Supplemental Materials

Comparative ACE2 variation and primate COVID-19 risk

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Supplemental Table S1. Gene IDs and NCBI accession numbers of *ACE2* gene sequences included in the study.

Species	Common Name	Gene ID	NCBI Accession Number	Notes
Homo sapiens	human	59272	NM_001371415.1	
Pan troglodytes	chimpanzee	465511	XM_016942979.1	
Pan paniscus	bonobo	100970340	XM_008974180.1	
Gorilla gorilla	gorilla	101142534	XM_019019204.1	
Pongo abelii	Sumatran orangutan	100171441	NM_001131132.2	
Nomascus leucogenys	northern white-cheeked gibbon	100602708	XM_003261084.3	
Hylobates moloch	silvery gibbon	116811532	XM_032756617.1	
Rhinopithecus roxellana	golden snub-nosed monkey	104664530	XM_010366065.2	
Piliocolobus tephrosceles	Ugandan red colobus	111531712	XM_023199053.2	
Macaca mulatta	rhesus macaque	712790	NM_001135696.1	
Macaca nemestrina	pigtail macaque	105478157	XM_011735203.2	
Macaca fascicularis	long-tailed macaque	102130864	XM_005593037.2	
Cercocebus atys	sooty mangabey	105574684	XM_012035809.1	
Mandrillus leucophaeus	drill	105550583	XM_011995533.1	
Papio anubis	olive baboon	101008749	XM_021933040.1	
Theropithecus gelada	gelada	112615413	XM_025372062.1	
Chlorocebus sabaeus	vervet	103231639	XM_007991113.1	
Alouatta palliata	mantled howler monkey	N/A	N/A	unpublished draft genome, sequence in supplemental file
Aotus nancymaae	Ma's night monkey	105705080	XM_012434682.2	
Cebus capucinus imitator	white-faced capuchin	108291904	XM_017512376.1	
Sapajus apella	tufted capuchin	116556688	XM_032285963.1	
Saimiri boliviensis	Bolivian squirrel monkey	101045190	XM_010336623.1	
Callithrix jacchus	common marmoset	100408882	XM_017968359.1	
Carlito syrichta	Philippine tarsier	103267011	XM_008064619.1	
Microcebus murinus	gray mouse lemur	105882317	XM_020285237.1	Exon 15 manually corrected, NCBI

				annotation incorrect
Propithecus coquereli	Coquerel's sifaka	105805773	XM_012638731.1	
Otolemur garnettii	Northern greater galago	100951881	XM_003791864.2	
Eulemur flavifrons	blue-eyed black lemur	N/A	LGHW01000591.1, scaffold 590	*ACE2* not annotated, identified via BLAST
Daubentonia madagascariensis	aye-aye	N/A	PVJZ01006595.1, scaffold 13170	*ACE2* not annotated, identified via BLAST
Rhinolophus sinicus	Chinese rufous horseshoe bat	N/A	GQ999933.1	From [1]
Rhinolophus pusillus	least horseshoe bat	N/A	GQ999938.1	
Rhinolophus macrotis	big-eared horseshoe bat	N/A	GQ999932.1	
Rhinolophus pearsonii	Pearson's horseshoe bat	N/A	EF569964.1	
Rhinolophus ferrumequinum	greater horseshoe bat	N/A	GQ999931.1	
Myotis daubentonii	Daubenton's bat	N/A	GQ999937.1	
Hipposideros pratti		N/A	GQ999934.1	
Felis catus	domestic cat	554349	NM_001039456.1	
Canis lupus	domestic dog	480847	NM_001165260.1	
Sus scrofa	domestic pig	100144303	NM_001123070.1	
Mustela putorius	ferret	101673097	NM_001310190.1	
Manis javanica	Malayan pangolin	108390919	XM_017650257.1	

Supplementary Table S2. Results of alanine scanning mutagenesis experiments predicting critical binding sites between ACE2 and Sars-CoV-2 receptor binding domain. Residues whose mutation to alanine decrease the binding energy by $\Delta\Delta G_{bind} \geq 1.0$ kcal/mol are considered to be significant for binding (in bold). [+]Denotes sites also implicated by Yan et al.[2]

Residue site	ΔΔG (kcal/mol)[a]
41[+]	**4.1**
355	**3.5**
42[+]	**2.3**
83	**2.1**
357[+]	**2**
38	**1.4**
37	**1.2**
24[+]	**1.1**
353[+]	**1.1**
27	0.7
34[+]	0.7
31	0.6
30[+]	0.6
35	0.5
79	0.5
45	0.5
28	0.3
82[+]	0.2
330	0.2
351	0.03

[a]The computational alanine mutagenesis analysis was performed with Rosetta Software and PDB file 6M0J.

Supplementary Table S3. Pairwise identities of ACE2 nucleotide sequences between all species in our study. Number indicates the percentage of bases that are identical across the full length of the gene sequence.

	Aloualta palliata	*A. nancymaae*	*C. capucinus*	*S. apella*	*S. boliviensis*	*C. jacchus*	*C. atys*	*M. leucophaeus*	*M. fascicularis*	*M. nemestrina*	*P. anubis*	*T. gelada*	*M. mulatta*	*P. ephrosceles*	*R. roxellana*	*C. sabaeus*	*G. gorilla*	*H. sapiens*	*P. paniscus*	*P. troglodytes*	*P. abelii*	*H. moloch*	*N. leucogenys*	*D. madagascariensis*	*E. flavifrons*	*P. coquereli*	*M. murinus*	*O. garnettii*	*C. syrichta*	*C. lupus*	*F. catus*	*M. putorius*	*M. javanica*	*H. pratti*	*R. ferrum-equinum*	*R. macrotis*	*R. pusillus*	*R. sinicus*	*R. pearsonii*	*M. daubentonii*
Aotus nancymaae	97.35																																							
Cebus capucinus	97.28	97.78																																						
Sapajus apella	97.48	97.97	99.47																																					
Saimiri boliviensis	97.11	97.93	98.03	98.14																																				
Callithrix jacchus	97.19	97.68	97.61	97.85	97.52																																			
Cercocebus atys	94.62	94.5	94.51	94.71	94.67	94.21																																		
Mandrillus leucophaeus	94.54	94.42	94.43	94.62	94.58	94.13	99.67																																	
Macaca fascicularis	94.79	94.67	94.55	94.75	94.75	94.29	99.42	99.34																																
Macaca nemestrina	94.87	94.75	94.63	94.83	94.83	94.38	99.5	99.42	99.92																															
Papio anubis	94.83	94.62	94.59	94.79	94.79	94.33	99.5	99.42	99.67	99.75																														
Theropithecus gelada	94.71	94.58	94.55	94.75	94.83	94.29	99.59	99.5	99.5	99.59	99.75																													
Macaca mulatta	94.67	94.54	94.43	94.62	94.54	94.17	99.17	99.09	99.59	99.67	99.42	99.26																												
Piliocolobus tephrosceles	94.75	94.62	94.59	94.79	94.79	94.33	98.76	98.59	98.84	98.92	98.92	98.84	98.68																											
Rhinopithecus roxellana	94.79	94.54	94.59	94.79	94.79	94.33	98.92	98.76	98.97	99.05	99.05	98.97	98.72	99.05																										
Chlorocebus sabaeus	94.54	94.33	94.34	94.54	94.54	94.13	98.97	98.88	99.01	99.09	99.05	99.05	98.76	98.51	98.59																									
Gorilla gorilla	94.58	94.33	94.34	94.54	94.71	94.25	96.94	96.73	96.94	97.02	97.02	97.02	96.69	96.98	97.06	96.77																								
Homo sapiens	94.62	94.54	94.55	94.75	94.83	94.46	97.02	96.82	97.02	97.11	97.11	97.11	96.77	97.06	97.15	96.86	99.26																							
Pan paniscus	94.54	94.46	94.47	94.67	94.75	94.38	97.02	96.82	97.02	97.02	97.02	97.02	96.69	96.98	97.06	96.77	99.17	99.42																						
Pan troglodytes	94.54	94.46	94.47	94.67	94.75	94.38	97.02	96.82	96.94	97.02	97.02	97.02	96.69	96.98	97.06	96.77	99.17	99.42	99.92																					
Pongo abelii	94.62	94.38	94.39	94.58	94.71	94.38	97.15	96.94	97.15	97.23	97.23	97.19	96.9	97.15	97.27	96.82	98.3	98.47	98.39	98.39																				
Hylobates moloch	94.83	94.67	94.51	94.71	94.83	94.42	96.94	96.73	96.94	97.02	97.02	96.98	96.69	96.94	97.06	96.65	98.22	98.3	98.3	98.3	98.26																			
Nomascus leucogenys	94.87	94.62	94.47	94.67	94.87	94.46	96.94	96.73	96.94	97.02	97.02	96.98	96.69	96.94	97.06	96.61	98.26	98.26	98.26	98.26	98.35	99.26																		
Daubentonia madagascariensis	89.66	89.58	89.42	89.74	89.66	89.37	90.24	90.16	90.24	90.32	90.32	90.36	90.07	90.16	90.28	90.16	89.99	90.2	90.12	90.12	90.24	90.36	90.2																	
Eulemur flavifrons	88.67	88.5	88.31	88.54	88.63	88.46	88.96	88.96	89.25	89.25	89.21	89.25	89	89	88.96	88.96	89	89.12	89.12	89.04	89.08	89.08	89.25	93.22																
Propithecus coquereli	89.16	89.16	88.89	89.12	89.04	88.96	89.66	89.66	89.74	89.83	89.74	89.78	89.58	89.7	89.62	89.62	89.5	89.7	89.7	89.7	89.66	89.7	89.7	94.54	95.37															
Microcebus murinus	88.5	88.3	88.06	88.3	88.25	88.34	88.54	88.54	88.71	88.79	88.71	88.71	88.54	88.79	88.83	88.83	88.96	88.92	88.75	88.75	88.88	88.75	88.92	93.13	94.71	95.16														
Otolemur garnettii	86.35	86.19	86.07	86.39	86.48	86.1	86.35	86.27	86.31	86.39	86.31	86.44	86.15	86.56	86.56	86.48	86.52	86.48	86.39	86.39	86.35	86.44	86.48	90.24	89	89.91	89.29													
Carlito syrichta	87.84	87.39	87.56	87.76	87.84	87.68	87.88	87.88	88.01	88.09	88.09	88.13	87.88	88.13	88.05	87.92	88.17	87.92	88.05	88.05	87.97	87.97	88.09	87.76	86.64	87.26	86.97	84.66												
Canis lupus	86.93	86.77	86.78	86.77	87.14	86.68	87.26	87.1	87.3	87.39	87.39	87.34	87.22	87.3	87.39	87.06	87.06	87.01	87.1	87.1	87.1	87.3	87.22	88.21	86.72	87.68	86.6	85.4	85.36											
Felis catus	86.64	86.52	86.78	86.85	86.97	86.39	86.77	86.64	86.85	86.93	86.85	86.89	86.68	86.97	86.97	86.6	86.81	86.93	87.1	87.1	86.93	87.22	87.1	87.92	86.85	87.51	86.31	85.24	85.32	92.6										
Mustela putorius furo	85.73	85.65	85.49	85.65	85.9	85.57	85.86	85.65	85.81	85.9	85.86	85.9	85.77	85.94	85.98	85.57	85.98	85.86	85.98	85.98	85.73	85.98	86.1	86.72	85.32	86.44	85.07	84.37	84.62	92.22	91.36									
Manis javanica	86.06	85.81	86.03	86.23	86.06	86.02	86.6	86.48	86.6	86.68	86.77	86.64	86.56	86.68	86.72	86.39	86.6	86.68	86.6	86.6	86.72	86.72	86.68	87.68	86.02	87.26	85.81	84.78	84.99	89.16	89.16	88.3								
Hipposideros pratti	85.21	84.84	85.3	85.21	84.84	85.12	85.77	85.67	85.77	85.86	85.58	85.67	85.77	85.77	85.49	85.67	85.58	85.58	85.4	85.49	85.86	85.95	85.95	85.58	85.77	85.58	84.65	82.42	82.88	87.16	86.98	85.58	86.79							
Rhinolophus ferrumequinum	86.1	85.73	85.83	85.98	85.86	85.61	86.68	86.48	86.68	86.77	86.68	86.77	86.64	86.77	86.97	86.64	86.23	86.39	86.48	86.48	86.52	86.48	86.48	87.26	85.61	86.89	85.4	84.33	84.04	88.5	88.46	87.01	87.3	90.98						
Rhinolophus macrotis	85.69	85.19	85.49	85.57	85.44	85.11	85.98	85.86	85.98	86.06	85.98	86.06	85.86	86.06	86.19	85.94	85.61	85.69	85.77	85.77	85.81	85.86	85.77	87.14	85.65	86.81	85.4	84.33	83.62	87.88	88.21	86.48	87.47	90.05	95.91					
Rhinolophus pusillus	85.44	84.95	85.25	85.32	85.19	84.86	85.73	85.61	85.73	85.81	85.73	85.81	85.61	85.81	85.94	85.77	85.44	85.53	85.53	85.53	85.65	85.61	85.53	86.52	85.07	86.39	84.9	83.87	83.33	87.34	87.63	86.19	86.97	89.77	95.45	98.39				
Rhinolophus sinicus	85.69	85.11	85.33	85.48	85.36	85.03	85.77	85.65	85.73	85.81	85.73	85.86	85.61	85.81	85.94	85.81	85.44	85.53	85.53	85.53	85.57	85.61	85.53	86.56	85.07	86.23	84.86	83.79	83.29	87.43	87.76	86.06	86.81	89.86	95.45	97.52	97.02			
Rhinolophus pearsonii	85.9	85.32	85.54	85.69	85.57	85.4	85.98	85.81	85.94	86.02	85.94	86.02	85.81	86.02	86.15	85.9	85.65	85.65	85.65	85.65	85.77	85.9	85.81	86.85	85.4	86.56	85.19	84.08	83.71	88.05	88.17	86.56	87.06	90.05	95.66	97.02	96.36	96.94		
Myotis daubentonii	86.7	85.77	86.23	86.33	86.05	85.95	86.6	86.7	86.6	86.7	86.6	86.7	86.6	86.7	86.7	86.7	86.33	86.33	86.14	86.23	86.51	86.6	86.79	87.44	86.7	87.16	86.33	84.65	85.4	86.33	86.6	85.3	86.05	86.6	87.53	87.63	86.98	87.35	86.98	
Sus scrofa	84.95	84.66	84.71	84.82	84.7	84.49	84.57	84.37	84.53	84.62	84.57	84.66	84.49	84.62	84.74	84.37	84.74	84.66	84.66	84.66	84.7	84.9	84.9	85.36	84.86	85.44	84.33	82.59	82.59	86.19	87.14	86.15	85.24	84.19	85.61	85.32	84.99	84.74	84.99	83.72

Supplementary Table S4. Pairwise identities of ACE2 protein sequences between all species in our study. Number indicates the percentage of residues that are identical across the full length of the protein sequence.

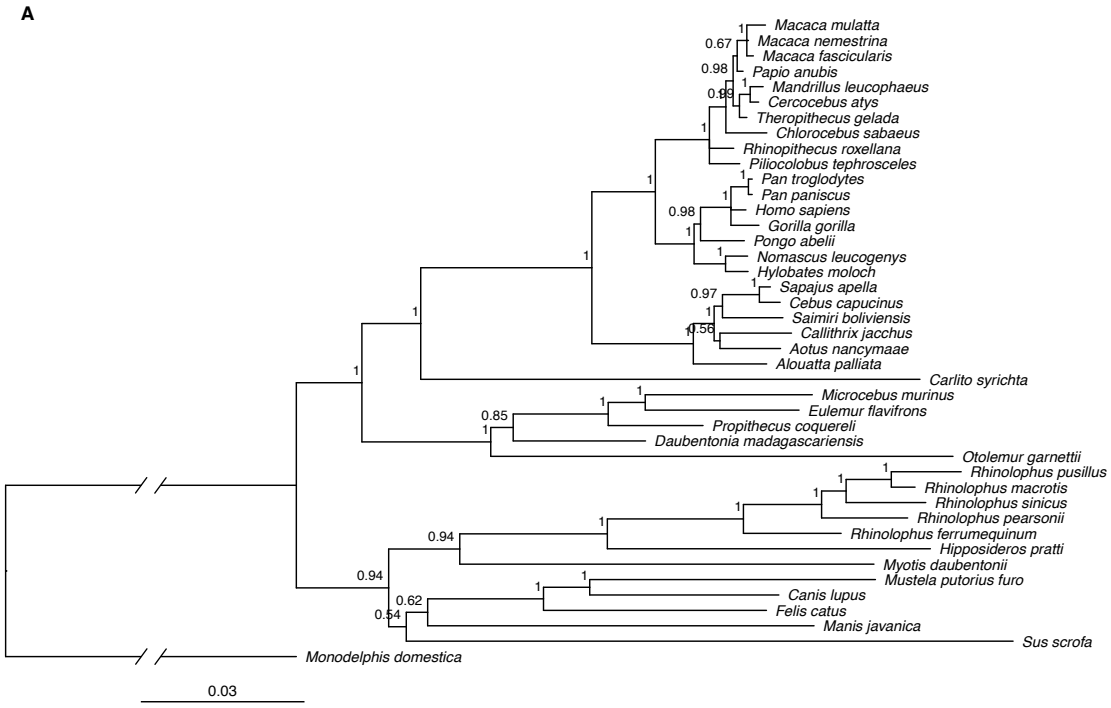
	A.louatta palliata	*A. nancymaae*	*C. capucinus*	*S. apella*	*S. boliviensis*	*C. jacchus*	*C. atys*	*M. leucophaeus*	*M. fascicularis*	*M. nemestrina*	*M. mulatta*	*P. anubis*	*T. gelada*	*R. roxellana*	*C. sabaeus*	*P. tephrosceles*	*G. gorilla*	*H. sapiens*	*P. paniscus*	*P. troglodytes*	*H. moloch*	*N. leucogenys*	*P. abelii*	*D. madagascariensis*	*E. flavifrons*	*M. murinus*	*O. garnettii*	*P. coquereli*	*C. syrichta*	*C. lupus*	*F. catus*	*M. putorius*	*M. javanica*	*S. scrofa*	*H. pratti*	*R. ferrumequinum*	*R. macrotis*	*R. pusillus*	*R. sinicus*	*R. pearsonii*
Aotus nancymaae	96.89																																							
Cebus capucinus	97.02	97.89																																						
Sapajus apella	97.02	97.89	99.51																																					
Saimiri boliviensis	95.9	96.89	97.77	97.52																																				
Callithrix jacchus	95.78	96.77	97.15	97.14	96.27																																			
Cercocebus atys	91.55	92.05	92.06	92.05	91.68	90.68																																		
Mandrillus leucophaeus	91.3	91.8	91.81	91.8	91.43	90.43	99.63																																	
Macaca fascicularis	91.55	92.05	92.06	92.05	91.55	90.68	99.01	98.88																																
Macaca nemestrina	91.68	92.17	92.18	92.17	91.68	90.81	99.13	99.01	99.88																															
Macaca mulatta	91.3	91.8	91.81	91.8	91.3	90.43	98.76	98.63	99.5	99.63																														
Papio anubis	91.55	92.05	92.06	92.05	91.55	90.68	99.01	99.01	99.25	99.38	99.01																													
Theropithecus gelada	91.68	92.17	92.18	92.17	91.8	90.81	99.25	99.25	99.13	99.25	98.88	99.63																												
Rhinopithecus roxellana	91.06	91.3	91.56	91.55	91.18	90.19	98.14	98.01	98.26	98.39	98.01	98.26	98.39																											
Chlorocebus sabaeus	91.3	91.55	91.56	91.55	91.18	90.56	98.26	98.14	98.39	98.51	98.14	98.26	98.39	97.39																										
Piliocolobus tephrosceles	91.3	91.55	91.81	91.8	91.55	90.43	97.76	97.64	97.89	98.01	97.64	97.89	98.01	97.89	97.14																									
Gorilla gorilla	92.42	91.93	92.3	92.3	91.8	91.43	95.28	95.03	95.28	95.4	95.03	95.28	95.4	95.4	94.91	95.16																								
Homo sapiens	92.17	92.17	92.55	92.55	92.05	91.68	95.16	94.91	95.16	95.28	94.91	95.28	95.28	95.28	94.78	95.03	99.01																							
Pan paniscus	92.05	91.93	92.3	92.3	91.8	91.55	95.03	94.78	95.28	95.16	94.78	95.03	95.16	95.16	94.66	94.91	98.76	99.01																						
Pan troglodytes	92.05	91.93	92.3	92.3	91.8	91.55	95.03	94.78	95.03	95.16	94.78	95.03	95.16	95.16	94.66	94.91	98.76	99.01	99.75																					
Hylobates moloch	92.42	92.17	92.3	92.3	91.68	91.43	94.78	94.53	94.78	94.91	94.53	94.78	94.91	94.91	94.29	94.66	98.01	98.01	98.01	98.01																				
Nomascus leucogenys	92.3	91.93	92.06	92.05	91.68	91.18	94.66	94.41	94.53	94.66	94.29	94.53	94.78	94.78	94.16	94.53	98.01	97.76	97.76	97.76	98.76																			
Pongo abelii	91.8	91.68	92.06	92.05	91.68	91.18	95.28	95.03	95.16	95.28	94.91	95.16	95.4	95.4	94.78	95.16	98.14	98.14	97.89	97.89	97.52	97.64																		
Daubentonia madagascariensis	85.84	86.09	86.47	86.34	85.71	85.34	86.83	86.71	86.71	86.83	86.46	86.83	86.96	86.46	86.21	86.34	86.34	86.83	86.58	86.58	86.58	86.21	86.34																	
Eulemur flavifrons	83.23	83.11	83.61	83.48	82.98	82.73	84.35	84.47	84.6	84.47	84.1	84.6	84.6	83.73	84.1	84.35	84.22	84.35	84.35	84.1	84.22	84.1	83.98	87.58																
Microcebus murinus	83.85	83.11	83.86	83.85	83.23	83.35	83.73	83.73	83.85	83.98	83.6	83.73	83.85	83.73	84.1	84.1	84.6	84.1	83.73	83.73	83.85	83.85	83.98	87.95	90.81															
Otolemur garnettii	81.74	81.74	81.99	82.11	81.49	81.12	81.61	81.49	81.74	81.86	81.49	81.74	81.86	81.74	81.49	82.36	81.74	81.86	81.74	81.74	81.61	81.37	81.49	84.6	83.11	83.85														
Propithecus coquereli	84.84	85.09	85.22	85.22	84.84	84.35	85.96	85.96	86.09	86.21	85.84	85.96	86.09	85.47	85.47	86.09	85.47	85.71	85.84	85.84	85.96	85.47	85.22	90.19	91.93	91.68	84.97													
Carlito syrichta	83.73	83.35	83.61	83.73	83.48	83.35	83.85	83.73	83.85	83.98	83.6	83.85	84.1	83.73	83.73	84.35	84.72	84.1	84.22	84.22	84.1	84.35	84.22	82.36	80.99	81.74	79.88	82.11												
Canis lupus	81.99	82.11	82.37	82.24	81.99	81.12	83.48	83.23	83.35	83.48	83.11	83.73	83.6	83.23	83.11	83.35	83.23	83.35	83.35	83.35	83.35	82.86	83.35	82.36	80.25	81.37	80.62	82.48	79.88											
Felis catus	83.73	84.22	84.73	84.6	84.35	83.35	84.84	84.6	84.72	84.84	84.47	84.84	84.97	84.72	84.35	84.84	84.97	85.22	85.34	85.34	85.59	85.22	84.97	84.72	81.86	82.48	81.49	84.35	80.75	90.56										
Mustela putorius furo	81.61	82.24	82.37	82.24	82.11	81.12	82.61	82.36	82.48	82.61	82.36	82.61	82.73	82.61	82.11	82.73	82.86	82.61	82.98	82.98	82.73	82.48	82.24	82.36	79.5	80	80.25	82.61	80.62	89.57	89.69									
Manis javanica	83.6	83.98	84.11	84.1	83.73	82.98	85.22	84.97	85.22	85.34	84.97	85.47	85.47	85.22	84.84	85.47	84.97	84.84	84.97	84.97	84.72	84.6	84.72	84.6	81.49	82.24	81.24	83.98	81.86	86.21	87.33	86.58								
Sus scrofa	81.24	81.12	81.25	81.24	80.62	80.37	81.24	80.99	81.12	81.24	80.87	81.24	81.37	81.24	80.87	80.87	81.61	81.37	81.37	81.37	81.49	81.49	81.61	81.74	80.62	81.24	77.89	81.86	79.25	81.99	83.98	83.85	82.61							
Hipposideros pratti	77.65	77.65	78.49	78.49	78.21	76.82	78.21	78.21	77.93	78.21	77.65	77.93	78.21	77.37	78.21	77.65	77.93	77.37	77.37	77.65	77.65	77.65	77.37	77.93	77.37	76.82	73.74	77.93	74.3	78.49	80.73	78.21	80.73	76.54						
Rhinolophus ferrumequinum	80	80.37	80.75	80.75	80.37	79.75	81.74	81.49	81.61	81.74	81.37	81.74	81.86	81.99	81.49	81.49	81.24	81.49	81.61	81.61	81.37	80.99	81.49	80.12	77.27	77.14	77.64	79.25	76.77	81.74	83.73	80.99	83.11	80.37	83.52					
Rhinolophus macrotis	79.88	80.12	80.75	80.75	80.37	79.5	80.87	80.62	80.75	80.87	80.5	80.87	80.99	80.87	80.62	80.62	80.62	80.87	80.99	80.99	80.75	80.37	80.75	80.5	77.76	78.51	78.26	79.88	76.02	81.74	84.35	81.12	83.73	80.5	84.36	92.42				
Rhinolophus pusillus	79.88	79.88	80.5	80.5	79.88	79.25	80.37	80.12	80.25	80.37	80	80.37	80.5	80.37	80.37	80.12	80.37	80.5	80.62	80.62	80.5	80.25	80.37	79.75	77.39	78.14	77.52	79.25	76.27	81.61	84.1	81.49	83.35	80.99	84.08	91.8	96.77			
Rhinolophus sinicus	79.88	80	80.63	80.62	80	79.38	80.25	80	80.12	80.25	79.88	80.25	80.37	80.25	80.37	80	80	80.12	80.25	80.25	80	79.75	80	79.5	77.14	77.39	77.14	78.88	76.02	80.75	83.35	80.25	82.24	79.63	84.08	92.3	95.28	94.29		
Rhinolophus pearsonii	80.87	80.87	81.5	81.49	81.12	80.37	81.12	80.87	80.99	81.12	80.75	81.12	81.24	81.12	80.87	80.87	81.37	81.37	81.49	81.49	81.49	81.12	81.24	80.37	77.76	78.39	78.26	79.88	77.27	82.11	84.22	81.24	82.98	80.37	83.8	92.3	94.91	93.42	94.78	
Myotis daubentonii	79.89	79.89	80.17	80.17	79.89	78.77	80.17	80.17	79.89	80.17	79.61	79.89	80.17	79.33	79.89	79.61	79.33	78.77	78.77	79.05	79.05	79.05	78.77	80.17	79.33	78.49	77.09	79.61	77.09	77.37	80.45	78.77	79.05	77.09	79.05	77.93	79.89	79.05	78.77	78.21

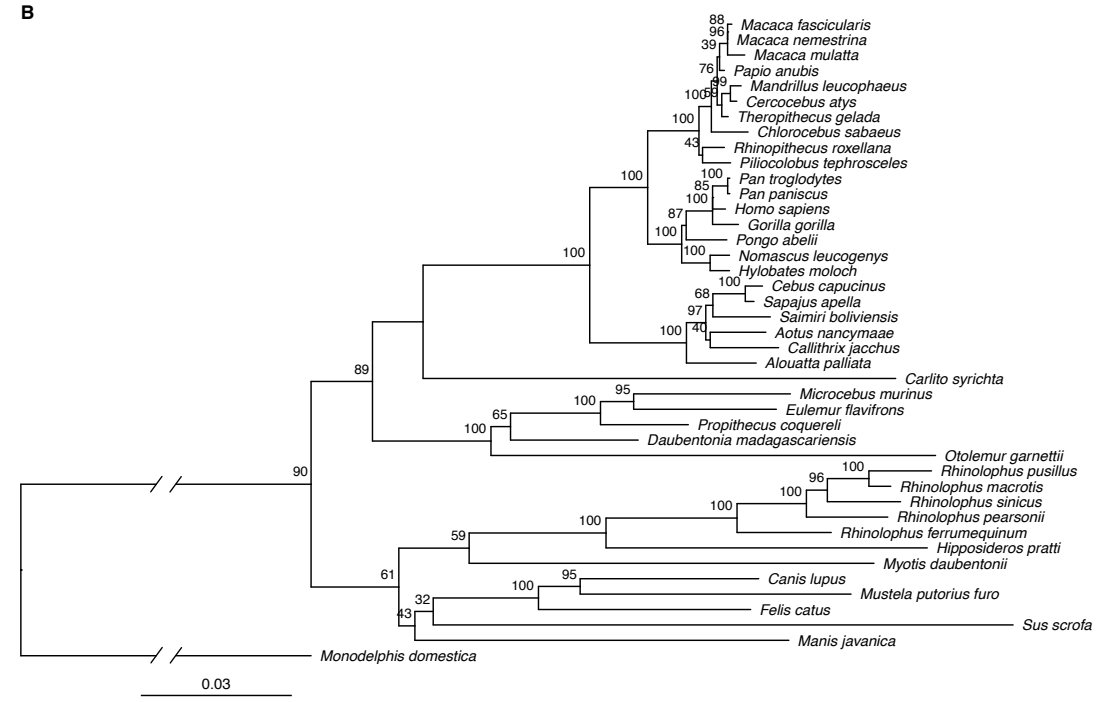
Supplementary Table S5. Pairwise similarities of ACE2 protein sequences between all species in our study. Number indicates the percentage of residues that are similar (score ≥1 in the BLOSUM62 matrix) across the full length of the protein sequence.

	Aloualta pallata	*A. nancymaae*	*C. capucinus*	*S. apella*	*S. boliviensis*	*C. jacchus*	*C. atys*	*M. leucophaeus*	*M. fascicularis*	*M. nemestrina*	*M. mulatta*	*P. anubis*	*T. gelada*	*R. roxellana*	*C. sabaeus*	*P. tephrosceles*	*G. gorilla*	*H. sapiens*	*P. paniscus*	*P. troglodytes*	*H. moloch*	*N. leucogenys*	*P. abelii*	*D. madagascar-iensis*	*E. flavifrons*	*M. murinus*	*O. garnettii*	*P. coquereli*	*C. syrichta*	*C. lupus*	*F. catus*	*M. putorius*	*M. javanica*	*S. scrofa*	*H. pratti*	*R. ferrum-equinum*	*R. macrotis*	*R. pusillus*	*R. sinicus*	*R. pearsonii*
Aotus nancymaae	98.26																																							
Cebus capucinus	98.63	98.63																																						
Sapajus apella	98.76	98.76	99.88																																					
Saimiri boliviensis	97.76	98.01	98.39	98.51																																				
Callithrix jacchus	97.76	97.89	98.26	98.39	97.76																																			
Cercocebus atys	96.27	96.15	96.15	96.27	95.78	95.4																																		
Mandrillus leucophaeus	96.02	95.9	95.9	96.02	95.65	95.16	99.63																																	
Macaca fascicularis	96.52	96.4	96.15	96.27	96.02	95.53	99.38	99.25																																
Macaca nemestrina	96.52	96.4	96.15	96.27	96.02	95.53	99.38	99.25	100																															
Macaca mulatta	96.27	96.15	95.9	96.02	95.78	95.28	99.13	99.01	99.75	99.75																														
Papio anubis	96.65	96.4	96.27	96.4	96.15	95.65	99.38	99.25	99.75	99.75	99.5																													
Theropithecus gelada	96.65	96.52	96.4	96.52	96.27	95.78	99.5	99.38	99.63	99.63	99.38	99.88																												
Rhinopithecus roxellana	96.4	96.02	96.15	96.27	96.02	95.53	98.63	98.51	99.01	99.01	98.76	99.01	99.13																											
Chlorocebus sabaeus	96.02	95.65	95.65	95.78	95.4	94.91	98.88	98.76	99.01	99.01	98.76	98.76	98.88	98.26																										
Piliocolobus tephrosceles	96.27	95.9	96.02	96.15	95.9	95.4	98.51	98.39	98.88	98.88	98.63	98.88	99.01	99.13	98.14																									
Gorilla gorilla	96.27	95.53	95.9	96.02	95.65	95.4	97.52	97.27	97.76	97.76	97.52	97.76	97.89	98.01	97.14	97.89																								
Homo sapiens	96.02	95.53	95.9	96.02	95.65	95.4	97.52	97.27	97.76	97.76	97.52	97.64	97.89	98.01	97.14	97.89	99.5																							
Pan paniscus	95.9	95.4	95.78	95.9	95.53	95.4	97.52	97.27	97.64	97.64	97.39	97.64	97.76	97.89	97.14	97.76	99.38	99.38																						
Pan troglodytes	95.9	95.4	95.78	95.9	95.53	95.4	97.52	97.27	97.64	97.64	97.39	97.64	97.76	97.89	97.14	97.76	99.38	99.38	100																					
Hylobates moloch	96.15	95.65	96.02	96.15	95.78	95.53	97.64	97.39	97.89	97.89	97.64	97.89	98.01	98.14	97.27	98.01	99.13	99.13	99.01	99.01																				
Nomascus leucogenys	96.27	95.78	96.15	96.27	95.9	95.65	97.76	97.52	98.01	98.01	97.76	98.01	98.14	98.26	97.39	98.14	99.25	99.25	99.13	99.13	99.75																			
Pongo abelii	96.27	95.78	96.15	96.27	95.9	95.65	97.76	97.52	98.01	98.01	97.76	98.01	98.14	98.26	97.39	98.14	99.25	99.25	99.13	99.13	99.38	99.5																		
Daubentonia madagascarien	92.8	92.55	92.67	92.8	92.17	92.05	93.29	93.17	93.54	93.54	93.29	93.66	93.79	93.42	92.8	93.29	93.04	93.29	92.92	92.92	93.17	93.17	93.29																	
Eulemur flavifrons	91.8	91.93	91.93	92.05	91.68	91.3	92.55	92.42	93.04	93.04	92.8	92.92	92.8	92.3	92.17	92.42	91.8	92.05	91.68	91.68	92.17	92.17	92.05	94.16																
Microcebus murinus	91.3	91.18	91.3	91.43	91.06	90.68	91.8	91.68	92.05	92.05	91.8	92.17	92.3	92.3	92.05	92.67	92.05	92.05	91.68	91.68	91.8	91.93	92.05	94.04	95.16															
Otolemur garnettii	89.69	89.32	89.32	89.44	89.19	88.82	89.19	89.07	89.32	89.32	89.07	89.44	89.57	89.57	88.94	89.94	89.44	89.44	89.07	89.07	89.32	89.32	89.44	91.8	90.81	91.68														
Propithecus coquerelli	91.93	92.3	91.8	91.93	91.8	91.43	92.92	92.8	93.17	93.17	92.92	93.29	93.42	92.8	92.55	93.29	92.55	92.8	92.67	92.67	92.8	92.8	92.8	94.91	96.27	96.15	91.55													
Carlito syrichta	91.43	90.93	91.43	91.55	91.3	91.18	91.18	91.06	91.43	91.43	91.18	91.55	91.68	91.68	90.93	92.05	92.05	91.8	91.93	91.93	91.8	91.8	91.68	90.56	89.19	89.81	88.57	89.94												
Canis lupus	91.3	91.06	91.18	91.3	90.93	90.56	92.05	91.8	92.17	92.17	91.93	92.3	92.42	92.3	91.55	92.3	91.8	91.68	91.68	91.68	92.05	91.93	92.05	91.43	89.94	90.43	89.57	91.06	89.19											
Felis catus	92.42	92.17	92.3	92.42	92.17	91.55	92.55	92.3	92.67	92.67	92.42	92.8	92.92	92.92	91.93	92.92	92.3	92.3	92.17	92.17	92.55	92.42	92.55	92.67	91.3	91.43	90.56	92.42	89.57	94.53										
Mustela putorius furo	91.55	91.18	91.18	91.3	91.18	90.68	91.8	91.55	91.8	91.8	91.43	91.93	92.05	91.93	91.3	92.05	91.8	91.55	91.68	91.68	91.68	91.55	91.55	91.43	90.43	89.81	89.19	91.43	89.32	94.16	95.03									
Manis javanica	91.3	91.06	91.06	91.18	90.81	90.43	91.55	91.3	91.68	91.68	91.43	91.8	91.93	91.93	91.18	92.05	91.55	91.3	91.18	91.18	91.43	91.55	91.55	92.3	90.06	90.93	89.69	91.06	88.94	91.93	92.42	93.04								
Sus scrofa	89.94	89.81	90.06	90.19	89.57	89.57	90.68	90.43	90.81	90.81	90.56	90.93	90.93	90.93	90.43	90.56	90.68	90.68	90.56	90.56	90.81	90.93	90.81	90.56	90.19	90.31	88.32	90.31	87.83	90.56	91.93	90.81	90.43							
Hipposideros pratti	86.31	85.75	86.31	86.31	86.03	85.47	86.87	86.87	86.87	86.87	86.31	86.87	86.87	86.31	86.59	86.03	86.03	85.75	85.75	85.75	86.31	86.31	85.75	87.15	86.87	86.03	84.36	86.31	82.96	87.43	87.99	86.59	87.71	85.75						
Rhinolophus ferrumequinum	90.19	90.06	90.19	90.31	89.94	89.69	90.81	90.56	90.81	90.81	90.56	90.93	91.06	90.93	90.56	90.81	90.31	90.31	90.19	90.19	90.31	90.43	90.43	89.57	88.7	88.57	88.32	89.19	87.08	89.81	91.18	89.32	89.94	89.32	92.18					
Rhinolophus macrotis	89.94	89.69	90.06	90.19	89.81	89.32	90.56	90.31	90.56	90.56	90.31	90.68	90.81	90.68	90.31	90.56	90.06	90.06	89.94	89.94	90.06	90.19	90.06	89.69	88.7	89.07	88.82	89.44	86.58	89.94	91.06	89.57	90.43	88.7	91.34	95.65				
Rhinolophus pusillus	90.19	89.94	90.31	90.43	89.81	89.57	90.56	90.31	90.56	90.56	90.31	90.68	90.81	90.68	90.56	90.56	89.94	90.06	89.94	89.94	89.94	90.06	90.06	89.44	88.45	88.82	88.32	88.94	86.83	89.81	90.81	89.81	90.19	88.82	91.06	95.53	97.89			
Rhinolophus sinicus	90.43	90.19	90.56	90.68	89.94	89.81	90.19	89.94	90.19	90.19	89.94	90.31	90.43	90.31	90.19	90.19	89.69	89.69	89.57	89.57	89.69	89.81	89.69	89.07	88.2	88.32	87.45	88.82	86.34	89.19	90.43	88.94	89.19	88.57	89.11	95.03	97.39	97.02		
Rhinolophus pearsonii	90.56	90.31	90.68	90.81	90.43	90.19	91.06	90.81	91.06	91.06	90.81	91.18	91.3	91.18	90.81	91.06	90.56	90.56	90.43	90.43	90.56	90.68	90.56	89.69	88.45	88.82	88.7	89.44	86.96	90.81	91.3	89.69	89.69	88.82	89.94	95.53	97.39	96.27	97.14	
Myotis daubentonii	87.43	86.87	86.87	87.15	86.59	85.75	87.71	87.71	87.71	87.71	87.15	87.71	87.71	87.15	87.43	86.87	86.31	86.03	86.03	86.03	86.31	86.31	86.03	88.55	88.83	87.71	86.59	88.27	85.75	87.15	88.27	87.99	87.71	87.71	87.15	88.27	87.99	88.55	87.71	86.87

Supplementary Table S6. Full results of the codeml analyses of adaptive evolution across *ACE2* gene sequences.

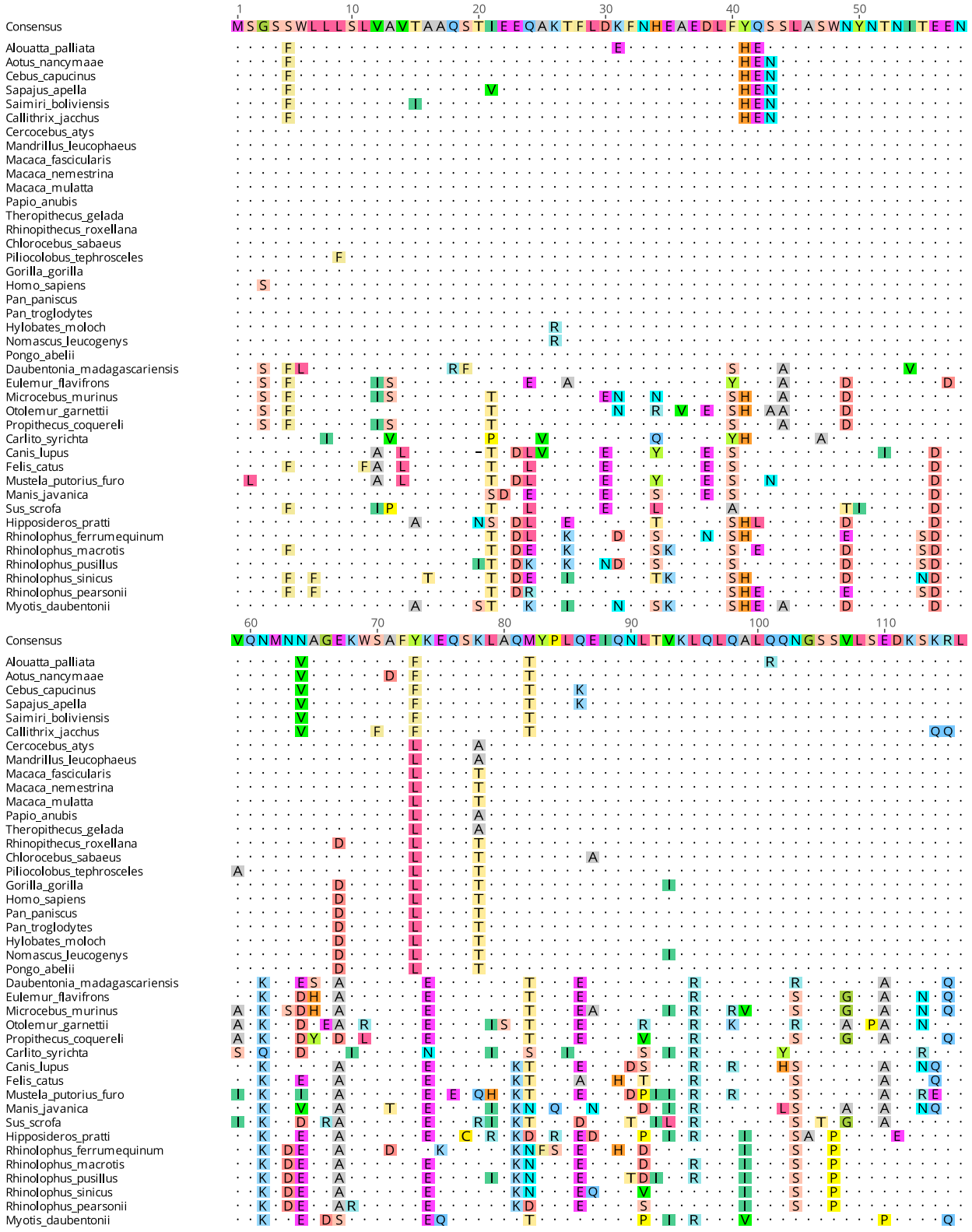
codeml analysis	Foreground branch	Model	kappa	treeLength	number of parameters	omega	proportion	lnL	LRT	p	positively selected sites
branch-site model	platyrrhine	null	3.08706	3.33363	79	background: $\omega 0$ = 0.07549, $\omega 1$ = 1.00000, $\omega 2a$ = 0.07549, $\omega 2b$ = 1.00000; foreground: $\omega 0$ = 0.07549, $\omega 1$ = 1.00000, $\omega 2a$ = 1.00000, $\omega 2b$ = 1.00000	p0 = 0.63315, p1 = 0.35752, p2a = 0.00596, p2b = 0.00337	-15583.14271			
branch-site model	platyrrhine	alternative	3.08849	3.3349	80	background: $\omega 0$ = 0.07584, $\omega 1$ = 1.00000, $\omega 2a$ = 0.07584, $\omega 2b$ = 1.00000; foreground: $\omega 0$ = 0.07584, $\omega 1$ = 1.00000, $\omega 2a$ = 6.21808, $\omega 2b$ = 6.21808	p0 = 0.63821, p1 = 0.35912, p2a = 0.00171, p2b = 0.00096	-15582.82647	0.632472	0.4264500154	n/a
branch-site model	bats	null	3.08122	3.33427	79	background: $\omega 0$ = 0.07232, $\omega 1$ = 1.00000, $\omega 2a$ = 0.07232, $\omega 2b$ = 1.00000; foreground: $\omega 0$ = 0.07232, $\omega 1$ = 1.00000, $\omega 2a$ = 1.00000, $\omega 2b$ = 1.00000	p0 = 0.58383, p1 = 0.32072, p2a = 0.06161, p2b = 0.03384	-15579.5976			
branch-site model	bats	alternative	3.12988	3.35579	80	background: $\omega 0$ = 0.07530, $\omega 1$ = 1.00000, $\omega 2a$ = 0.07530, $\omega 2b$ = 1.00000; foreground: $\omega 0$ = 0.07530, $\omega 1$ = 1.00000, $\omega 2a$ = 10.53445, $\omega 2b$ = 10.53445	p0 = 0.62612, p1 = 0.33778, p2a = 0.02345, p2b = 0.01265	-15558.2729	42.649394	0	7L (0.917), **24Q (0.998**)**, 27T (0.718), **31E (0.959*)**, 34H (0.887), **35E (0.974*)**, 42E (0.652), 91L (0.888), **298V (0.959*)**, 478W (0.505), 483E (0.768), 549E (0.807), 565P (0.939), **568L (0.998**)**, 569A (0.764), **575G (0.965*)**, 658V (0.810), 771K (0.570)
branch-site model	catarrhines	null	3.08696	3.33682	79	background: $\omega 0$ = 0.07190, $\omega 1$ = 1.00000, $\omega 2a$ = 0.07190, $\omega 2b$ = 1.00000; foreground: $\omega 0$ = 0.07190, $\omega 1$ = 1.00000, $\omega 2a$ = 1.00000, $\omega 2b$ = 1.00000	p0 = 0.59837, p1 = 0.33784, p2a = 0.04077, p2b = 0.02302	-15581.0318			
branch-site model	catarrhines	alternative	3.10444	3.33652	80	background: $\omega 0$ = 0.07498, $\omega 1$ = 1.00000, $\omega 2a$ = 0.07498, $\omega 2b$ = 1.00000; foreground: $\omega 0$ = 0.07498, $\omega 1$ = 1.00000, $\omega 2a$ = 8.98776, $\omega 2b$ = 8.98776	p0 = 0.63077, p1 = 0.35602, p2a = 0.00845, p2b = 0.00477	-15573.75876	14.546074	0.000136773355	206D (0.786), **249M (0.962*)**, 338D (0.581), **653A (0.958*)**, 657K (0.511), **658V (0.957*)**, 706M (0.827), 729P (0.798), 732G (0.616), 788K (0.581)
branch-site model	strepsirrhines	null	3.0744	3.34127	79	background: $\omega 0$ = 0.06994, $\omega 1$ = 1.00000, $\omega 2a$ = 0.06994, $\omega 2b$ = 1.00000; foreground: $\omega 0$ = 0.06994, $\omega 1$ = 1.00000, $\omega 2a$ = 1.00000, $\omega 2b$ = 1.00000	p0 = 0.59047, p1 = 0.30920, p2a = 0.06585, p2b = 0.03448	-15576.45584			
branch-site model	strepsirrhines	alternative	3.08067	3.34233	80	background: $\omega 0$ = 0.07170, $\omega 1$ = 1.00000, $\omega 2a$ = 0.07170, $\omega 2b$ = 1.00000; foreground: $\omega 0$ = 0.07170, $\omega 1$ = 1.00000, $\omega 2a$ = 1.38404, $\omega 2b$ = 1.38404	p0 = 0.60671, p1 = 0.31603, p2a = 0.05080, p2b = 0.02646	-15576.03928	0.83312	0.3613718973	n/a
cladeC model	n/a	M2a_rel (cla	2.99711	3.34639	80	$\omega 0$ = 0.03668, $\omega 1$ = 1.00000, $\omega 2$ = 0.36059	p0 = 0.50433, p1 = 0.27145, p2 = 0.22423	-15575.33101			
cladeC model	n/a	cladeC	3.07137	3.34517	83	$\omega 0$ = 0.05915, $\omega 1$ = 1.00000, $\omega 2$ = 0.08051, $\omega 3$ = 1.12260, $\omega 4$ = 0.23634, $\omega 5$ = 1.34632	p0 = 0.58058, p1 = 0.33089, p2-5 = 0.08853	-15561.96782	26.72638	0.000006718510	n/a

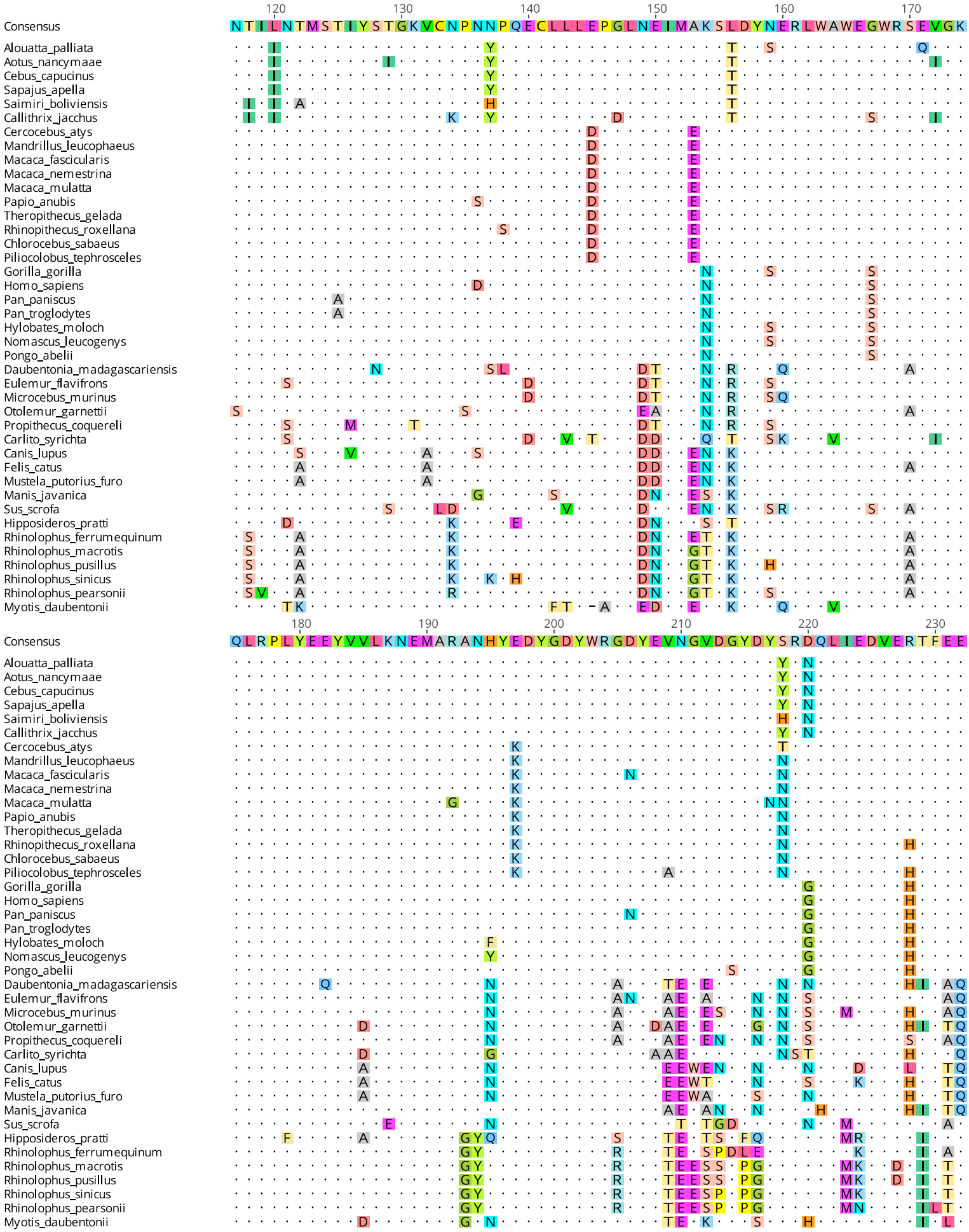




Supplemental Figure S1. *ACE2* gene trees built with (A) a Bayesian approach (Mr Bayes[3]) and (B) a maximum likelihood approach (RAxML[4]), using *Monodelphis domestica* as an outgroup. Node labels indicate (A) posterior probabilities or (B) bootstrap support. Scale bars indicate substitutions per site.

Supplementary Figure S2. Full-length alignment of ACE2 protein sequences.

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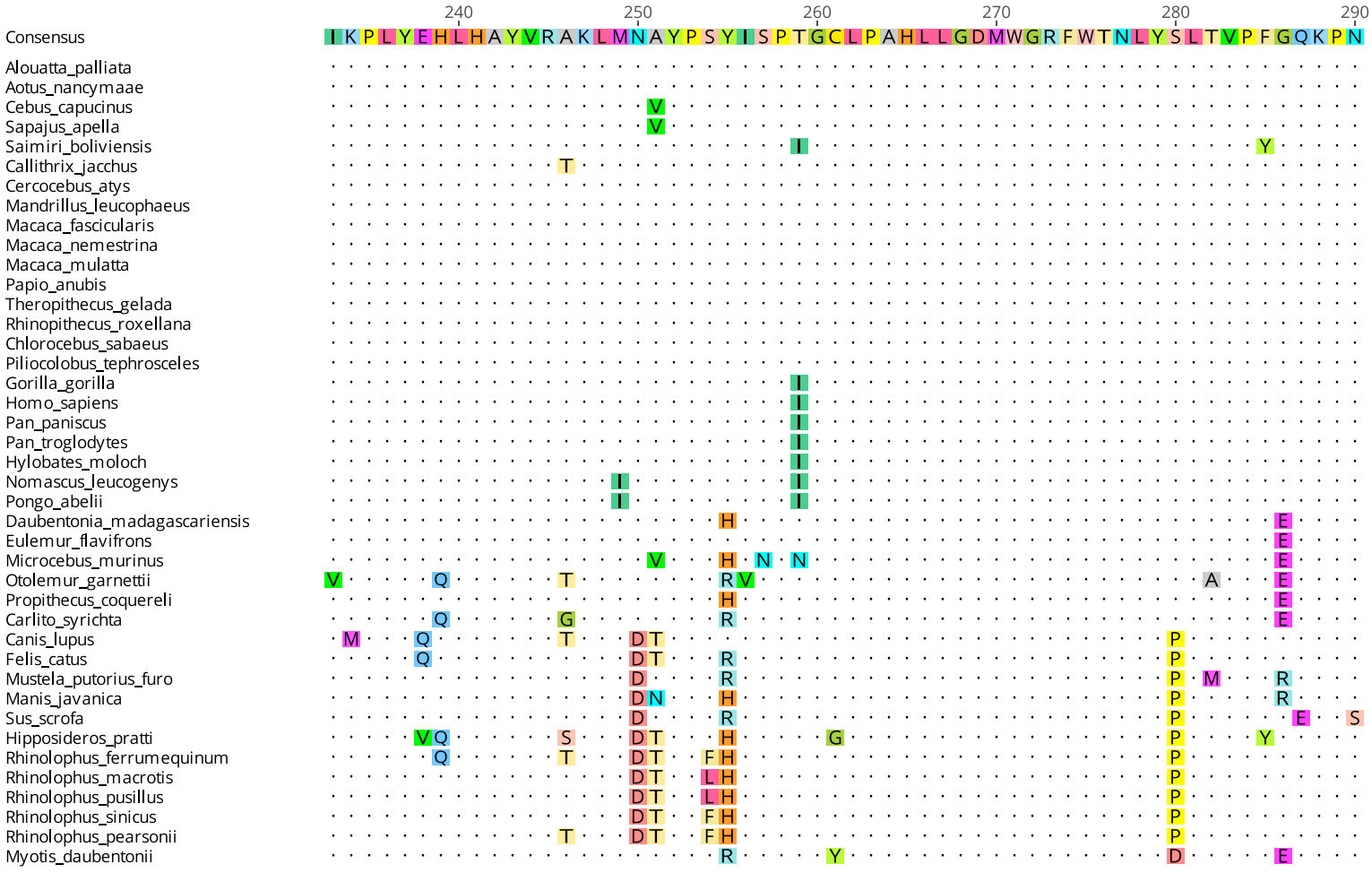
Alouatta_palliata
Aotus_nancymaae
Cebus_capucinus
Sapajus_apella
Saimiri_boliviensis
Callithrix_jacchus
Cercocebus_atys
Mandrillus_leucophaeus
Macaca_fascicularis
Macaca_nemestrina
Macaca_mulatta
Papio_anubis
Theropithecus_gelada
Rhinopithecus_roxellana
Chlorocebus_sabaeus
Piliocolobus_tephrosceles
Gorilla_gorilla
Homo_sapiens
Pan_paniscus
Pan_troglodytes
Hylobates_moloch
Nomascus_leucogenys
Pongo_abelii
Daubentonia_madagascariensis
Eulemur_flavifrons
Microcebus_murinus
Otolemur_garnettii
Propithecus_coquereli
Carlito_syrichta
Canis_lupus
Felis_catus
Mustela_putorius_furo
Manis_javanica
Sus_scrofa
Hipposideros_pratti
Rhinolophus_ferrumequinum
Rhinolophus_macrotis
Rhinolophus_pusillus
Rhinolophus_sinicus
Rhinolophus_pearsonii
Myotis_daubentonii
180 190 200 210 220 230
Consensus QLRPLYEEYVVLKNEMARANHYEDYGDYWRGDYEVNGVDGYDYSRDQLIEDVERTFEE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Consensus
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Aotus_nancymaae
Cebus_capucinus
Sapajus_apella
Saimiri_boliviensis
Callithrix_jacchus
Cercocebus_atys
Mandrillus_leucophaeus
Macaca_fascicularis
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Macaca_mulatta
Papio_anubis
Theropithecus_gelada
Rhinopithecus_roxellana
Chlorocebus_sabaeus
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Homo_sapiens
Pan_paniscus
Pan_troglodytes
Hylobates_moloch
Nomascus_leucogenys
Pongo_abelii
Daubentonia_madagascariensis
Eulemur_flavifrons
Microcebus_murinus
Otolemur_garnettii
Propithecus_coquereli
Carlito_syrichta
Canis_lupus
Felis_catus
Mustela_putorius_furo
Manis_javanica
Sus_scrofa
Hipposideros_pratti
Rhinolophus_ferrumequinum
Rhinolophus_macrotis
Rhinolophus_pusillus
Rhinolophus_sinicus
Rhinolophus_pearsonii
Myotis_daubentonii
300 310 320 330 340
Consensus
IDVTDAMVNQAWDAQRIFKEAEKFFVSVGLPNMTQGFWENSMLTEPGDGQKVVCHPTA

350 360 370 380 390 400
Consensus WDLGKGDFRIXMCTKVTMDDFLTAHHEMGHIQYDMAYAAQPFLLRNGANEGFHEAVGE
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Aotus_nancymaae
Cebus_capucinus
Sapajus_apella
Saimiri_boliviensis
Callithrix_jacchus
Cercocebus_atys
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Gorilla_gorilla
Homo_sapiens
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Pan_troglodytes
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Nomascus_leucogenys
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Otolemur_garnettii
Propithecus_coquereli
Carlito_syrichta
Canis_lupus
Felis_catus
Mustela_putorius_furo
Manis_javanica
Sus_scrofa
Hipposideros_pratti
Rhinolophus_ferrumequinum
Rhinolophus_macrotis
Rhinolophus_pusillus
Rhinolophus_sinicus
Rhinolophus_pearsonii
Myotis_daubentonii
410 420 430 440 450 460
Consensus IMSLSAATPKHLKSIGLLSPDFQEDNETEINFLLKQALTIVGTLPFTYMLEKWRWMVF
Alouatta_palliata
Aotus_nancymaae
Cebus_capucinus
Sapajus_apella
Saimiri_boliviensis
Callithrix_jacchus
Cercocebus_atys
Mandrillus_leucophaeus
Macaca_fascicularis
Macaca_nemestrina
Macaca_mulatta
Papio_anubis
Theropithecus_gelada
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Mustela_putorius_furo
Manis_javanica
Sus_scrofa
Hipposideros_pratti
Rhinolophus_ferrumequinum
Rhinolophus_macrotis
Rhinolophus_pusillus
Rhinolophus_sinicus
Rhinolophus_pearsonii
Myotis_daubentonii

470 480 490 500 510 520
Consensus K G E I P K D Q W M K K W W E M K R E I V G V V E P V P H D E T Y C D P A S L F H V S N D Y S F I R Y Y T R T L Y Q
Alouatta_palliata
Aotus_nancymaae
Cebus_capucinus
Sapajus_apella
Saimiri_boliviensis
Callithrix_jacchus
Cercocebus_atys
Mandrillus_leucophaeus
Macaca_fascicularis
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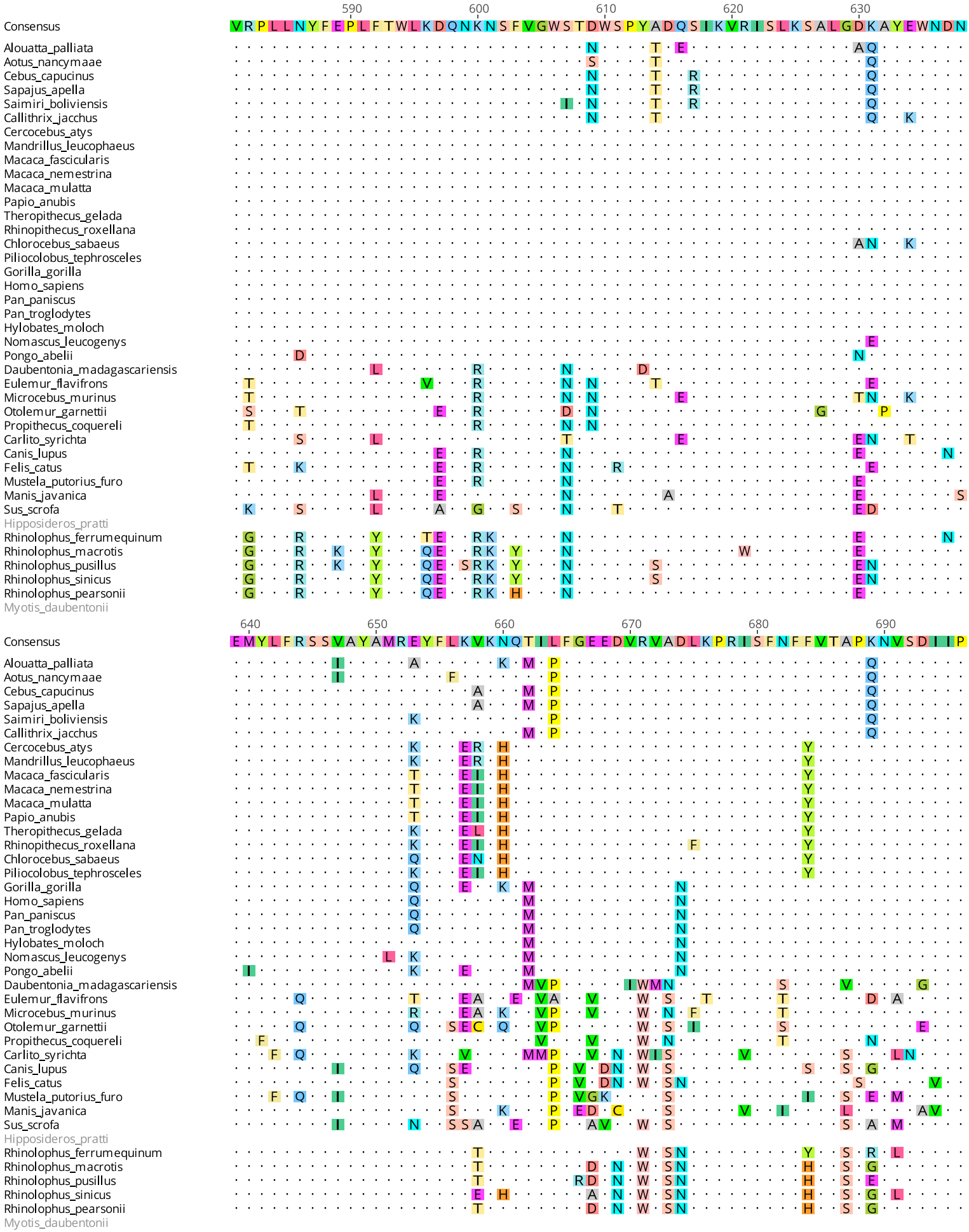
Rhinolophus_macrotis
Rhinolophus_pusillus
Rhinolophus_sinicus
Rhinolophus_pearsonii
Myotis_daubentonii
530 540 550 560 570 580
Consensus F Q F Q E A L C Q A A K H E G P L H K C D I S N S T E A G Q K L L N M L R L G K S E P W T L A L E N V V G A K N M N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Aotus_nancymaae
Cebus_capucinus
Sapajus_apella
Saimiri_boliviensis
Callithrix_jacchus
Cercocebus_atys
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Propithecus_coquereli
Carlito_syrichta
Canis_lupus
Felis_catus
Mustela_putorius_furo
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Sus_scrofa
Hipposideros_pratti
Rhinolophus_ferrumequinum
Rhinolophus_macrotis
Rhinolophus_pusillus
Rhinolophus_sinicus
Rhinolophus_pearsonii
Myotis_daubentonii
640 650 660 670 680 690
Consensus EMYLFRSSVAYAMREYFLKVKNQTILFGEEDVRVADLKPRISFNFFVTAPKNVSDIIP
Alouatta_palliata
Aotus_nancymaae
Cebus_capucinus
Sapajus_apella
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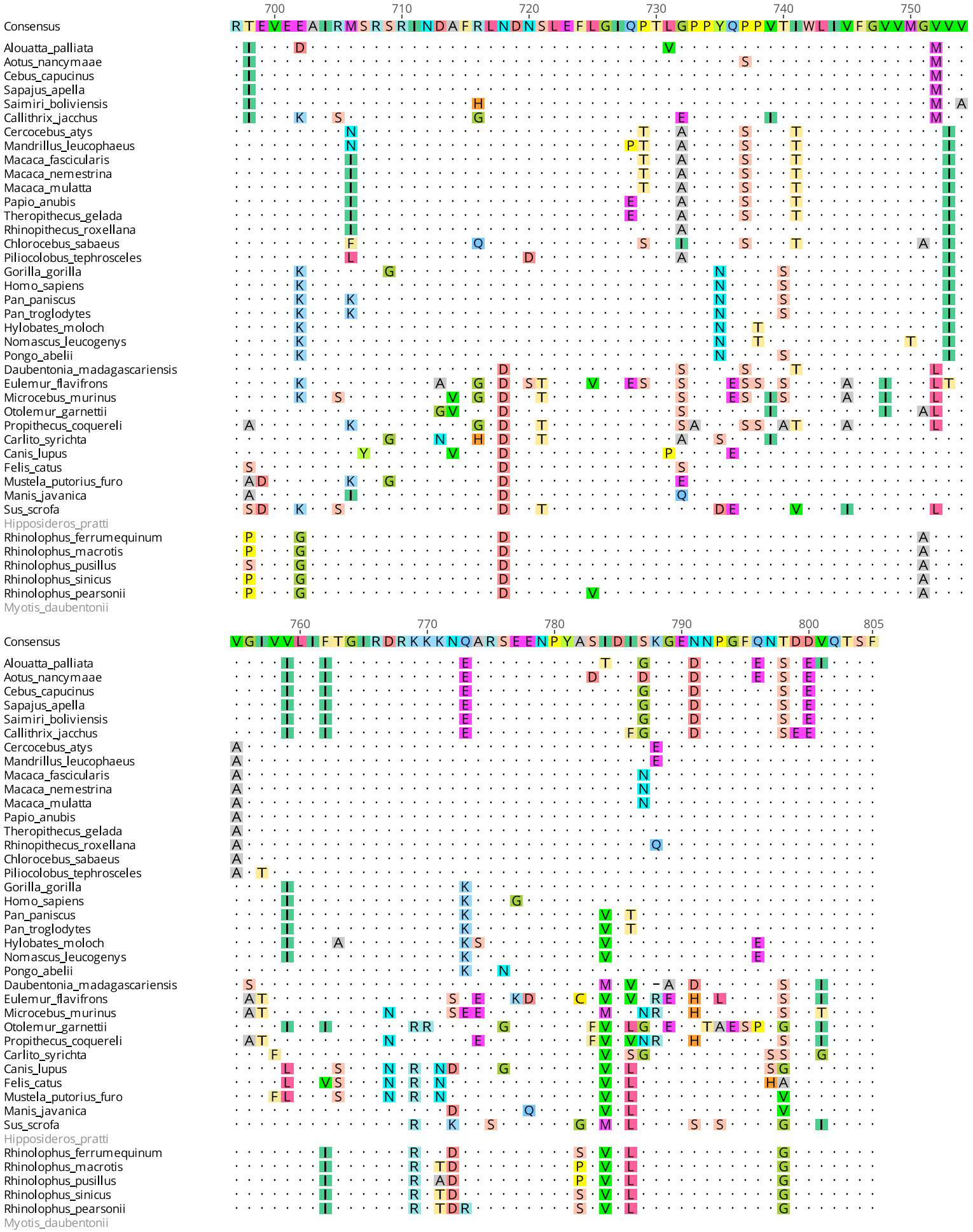
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Saimiri_boliviensis
Callithrix_jacchus
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Rhinolophus_pusillus
Rhinolophus_sinicus
Rhinolophus_pearsonii
Myotis_daubentonii
760 770 780 790 800 805
Consensus
Alouatta_palliata
Aotus_nancymaae
Cebus_capucinus
Sapajus_apella
Saimiri_boliviensis
Callithrix_jacchus
Cercocebus_atys
Mandrillus_leucophaeus
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Rhinolophus_pusillus
Rhinolophus_sinicus
Rhinolophus_pearsonii
Myotis_daubentonii

References

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4. Stamatakis, A. RAxML version 8: a tool for phylogenetic analysis and post-analysis of large phylogenies. *Bioinformatics* **30**, 1312–1313 (2014).