

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

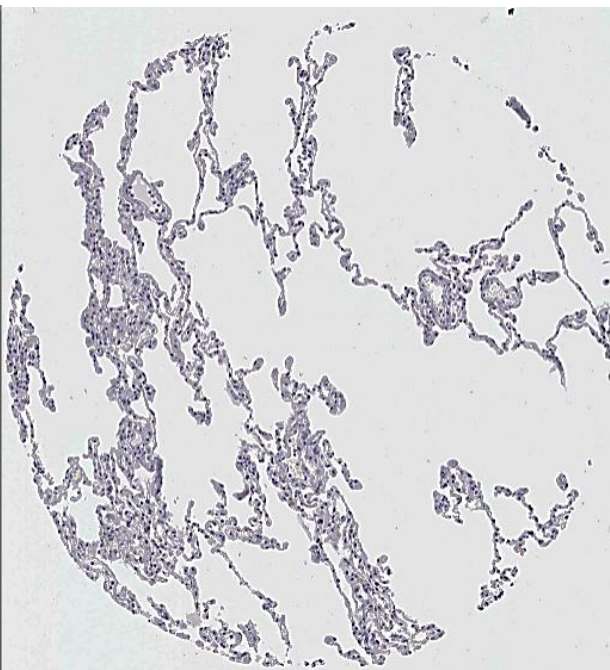
In addition to the blood cell type data generated within the Human Protein Atlas project, data from 15 blood cell types by Schmiedel *et al.* and 29 blood cell types as well as total PBMC by Monaco *et al.* have been incorporated into the Blood Atlas.

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.

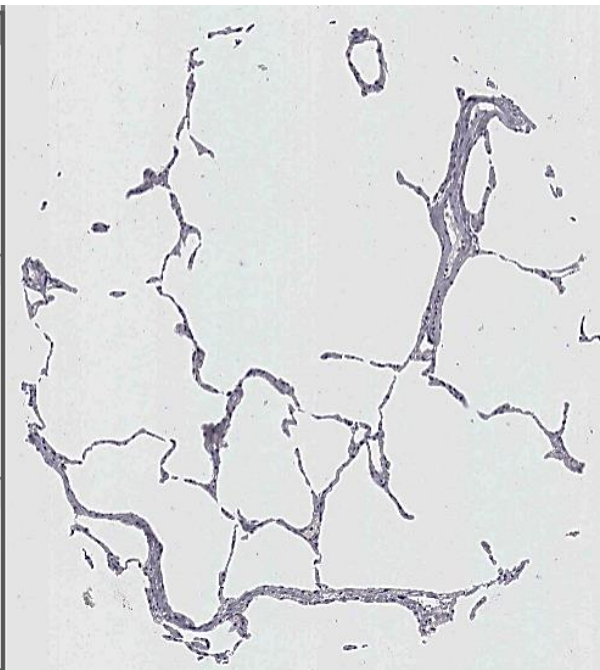
The Monaco dataset contains data for 29 immune cell types within the peripheral blood mononuclear cell (PBMC) fraction of healthy donors using RNA-seq and flow cytometry. TPM values per transcript for 29 immune cells as well as total PBMC were mapped to the corresponding transcripts in the Ensembl version 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>

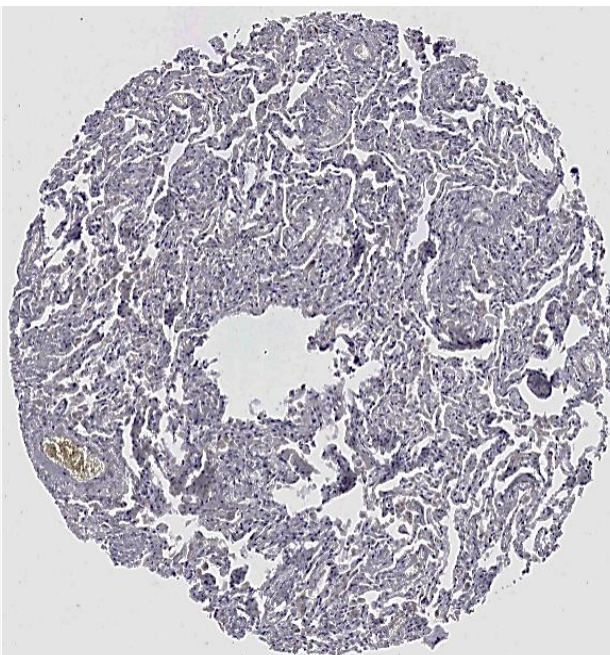
Lung
HPA000288
Female, age 61
Lung (T-28000)
Normal tissue, NOS (M-00100)
Patient id: 705
Macrophages
Staining: Low
Intensity: Weak
Quantity: 75%-25%
Location: Cytoplasmic/ membranous
Pneumocytes
Staining: Not detected
Intensity: Negative
Quantity: None
Location: None



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

Macrophages

Staining: Medium

Intensity: Moderate

Quantity: 75%-25%

Location: Cytoplasmic/
membranous

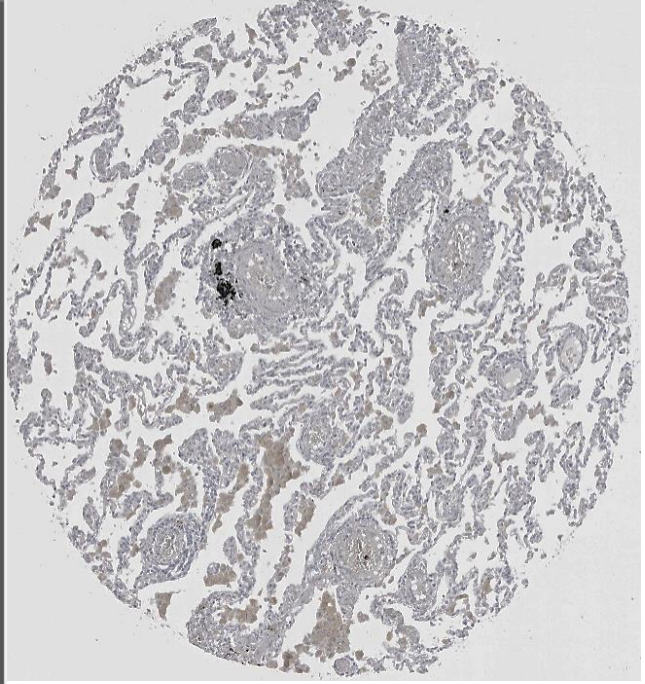
Pneumocytes

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

Macrophages

Staining: Medium

Intensity: Moderate

Quantity: 75%-25%

Location: Cytoplasmic/
membranous

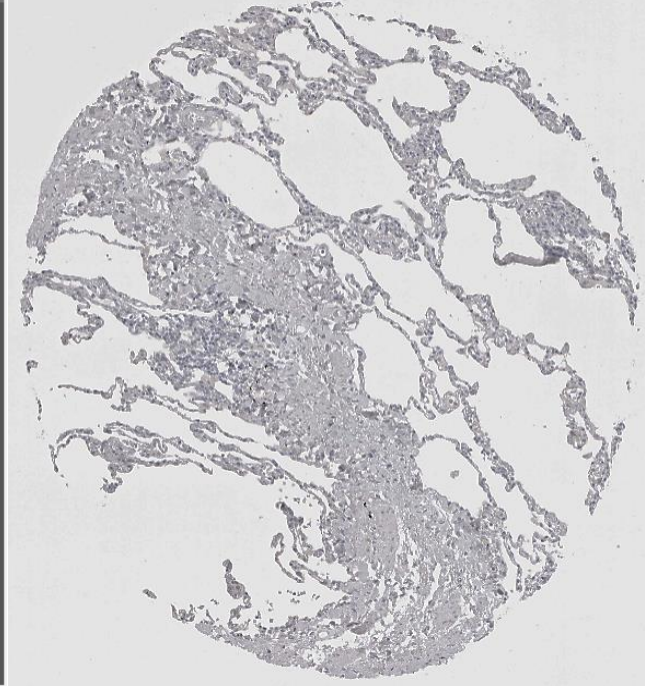
Pneumocytes

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

Macrophages

Staining: 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

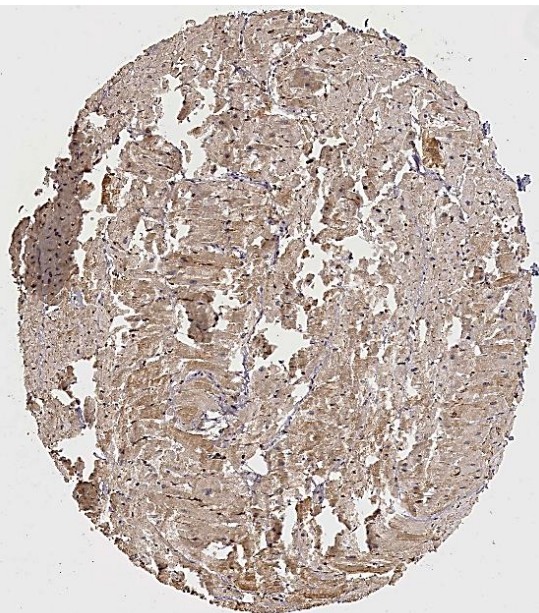
Myocytes

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

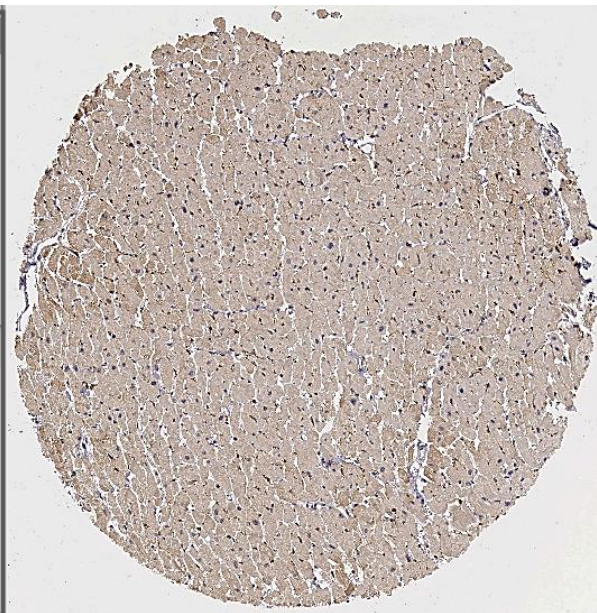
Myocytes

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

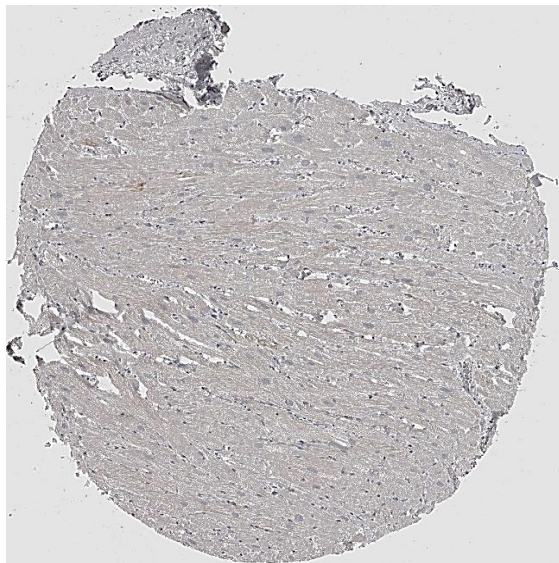
Myocytes

Staining: **Not detected**

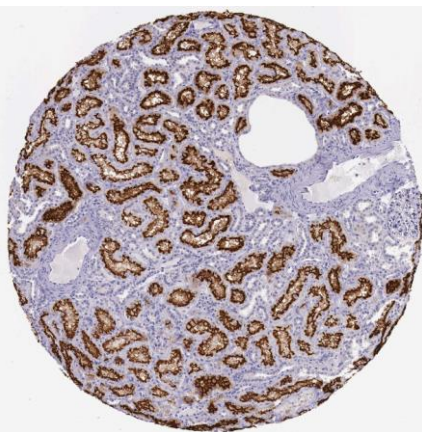
Intensity: **Negative**

Quantity: **None**

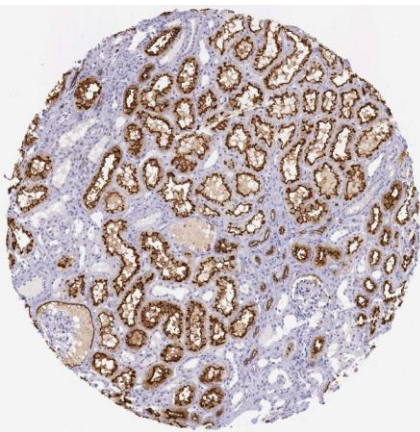
Location: **None**



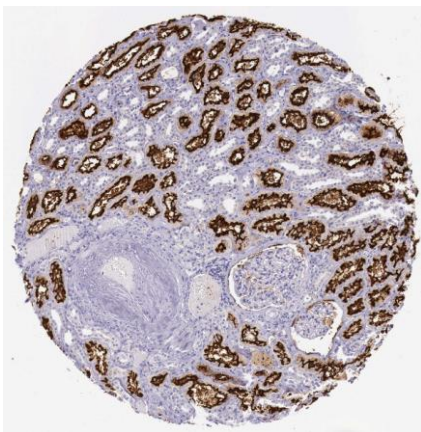
Kidney	
HPA000288	
Female, age 52	
Kidney (T-71000)	
Normal tissue, NOS (M-00100)	
Patient id: 1263	
Cells in glomeruli	
Staining:	Not detected
Intensity:	Negative
Quantity:	None
Location:	None
Cells in tubules	
Staining:	High
Intensity:	Strong
Quantity:	75%-25%
Location:	Cytoplasmic/ membranous



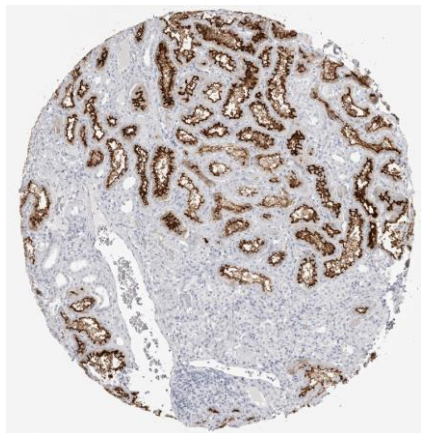
Kidney	
HPA000288	
Male, age 36	
Kidney (T-71000)	
Normal tissue, NOS (M-00100)	
Patient id: 924	
Cells in glomeruli	
Staining:	Not detected
Intensity:	Negative
Quantity:	None
Location:	None
Cells in tubules	
Staining:	High
Intensity:	Strong
Quantity:	75%-25%
Location:	Cytoplasmic/ membranous



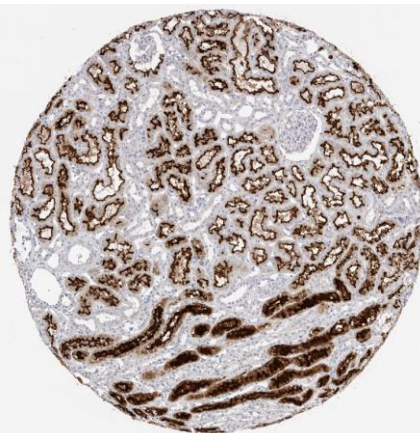
Kidney	
HPA000288	
Male, age 61	
Kidney (T-71000)	
Normal tissue, NOS (M-00100)	
Patient id: 443	
Cells in glomeruli	
Staining:	Not detected
Intensity:	Negative
Quantity:	None
Location:	None
Cells in tubules	
Staining:	High
Intensity:	Strong
Quantity:	75%-25%
Location:	Cytoplasmic/ membranous



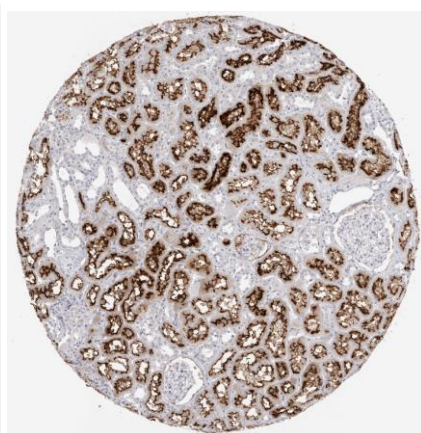
Kidney	
CAB026174	
Female, age 56	
Kidney (T-71000)	
Normal tissue, NOS (M-00100)	
Patient id: 1933	
Cells in glomeruli	
Staining:	Not detected
Intensity:	Negative
Quantity:	None
Location:	None
Cells in tubules	
Staining:	High
Intensity:	Strong
Quantity:	75%-25%
Location:	Cytoplasmic/ membranous



Kidney	
CAB026174	
Male, age 16	
Kidney (T-71000)	
Normal tissue, NOS (M-00100)	
Patient id: 1767	
Cells in glomeruli	
Staining:	Not detected
Intensity:	Negative
Quantity:	None
Location:	None
Cells in tubules	
Staining:	High
Intensity:	Strong
Quantity:	75%-25%
Location:	Cytoplasmic/ membranous



Kidney	
CAB026174	
Male, age 70	
Kidney (T-71000)	
Normal tissue, NOS (M-00100)	
Patient id: 3356	
Cells in glomeruli	
Staining:	Not detected
Intensity:	Negative
Quantity:	None
Location:	None
Cells in tubules	
Staining:	High
Intensity:	Strong
Quantity:	75%-25%
Location:	Cytoplasmic/ membranous



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 μ m 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

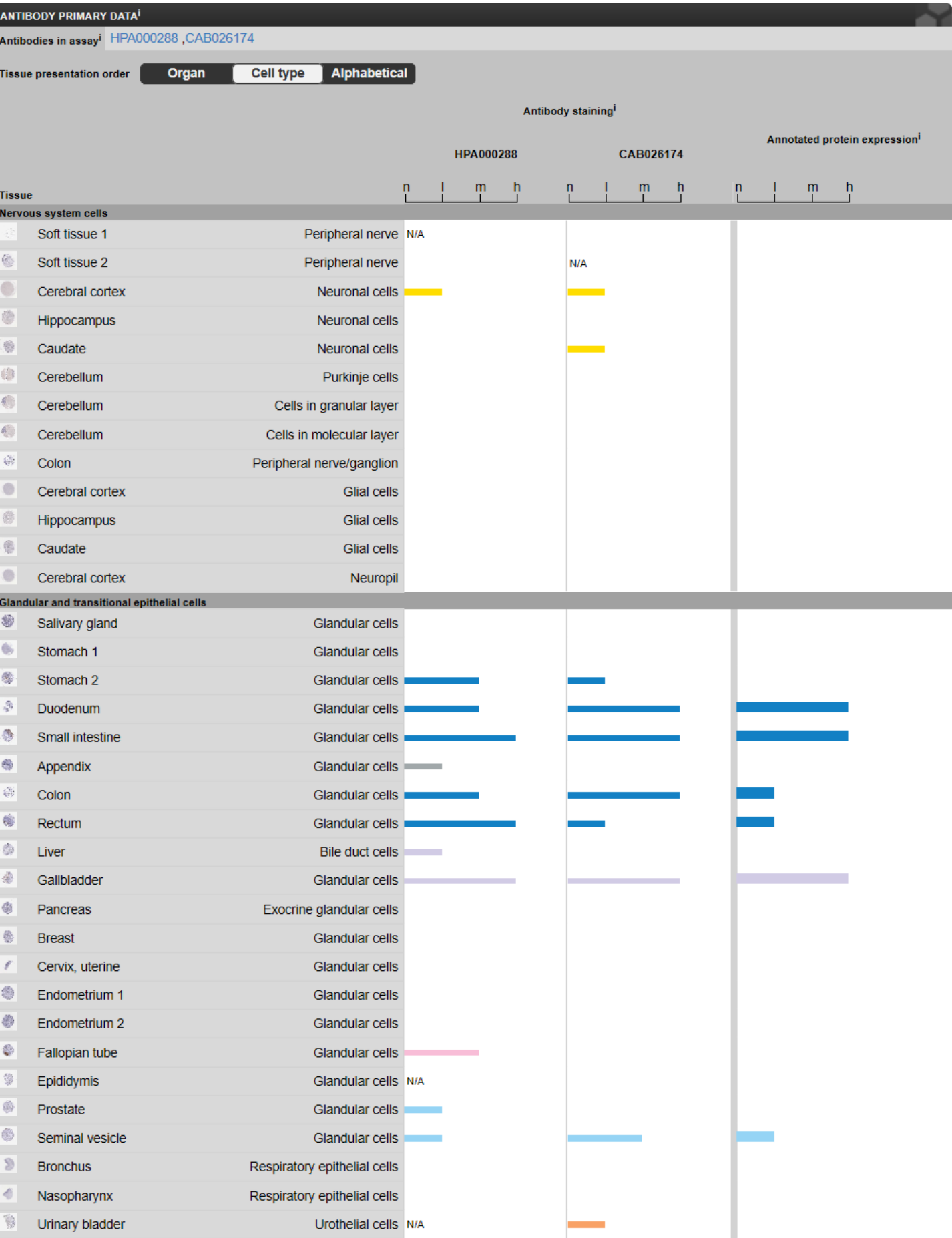
1	cerebrum	0.027		prostate	0.74	
2	cerebellum	0		ovary	1.2	
3	brain stem	0.0669		testis	3.7	
4	corpus callosum/glia	0		heart	2.021	
5	pineal gland	0.426		muscle	0.508	
6	peripheral nerve	0		esophagus	0.627	
7	spine	0.089		stomach	0	
8	retina	0		intestine	5.69	
9	eye	0		colon	2.424	
10	artery/aorta	0.335		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						




































Supplementary Data 2




















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.

Expression of ACE2 in human tissues




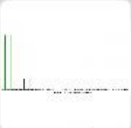


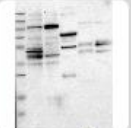






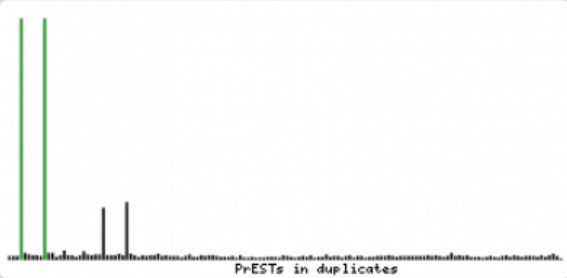


Hematopoietic cells					
	Skin 1	Langerhans			
	Bone marrow	Hematopoietic cells			
	Lymph node	Germinal center cells			
	Tonsil	Germinal center cells			
	Lymph node	Non-germinal center cells			
	Tonsil	Non-germinal center cells			
	Spleen	Cells in white pulp			
	Spleen	Cells in red pulp			
	Appendix	Lymphoid tissue			
	Lung	Macrophages	<div></div>	<div></div>	
Squamous epithelial cells					
	Skin 1	Keratinocytes		<div></div>	
	Skin 2	Epidermal cells			
	Vagina	Squamous epithelial cells			
	Cervix, uterine	Squamous epithelial cells			
	Oral mucosa	Squamous epithelial cells			
	Tonsil	Squamous epithelial cells			
	Esophagus	Squamous epithelial cells			
Endocrine cells					
	Pancreas	Islets of Langerhans			
	Thyroid gland	Glandular cells			
	Parathyroid gland	Glandular cells			
	Adrenal gland	Glandular cells	<div></div>		<div></div>
	Testis	Leydig cells	<div></div>	<div></div>	<div></div>
Mesenchymal cells					
	Adipose tissue	Adipocytes			
	Soft tissue 1	Chondrocytes		N/A	
	Soft tissue 1	Fibroblasts			
	Soft tissue 2	Fibroblasts			
	Soft tissue 2	Chondrocytes	N/A	N/A	
	Skin 1	Fibroblasts			
	Skeletal muscle	Myocytes			
	Heart muscle	Myocytes	<div></div>		
	Smooth muscle	Smooth muscle cells			
	Endometrium 1	Cells in endometrial stroma			
	Endometrium 2	Cells in endometrial stroma			
	Ovary	Ovarian stroma cells	<div></div>		
	Breast	Adipocytes			

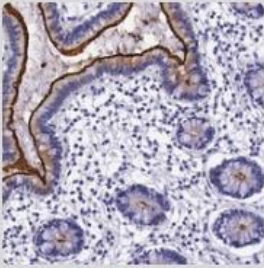
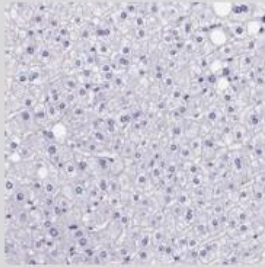
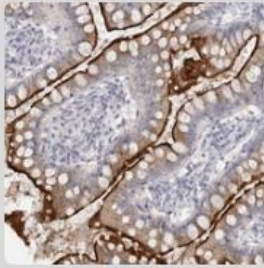
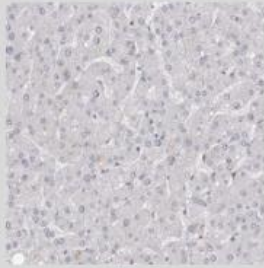
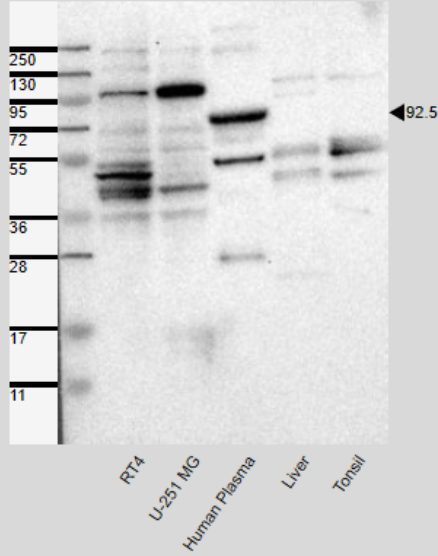
Other cells					
	Liver	Hepatocytes			
	Skin 1	Melanocytes			
	Kidney	Cells in glomeruli			
	Kidney	Cells in tubules			
	Lung	Pneumocytes			
	Testis	Cells in seminiferous ducts			
	Ovary	Follicle cells			
	Colon	Endothelial cells			
	Placenta	Decidual cells	N/A		
	Cerebral cortex	Endothelial cells			
	Placenta	Trophoblastic cells			
	Breast	Myoepithelial cells			
Staining summary ⁱ	HPA000288	Strong cytoplasmic and membranous positivity was seen in glandular cells of gastrointestinal tract, gallbladder, renal tubules and testis. Remaining normal tissues were generally negative.			
	CAB026174	Strong membranous positivity was observed in renal tubules, gall bladder and intestinal cells. Testicular cells showed strong cytoplasmic staining. The remaining normal tissues were generally negative.			

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

Antibody Information

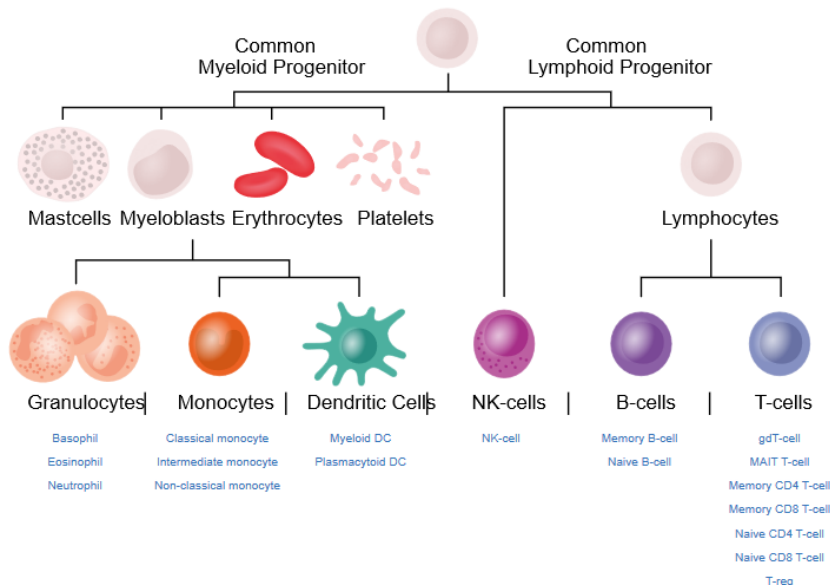
Antibody HPA000288				Antibody CAB026174				
ANTIBODY INFORMATION								
Provider	Atlas Antibodies Sigma-Aldrich			R&D Systems				
Product name	HPA000288			MAB933				
Host species	Rabbit			Mouse				
Clonality ⁱ	pAb			mAb				
Purity	Affinity purified using the PrEST-antigen as affinity ligand			Protein 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								
	ICC	IHC 	WB	PA 	ICC	IHC 	WB 	PA
PROTEIN ARRAY								
Validation ⁱ								
	Approved							
	Pass with quality comment low specificity (binding to 1-2 PrESTs >15% and <40%).							
								
Antibody specificity analysis with protein arrays. Predicted and matching interactions are shown in green.								
Antibody dilution: 1:2000								

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

IMMUNOHISTOCHEMISTRY ⁱ		
Validation ⁱ	<div> <div>Enhanced - Orthogonal</div> <div>Antibody staining mainly consistent with RNA expression data across 36 tissues.</div> <div> <div>HIGH EXPRESSION</div>  <div>Small intestine</div> <div>RNA expression: 122.0 NX</div> </div> <div> <div>LOW EXPRESSION</div>  <div>Liver</div> <div>RNA expression: 1.2 NX</div> </div> </div>	<div> <div>Enhanced - Orthogonal</div> <div>Antibody staining mainly consistent with RNA expression data across 36 tissues.</div> <div> <div>HIGH EXPRESSION</div>  <div>Small intestine</div> <div>RNA expression: 122.0 NX</div> </div> <div> <div>LOW EXPRESSION</div>  <div>Liver</div> <div>RNA expression: 1.2 NX</div> </div> </div>
	<div>Retrievalⁱ</div> <div>Antibody dilution</div> <div>Literature conformityⁱ</div> <div>RNA consistencyⁱ</div>	<div>Retrievalⁱ</div> <div>Antibody dilution</div> <div>Literature conformityⁱ</div> <div>RNA consistencyⁱ</div>
WESTERN BLOT ⁱ		
Validation ⁱ	<div> <div>Uncertainⁱ</div> <div>Only bands not corresponding to the predicted size. Analysis performed using a standard panel of samples.</div> <div>Antibody dilution: 1:500</div> </div>	<div> <div>Supportedⁱ</div> <div>Band of predicted size in kDa (+/-20%) with additional bands present. Analysis performed using a standard panel of samples.</div>  <div>Antibody dilution: 1:500</div> </div>
RELEVANT PUBLICATIONS		
<div> <div>Gene expression profiling of metaplastic lineages identifies CDH17 as a prognostic marker in early stage gastric cancer</div> <div>Lee HJ et al</div> <div>Gastroenterology 2010;139(1):213-25.e3</div> <div>Variance decomposition of protein profiles from antibody arrays using a longitudinal twin model</div> <div>Kato BS et al</div> <div>Proteome Sci 2011;9:73</div> </div>		



Hematopoietic Stem Cell










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				Committed DC progenitor		
Surface marker	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.
CADM1	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.
XCR1	–	–	–	–	+	–	–

^aCD3, CD19, CD20, CD56, CD66abce.

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

<https://www.frontiersin.org/articles/10.3389/fimmu.2017.00499/full>

GENERAL INFORMATION¹

Gene name ¹	ACE2
Gene description	Angiotensin I converting enzyme 2
Predicted location ¹	Membrane, Secreted

HUMAN PROTEIN ATLAS INFORMATION

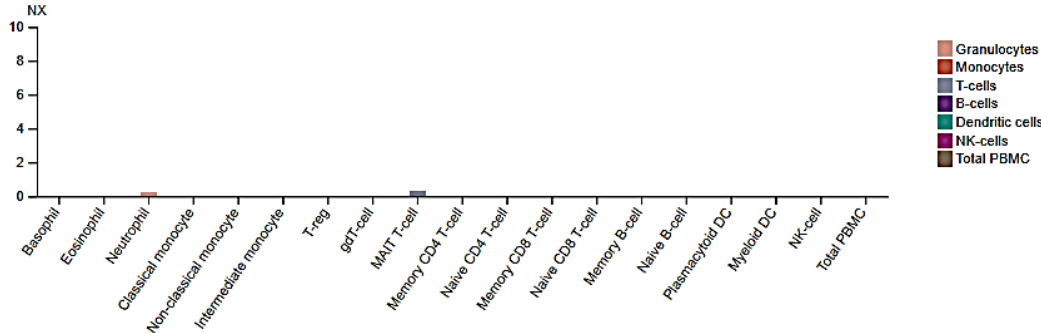
Secretome annotation ⁱ	Secreted to blood
Secretome annotation comment	Secreted form from proteolytic cleavage or shedding
RNA blood cell lineage specificity ⁱ	Not detected
RNA blood cell lineage distribution ⁱ	Not detected
RNA blood cell type specificity ⁱ	Not detected
RNA blood cell type distribution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

BLOOD CELL TYPE EXPRESSION (RNA)ⁱ

Consensus datasetⁱ

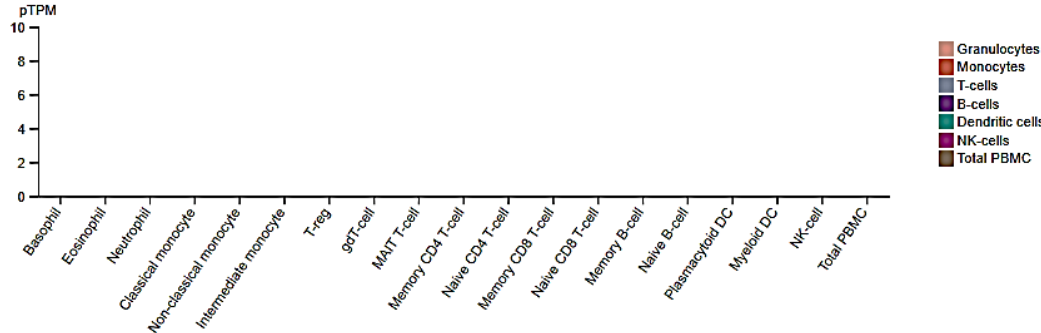
RNA cell type specificity: Not detected

Lineage Expression Alphabetical



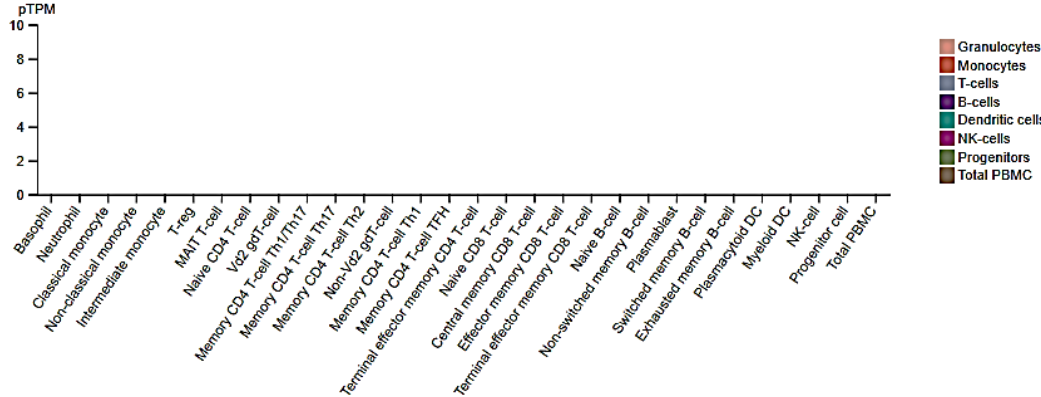
HPA scaled datasetⁱ

Lineage Expression Alphabetical



Monaco scaled datasetⁱ

Lineage Expression Alphabetical



Schmiedel datasetⁱ

Lineage Expression Alphabetical

