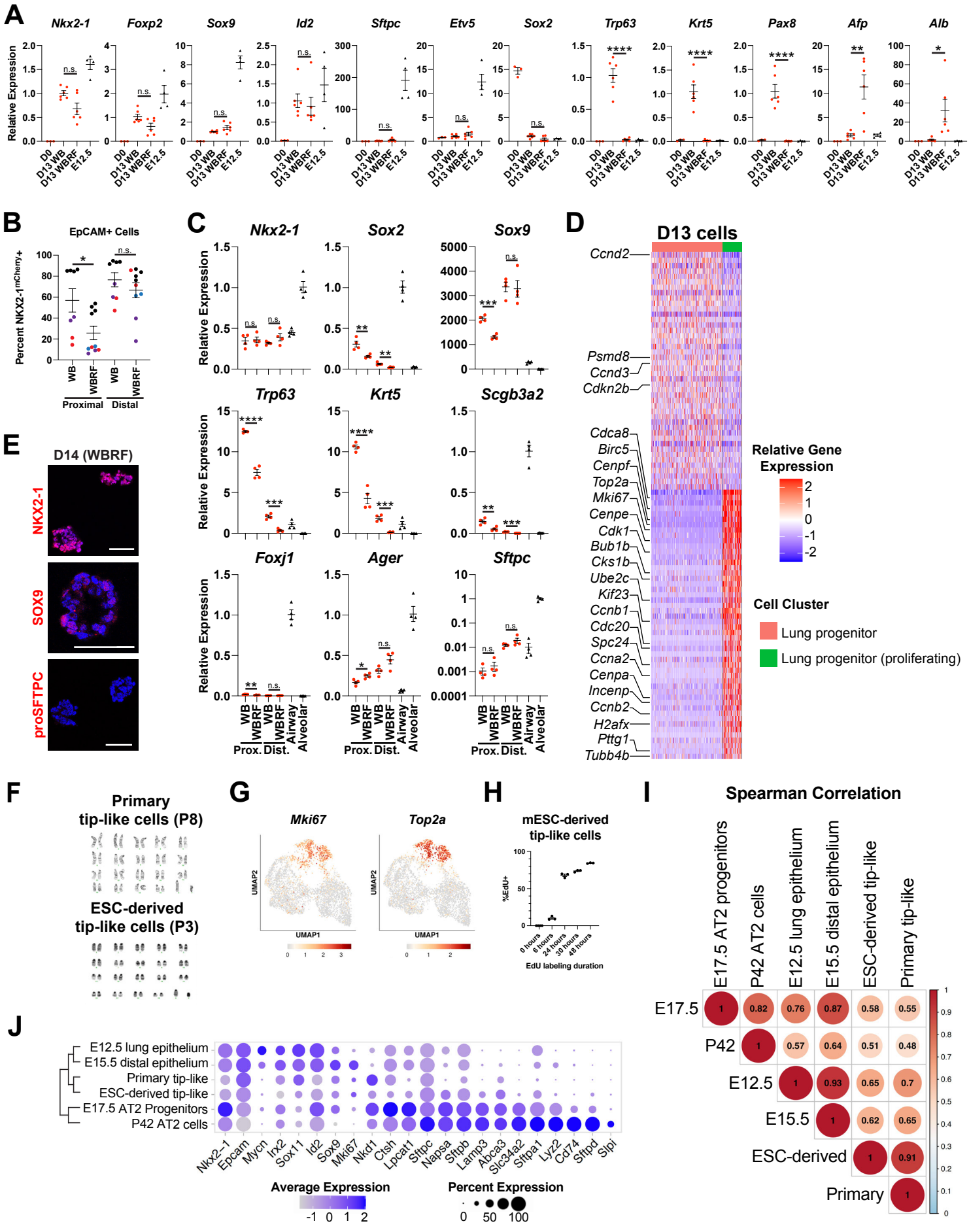
Fig. S1


A
Nkx2-1
Foxp2
Sox9
Id2
Sftpc
Etv5
Sox2
Trp63
Krt5
Pax8
Afp
Alb
Relative Expression
D0
D13 WB
D13 WBRF
E12.5
B
EpCAM+ Cells
Percent NKX2-1mCherry+
WB
WBRF
Proximal
Distal
C
Nkx2-1
Sox2
Sox9
Trp63
Krt5
Scgb3a2
Foxj1
Ager
Sftpc
Relative Expression
Prox.
Dist.
Airway
Alveolar
D
D13 cells
Ccnd2
Psmd8
Ccnd3
Cdkn2b
Cdca8
Birc5
Cenpf
Top2a
Mki67
Cenpe
Cdk1
Bub1b
Cks1b
Ube2c
Kif23
Ccnb1
Cdc20
Spc24
Ccna2
Cenpa
Incenp
Ccnb2
H2afx
Pttg1
Tubb4b
Relative Gene Expression
Cell Cluster
Lung progenitor
Lung progenitor (proliferating)
E
D14 (WBRF)
NKX2-1
SOX9
proSFTPC
F
Primary tip-like cells (P8)
ESC-derived tip-like cells (P3)
G
Mki67
Top2a
UMAP1
UMAP2
H
mESC-derived tip-like cells
%EdU+
0 hours
6 hours
24 hours
30 hours
48 hours
EdU labeling duration
I
Spearman Correlation
E17.5 AT2 progenitors
P42 AT2 cells
E12.5 lung epithelium
E15.5 distal epithelium
ESC-derived tip-like
Primary tip-like
E17.5
P42
E12.5
E15.5
ESC-derived
Primary
1
0.82
0.76
0.87
0.58
0.55
0.57
0.64
0.51
0.48
0.93
0.65
0.7
0.62
0.65
0.91
J
E12.5 lung epithelium
E15.5 distal epithelium
Primary tip-like
ESC-derived tip-like
E17.5 AT2 Progenitors
P42 AT2 cells
Nkx2-1
Epcam
Mycn
Irx2
Sox11
Id2
Sox9
Mki67
Nkd1
Ctsh
Lpcat1
Sftpc
Napsa
Sftpb
Lamp3
Abca3
Slc34a2
Sftpa1
Lyz2
Cd74
Sftpd
Slpi
Average Expression
Percent Expression

Supplemental Figure 1: Characterization of ESC-derived Lung Epithelial Progenitors and ESC-derived Tip-like Cells, Related to Figures 1, 2

(A) Analysis of gene expression by RT-qPCR at day 13 of WB and WBRF lung specification protocols compared to ESCs (D0) and freshly collected E12.5 SOX9+ epithelium. n.s. not significant, * $p<0.05$, ** $p<0.01$, **** $p<0.0001$ by unpaired, two-tailed Student's t-test. n= 3, 6, 6, 4 biological replicates. Error bars = mean +/- SEM.

(B) The percent of cells that were NKX2-1^{mCherry}+ based on specification (WB vs WBRF) and differentiation (Proximal vs Distal) protocols. Dot color indicates biological replicates performed in the same batch. n.s. not significant, * $p<0.05$ by one-way ANOVA. n= 8, 10, 8, 10 biological replicates. Error bars = mean +/- SEM.

(C) RT-qPCR analysis of gene expression in day 26 NKX2-1^{mCherry}+ cells of proximal and distal differentiation protocols. Cultured cells were compared to freshly collected epithelial cells from adult mouse lungs (Airway and Alveolar). n.s. not significant, * $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$ by unpaired, two-tailed Student's t-test. n= 4 biological replicates. Error bars = mean +/- SEM.

(D) Row-normalized heatmap of the top 50 most up-regulated and top 50 most down-regulated genes (with adj. p-value <0.05, ordered by logFC) between the clusters Lung progenitor and Lung progenitor (proliferating) in day 13 of the WBRF specification protocol. Annotated genes are associated with proliferation.

(E) Representative immunofluorescence confocal microsocopy of paraffin tissue sections prepared from day 14 cells cultured in the WBRF specification protocol. Staining performed with antibodies against NKX2-1, SOX9, or proSFTPC. Nuclei stained with Hoechst, scale bars are 200um.

(F) Representative G-banding indicates karyotypically normal primary and ESC-derived tip-like cells.

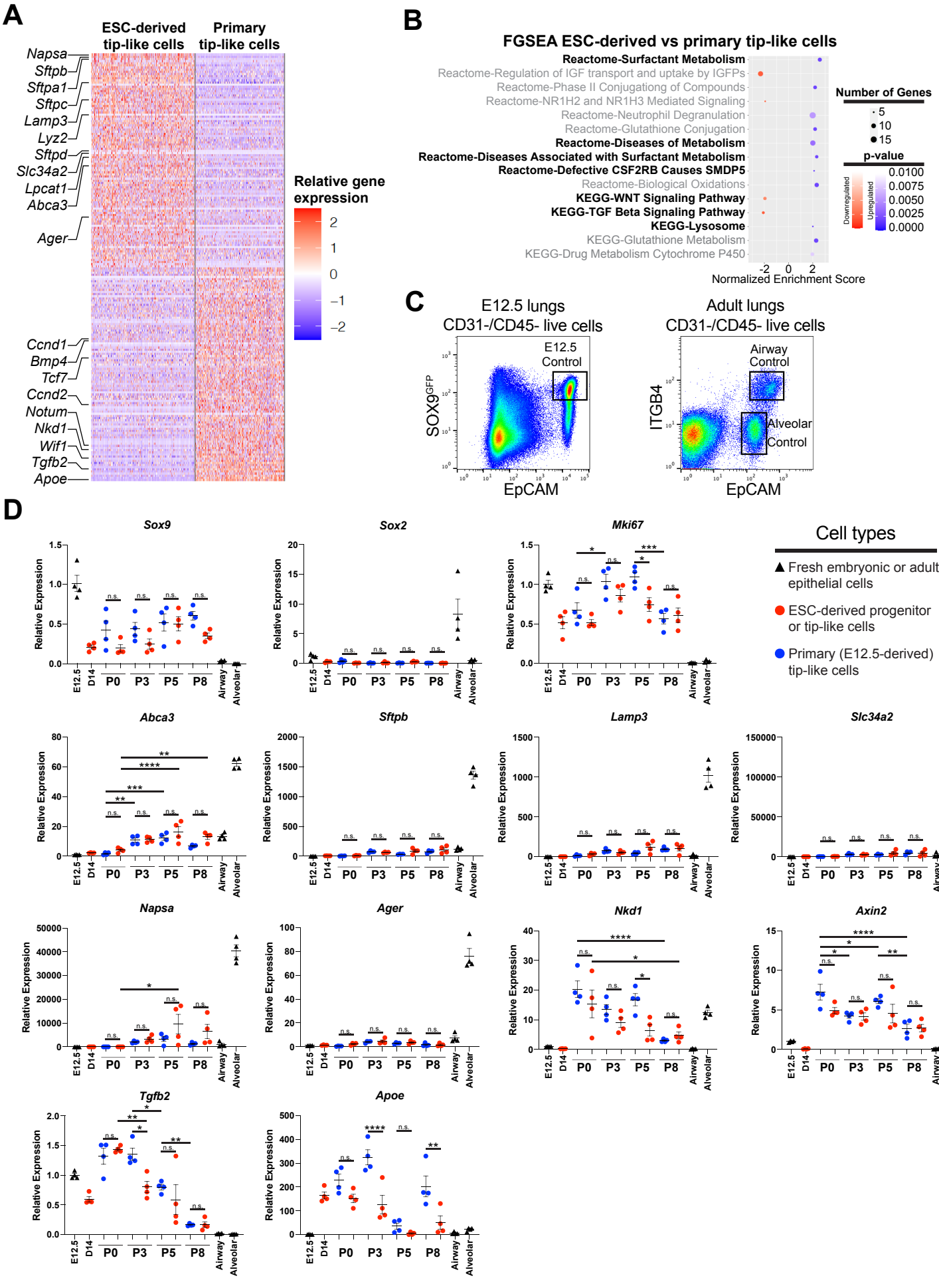
(G) UMAP plots displaying expression of *Mki67* and *Top2a* in primary and ESC-derived tip-like cells.

(H) Percent EdU labeling of ESC-derived tip-like cells with different durations of EdU labeling prior to collection.

(I) Spearman Correlation using the top 1000 most variable genes when comparing ESC-derived tip-like cells, primary tip-like cells, and primary distal lineages[36].

(J) Hierarchical clustering of cell populations from figure S1I based on expression of lung epithelial markers and AT2 differentiation markers.

Fig. S2


A
ESC-derived tip-like cells
Primary tip-like cells
Napsa
Sftpb
Sftpa1
Sftpc
Lamp3
Lyz2
Sftpd
Slc34a2
Lpcat1
Abca3
Ager
Ccnd1
Bmp4
Tcf7
Ccnd2
Notum
Nkd1
Wif1
Tgfb2
Apoe
Relative gene expression
2
1
0
−1
−2
B
FGSEA ESC-derived vs primary tip-like cells
Reactome-Surfactant Metabolism
Reactome-Regulation of IGF transport and uptake by IGFPs
Reactome-Phase II Conjugationg of Compounds
Reactome-NR1H2 and NR1H3 Mediated Signaling
Reactome-Neutrophil Degranulation
Reactome-Glutathione Conjugation
Reactome-Diseases of Metabolism
Reactome-Diseases Associated with Surfactant Metabolism
Reactome-Defective CSF2RB Causes SMDP5
Reactome-Biological Oxidations
KEGG-WNT Signaling Pathway
KEGG-TGF Beta Signaling Pathway
KEGG-Lysosome
KEGG-Glutathione Metabolism
KEGG-Drug Metabolism Cytochrome P450
-2 0 2
Normalized Enrichment Score
Number of Genes
5
10
15
p-value
0.0100
0.0075
0.0050
0.0025
0.0000
Downregulated
Upregulated
C
E12.5 lungs
CD31-/CD45- live cells
E12.5 Control
SOX9GFP
EpCAM
Adult lungs
CD31-/CD45- live cells
Airway Control
Alveolar Control
ITGB4
EpCAM
D
Sox9
Sox2
Mki67
Abca3
Sftpb
Lamp3
Slc34a2
Napsa
Ager
Nkd1
Axin2
Tgfb2
Apoe
Relative Expression
E12.5
D14
P0
P3
P5
P8
Airway
Alveolar
Cell types
Fresh embryonic or adult epithelial cells
ESC-derived progenitor or tip-like cells
Primary (E12.5-derived) tip-like cells

Supplemental Figure 2: Transcriptomic Analysis of ESC-derived and Primary Tip-like Cells, Related to Figure 2

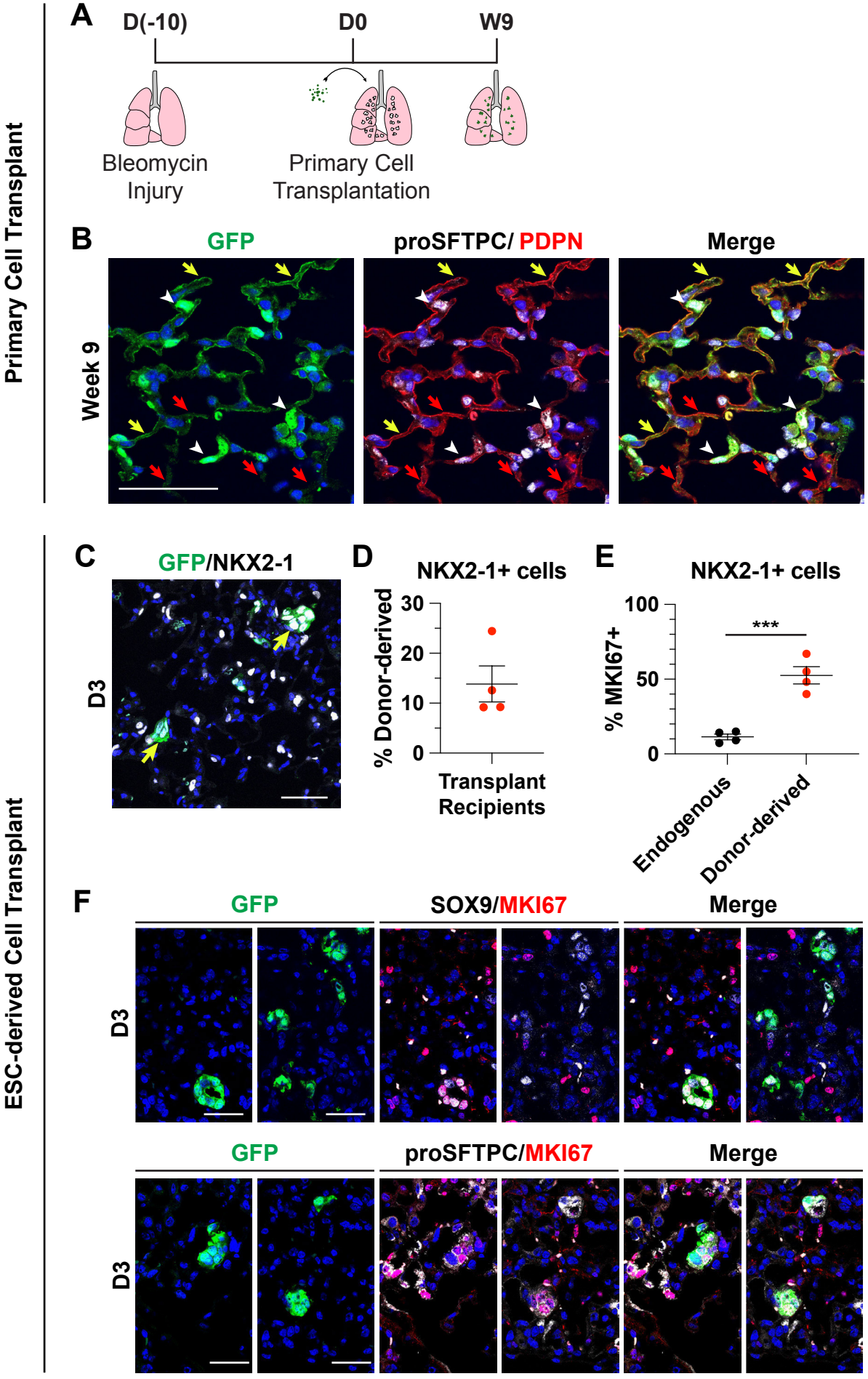
(A) Row-normalized heatmap of the top 100 most up-regulated and top 100 most down-regulated genes (with adj. p-value <0.05, ordered by logFC) between ESC-derived and Primary Tip-like Cells. Annotated genes are associated with surfactant metabolism or signaling pathways identified in supplemental figure 3B.

(B) FGSEA-identified Reactome and KEGG categories that are differentially regulated between ESC-derived and primary tip-like cells. The highlighted categories contain genes associated with AT2 function or prominent signaling pathways in lung development. Shown here are the 15 categories with the lowest p-value, a full list can be found in Table S2.

(C) Representative gating used to collect E12.5 SOX9+ epithelial cells and adult epithelial cells as primary controls for RT-qPCR.

(D) Analysis of gene expression by RT-qPCR. Primary and ESC-derived tip-like cells from multiple passages are compared against lung epithelial progenitors from day 14 of the WBRF protocol (D14) and freshly sorted lung epithelial cells from embryonic (E12.5) and adult (Airway and Alveolar) mouse lungs. n.s. not significant, * $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$ by one-way ANOVA. n= 4 biological replicates. Error bars = mean +/- SEM.

Fig. S3


Primary Cell Transplant
A
D(-10)
D0
W9
Bleomycin Injury
Primary Cell Transplantation
B
GFP
proSFTPC/ PDPN
Merge
Week 9
ESC-derived Cell Transplant
C
GFP/NKX2-1
D3
D
NKX2-1+ cells
% Donor-derived
30
20
10
0
Transplant Recipients
E
NKX2-1+ cells
% MKI67+
100
50
0
***
Endogenous
Donor-derived
F
GFP
SOX9/MKI67
Merge
D3
GFP
proSFTPC/MKI67
Merge
D3

Supplemental Figure 3: Transplantation of Primary Tip-like cells into an Immunocompetent Recipient and Progenitor State of ESC-derived Tip-like Cells at 3 Days Post Transplantation, Related to Figure 3

(A) Schematic for transplantation of GFP+ primary cells into bleomycin injured lungs with later histological assessment of recipient lungs.

(B) Representative immunofluorescence confocal microscopy of donor-derived cells at 9 weeks post-transplantation with antibodies detecting GFP, proSFTPC, and PDPN. White arrowheads indicate cuboidal proSFTPC+/GFP+ cells and yellow arrows indicate thin PDPN+/GFP+ cells. Nuclei stained with Hoechst, scale bar is 50um.

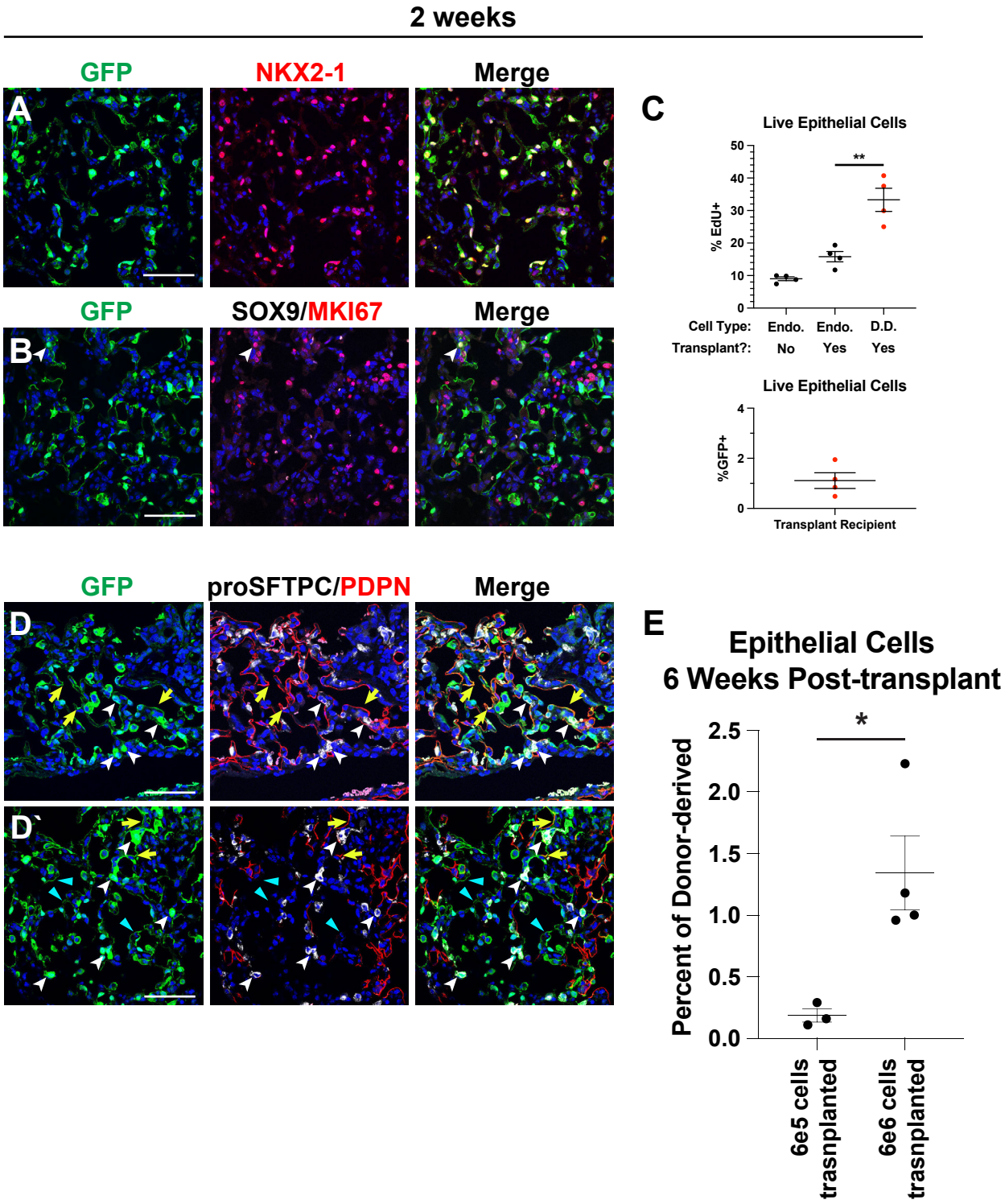
(C) Representative immunofluorescence confocal microscopy of lung tissue sections containing donor-derived cells at 3 days post-transplantation. Sections stained with antibodies detecting GFP and NKX2-1. Yellow arrows indicate representative GFP+/NKX2-1+ cells. Nuclei stained with Hoechst, scale bar is 50um.

(D) Percent of NKX2-1+ cells that were GFP+ donor-derived cells in analyzed confocal images from 3 days post-transplantation.

(E) Percent of endogenous and donor-derived NKX2-1+ cells that expressed MKI67.

(F) Representative immunofluorescence confocal microscopy of lung tissue sections containing donor-derived cells at 3 days post-transplantation. Sections stained with antibodies detecting GFP, proSFTPC, SOX9, and MKI67. Nuclei stained with Hoechst, scale bars are 25um.

Fig. S4


2 weeks
GFP
NKX2-1
Merge
A
GFP
SOX9/MKI67
Merge
B
C
Live Epithelial Cells
% EdU+
50
40
30
20
10
0
**
Cell Type:
Endo.
Endo.
D.D.
Transplant?:
No
Yes
Yes
Live Epithelial Cells
%GFP+
4
2
0
Transplant Recipient
GFP
proSFTPC/PDPN
Merge
D
D`
E
Epithelial Cells
6 Weeks Post-transplant
*
Percent of Donor-derived
2.5
2.0
1.5
1.0
0.5
0.0
6e5 cells trasnplanted
6e6 cells trasnplanted

Supplemental Figure 4: Donor-derived Cells Have Differentiated and Become Less Proliferative by 2 Weeks Post-transplantation, Related to Figure 3

(A) Representative immunofluorescence confocal microscopy of lung tissue sections indicating donor-derived cells (GFP+) at 2 weeks post-transplantation of ESC-derived tip-like cells. The majority of GFP+ donor-derived cells are NKX2-1+. Nuclei stained with Hoechst, scale bars are 50um.

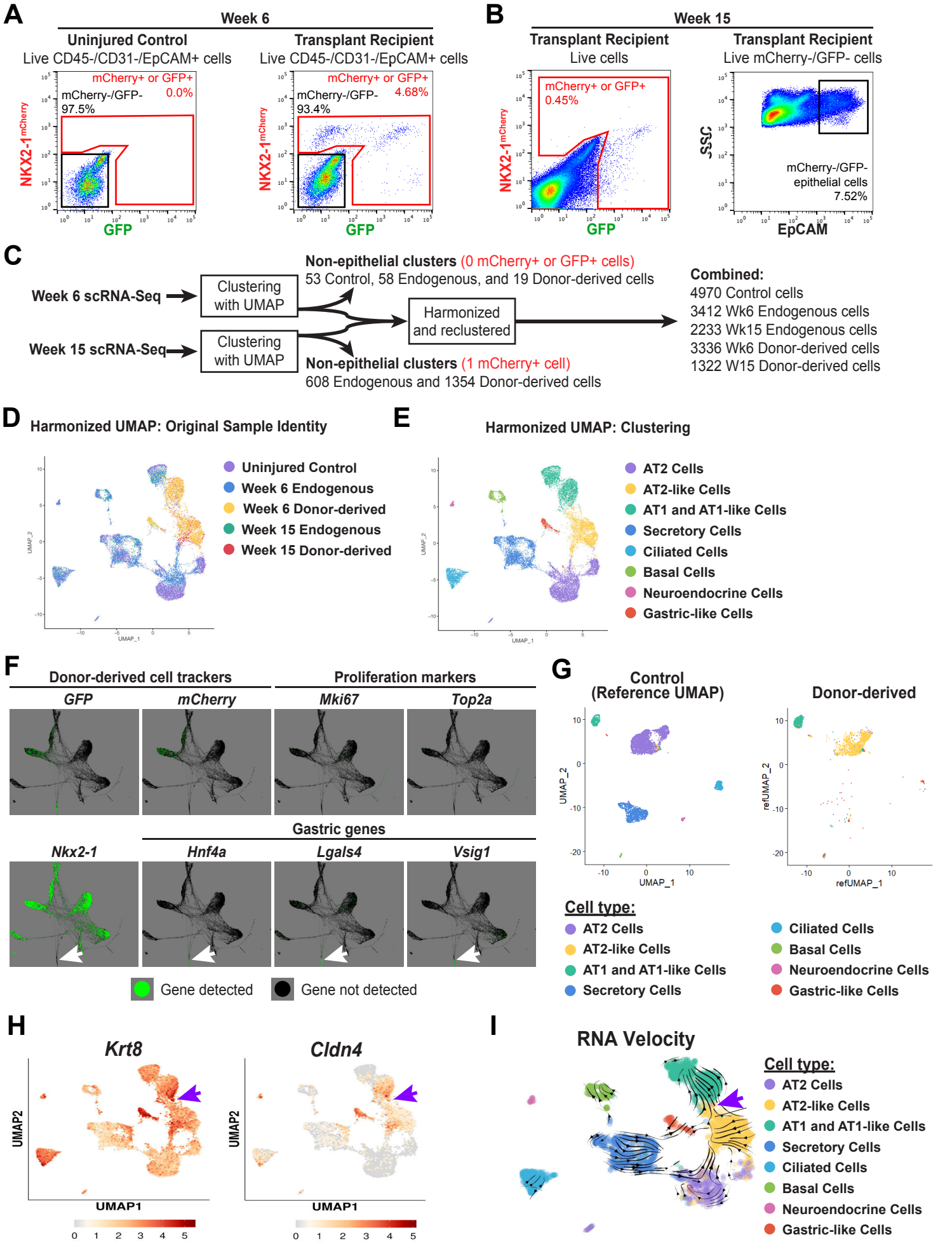
(B) At this time point donor-derived cells are SOX9- and only a small fraction are MKI67+ (white arrowhead). Nuclei stained with Hoechst, scale bars are 50um.

(C) Percent EdU labeling of endogenous and donor-derived cells for the first 2 weeks following transplantation of ESC-derived tip-like cells or media only and the percent of EdU+ cells that were GFP+. Lobes were pruned down to regions containing GFP+ cells, or similar regions in no transplant controls, prior to digestion into single cell suspension. Endo. = endogenous, D.D. = donor-derived. ** = p. value < 0.01 by unpaired, two-tailed Student's t-test. n= 4 biological replicates. Error bars = mean +/- SEM.

(D) At this time point donor-derived cells include both cuboidal proSFTPC+ (white arrowheads) and thin PDPN+ (yellow arrows) donor-derived cells. Some donor-derived clusters (D`) are primarily composed of cuboidal proSFTPC+ (white arrowheads) and thin PDPN- cells (blue triangles). Nuclei stained with Hoechst, scale bars are 50um.

(E) Flow cytometry quantitation of the percent of live epithelial (EpCAM+/CD45-/CD31-) cells that are donor-derived in whole lungs 6 weeks after transplantation of 6e5 or 6e6 ESC-derived tip-like cells. * = p. value < 0.05 by unpaired, two-tailed Student's t-test. n= 3,4 biological replicates. Error bars = mean +/- SEM.

Fig. S5


A
Week 6
Uninjured Control
Live CD45-/CD31-/EpCAM+ cells
mCherry+ or GFP+ 0.0%
mCherry-/GFP- 97.5%
NKX2-1 mCherry
GFP
Transplant Recipient
Live CD45-/CD31-/EpCAM+ cells
mCherry+ or GFP+ 4.68%
mCherry-/GFP- 93.4%
NKX2-1 mCherry
GFP
B
Week 15
Transplant Recipient
Live cells
mCherry+ or GFP+ 0.45%
NKX2-1 mCherry
GFP
Transplant Recipient
Live mCherry-/GFP- cells
SSC
mCherry-/GFP- epithelial cells 7.52%
EpCAM
C
Week 6 scRNA-Seq
Week 15 scRNA-Seq
Clustering with UMAP
Clustering with UMAP
Non-epithelial clusters (0 mCherry+ or GFP+ cells)
53 Control, 58 Endogenous, and 19 Donor-derived cells
Harmonized and reclustered
Non-epithelial clusters (1 mCherry+ cell)
608 Endogenous and 1354 Donor-derived cells
Combined:
4970 Control cells
3412 Wk6 Endogenous cells
2233 Wk15 Endogenous cells
3336 Wk6 Donor-derived cells
1322 W15 Donor-derived cells
D
Harmonized UMAP: Original Sample Identity
UMAP_2
UMAP_1
Uninjured Control
Week 6 Endogenous
Week 6 Donor-derived
Week 15 Endogenous
Week 15 Donor-derived
E
Harmonized UMAP: Clustering
UMAP_2
UMAP_1
AT2 Cells
AT2-like Cells
AT1 and AT1-like Cells
Secretory Cells
Ciliated Cells
Basal Cells
Neuroendocrine Cells
Gastric-like Cells
F
Donor-derived cell trackers
Proliferation markers
GFP
mCherry
Mki67
Top2a
Gastric genes
Nkx2-1
Hnf4a
Lgals4
Vsig1
Gene detected
Gene not detected
G
Control (Reference UMAP)
Donor-derived
UMAP_2
UMAP_1
refUMAP_2
refUMAP_1
Cell type:
AT2 Cells
AT2-like Cells
AT1 and AT1-like Cells
Secretory Cells
Ciliated Cells
Basal Cells
Neuroendocrine Cells
Gastric-like Cells
H
Krt8
Cldn4
UMAP2
UMAP1
0 1 2 3 4 5
I
RNA Velocity
Cell type:
AT2 Cells
AT2-like Cells
AT1 and AT1-like Cells
Secretory Cells
Ciliated Cells
Basal Cells
Neuroendocrine Cells
Gastric-like Cells

Supplemental Figure 5: Sort Purification and Identification of Endogenous and Donor-derived Cell Types, Related to Figure 4

(A) Gating for FACS-based collection of endogenous (mCherry-/GFP-) and donor-derived (mCherry+ or GFP+) lung epithelial cells from an uninjured control and a transplant recipient at 6 weeks post-transplantation of ESC-derived tip-like cells.

(B) Gating for FACS-based collection of endogenous epitheilal (mCherry-/GFP-/EpCAM+) and donor-derived (mCherry+ or GFP+) cells at 15 weeks post-transplantation of ESC-derived tip-like cells.

(C) Pipeline for analysis of scRNA-seq data including exclusion of non-epithelial lineages based on minimal presence of true donor-derived cells in these populations.

(D) Epithelial cells from both timepoints were combined using harmonization to generate a single UMAP plot.

(E) Cells were clustered using the Louvain algorithm followed by combining overlapping clusters. Clusters were then identified based on cell type signatures outlined in Table S3.

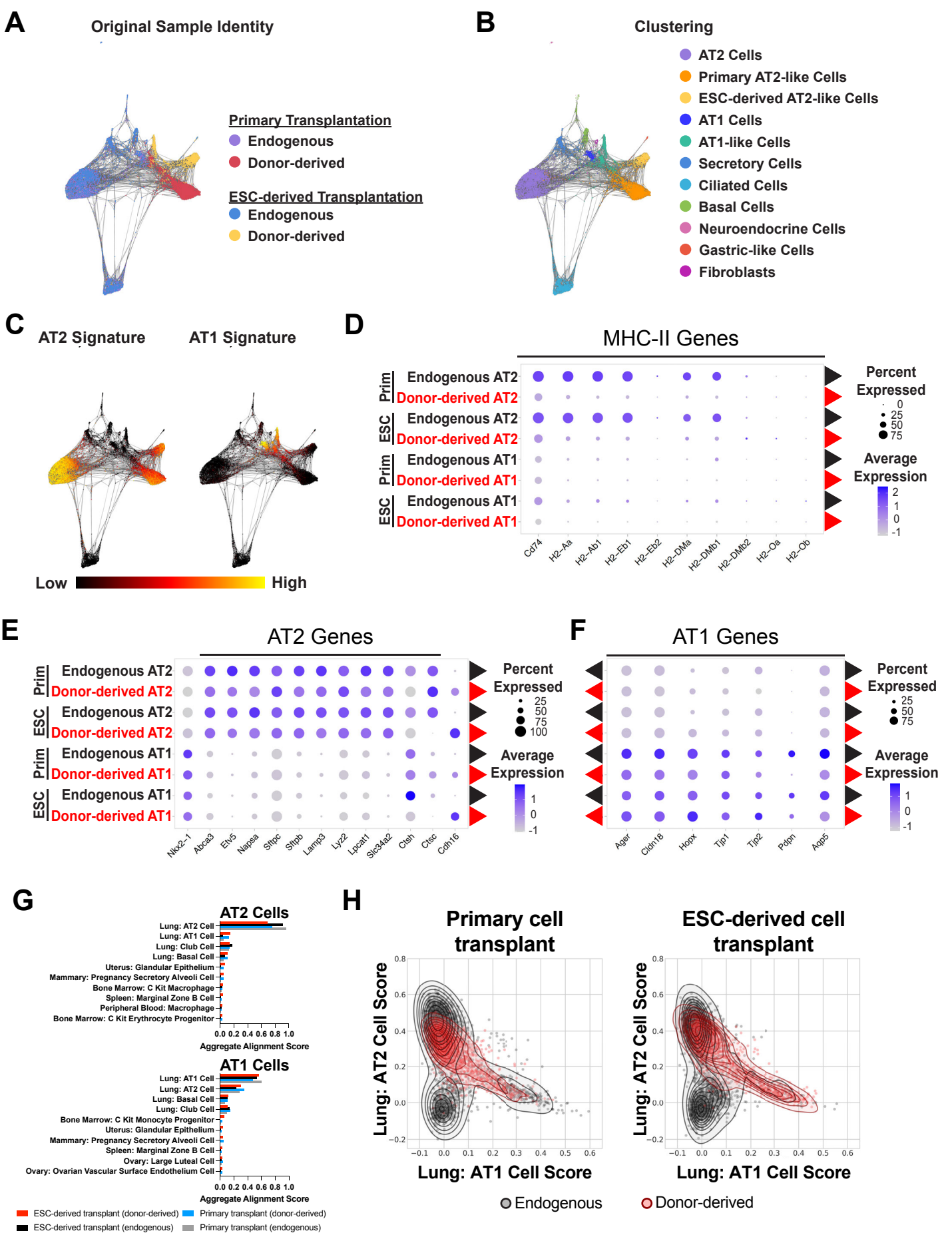
(F) SPRING plots indicating cells with detectable expression of *GFP*, *mCherry*, proliferation markers, *Nkx2-1*, and gastric genes in endogenous and donor-derived cells at 6 and 15 weeks post-transplantation. See figure 4 for annotation of SPRING plot by sample origin or cell type. White arrows indicate the gastric-like cells.

(G) Multimodal reference mapping using samples from figure S5D, E and figure 4. Donor-derived cells are mapped onto the reference created from the uninjured control.

(H) UMAP of combined cell transplantation samples from S5D, E and figure 4 displaying expression of transitional cell markers. The purple arrow indicates a subpopulation high for transitional cell markers.

(I) RNA velocity analysis of endogenous and donor-derived cells from figure S5E.

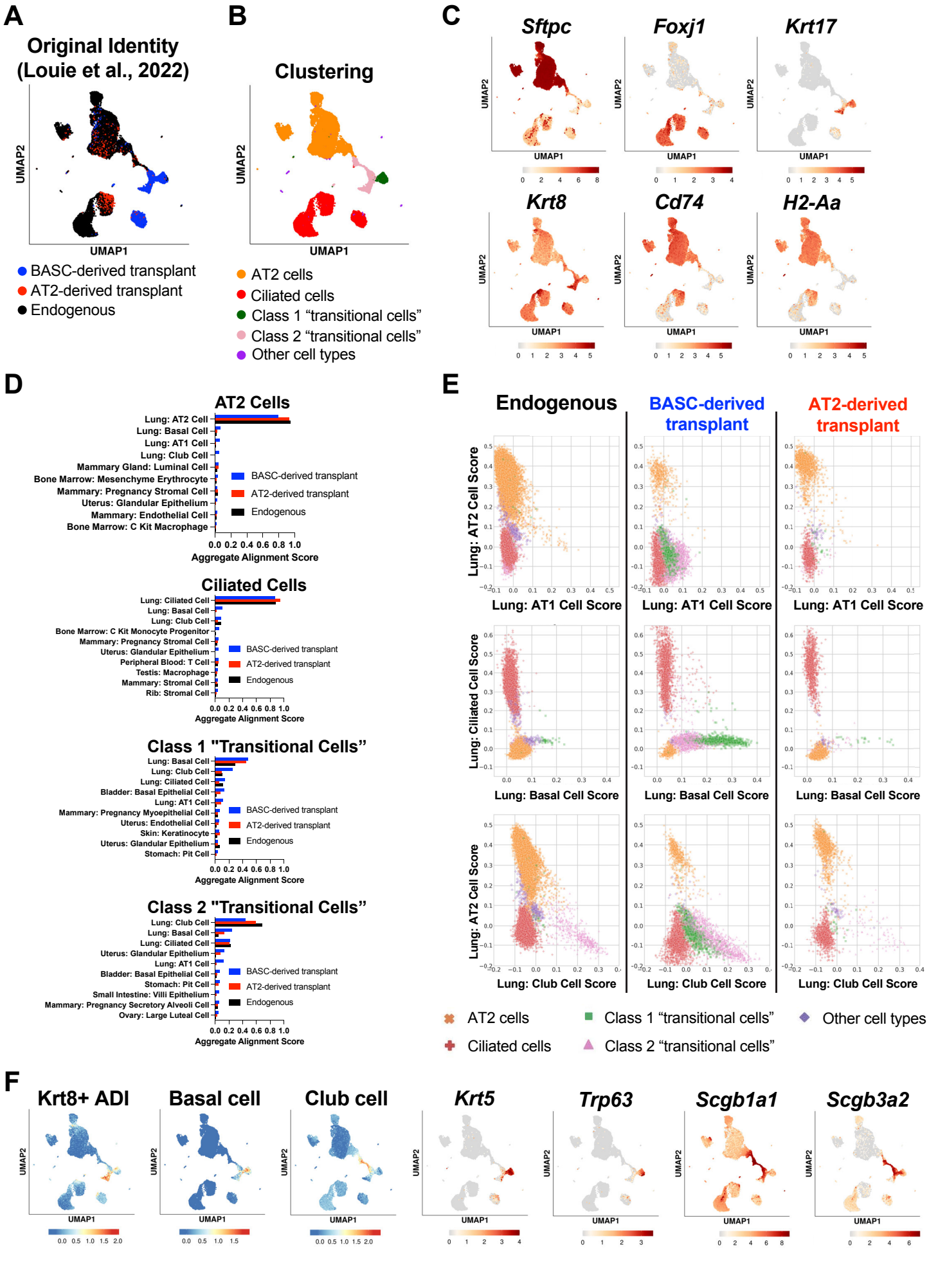
Fig. S6


A
Original Sample Identity
Primary Transplantation
Endogenous
Donor-derived
ESC-derived Transplantation
Endogenous
Donor-derived
B
Clustering
AT2 Cells
Primary AT2-like Cells
ESC-derived AT2-like Cells
AT1 Cells
AT1-like Cells
Secretory Cells
Ciliated Cells
Basal Cells
Neuroendocrine Cells
Gastric-like Cells
Fibroblasts
C
AT2 Signature
AT1 Signature
Low
High
D
MHC-II Genes
Prim
Endogenous AT2
Donor-derived AT2
ESC
Endogenous AT2
Donor-derived AT2
Prim
Endogenous AT1
Donor-derived AT1
ESC
Endogenous AT1
Donor-derived AT1
Cd74
H2-Aa
H2-Ab1
H2-Eb1
H2-Eb2
H2-DMa
H2-DMb1
H2-DMb2
H2-Oa
H2-Ob
Percent Expressed
0
25
50
75
Average Expression
2
1
0
-1
E
AT2 Genes
Prim
Endogenous AT2
Donor-derived AT2
ESC
Endogenous AT2
Donor-derived AT2
Prim
Endogenous AT1
Donor-derived AT1
ESC
Endogenous AT1
Donor-derived AT1
Nkx2-1
Abca3
Etv5
Napsa
Sftpc
Sftpb
Lamp3
Lyz2
Lpcat1
Slc34a2
Ctsh
Ctsc
Cdh16
Percent Expressed
25
50
75
100
Average Expression
1
0
-1
F
AT1 Genes
Ager
Cldn18
Hopx
Tjp1
Tjp2
Pdpn
Aqp5
Percent Expressed
25
50
75
Average Expression
1
0
-1
G
AT2 Cells
Lung: AT2 Cell
Lung: AT1 Cell
Lung: Club Cell
Lung: Basal Cell
Uterus: Glandular Epithelium
Mammary: Pregnancy Secretory Alveoli Cell
Bone Marrow: C Kit Macrophage
Spleen: Marginal Zone B Cell
Peripheral Blood: Macrophage
Bone Marrow: C Kit Erythrocyte Progenitor
0.0 0.2 0.4 0.6 0.8 1.0
Aggregate Alignment Score
AT1 Cells
Lung: AT1 Cell
Lung: AT2 Cell
Lung: Basal Cell
Lung: Club Cell
Bone Marrow: C Kit Monocyte Progenitor
Uterus: Glandular Epithelium
Mammary: Pregnancy Secretory Alveoli Cell
Spleen: Marginal Zone B Cell
Ovary: Large Luteal Cell
Ovary: Ovarian Vascular Surface Endothelium Cell
0.0 0.2 0.4 0.6 0.8 1.0
Aggregate Alignment Score
ESC-derived transplant (donor-derived)
Primary transplant (donor-derived)
ESC-derived transplant (endogenous)
Primary transplant (endogenous)
H
Primary cell transplant
ESC-derived cell transplant
Lung: AT2 Cell Score
Lung: AT1 Cell Score
Endogenous
Donor-derived

Supplemental Figure 6: Primary and ESC-derived Tip-like Cell Transplants Give Rise to Transcriptionally Similar Donor-derived Cells, Related to Figure 5, 6

(A) SPRING plot of data generated from scRNA-seq of parallel ESC-derived and primary tip-like cell transplant recipients at 8 weeks post-transplant.
(B) Cell-type annotation of clusters based on supervised Louvain clustering and expression of lung epithelial cell signatures.
(C) Expression of AT2 and AT1 cell signatures. Gene sets comprising each signature can be found in Supplementary Table 3.
(D) Expression of MHC-II genes in donor-derived (red) and endogenous (black) cells.
(E) Expression of AT2 genes in donor-derived (red) and endogenous (black) cells.
(F) Expression of AT1 genes in donor-derived (red) and endogenous (black) cells.
(G) The top ten aggregate alignment scores for donor-derived AT2-like cells and the corresponding scores for endogenous AT2 cells. The top ten aggregate alignment scores for donor-derived AT1-like cells and the corresponding scores for endogenous AT1 cells. All reference cell types are from adult mice (Mouse Cell Atlas or Control sample as delineated in Figure 4) [50].
(H) Individual alignment scores for all donor-derived and endogenous epithelial cells against reference adult lung AT1 and AT2 cells. Each cell is annotated based on sample type. See also Tables S8-S11.

Fig. S7


A
Original Identity
(Louie et al., 2022)
UMAP2
UMAP1
BASC-derived transplant
AT2-derived transplant
Endogenous
B
Clustering
UMAP2
UMAP1
AT2 cells
Ciliated cells
Class 1 “transitional cells”
Class 2 “transitional cells”
Other cell types
C
Sftpc
Foxj1
Krt17
Krt8
Cd74
H2-Aa
UMAP2
UMAP1
D
AT2 Cells
Lung: AT2 Cell
Lung: Basal Cell
Lung: AT1 Cell
Lung: Club Cell
Mammary Gland: Luminal Cell
Bone Marrow: Mesenchyme Erythrocyte
Mammary: Pregnancy Stromal Cell
Uterus: Glandular Epithelium
Mammary: Endothelial Cell
Bone Marrow: C Kit Macrophage
BASC-derived transplant
AT2-derived transplant
Endogenous
0.0 0.2 0.4 0.6 0.8 1.0
Aggregate Alignment Score
Ciliated Cells
Lung: Ciliated Cell
Lung: Basal Cell
Lung: Club Cell
Bone Marrow: C Kit Monocyte Progenitor
Mammary: Pregnancy Stromal Cell
Uterus: Glandular Epithelium
Peripheral Blood: T Cell
Testis: Macrophage
Mammary: Stromal Cell
Rib: Stromal Cell
Class 1 "Transitional Cells”
Lung: Basal Cell
Lung: Club Cell
Lung: Ciliated Cell
Bladder: Basal Epithelial Cell
Lung: AT1 Cell
Mammary: Pregnancy Myoepithelial Cell
Uterus: Endothelial Cell
Skin: Keratinocyte
Uterus: Glandular Epithelium
Stomach: Pit Cell
Class 2 "Transitional Cells”
Lung: Club Cell
Lung: Basal Cell
Lung: Ciliated Cell
Uterus: Glandular Epithelium
Lung: AT1 Cell
Bladder: Basal Epithelial Cell
Stomach: Pit Cell
Small Intestine: Villi Epithelium
Mammary: Pregnancy Secretory Alveoli Cell
Ovary: Large Luteal Cell
E
Endogenous
BASC-derived transplant
AT2-derived transplant
Lung: AT2 Cell Score
Lung: AT1 Cell Score
Lung: Ciliated Cell Score
Lung: Basal Cell Score
Lung: Club Cell Score
AT2 cells
Ciliated cells
Class 1 “transitional cells”
Class 2 “transitional cells”
Other cell types
F
Krt8+ ADI
Basal cell
Club cell
Krt5
Trp63
Scgb1a1
Scgb3a2
UMAP2
UMAP1

Supplemental Figure 7: Transplantation of cultured adult lung epithelial cells gives rise to mature AT2 cells and non-alveolar epithelial lineages, Related to Figure 5, 6

(A) UMAP of combined cell transplantation samples from (Louie et al., 2022)[15].
(B) UMAP with annotation of cell types based on supervised Louvain clustering and expression of marker genes.
(C) UMAP plots displaying expression of the indicated genes.
(D) The top ten aggregate alignment scores for donor-derived AT2 cells following a BASC-derived transplant as well as the corresponding scores for donor-derived AT2 cells following a AT2-derived transplant and endogenous AT2 cells. Similar graphs are shown for ciliated cells and "transitional cells". All reference cell types are from adult mice (Mouse Cell Atlas or Control sample as delineated in Figure 4) [50].
(E) Individual alignment scores for all donor-derived and endogenous epithelial cells against the indicated reference cells. Each cell is annotated (by color and shape shown in the key below the graphs) based on cell type as determined in figure S7B.
(F) UMAP plots displaying expression of cell type signature (top 30 DEGs for each cell type)[39] or the indicated gene.

Supplemental Table 3: Lung Epithelial Cell Type Gene Signatures, Related to Figure 4

AT1 Cell Gene Signature	AT2 Cell Gene Signature	Ciliated Cell Gene Signature	Secretory Cell Gene Signature	Basal Cell Gene Signature	Neuroendocrine Gene Signature
Ager	Abca3	1110017D15Rik	5330417C22Rik	Apoe	Nov
Akap5	Acot7	1700001C02Rik	Acsm1	Dcn	Resp18
Aqp5	Acoxl	1700007K13Rik	Aldh1a7	Dapl1	Ascl1
Cldn18	Acsl4	1700016K19Rik	Cckar	Aqp3	Scg5
Clic3	Ank3	Ak7	Cldn10	Krt5	Chgb
Clic5	Atp8a1	BC051019	Cyp2f2	Krt15	Pcsk1
Col4a3	Cd74	Ccdc113	Fmo3	Fxyd3	Calca
Col4a4	Cebpa	Ccdc153	Gabrp	Ltbp4	Meis2
Cryab	Cpm	Cfap126	Gpx2	Dlk2	Nnat
Cyp2b10	Ctsh	Cfap45	Gsta2	Trp63	Cplx2
Emp2	Cxcl15	Cfap53	Gsta4	Wnt4	Cd9
Fam189a2	Dram1	Cyp2s1	Hp	Krt17	Piezo2
Gprc5a	Egfl6	Dnali1	Iyd	Tpt1	Col8a1
Hopx	Elovl1	Drc1	Kcnk2	Tmem176b	Pnmal2
Hs2st1	Etv5	Fam183b	Ldhb	Dst	Cdc14b
Igfbp2	Fabp5	Foxj1	Lrrc26	Col17a1	Pkib
Krt7	Fasn	Gm867	Lypd2	Aqp4	Tmem158
Lmo7	Hc	Lrriq1	Mgat3	Hcar2	Ptn
Mal2	Lamp3	Mlf1	Mgst1	Defb1	Hist3h2ba
Pdpn	Lgi3	Mns1	Pigr	Spon2	Pcsk1n
Prdx6	Lpcat1	Nme5	Pon1		
Pxdc1	Lyz2	Nme9	Por		
Rtkn2	Mlc1	Pifo	Rassf9		
Scnn1g	Muc1	Riiad1	Reep6		
Spock2	Napsa	Rsph1	Retnla		
Tspan8	Npc2	Smim5	Scgb1a1		
Vegfa	Ppp1r14c	Sntn	Scgb3a2		
	S100g	Spaca9	Selenbp1		
	Scd1	Tekt1	Slc16a11		
	Sfta2		Wfdc2		
	Sftpa1				
	Sftpb				
	Sftpc				
	Sftpd				
	Slc34a2				
	Zdhhc3				

This table contains lists of genes that are selectively upregulated in the predominant lung epithelial cell types and were used to generate cell type gene expression signatures used to identify cell types in scRNA-seq datasets. See the methods section for cutoffs used to generate these lists.