

Supplementary Figure 5. Scgb1a1+ marked cells in lung injury and triple transgenic models of pulmonary lineage ablation. A and B, Representative epifluorescence images of tumor-bearing lungs (A; top), as well as merged fluorescent microscopy images of lung tumors (merges of endogenous mT and mG stained with Hoechst 33258; A, bottom) and data summary of mG+ tumors and tumor cells (B) of six-week-old mT/mG; Scgb1a1. Cre mice that received saline (n = 12) or 0.08 units bleomycin (n = 13) intratracheally, were allowed to recover for one month, and subsequently received ten weekly intraperitoneal injections of 1 g/Kg urethane to be sacrificed six months after first urethane injection. Arrows and dashed outlines in (A) indicate tumors. Note the enrichment of lung adenocarcinomas in mG+ cells in response to bleomycin, which depletes resident alveolar type II (ATII) cells, as shown in Figure 4B. C and D, Representative fluorescent microscopic images [C: merges of Hoechst 33258-stained endogenous mT and mG immunostained for surfactant protein C (SFTPC, left) or Clara cell secretory protein (CCSP, right)] and data summary of percentage of mG+ airway cells (D; n = 5 mice/group) of mT/mG; Scgb1a1. Cre mice after intraperitoneal injection of 250 mg/Kg naphthalene given at six weeks of age. Arrows denote naphthalene-induced airway epithelial gaps that are restored by mG+CCSP+SFTPC- cells. **E** and **F**, Representative lung sections of 12-week-old mT/mG;Scgb1a1.Cre, mT/mG;Lvz2.Cre, mT/mG;Scgb1a1.Cre;Dta, and mT/mG;Lyz2.Cre;Dta mice (E; n = 6/group) and data summary of airway (top) and alveolar (bottom) mG+ cells (F; n = 6/group). Note increased bronchial (b) and alveolar (a) size, complete airway epithelial denudement, and prominent distortion of bronchial and alveolar structure of mT/mG;Scgb1a1.Cre;Dta mice compared with other strains, mimicking human emphysema. Note also mG+ alveolar macrophages (AM Φ) in mT/mG; Lyz2. Cre; Dta mice (arrows). Measurements were from at least five non-overlapping tumor, airway, or alveolar fields/lung. Data are given as mean \pm SD. ns, *, and ***: P > 0.05, P < 0.05, and P < 0.001, respectively, for the indicated comparisons by unpaired Student's t-test (B), for comparison with time-point zero by one-way ANOVA with Bonferroni post-tests (D), or for comparison of the indicated columns to all other

groups by one-way ANOVA with Bonferroni post-tests (F). mG, membranous green fluorescent protein fluorophore; mT, membranous tomato fluorophore.