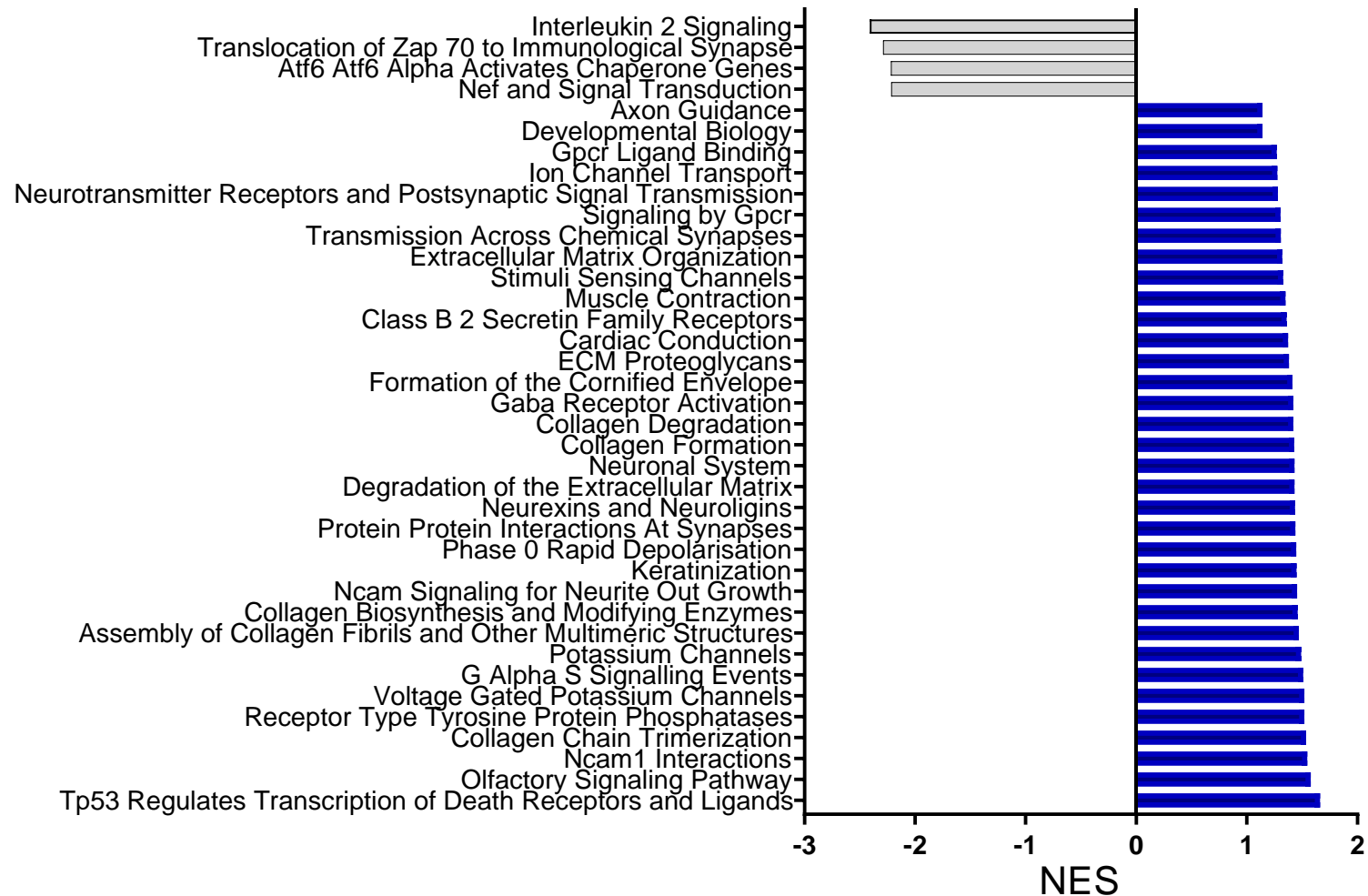
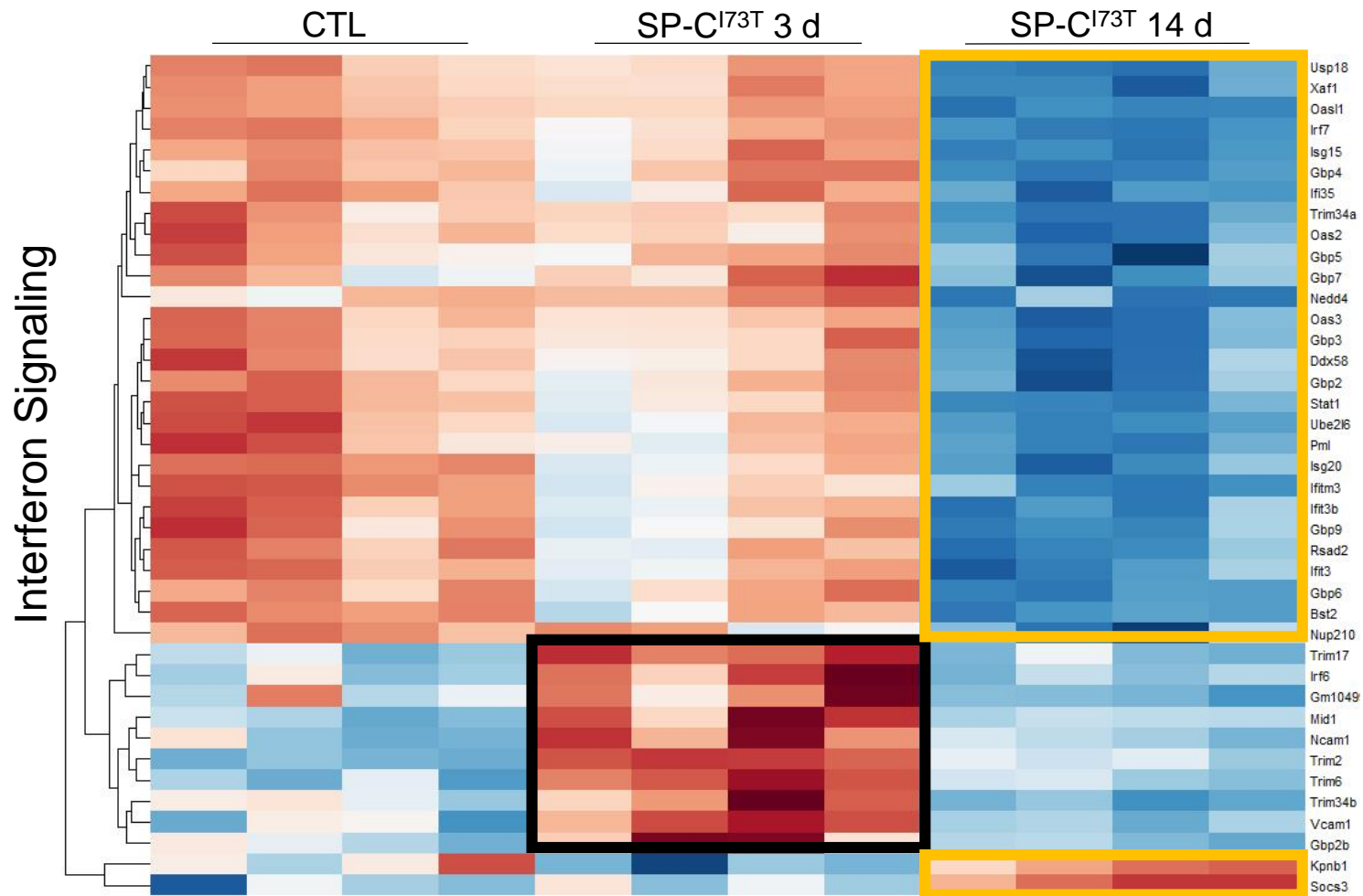


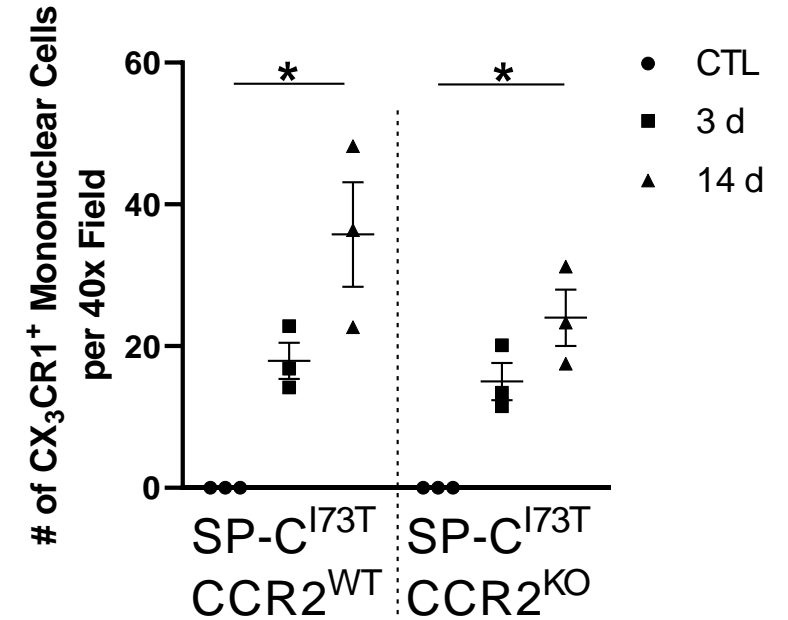
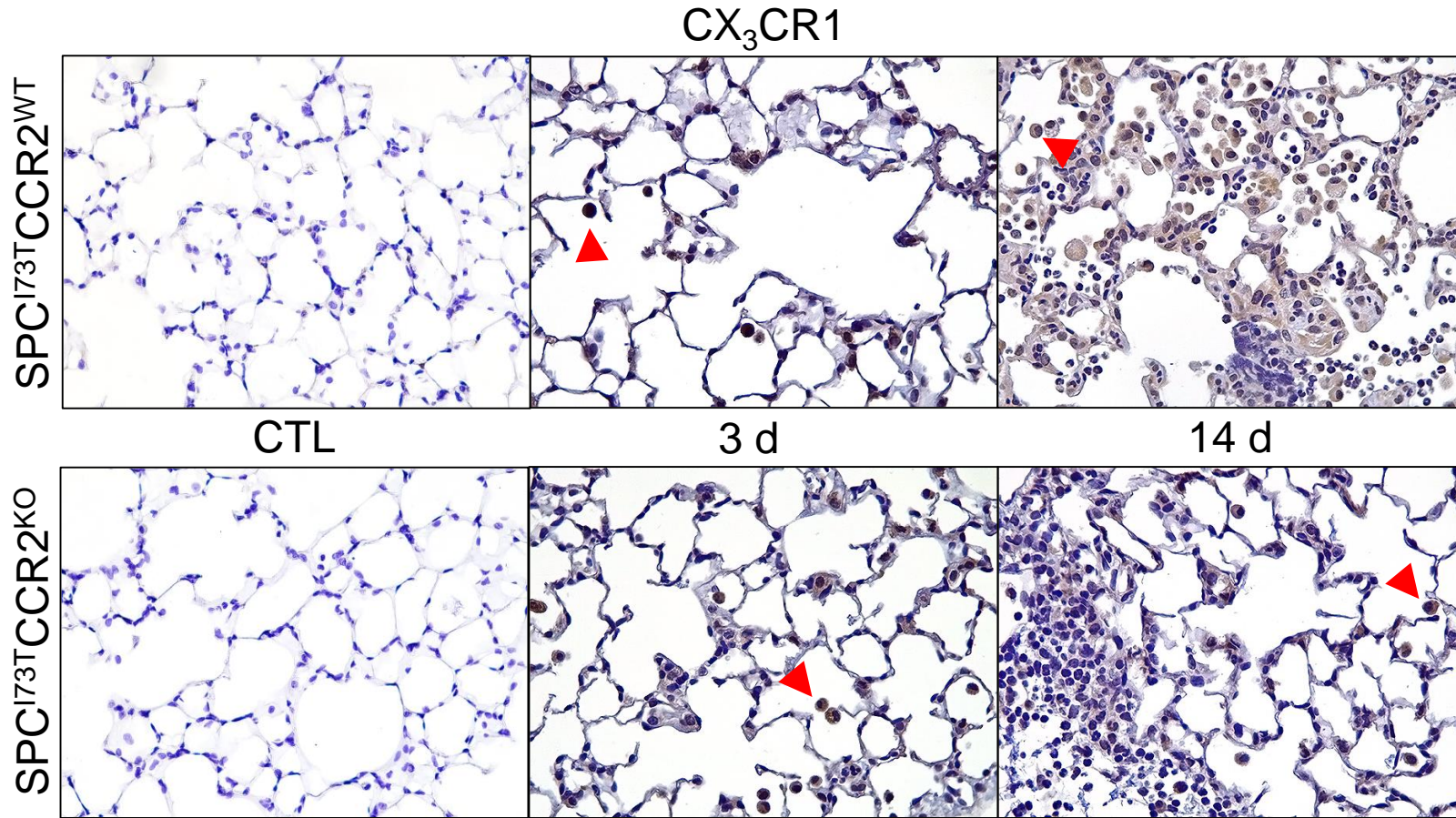
**Supplementary Figure 1. Flow cytometric gating strategy.** Gating strategy used to identify inflammatory cell subsets in control (CTL, oil treated SP-C<sup>I73T</sup> mice) or SP-C<sup>I73T</sup> mice 3 d and 14 d after injury. Cells were gated on CD45<sup>+</sup> following the exclusion of dead cells and doublets. Populations were identified based on a previously published protocol (Venosa *et al.*, 2019). Alveolar macrophages were gated based on SigF<sup>+</sup>CD11b<sup>-</sup> expression and confirmed using CD11c, CD64. Sequential gating of neutrophils (CD11b<sup>+</sup>Ly6G<sup>+</sup>), eosinophils (SigF<sup>+</sup>CD11b<sup>+</sup>CD11c<sup>-</sup>), lymphocytes (CD3<sup>+</sup>CD11b<sup>-</sup>), and monocytes (CD11b<sup>+</sup>CD64<sup>+</sup>Ly6C<sup>+</sup>). Monocytes (highlighted in the red box) were sorted and analyzed via RNA-sequencing.



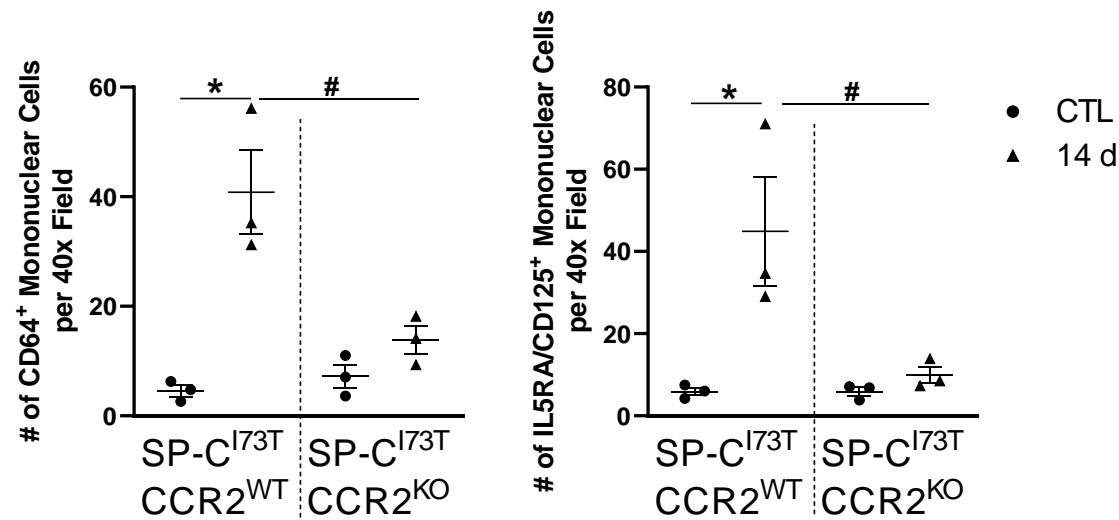
**Supplementary Figure 2. Positively and negatively enriched pathways of flow cytometry sorted CD11b<sup>+</sup>Ly6C<sup>hi</sup> monocytes following SP-C<sup>I73T</sup> induced injury.** Differentially expressed genes of CD11b<sup>+</sup>Ly6C<sup>hi</sup> monocytes isolated 3 d post SP-C<sup>I73T</sup> induced injury were analyzed using Reactome database to highlight negatively (grey bars) and positively (blue bars) enriched signaling pathways (normalized enrichment score, NES) compared to control (CTL, oil treated SP-C<sup>I73T</sup> mice). A fold change > 1.5 and false discovery rate [q-value] < 0.05 was considered significant.



**Supplementary Figure 3. Interferon-associated gene expression of flow cytometry sorted CD11b<sup>+</sup>Ly6C<sup>hi</sup> monocytes following SP-C<sup>I73T</sup> induced injury.** Differentially expressed genes in CD11b<sup>+</sup>Ly6C<sup>hi</sup> monocytes isolated from control (CTL, oil treated SP-C<sup>I73T</sup> mice) or SP-C<sup>I73T</sup> mice 3 d and 14 d after injury. Heat-map showing expression of significantly regulated genes involved in ‘Interferon Signaling’ using Reactome database. A fold change > 1.5 and false discovery rate [q-value] < 0.05 was considered significant. Note **black boxes** represent genes uniquely expressed 3 d after SP-C<sup>I73T</sup> injury; **orange boxes** represent genes uniquely expressed 14 d after SP-C<sup>I73T</sup> injury.

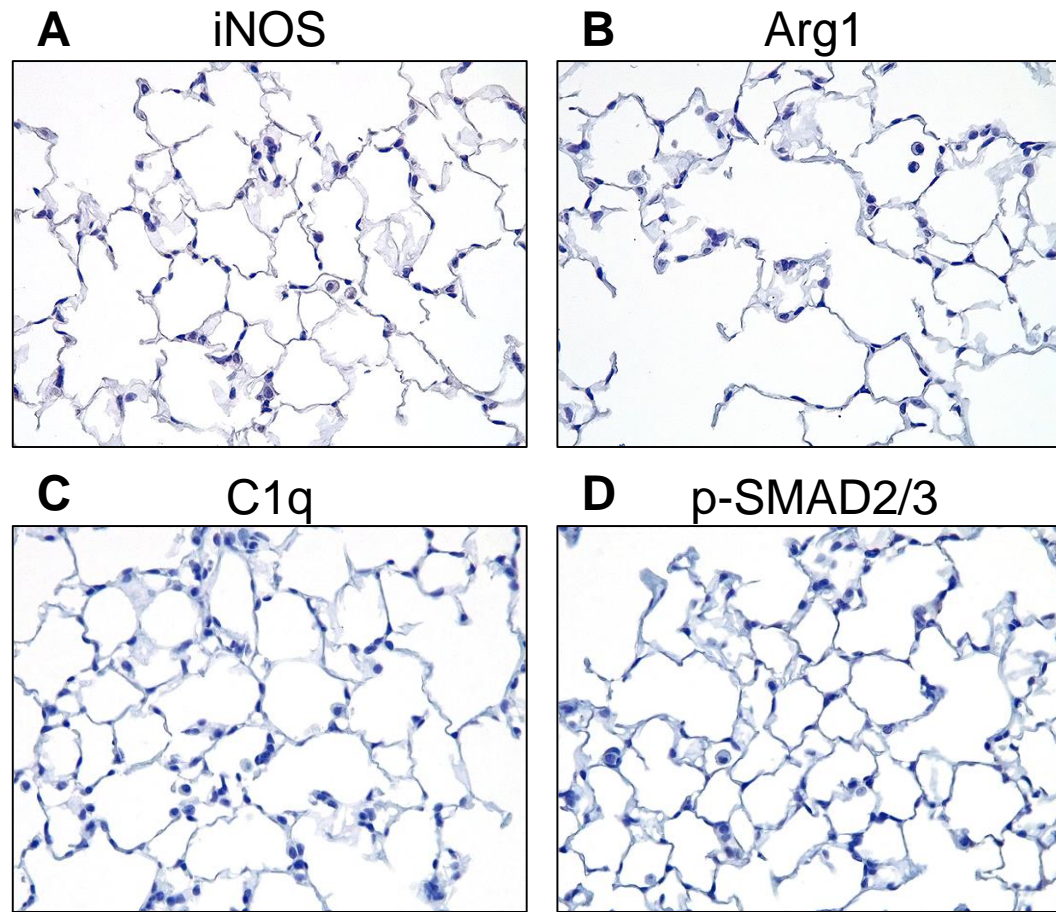


**Supplementary Figure 4. Effects of CCR2 monocyte ablation on CX<sub>3</sub>CR1 expression following SP-C<sup>I73T</sup> induced injury.** Histochemical analysis of control (CTL, tamoxifen treated SP-C<sup>WT</sup> or oil treated SP-C<sup>I73T</sup> mice), SP-C<sup>I73T</sup>CCR2<sup>WT</sup> and SP-C<sup>I73T</sup>CCR2<sup>KO</sup> lung sections 14 d post injury immunostained with antibody to CX<sub>3</sub>CR1. Protein expression was visualized using a DAB Vectastain kit (brown). Arrowheads indicate cells expressing the receptor. Original magnification, 400x. Right panel represents quantification of CX<sub>3</sub>CR1 expression in mononuclear cells following SP-C<sup>I73T</sup> induced injury. 40x images from 5 foci of injury were acquired, acquired and averaged. Data are represented as mean ± SEM (N=3/study group). All analysis was considered significant \*p<0.05 compared to control mice by One-Way ANOVA, using Tukey post- hoc test.



**Supplementary Figure 5. Immunohistochemical analysis of monocyte/macrophage maturation and recruitment in SP-C<sup>I73T</sup> mice.**

Quantification of histochemical analysis of control (CTL, tamoxifen treated SP-C<sup>WT</sup> or oil treated SP-C<sup>I73T</sup> mice), SP-C<sup>I73T</sup>CCR2<sup>WT</sup> and SP-C<sup>I73T</sup>CCR2<sup>KO</sup> lung sections 14 d post injury immunostained with antibody to CD64 and CD125/IL5RA. Panels depict average number of mononuclear cells present in 40x images acquired from 5 foci of injury. Data are represented as mean ± SEM (N=3/study group). All analysis was considered significant \*p<0.05 compared to control mice; #p<0.05 compared to SP-C<sup>I73T</sup>CCR2<sup>WT</sup> mice by One-Way ANOVA, using Tukey post- hoc test.



**Supplementary Figure 6. Expression of inflammatory and maturity markers in control SP-C<sup>I73T</sup>CCR2<sup>KO</sup> mice.**

Histochemical analysis of oil treated (control) SP-C<sup>I73T</sup>CCR2<sup>KO</sup> lung sections immunostained with antibody to (A) iNOS and (B) Arg1, (C) C1q and (D) p-SMAD2/3. Protein expression was visualized using a DAB Vectastain kit (brown). Original magnification, 400x.