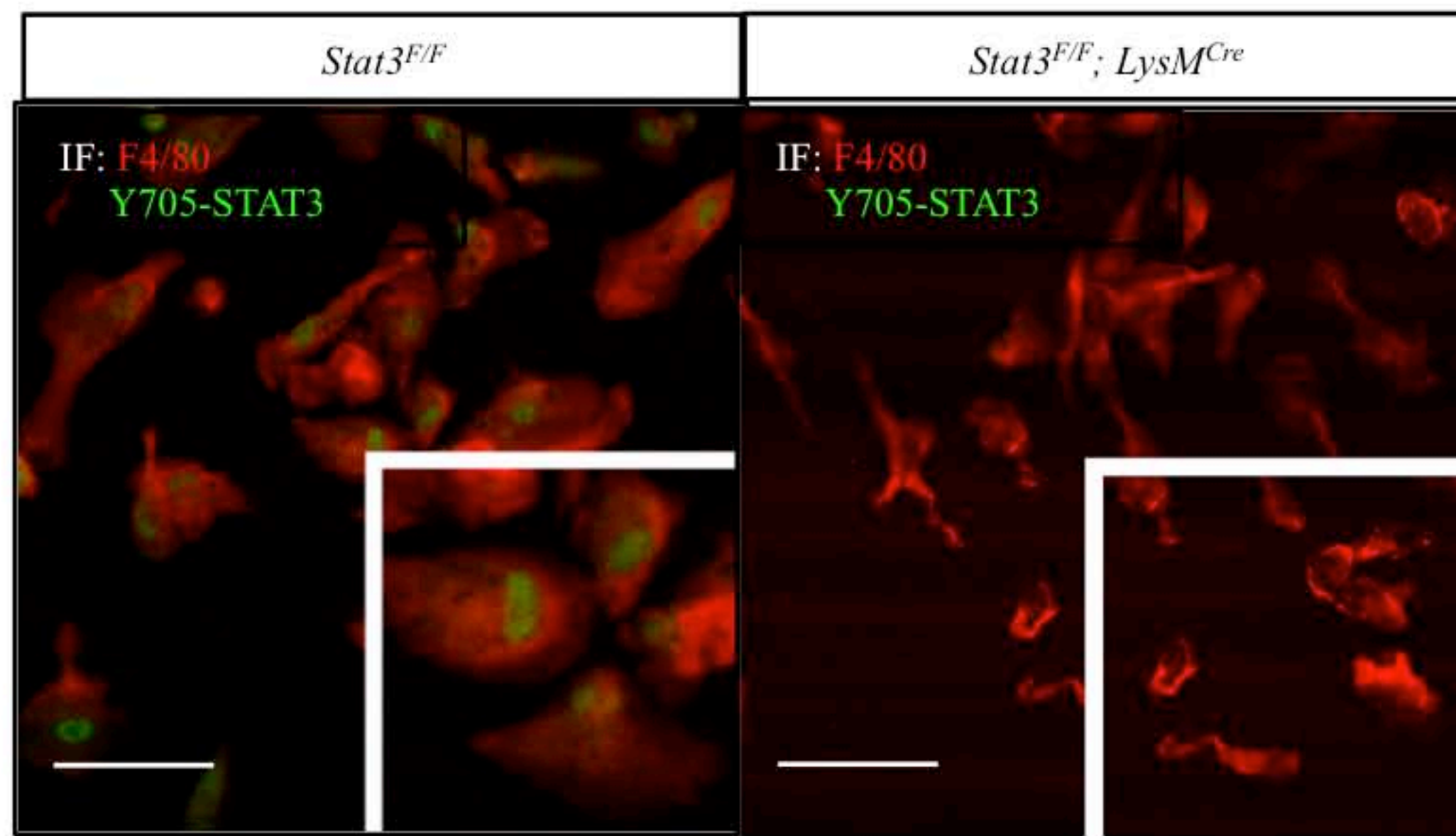


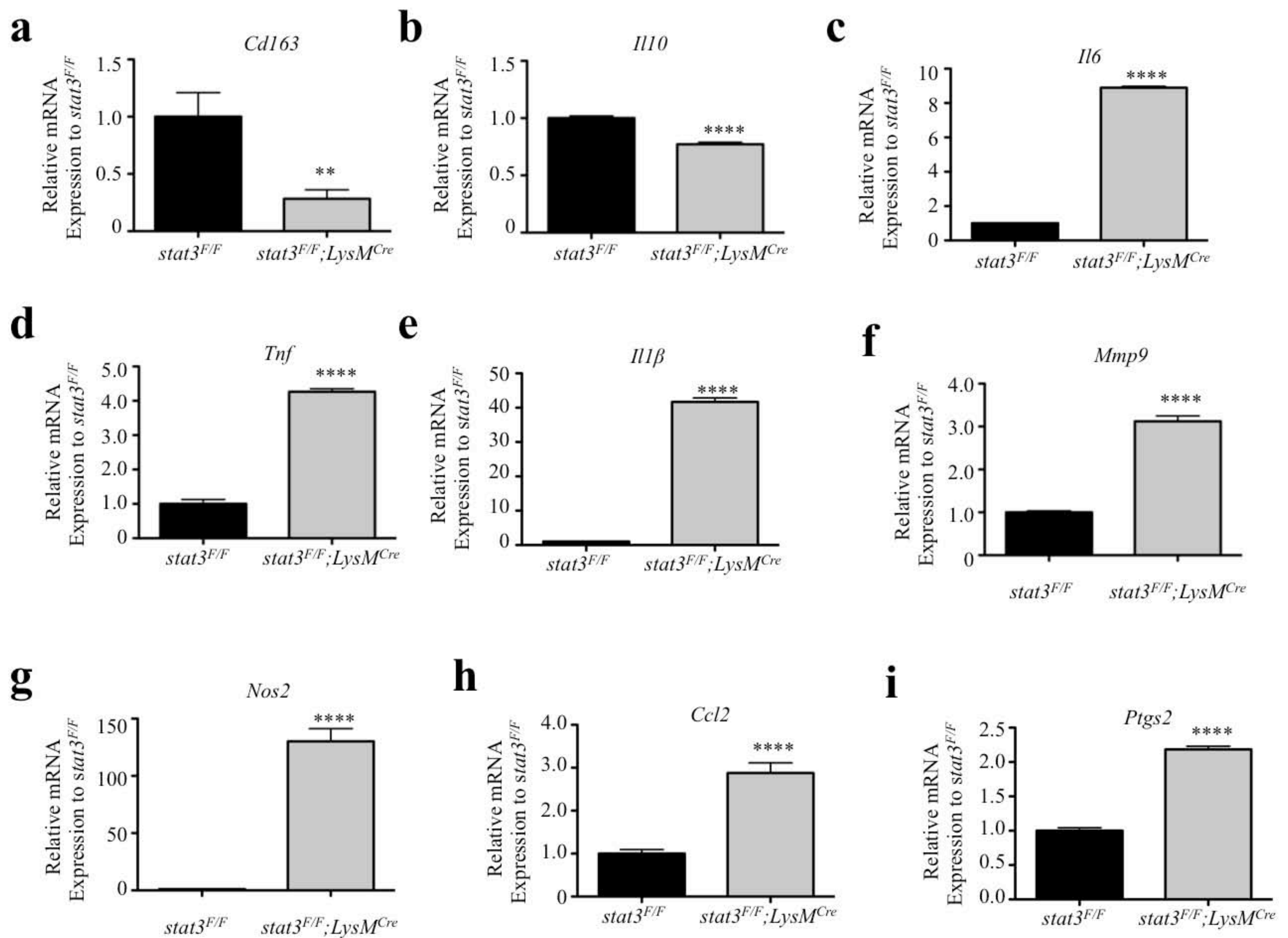
Supplementary Figure. 1. IL10 production is increased in serum and CNV complexes of old mice. (a) Serum level of IL10 was measured by ELISA in 3 month- (3 Mo, n=8) and 18 month-old (18 Mo, n=9) mice. (b) Choroidal neovascularization (CNV) was induced in 3 Mo (left panel) and 18 Mo (right panel) mice. After 7 days, eyes were cross-sectioned and stained for F4/80 (macrophage marker), IL10 and Dapi (nuclei). Scale bar = 100 μ m. ONL, outer nuclear layer.



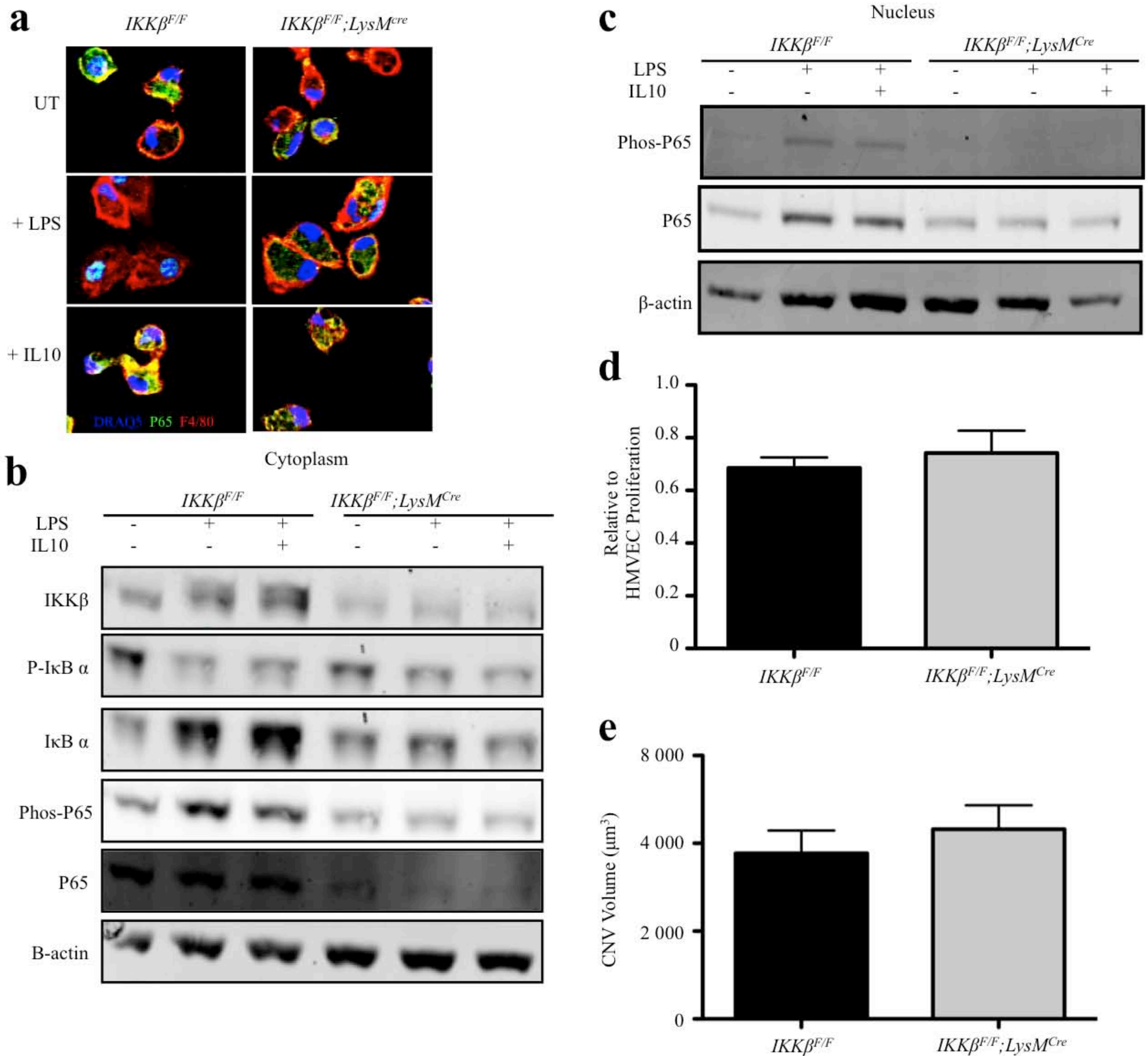
Supplementary Figure. 2. *IL10-r2*^{-/-} macrophages are resistant to M2 polarization after IL10 treatment. Peritoneal macrophages from *IL10r2*^{-/-} mice were treated with IL10 for 18 hours. **(a)** *Arg1* and **(b)** *Cd163* mRNA expression were measured by quantitative real-time PCR. Values are expressed as mean + SEM relative to untreated macrophage. At least three biological replicates were analyzed. (Student unpaired t test; ***p < 0.001, **p < 0.01). **(c)** Representative immunoblot for Y705-STAT3, STAT3 α , Arginase1, and β -actin after 18 hours of treatment with IL10. Values underneath the blot indicate expression relative to β -actin.



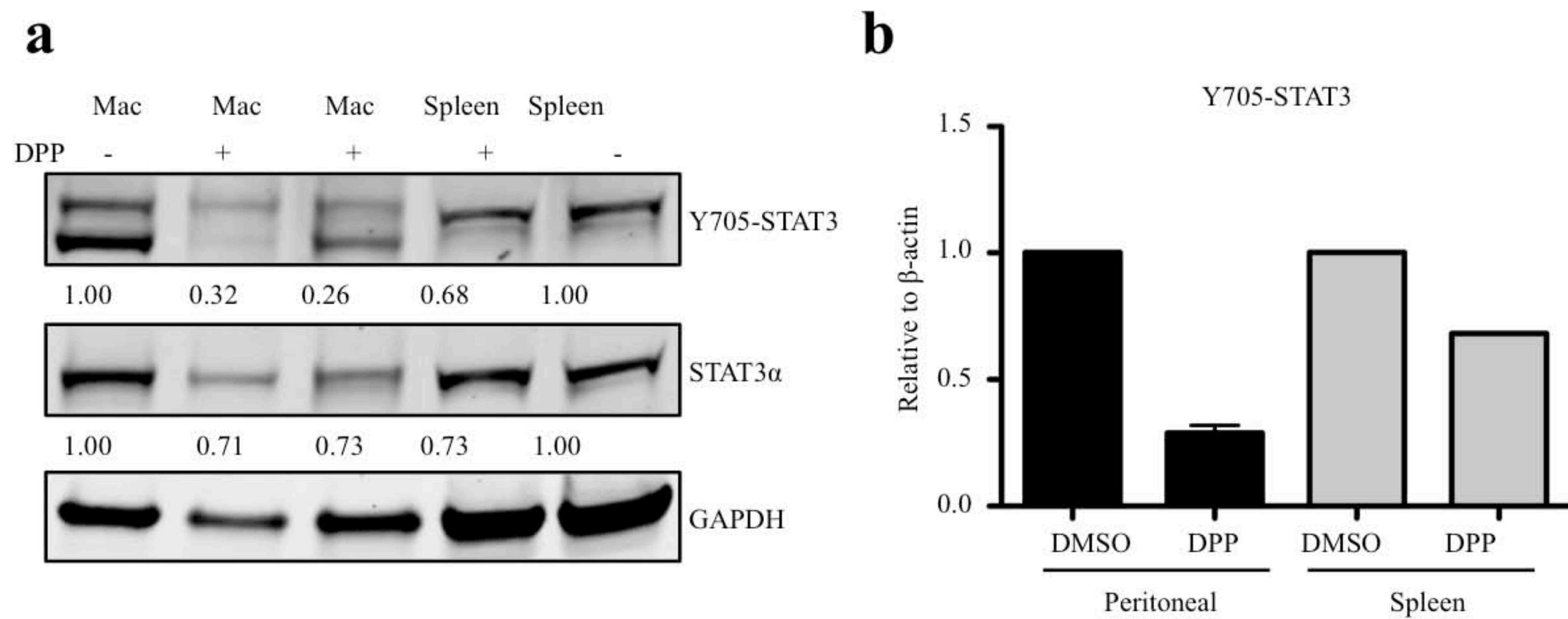
Supplementary Figure. 3. *Stat3^{F/F}; LysM^{Cre}* macrophages fails to respond to IL10 treatment through STAT3 signaling. Immunohistochemical image of phospho-STAT3 (green) after IL10 treatment in *STAT3^{F/F};LysM^{Cre}* and littermate controls (*STAT3^{F/F}*). F4/80 (red) is used as a macrophage marker protein. *STAT3^{F/F};LysM^{Cre}* macrophages do not respond to IL10 cytokine via Stat3 signaling. Representative images of staining from 3 independent experiments are shown. Scale bar = 50 μ m.



Supplementary Fig. 4. Baseline polarization of *Stat3^{F/F}; LysM^{Cre}* macrophage. Baseline macrophage polarization was determined using quantitative real-time qPCR. M2 markers (a) *Cd163* and (b) *Il10* were significantly down regulated in *STAT3^{F/F};LysM^{Cre}* while M1 markers (c) *Il6*, (d) *Tnf*, (e) *Il1 β* , (f) *Mmp9*, (g) *Nos2*, (h) *Ccl2*, and (i) *Ptgs2* were elevated. Values are expressed as mean + SEM relative to *STAT3^{F/F}*. (n > 5 biological replicate per group, unpaired t test; * p < 0.05, ** p < 0.01, ***p < 0.001 compared to *STAT3^{F/F}* macrophage).

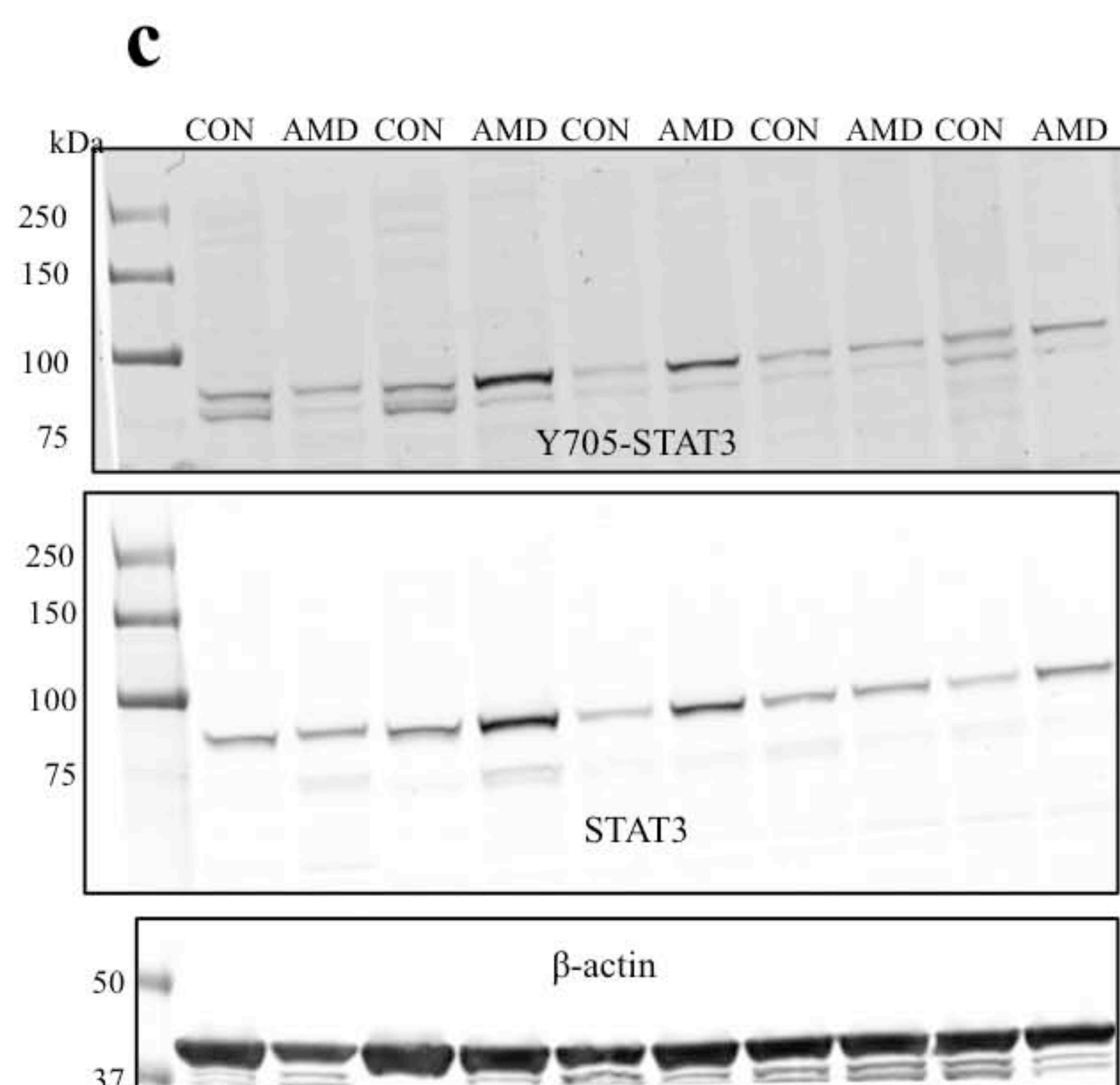
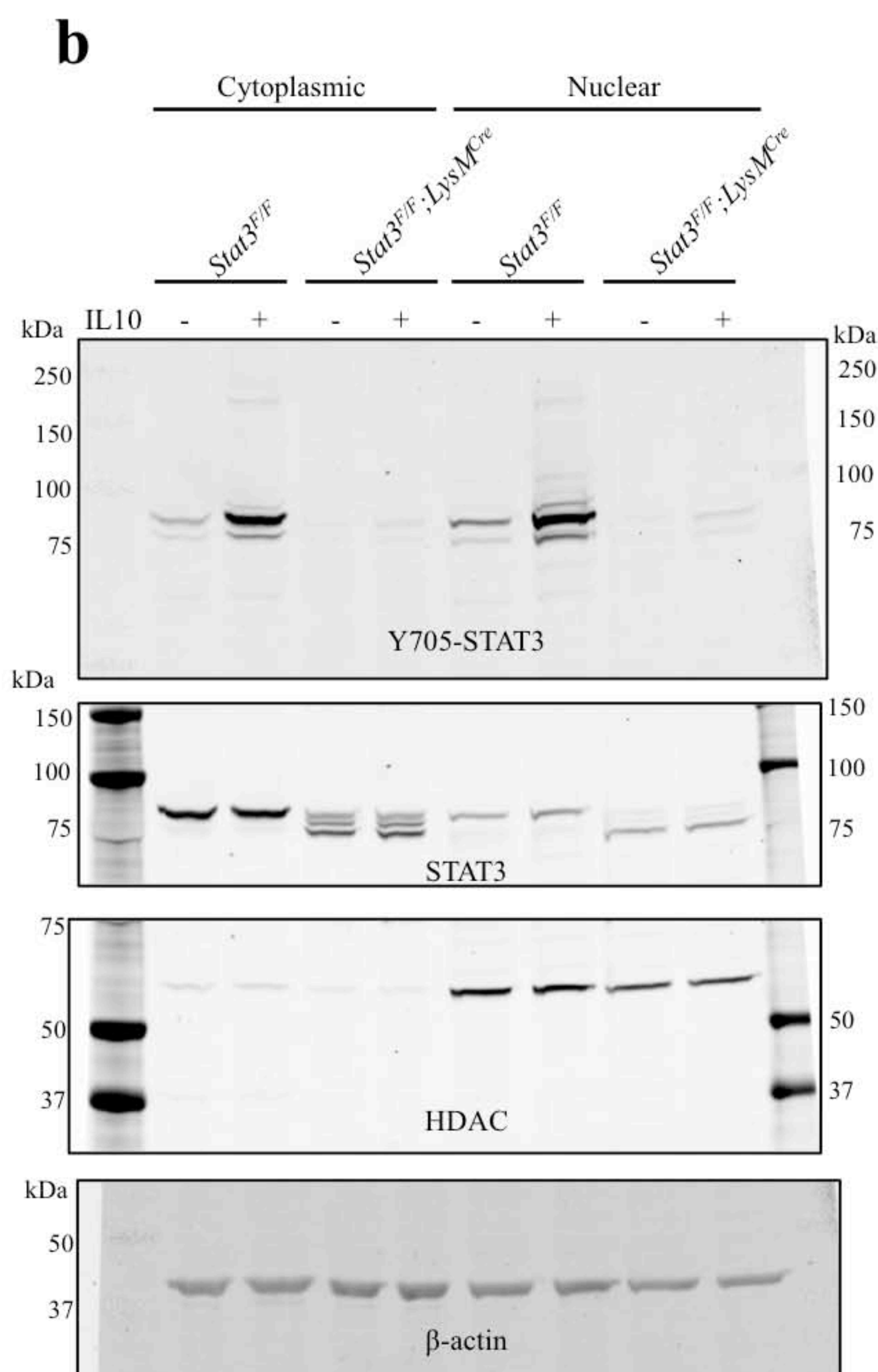
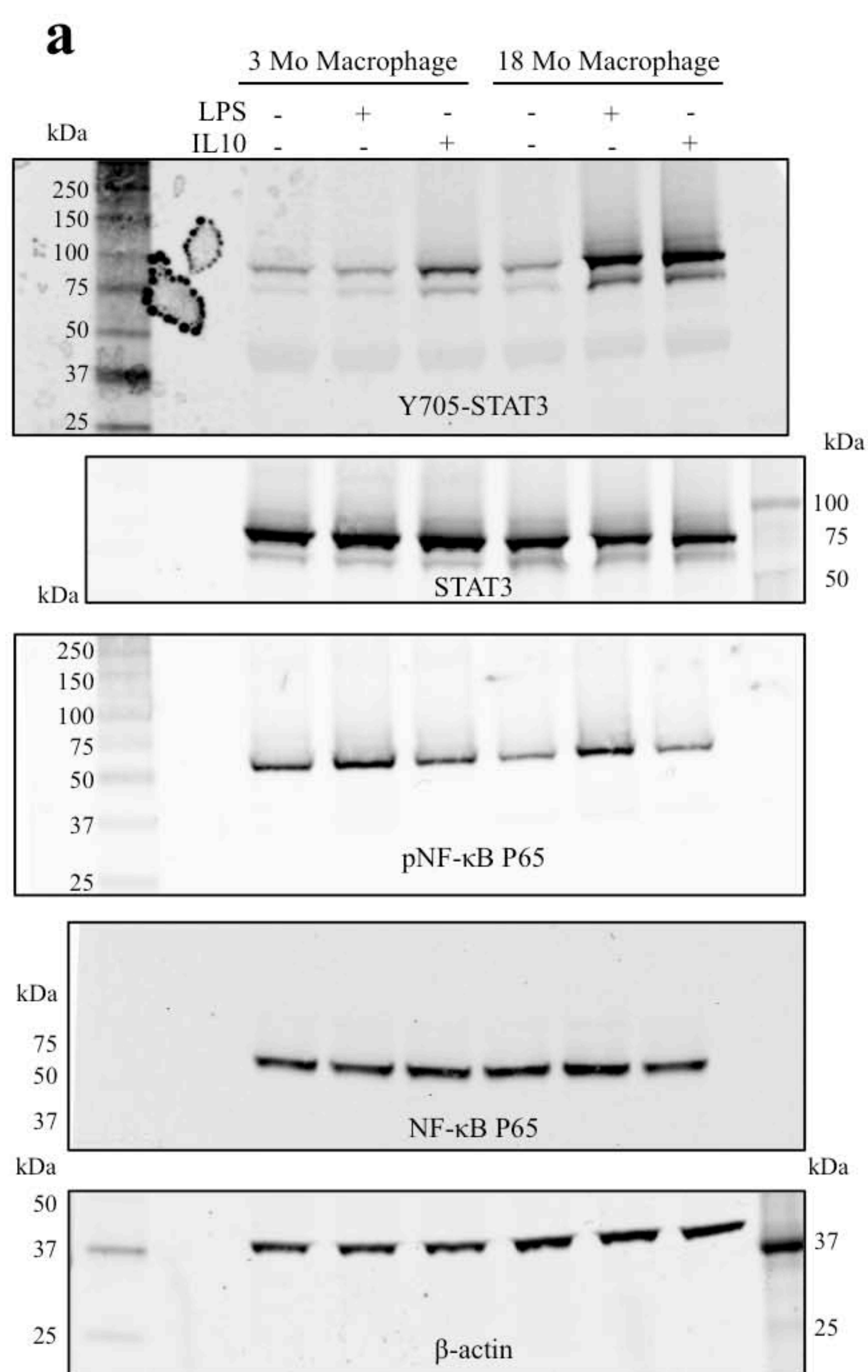


Supplementary Figure. 5. NF- κ B pathway in macrophages is not involved in regulation of angiogenesis *in vivo* and *in vitro*. (a) Peritoneal macrophages isolated from *IKK $\beta^{F/F};LysM^{Cre}$* or *IKK $\beta^{F/F}$* control mice were treated with LPS (100 ng/ml) or IL10 (100 ng/ml) for 18 hr. Immunohistochemical analysis was performed to visualize the NF- κ B signaling pathway by tracing nuclear P65 expression after treatment. Representative images of the staining are shown. F4/80 and DRAQ5 were used to counterstain for macrophage and nuclei, respectively. Immunoblot for IKK β , phospho-IkB α , IkB α , phospho-P65 and P65 subunit expression in (b) cytoplasmic and (c) nuclear lysate of *IKK $\beta^{F/F};LysM^{Cre}$* macrophage and *IKK $\beta^{F/F}$* control. β -actin was used for loading control. Representative blots from 3 independent experiments are shown. (d) HMVEC proliferation assay demonstrates that *IKK $\beta^{F/F};LysM^{Cre}$* does not affect HMVEC proliferation compared to littermate *IKK $\beta^{F/F}$* control. N = 20 co-cultures for each genotype. Student's unpaired *t* test. *p* value is not significant. (e) Laser induced choroidal neovascularization performed in *IKK $\beta^{F/F};LysM^{Cre}$* and *IKK $\beta^{F/F}$* control. Mice were perfused with FITC labeled dextran to visualize CNV and to quantify CNV volume. N > 10 individual mice for each genotype. Student's unpaired *t* test. *p* value is not significant.



Supplementary Figure. 6. 5,15-DPP inhibits STAT3 activation *in vivo*.

(a) 18 month old female mice received daily 5,15-DPP (15mg/kg) or DMSO i.p. injections for 5 days before CNV injury and continued to receive injection until time for analysis. On the day of perfusion with FITC-labeled dextran peritoneal macrophages and the spleen were isolated. Whole cell lysate from macrophages and spleen were subjected to Western blot analysis for Y705-STAT3, STAT3 α and GAPDH. **(b)** Band intensity was measured and normalized to untreated (DPP (-)) samples.



Supplementary Figure. 7. Full size blot images of sections presented in the manuscript.
Full blots of sections shown in Figure 1d (a), Figure 3a (b) and Figure 7a (c).

