

Atlas of ACE2 gene expression in mammals reveals novel insights in transmission of SARS-CoV-2

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Running title: Mammalian ACE2 expression and SARS-CoV-2 susceptibility

Keywords: COVID-19, 2019-nCoV, novel coronavirus, potential host, susceptibility

Abstract

Background: COVID-19 has become a worldwide pandemic. It is caused by a novel coronavirus named SARS-CoV-2 with elusive origin. SARS-CoV-2 infects mammalian cells by binding to ACE2, a transmembrane protein. Therefore, the conservation of ACE2 and its expression pattern across mammalian species, which are yet to be comprehensively investigated, may provide valuable insights into tracing potential hosts of SARS-CoV-2.

Methods: We analyzed gene conservation of ACE2 across mammals and collected more than 140 transcriptome datasets from human and common mammalian species, including presumed hosts of SARS-CoV-2 and other animals in close contact with humans. In order to enable comparisons across species and tissues, we used a unified pipeline to quantify and normalize ACE2 expression levels.

Results: We first found high conservation of ACE2 genes among common mammals at both DNA and peptide levels, suggesting that a broad range of mammalian species can potentially be the hosts of SARS-CoV-2. Next, we showed that high level of ACE2 expression in certain human tissues is consistent with clinical symptoms of COVID-19 patients. Furthermore, we observed that ACE2 expressed in a species-specific manner in the mammals examined. Notably, high expression in skin and eyes in cat and dog suggested that these animals may play roles in transmitting SARS-CoV-2 to humans.

Conclusions: Through building the first atlas of ACE2 expression in pets and livestock, we identified species and tissues susceptible to SARS-CoV-2 infection, yielding novel insights into the viral transmission.

Introduction

In December 2019, outbreak of a novel coronavirus disease (COVID-19), a severe respiratory disease, and since spread rapidly throughout the country. A worldwide pandemic soon followed, with over 600,000 COVID-19 cases reported across 190 countries and territories by end of March 2020 and the number continues to rise sharply. After taking strong quarantine measures and national-wide lockdowns, the number of confirmed diagnoses is rapidly declining in China since February 2020. However, the endemic epicenter had since shifted to Italy and later to the United States. COVID-19 is becoming a global challenge to public health and continues to gather close attention.

The culprit of this pandemic is a new coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)¹, which belongs to the same beta coronavirus family as SARS-CoV and MERS-CoV, the other two viruses that caused outbreaks in the past two decades². Among myriad biological questions to be answered regarding SARS-CoV-2, one that is crucial and has intrigued much interest is the host origin and its mode of transmission to humans. SARS-CoV-2 and SARS-CoV are closely related, and both invade human cells via attaching their S proteins to a host transmembrane protein called angiotensin converting enzyme 2 (ACE2) as the entry point³. Using transcriptome data, some studies analyzed spatial expression patterns of ACE2 in various tissues and cell types of the human body, and reported that the receptor gene is indeed expressed in the lungs⁴⁻⁶. The connections between ACE2 expression and viral infection are further supported by cases from the United States, which confirmed for the first time the presence of SARS-CoV-2 in both the upper respiratory tract and stool

sample of COVID-19 patients⁷.

Some studies have suggested that the original host of SARS-CoV-2 may be bats². However, in the case of COVID-19, the outbreak occurred in winter when bats were under hibernation, making them unlikely to be the direct source of human infection. Hence, SARS-CoV-2 was likely transmitted to humans through some small carnivores like civet, the intermediate host of SARS-CoV. Recent studies have pointed to pangolins as the natural host of the virus, while minks being the possible intermediate host⁸⁻¹⁰. Virus tracing has thus been continuously carried out and attracted much attention. The mystery remains as which wild animals are definitive and intermediate hosts of the new coronavirus, and virus tracing has been continuously carried out and attracted much attention. Furthermore, is it possible that some of the animals living in close proximity to humans may also be susceptible to the virus and could potentially become additional hosts to SARS-CoV-2 hence further facilitating its transmission?

In attempt to address these questions, in this study we focused on the ACE2 gene, the host receptor of SARS-CoV-2 and other coronaviruses, and used quantitative data from various mammalian species to infer their susceptibility to SARS-CoV-2 infection. Since SARS-CoV-2 invade both bat and human cells via ACE2, we reasoned that if animals have ACE2 proteins similar to human, they could also become the targets of SARS-CoV-2, we thus evaluated the conservation of ACE2 gene across mammals. We further investigated ACE2 expression in various tissues among human and common mammals. In particular, we included species that live in close proximity with humans, i.e., pets and livestock. Our analyses identified potential species susceptible to SARS-

CoV-2 and yielded novel insights into virus tracing and transmission, which may further contribute to the prevention and control of the COVID-19 pandemic.

Methods

Reference genomes and gene annotations

A total of 12 mammalian species were investigated in this study: *Homo sapiens* (human), *Mus musculus* (mouse), *Rhinolophus sinicus* (Chinese rufous horseshoe bat), *Manis javanica* (pangolin), *Felis catus* (cat), *Canis lupus familiaris* (dog), *Mustela putorius furo* (ferret), *Mesocricetus auratus* (hamster), *Bos taurus* (cow), *Sus scrofa* (pig), *Oryctolagus cuniculus* (rabbit), and *Capra hircus* (goat). Among these mammals, bats and pangolins are presumed candidates of definitive and intermediate hosts of SARS-CoV-2, respectively^{2,11}; cats, dogs, ferrets and hamsters are common pets; cows, pigs, rabbits and goats are common livestock. Latest versions of reference genomes and RefSeq gene annotations¹² for these species were downloaded from NCBI (National Center for Biotechnology Information)¹³. Detailed information was described in Table S1 in Supplementary data.

Transcriptome data collection

Transcriptome data for various mammalian tissues generated from 142 RNA-seq experiments (whole transcriptome shotgun sequencing) was collected from publicly available sources. Briefly, human data was from the GTEx (Genotype-Tissue Expression) project¹⁴, ENCODE (ENCyclopedia Of DNA Elements) project¹⁵, and

Frausto et al.¹⁶; bat data was from Dong et al.¹⁷; pangolin data was from Ma et al.¹⁸ and Mohamed Yusoff et al.¹⁹; cat data was from 99 Lives Cat Genome Sequencing Initiative project; dog data was from Hoepfner et al.²⁰, Lindblad-Toh et al.²¹ and Sudharsan et al.²²; ferret and rabbit data was from Chen et al.²³; hamster and goat data was from Fushan et al.²⁴; cow data was from Merkin et al.²⁵; and pig data was from Summers et al.²⁶. Detailed information on accession numbers and tissues for each species was listed in Table S2 in Supplementary data.

Transcriptome data analysis

All the transcriptome data was analyzed using a unified pipeline. Briefly, raw RNA-seq reads were first preprocessed to trim sequencing adapters and low-quality cycles using Ktrim software²⁷ with default parameters; the preprocessed reads were then aligned to corresponding reference genomes using STAR software²⁸ with default parameters. Key statistics during preprocessing and alignment was present in Table S2 in Supplementary data. The vast majority (141/142) of the samples had more than 10 million uniquely mapped reads (median: 27.8 million), indicating sufficient sequencing depths for reliable gene expression quantifications²⁹, which was performed using featureCounts³⁰ software with default parameters against RefSeq gene annotations¹². Considering that the reference genomes and gene annotations for most of the species included in this study are far from complete, in order to avoid potential biases of the conventional FPKM (Fragments per Kilobase Million) values, we used ACTB (Actin Beta) gene from each RNA-seq experiment to normalize ACE2 expression for

appropriate comparisons across species and tissue types. ACTB is a housekeeping gene that is abundantly and stably expressed in most cell types, and is commonly used as an internal control for gene expression normalizations³¹. In addition, ACTB gene is also conserved in all the species investigated in this study. The following formula was used to calculate normalized ACE2 expression:

$$ACE2 \text{ expression} = \frac{\text{No. of reads mapped to ACE2} / \text{length of ACE2}}{\text{No. of reads mapped to ACTB} / \text{length of ACTB}} \times 10000$$

We used 10000 as a scale factor here because ACE2 was typically expressed at much lower levels than ACTB. Meanwhile, since data from the GTEx project was provided as preprocessed values, these GTEx values were used directly in the above formula in lieu of number of mapped reads and gene length.

Results

Conservation of ACE2 gene in mammals

We first examined the conservation of ACE2 across mammalian species. A snapshot obtained from the UCSC genome browser³² was shown in Figure 1A, which demonstrated high conservation of ACE2 gene's exons in DNA level. Next we examined the conservation of ACE2 at the peptide level by searching the UniProt database³³ for ACE2 protein sequences in mammals. We limited the analysis to species listed in Methods (plus rats) and discarded duplicate records as well as records with abnormally short sequences (< 300 amino acids), leaving 24 ACE2 protein sequences

for subsequent analyses. Pairwise alignment results showed that 23 non-human ACE2 proteins share high level of similarity to the human ACE2 protein, with the identity scores ranging from 78.6% to 85.2% and a median score of 81.9%. Notably, for the two virus-binding hotspots (i.e., the 31th and 353th amino acid)³⁴, all the mammals except mice and rats share the same amino acids to the human ACE2 protein (Table S3 in Supplementary data). Surprisingly, in contrast to conventional phylogenetic tree generated using genomic data, the phylogenetic tree based on the ACE2 proteins showed that, cats and dogs were the species closest to human instead of mice among the mammals included in this analysis (Figure 1B). Taken together, the conservation analysis showed that ACE2 gene was highly conserved among common mammals at both DNA and peptide levels, suggesting that SARS-CoV-2 can potentially bind to ACE2 proteins in these mammals with high affinity².

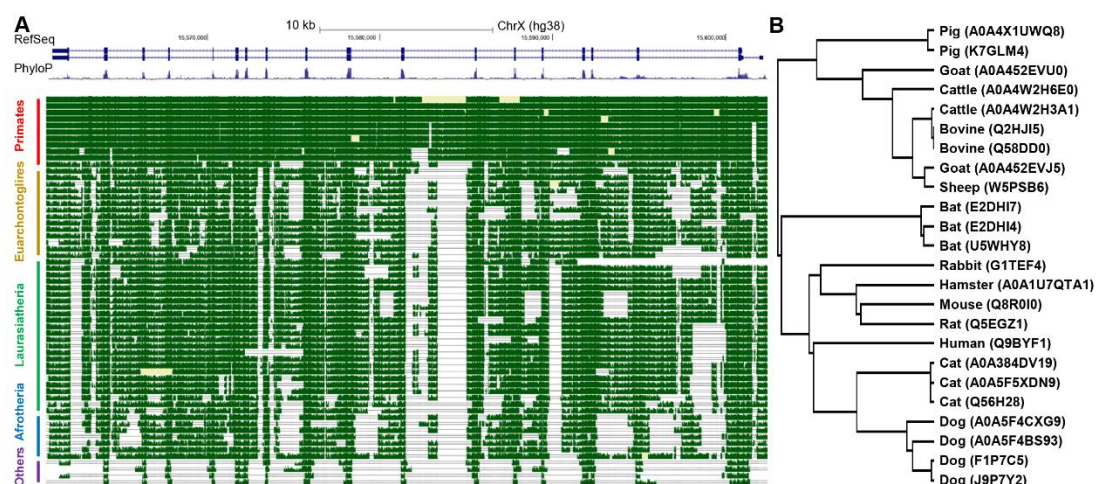
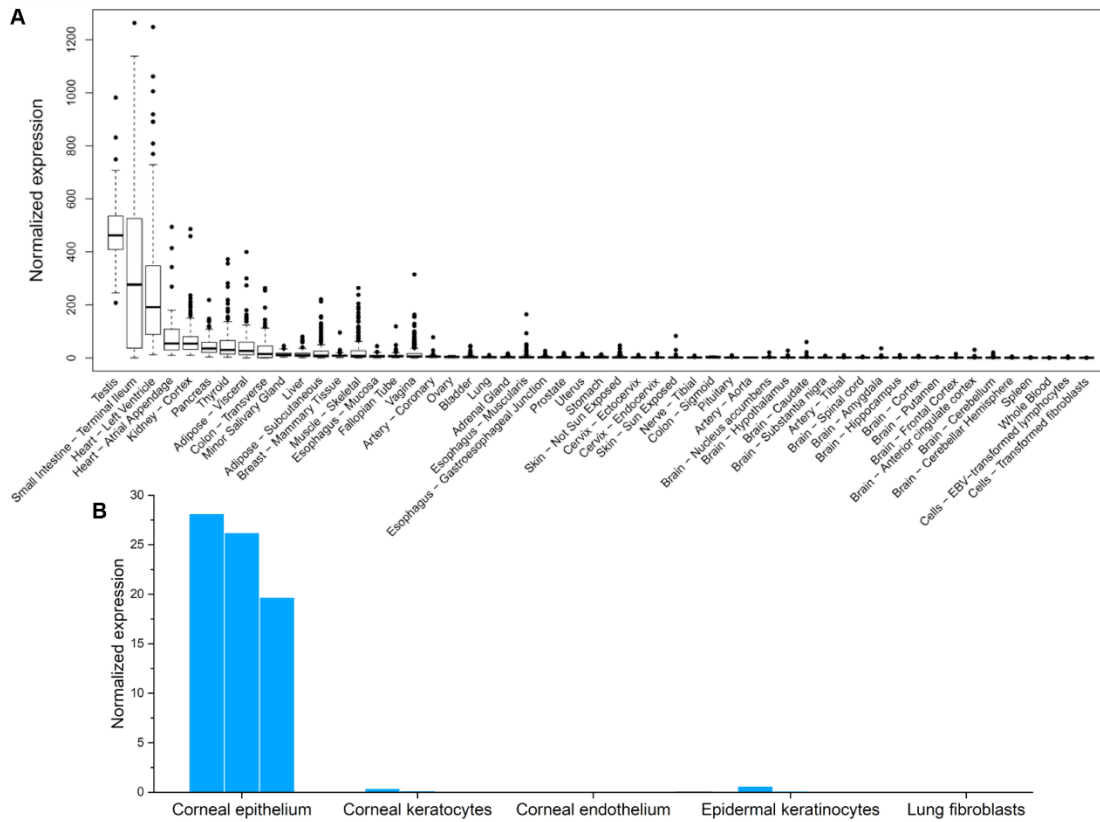


Figure 1. Conservation analysis of ACE2 gene. (A) Snapshot from the UCSC genome browser showing the DNA level conservation of ACE2 gene. Note that horse was removed due to lack of pair-wise alignment data. (B) Phylogenetic tree based on mammal ACE2 protein sequences from UniProt database. The top panel in (A) is RefSeq annotation of ACE2 gene in human (which contains two isoforms), the middle panel is conservation scores among 100 vertebrates, higher values denote higher levels of conservation), and the best-in-genome pairwise alignments among 42 mammals are plotted in the bottom panel. For (B), the protein accession number in UniProt were shown in parentheses and some species has multiple records.

Expression profile of ACE2 gene in human tissues

We then profiled the expression patterns of ACE2 gene in human tissues. Data from the GTEx project showed that ACE2 was expressed in various tissues, including testis, intestines, heart, kidney, and pancreas (Figure 2A). It was worth noting that our normalized ACE2 expression pattern was similar to the original version obtained from the GTEx portal (Figure S1 in Supplementary data), except that our analysis highlighted the heart as the tissue with 3rd highest ACE2 expression.

We also collected transcriptome data from tissues that were not in the GTEx datasets, including cornea, epidermal keratinocytes, and lung fibroblasts. These tissues are frequently exposed to the air. ACE2 gene was expressed in corneal epithelial cells (Figure 2B), suggesting that the eye could be vulnerable to SARS-CoV-2 infections. In contrast, ACE2 was not expressed in epidermal keratinocytes nor lung fibroblasts, which was consistent with the above analysis based on GTEx data. This result was also consistent with a previous report based on single-cell RNA-seq data that ACE2 was only expressed in the alveolar type 2 (AT2) cells in lungs³⁵.



Expression pattern of ACE2 gene in mice

Mouse is the most widely used model species in biomedical studies, including those related to SARS-CoV-2. We extracted the expression data of murine Ace2 gene from Tabula Muris project³⁶, which investigated various murine tissues using single-cell RNA-seq experiments. Murine Ace2 gene was expressed in kidney, heart, intestine, and pancreas (Figures 3 and S1 in Supplementary data), a pattern similar to human (Figure 2A). However, murine Ace2 gene was not expressed in any cell types in lungs, while expressed in tongue and skin (Figure 3B). The data also suggested that ACE2 gene expression pattern could be species-specific among mammals. In particular, lung-related symptoms may not be expected when infecting SARS-CoV-2 to normal mice.

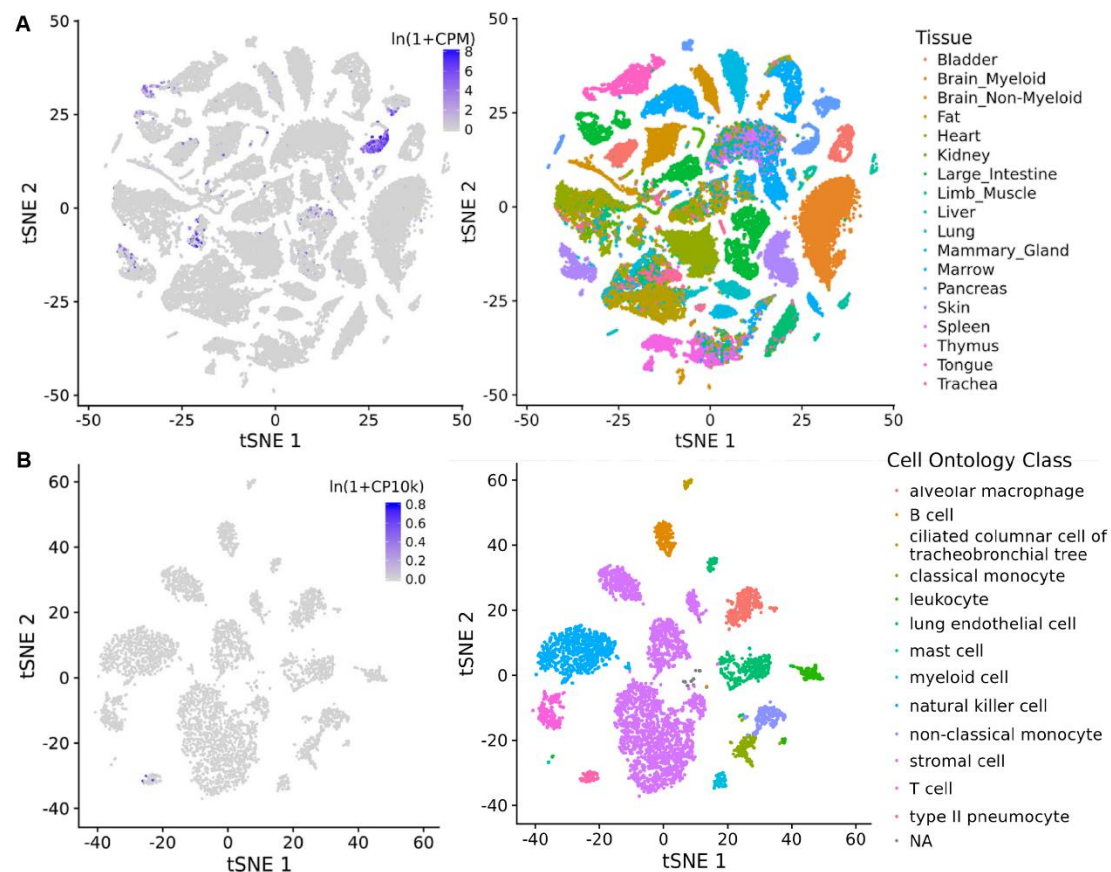


Figure 3. Expression of ACE2 in murine tissues. Data was obtained from the Tabula Muris project. (A) Expression in all cells isolated using FACS protocol (left) and corresponding tissue origin of these cells (right). Note that the cells were clustered using t-SNE (t-distributed Stochastic Neighbor Embedding) algorithm based on their transcriptome. (B) Expression in lung tissue.

Expression patterns of ACE2 gene in other mammals

Bats and pangolins are hypothesized to be the definitive and intermediate hosts of SARS-Cov-2². We profiled the expression of ACE2 in various tissues in Chinese rufous horseshoe bats and Malayan pangolins. ACE2 gene was highly expressed in most tissues examined in both bats and in pangolin, including those frequently exposed to the air, e.g., lungs in bats and tongue in pangolins (Figure 4).

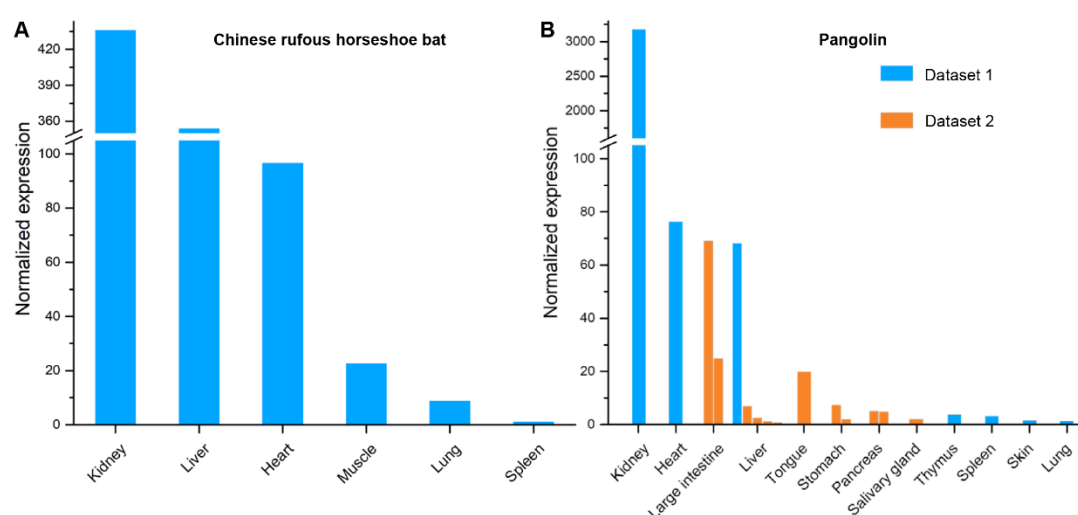


Figure 4. Expression of ACE2 gene in (A) bat and (B) pangolin tissues. Two datasets for pangolin tissues were collected and labelled with different colors. Replicate experiments for some tissues were available and were shown as multiple bars.

Pets are the most intimate animals to humans and may thus very likely to be contracted by human COVID-19 patients or to transmit the virus to humans if they are infected. We examined ACE2 expression patterns in cats and dogs, the most popular pets worldwide, as well as ferrets and hamsters, which are also very common in China. ACE2 gene was highly expressed in various tissues in these animals, such as kidney, heart and liver (Figures 5A-5C and S2A in Supplementary data). For cats, ACE2 was also highly expressed in skin, ear tip, lungs, and retina; for dogs, ACE2 was expressed in skin and retina. This data suggested that cats and dogs may be highly susceptible to SARS-CoV-2 infection. In addition, we also observed ACE2 expression in the lungs of cats and ferrets, which suggested that these animals may be more suitable for SARS-CoV-2 studies than rodent models^{2,37}.

Besides pets, livestock are another category of mammals that are frequently in direct contact with humans. We profiled the ACE2 expression in cows, pigs, rabbits (which can also serve as pets), and goats. In these animals, ACE2 was highly expressed in multiple tissues including kidney, liver, and heart, but not in muscles (Figures 5D-5F and S2B in Supplementary data). ACE2 was also highly expressed in the fat of pigs. The data suggested that storage of fresh or undercooked meat, especially viscera tissues, might be risky.

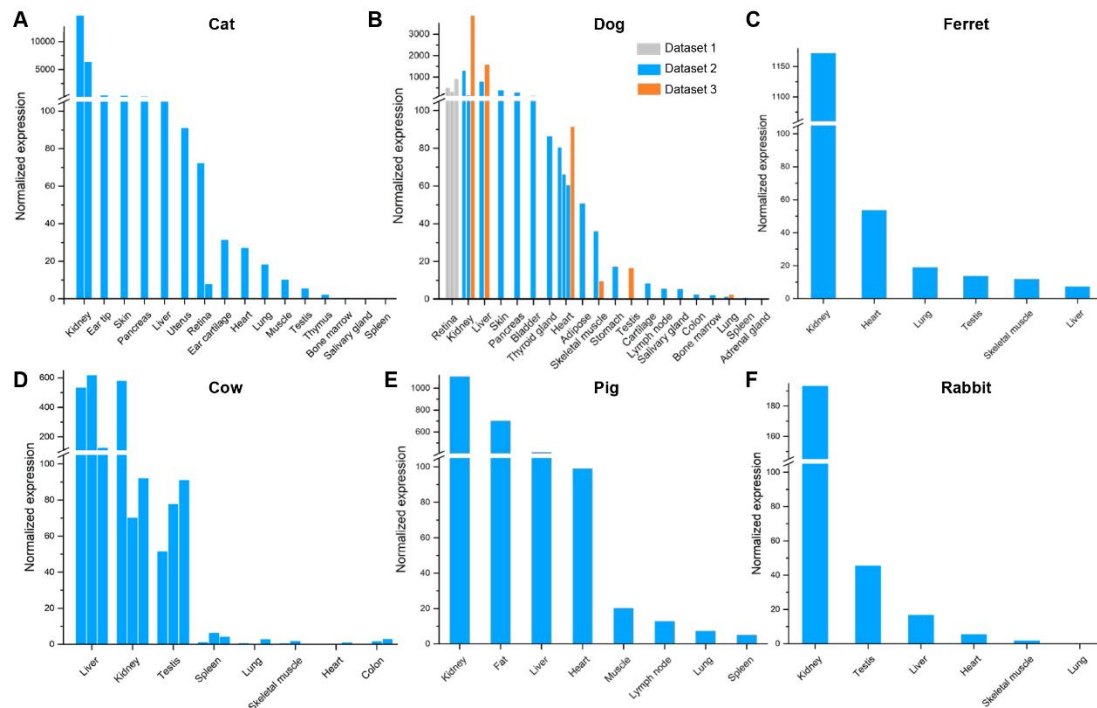


Figure 5. Expression of ACE2 in (A) cat, (B) dog, (C) ferret, (D) pig, (E) cow and (F) rabbit tissues. Three datasets for dog tissues were collected and labelled with different colors. Replicate experiments for some tissues were available and were shown as multiple bars.

Discussion

We showed that ACE2 expression profile in human tissues was in agreement with clinical observations of SARS-CoV-2 infected individuals. For example, ACE2 was by far most strongly expressed in testis. SARS is known to cause orchitis and destruction to male germ cells³⁸. Similar effect from COVID-19 was speculated, but a most recent study had just provided the first direct evidence that SARS-CoV-2 infection impacts male sex hormones³⁹. Similarly, small intestine is the tissue with the second highest level of ACE2 expression, while SARS-CoV-2 was found in stool samples of COVID-19 patients both in China and the United States^{7,42}, even after the viral RNA decreased to undetectable level in respiratory tract⁴³. Additionally, we found in our normalized dataset that heart tissues also had the third highest level of ACE2 expression. This observation is also in line with reports showing that COVID-19 patients complicated with cardiac diseases are subject to the highest mortality risk^{40,41}. Together, the consistence between our results and clinical observations demonstrated that ACE2 expression is a reasonable indicator for susceptibility to SARS-CoV-2 infection.

Our analyses showed that mammalian ACE2 genes are highly conserved across lineages and exhibit broad expression patterns. However, tissue-specific expression profiles varied from species to species, suggesting certain mammals may be the hosts of SARS-CoV-2, i.e., carriers without significant symptoms. Compared to humans, other mammals examined in this study either don't express ACE2 in their testes, or at a low level. On the contrary, among non-human species kidney was almost always the tissue with highest ACE2 expression. Meanwhile, it is worth noting that mouse is a

common model species for many human medical studies, including COVID-19. However, we showed that in ACE2 proteins, mice and rats are the only mammals that have different amino acids in the two virus-binding hotspots from humans, which is consistent with previous *in vitro* virus infection experiments². Moreover, ACE2 was barely expressed in any of the cell types in murine lungs. Thus, both observations argue against using mice as the optimal animal model for studying coronavirus related diseases.

Most notably, our analyses revealed that ACE2 expression levels are particularly high in cats and dogs. Especially in cats, expression levels in top four ACE2 expression hotspot tissues are all magnitudes higher than any other mammals examined. Intriguingly, in the ACE2 phylogenetic tree, both cats and dogs are also cluster closer to humans than other mammals (Figure 1B), suggesting potentially higher affinity to coronaviruses in these pets. SARS-CoV is known to infect cats⁴⁴, while SARS-CoV-2 positive cats and dogs had also been reported^{45,46}, therefore our analyses suggest high possibility that cats and dogs can host SARS-CoV-2. Furthermore, in both cats and dogs, skin had high abundant ACE2 expression, so did ear tip in cats and retina in dogs. High ACE2 expression levels in these exterior body parts makes them particularly likely to host SARS-CoV-2 and pass on to humans via skin to skin contact. Stray animals can even be more serious transmitters of coronaviruses. It is estimated that there are approximately 500 million stray dogs and similar number of stray cats worldwide⁴⁷. Cats and dogs are sometimes slaughtered for meat, including a large proportion of stray ones⁴⁸. Therefore, it is likely that cats and dogs may have contributed to the COVID-

19 pandemic. For the least, people should also be vigilant with handling of pets in the effort of containing the spread of SARS-CoV-2.

In conclusion, in this study, we had reported the high conservation and built the first expression atlas of ACE2 gene in common mammals. Our analyses revealed species and tissues susceptible to SARS-CoV-2 infection, thus yielding novel insights in tracing the origin and transmission of the virus.

Acknowledgements

This work has been supported by Shenzhen Bay Laboratory and Beijing Huayuan Academy of Biotechnology.

Conflict of interest: none declared.

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Supplementary materials

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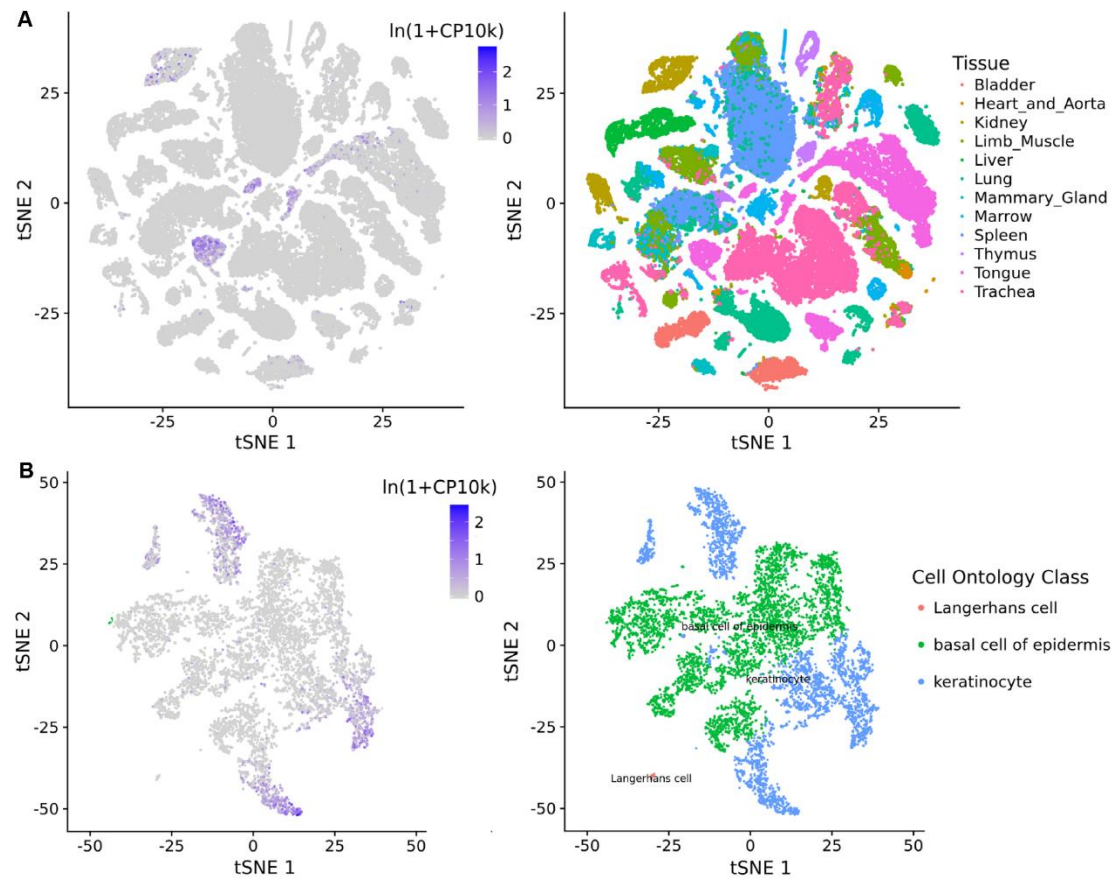


Figure S2. Expression of ACE2 in murine tissues. The data was obtained from Tabula Muris project. (A) All tissues. (B) Tongue.

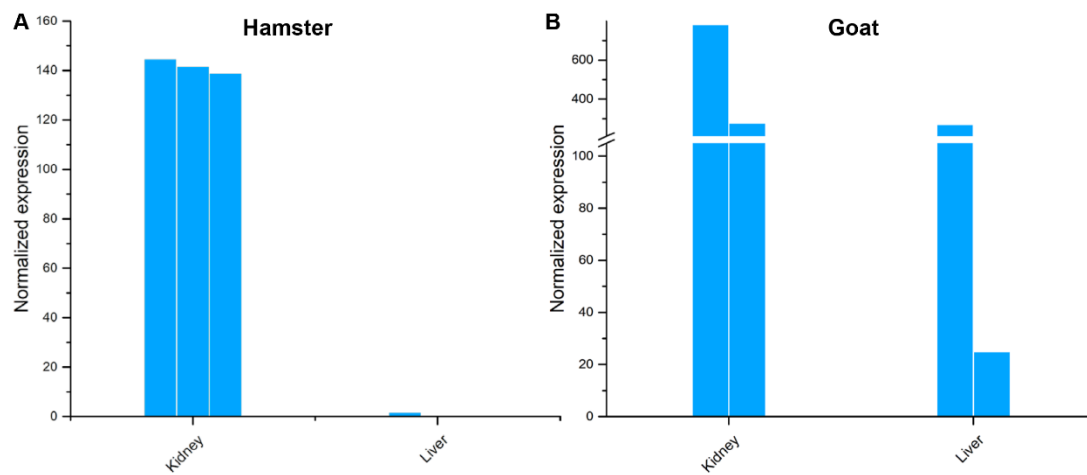


Figure S3. Expression of ACE2 in (A) hamster and (B) goat tissues.

Table S1. Reference genomes and gene annotation used in this study.

Species	Common name	Assembly name	Assembly accession	Annotation release ID
<i>Homo sapiens</i>	Human	GRCh38.p13	GCF_000001405.39	109
<i>Rhinolophus sinicus</i>	Bat	ASM188883v1	GCF_001888835.1	100
<i>Manis javanica</i>	Manis	ManJav1.0	GCF_001685135.1	100
<i>Felis catus</i>	Cat	Felis_catus_9.0	GCF_000181335.3	104
<i>Canis lupus familiaris</i>	Dog	CanFam3.1	GCF_000002285.3	105
<i>Mustela putorius furo</i>	Ferret	MusPutFur1.0	GCF_000215625.1	101
<i>Mesocricetus auratus</i>	Hamster	MesAur1.0	GCF_000349665.1	102
<i>Bos taurus</i>	Cow	ARS-UCD1.2	GCF_002263795.1	106
<i>Sus scrofa</i>	Pig	Sscrofa11.1	GCF_000003025.6	106
<i>Oryctolagus cuniculus</i>	Rabbit	OryCun2.0	GCF_000003625.3	102
<i>Capra hircus</i>	Goat	ARS1	GCF_001704415.1	102

Table S2. Accession and statistics of the transcriptome data compiled in this study.

Species	Data source	Sample ID	Tissue information	Total reads	Ktrim preprocessed	STAR aligned	Mappability(%)
Homo sapiens	ENCODE	NHEK.rep1	Epidermal	68,932,471	42,944,842	36,715,777	81.9
		NHEK.rep2	Epidermal	68,995,645	60,849,039	58,067,559	89.2
		NHLF.rep1	Lung fibroblasts	67,321,664	59,671,441	56,028,139	88.5
		NHLF.rep2	Lung fibroblasts	67,164,915	55,872,307	50,225,300	89.0
	GSE121922	SRR8129827	Corneal epithelium	21,384,188	21,063,173	17,912,697	85.0
		SRR8129828	Corneal epithelium	20,913,971	20,625,789	17,502,545	84.9
		SRR8129829	Corneal epithelium	19,466,412	19,187,323	16,184,315	84.4
		SRR8129830	Corneal keratocytes	21,730,275	21,495,198	18,156,122	84.5
		SRR8129831	Corneal keratocytes	18,799,079	18,527,115	15,575,797	84.1
		SRR8129832	Corneal keratocytes	18,996,222	18,718,811	15,701,517	83.9
		SRR8129833	Corneal endothelium	13,389,782	13,138,066	10,564,327	80.4
		SRR8129834	Corneal endothelium	12,285,592	12,019,769	9,653,549	80.3
		SRR8129835	Corneal endothelium	13,928,169	13,644,250	10,959,195	80.3
Rhinolophus sinicus	SRP063381	SRR2273931	Kidney	30,337,622	29,795,046	26,698,695	89.6
		SRR2273875	Liver	30,559,494	30,057,890	27,893,166	92.8
		SRR2273739	Heart	27,788,814	27,274,122	22,964,399	84.2
		SRR2273816	Muscle	32,875,990	32,299,770	25,715,822	79.6
		SRR2273738	Brain	33,101,848	32,507,454	30,637,988	94.3
		SRR2273740	Lung	34,488,781	33,837,363	32,558,189	96.2
		SRR2273762	Spleen	22,008,969	20,889,127	11,166,880	53.5
Manis javanica	SRP156258	SRR7641079	Pancreas	24,856,498	24,856,472	20,906,101	84.1
		SRR7641080	Liver	21,967,580	21,967,553	18,689,870	85.1
		SRR7641081	Liver	23,980,609	23,980,571	19,980,166	83.3
		SRR7641082	Pancreas	24,376,771	24,376,734	20,839,958	85.5
		SRR7641083	Tongue	28,411,058	28,411,029	24,114,077	84.9
		SRR7641084	Salivary glands	22,444,882	22,444,842	19,046,428	84.9
		SRR7641085	Stomach	22,856,344	22,856,313	19,682,763	86.1
		SRR7641086	Stomach	25,508,428	25,508,397	21,964,813	86.1
		SRR7641087	Liver	25,805,479	25,805,442	21,541,960	83.5
		SRR7641088	Liver	28,768,081	28,768,050	24,409,509	84.9
	SRP064341	SRR7641089	Large Intestine	29,573,813	29,573,794	25,137,147	85.0
		SRR7641090	Large Intestine	20,449,264	20,449,253	18,203,703	89.0
		SRR3923846	Skin	24,805,754	24,493,823	21,702,376	88.6
		SRR2561214	Lungs	45,883,537	45,883,536	43,005,271	93.7
		SRR2561215	Spleen	52,632,086	52,632,086	49,422,337	93.9
		SRR2561213	Liver	45,306,423	45,306,423	42,722,562	94.3
		SRR2561216	Thymus	41,532,741	41,532,741	39,554,501	95.2
		SRR2561212	Kidney	42,419,462	42,419,462	40,640,322	95.8
		SRR2561211	Heart	47,079,243	47,079,243	45,497,321	96.6
Felis catus	SRP071078	SRR3200449	Lung	61,604,161	59,373,190	52,323,679	88.1
		SRR3200451	Muscle	53,498,415	51,628,230	44,553,838	86.3
		SRR3200453	Liver	66,486,821	64,279,254	54,290,629	84.5
		SRR3200454	Ear Tip	61,849,569	59,863,742	49,458,043	82.6
		SRR3200455	Ear cartilage	74,477,894	72,375,687	67,892,280	93.8

		SRR3200457	Retina	54,310,271	52,850,253	46,389,760	87.8
		SRR3200458	Uterus	51,634,724	48,975,318	40,155,738	82.0
		SRR3200459	Bone marrow	36,096,745	33,351,045	24,701,766	74.1
		SRR3200460	Kidney	60,295,175	58,082,781	43,644,190	75.1
		SRR3200462	Testes	80,274,030	77,645,779	70,923,239	91.3
		SRR3200465	Retina	58,621,360	57,043,848	51,114,268	89.6
		SRR3200469	Pancreas	83,078,528	80,123,579	74,509,518	93.0
		SRR3200470	Skin	66,777,859	64,602,457	55,718,935	86.3
		SRR3200471	Heart	107,724,558	104,532,937	67,788,907	64.9
		SRR3200473	Kidney	47,219,252	45,690,466	34,964,638	76.5
		SRR3218714	Spleen	60,725,845	58,500,972	49,693,589	84.9
		SRR3218715	Thymus	52,195,042	49,203,820	41,479,120	84.3
		SRR3218716	Spleen	42,845,814	41,577,135	34,374,919	82.7
		SRR3218717	Salivary gland	56,827,581	54,141,092	45,207,119	83.5
Canis lupus familiaris	GSE97638	SRR5443379	Neural retina	18,158,136	18,138,066	17,449,363	96.2
		SRR5443380	Neural retina	25,489,581	25,465,359	24,490,231	96.2
		SRR5443381	Neural retina	12,003,881	11,992,690	11,535,499	96.2
	SRP114662	SRR8996983	Adipose	45,152,409	43,618,974	40,633,451	93.2
		SRR8996995	Adrenal gland	55,999,077	54,435,675	42,867,568	78.8
		SRR8996996	Bladder	25,629,091	24,710,475	23,381,661	94.6
		SRR8996993	Bone marrow	72,272,259	69,830,421	59,939,651	85.8
		SRR8996994	Cartilage	53,915,899	52,097,984	49,142,410	94.3
		SRR8997000	Colon	44,721,489	43,036,543	40,558,438	94.2
		SRR8997001	Kidney (cortex)	57,787,581	56,189,631	51,652,382	91.9
		SRR8997002	Kidney (medulla)	44,087,155	42,677,016	39,643,305	92.9
		SRR8996964	Heart (left atrium)	46,569,235	45,213,751	42,470,278	93.9
		SRR8996963	Heart (left ventricle)	45,991,318	44,449,475	42,594,327	95.8
		SRR8996969	Heart (right ventricle)	46,648,476	45,117,648	42,915,864	95.1
		SRR8996966	Liver	51,692,060	49,953,096	46,598,407	93.3
		SRR8996965	Lung	46,168,334	44,590,607	40,816,349	91.5
		SRR8996968	Lymph node	62,480,995	60,629,005	51,758,660	85.4
		SRR8996967	Pancreas	55,283,372	53,379,088	46,388,546	86.9
		SRR8996972	Salivary gland	43,256,190	41,697,927	36,926,974	88.6
		SRR8996971	Skeletal muscle	45,631,797	44,233,179	41,948,357	94.8
		SRR8997043	Skin	43,200,562	41,534,641	38,317,594	92.3
		SRR8997044	Spleen	26,950,137	26,050,311	21,795,307	83.7
		SRR8997045	Stomach	55,518,261	53,647,070	50,276,470	93.7
		SRR8997046	Thyroid gland	48,423,432	46,874,668	43,968,733	93.8
	GSE97638	SRR6206901	Heart	31,934,896	28,297,899	25,005,163	88.4
		SRR6206906	Kidney	35,927,711	31,403,005	27,697,606	88.2
		SRR6206911	Liver	33,858,041	30,213,606	23,632,522	78.2
		SRR6206916	Lung	29,502,542	25,638,471	21,877,766	85.3
		SRR6206921	Skeletal Muscle	32,712,735	28,511,422	24,698,601	86.6
		SRR6206926	Testis	35,435,315	30,667,393	26,339,541	85.9
Mustela putorius furo	GSE106077	SRR6206902	Heart	29,394,130	27,861,205	26,291,047	94.4
		SRR6206907	Kidney	27,472,302	25,711,807	24,206,747	94.2
		SRR6206912	Liver	27,454,811	25,996,290	24,282,703	93.4
		SRR6206917	Lung	26,849,508	25,065,001	23,473,250	93.7
		SRR6206922	Skeletal muscle	30,505,719	28,822,176	27,180,993	94.3

		SRR6206927	Testis	27,024,467	25,551,148	23,846,337	93.3
Mesocricetus auratus	GSE43013	SRR636857	Liver	22,166,056	21,444,610	19,015,456	88.7
		SRR636858	Liver	15,859,602	15,549,003	13,966,154	89.8
		SRR636859	Liver	19,789,823	19,142,756	16,996,355	88.8
		SRR636907	Kidney	21,084,573	20,327,600	18,417,620	90.6
		SRR636908	Kidney	22,131,879	21,703,453	19,566,391	90.2
		SRR636909	Kidney	16,437,102	16,098,938	14,838,431	92.2
Bos taurus	GSE41637	SRR594474	Colon	119,761,742	108,567,519	100,493,689	92.6
		SRR594475	Heart	117,554,231	102,808,834	99,087,699	96.4
		SRR594476	Kidney	115,720,336	107,048,435	102,311,713	95.6
		SRR594477	Liver	103,019,718	96,471,480	91,471,456	94.8
		SRR594478	Lung	103,196,444	94,356,596	89,631,315	95.0
		SRR594479	Skeletal muscle	113,227,169	100,258,839	95,034,372	94.8
		SRR594480	Spleen	116,884,523	106,487,738	98,708,719	92.7
		SRR594481	Testes	107,483,976	98,479,248	94,432,393	95.9
		SRR594483	Colon	32,336,017	26,359,467	23,192,961	88.0
		SRR594484	Heart	21,185,451	19,043,822	17,832,960	93.6
		SRR594485	Kidney	27,567,792	23,849,700	22,038,194	92.4
		SRR594486	Liver	26,021,524	22,615,391	20,906,823	92.5
		SRR594487	Lung	22,498,703	19,783,813	18,090,439	91.4
		SRR594488	Skeletal muscle	27,439,293	23,672,541	21,740,316	91.8
		SRR594489	Spleen	24,283,167	20,956,751	18,126,163	86.5
		SRR594490	Testes	38,368,885	28,286,737	25,950,324	91.7
		SRR594492	Colon	23,173,287	20,517,583	18,384,896	89.6
		SRR594493	Heart	37,897,106	29,975,705	28,038,599	93.5
		SRR594494	Kidney	22,535,945	19,780,690	18,307,870	92.6
		SRR594495	Liver	29,192,793	25,348,304	23,247,486	91.7
		SRR594496	Lung	35,817,736	28,434,425	26,123,049	91.9
		SRR594497	Skeletal muscle	24,842,489	21,711,317	20,211,951	93.1
		SRR594498	Spleen	31,925,721	25,398,752	21,828,414	85.9
		SRR594499	Testes	25,780,071	19,749,083	18,213,999	92.2
Sus scrofa	ERP009821	ERR789443	Fat	47,223,701	46,255,200	40,704,383	88.0
		ERR789444	Heart	46,474,210	45,751,115	40,401,277	88.3
		ERR789445	Kidney	47,565,661	46,737,485	41,432,264	88.7
		ERR789446	Liver	52,484,784	51,461,538	44,629,431	86.7
		ERR789447	Lung	42,115,278	41,036,112	33,759,440	82.3
		ERR789448	Lymph node	42,796,446	41,486,945	27,658,393	66.7
		ERR789449	Muscle	48,296,978	47,355,203	41,588,901	87.8
		ERR789450	Spleen	39,615,892	38,445,242	27,518,183	71.6
Oryctolagus cuniculus	GSE106077	SRR6206905	Kidney	59,053,890	50,965,385	44,586,791	87.5
		SRR6206925	Testis	64,474,890	55,281,359	47,267,601	85.5
		SRR6206910	Liver	55,990,721	48,037,240	42,156,774	87.8
		SRR6206900	Heart	55,064,609	47,251,883	40,998,926	86.8
		SRR6206920	Skeletal muscle	52,765,274	45,154,347	38,691,448	85.7
		SRR6206915	Lung	51,028,249	43,500,838	36,326,098	83.5
Capra hircus	GSE43013	SRR636844	Liver	15,873,867	15,539,416	14,327,927	92.2
		SRR636845	Liver	16,454,606	16,090,806	13,168,242	81.8
		SRR636894	Kidney	25,499,168	23,266,061	19,900,921	85.5
		SRR636895	Kidney	36,708,994	31,839,681	26,278,586	82.5

Table S3. Alignment result of mammal ACE2 protein sequences in UniProt.

A0A4X1UWQ8 PIG	MSGSFWLLLSLIPVTAAQSTTEELAKTFLEKFNLEAEDLAYQSSSLASWNYNTNITDENIQ
K7GLM4 PIG	MSGSFWLLLSLIPVTAAQSTTEELAKTFLEKFNLEAEDLAYQSSSLASWNYNTNITDENIQ
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A0A4W2H6E0 BOBOX	MTGSFWLLLSLVAVTAAQSTTEEQAKTFLEKFNHEAEDLSYQSSSLASWNYNTNITDENVQ
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Q2HJI5 BOVIN	MTGSFWLLLSLVAVTAAQSTTEEQAKTFLEKFNHEAEDLSYQSSSLASWNYNTNITDENVQ
ACE2 BOVIN	MTGSFWLLLSLVAVTAAQSTTEEQAKTFLEKFNHEAEDLSYQSSSLASWNYNTNITDENVQ
A0A452EVJ5 CAPHI	MTGSFWLLLSLVAVTAAQSTTEEQAKTFLEKFNHEAEDLSYQSSSLASWNYNTNITDENVQ
W5PSB6 SHEEP	MTGSFWLLLSLVAVTAAQSTTEGQAKTFLEKFNHEAEDLSYQSSSLASWNYNTNITDENVQ
E2DHI7 9CHIR	MSGSFWLLLSLVAVTTAQSTTEDRAKTFLEKFNHEAEDLSYQSSSLASWDYNTNINDENVQ
E2DHI4 9CHIR	MSGSFWLLLSLVAVTTAQSTTEDEAKIFLDKFNKAEEDLSHQSSSLASWDYNTNINDENVQ
U5WHY8 9CHIR	MSGSSWLLLSLVAVTTAQSTTEDEAKMFLDKFNKAEEDLSHQSSSLASWDYNTNINDENVQ
G1TEF4 RABIT	MSGSSWLLLSLVAVTAAQSTIEELAKTFLEKFNQEAEDLSYQSALASWDYNTNITEENVQ
A0A1U7QTA1 MESAU	MSSSSWLLLSLVAVTTAQSIIEEQAKTFLEKFNQEAEDLSYQSALASWNYNTNITEENAO
ACE2 MOUSE	MSSSSWLLLSLVAVTTAQSLTEENAKTFLEKFNQEAEDLSYQSSSLASWNYNTNITEENAO
ACE2 RAT	MSSSCWLLLSLVAVATAQSLIEEKAESFLNKFQEAEDLSYQSSSLASWNYNTNITEENAO
ACE2 HUMAN	MSSSSWLLLSLVAVTAAQSTIEEQAKTFLEKFNHEAEDLFYQSSSLASWNYNTNITEENVQ
A0A384DV19 FELCA	MSGSFWLLLSFAALTAAQSTTEELAKTFLEKFNHEAEELS YQSSSLASWNYNTNITDENVQ
A0A5F5XDN9 FELCA	MSGSFWLLLSFAALTAAQSTTEELAKTFLEKFNHEAEELS YQSSSLASWNYNTNITDENVQ
ACE2 FELCA	MSGSFWLLLSFAALTAAQSTTEELAKTFLEKFNHEAEELS YQSSSLASWNYNTNITDENVQ
A0A5F4CXG9 CANLF	MSGSSWLLLSLAALTAAQS-TEDLVKTFLEKFN YEAEELS YQSSSLASWNYNINITDENVQ
A0A5F4BS93 CANLF	MSGSSWLLLSLAALTAAQS-TEDLVKTFLEKFN YEAEELS YQSSSLASWNYNINITDENVQ
F1P7C5 CANLF	MSGSSWLLLSLAALTAAQS-TEDLVKTFLEKFN YEAEELS YQSSSLASWNYNINITDENVQ
J9P7Y2 CANLF	MSGSSWLLLSLAALTAAQS-TEDLVKTFLEKFN YEAEELS YQSSSLASWNYNINITDENVQ
	*:. * *:***: :::*** * .: **:*** :*: * :*:***: ** **:. ** *
A0A4X1UWQ8 PIG	KMNDAKWSAFYEEQSRIAKTYPLDEIQTLILKRQLQALQQSGTSGLSADKSKRLNTIL
K7GLM4 PIG	KMNDAKWSAFYEEQSRIAKTYPLDEIQTLILKRQLQALQQSGTSGLSADKSKRLNTIL
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A0A4W2H6E0 BOBOX	KMNEARAKWSAFYEEQSRMAKTYSLLEEIQNLTLKRQLKALQHSGTSLSAEKSkrLNTIL
A0A4W2H3A1 BOBOX	KMNEARAKWSAFYEEQSRMAKTYSLLEEIQNLTLKRQLKALQHSGTSLSAEKSkrLNTIL
Q2HJI5 BOVIN	KMNEARAKWSAFYEEQSRMAKTYSLLEEIQNLTLKRQLKALQHSGTSLSAEKSkrLNTIL
ACE2 BOVIN	KMNEARAKWSAFYEEQSRMAKTYSLLEEIQNLTLKRQLKALQHSGTSLSAEKSkrLNTIL
A0A452EVJ5 CAPHI	KMNEARAKWSAFYEEQSRMARTYSLEEIQNLTLKRQLKALQHSGTSLSAEKSkrLNMIL
W5PSB6 SHEEP	KMNEARAKWSAFYEEQSRMARTYSLEEIQNLTLKRQLKALQHSGTSLSAEKSkrLNTIL
E2DHI7 9CHIR	KMDEAGAKWSAFYEEQSKLAKNYPLEQIQNVTVKLQLQLQQSGSPVLSEDKSKRLNSIL
E2DHI4 9CHIR	KMDEAGAKWSAFYEEQSKLAKNYPLEQIQNVTVKLQLQLQLQQSGSPVLSEDKSKRLNSIL
U5WHY8 9CHIR	KMDEAGAKWSAFYEEQSKLAKNYSLEQIQNVTVKLQLQLQLQQSGSPVLSEDKSKRLNSIL
G1TEF4 RABIT	KMNDAEAKWSAFYEEQSKLAKTYPSQEVQNLTVKRQLQALQQSGSSALSADKSKQLNTIL
A0A1U7QTA1 MESAU	KMNEAAKWSAFYEEQSKLAKNYSLEQEVQNLTIKRQLQALQQSGSSALSADKKNKQLNTIL
ACE2 MOUSE	KMSEAAKWSAFYEEQSKTAQSFSLQEIQTPIIKRQLQALQQSGSSALSADKKNKQLNTIL
ACE2 RAT	KMNEAAKWSAFYEEQSKIAQNFSLEQIQNATIKRQLKALQQSGSSALSPDKNKQLNTIL
ACE2 HUMAN	NMNNAGDKWSAFLKEQSTLAQMYPLQEIQNLTIVKLQLQALQQSGSSVLSADKSKRLNTIL
A0A384DV19 FELCA	KMNEAGAKWSAFYEEQSKLAKTYPLAEIHNTTVKRQLQALQQSGSSVLSADKSKRLNTIL
A0A5F5XDN9 FELCA	KMNEAGAKWSAFYEEQSKLAKTYPLAEIHNTTVKRQLQALQQSGSSVLSADKSKRLNTIL
ACE2 FELCA	KMNEAGAKWSAFYEEQSKLAKTYPLAEIHNTTVKRQLQALQQSGSSVLSADKSKRLNTIL
A0A5F4CXG9 CANLF	KMNNAGAKWSAFYEEQSKLAKTYPLEEIQDSTVKRQLRALQHSGSSVLSADKNQRLNTIL
A0A5F4BS93 CANLF	KMNNAGAKWSAFYEEQSKLAKTYPLEEIQDSTVKRQLRALQHSGSSVLSADKNQRLNTIL
F1P7C5 CANLF	KMNNAGAKWSAFYEEQSKLAKTYPLEEIQDSTVKRQLRALQHSGSSVLSADKNQRLNTIL
J9P7Y2 CANLF	KMNNAGAKWSAFYEEQSKLAKTYPLEEIQDSTVKRQLRALQHSGSSVLSADKNQRLNTIL
	:*:. * ***** :*** *: : ::: :* **: **:*. : ** :*.: : *
A0A4X1UWQ8 PIG	NTMSTIYSSGKVLDPNPNQECVLPLEPGLDEIMENSKDYSRRLWAWESWRAEVGKQLRPLY
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A0A452EVU0 CAPHI	Q-----LYDLIDICLDDIMENSRDYNRRLLWAWEGWRAEVGKQLRPLY
A0A4W2H6E0 BOBOX	NKMSTIYSTGKVLDPN-TQECLALEPGLDDIMENSRDYNRRLLWAWEGWRAEVGKQLRPLY
A0A4W2H3A1 BOBOX	NKMSTIYSTGKVLDPN-TQECLALEPGLDDIMENSRDYNRRLLWAWEGWRAEVGKQLRPLY
Q2HJI5 BOVIN	NKMSTIYSTGKVLDPN-TQECLALEPGLDDIMENSRDYNRRLLWAWEGWRAEVGKQLRPLY

NKMSTIYSTGKVLDPN-TQECLALEPGLDDIMENS RDYNRRLWAWEGWRAEVGKQLRPLY
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 STMSTIYSTGKVCNQSNPQECFLLEPGLDEIMAKSTDYNERLWAWEGWRSVVGKQLRPLY
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A0A4X1UWQ8 PIG
K7GLM4 PIG
A0A452EVU0 CAPHI
A0A4W2H6E0 BOBOX
A0A4W2H3A1 BOBOX
Q2HJI5 BOVIN
ACE2 BOVIN
A0A452EVJ5 CAPHI
W5PSB6 SHEEP
E2DHI7 9CHIR
E2DHI4 9CHIR
U5WHY8 9CHIR
G1TEF4 RABIT
A0A1U7QTA1 MESAU
ACE2 MOUSE
ACE2 RAT
ACE2 HUMAN
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A0A5F5XDN9 FELCA
ACE2 FELCA
A0A5F4CXG9 CANLF
A0A5F4BS93 CANLF
F1P7C5 CANLF
J9P7Y2 CANLF

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EEYVVLLENEMARAN-----NYEDYGDYWRGDYEVGTGDYDYSRNQLMEDVERT
EEYVVLLENEMARAN-----NYEDYGDYWRGDYEVGTGDYDYSRNQLMEDVERT
EEYVVLLENEMARANSKCSHFLLFETDYEDYGDYWRGDYEVGTAGDYDYSRDQLMKDVERT
EEYVVLLENEMARAN-----NYEDYGDYWRGDYEVGTAGDYDYSRDQLMKDVERT
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EEYVVLLENEMARAN-----NYEDYGDYWRGDYEVGTAGDYDYSRDQLMKDVERT
EEYVVLLENEMARAN-----NYEDYGDYWRGDYEVGTAGDYDYSRDQLMKDVERT
EEYVVLLENEMARAN-----NYEDYGDYWRGDYEVGTAGDYDYSRDQLMKDVERT
EEYVVLLENEMARAN-----NYEDYGDYWRGDYEVGTAGDYDYSRDQLMKDVERT
EEYVVLKKNEMARGY-----HYEDYGDYWRRDYETEESPGPGYSRDQLMKDVERI
EEYVVLKKNEMARGY-----HYEDYGDYWRRDYETEESPGPGYSRDQLMKDVERI
EEYVVLKKNEMARGY-----HYEDYGDYWRRDYETEESPGPGYSRDQLMKDVERI
EEYVVLKKNEMARAN-----NYEDYGDYWRADYEAEGADGYDYSRSQLIDDVERT
EEYVVLKKNEMARAN-----NYEDYGDYWRGDYEAEGADGYNNGNQLIEDVERT
EEYVVLKKNEMARAN-----NYNDYGDYWRGDYEAEGADGYNYNRNQLIEDVERT
EEYVVLKKNEMARAN-----NYEDYGDYWRGDYEAEGVEGYNYNRNQLIEDVENT
EEYVVLKKNEMARAN-----HYEDYGDYWRGDYEVNGVDGYDYSRQQLIEDVEHT
EEYVALKNEMAK-----NYEDYGDYWRGDYEEEWTDGYNYSRSQLIKDVEHT
EEYVALKNEMAKSK-----QYEDYGDYWRGDYEEEWTDGYNYSRSQLIKDVEHT
EEYVALKNEMARAN-----NYEDYGDYWRGDYEEEWTDGYNYSRSQLIKDVEHT
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EEYVALKNEMARAN-----NYEDYGDYWRGDYEEEWENGYNYSRNQLIDDVEHT
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A0A4X1UWQ8 PIG
K7GLM4 PIG
A0A452EVU0 CAPHI
A0A4W2H6E0 BOBOX
A0A4W2H3A1 BOBOX
Q2HJI5 BOVIN
ACE2 BOVIN
A0A452EVJ5 CAPHI
W5PSB6 SHEEP
E2DHI7 9CHIR
E2DHI4 9CHIR
U5WHY8 9CHIR
G1TEF4 RABIT
A0A1U7QTA1 MESAU
ACE2 MOUSE

[illegible]

ACE2 RAT	FKEIKPLYEQLHAYVRTKLMEVYPSYISPTGCLPAHL-LGDMWGRFWTNLYPLTTPFLQK
ACE2 HUMAN	FEEIKPLYEHLHAYVRAKLMNAYPSYISPIGCLPAHL-LGDMWGRFWTNLYSLTVPFQK
A0A384DV19 FELCA	FTQIKPLYQHLHAYVRAKLMDTYPSTRISPTGCLPAHL-LGDMWGRFWTNLYPLTVPFQK
A0A5F5XDN9 FELCA	FTQIKPLYQHLHAYVRAKLMDTYPSTRISPTGCLPAHL-LGDMWGRFWTNLYPLTVPFQK
ACE2 FELCA	FTQIKPLYQHLHAYVRAKLMDTYPSTRISPTGCLPAHL-LGDMWGRFWTNLYPLTVPFQK
A0A5F4CXG9 CANLF	FTQIMPLYQHLHAYVRTKLMDTYPSTRISPTGCLPAHL-LGDMWGRFWTNLYPLTVPFQK
A0A5F4BS93 CANLF	FTQIMPLYQHLHAYVRTKLMDTYPSTRISPTGCLPAHL-LGDMWGRFWTNLYPLTVPFQK
F1P7C5 CANLF	FTQIMPLYQHLHAYVRTKLMDTYPSTRISPTGCLPAHL-LGDMWGRFWTNLYPLTVPFQK
J9P7Y2 CANLF	FTQIMPLYQHLHAYVRTKLMDTYPSTRISPTGCLPAHL-LGDMWGRFWTNLYPLTVPFQK
	* : * * * * : : * * * : * * * * . . * * * * * * * * * : * * * * * * * * * * * * . * * . *
A0A4X1UWQ8 PIG	PSIDVTEAMVNSQSWDAVRIFEEAEKFFVSIGLPNMTQGFWNNSMLTEPGDGRKVVCHPTA
K7GLM4 PIG	PSIDVTEAMVNSQSWDAIRIFEEAEKFFVSIGLPNMTQGFWNNSMLTEPGDGRKVVCHPTA
A0A452EVU0 CAPHI	PSIDVTEKMKNQSWDAERIFKEAEKFFVSIGLPYMTQGFWNNSMLTEPGDGRKVVCHPTA
A0A4W2H6E0 BOBOX	PSIDVTEKMENQSWDAERIFKEAEKFFVSISLPYMTQGFWDNSMLTEPGDGRKVVCHPTA
A0A4W2H3A1 BOBOX	PSIDVTEKMENQSWDAERIFKEAEKFFVSISLPYMTQGFWDNSMLTEPGDGRKVVCHPTA
Q2HJI5 BOVIN	PSIDVTEKMENQSWDAERIFKEAEKFFVSISLPYMTQGFWDNSMLTEPGDGRKVVCHPTA
ACE2 BOVIN	PSIDVTEKMENQSWDAERIFKEAEKFFVSISLPYMTQGFWDNSMLTEPGDGRKVVCHPTA
A0A452EVJ5 CAPHI	PSIDVTEKMKNQSWDAERIFKEAEKFFVSIGLPYMTQGFWNNSMLTEPGDGRKVVCHPTA
W5PSB6 SHEEP	PSIDVTEKMKNQSWDAERIFKEAEKFFVSIGLPYMTQGFWDNSMLTEPGDGRKVVCHPTA
E2DHI7 9CHIR	PNIDVTDEMLKQGWADDRIFKEAEKFFVSVGLPNMTEGFWNNSMLTEPGDGRKVVCHPTA
E2DHI4 9CHIR	PNIDVTDEMLKQGWADDRIFKEAEKFFVSVGLPNMTEGFWNNSMLTEPGDGRKVVCHPTA
U5WHY8 9CHIR	PNIDVTDEMLKQGWADDRIFKEAEKFFVSVGLPNMTEGFWNNSMLTEPGDGRKVVCHPTA
G1TEF4 RABIT	PNIDVTDTMVNQGWDAERIFKEAEKFFVSVGLPSMTQGFWNSMLTEPGDGRKVVCHPTA
A0A1U7QTA1 MESAU	PNIDVTDAMVNQGWNAERIFKEAEKFFVSVGLPYMTQGFWNSMLTEPDGDRKVVCHPTA
ACE2 MOUSE	PNIDVTDAMNQGWDARERIFQEAEEKFFVSVGLPHMTQGFWANSMLTEPADGRKVVCHPTA
ACE2 RAT	PNIDVTDAMVNQSWDAERIFKEAEKFFVSVGLPQMTPGFWTNSMLTEPGDGRKVVCHPTA
ACE2 HUMAN	PNIDVTDAMVDQAWDAQRIFKEAEKFFVSVGLPNMTQGFWNSMLTEPDGNVQKAVCHPTA
A0A384DV19 FELCA	PNIDVTDAMVNQSWDARRIFKEAEKFFVSVGLPNMTQGFWNSMLTEPGDSRKVVCHPTA
A0A5F5XDN9 FELCA	PNIDVTDAMVNQSWDARRIFKEAEKFFVSVGLPNMTQGFWNSMLTEPGDSRKVVCHPTA
ACE2 FELCA	PNIDVTDAMVNQSWDARRIFKEAEKFFVSVGLPNMTQGFWNSMLTEPGDSRKVVCHPTA
A0A5F4CXG9 CANLF	PNIDVTNAMVNQSWDARKIFKEAEKFFVSVGLPNMTQGFWNSMLTEPSDSRKVVCHPTA
A0A5F4BS93 CANLF	PNIDVTNAMVNQSWDARKIFKEAEKFFVSVGLPNMTQGFWNSMLTEPSDSRKVVCHPTA
F1P7C5 CANLF	PNIDVTNAMVNQSWDARKIFKEAEKFFVSVGLPNMTQGFWNSMLTEPSDSRKVVCHPTA
J9P7Y2 CANLF	PNIDVTNAMVNQSWDARKIFKEAEKFFVSVGLPNMTQGFWNSMLTEPSDSRKVVCHPTA
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A0A4X1UWQ8 PIG	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAIQPYLLRNGANEGFHEAVGEIM
K7GLM4 PIG	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAIQPYLLRNGANEGFHEAVGEIM
A0A452EVU0 CAPHI	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYATQPYLLRNGANEGFHEAVGEIM
A0A4W2H6E0 BOBOX	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPYLLRNGANEGFHEAVGEIM
A0A4W2H3A1 BOBOX	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPYLLRNGANEGFHEAVGEIM
Q2HJI5 BOVIN	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPYLLRNGANEGFHEAVGEIM
ACE2 BOVIN	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPYLLRNGANEGFHEAVGEIM
A0A452EVJ5 CAPHI	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYATQPYLLRNGANEGFHEAVGEIM
W5PSB6 SHEEP	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYATQPYLLRNGANEGFHEAVGEIM
E2DHI7 9CHIR	WDLGKGDFRIKMCTKVTMEDFLTAHHEMGHIQYDMVYASQPYLLRNGANEGFHEAVGEIM
E2DHI4 9CHIR	WDLGKGDFRIKMCTKVTMEDFLTAHHEMGHIQYDMAYASQPYLLRNGANEGFHEAVGEIM
U5WHY8 9CHIR	WDLGKGDFRIKMCTKVTMEDFLTAHHEMGHIQYDMAYASQPYLLRNGANEGFHEAVGEIM
G1TEF4 RABIT	WDLGKGDFRIKMCTKVTMDNFLTAAHHEMGHIQYDMAYATQPFLLRNGANEGFHEAVGEIM
A0A1U7QTA1 MESAU	WDLGKGDFRIKMCTKVTMDNFLTAAHHEMGHIQYDMAYATQPFLLRNGANEGFHEAVGEIM
ACE2 MOUSE	WDLGHGDFRIKMCTKVTMDNFLTAAHHEMGHIQYDMAYARQPFLLRNGANEGFHEAVGEIM
ACE2 RAT	WDLGHGDFRIKMCTKVTMDNFLTAAHHEMGHIQYDMAYAKQPFLLRNGANEGFHEAVGEIM
ACE2 HUMAN	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPFLLRNGANEGFHEAVGEIM
A0A384DV19 FELCA	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAVQPFLLRNGANEGFHEAVGEIM
A0A5F5XDN9 FELCA	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAVQPFLLRNGANEGFHEAVGEIM
ACE2 FELCA	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAVQPFLLRNGANEGFHEAVGEIM
A0A5F4CXG9 CANLF	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPFLLRNGANEGFHEAVGEIM
A0A5F4BS93 CANLF	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPFLLRNGANEGFHEAVGEIM
F1P7C5 CANLF	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPFLLRNGANEGFHEAVGEIM
J9P7Y2 CANLF	WDLGKGDFRIKMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPFLLRNGANEGFHEAVGEIM

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A0A4X1UWQ8 PIG	SLSAATPHYLKALGLLPPDFYEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
K7GLM4 PIG	SLSAATPHYLKALGLLPPDFYEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A452EVU0 CAPHI	SLSAATPHYLKALGLLAPDFYEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A4W2H6E0 BOBOX	SLSAATPHYLKALGLLAPDFHEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A4W2H3A1 BOBOX	SLSAATPHYLKALGLLAPDFHEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
Q2HJ15 BOVIN	SLSAATPHYLKALGLLAPDFHEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
ACE2 BOVIN	SLSAATPHYLKALGLLAPDFHEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A452EVJ5 CAPHI	SLSAATPHYLKALGLLAPDFYEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
W5PSB6 SHEEP	SLSAATPHYLKALGLLAPDFYEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
E2DHI7 9CHIR	SLSVATPKHLKTMGLLSPDFHEDNETEINFLKQALNIVGTLPTTYMLEKWRWMVFKGEI
E2DHI4 9CHIR	SLSVATPKHLKTMGLLSPDFREDNETEINFLKQALNIVGTLPTTYMLEKWRWMVFKGEI
U5WHY8 9CHIR	SLSVATPKHLKTMGLLSPDFREDNETEINFLKQALNIVGTLPTTYMLEKWRWMVFKGEI
G1TEF4 RABIT	SLSAATPEHLKSIGLLPSDFHEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A1U7QTA1 MESAU	SLSAATPEHLKSIGLLPSDFQEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGDI
ACE2 MOUSE	SLSAATPKHLKSIGLLPSDFQEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFRGEI
ACE2 RAT	SLSAATPKHLKSIGLLPSNFQEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKDKI
ACE2 HUMAN	SLSAATPKHLKSIGLLSPDFQEDNETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A384DV19 FELCA	SLSAATPNHLKTIGLLSPGFSEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A5F5XDN9 FELCA	SLSAATPNHLKTIGLLSPGFSEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
ACE2 FELCA	SLSAATPNHLKTIGLLSPGFSEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A5F4CXG9 CANLF	SLSAATPNHLKNIGLLPPSFFEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
A0A5F4BS93 CANLF	SLSAATPNHLKNIGLLPPSFFEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
F1P7C5 CANLF	SLSAATPNHLKNIGLLPPSFFEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI
J9P7Y2 CANLF	SLSAATPNHLKNIGLLPPSFFEDSETEINFLKQALTIVGTLPTTYMLEKWRWMVFKGEI

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A0A4X1UWQ8 PIG	PKEQWMQKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
K7GLM4 PIG	PKEQWMQKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
A0A452EVU0 CAPHI	PKQQWMEKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
A0A4W2H6E0 BOBOX	PKQQWMEKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
A0A4W2H3A1 BOBOX	PKQQWMEKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
Q2HJ15 BOVIN	PKQQWMEKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
ACE2 BOVIN	PKQQWMEKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
A0A452EVJ5 CAPHI	PKQQWMEKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
W5PSB6 SHEEP	PKQQWMEKWWEMKREIVGVVEPLPHDETYCDPACLFHVAEDYSFIRYYTRTIYQFQFHEA
E2DHI7 9CHIR	PKEEWMKKWWEMKRKIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIFEFQFHEA
E2DHI4 9CHIR	PKEEWMKKWLEMKRKIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIFEFQFHEA
U5WHY8 9CHIR	PKEEWMKKWWEMKRKIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIFEFQFHEA
G1TEF4 RABIT	PKEQWMQKWWEMKREIVGVVEPMPHDETYCDPAALFHVANDYSFIRYYTRTIYQFQFQEA
A0A1U7QTA1 MESAU	PKEQWMEKWWEMKREIVGVVEPLPHDETYCDPAALFHVSNDSFIRYYTRTIYQFQFQEA
ACE2 MOUSE	PKEQWMKKWWEMKREIVGVVEPLPHDETYCDPASLFHVSNDSFIRYYTRTIYQFQFQEA
ACE2 RAT	PREQWTKKWWEMKREIVGVVEPLPHDETYCDPASLFHVSNDSFIRYYTRTIYQFQFQEA
ACE2 HUMAN	PKDQWMKKWWEMKREIVGVVEPVPHDETYCDPASLFHVSNDSFIRYYTRTLYQFQFQEA
A0A384DV19 FELCA	PKEQWMQKWWEMKREIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIYQFQFQEA
A0A5F5XDN9 FELCA	PKEQWMQKWWEMKREIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIYQFQFQEA
ACE2 FELCA	PKEQWMQKWWEMKREIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIYQFQFQEA
A0A5F4CXG9 CANLF	PKDQWMKTWWEMKRNIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIYQFQFQEA
A0A5F4BS93 CANLF	PKDQWMKTWWEMKRNIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIYQFQFQEA
F1P7C5 CANLF	PKDQWMKTWWEMKRNIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIYQFQFQEA
J9P7Y2 CANLF	PKDQWMKTWWEMKRNIVGVVEPVPHDETYCDPASLFHVANDYSFIRYYTRTIYQFQFQEA

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A0A4X1UWQ8 PIG	LCRTAKHEGPLYKCDISNSTEAGQKLLQMLSLGKSEPWTALLENIVGVKTMVDPKPLLSYF
K7GLM4 PIG	LCRTAKHEGPLYKCDISNSTEAGQKLLQMLSLGKSEPWTALLENIVGVKTMVDPKPLLSYF
A0A452EVU0 CAPHI	LCKTAKHEGALFKCDISNSTEAGQRLQLMLRLGKSEPWTALLENIVGIKTMVDPKPLLSYF
A0A4W2H6E0 BOBOX	LCKTAKHEGALFKCDISNSTEAGQRLQLMLRLGKSEPWTALLENIVGIKTMVDPKPLLSYF
A0A4W2H3A1 BOBOX	LCKTAKHEGALFKCDISNSTEAGQRLQLMLRLGKSEPWTALLENIVGIKTMVDPKPLLSYF
Q2HJ15 BOVIN	LCKTAKHEGALFKCDISNSTEAGQRLQLMLRLGKSEPWTALLENIVGIKTMVDPKPLLSYF
ACE2 BOVIN	LCKTAKHEGALFKCDISNSTEAGQRLQLMLRLGKSEPWTALLENIVGIKTMVDPKPLLSYF

ACE2 HUMAN	YAMRQYFLKVKNQMILFGEEDVRVANLKPRISFNFFVTAPKNVSDIIPRTEVEKAIRMSR
A0A384DV19 FELCA	YAMREYFSKVKNQTI PFVEDNVWVSNLKPRISFNFFVTASKNVSDVIPRSEVEEAIIRMSR
A0A5F5XDN9 FELCA	YAMREYFSKVKNQTI PFVEDNVWVSNLKPRISFNFFVTASKNVSDVIPRSEVEEAIIRMSR
ACE2 FELCA	YAMREYFSKVKNQTI PFVEDNVWVSNLKPRISFNFFVTASKNVSDVIPRSEVEEAIIRMSR
A0A5F4CXG9 CANLF	YAMRQYFSEVKNQTI PFVEDNVWVSDLKPRISFNFFVTS PGNVSDIIPRTEVEEAIIRMYR
A0A5F4BS93 CANLF	YAMRQYFSEVKNQTI PFVEDNVWVSDLKPRISFNFFVTS PGNVSDIIPRTEVEEAIIR---
F1P7C5 CANLF	YAMRQYFSEVKNQTI PFV-----MYR
J9P7Y2 CANLF	YAMRQYFSEVKNQTI PFVEDNVWVSDLKPRISFNFFVTS PGNVSDIIPRTEVEEAIIRMYR
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A0A4X1UWQ8 PIG	SRINDAFRLDDNTLEFLGIQPTLGPPDEPPVTWLIIFGVVMGLVVVGIVVLIFTGIRDR
K7GLM4 PIG	SRINDAFRLDDNTLEFLGIQPTLGPPDEPPVTWLIIFGVVMGLVVVGIVVLIFTGIRDR
A0A452EVU0 CAPHI	DRINDAFQLDDNSLEFLGIQPTLRPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRDQ
A0A4W2H6E0 BOBOX	DRINDVFLQDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRNR
A0A4W2H3A1 BOBOX	DRINDVFLQDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRNR
Q2HJ15 BOVIN	DRFNDVFLQDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRNR
ACE2 BOVIN	DRINDVFLQDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRNR
A0A452EVJ5 CAPHI	DRINDAFQLDDNSLEFLGIQPTLRPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRDQ
W5PSB6 SHEEP	DRINDAFQLDDNSLEFLGIQPTLRPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRDQ
E2DHI7 9CHIR	SRINDAFRLDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRDR
E2DHI4 9CHIR	SRINDAFRLDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRDR
U5WHY8 9CHIR	SRINDAFRLDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVVLIFTGIRDR
G1TEF4 RABIT	SRINDIFRLDDNSLEFLVGIQPTLEPPYESPVPIWLVVFGVVMGMIVIGIVVLIFTGIKDR
A0A1U7QTA1 MESAU	GRINDVFLQDDNSLEFLGINPTLSPPYEPPVTIWLIIFGVVMGIVVVGIIILIFTGIKGR
ACE2 MOUSE	GRINDVFLQDDNSLEFLGIHPTLEPPYEPPVTIWLIIFGVVMALVVVGIIILIVTGIKGR
ACE2 RAT	GRINDIFGLNDNSLEFLGIYPTLKPPYEPPVTIWLIIFGVVMGTVVVGIVILIVTGIKGR
ACE2 HUMAN	SRINDAFRLNDNSLEFLGIQPTLGPPNQPPVSIWLIIFGVVMGVIVVGIVILIFTGIRDR
A0A384DV19 FELCA	SRINDAFRLDDNSLEFLGIQPTLSPPYEPPVTIWLIIFGVVMGVVVGIVLLIVSGIRNR
A0A5F5XDN9 FELCA	SRINDAFRLDDNSLEFLGIQPTLSPPYEPPVTIWLIIFGVVMGVVVGIVLLIVSGIRNR
ACE2 FELCA	SRINDAFRLDDNSLEFLGIQPTLSPPYEPPVTIWLIIFGVVMGVVVGIVLLIVSGIRNR
A0A5F4CXG9 CANLF	SRINDVFLRDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVLLIFSGIRNR
A0A5F4BS93 CANLF	-----
F1P7C5 CANLF	SRINDVFLRDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVLLIFSGIRNR
J9P7Y2 CANLF	SRINDVFLRDDNSLEFLGIQPTLGPPYEPPVTIWLIIFGVVMGVVVGIVLLIFSGIRNR
A0A4X1UWQ8 PIG	RKKKQASSEENPYGSMDLSK-----GESNSGFQNGDDIQTSF
K7GLM4 PIG	RKKKQASSEENPYGSMDLSK-----GESNSGFQNGDDIQTSF
A0A452EVU0 CAPHI	RKKKQASSEENPYGSVD-----LNKG--ENNSGFQNTDDVQTSL
A0A4W2H6E0 BOBOX	RKHDSGLQNDENLRVQQQAVKVDIPRNSLKATVPFSNSHEKLR--
A0A4W2H3A1 BOBOX	RKKKQASSEENPYGSVD-----LNKGE--NNSGFQNI DDVQTSL
Q2HJ15 BOVIN	RKKKQASSEENPYGSVD-----LNKGE--NNSGFQNI DDVQTSL
ACE2 BOVIN	RKKKQASSEENPYGSVD-----LNKGE--NNSGFQNI DDVQTSL
A0A452EVJ5 CAPHI	RKKKQASSEENPYGSVD-----LNKGE--NNSGFQNTDDVQTSL
W5PSB6 SHEEP	RKKKQASSEENPYGSVD-----LNKGE--NNSGFQNTDDVQTSL
E2DHI7 9CHIR	RKTDQARSEENPYSSVDLSK-----GENNPGFQNGDDVQTSF
E2DHI4 9CHIR	RKTDQARSEENPYSSVDLSK-----GENNPGFQNGDDVQTSF
U5WHY8 9CHIR	RKTDQARSEENPYSSVDLSK-----GENNPGFQNGDDVQTSF
G1TEF4 RABIT	RKQKQAKREENPYGFVDMASK-----GENNSGFQNSDDIQTSF
A0A1U7QTA1 MESAU	KKKNETKREENPYDSVDIGK-----GESNAGFLSNDDAQTSF
ACE2 MOUSE	KKKNETKREENPYDSMDIGK-----GESNAGFQNSDDAQTSF
ACE2 RAT	KKKNETKREENPYDSMDIGK-----GESNAGFQNSDDAQTSF
ACE2 HUMAN	KKKNKARSGENPYASIDISK-----GENNPGFQNTDDVQTSF
A0A384DV19 FELCA	RKNNQARSEENPYASVDLSK-----GENNPGFQHADDVQTSF
A0A5F5XDN9 FELCA	RKNNQARSEENPYASVDLSK-----GENNPGFQHADDVQTSF
ACE2 FELCA	RKNNQARSEENPYASVDLSK-----GENNPGFQHADDVQTSF
A0A5F4CXG9 CANLF	RKWPSLSSP-----
A0A5F4BS93 CANLF	--NDQARGEENPYASVDLSK-----GENNPGFQNVDDAQTSF
F1P7C5 CANLF	RKNDQARGEENPYASVDLSK-----GENNPGFQNVDDAQTSF
J9P7Y2 CANLF	RKNDQARGEENPYASVDLSK-----GENNPGFQNVDDAQTSF