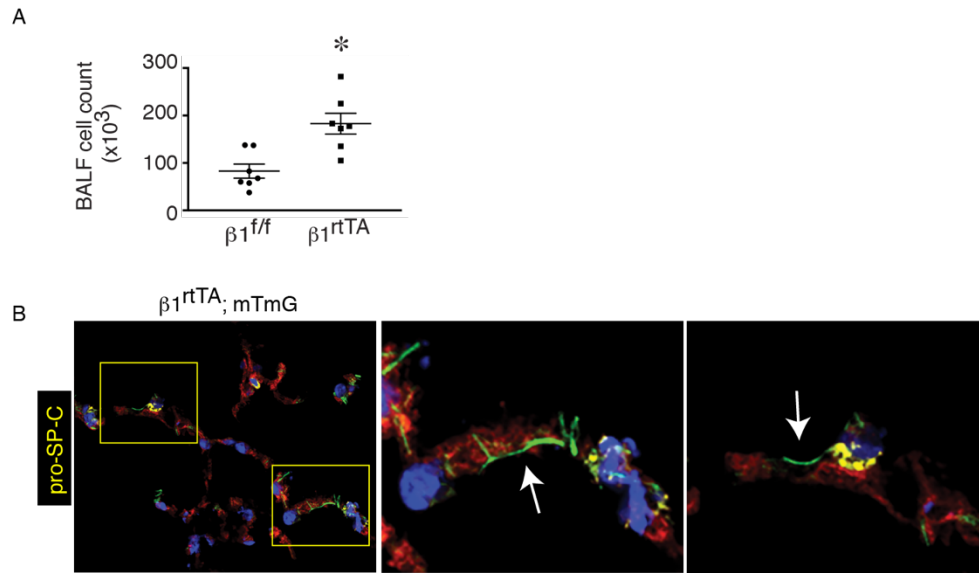
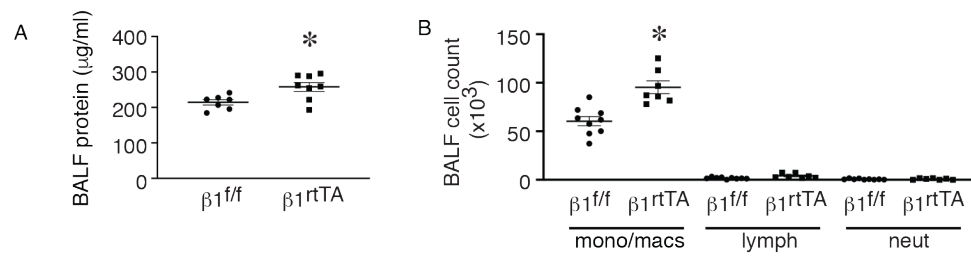


Supp. Figure 1



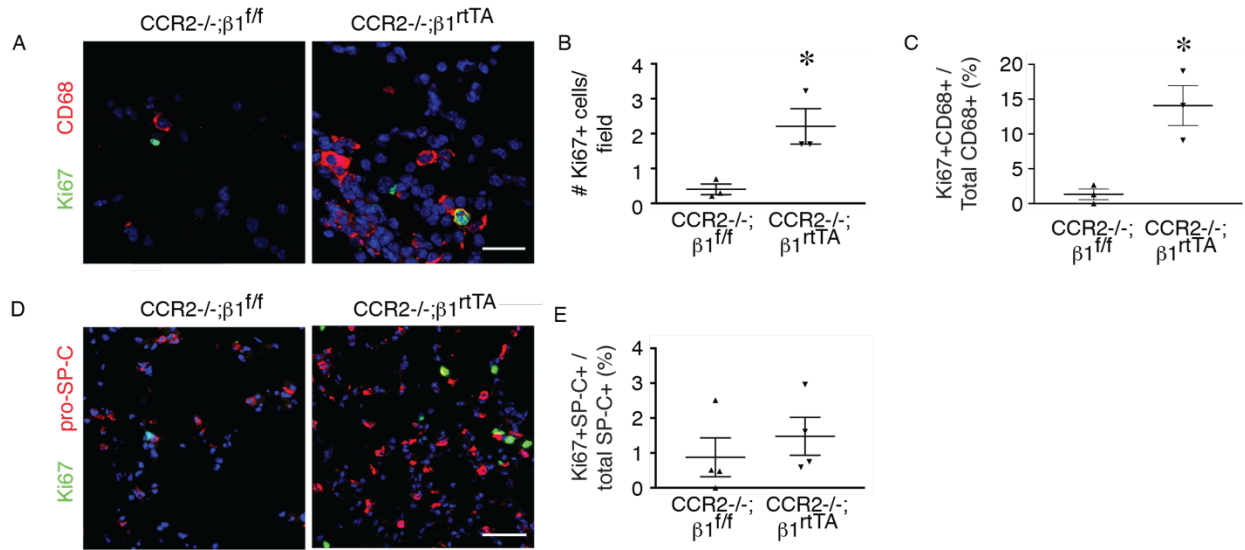
Supp. Figure 1. (A) Increased bronchoalveolar lavage fluid (BALF) cell count in 24-month-old $\beta 1^{rtTA}$ mice compared to $\beta 1^{f/f}$ mice (n = 7 mice/ group). (B) GFP+ type 1 AECs (green, noted by arrows) derived from $\beta 1$ deficient Cre recombinase activated type 2 AECs (marked by pro-SP-C in yellow) are shown 24-month-old $\beta 1^{rtTA}; mTmG$ mice.

Supp. Figure 2



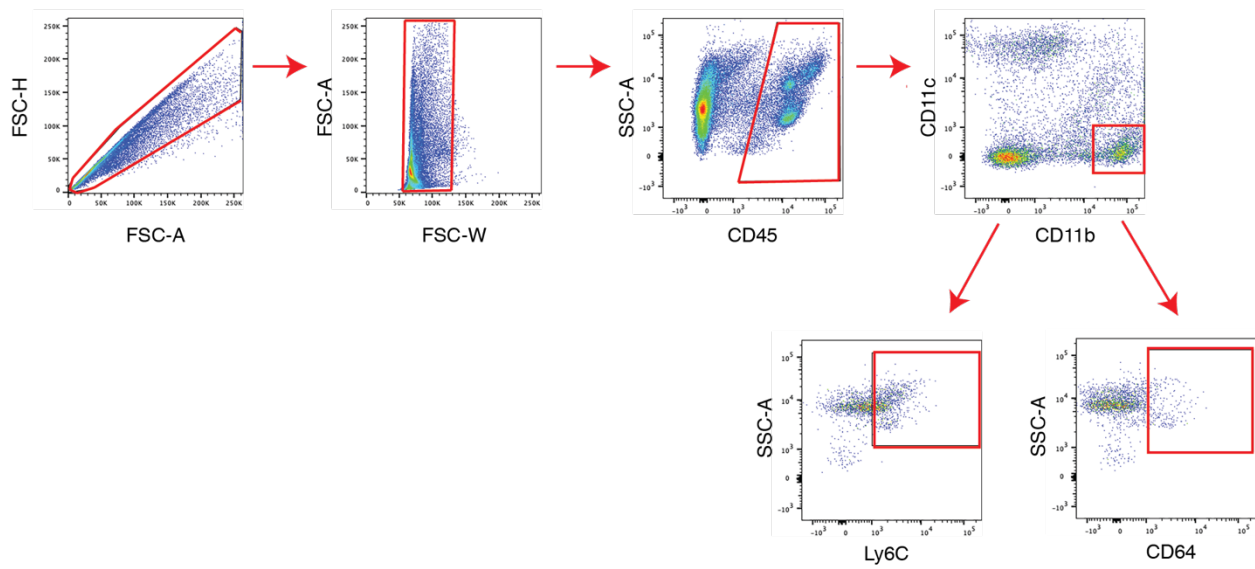
Supp. Figure 2 (A) Increased BALF protein in 3-month-old $\beta 1^{rtTA}$ mice ($n = 7$ $\beta 1^{f/f}$ mice, 8 $\beta 1^{rtTA}$ mice). (B) Increased monocyte-macrophages in BALF from 3-month-old $\beta 1^{rtTA}$ mice ($n = 9$ $\beta 1^{f/f}$ mice, 7 $\beta 1^{rtTA}$ mice). * $p < 0.05$ by 2-tailed Student's t test.

Supp. Figure 3



Supp. Figure 3. (A) Lung sections immunostained for Ki67 (green) and CD68 (red) demonstrate increase in total # of proliferating cells, quantified in (B), and an increase in proliferating CD68+ macrophages in $CCR2^{-/-};\beta1^{rtTA}$ lungs, quantified in (C) (20 sections/ mouse; n = 3 mice/ group). (D) Lung sections immunostained for Ki67 (green) and pro-SP-C (red) demonstrate no difference in the percent of proliferating type 2 AECs in $CCR2^{-/-};\beta1^{rtTA}$ lungs compared to $CCR2^{-/-};\beta1^{f/f}$ lungs, quantified in (E) (20 sections/ mouse; n = 4 mice/ group). Scale bar = 50 μm for A, D. * $p < 0.05$ by 2-tailed Student's t test.

Supp. Figure 4



Supp. Figure 4. Representative gating strategy for CD45⁺ CD11b⁺ CD11c⁻ gate in Fig. 7A-D.

Supplemental Table 1. Monocyte Media Cytokine Multiplex

Analyte	$\beta 1^{f/f}$	$\beta 1^{rtTA}$
	pg/ml (st dev)	pg/ml (st dev)
CCL2	3.74 (0.89)	3.41 (0.33)
Eotaxin	4.25 (2.28)	3.74 (0.80)
G-CSF	9.35 (6.32)	6.08 (1.38)
GM-CSF	4.45 (2.22)	3.87 (1.01)
IFN γ	5.91 (2.02)	4.46 (0.94)
IL-1 α	4.13 (2.07)	3.69 (0.79)
IL-1 β	7.91 (3.24)	5.97 (1.51)
IL-2	4.12 (1.98)	3.52 (0.59)
IL-3	4.22 (2.21)	3.85 (0.99)
IL-4	4.72 (2.13)	3.33 (0.32)
IL-5	4.79 (2.80)	4.1 (1.24)
IL-6	12.57 (8.55)	7.44 (2.34)
IL-7	4.88 (2.81)	4.45 (1.44)
IL-9	4.39 (2.23)	3.63 (0.68)
IL-10	4.94 (1.75)	4.23 (1.22)
IL-12(p40)	4.21 (2.12)	3.72 (0.61)
IL-12(p70)	4.16 (2.14)	3.47 (0.46)
IL-13	4.13 (2.07)	3.80 (1.07)
IL-15	4.74(2.22)	4.03 (1.12)
IL-17	4.91 (2.27)	4.2 (1.18)
IP-10	6.38 (3.98)	4.2 (1.18)
LIF	4.38 (2.31)	3.66 (0.73)
LIX	9.67 (4.99)	7.94 (2.44)
KC	3.29 (0.21)	8.47 (9.28)
M-CSF	4.32 (2.25)	3.61 (0.48)
MIG	4.09 (2.00)	3.69 (0.76)
MIP-1 α	8.91 (5.95)	5.9 (2.06)
MIP-1 β	36.11 (38.31)	16.17 (14.71)
MIP-2	15.17 (18.00)	4.81 (1.06)
RANTES	30.45 (34.90)	20.51 (18.34)
VEGF	7.07 (3.17)	6.18 (2.60)
TNF α	18.6 (12.90)	12.18 (5.95)

Supp. Table 1. No difference in inflammatory analytes from $\beta 1^{rtTA}$ and $\beta 1^{f/f}$ monocyte-macrophage conditioned media. Cytokine multiplex analysis on monocyte-macrophage conditioned media from $\beta 1^{f/f}$ and $\beta 1^{rtTA}$ lungs. (n = 5 $\beta 1^{f/f}$, 6 $\beta 1^{rtTA}$ mice/ group). Groups compared by 2-tailed Student's t test, but all groups were nonsignificant with $p > 0.05$.

Supplemental Table 2. AEC Media Cytokine Multiplex

Analyte	$\beta 1^{ff}$ pg/ml (st dev)	$\beta 1^{rtTA}$ pg/ml (st dev)
CCL2	34.13 (36.35)	122.14 (95.51)*
Eotaxin	3.31 (0.24)	5.23 (4.20)
G-CSF	80.42 (91.07)	275.36 (192.32)*
GM-CSF	15.92 (13.27)	41.37 (31.73)*
IFN γ	3.93 (1.30)	3.95 (1.18)
IL-1 α	31.26 (25.42)	32.88 (20.05)
IL-1 β	4.95 (1.49)	8.93 (6.30)
IL-2	8.67 (5.62)	7.74 (3.32)
IL-3	3.20 (0)	3.20 (0)
IL-4	3.33 (.43)	3.96 (2.11)
IL-5	6.07 (3.62)	15.02 (11.81)*
IL-6	243.13 (368.62)	774.16 (672.49)*
IL-7	3.20 (0)	3.20 (0)
IL-9	61.42 (31.29)	62.08 (26.22)
IL-10	9.95 (9.05)	9.38 (5.44)
IL-12(p40)	3.76 (0.96)	3.74 (0.77)
IL-12(p70)	3.74 (0.90)	4.22 (0.94)
IL-13	11.73 (0)	11.73 (0)
IL-15	3.60(0.55)	4.49 (1.19)*
IL-17	3.2 (0)	3.26 (0.20)
IP-10	29.61 (18.06)	76.91 (57.46)*
LIF	11.42 (7.52)	23.49 (13.95)*
LIX	16.96 (26.28)	41.22 (39.14)
KC	324.81 (374.16)	986.96 (809.59)*
M-CSF	3.65 (0.92)	4.01 (1.14)
MIG	3.36 (0.34)	5.13 (2.79)*
MIP-1 α	38.17 (44.39)	55.13 (40.21)
MIP-1 β	29.54 (45.16)	46.55 (42.57)
MIP-2	619.50 (485.09)	87.01 (519.44)
RANTES	6.14 (2.43)	7.36 (4.35)
VEGF	41.24 (46.81)	71.46 (35.19)
TNF α	4.83 (1.55)	4.62 (1.00)

Supp. Table 2. Increased inflammatory analytes from $\beta 1^{rtTA}$ type 2 AEC media. Cytokine multiplex analysis on media collected from primary type 2 AECs isolated from $\beta 1^{ff}$ and $\beta 1^{rtTA}$ mice. (n= 11-12/ group). * $p < 0.05$ by 2-tailed Student's t test.

Supplemental Table 3. Tissue Lysate Cytokine Multiplex

Analyte	$\beta 1^{ff}$	CCR2-/-; $\beta 1^{ff}$	$\beta 1^{rtTA}$	CCR2-/-; $\beta 1^{rtTA}$
	pg/ml (st dev)	pg/ml (st dev)	pg/ml (st dev)	pg/ml (st dev)
CCL2	10.25 (7.48)	12.54 (5.87)	14.69 (5.43)	48.49 (16.38) ^{a,c}
Eotaxin	3.26 (0.10)	3.20 (0)	4.46 (1.62)	19.36 (18.79)
G-CSF	42.91 (74.00)	4.19 (2.22)	440.37 (284.34)	1004.54 (805.28) ^{a,b}
GM-CSF	4.08 (1.42)	3.35 (0.20)	11.70 (5.81)	47.08 (34.13) ^a
IFN γ	3.20 (0)	3.20 (0)	5.63 (3.18)	42.69 (69.44)
IL-1 α	42.97 (22.59)	23.51 (3.47)	404.81 (193.31)	1430.88 (1523.56) ^{a,b}
IL-1 β	9.59 (6.93)	6.93 (2.25)	109.34 (83.23)	450.61 (213.01) ^{a,b,c}
IL-2	3.32 (0.29)	3.20 (0)	5.55 (2.45)	4.70 (1.69)
IL-3	3.20 (0)	3.31 (0.21)	3.20 (0)	3.20 (0)
IL-4	3.20 (0)	3.20 (0)	3.20 (0)	3.20 (0)
IL-5	3.20 (0)	3.20 (0)	3.20 (0)	5.89 (4.22)
IL-6	111.43 (245.95)	30.12 (25.84)	1753.65 (1738.10)	8933.67 (5477.94) ^{a,b,c}
IL-7	3.20 (0)	3.20 (0)	3.20 (0)	3.20 (0)
IL-9	217.58 (49.04)	178.80 (98.65)	184.83 (103.09)	192.32 (65.29)
IL-10	3.44 (0.39)	4.44 (2.48)	5.46 (1.45)	12.31 (6.36) ^{a,b,c}
IL-12(p40)	3.53 (0.51)	3.58 (0.38)	4.91 (1.71)	5.78 (1.70)
IL-12(p70)	3.41 (0.43)	3.20 (0)	5.64 (1.95)	13.01 (2.89) ^{a,b,c}
IL-13	4.42 (0.89)	6.31 (2.32)	10.30 (5.18)	22.62 (12.09) ^{a,b,c}
IL-15	3.50 (0.48)	3.31 (0.21)	23.20 (31.73)	50.14 (22.81) ^{a,b}
IL-17	21.15 (42.64)	7.81 (9.22)	153.31 (303.19)	3289.61 (3660.91) ^a
IP-10	7.02 (3.59)	13.68 (12.19)	50.81 (96.95)	148.20 (157.77)
LIF	3.69 (1.19)	5.82 (5.23)	6.13 (4.26)	27.74 (24.95) ^a
LIX	224.59 (328.48)	80.23 (71.25)	1065.61 (657.09)	2297.17 (2051.08) ^{a,b}
KC	150.42 (184.16)	289.53 (256.45)	1798.74 (1673.42)	10435.50 (1902.10) ^{a,b,c}
M-CSF	3.20 (0)	3.20 (0)	3.90 (0.10)	6.27 (1.85)
MIG	5.13 (1.61)	13.73 (9.43)	15.78 (19.98)	86.25 (57.67) ^{a,b,c}
MIP-1 α	119.49 (81.91)	47.27 (36.53)	1390.23 (1364.85)	7773.33 (4642.49) ^{a,b,c}
MIP-1 β	21.88 (14.42)	35.50 (35.55)	462.82 (477.71)	1068.14 (814.03) ^{a,b}
MIP-2	6012.40 (7334.83)	2665.36 (1880.39)	19216.50(4829.08)	19291.50 (2707.78) ^{a,b,c,d}
RANTES	5.39 (3.77)	9.07 (6.81)	9.42 (11.24)	29.63 (35.38)
VEGF	3.20 (0)	3.20 (0)	3.20 (0)	3.20 (0)
TNF α	1709.72 (4024.86)	100.10 (58.34)	1490.39 (1930.89)	467.29 (305.10)

Supp. Table 3. Increased inflammatory analytes from $\beta 1^{rtTA}$ and CCR2-/-; $\beta 1^{rtTA}$ tissue lysates. Cytokine multiplex analysis on tissue lysate samples from $\beta 1^{ff}$, CCR2-/-; $\beta 1^{ff}$, $\beta 1^{rtTA}$, and CCR2-/-; $\beta 1^{rtTA}$ lungs. (n = 4-6 mice/ group). $p < 0.05$ by one-way ANOVA with secondary analysis by Tukey's test for multiple comparisons, $a = \beta 1^{ff}$ vs. CCR2-/-; $\beta 1^{rtTA}$, $b =$ CCR2-/-; $\beta 1^{ff}$ vs. CCR2-/-; $\beta 1^{rtTA}$, $c = \beta 1^{rtTA}$ vs. CCR2-/-; $\beta 1^{rtTA}$, $d = \beta 1^{ff}$ vs. CCR2-/-; $\beta 1^{ff}$.