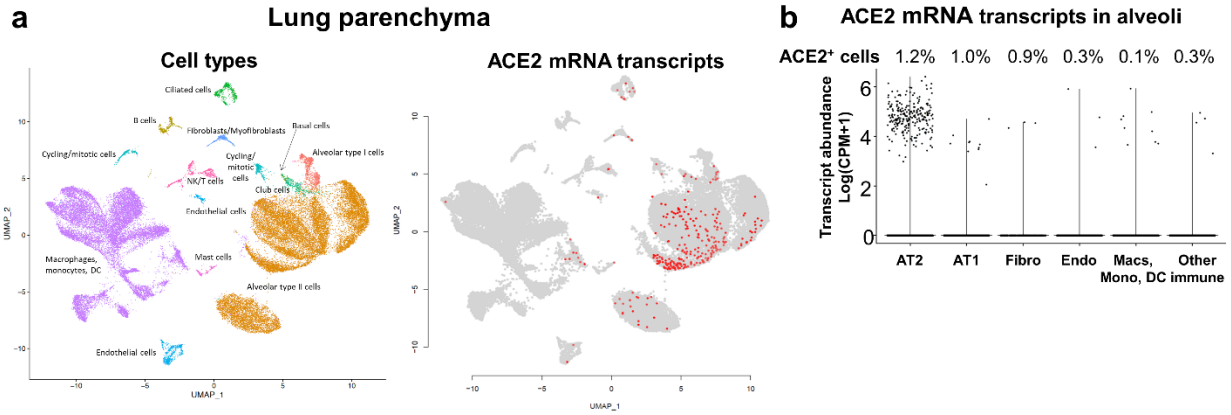
559 **Supplemental information:**

Supplemental Figure 1



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561 **Supplemental Figure 1.** Single-cell RNA sequencing reanalyses of ACE2 transcript abundance
562 in lung parenchyma (23). Summative observations from all donors. **a**) Uniform manifold
563 approximation and projection (UMAP) visualizations. Cells were clustered using a shared
564 nearest neighbor (SNN) approach. Cell types associated with each cluster were identified by
565 determining marker genes for each cluster. Each data point denotes a cell. On the right panel,
566 cells with ACE2 transcripts are shown in red. **b**) Violin plots representing ACE2 expression in
567 the alveoli. Airway cells (basal, mitotic, ciliated, club) are not shown. Percentage of $ACE2^+$ cells
568 within each cell type shows ACE2 transcripts in 1.2% of alveolar type II cells and in 0.1% of
569 macrophages, monocytes, or dendritic cells. Each data point denotes a cell, most cells have no
570 expression (0). AT2: alveolar type II. AT1: alveolar type I. Macs: Macrophages. Mono:
571 Monocytes. DC: dendritic cells. Other immune cells: B cells, mast cells, natural killer/T cells.
572 Endo: Endothelial. Fibro: Fibroblasts/myofibroblasts. NK: Natural killer. CPM: Counts per
573 million.

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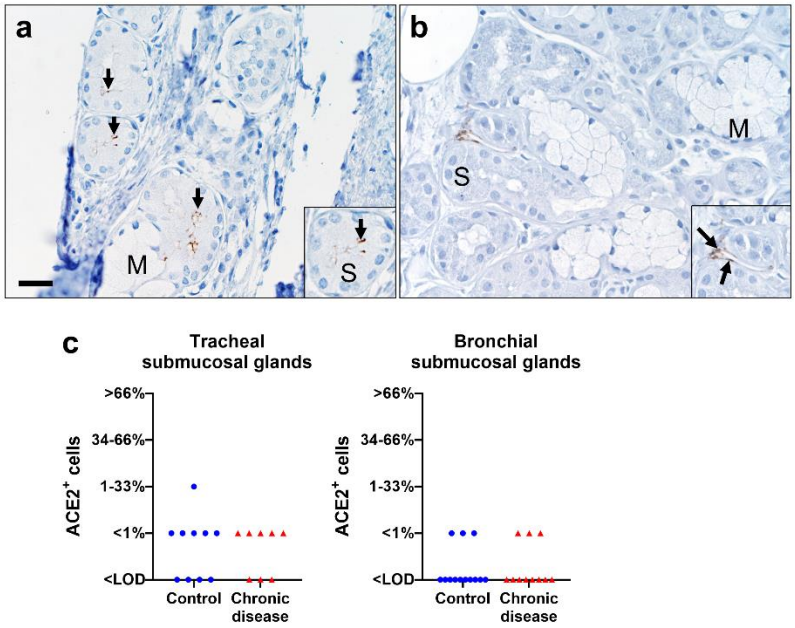
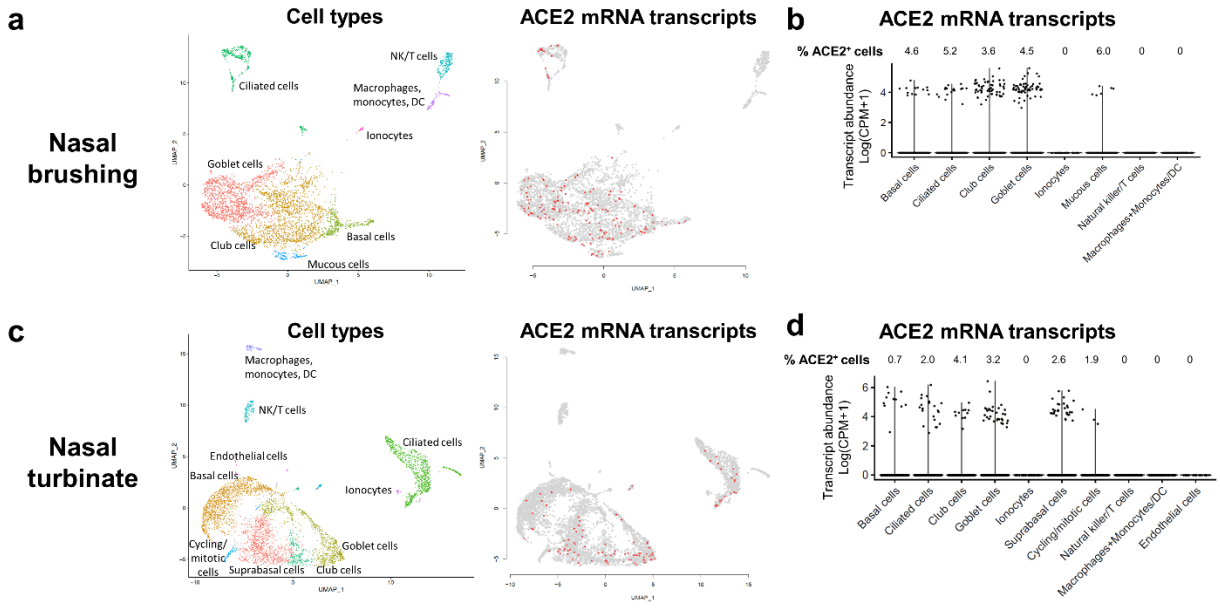
Supplemental Figure 2



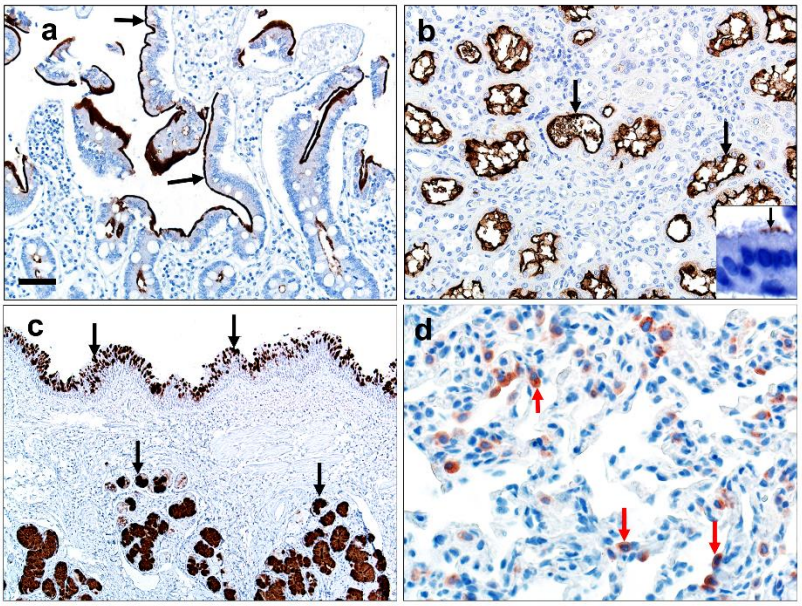
Supplemental Figure 2. Representative tissue section from submucosa of large airways (trachea/bronchi) showing ACE2 protein localization (brown color, black arrows) (**a, b**) and scores (**c**). **a**) Submucosal glands had uncommon to localized apical ACE2 protein (arrows) in serous (S) cells, but not mucous (M) cells. **b**) Submucosal glands also had absent to uncommon ACE2 protein (arrows) in the interstitium that centered on vascular walls and endothelium. This vascular staining was uncommonly seen in lung too and corresponded to the low levels seen in transcripts for these endothelial cells (Supplemental Figure 1a-b). Note the absence of ACE2 staining in serous (S) or mucous (M) cells of the gland (**b**). **c**) ACE2 protein scores for each subject for serous cells in submucosal glands from trachea and bronchi, in control versus chronic disease groups (P>0.9999, 0.9999, respectively, Mann-Whitney U test). Bar = 25 μm. LOD: Limit of detection.

Supplemental Figure 3



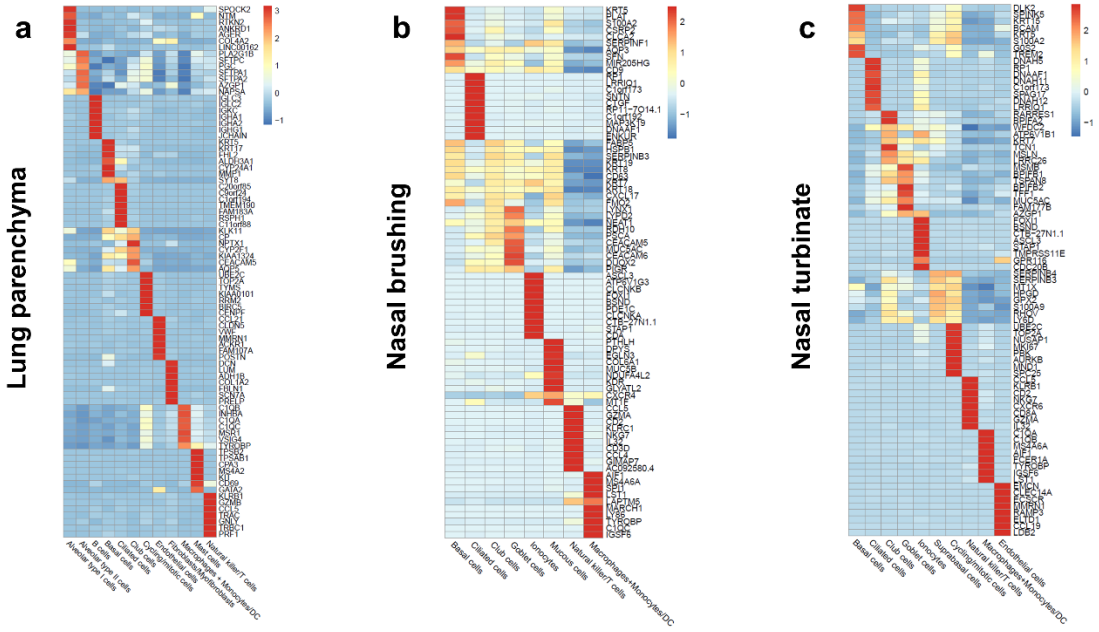
Supplemental Figure 3. Single-cell RNA sequencing reanalyses of ACE2 transcript abundance in nasal brushing (**a, b**) and nasal turbinate (**c, d**) (24). **a, c**) Uniform manifold approximation and projection (UMAP) visualizations. Cells were clustered using a shared nearest neighbor (SNN) approach. Cell types associated with each cluster were identified by determining marker genes for each cluster. Each data point denotes a cell. On the right panels, cells with ACE2 transcripts are shown in red. **b, d**) Violin plots representing ACE2 expression. In nasal turbinate and nasal brushing, percentage of $ACE2^+$ cells within each cell type shows ACE2 expression on epithelial cells. Each data point denotes a cell, most cells have no expression (0). DC: dendritic cells. NK: Natural killer. CPM: Counts per million.

Supplemental Figure 4



Supplemental Figure 4. Quality controls for ACE2 immunohistochemistry technique (**a, b**) and tissue quality (**c, d**). **a, b**) ACE2 protein (brown color, black arrows) was detected along the apical surface of small intestine enterocytes (**a**), renal tubule epithelium (**b**), and ciliated cells (**b, inset**) of primary airway cell cultures. These findings demonstrate specific detection of ACE2 protein in cells/tissues consistent with known ACE2 expression. **c**) Representative immunostaining of bronchus detected abundant MUC5B protein (brown color, black arrows) in mucous cells of surface epithelium (top) and submucosal glands (bottom). **d**) Representative sections of alveoli had SP-C^{+} alveolar type II cells (red color, red arrows). These results (**c, d**) demonstrate the tissues were intact and that immunostaining can be used to detect native airway (**c**) and lung (**d**) proteins. Bar = 40 (a, b), 80 (c), and 20 μm (d).

Supplemental Figure 5



Supplemental Figure 5. Single-cell RNA sequencing reanalyses of lung parenchyma (a) (23), nasal brushing (**b**) and nasal turbinate (**c**) (24). Heatmaps depicting the marker genes for each cluster that were used to assign cell types.

Supplemental Table 1. ACE2 protein reported in surface epithelium (SE) of human respiratory tract surface epithelium.

Reported Cases [n]	Primary Ab	SN	T	B	Br	Al	Summary comments
Non-diseased lungs / nasal [5 each]; diseased lungs [5] (17)	Polyclonal	SE (C++, basal cells in squamous epithelium)	n.d.	SE (C+)	n.d.	AT1 (C++); AT2 (C++)	Abundant ACE2 protein in lung epithelia
Non-diseased lungs [5] (18)	Undefined	n.d.	SE (C+, A+)	SE (C+, A+)	n.d.	"Alveoli" (A+) Mac (A+)	ACE2 is present on epithelia in several parts of the respiratory tract and macrophages
Lung [undefined] (19)	Polyclonal	n.d.	n.d.	SE (C+, N+, M+)	n.d.	AT1− AT2 (N+)	ACE2 is present in bronchial epithelium, AT2 cells and macrophages
Sinus [undefined] and Lung [undefined, same tissues as above] (20)	Polyclonal	SE (N++)	SE (−)	SE (C+, N++)	n.d.	AT1− AT2 (N++)	ACE2 is present in sinus and bronchial epithelium, AT2 cells and macrophages

Non-diseased: The cause of death was not directly related to lung disease

n.d.: Not described

Tissues: Sinonasal (SN), trachea (T), bronchi (B), bronchioles (Br), and alveoli (Al)

Cellular localization: cytoplasmic (C), nuclear (N), apical membrane (A)

Cells: Surface epithelium (SE), alveolar type I cells (AT1), alveolar type II cells (AT2), alveolar macrophages (Mac)

ACE2 protein (based on published reports/figures): negative (−), weak (+), moderate to abundant (++)

Supplemental Table 2. Donor demographics and ACE2 distribution scores for each tissue region.

Case #	Group	Age (yrs)	Sex	Comorbidities	Trachea	Bronchi	Bronchioles	Alveoli
1	Control	5	F	Trauma	NA	2	2	1
2	Control	57	M	Arrhythmia	0	0	0	1
3	Control	31	M	Stroke (Joubert syndrome)	1	1	0	0
4	Control	53	F	Trauma	NA	0	0	1
5	Control	2	M	Brain hemorrhage	0	0	0	1
6	Control	2	M	Trauma	0	0	1	2
7	Control	0.5	M	Spinomuscular atrophy	NA	0	1	0
8	Control	71	M	Stroke, Parkinson's disease, nonsmoker	0	1	1	0
9	Control	4	F	Trauma	0	0	0	2
10	Control	1.2	M	Trauma	0	NA	1	1
11	Control	53	F	Trauma, nonsmoker	0	0	2	0
12	Control	26	F	NA	0	NA	0	0
13	Control	27	F	NA	NA	0	1	0
14	Control	64	M	NA	NA	1	1	0
15	Chronic disease	53	F	Smoker	0	NA	0	1
16	Chronic disease	60	M	COPD, smoker	NA	NA	0	1
17	Chronic disease	32	M	COPD, smoker	0	0	0	1
18	Chronic disease	68	M	COPD	NA	1	0	1
19	Chronic disease	68	F	COPD	NA	NA	1	1
20	Chronic disease	9	M	Asthma	0	0	0	1
21	Chronic disease	25	F	Cystic fibrosis	NA	0	0	0
22	Chronic disease	47	F	Cardiovascular disease	1	2	2	1
23	Chronic disease	27	M	Cystic fibrosis	0	NA	NA	1
24	Chronic disease	50	F	Cardiovascular disease, diabetes, asthma	NA	0	0	0
25	Chronic disease	37	M	Drug use, smoker	0	0	0	0
26	Chronic disease	38	M	Asthma (status asthmaticus)	0	0	0	0
27	Chronic disease	32	M	Cystic fibrosis	NA	NA	0	1
28	Chronic disease	58	F	Cardiovascular disease, diabetes, NASH	0	0	0	1
29	Chronic disease	19	F	Cystic fibrosis	NA	0	0	0

NA: Not available for analyses / COPD: Chronic obstructive pulmonary disease / NASH: Non-alcoholic steatohepatitis.

Scoring: 0 = below limit of immunohistochemical detection; 1 = rare (<1%); 2 = 1-33%; 3 = 34-66%; 4 = >66% of cells.

Supplemental Table 3. Parameters for immunohistochemistry on fixed tissues.

Target	Primary Antibody	Antigen Retrieval	Secondary Reagents
Allograft Inflammatory Factor 1 (AIF1)	Anti-AIF1 polyclonal (#019-19741, Wako Pure Chemical Industries, Ltd., Richmond, VA USA) in diluent 1:1000 x 1 hour	HIER, Citrate buffer pH 6.0, 110˚C for 15 min; 20 min cool down (Decloaking Chamber Plus, Biocare Medical, Concord, CA USA)	Dako EnVision+ System-HRP Labeled Polymer Anti-rabbit, 30 min (Dako North America, Inc., Carpentaria, CA USA) AEC chromogen, counterstain.
Angiotensin-Converting Enzyme 2 (ACE2)	Anti-ACE2, monoclonal (MAB933, R&D Systems, Minneapolis, MN USA) in diluent at 1:100 x 1 hour.	HIER, Citrate Buffer, pH 6.0, 110˚C for 15 minutes; 20 min cool down (Decloaking Chamber Plus, Biocare Medical, Concord, CA USA)	Dako EnVision+ System-HRP Labeled Polymer Anti-mouse, 60 min (Dako North America, Inc., Carpentaria, CA USA), DAB Chromogen, counterstain.
MUC5B	Rabbit anti-MUC5B polyclonal, (LSBio #LS-B8121, LifeSpan BioSciences, Inc., Seattle, WA) in Dako Antibody Diluent (Dako North America, Inc., Carpentaria, CA); 1:60,0000/30 min	HIER, Citrate buffer pH 6.0, 110˚C for 15min; 20 min cool down	Step 1: Biotinylated anti-Rabbit IgG (H+L) (Vector Laboratories, Inc., Burlingame, CA) in Dako Wash Buffer (Dako North America, Inc., Carpentaria, CA); 1:500, 30 min Step 2: Vectastain ABC Kit (Vector Laboratories, Inc., Burlingame, CA), 30min. DAB Chromogen, counterstain.
Surfactant Protein – C (SP-C)	Anti-SP-C, polyclonal (PA5-71680, Thermo Fisher Scientific, Waltham, MA USA) in diluent 1:100 x 1 hour	HIER, Citrate Buffer, pH 6.0, 110˚C for 15 minutes; 20 min cool down (Decloaking Chamber Plus, Biocare Medical, Concord, CA USA)	Dako EnVision+ System-HRP Labeled Polymer Anti-rabbit, 60 min (Dako North America, Inc., Carpentaria, CA USA), AEC chromogen, counterstain.

HIER – Heat-induced epitope retrieval

DAB – 3,3'-Diaminobenzidine (produces brown stain)

AEC - aminoethyl carbazole (produces red stain)

Counterstain – Harris hematoxylin (blue color)