

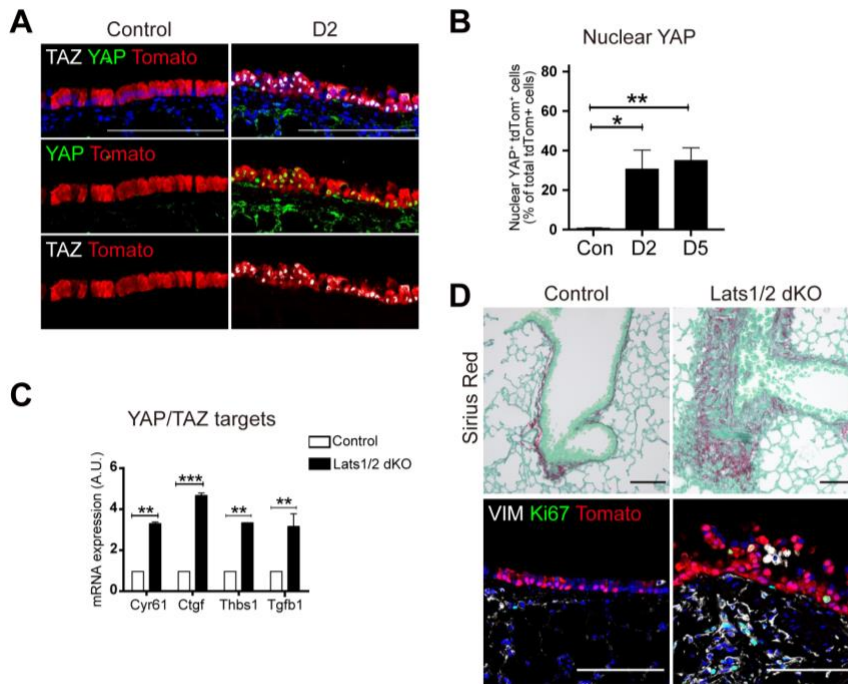
Appendix

Airway secretory cell fate conversion via YAP-mTORC1-dependent essential amino acid metabolism

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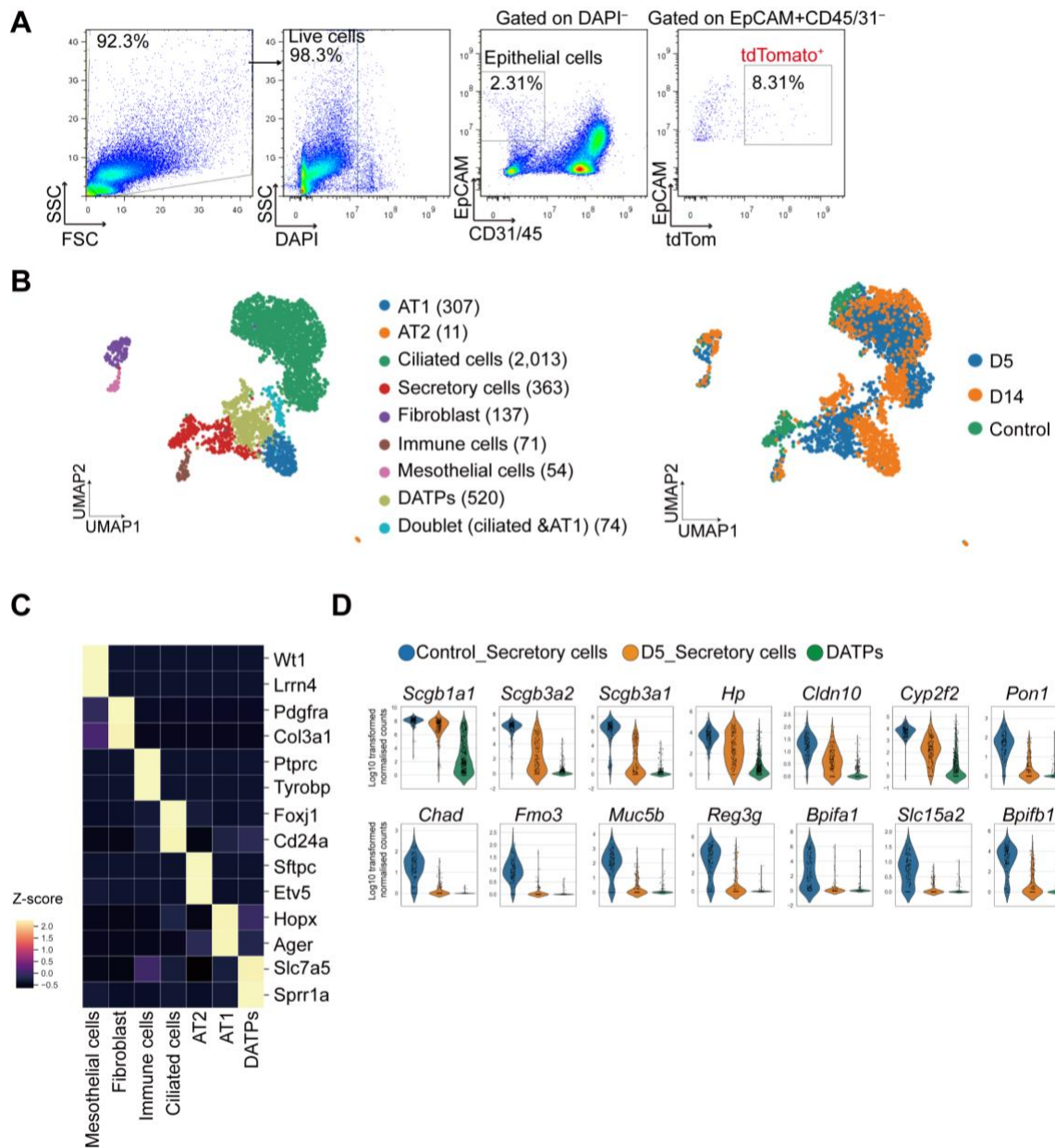
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Appendix Figure S1. Activation of YAP/TAZ by *Lats1/2* deletion leads to peribronchiolar fibrosis

- A** Representative IF images showing the expression of YAP and TAZ in control and *Lats1/2* dKO lungs at day 2 post tamoxifen treatment. Tomato (for secretory lineage, red), TAZ (white), YAP (green), and DAPI (blue). Scale bars, 100 μ m.
- B** Quantification of nuclear YAP in *Scgbl1* lineage-labeled cells of control and *Lats1/2* dKO lungs at day 2 and 5 post tamoxifen treatment. Data are presented as mean \pm SEM (n=3, each group). *p<0.05, **p<0.01.
- C** qPCR analysis of YAP/TAZ target genes (*Cyr61*, *Ctgf*, *Thbs1*, *Tgfb1*) in freshly isolated *Scgbl1* lineage-labeled cells of control and *Lats1/2* dKO lungs at day 2 post tamoxifen treatment. Data are presented as mean \pm SEM (n=3, each group). **p<0.01, ***p<0.001.
- D** Representative images of Sirius red staining for collagen (top) and IF images of proliferating mesenchymal cells (bottom) in control and *Lats1/2* dKO lungs at day 7 post tamoxifen treatment. Tomato (for secretory lineage, red), VIM (Vimentin for mesenchyme, white), Ki67 (for proliferating cells, green), and DAPI (blue). Scale bars, 100 μ m.



Appendix Figure S2. Unfiltered single cell RNA sequencing results

- A** Flow cytometry sorting scheme for isolating *Scgb1a1* lineage-labeled tdTomato⁺ cells from control lungs at day 5 post tamoxifen treatment and *Lats1/2* dKO lungs at day 5 and 14 post tamoxifen treatment for scRNA-sequencing.
- B** UMAP plot showing unfiltered cell clusters identified in merged single-cell transcriptomes from control and *Lats1/2* dKO lungs at day 5 and 14 post tamoxifen treatment.
- C** Heatmap of representative cell marker genes of each cell cluster.
- D** Violin plot of secretory cell markers in secretory cells and DATP cells of control and *Lats1/2* dKO lungs. Of note, most of the secretory marker genes are dramatically lost in *Lats1/2*-deficient secretory cells at day 5 post tamoxifen induction.