

Supplementary Data 1

Symptoms of new coronavirus infection disease (COVID-19): Clinical symptoms such as thrombosis other than pneumonia

Hayashi T, Abiko K, Madai M, Yaegashi N, Konishi I.

Immunohistochemistry - tissues

The Human Protein Atlas contains images of histological sections from normal and cancer tissues obtained by immunohistochemistry. Antibodies are labeled with DAB (3,3'-diaminobenzidine) and the resulting brown staining indicates where an antibody has bound to its corresponding antigen. The section is furthermore counterstained with hematoxylin to enable visualization of microscopical features. Tissue microarrays are used to show antibody staining in samples from 144 individuals corresponding to 44 different normal tissue types (movie about tissue microarray production and immunohistochemical staining). Each sample is represented by 1 mm tissue cores, resulting in a total number of 576 images for each antibody. Normal tissues are represented by samples from three individuals each, one core per individual, except for endometrium, skin, soft tissue and stomach, which are represented by samples from six individuals each and parathyroid gland, which is represented by one sample. Protein expression is annotated in 76 different normal cell types present in these tissue samples. A small fraction of the 576 images are missing for most antibodies due to technical issues. Specimens containing normal tissue have been collected and sampled from anonymized paraffin embedded material of surgical specimens, in accordance with approval from the local ethics committee. For selected proteins extended tissue profiling is performed in addition to standard tissue microarrays. Examined tissues include mouse brain, human lactating breast, eye, thymus and extended samples of adrenal gland, skin and brain.

Since specimens are derived from surgical material, normal is here defined as non-neoplastic and morphologically normal. It is not always possible to obtain fully normal tissues and thus several of the tissues denoted as normal will include alterations due to inflammation, degeneration and tissue remodeling. In rare tissues, hyperplasia or benign proliferations are included as exceptions. It should also be noted that within normal morphology there may exist interindividual differences and variations due to primary diseases, age, sex etc. Such differences may also affect protein expression and thereby immunohistochemical staining patterns.

FANTOM5 CAGE data

The Functional Annotation of Mammalian Genomes 5 (FANTOM5) project provides comprehensive expression profiles and functional annotation of mammalian cell-type specific transcriptomes using Cap Analysis of Gene Expression (CAGE) (Takahashi H *et al.*, 2012), which is based on a series of full-length cDNA technologies developed in RIKEN. CAGE data for 60 of their tissues was obtained from the FANTOM5 repository and mapped to ENSEMBL. The normalized Tags Per Million for each gene were calculated and included in the Human Protein Atlas.

External blood RNA-seq data

In addition to the blood cell type data generated within the Human Protein Atlas project, data from 15 blood cell types by Schmiedel *et al.* and 29 blood cell types as well as total PBMC by Monaco *et al.* have been incorporated into the Blood Atlas.

The Schmiedel dataset is available at the DICE (Database of Immune Cell Expression, Expression quantitative trait loci (eQTLs) and Epigenomics) database, which was established to address how genetic variants associated with risk for human diseases affect gene expression in various cell types. The TPM values per gene for 15 immune cell types were mapped to the corresponding genes in the Ensembl version used in the Human Protein Atlas.

The Monaco dataset contains data for 29 immune cell types within the peripheral blood mononuclear cell (PBMC) fraction of healthy donors using RNA-seq and flow cytometry. TPM values per transcript for 29 immune cells as well as total PBMC were mapped to the corresponding transcripts in the Ensembl version used in the Human Protein Atlas and summarized to pTPM values based only on protein coding transcripts.

<https://www.proteinatlas.org/about/assays+annotation#ihk>

Lung**HPA000288**

Female, age 61
Lung (T-28000)
Normal tissue, NOS (M-00100)
Patient id: 705

Macrophages

Staining: **Low**

Intensity: **Weak**

Quantity: **75%-25%**

Location: **Cytoplasmic/
membranous**

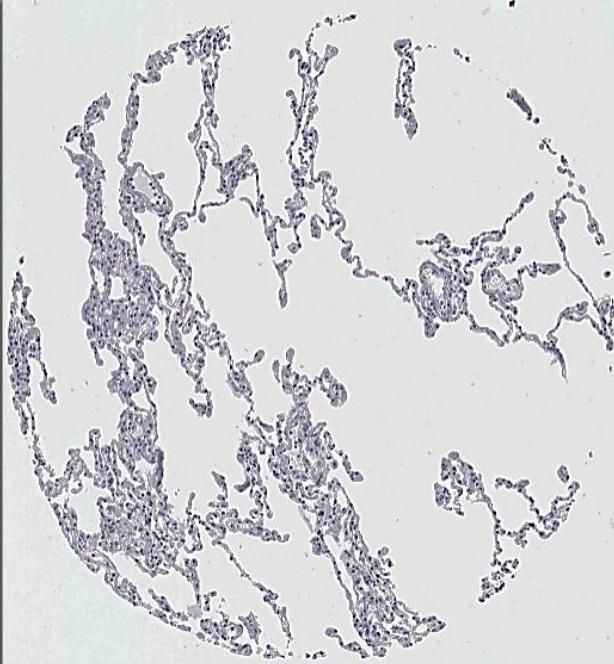
Pneumocytes

Staining: **Not detected**

Intensity: **Negative**

Quantity: **None**

Location: **None**

**Lung****HPA000288**

Female, age 75
Lung (T-28000)
Normal tissue, NOS (M-00100)
Patient id: 496

Macrophages

Staining: **Low**

Intensity: **Weak**

Quantity: **75%-25%**

Location: **Cytoplasmic/
membranous**

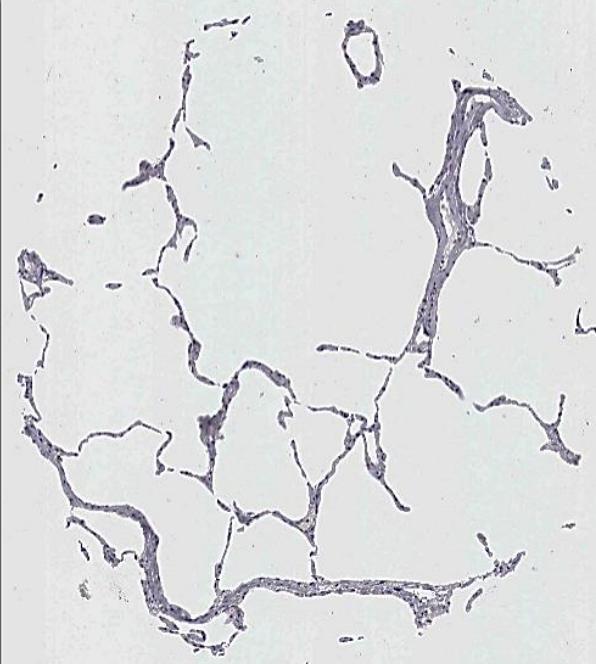
Pneumocytes

Staining: **Not detected**

Intensity: **Negative**

Quantity: **None**

Location: **None**

**Lung****HPA000288**

Male, age 73
Lung (T-28000)
Normal tissue, NOS (M-00100)
Patient id: 218

Macrophages

Staining: **Low**

Intensity: **Weak**

Quantity: **75%-25%**

Location: **Cytoplasmic/
membranous**

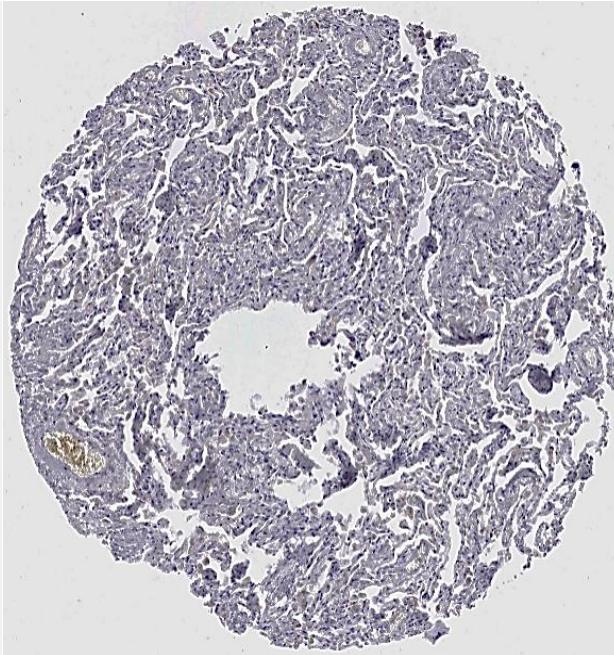
Pneumocytes

Staining: **Not detected**

Intensity: **Negative**

Quantity: **None**

Location: **None**



Lung**CAB026174**

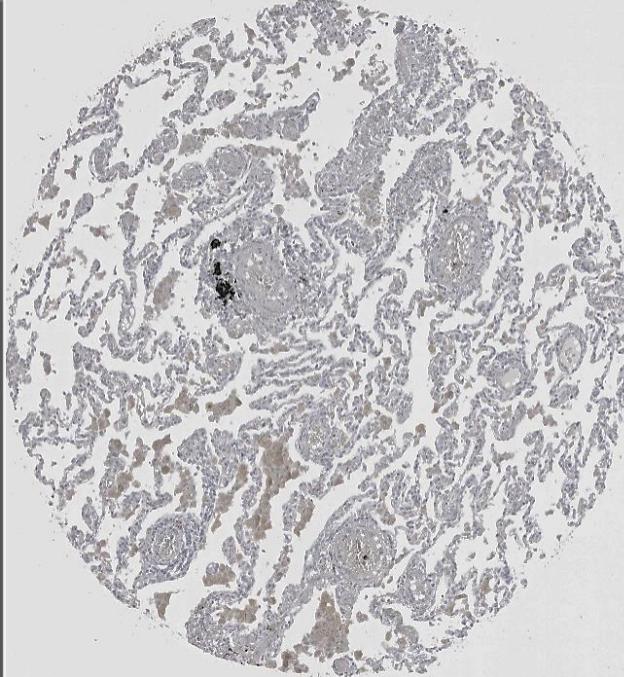
Female, age 49

Lung (T-28000)

Bronchus (T-26000)

Normal tissue, NOS (M-00100)

Patient id: 2268

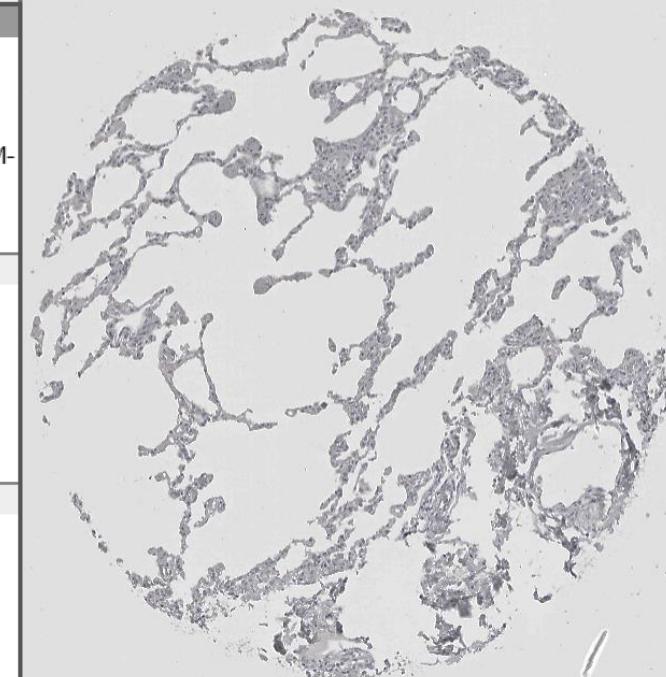
MacrophagesStaining: **Medium**Intensity: **Moderate**Quantity: **75%-25%**Location: **Cytoplasmic/
membranous****Pneumocytes**Staining: **Not detected**Intensity: **Negative**Quantity: **None**Location: **None****Lung****CAB026174**

Male, age 21

Lung (T-28000)

Normal tissue, NOS (M-00100)

Patient id: 2101

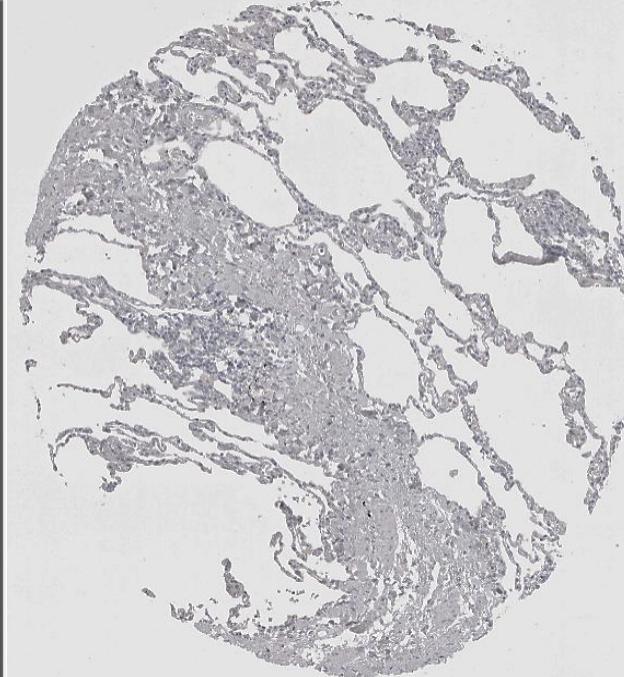
MacrophagesStaining: **Medium**Intensity: **Moderate**Quantity: **75%-25%**Location: **Cytoplasmic/
membranous****Pneumocytes**Staining: **Not detected**Intensity: **Negative**Quantity: **None**Location: **None****Lung****CAB026174**

Male, age 59

Lung (T-28000)

Normal tissue, NOS (M-00100)

Patient id: 2222

MacrophagesStaining: **Medium**Intensity: **Moderate**Quantity: **75%-25%**Location: **Cytoplasmic/
membranous****Pneumocytes**Staining: **Not detected**Intensity: **Negative**Quantity: **None**Location: **None**

Heart muscle**HPA000288**

Female, age 19

Heart (T-32000)

Normal tissue, NOS (M-00100)

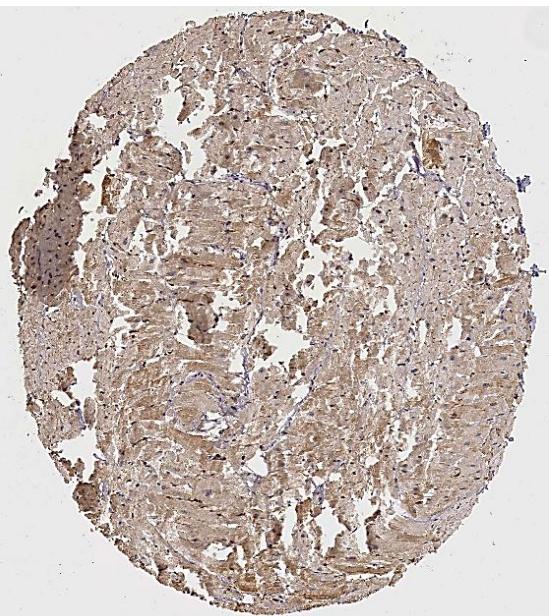
Patient id: 2524

Myocytes

Staining: Medium

Intensity: Moderate

Quantity: >75%

Location: Cytoplasmic/
membranous**Heart muscle****HPA000288**

Female, age 54

Heart (T-32000)

Normal tissue, NOS (M-00100)

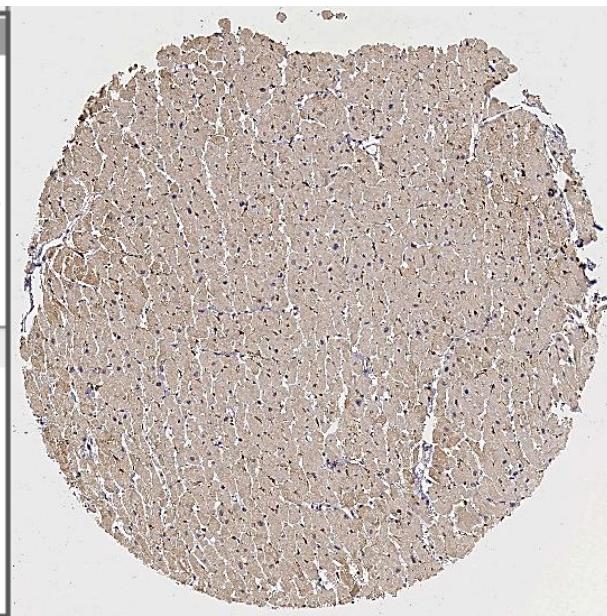
Patient id: 2523

Myocytes

Staining: Medium

Intensity: Moderate

Quantity: >75%

Location: Cytoplasmic/
membranous**Heart muscle****CAB026174**

Male, age 49

Heart (T-32000)

Normal tissue, NOS (M-00100)

Patient id: 2278

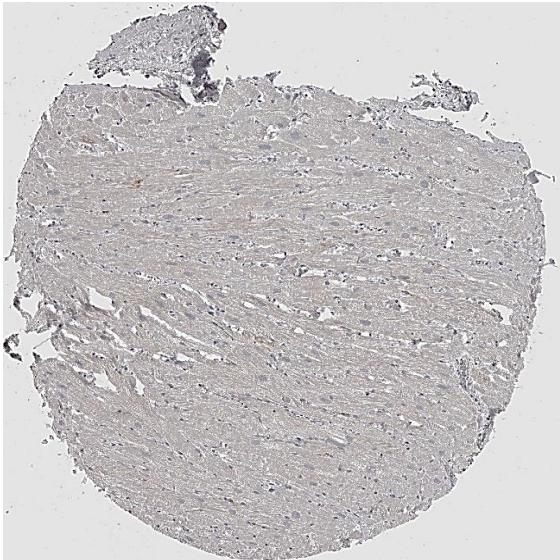
Myocytes

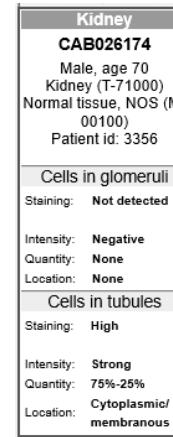
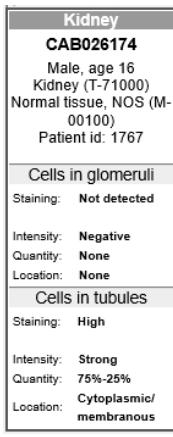
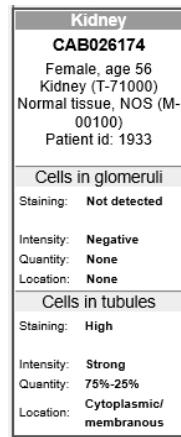
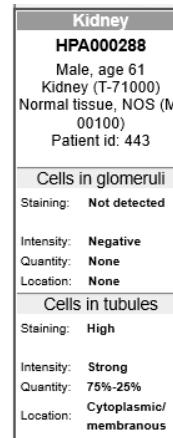
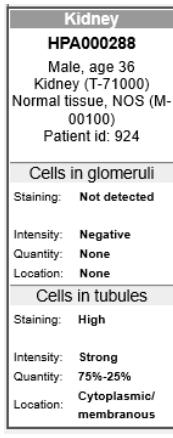
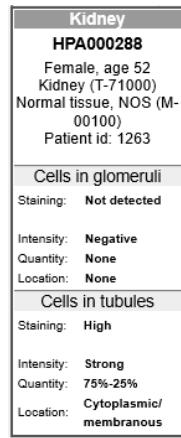
Staining: Not detected

Intensity: Negative

Quantity: None

Location: None





The normal histology section of the dictionary is based on representative sections from human tissues. Tissues have been collected from clinical specimens sent to the Department of Pathology at the Uppsala Akademiska hospital, Uppsala, Sweden for diagnostics. All specimens have been collected with consent of patients. All samples have been anonymized in accordance with ethical approval. Examples of normal tissue histology have been selected from regions in these surgical specimens where morphology appears as normal.

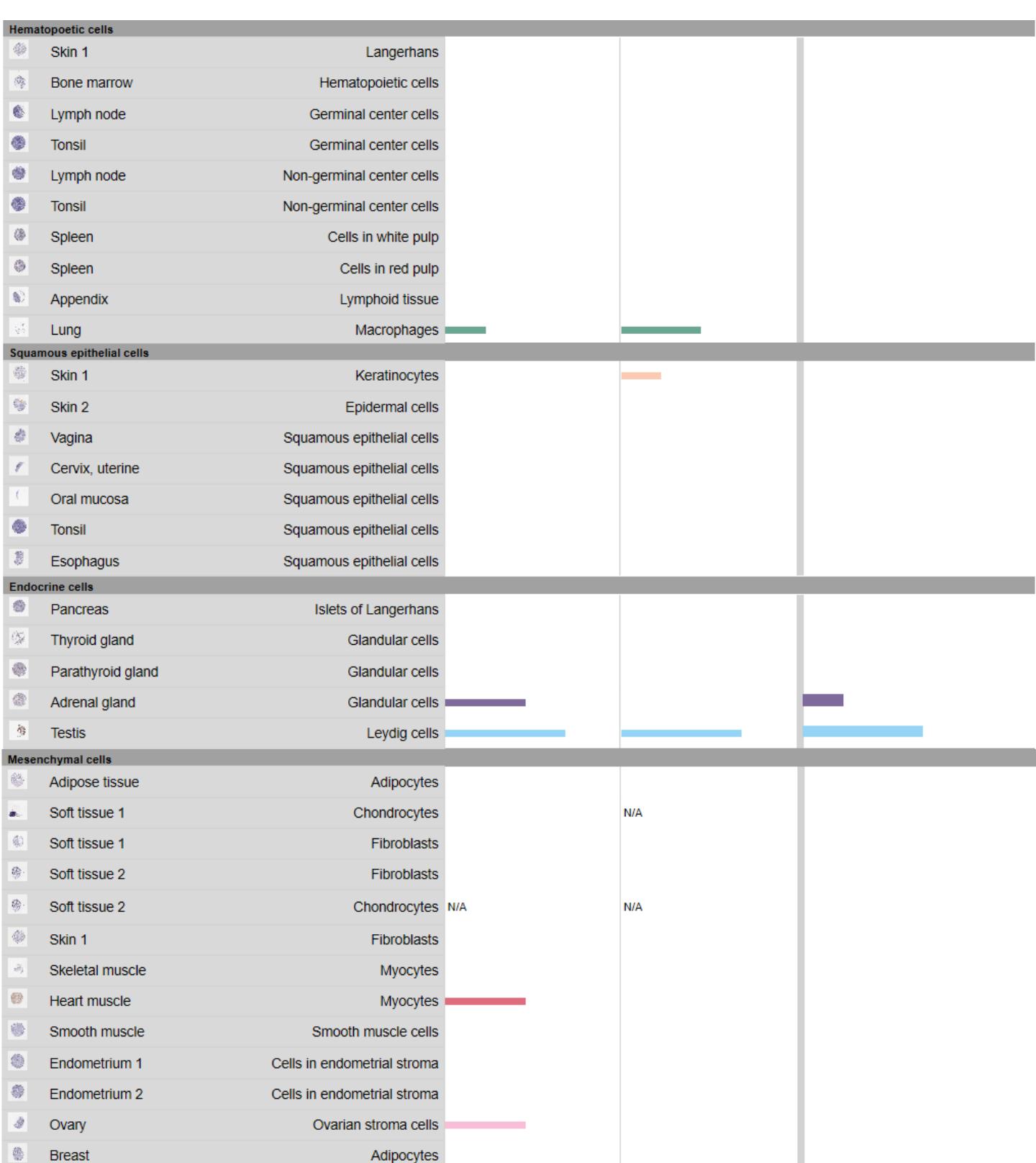
Tissues used in the dictionary have been formalin fixed, paraffin embedded and cut in 4 μm thin sections and placed on glass slides. Glass slides containing tissue sections have been stained using hematoxylin-eosin (HE). Hematoxylin stains cell nuclei blue and eosin stains the cytoplasm and membrane of cells together with connective tissue and extracellular matrix in various shades of red color. Following HE-staining, the sections of tissue have been scanned to obtain high-quality images corresponding to 40x magnification in a microscope.

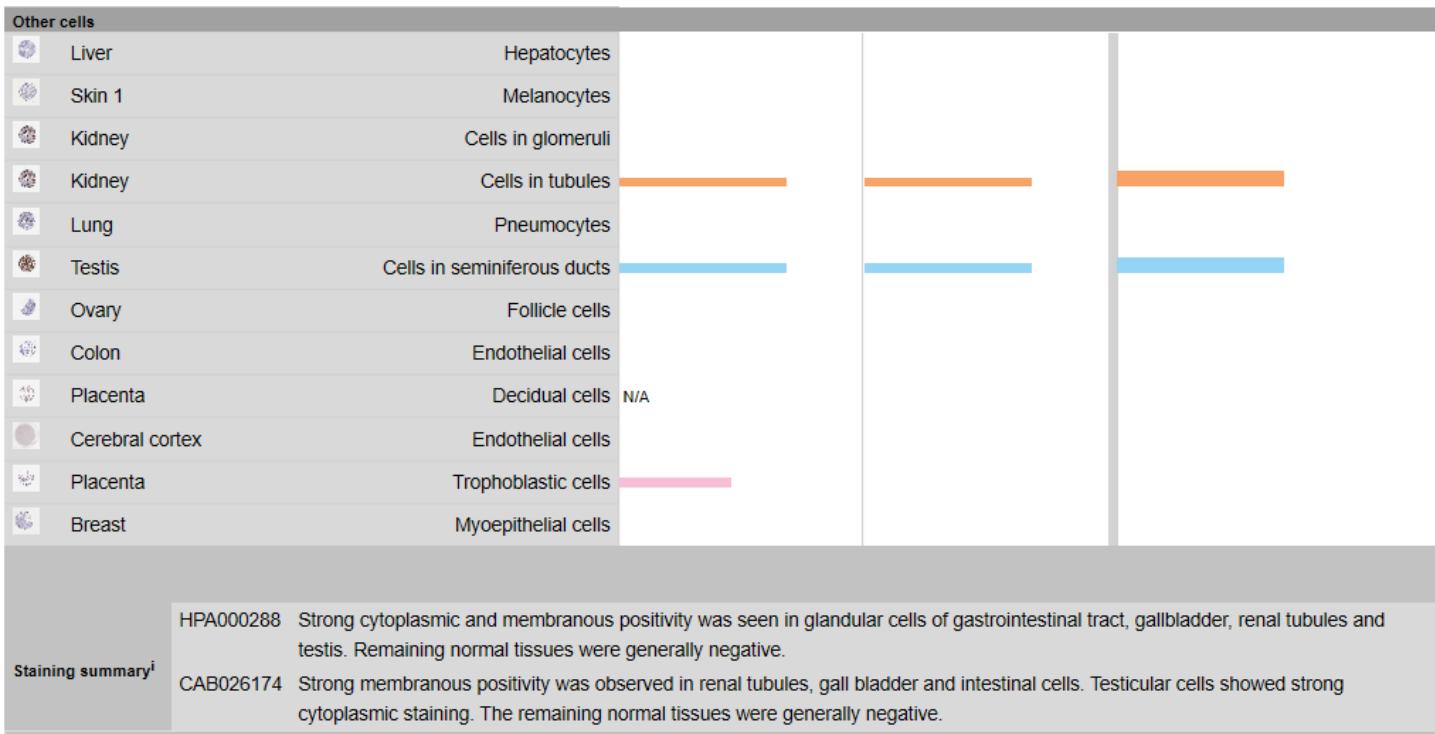
Histology is defined as the study of microscopical anatomy of cells. Assessment of histology provides important and basic information for our understanding of biology and medicine. Histology is also an integral part of pathology and microscopy-based diagnostics. Histological structures, in terms of pathological consideration, are thus important to recognize and relate to when distinguishing a particular disease from normal. In particular, inter-individual variations of the norm (for example related to age) can pose a challenge when distinguishing normal from a pathological condition.

<https://www.proteinatlas.org/learn/dictionary/normal>

FANTOM5 CAGE data: ACE2 expression in human tissues

1	cerebrum	0.027	prostate	0.74
2	cerebellum	0	ovary	1.2
3	brain stem	0.0669	testis	3.7
4	corpus callosum/glia	0	heart	2.021
5	pineal gland	0.426	muscle	0.508
6	peripheral nerve	0	esophagus	0.627
7	spine	0.089	stomach	0
8	retina	0	intestine	5.69
9	eye	0	colon	2.424
10	artery/aorta	0.335	liver/hepato	0.84
11	vein	0.338	lung	0.317
12	lymphnode	0.4078	bladder	0
13	spleen	0	kidney	2.86
14	thymus	0	pituitary	0
15	bone marrow	2.98	thyroid/parathyroid	2.4
16	adipose	1.57	adrenal gland	0.189
17	bone	0	pancreas	1.738
18	skin	0	breast	1.8
19	uterus	0.26	salivary	0.357
20	placenta	3.21		
21				

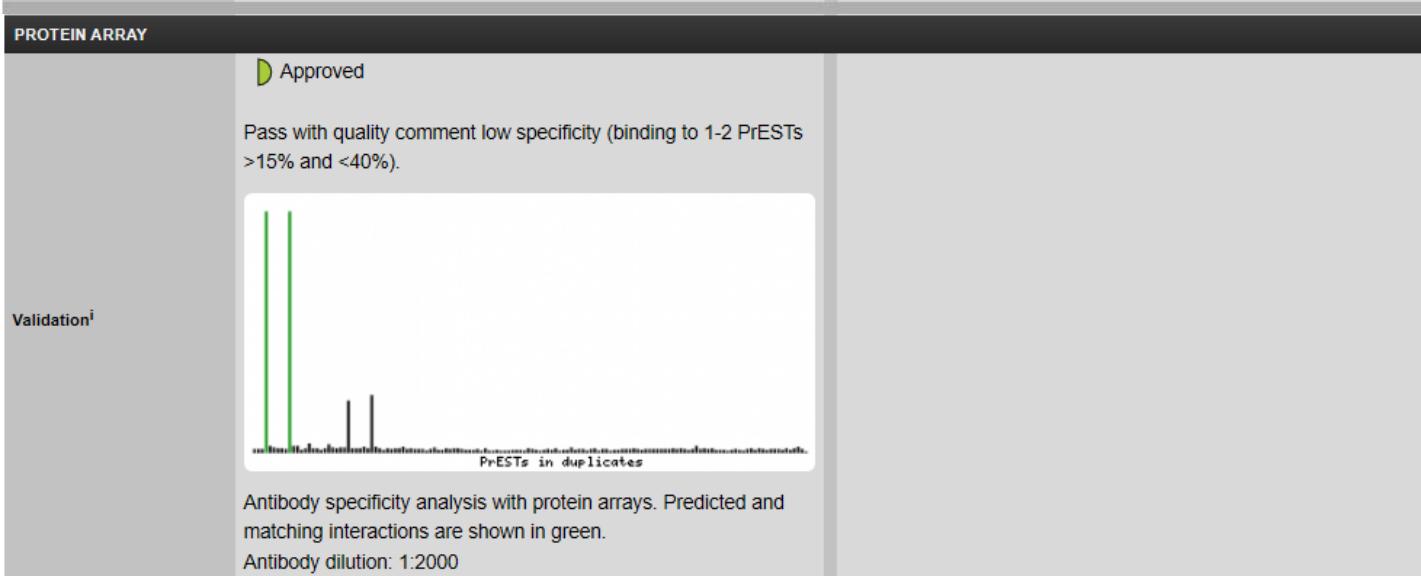




<https://www.proteinatlas.org/ENSG00000130234-ACE2/tissue/primary+data>

Antibody Information

ANTIBODY INFORMATION		Antibody HPA000288	Antibody CAB026174
Provider	Atlas Antibodies Sigma-Aldrich		R&D Systems
Product name	HPA000288		MAB933
Host species	Rabbit		Mouse
Clonality ⁱ	pAb		mAb
Purity	Affinity purified using the PrEST-antigen as affinity ligand		Protein A/G
Released in version ⁱ	1.2		5
References ⁱ	2		
Proper citation	Atlas Antibodies Cat#HPA000288, RRID:AB_1078160		n/a
Validation summary ⁱ	<div style="display: flex; justify-content: space-around; align-items: center;"> N/A N/A </div> <p>ICC IHC WB PA</p>	<div style="display: flex; justify-content: space-around; align-items: center;"> N/A N/A </div> <p>ICC IHC WB PA</p>	

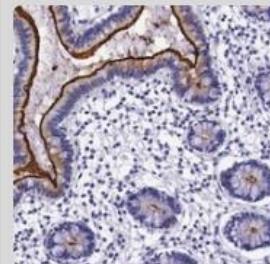


<https://www.proteinatlas.org/ENSG00000130234-ACE2/antibody>

● Enhanced - Orthogonal

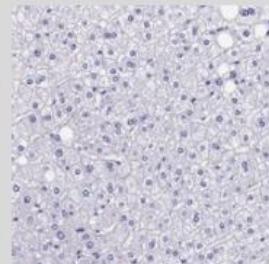
Antibody staining mainly consistent with RNA expression data across 36 tissues.

HIGH EXPRESSION



Small intestine

LOW EXPRESSION



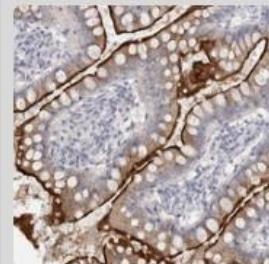
Liver



● Enhanced - Orthogonal

Antibody staining mainly consistent with RNA expression data across 36 tissues.

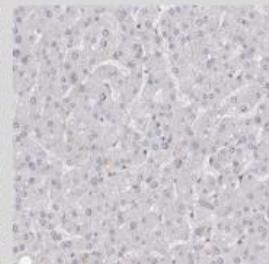
HIGH EXPRESSION



Small intestine

RNA expression: 122.0 NX

LOW EXPRESSION



Liver

RNA expression: 1.2 NX



Validationⁱ

Retrievalⁱ

HIER pH9

Antibody dilution

1:250

Literature conformityⁱ

Partly consistent with extensive gene/protein characterization data.

RNA consistencyⁱ

Consistent with RNA expression data.

HIER pH6

1:5000

Partly consistent with extensive gene/protein characterization data.

Consistent with RNA expression data.

WESTERN BLOTHⁱ

● Uncertainⁱ

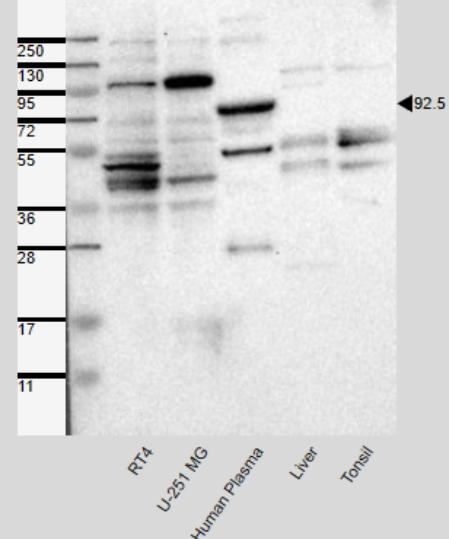
Only bands not corresponding to the predicted size.
Analysis performed using a standard panel of samples.

Antibody dilution: 1:500

● Supportedⁱ

Band of predicted size in kDa (+/-20%) with additional bands present.

Analysis performed using a standard panel of samples.



Antibody dilution: 1:500

Validationⁱ

RELEVANT PUBLICATIONS

Gene expression profiling of metaplastic lineages identifies CDH17 as a prognostic marker in early stage gastric cancer
Lee HJ et al

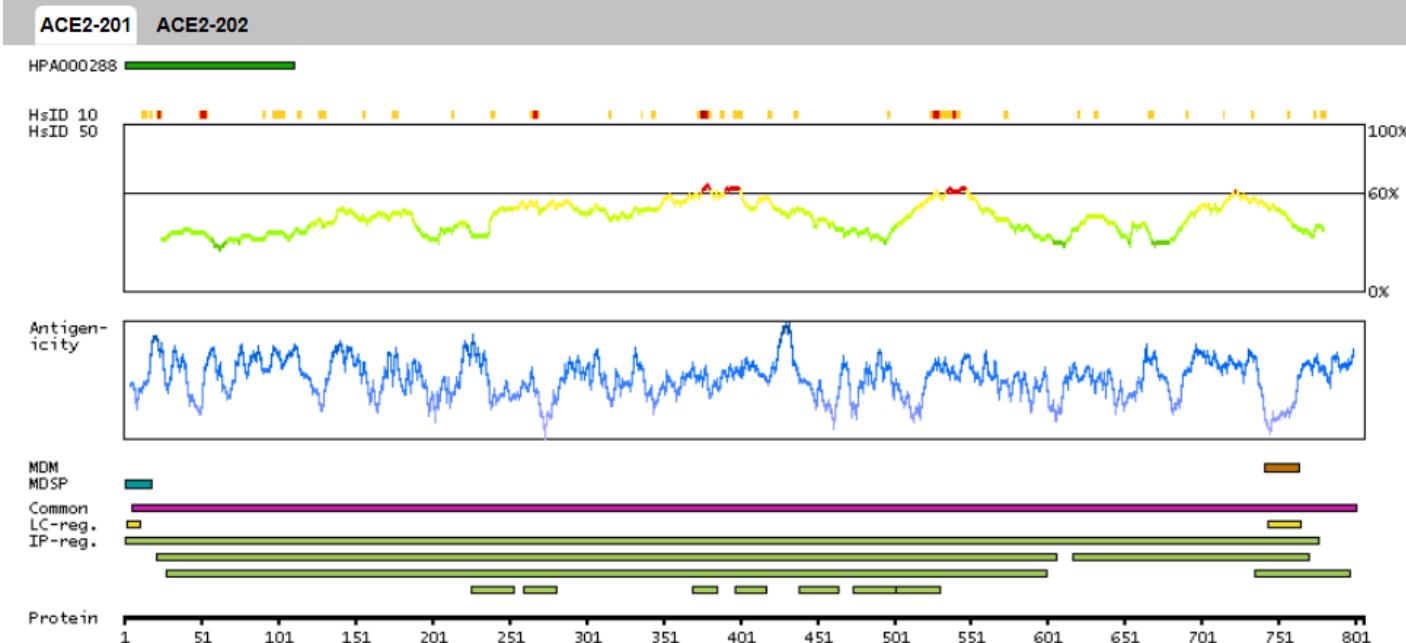
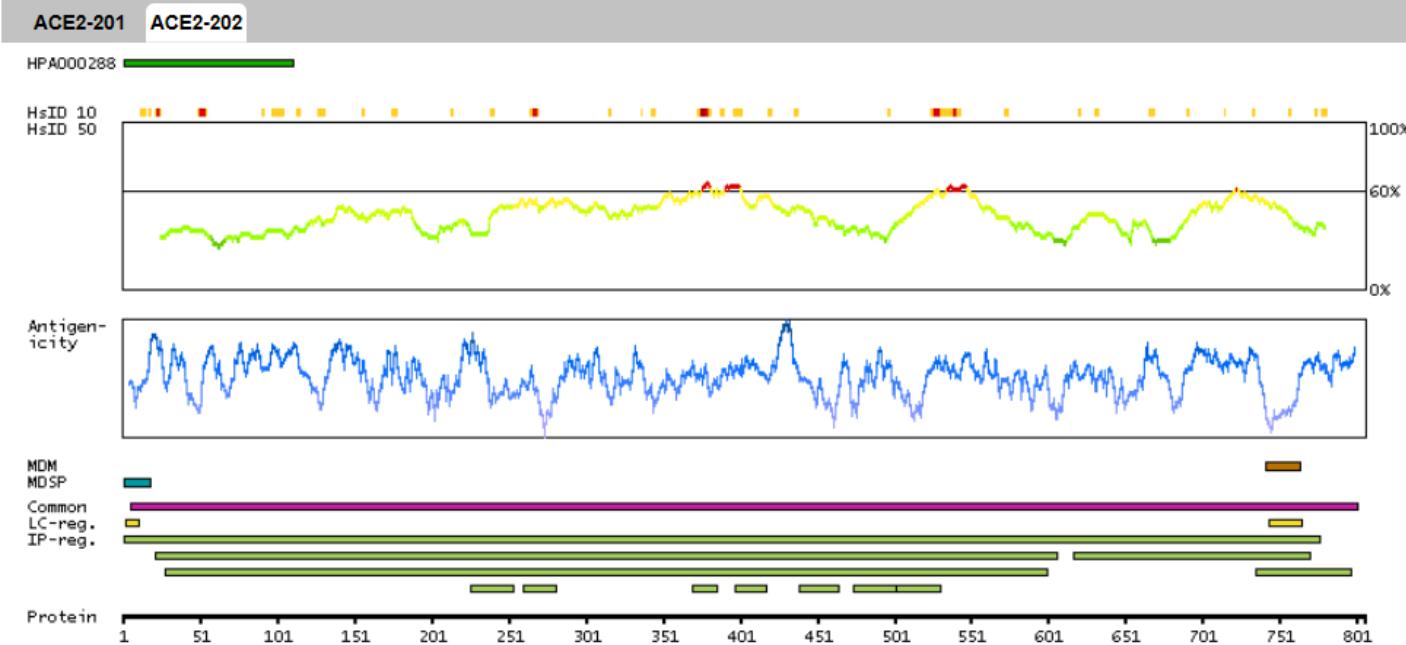
Gastroenterology 2010;139(1):213-25.e3

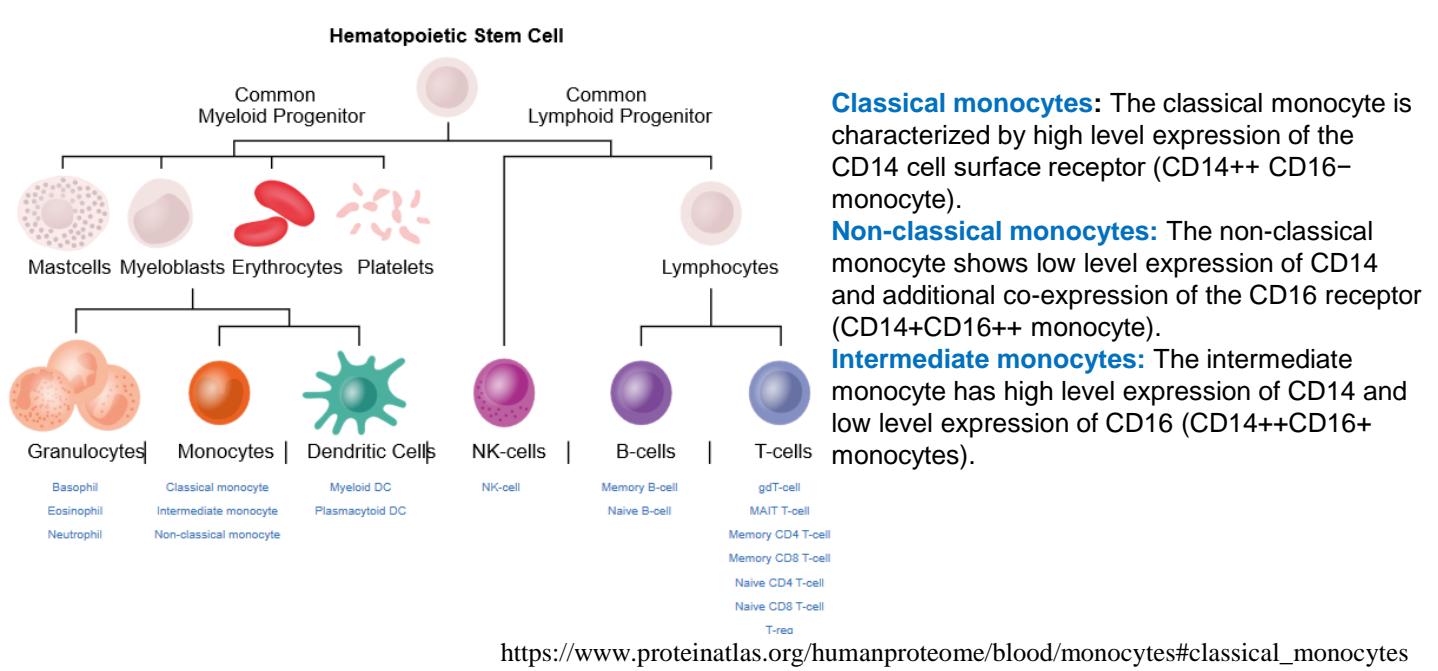
Variance decomposition of protein profiles from antibody arrays using a longitudinal twin model
Kato BS et al

Proteome Sci 2011;9:73

ANTIGEN INFORMATION

Antigen	Recombinant protein fragment	Recombinant protein
Length (aa)	111	
Antigen sequence	MSSSSWLLSLVAVTAAQSTIEEQAKTFLDKFNHEAEDLFYQSSLASWNY NTNITEENVQNMNNAGDKWSAFLKEQSTLAQMYPLQEIQNLTVKLQLQAL QQNGSSVLSED	
Matching transcripts	ACE2-201 - ENSP00000252519 [100%] ACE2-202 - ENSP00000389326 [100%]	
Matching mouse transcripts	ENSMUSP00000073626 [74%] ENSMUSP00000107890 [74%] ENSMUSP00000140827 [29%] ENSMUSP00000006629 [24%]	

ANTIGEN VIEWⁱANTIGEN VIEWⁱ



Classical monocytes: The classical monocyte is characterized by high level expression of the CD14 cell surface receptor (CD14++ CD16- monocyte).

Non-classical monocytes: The non-classical monocyte shows low level expression of CD14 and additional co-expression of the CD16 receptor (CD14+CD16++ monocyte).

Intermediate monocytes: The intermediate monocyte has high level expression of CD14 and low level expression of CD16 (CD14++CD16+ monocytes).

https://www.proteinatlas.org/humanproteome/blood/monocytes#classical_monocytes

TABLE 1 | Cell surface markers of mononuclear phagocytes in human lungs.

Ontogeny	Macrophages				Monocytes			Committed DC progenitor		
	Alveolar macrophages	Interstitial macrophages	Tissue monocytes	Monocyte-derived DC	cDC1 CD141+ MDC (IRF8 dependent)	cDC2 CD1c+ MDC (IRF4 dependent)	PDC			
AF	++	-	-	-	-	-	-	-	-	-
BTLA	n.d.	n.d.	n.d.	-	++	+	n.d.	+	n.d.	n.d.
CADM1	n.d.	n.d.	n.d.	n.d.	+	-	n.d.	-	n.d.	n.d.
CD1a	-	-	-	-/+	-	-	-/+	-	-	-
CD1c	-	-	-	+	-	-	+	-	-	-
CD11b	+	+	+	+	-	-	+	+	-	-
CD11c	+	+	+	+	+	+	+	+	-	-
CD14	-	+	+	+	-	-	-	-	-	-
CD16	+	+	++	-	-	-	-	-	-	-
CD64	+	+	+	-	+	+	+	-	-	-
CD103	+	n.d.	-	-	-/+	+	+	+	+	+
CD123	-	-	-	-/+	-	-	-/+	-	-	+
CD141	+	-	-	-/+	++	+	-	-	-	-
CD163	+	+	+	+	-	-	-	-	-	-
CD169	+	-	n.d.	-	-	-	-	-	-	-
CD172a	n.d.	n.d.	n.d.	+	-	-	+	-	n.d.	-
CD206	+	+	+	+	-	-	+	-	-	-
CD207	n.d.	n.d.	n.d.	n.d.	-	-	-/+	-	-	-
CD303	-	-	-	-	-	-	-	-	-	+
Clec9A	-	-	-	-	+	-	-	-	-	-
HLA-DR	+	+	+	+	++	++	++	++	++	++
Lineage ^a	-	-	-	-	-	-	-	-	-	-
TGFbR	n.d.	n.d.	n.d.	n.d.	+	+	+	+	n.d.	n.d.
XCR1	-	-	-	-	+	-	-	-	-	-

^aCD3, CD19, CD20, CD56, CD66abc.

n.d., not determined; DCs, dendritic cells; PDC, plasmacytoid DC; cDC, classical DC; IRF, interferon regulatory factor; MDC, myeloid DC.

GENERAL INFORMATIONⁱ

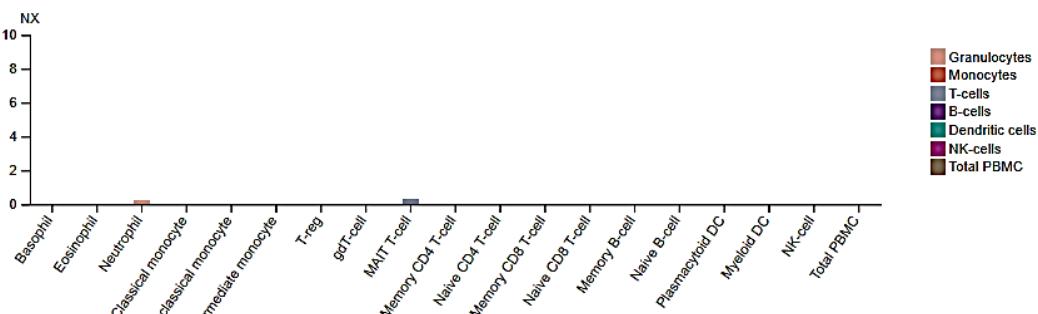
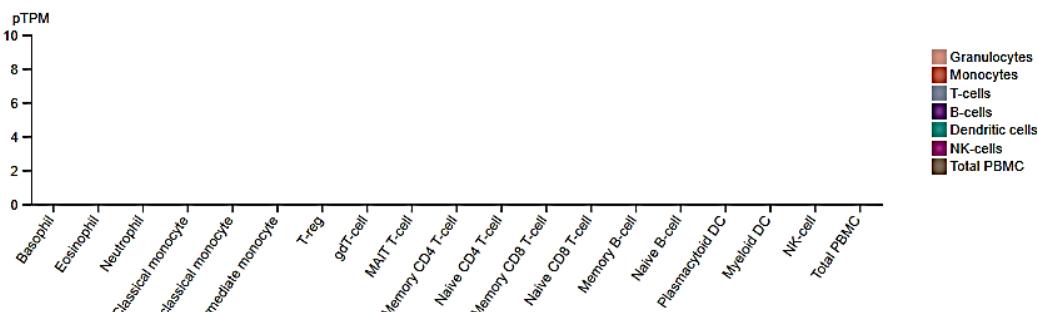
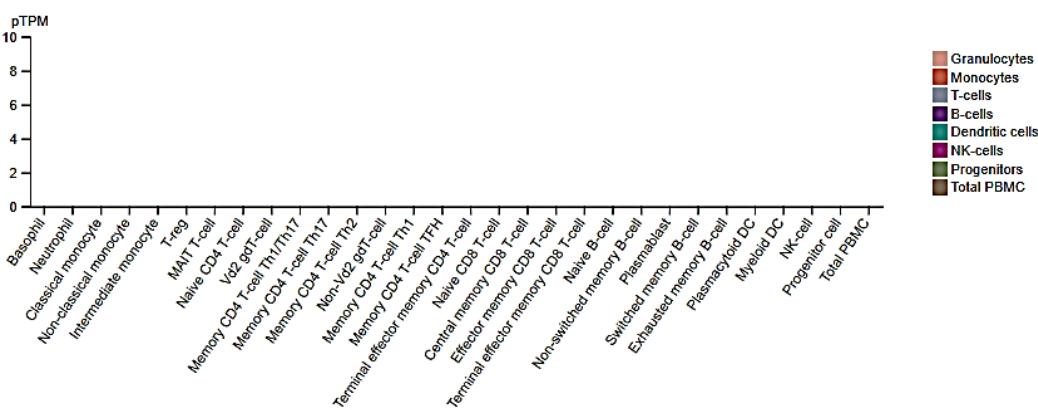
Gene name ⁱ	ACE2
Gene description	Angiotensin I converting enzyme 2
Predicted location ⁱ	Membrane,Secreted

HUMAN PROTEIN ATLAS INFORMATION

Secretome annotation ⁱ	Secreted to blood
Secretome annotation comment	Secreted form from proteolytic cleavage or shedding
RNA blood cell lineage specificity ⁱ	Not detected
RNA blood cell lineage distribution ⁱ	Not detected
RNA blood cell type specificity ⁱ	Not detected
RNA blood cell type distribution ⁱ	Not detected
Blood-based immunoassay ⁱ	Not detected
Mass spectrometry ⁱ	Detected

BLOOD CELL TYPE EXPRESSION (RNA)ⁱConsensus datasetⁱ

RNA cell type specificity: Not detected

[Lineage](#) [Expression](#) [Alphabetical](#)HPA scaled datasetⁱ[Lineage](#) [Expression](#) [Alphabetical](#)Monaco scaled datasetⁱ[Lineage](#) [Expression](#) [Alphabetical](#)Schmiedel datasetⁱ[Lineage](#) [Expression](#) [Alphabetical](#)