

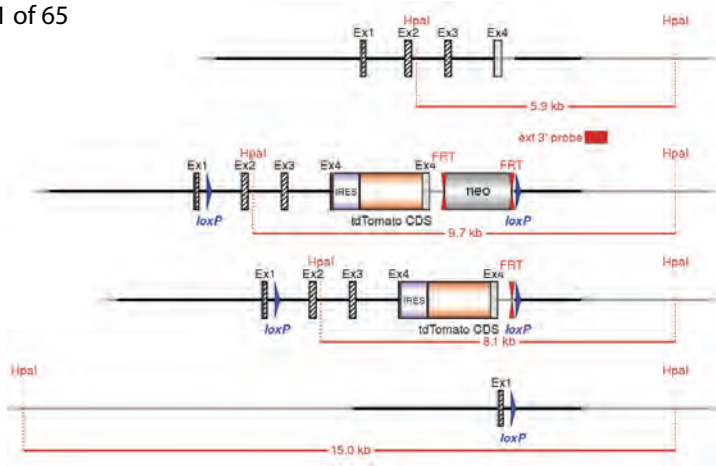
Supplementary Figure 1 Quantification of proliferating epithelial cells during *N.b.* infection and demonstration of IL-4R alpha-independent TFF2 induction.

(a-b) Isotype controls for (a) naive and (b) d5 post-infection of Ym1/Ki-67 staining in **Figure 1c**. Donkey anti-goat (Cy2) and donkey anti-rabbit (Cy3) secondary antibodies were added in the absence of primary antibodies.

(c) Flow cytometry gating strategy for the identification of distal lung epithelial cells within single cell suspensions of lung tissue digests: Selection of singlets, fluorescence minus one (FMO) gating for aqua viability dye, dead cell exclusion using aqua viability dye, FMO for CD45⁻ EpCAM⁺ epithelia, representative positive staining for EpCAM⁺ cells, FMO for pro-SPC staining, positive pro-Spc staining, and (k) BrdU FMO in the proSPC gate, positive staining for BrDU EpCAM gate.

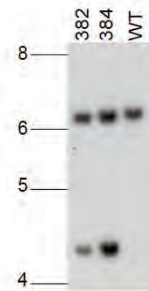
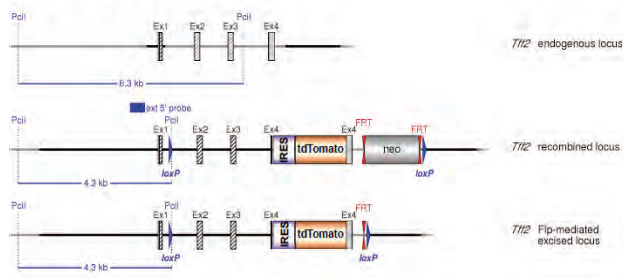
(d) Quantification of total numbers of CD45⁻ EpCAM⁺ pro-SPC⁺ epithelia at d4 following *N.b.* infection. Each symbol represents an individual mouse. (e) lung mRNA transcripts for each TFF family member in WT vs IL-4R $\alpha^{-/-}$ mice following *N. b.* infection (N=3-4/group).

a



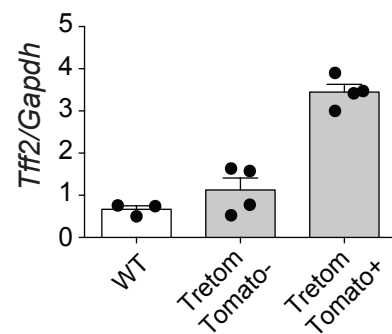
b

- 5' Southern blot



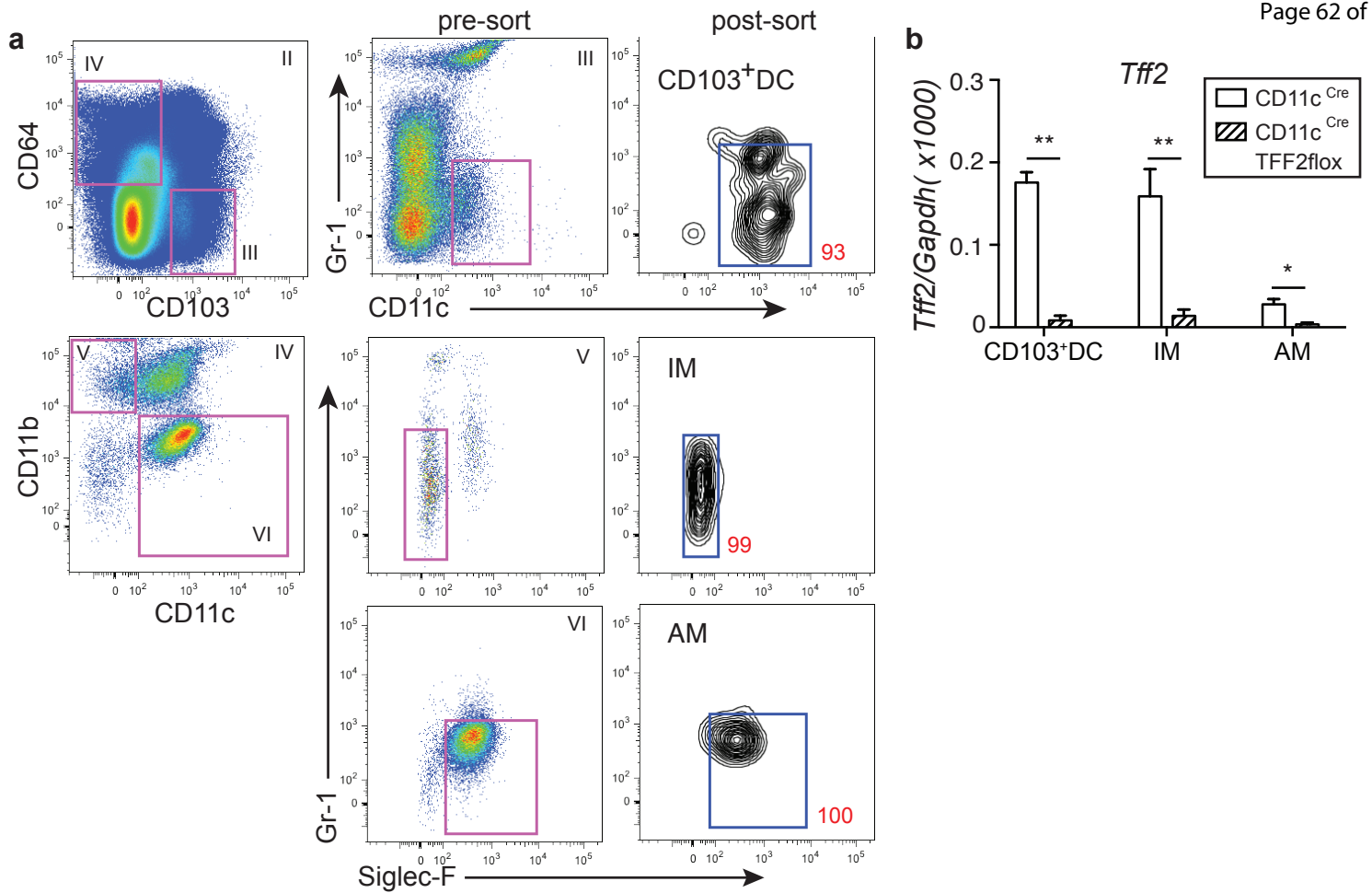
c

Gastric epithelia



Supplementary Figure 2. TFF2 fluorescent reporter mouse (Tre-Tom) and TFF2 expressing gastric cells

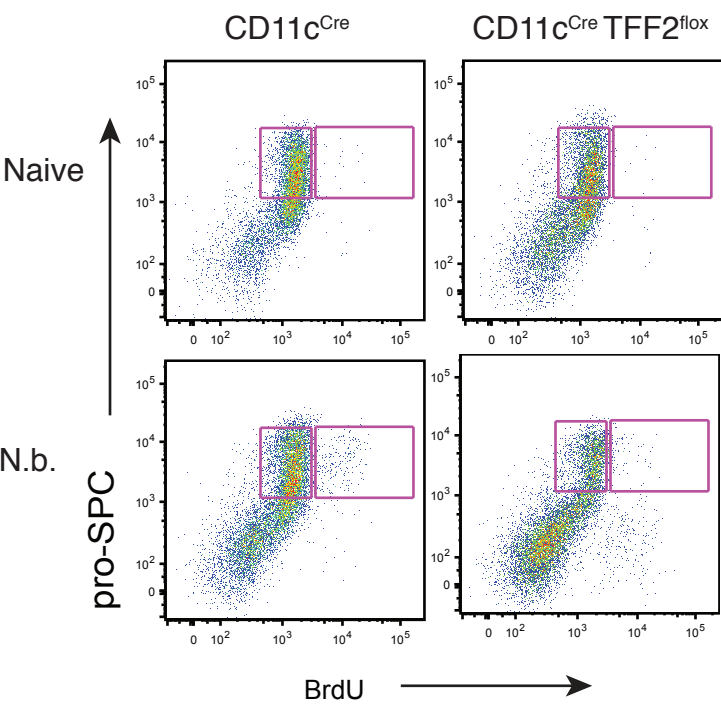
(a) Genomic C57BL/6 embryonic stem (ES) cell DNA was used to generate a targeting vector that possessed homology to the single *Tff2* isoform that encodes a 129 aa protein (NP_033389). The targeting vector contained long and short homology arms of 6.4 and 1.6kb, respectively, with loxP sites flanking *Tff2* exons 2-4 and an IRES td-Tomato reporter downstream of the endogenous STOP codon. Targeted C57BL/6 ES were injected into blastocysts from albino C57BL/6 (C57BL/CJ-Tyrc-2J/J) chimeras identified and bred to deleter strains. Schematic shows the outcome following breeding of Tre-Tom mice with Flp recombinase or cre-deleter strains. (b) Southern blot was used to confirm homologous recombination at the 5' end using an internal homology arm to detect Pci generated fragments. (c) Expression of *Tff2* in sorted gastric epithelial cells from WT and Tretom reporter mice. Symbols represent individual mouse.



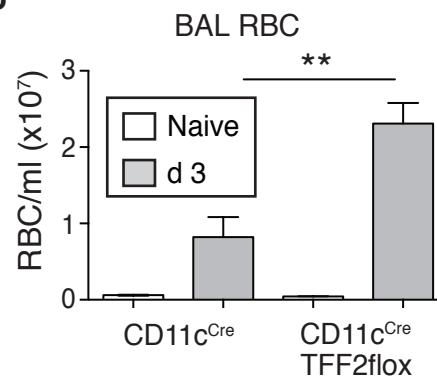
Supplementary Figure 3 Expression of *Tff2* in multiple lung myeloid cells

(a) Sorting strategy for lung myeloid cells at d4 following *N.b.* infection. Pre-sort gating and post-sort purity check from a representative mouse are shown. (b) *Tff2* expression levels in sorted myeloid subsets in the lung at d4 post-*N.b.* infection. (N=4). * $p < 0.05$ and **, $p < 0.01$ and ***, $p < 0.005$ as determined by Student's t-test.

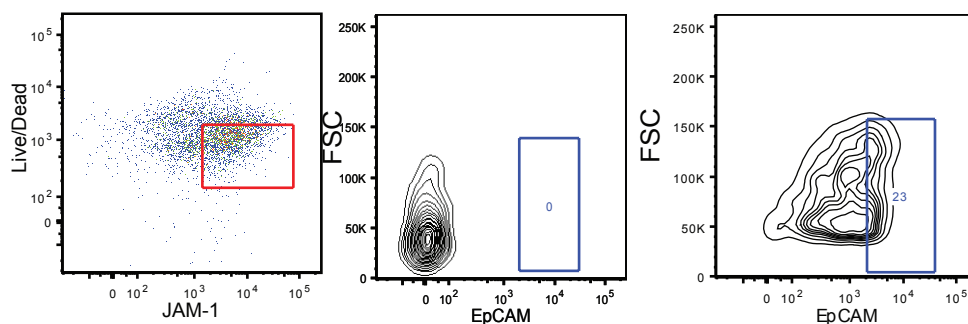
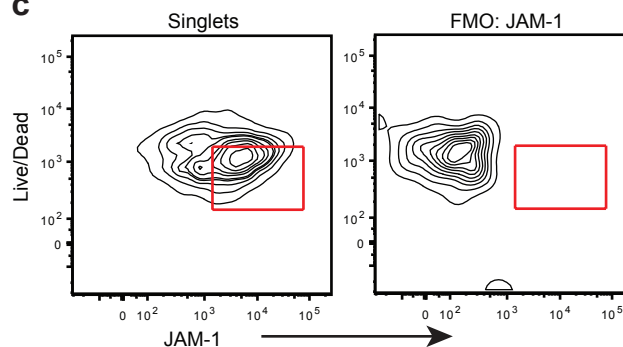
a



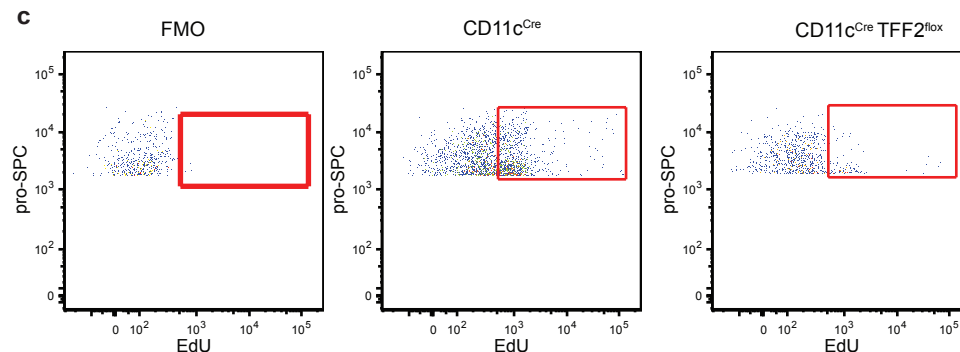
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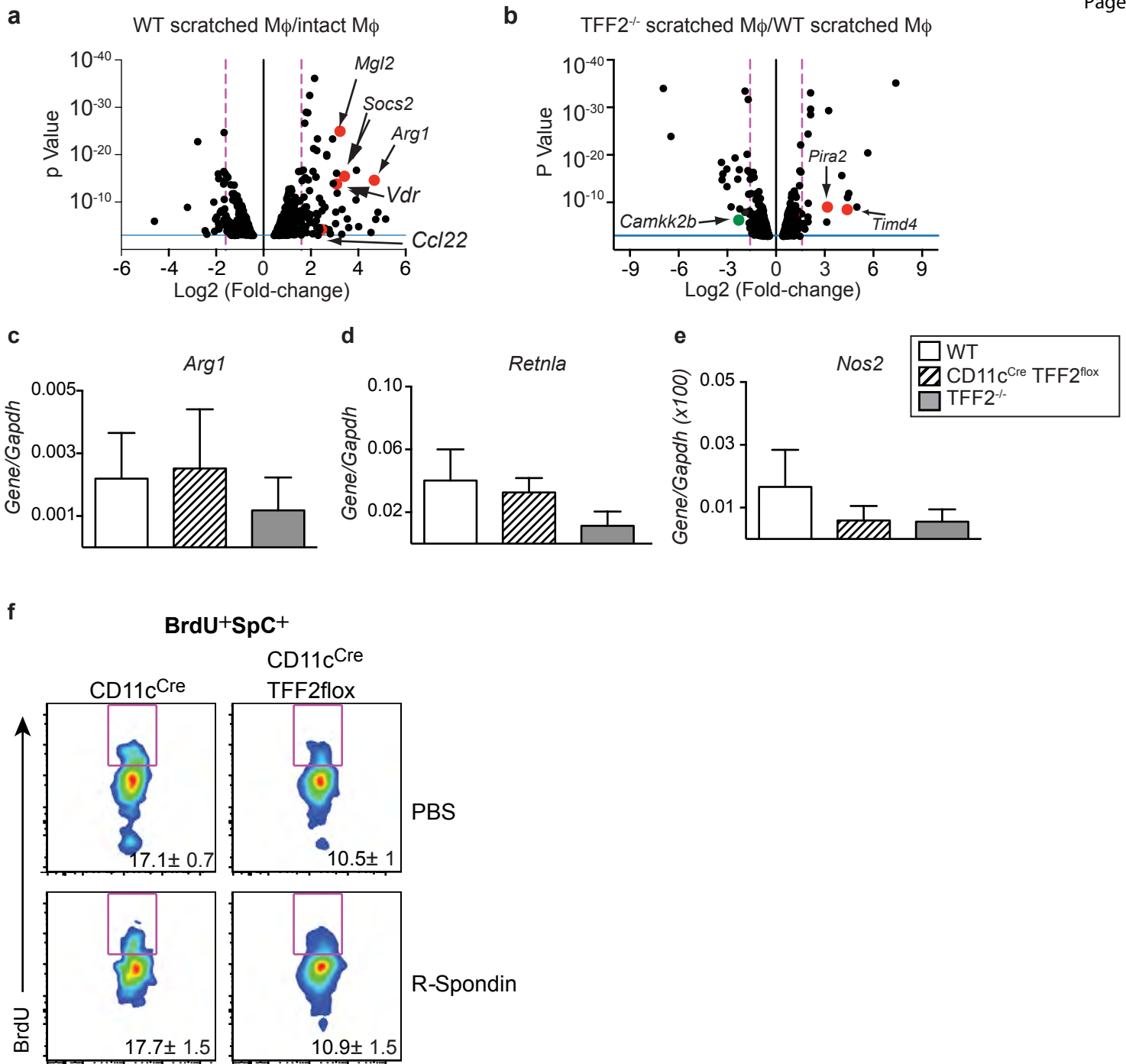


c



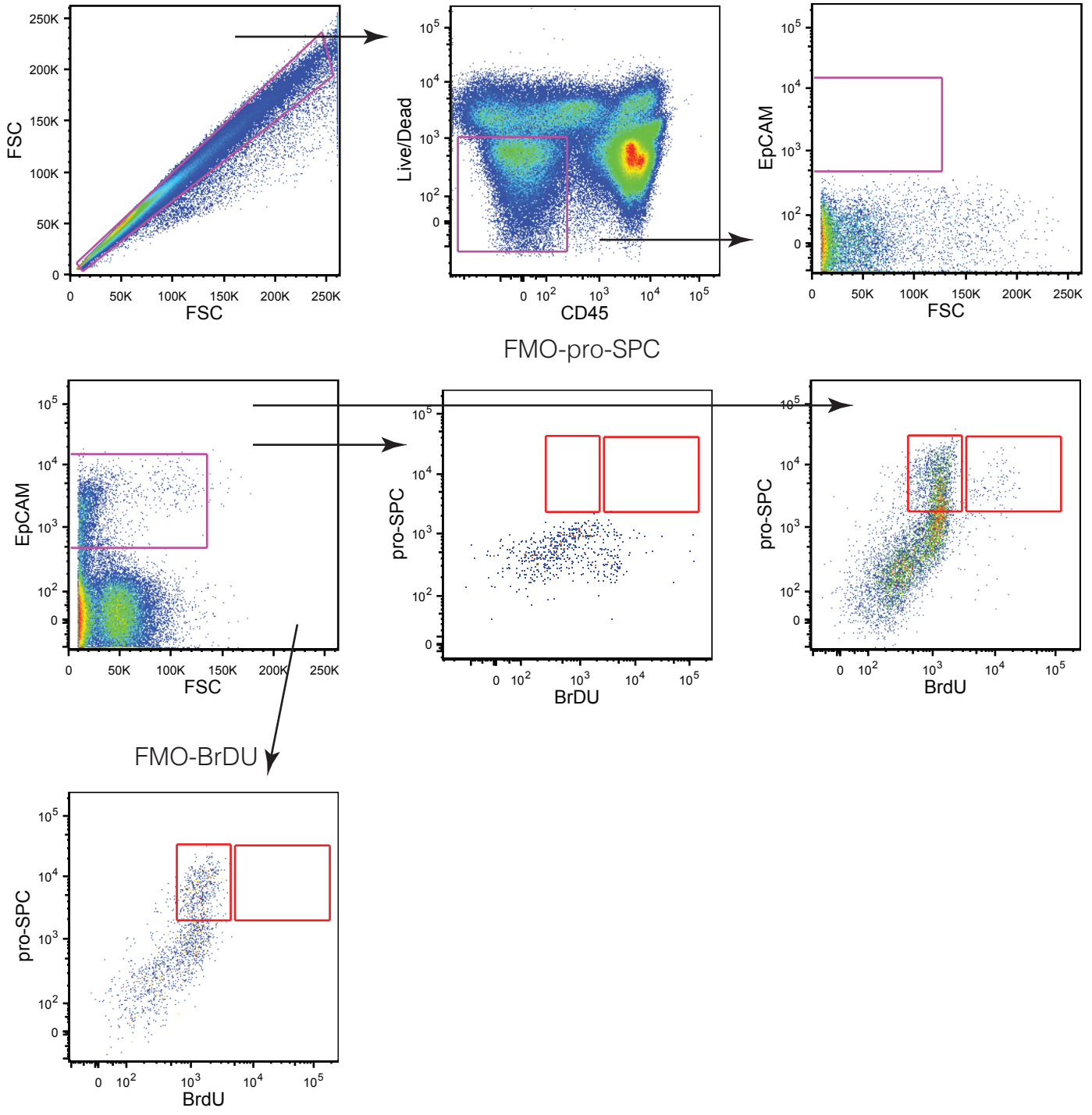
Supplementary Figure 4 TFF2 produced by lung meloid cells is critical in pathogenesis during *N.b.* infection

(a) Representative dot plots showing gating strategy for pro-SPC pos BrdU pos ATII cells pre and post *N.b.* infection (b) Numbers of RBC in BAL fluid at d3 following *N.b.* infection. (c) Gating strategy for MERA to identify live JAM-1 positive epithelia recovered from the apical side of the transwell insert. (c) EdU FMO for pro-SPC positive cells within the CD45 neg, EpCAM positive pro-SPC pos gate in BrdU experiments at day 9 for Bleomycin experiments.



Supplementary Figure 5 Gene expression of BMM or AM upon exposure to injury and the effect of R-spondin on epithelial proliferation after *N.b.* infection

(a,b) Volcano plots showing results of RNASeq comparing WT BMM recovered from MERA that were exposed to (a) intact or scratched MTEC and (b) WT or TFF2^{-/-} BMM exposed to damaged MTEC. (c-e) Sorted AM from WT, CD11c^{Cre}-TFF2^{lox} or TFF2^{-/-} at d4 post-*N.b.* infection were subjected to QRT-PCR to assess (c) *Arg1*, (d) *Retnla* and (e) *Nos2* levels. N=3/group. (f) Lungs were collected from CD11c^{Cre} or CD11c^{Cre}-TFF2^{lox} mice, treated with PBS or R-spondin, on d4 post-*N.b.*infection. Percentages of CD45 neg, EpCAM pos BrdU⁺SpC⁺ were analyzed by flow cytometry. Numbers indicate mean \pm SEM from 5 samples.



Supplementary Figure 6 Gating ancestry to identify BrdU positive ATII cells

Selection of singlets, dead cell exclusion using aqua viability dye fluorescence minus one (FMO) gating for FMO for CD45⁻ EpCAM⁺ epithelia, representative positive staining for EpCAM⁺ cells, FMO for pro-SPC staining, positive pro-Spc staining, and (k) BrdU FMO in the proSPC gate.