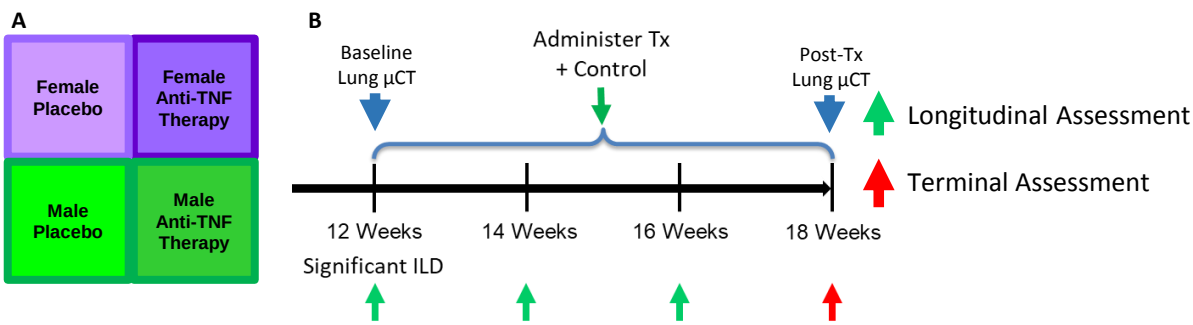
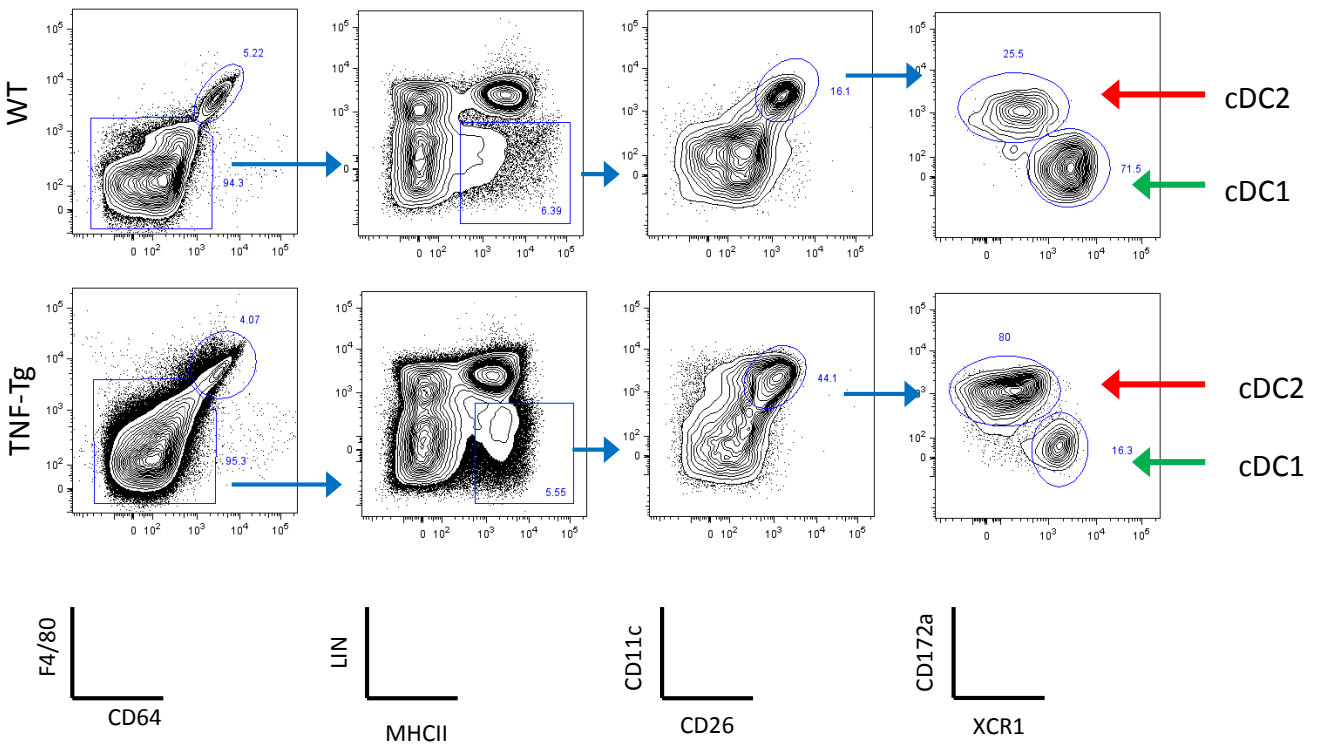
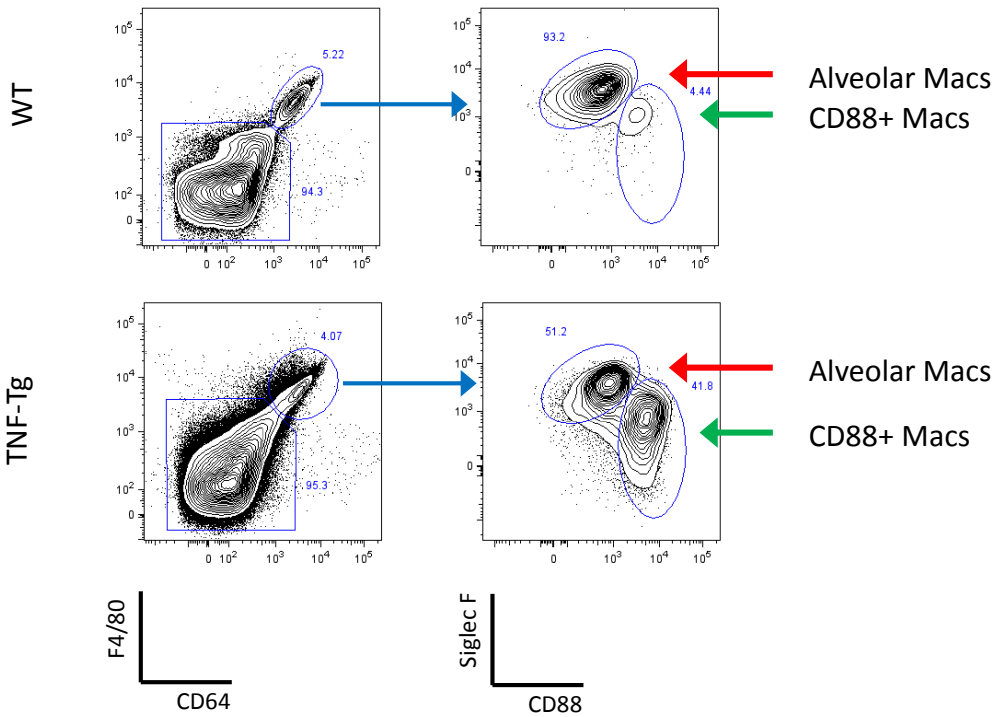


Supplemental Figure 1. Experimental outline to evaluate reversibility of articular and pulmonary pathology in TNF-Tg mice treated with anti-TNF mAb versus placebo. Four cohorts of TNF-Tg mice on a C57/BL6 background (n=6) were studied as outlined in (A). Mice >12 weeks of age were randomized into treatment groups based on a minimum post-expiratory lung tissue volume of 400mm3 (known to correspond to significant ILD, Bell at al 2018 PLoS), determined via 3D micro-CT (µCT) screening. Murine anti-human TNF mAb (CNTO12) or irrelevant IgG1 isotype placebo control mAb (CNTO151) were administered at 10mg/kg/wk via I.P. injection for six weeks total. B) Longitudinal, noninvasive, in vivo measurements (weight, grip strength, and ultrasound), were obtained biweekly, including prior to sacrifice (green arrows). µCT scans were taken at the onset of the study, and prior to sacrifice (blue arrows). Terminal measurements at time of sacrifice included histologic and/or flow cytometric analysis of lung, knee joint and popliteal lymph node tissue (red arrows).



Supplemental Figure 2. Conventional dendritic cell 2 (cDC2) population is substantially increased in lungs of TNF-Tg mice with ILD. Right lung tissue from 3.5 month old male and female WT and TNF-Tg mice (n=3 per group) were harvested and processed for multicolor flow cytometry and the experiment was performed in duplicate with similar results (total n=24). Representative dot plots of CD45+ gated cells from a female WT and TNF-Tg mouse are shown to illustrate the gating strategy used to isolate the cDC 1(LIN- (CD3-/CD19-) MHCII++ CD11c++ CD26+CD172a- XCR1+) and cDC 2 (LIN- (CD3-/CD19-) MHCII++ CD11c++ CD26+CD172a+ XCR1-) populations as previously described by Guilliams et al (Immunity, 2016). Note the significant increase in the proportion (1.71+/-0.32% vs. 0.17+/-0.13% (cDC2) and (0.47+/-0.12% vs. 0.37+/-0.19% (cDC1)) and absolute cell numbers (4652+/-1619 vs 184+/-99.7 (cDC2) and (1259+/-581 vs 435+/-165 (cDC1)) of cDC2 (red arrow) vs. cDC1 (green arrow) respectively in TNF-Tg vs. WT lungs ($p<0.0001$).



Supplemental Figure 3. Increased macrophage populations in TNF-Tg lungs with ILD. Additional flow cytometry analyses were performed on the lung cells described in Supplemental Figure 1, which were stained for macrophage markers. Representative dot plots are shown to illustrate the initial gating on the F4/80+/CD64+ double positive population (left), and the subsequent analysis of alveolar macrophages (Siglec F++/CD88lo) vs. the Siglec F+/CD88+ macrophage population (right). Note the significant increase in the proportion (30+/-9% vs. 4+/-1% (CD88+)) and 63+/-11% vs. 93+/-2% (Alveolar) and absolute cell numbers (5181+/-2336 vs 225+/-86 (CD88+) and 11081+/-4656 vs 5921+/-3526) of CD88+ macrophages (green arrow) vs. Alveolar macrophages (red arrow) respectively in TNF-Tg vs. WT lungs ($p<0.0001$).

	CD3+ (T cells)	CD19+ (B cells)	CD11b-CD11c+++MCHII+SigF+ (Alveolar Macs)	CD11b-CD11c+++MCHII+SigF- (cDC1)	CD11b++CD11c++MCHII+SigF- (cDC2)	CD11b++CD11c+ (Activated Monos)	CD11b+CD11c- (Undifferentiated Mono/Macs)	CD11b++CD11c- (Monos)
WT F	815,475+/-2%	1,677,324+/-4%	133,620+/-0.4%	19,650+/-0.2%	11,790+/-0.1%	113,970+/-0.2%	267,240+/-1%	510,900+/-2%
Placebo F	403,232,500 +/-1%	8,228,544.5+/-4%	598,345+/-1%	114,466+/-0.1%	780,450+/-0.8%	4,812,775+/-3%	1,014,585+/-2%	2,861,650+/-4%
Anti-TNF F	631,300+/-3%	1,629,824+/-7%	261,080+/-4%	25,680+/-0.2%	12,840+/-0.2%	248,240+/-2%	226,840+/-1%	684,800+/-5%
WT M	814,088+/-3%	1,706,100+/-4%	125,840+/-1%	9,680+/-0.1%	4,840+/-0.1%	203280+/-2%	314,600+/-1%	1,161,600+/-4%
Placebo M	1,937,490+/-0.8%	4,665,172+/-6%	873,770+/-2%	56,985+/-0.1%	322,915+/-0.3%	4,387,845+/-3%	1,576,585+/-3%	2,849,250+/-4%
Anti-TNF M	546,150+/-2%	1,256,476+/-7%	178,740+/-2%	19,860+/-0.2%	9,268+/-0.1%	148,950+/-0.8%	201,910+/-0.6%	662,000+/-3%

Supplemental Table 1. Absolute number of lung cell subsets in WT and TNF-Tg mice. The absolute number of cell populations from lung of WT and TNF-Tg mice as described in Figure 6 of the main manuscript are provided in table form above.