

Small Animal Model ACE2 and Antibody Response Comparison

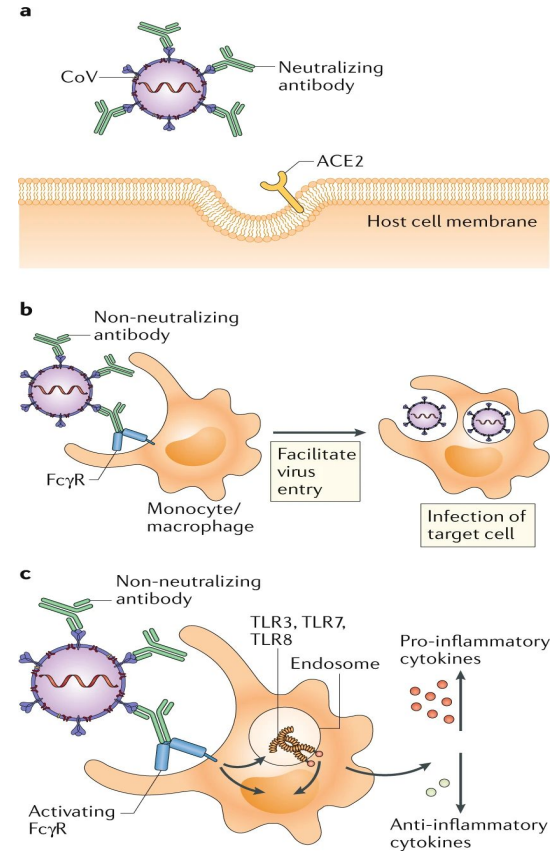
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Outline

- Efficacy of RBD nAb in vivo in Syrian hamsters shows promise for human studies
- Syrian hamsters as a model for studying respiratory diseases in humans
- Small animal model ACE2 sequences showed varied relationships
- Comparison of ACE2 sequences in humans vs. small animal models
- SARS-CoV-2 Antibody Neutralizing Potencies
- Future neutralizing antibody work using small animal models

Neutralizing antibodies to the cause of SARS-CoV-2 can help guide vaccine design

- Enrolled recovered SARS-CoV-2 patients (Rogers et al, 2020)
- Isolated potent neutralizing antibodies (nAbs)
 - Two epitopes on the RBD and non-RBD epitopes on the spike protein
- Found an nAb to SARS-CoV-2 and demonstrated its efficacy in small animals
 - Likely useful in medical interventions in humans



Mechanism of neutralizing antibodies (Iwasaki and Yang, 2020)

Efficacy of RBD nAb in vivo in Syrian hamsters shows promise for human studies

- The most potent Abs target the RBD-A epitope, which overlaps with the ACE2 binding site (Rogers et al, 2020)
- RBD-A nAbs were able to compete with ACE2
- Vaccine development should focus on the RBD, as there are strong nAb responses visible (Rogers et al, 2020)
- Multiple small animal model studies on SARS-CoV-2 found promising nAbs

How similar are the ACE2 receptors for SARS-CoV-2 within small-animal models compared to humans with reference to neutralizing antibody activity?

- Small animal models used for biomedical research to test therapies
 - Done prior to human clinical trials
- Most commonly used small animal models:
 - Syrian hamsters, mice, rats, guinea pigs, monkeys, rabbits, ferrets



Syrian hamster in the lab (Cohen, 2020)

Syrian hamsters as a model for studying diseases in humans

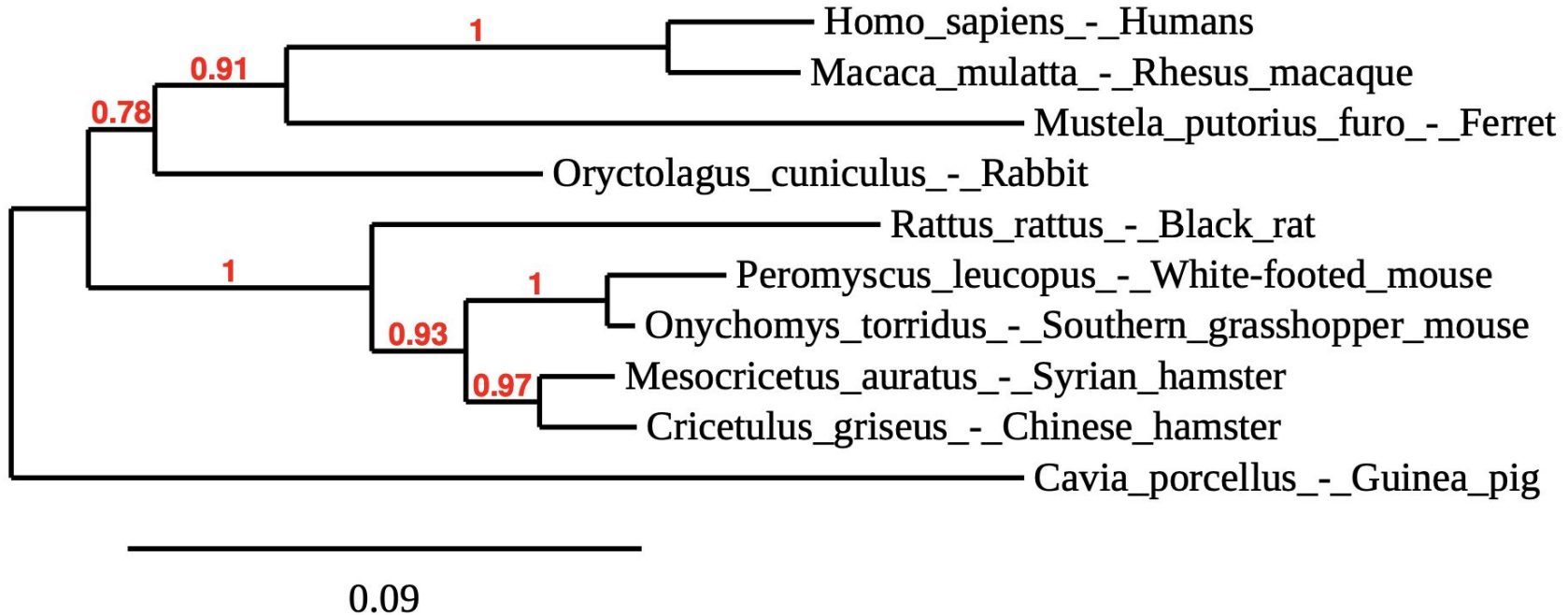
- Our species have similar immune responses to infectious pathogens
- This makes them ideal for studying
 - Pathogenesis of parasitic, viral, and bacterial infections
 - The efficacy and interactions of medications and vaccines
- Comparing our ACE2 sequences is aimed at examining this similarity



Female S. hamster named Vince (Jennison, 2006)

Syrian hamsters as a model... (Maio et al. 2019)

Small animal model ACE2 sequences showed varied relationships

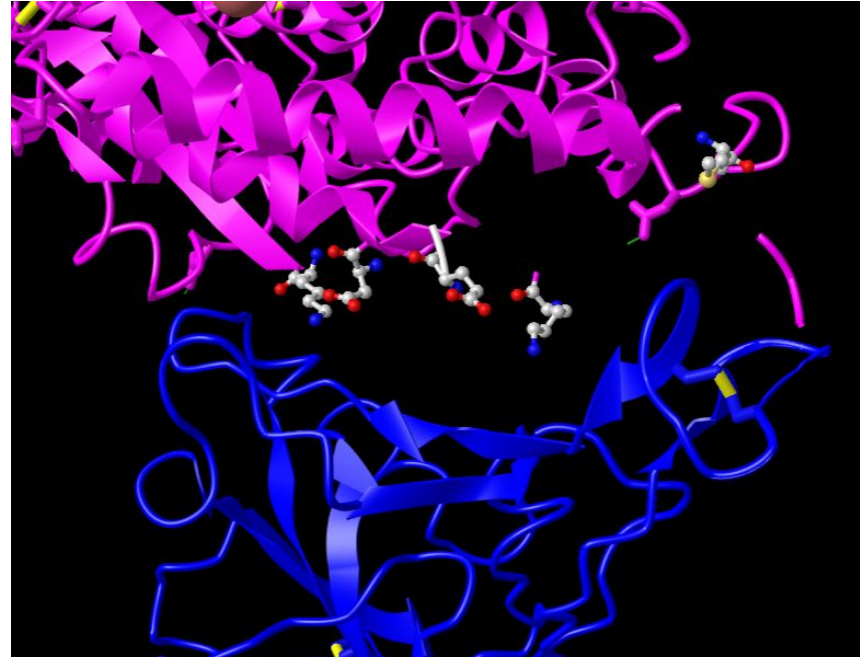


Visualization of Human Critical Residues was Made Using iCn3D Viewer

Here the human ACE2 is in pink and the SARS-CoV-2 spike protein in blue.

This was done by selecting the following residues & displaying them in the ball and stick style with atom colouring.

- K31
- E35
- D38
- M82
- K353



ACE2 percent sequence similarities show wide range of similarity to Syrian hamsters

ACE2 Sequence Similarities	Domestic Guinea Pig	Black Rat	Domestic Ferret	Human	Rhesus monkey	Rabbit	White-Footed Mouse	Southern Grasshopper Mouse	Chinese Hamster		
Syrian Hamster	92.4	94.2	94.5	95.8	95.8	96	98.4	98.8	99.4		

- Most commonly used small animal models show close similarity
- Humans and rhesus monkeys are the most similar sequences

Comparison of ACE2 critical residues

ACE2 Critical Residue	Domestic Guinea Pig	Domestic Ferret	Human	Rhesus Monkey	Rabbit	Black Rat	White-Footed Mouse	Southern Grasshopper Mouse	Syrian Hamster	Chinese Hamster
31	K	K	K	K	K	E	K	K	K	K
35	K	E	E	E	E	E	E	E	E	E
38	D	E	D	D	D	D	D	D	D	D
82	A	T	M	M	T	N	N	N	N	N
353	K	K	K	K	K	H	K	K	K	K

Comparison of ACE2 sequences in humans vs. small animal models

	Description	Common Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
✓	angiotensin converting enzyme 2 [Macaca mulatta]	Rhesus monkey	1596	1596	98%	0.0	95.34%	805	ACI04574.1
✓	angiotensin I converting enzyme 2 [Oryctolagus cuniculus]	rabbit	1440	1440	98%	0.0	84.76%	805	QHX39726.1
✓	angiotensin-converting enzyme 2 [Mesocricetus auratus]	golden hamster	1398	1398	98%	0.0	84.26%	805	XP_005074266.1
✓	angiotensin-converting enzyme 2 [Cricetulus griseus]	Chinese hamster	1394	1394	98%	0.0	84.01%	805	XP_027288607.1
✓	angiotensin-converting enzyme 2 [Onychomys torridus]	southern grasshopper mouse	1388	1388	98%	0.0	83.75%	805	XP_036030683.1
✓	angiotensin-converting enzyme 2 [Peromyscus leucopus]	white-footed mouse	1373	1373	98%	0.0	82.87%	805	XP_028743609.1
✓	angiotensin-converting enzyme 2 precursor [Mustela putorius furo]	domestic ferret	1369	1369	97%	0.0	82.74%	805	NP_001297119.1
✓	angiotensin-converting enzyme 2 [Rattus rattus]	black rat	1320	1320	100%	0.0	79.31%	793	XP_032746145.1
✓	LOW QUALITY PROTEIN: angiotensin-converting enzyme 2 [Cavia porcellus]	domestic guinea pig	1285	1285	100%	0.0	77.27%	813	XP_023417808.1

Comparison of ACE2 sequences in humans vs. small animal models

angiotensin-converting enzyme 2 [*Macaca nemestrina*]

Sequence ID: [XP_011733505.1](#) Length: 805 Number of Matches: 1

[See 7 more title\(s\) ▼](#) [See all Identical Proteins\(IPG\)](#)

Range 1: 12 to 805				GenPart	Graphics	▼ Next Match & Previous Match		
Score	Expect Method		Identities		Positives	Gaps		
1596 bits(4133)	0.0	Compositional matrix adjust.	757/794(95%)	757/794(95%)	0/794(0%)	0/794(0%)		
Query	12	1	VAVTAAGSTLEEAKTFLDKPHNEAEFLVQSSLASMYNTNTINEVQNNINAGDKWSA					71
Subject	12	1	N.....D.....E.....					71
Query	72	1	FLKEGTLAQMYPLOEQINLTVKLQALQNGSSVLSDEKSKRLNTLNTSTYSTGK					131
Subject	72	1						131
Query	132	1	VGNPNPGCELLLEPLNEIMANSLDYNERLWAWESRSEVGKQLRPLYEYVVLNNEMA					191
Subject	132	1	N.....D.....E.....					191
Query	192	1	RAHNYEDGYDNRGDEYEWGVGDEYDSRGSLDEVDHEETKPLVELHLYAVAKLMA					251
Subject	192	1	K.....R.....D.....					251
Query	252	1	YPSYSITGCLPAHLGDGMGRFNTLVSYPFGQKPIZVDAMVDQAADQAFKEA					311
Subject	252	1	T.....N.....N.....					311
Query	312	1	EKFFYSVPLRWMTQGWENSLTDPMQVQKAVCHPTAMDLQGRFLRLCTYTMDFLT					371
Subject	312	1	V.....					371
Query	372	1	AHHGIMGIDYMAAAQPLLRNGANGFEAVEIMSLSATPKHLSTGLSPFOED					431
Subject	372	1						431
Query	432	1	NETEINFLLKQALTIVGTLFPTVLTLEKRWMMFKGEIPKDMQNMWEMRGVGVPEP					491
Subject	432	1						491
Query	492	1	PHDETYPDAPSLHVSNDYSFIRIYTRLVQFQFEALCQAQKHGFLPKDCINSSTEAG					551
Subject	492	1						551
Query	552	1	QKLPNRLKSGKEMPTLALENVGAKPNVPLRLNVEFLPLTKLDKNQNSFVGSWTDS					611
Subject	552	1	L.....R.....					611
Query	612	1	PYADQSKVRISLKSALGQAYEMDNENYLFSSVAYAMRQYVLMQNMILFGEEDVR					671
Subject	612	1	T.....E.....H.....T.....					671
Query	672	1	VANLKPRISFNFFVAPKQNVSDIPRTEVEKATMPSRSDINAFRLMNSLEFLGQPTL					731
Subject	672	1	E.....I.....T.....					731
Query	732	1	GPMNPVPSVILFVGGMGTIVGIVLFTGIRORRKNKARSSEGPYASIDSKGEN					791
Subject	732	1	A.....Y.....S.....T.....A.....L.....V.....					791
Query	792	1	NPGFQNTDDVTSF					805
Subject	792	1						805

angiotensin I converting enzyme 2 [*Oryctolagus cuniculus*]Sequence ID: [QHX39726.1](#) Length: 805 Number of Matches: 1

Range 1: 12 to 805 GenPuzz Graphics				Next Match	Previous Match
Score	Expert Method		Identities	Positives	Gaps
1440 bits(3727) 0.0			Compositional matrix adjust. 673/794(85%)	733/794(92%)	0/794(0%)
Query	12	VAVTAQSTIEEQAKTFLDKHAEEDLVQSSLASWYNITNTEBWNQKQAKWKA			71
Subject	12	L.....E.....Q.....S.....R.....A.....D.....K.....D.....E.....A.....			71
Query	72	FLKEQSTLAQMPLTEQILNTVKLQLOAGNGSVLSEKSRKRNITLNTMSTYSTGK			131
Subject	72	Y.....K.....K.....T.....S.....V.....R.....S.....S.....A.....A.....Q.....G.....V.....			131
Query	132	VYNDPMQPECLLEPGLEIMANSIDYNERLWAMESWSEVGKQRLPYEYVVLKNEA			191
Subject	132	Q.....S.....Q.....F.....P.....D.....D.....K.....K.....T.....G.....V.....S.....G.....V.....			191
Query	192	RAMHEDYQWMDYGVNMGVDYQSGRLTDEVHTFEETPKLYHAYHAKUKAMA			251
Subject	192	N.....A.....D.....A.....A.....E.....A.....S.....D.....D.....R.....S.....D.....T.....D.....			251
Query	252	YPSYISPIGLPAHLGDMMGRFNTNLSYVFGKQKPIDVTDMVDQAWDAQIRFKEA			311
Subject	252	R.....T.....T.....T.....T.....T.....T.....T.....T.....T.....T.....G.....G.....E.....			311
Query	312	EKFVSVGLNMTQGFWENSLDTPGRQVAKCHPTAWDLGGKGFDRFLCTKTMDDFLT			371
Subject	312	S.....P.....H.....G.....S.....L.....H.....P.....E.....S.....D.....G.....V.....R.....L.....M.....K.....T.....			371
Query	372	AHHMGHTGYDMAYAAPFLRLNGANGFHEAGVIMSLSAKPHKLSTGLLSPDFQD			431
Subject	372	A.....H.....M.....G.....H.....T.....Y.....D.....M.....A.....Y.....A.....P.....F.....L.....R.....N.....G.....A.....F.....H.....E.....A.....G.....V.....I.....M.....S.....L.....S.....A.....K.....P.....H.....K.....L.....S.....T.....G.....L.....L.....S.....P.....D.....F.....Q.....D.....			431
Query	432	NETEINFLKQALTVIGTLPTFLMKLRWNVFKGEIKPDQMKKKMKMKREIVGVMP			491
Subject	432	N.....E.....T.....E.....I.....N.....F.....L.....K.....Q.....A.....L.....T.....V.....I.....G.....T.....L.....P.....T.....F.....L.....M.....K.....L.....R.....W.....N.....V.....F.....K.....G.....E.....I.....K.....P.....D.....Q.....M.....K.....K.....M.....K.....M.....K.....R.....E.....I.....V.....G.....M.....P.....			491
Query	492	PHDETCDPASLFFHSYSDISFRIYRYTRLVYQFOGALQAAHQEGHLKHCISINTEAG			551
Subject	492	P.....H.....D.....E.....T.....C.....D.....P.....A.....S.....L.....F.....F.....H.....S.....Y.....S.....D.....I.....S.....F.....R.....I.....Y.....R.....Y.....T.....R.....L.....V.....Y.....Q.....F.....O.....G.....A.....L.....Q.....A.....A.....H.....Q.....E.....G.....H.....L.....K.....H.....C.....I.....S.....I.....N.....T.....E.....A.....G.....			551
Query	552	QKLFNMLRLKSEFWTALLENVYGAKNNVRLNLNYPEFLTMKQDNQNSFVQWSTWS			611
Subject	552	Q.....K.....L.....F.....N.....M.....L.....R.....L.....K.....S.....E.....F.....W.....T.....A.....L.....E.....N.....V.....Y.....G.....A.....K.....N.....N.....V.....R.....L.....N.....L.....N.....Y.....P.....E.....F.....L.....T.....M.....K.....Q.....D.....N.....Q.....N.....S.....F.....V.....Q.....W.....S.....T.....W.....S.....			611
Query	612	PYADQSKIRVLSKLSAGKAYEMDQENYLFRSSVAYAMROYFLKQKQNLFGCEEDR			671
Subject	612	P.....Y.....A.....D.....Q.....S.....K.....I.....R.....V.....L.....S.....K.....L.....S.....A.....G.....K.....A.....Y.....E.....M.....D.....Q.....E.....N.....Y.....L.....F.....R.....S.....S.....V.....A.....Y.....A.....M.....R.....O.....Y.....F.....L.....K.....Q.....K.....Q.....N.....L.....F.....G.....E.....E.....D.....R.....			671
Query	672	VANLPRISFNFFYTPAKNVSDIIPRTKECAVMSRRSDINAFRLNDSLEFLGIPTL			731
Subject	672	V.....A.....N.....L.....P.....R.....I.....S.....F.....N.....F.....F.....Y.....T.....P.....A.....K.....N.....V.....S.....D.....I.....I.....P.....R.....T.....K.....E.....A.....V.....M.....S.....R.....R.....S.....D.....I.....N.....A.....F.....R.....L.....N.....D.....S.....L.....E.....F.....L.....G.....I.....P.....T.....L.....			731
Query	732	GPNPQPPVIMLVIFGVGMVGVIVGIVLIFTGIRDRKKKQAKARGENPYASIDISKEN			791
Subject	732	G.....P.....N.....P.....Q.....P.....P.....V.....I.....M.....L.....V.....I.....F.....G.....V.....M.....V.....G.....V.....I.....V.....G.....I.....V.....L.....I.....F.....T.....G.....I.....R.....D.....R.....K.....K.....Q.....A.....R.....G.....E.....N.....P.....Y.....A.....S.....I.....D.....I.....S.....K.....E.....N.....			791
Query	792	NPQGFONTDOVTSF 805			805
Subject	792	N.....P.....Q.....G.....F.....O.....N.....T.....D.....O.....V.....T.....S.....F..... 805			805

angiotensin-converting enzyme 2 [*Mesocricetus auratus*]Sequence ID: [XP_005074266.1](#) Length: 805 Number of Matches: 1

Range: 1 to 12 to 805			GenFigs	Graphics	Next Match		Previous Match			
Score	Expect	Method	Identities		Positives	Gaps				
1398 bits(3619)	0.0	Compositional matrix adjust.	669/794(84%)		727/794(91%)	0/794(0%)				
Query	12	VAVTAQGSITIEQAKTLDFKNFHEADFLFYSSLASWNYNTNTEENVQWNNQAKQKSA						71		
Subject	12	<u>T</u> <u>1</u> <u>2</u> <u>3</u> <u>4</u> <u>5</u> <u>6</u> <u>7</u> <u>8</u> <u>9</u> <u>10</u> <u>11</u> <u>12</u> <u>13</u> <u>14</u> <u>15</u> <u>16</u> <u>17</u> <u>18</u> <u>19</u> <u>20</u> <u>21</u> <u>22</u> <u>23</u> <u>24</u> <u>25</u> <u>26</u> <u>27</u> <u>28</u> <u>29</u> <u>30</u> <u>31</u> <u>32</u> <u>33</u> <u>34</u> <u>35</u> <u>36</u> <u>37</u> <u>38</u> <u>39</u> <u>40</u> <u>41</u> <u>42</u> <u>43</u> <u>44</u> <u>45</u> <u>46</u> <u>47</u> <u>48</u> <u>49</u> <u>50</u> <u>51</u> <u>52</u> <u>53</u> <u>54</u> <u>55</u> <u>56</u> <u>57</u> <u>58</u> <u>59</u> <u>60</u> <u>61</u> <u>62</u> <u>63</u> <u>64</u> <u>65</u> <u>66</u> <u>67</u> <u>68</u> <u>69</u> <u>70</u> <u>71</u> <u>72</u> <u>73</u> <u>74</u> <u>75</u> <u>76</u> <u>77</u> <u>78</u> <u>79</u> <u>80</u> <u>81</u> <u>82</u> <u>83</u> <u>84</u> <u>85</u> <u>86</u> <u>87</u> <u>88</u> <u>89</u> <u>90</u> <u>91</u> <u>92</u> <u>93</u> <u>94</u> <u>95</u> <u>96</u> <u>97</u> <u>98</u> <u>99</u> 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Query	72	FLKEQSTLAVYPLQETIQLTKYLQLOAQNGSSVSEDKSRILNTILNMTSTVSG						131		
Subject	72	<u>Y</u> <u>E</u> <u>1</u> <u>2</u> <u>3</u> <u>4</u> <u>5</u> <u>6</u> <u>7</u> <u>8</u> <u>9</u> <u>10</u> <u>11</u> <u>12</u> <u>13</u> <u>14</u> <u>15</u> <u>16</u> <u>17</u> <u>18</u> <u>19</u> <u>20</u> <u>21</u> <u>22</u> <u>23</u> <u>24</u> <u>25</u> <u>26</u> <u>27</u> <u>28</u> <u>29</u> <u>30</u> <u>31</u> <u>32</u> <u>33</u> <u>34</u> <u>35</u> <u>36</u> <u>37</u> <u>38</u> <u>39</u> <u>40</u> <u>41</u> <u>42</u> <u>43</u> <u>44</u> <u>45</u> <u>46</u> <u>47</u> <u>48</u> <u>49</u> <u>50</u> <u>51</u> <u>52</u> <u>53</u> <u>54</u> <u>55</u> <u>56</u> <u>57</u> <u>58</u> <u>59</u> <u>60</u> <u>61</u> <u>62</u> <u>63</u> <u>64</u> <u>65</u> <u>66</u> <u>67</u> <u>68</u> <u>69</u> <u>70</u> <u>71</u> <u>72</u> <u>73</u> <u>74</u> <u>75</u> <u>76</u> <u>77</u> <u>78</u> <u>79</u> <u>80</u> <u>81</u> <u>82</u> <u>83</u> <u>84</u> <u>85</u> <u>86</u> <u>87</u> <u>88</u> <u>89</u> <u>90</u> <u>91</u> <u>92</u> <u>93</u> <u>94</u> <u>95</u> <u>96</u> <u>97</u> <u>98</u> 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Comparison of ACE2 sequences in humans vs. small animal models

angiotensin-converting enzyme 2 [*Cricetulus griseus*]Sequence ID: [XP_027288607.1](#) Length: 805 Number of Matches: 1

[See 1 more title\(s\)](#)  [See all Identical Proteins\(IPG\)](#)

Range 1: 12 to 805 [GenPept](#) [Graphics](#) [▼ Next Match](#) [▲ Previous Match](#)

Score	Expect	Method	Identities		Positives		Gaps	
1394	bits(3609)	0.0	Compositional matrix adjust. 667/794(84%)		726/794(91%)		0/794(0%)	
Query	12	VAITAAAGSTIEEQAKTLDKFNHEADLEFYSSLASMWNVITZFNWNNNAQAGK						71
Subject	12	.T...T...I...Q...S...A...N...K...E...A...E...						71
Query	72	FLKEQSTLAQNPLOEIQNLITLQLQALQNGSSVLSEDKSRILNTLNKSTISYSGK						131
Subject	72	.Y...K...KN..S...V...II..R...A...S...N...Q...E...						131
Query	132	WQNPONPQGLDLEPLGNLWNLSDYLERLWAEHSVQGLRLPYEYVYLVKRNA						191
Subject	132	...K...L...L...DD...T...T...G...A...						191
Query	192	RAWHYEDGYCDLWRGQYVGVGDYDSRGQILEDEVEHTFEELPYEHLHAYRAKLNA						251
Subject	192	...K...D...K...HE..A...N..NGL...R...T...T...T...DT						251
Query	252	VPYSYIPGICLPAHLGDWGRFNITLVSITPFQGNPIVDIADWDADQRIEFGA						311
Subject	252	...F...T...T...F...T...N...G...E...E...						311
Query	312	EKFFVSGLVPMHTQGFENSLMTPDQAGKVCAPTAMDLGKGFIRLCTKVTYMDLFT						371
Subject	312	...L...L...L...P...D...D...D...D...D...V...						371
Query	372	AHHEGHQIWMYAAQAPFLFRNANGEGFHAEGEISLTSAPKHLISGLLSPSDH.N						431
Subject	372	...T...F...L...P...H...H...P...H...H...H...H...H...						431
Query	432	NETEIFLKLQALITGVLTPTFLYELKWRNMFKEGPKDQMKQWQKREIVYGVPEV						491
Subject	432	...L...L...L...L...L...L...L...L...L...L...L...L...						491
Query	492	PHQETYCPASLFWNSQYDSIFRYRTILYQFOEALCEAKHGELPHKIDISNTEAG						551
Subject	492	...L...L...L...L...L...L...L...L...L...L...L...L...						551
Query	552	QKLNFLNRLKGSFNTALBNVGDQGNVRLPILYFELPTLNDQGNQSVFQWSTONS						611
Subject	552	...L...L...L...L...L...L...L...L...L...L...L...L...						611
Query	612	PYADQSKIRISKLSDGKAYEWNMENYLFSSVAYRQYFKVKNQMLFGEDVR						671
Subject	612	...L...L...L...L...L...L...L...L...L...L...L...L...						671
Query	672	VANLKRISFNFFVTPQNSDITPREVEAKIRSRINDAIRDFSNLSEFLGIQPTL						731
Subject	672	...L...V...L...S...Q...N...E...V...F...G...V...G...D...						731
Query	732	GPNPQPVSVTLIVFGVWNIIVGVILVITGIRDRKKKNKAKSGENPVSYSIKGEN						791
Subject	732	...L...Y...T...T...I...I...V...I...V...I...V...I...V...						791
Query	792	MPGQNTDQVTSF 895						851
Subject	792	...L...L...L...L...L...L...L...L...L...L...L...L...						851

angiotensin-converting enzyme 2 [*Onychomys torridus*]Sequence ID: [XP_036030683.1](#) Length: 805 Number of Matches: 1

Range 1: 12 to 805 [GenPept](#) [Graphics](#) [▼ Next Match](#) [▲ Previous Match](#)

[illegible]angiotensin-converting enzyme 2 [*Peromyscus leucopus*]Sequence ID: [XP_028743609.1](#) Length: 805 Number of Matches: 1Range 1: 12 to 805 [GenPept](#) [Graphics](#) [▼ Next Match](#) [▲ Previous Match](#)[illegible]

Comparison of ACE2 sequences in humans vs. small animal models

angiotensin-converting enzyme 2 precursor [Mustela putorius furo]

Sequence ID: [NP_001297119.1](#) Length: 805 Number of Matches: 1
[See 3 more title\(s\)](#) [See all Identical Proteins\(PG\)](#)

Range 1: 18 to 805 [GenPept](#) [Graphics](#) [▼ Next Match](#) [▲ Previous](#)

Score	Expect	Method	Identities	Positives	Gaps
1369 bits(3544)	0.0	Compositional matrix adjust.	652/788(83%)	723/788(91%)	0/788(0%)
Query 18	OSTIEEQAKTFLDKFNHEAEDLYQSSLASMYNTNITEENVQNMNINAGDKWSAFLEKQS	77			
Sbjct 18	...T.DL...E...Y...E.S.N...D.I.K.I.A...YE.E	77			
Query 78	TLAOMYPLQEIQLTVKQLQALQNGSSVLSEDKSKRLNTILNTMSTIYSTGKVONPON	137			
Sbjct 78	QH.KT...E...DPIT.R.R...S...A.RE...A...A.N	137			
Query 138	PQECLLLEPGLENETMANSIDYNERLMAWESMRSEVGKOLRLPYEEYVLKNEMARAHYE	197			
Sbjct 138	...DD...E.K...G...A...R...A...N...S...Y...	197			
Query 198	DYGDYWRGDEYVINGVDGYDSRGLIEDVEHTFEETKPYEHLHAYVRALKMAYPSYS	257			
Sbjct 198	...EEMA...S...N...TQ...D...R...A...	257			
Query 258	PIGCLPAHLGDMGRFNTNLYSLTVPFQKPNIDVTDAWQAWDAQRIKFAEKFFVS	317			
Sbjct 258	...T...P.H...R...N.S...R...E...Y...	317			
Query 318	VGLPNMTGFWENSHLTPGNVQKAVCHPTAMDLGKGFRLNLTCTMDOLFATHEHMG	377			
Sbjct 318	...E...Q...E.DMR.V...D...P...S...D...	377			
Query 378	HIQYDMAYAAQPLLRNGANEHGEAVGEIMSLSAATPKHLKSIGLLSPDFQEDNETEIN	437			
Sbjct 378	...E...N...N...P...S...D...	437			
Query 438	FLLKQALITVGLTPTFYMLEKRMVFKGEIPKQDMKMKREIVGVVPEVPVPHDET	497			
Sbjct 438	...E...Q...D...R...E...A...R...E...	497			
Query 498	CDPASLFHVSNDYSFIRYTRTLVYQFQFQALCAQAKHEGLHKDINSNSTEAGQKHE	557			
Sbjct 498	...A...A...R...I...Y...S...R...F...	557			
Query 558	LRLGKSEPHTLALENYVGAKMNNRPLNLYFEPLFWLTKDQKNSFVHGSWDSPADDS	617			
Sbjct 558	...S.R.K...F...R...T.D...E...R...N...	617			
Query 618	IKVRISLKSADGKAYEMNDENHYLFSSVAYAMRYFKLKNQNMILFGEEDVRVANKP	677			
Sbjct 618	...E...F.Q.I...E.S...T.P.VK...SD...	677			
Query 678	RISPNFFVTAPKNSVDIIPRTEVEKATMRSKRSINDAFRLNLSLGIPTLGPNNQ	737			
Sbjct 678	...I.S.E.H...AD...E...K...G...D...E...Y...	737			
Query 738	PVSLNLTIVFGVMMGVIVGIVLFTGIIRDRKKNKARSGENPYASIDISKGENPFGQ	797			
Sbjct 738	...T...V...FL...S...N.R.N.Q...E...V.L...	797			
Query 798	TDDVQTSF	805			
Sbjct 798	V.....	805			

angiotensin-converting enzyme 2 [Rattus rattus]

Sequence ID: [XP_032748145.1](#) Length: 793 Number of Matches: 5

Range 1: 1 to 793 [GenPept](#) [Graphics](#) [▼ Next Match](#) [▲ Previous](#)

Score	Expect	Method	Identities	Positives	Gaps
1320 bits(3416)	0.0	Compositional matrix adjust.	640/807(79%)	709/807(87%)	16/807(1%)
Query 1	MSSSSWLLLSLVATAQSTIEEQAKTFLDKFNHEAEDLYQSSLASMYNTNITEENVQ	60			
Sbjct 1	...R.P...AT...L...K.ES...N...Q...S...A...	60			
Query 61	MNNINAGDKWSAFLEKQSTLAOMYPLQEIQLTVKQLQALQNGSSVLSEDKSKRLNTIL	120			
Sbjct 61	K...E.AA...YE...KI...NFS...DA.I.R...S...A.P.N.Q...	120			
Query 121	NTMSTIYSTGKVONPONPQECLLLEPGLENETMANSIDYNERLMAWESMRSEVGKOLRLPY	180			
Sbjct 121	...SM...FV...D...T.T...R...G.A...	180			
Query 181	EYVVLKNEMARAHYEDYDGYWRGDEYVINGVDGYDSRGLIEDVEHTFEETKPYEHL	240			
Sbjct 181	...T...AE...E.N.N.N...	240			
Query 241	HAYVRALKMAYPSYISPIGCLPAHLGDMGRFNTNLYSLTVPFQKPNIDVTDAWQ	300			
Sbjct 241	...T...DV...P...T...L...N...	300			
Query 301	AWDAQRIKFAEKFFVSGLPNMTGFWENSHLTPGNVQKAVCHPTAMDLGKGFRLN	360			
Sbjct 301	S...E...Q...P...T...E.DDR.V...H...K...	360			
Query 361	CTKVITMDLTAHHEHGHQYDMAYAAQPLLRNGANEHGEAVGEIMSLSAATPKHLKS	420			
Sbjct 361	...N...K...	420			
Query 421	IGLLSPDFQEDNETEINFLKQALITVGLTPTFYMLEKRMVFKGEIPKQDMKMKRE	480			
Sbjct 421	...PSN...D...I...DDK...RE.TQ...	480			
Query 481	KREIVGVPEVPVPHDETCDPASLFHVSNDYSFIRYTRTLVYQFQFQALCAQAKHEGLH	540			
Sbjct 481	...L...SR...D...K...V...E.S...	540			
Query 541	KCDINSNSTEAGQKFLNMLRLGKSEPHTLALENYVGAKMNNRPLNLYFEPLFWLTKDQK	600			
Sbjct 541	...L...S.N.G...SR...D...K...Q...V...E.S...	600			
Query 601	NSFVQNSWDSPNS...YADGSKVRISLKSADGKAYEMNDENHYLFSSVAYAMRYFLKV	658			
Sbjct 601	...T...N...CDFT.CT...H...T...S...E...SRE	658			
Query 659	KNQMLFGEEDVRVANKPRTISFNFFVTAPKNSVDIIPRTEVEKATMRSKRSINDAFRLN	718			
Sbjct 647	...TVP...A.N.SD...V...S...E...G...I.G...	706			
Query 719	DNSLEFLGIPTLGPNNQPVSLIVFGVMMGVIVGIVLFTGIIRDRKKNKARSGE	778			
Sbjct 707	...Y...K...YE...T...I...WV...V...V...K...G...ETKRE...	766			
Query 779	NPYASIDISKGENPFGQNTDDVQTSF	805			
Sbjct 767	...D.V.G...S.A...S.A...S...	793			

LOW QUALITY PROTEIN: angiotensin-converting enzyme 2 [Cavia porcellus]

Sequence ID: [XP_023417808.1](#) Length: 813 Number of Matches: 1

Range 1: 9 to 813 [GenPept](#) [Graphics](#) [▼ Next Match](#) [▲ Previous](#)

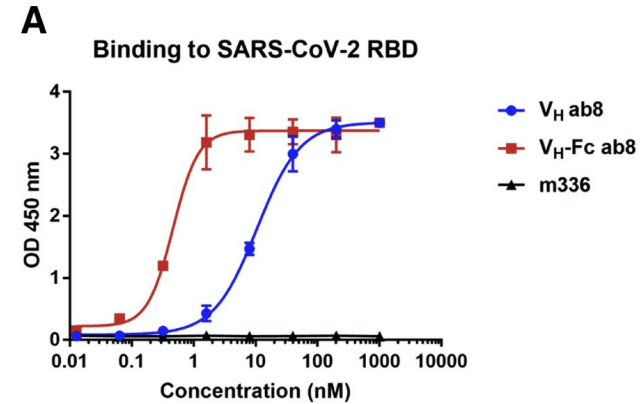
Score	Expect	Method	Identities	Positives	Gaps
1285 bits(3326)	0.0	Compositional matrix adjust.	622/805(77%)	704/805(87%)	0/805(0%)
Query 1	MSSSSWLLLSLVATAQSTIEEQAKTFLDKFNHEAEDLYQSSLASMYNTNITEENVQ	60			
Sbjct 9	...G.F.F.N...T...FNL...E...L...K...Y...D...D...	68			
Query 61	MNNINAGDKWSAFLEKQSTLAOMYPLQEIQLTVKQLQALQNGSSVLSEDKSKRLNTIL	120			
Sbjct 69	K.SE...GIL...YE...N.KA...D...R...R...S...GF.A...N.Q.S...	128			
Query 121	NTMSTIYSTGKVONPONPQECLLLEPGLENETMANSIDYNERLMAWESMRSEVGKOLRLPY	180			
Sbjct 129	...Y.SD...D...SK.T...L...G...K...	188			
Query 181	EYVVLKNEMARAHYEDYDGYWRGDEYVINGVDGYDSRGLIEDVEHTFEETKPYEHL	240			
Sbjct 189	...N...K...R...EDM...N...N...R...A...R...Q...	248			
Query 241	HAYVRALKMAYPSYISPIGCLPAHLGDMGRFNTNLYSLTVPFQKPNIDVTDAWQ	300			
Sbjct 249	...T...ET...R...V...E...E...Q...ES...	308			
Query 301	AWDAQRIKFAEKFFVSGLPNMTGFWENSHLTPGNVQKAVCHPTAMDLGKGFRLN	360			
Sbjct 309	S...EK...P...K...E.DG.V...M...N...K...	368			
Query 361	CTKVITMDLTAHHEHGHQYDMAYAAQPLLRNGANEHGEAVGEIMSLSAATPKHLKS	420			
Sbjct 369	...N...D...D...D...D...D...D...D...D...	428			
Query 421	IGLLSPDFQEDNETEINFLKQALITVGLTPTFYMLEKRMVFKGEIPKQDMKMKRE	480			
Sbjct 429	...N...G.KA.SS...LL...F...GEE...T.N.QE...IE.X.Q...	488			
Query 481	KREIVGVPEVPVPHDETCDPASLFHVSNDYSFIRYTRTLVYQFQFQALCAQAKHEGLH	540			
Sbjct 489	...I...K...D...K...N...V...	548			
Query 541	KCDINSNSTEAGQKFLNMLRLGKSEPHTLALENYVGAKMNNRPLNLYFEPLFWLTKDQK	600			
Sbjct 549	...L...K...K...S...T...D...K...Q...S...Q...R...	608			
Query 601	NSFVQNSWDSPNS...YADGSKVRISLKSADGKAYEMNDENHYLFSSVAYAMRYFLKV	658			
Sbjct 609	...D...E...SEE...ED.K.D...	668			
Query 661	QMLFGEEDVRVANKPRTISFNFFVTAPKNSVDIIPRTEVEKATMRSKRSINDAFRLN	720			
Sbjct 669	...TV...SW...SOWTH.V...T...E.N.N...K...D...L...V...GXX...	728			
Query 721	SLEFLGIPTLGPNNQPVSLIVFGVMMGVIVGIVLFTGIIRDRKKNKARSGENP	780			
Sbjct 729	HSGV...T...S...YE...T...D...LV...V.VI...R...KQKRE...	788			
Query 781	YASIDISKGENPFGQNTDDVQTSF	805			
Sbjct 789	...S.V.G...TA...SE.N...813				

Identifying key epitope regions within SARS-CoV-2

- SARS-CoV genome shares an 80% homology with SARS-CoV-2 (Grifoni et al., 2020)
 - Uses known antibody libraries and/or patient samples to select antibodies
- Most neutralizing antibodies target the RBD-A
 - competes with RBD of SARS-CoV-2
 - VHs may have an advantage for treatment of respiratory virus infections

SARS-CoV-2 Antibody Neutralizing Potencies

- Anti-RBD antibodies are mainly found in the V-gene family
 - Found enriched use of VH3-53 or VH3-66. VH3-53 and VH3-66 V-genes are closely related (Cao et al., 2020)
- Maintains similarities with human germline V-genes
 - VH-Fc ab8 shows complete neutralization at 36 mg/kg dosage in the lungs (Li et al., 2020)
 - STE90-C11 is tolerant to known RBD mutants



Antibody binding to SARS-CoV-2 RBD
(Li et al. 2020)

Further Research Questions

- Can further clinical trials be held using small animal models transduced with human ACE2 receptors?
- Should we rely on the prophylactic efficacy of the V-gene antibodies to treat at risk populations?
- Are small animals good models for human immune responses to SARS-CoV-2?
 - dosage
 - Respiratory response

Future neutralizing antibody work using small animal models

- Identify different neutralizing antibody regions that obtained promising results in SARS-CoV-2 studies
 - Rogers et al indicates vaccine development should focus on the RBD
- Compare common antibody regions in small animal models to observe similarities
- Potential studies could identify which small animal models work most efficiently for vaccine development

Summary

- Efficacy of RBD nAb in vivo in Syrian hamsters shows promise for human studies
- Syrian hamsters as a model for studying respiratory diseases in humans
- Small animal model ACE2 sequences showed varied relationships
- Comparison of ACE2 sequences in humans vs. small animal models
- SARS-CoV-2 Antibody Neutralizing Potencies
- Future neutralizing antibody work using small animal models

References

- Cohen, J. (2020). Mice, hamsters, ferrets, monkeys. Which lab animals can help defeat the new coronavirus?. Retrieved 6 December 2020, from <https://www.sciencemag.org/news/2020/04/mice-hamsters-ferrets-monkeys-which-lab-animals-can-help-defeat-new-coronavirus>
- Hassan, A. O., Case, J. B., Winkler, E. S., Thackray, L. B., Kafai, N. M., Bailey, A. L., ... & Turner, J. S. (2020). A SARS-CoV-2 infection model in mice demonstrates protection by neutralizing antibodies. *Cell*, 182(3), 744-753.
- Iwasaki, A., Yang, Y. The potential danger of suboptimal antibody responses in COVID-19. *Nat Rev Immunol* 20, 339–341 (2020). <https://doi.org/10.1038/s41577-020-0321-6>
- Jennison, A. (2006, April 19). *Vince the female Syrian hamster* [Photograph].
- Hassan, A. O., Case, J. B., Winkler, E. S., Thackray, L. B., Kafai, N. M., Bailey, A. L., ... & Turner, J. S. (2020). A SARS-CoV-2 infection model in mice demonstrates protection by neutralizing antibodies. *Cell*, 182(3), 744-753.
- Li, W., Schäfer, A., Kulkarni, S. S., Liu, X., Martinez, D. R., Chen, C., ... & Ura, M. L. (2020). High potency of a bivalent human VH domain in SARS-CoV-2 animal models. *Cell*, 183(2), 429-441.

References

- Rogers, T. F., Zhao, F., Huang, D., Beutler, N., Burns, A., He, W. T., Limbo, O., Smith, C., Song, G., Woehl, J., Yang, L., Abbott, R. K., Callaghan, S., Garcia, E., Hurtado, J., Parren, M., Peng, L., Ramirez, S., Ricketts, J., Ricciardi, M. J., ... Burton, D. R. (2020). Isolation of potent SARS-CoV-2 neutralizing antibodies and protection from disease in a small animal model. *Science (New York, N.Y.)*, 369(6506), 956–963.
<https://doi.org/10.1126/science.abc7520>
- Miao, J., Chard, L. S., Wang, Z., & Wang, Y. (2019). Syrian Hamster as an Animal Model for the Study on Infectious Diseases. *Frontiers in immunology*, 10, 2329.
<https://doi.org/10.3389/fimmu.2019.02329>
- Wan, Y., Shang, J., Graham, R., Baric, R., & Li, F. (2020). Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *Journal Of Virology*, 94(7). doi: 10.1128/jvi.00127-20

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