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Highly Conserved Binding Region of ACE2 as Receptor for SARS-CoV-2 between Human and Mammals

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Abstract:
In Belgium, case of new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection from owner to domestic cat was reported on March 27, 2020. So far, cases of SARS-CoV-2 infection from owners to their dogs have been reported. For the first time in the world, the case of SARS-CoV-2 transmission from the owner to a domestic cat has been confirmed. A tiger kept at a zoo in New York, USA, was reportedly infected with SRAS-CoV-2. It is believed that SRAS-CoV-2 has been transmitted to tiger from caretakers infected with SRAS-CoV-2. Therefore, we examined the homology of whole molecule and the 5 amino acids residues; KGDFR located in the binding region of the angiotensin converting enzyme-2 (ACE2) molecule, a receptor for the spike glycoprotein on the virion surface of SRAS-CoV-2, between humans, dogs, cats, tiger and other mammals. Although the transmission of human coronavirus to pets or animals is rare, the dangers of transmitting SARS-CoV-2 from animals or pets to humans have not been proven. Our findings with Shi's study provide important insights into the animal models for SARS-CoV-2 and animal management for COVID-19 control.

A novel human coronavirus that is now named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (formerly called 2019-nCoV) emerged in Wuhan, China, in late 2019 and is now causing a pandemic [1]. The genome of SARS-CoV-2 shares about 80% identity with that of SARS-CoV and is about 96% identical to the bat coronavirus BatCoV RaTG13 [2]. In the case of SARS-CoV, the spike glycoprotein on the virion surface mediates receptor recognition and membrane fusion [3,4,5]. During viral infection, the trimeric spike glycoprotein is cleaved into S1 and S2 subunits and S1 subunits are released in the transition to the post fusion conformation [4-7]. S1contains the receptor binding domain (RBD), which directly binds to the binding region located in the peptidase domain (PD) of angiotensin-converting enzyme 2 (ACE2), whereas S2 subunit is responsible for membrane fusion [5,6].

In Belgium, case of new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection from owner to domestic cat was reported on March 27, 2020. So far, cases of SARS-CoV-2 infection from owners to their dogs have been reported. For the first time in the world, the case of SARS-CoV-2 transmission from the owner to a domestic cat has been confirmed. A tiger kept at a zoo in New York, USA, was reportedly infected with SRAS-CoV-2. It is believed that SRAS-CoV-2 has been transmitted to tiger from caretakers who have been infected with SRAS-CoV-2. *Jianzhong Shi et al. in Science* 08 Apr 2020 report that cats are experimentally susceptible to airborne infection [7]. Therefore, we examined the whole molecule homology and the 5 amino acids residues; KGDFR located in the binding region of the angiotensin converting enzyme-2 (ACE2) molecule, a receptor for the spike glycoprotein on the virion surface of SRAS-CoV-2, between humans, dogs, cats, tiger and other mammals. As a result, the binding region with ACE2 molecule with SARS-CoV spike glycoprotein showed high homology and completely conserved the 5 amino acids residues: KGDFR between humans, dogs, cats, tiger, and other mammals. Although the transmission of human coronavirus to pets or animals is rare, the dangers of transmitting SARS-CoV-2 from animals or pets to humans have not been proven. The Belgian Health Service considers the zoonotic infection as a special case. However, the Belgian Health Service has called for individuals with SARS-CoV-2 to also avoid contact with pets or animals. Our findings with Shi's study provide important insights into the animal models for SARS-CoV-2 and animal management for COVID-19 control.

The Belgian Health Service reports that there is no medical evidence of SARS-CoV-2 transmission from pets to humans or other pets, the risk of SARS-CoV-2 transmission from pets to humans is much lower than in cases of SARS-CoV-2 transmission due to human contact. However, to prevent cross species transmitting SARS-CoV-2 from the owner to their pets, especially if the owner may be infected with SARS-

CoV-2, owners should avoid close contact with pets and refrain from licking their faces. The information from our examinations will support precision vaccine design and the discovery of antiviral therapeutics, accelerating medical countermeasure development.

Footnote

The materials (manuscript and figures) are original research, has not been previously published and has not been submitted for publication elsewhere while under consideration.

Disclosure

The authors declare no potential conflicts of interest. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Hayashi *et al.* Figure 1

angiotensin-converting enzyme 2 precursor [Homo sapiens]
NCBI Reference Sequence: **NP_001358344.1**
353..357 kgdfr /region_name="Interaction with SARS-CoV spike glycoprotein" /note="propagated from UniProtKB/Swiss-Prot (Q9BYF1.2)"

Species	Protein ID	Whole Homology		
Homo.	NP_001358344.1		301	awdaqrifke aekffvsvgl pnmtqgfwen smltdpgnvq kavchptawd lg**kgdfr**ilm
Dog#1	NP_001158732.1	**91.0%**	301	wdarkifkea ekffvsvglp nmtqefwgns mltepsdsrk vvchptawdl g**kgdfr**ikmc
Dog#2	XP_005641049.1	**92.0%**	301	wdarkifkea ekffvsvglp nmtqefwens mltepsdsrk vvchptawdl g**kgdfr**ikmc
Dog#3	XP_013966804.1	**92.0%**	301	wdarkifkea ekffvsvglp nmtqefwens mltepsdsrk vvchptawdl g**kgdfr**ikmc
Dog#4	XP_022271214.1	**79.0%**	181	darkifkeae kffvsvglpn mtqefwensm ltepsdsrkv vchptawdlg **kgdfr**ikmct
Cat#1	XP_023104564.1	**91.0%**	301	nqswdarrif keaekffvsv glpnmtqgfw ensmltepgd srkvvchpta wdlg**kgdfr**i
Cat#2	NP_001034545.1	**92.0%**	301	swdarrifke aekffvsvgl pnmtqgfwen smltepgdsr kvvchptawd lg**kgdfr**ikm
Tiger#1	XP_007090142.1	**92.0%**	291	nqswdarrif keaekffvsv glpnmtqgfw ensmltepgn sqkvvchpta wdlg**kgdfr**i
Bat#1	XP_014399780.1	**88.0%**	301	wdaekifkea ekfyisvglp smtpgfwnns mltepgdgrk vvchptawdl g**kgdfr**ikmc
Bat#2	XP_014399781.1	**88.0%**	301	wdaekifkea ekfyisvglp smtpgfwnns mltepgdgrk vvchptawdl g**kgdfr**ikmc
Bat#3	XP_014399782.1	**89.0%**	301	wdaekifkea ekfyisvglp smtpgfwnns mltepgdgrk vvchptawdl g**kgdfr**ikmc
Bat#4	XP_014399783.1	**80.0%**	301	wdaekifkea ekfyisvglp smtpgfwnns mltepgdgrk vvchptawdl g**kgdfr**ikmc
Bat#5	XP_024425698.1	**88.0%**	301	wdaqrifkea ekffksvglf smtqgfwdns mltkpddgre vvchptawdl gn**kdfr**ikmc
Bat#6	XP_024425699.1	**81.0%**	231	dqswdaqrif keaekffksv glfsmtqgfw dnsmltkpdd grevvchpta wdlgn**kdfr**i
Bat#7	XP_008153150.1	**88.0%**	301	wdaekifkea ekfymsvglp smtpgfwnns mltepgdgrk vvchptawdl g**kndfr**ikmc
Bat#8	XP_027986092.1	**88.0%**	301	wdaekifkea ekfymsvglp smtpgfwnns mltepgdgrk vvchptawdl g**kndfr**ikmc
Bat#9	XP_023609437.1	**88.0%**	301	wdaekifkea ekfyisvglp smtpgfwnns mltepgdgrk vvchptawdl g**kgdfr**ikmc
Bat#10	XP_023609438.1	**88.0%**	301	wdaekifkea ekfyisvglp smtpgfwnns mltepgdgrk vvchptawdl g**kgdfr**ikmc
Bat#11	XP_023609439.1	**89.0%**	301	wdaekifkea ekfyisvglp smtpgfwnns mltepgdgrk vvchptawdl g**kgdfr**ikmc
Bat#12	XP_028378317.1	**87.0%**	301	aqrifkeaek ffvsvglfnm tqgfwdnsml tkpddgrevv chptawdlg**k** **kdfr**ikmctk
Bat#13	XP_019522936.1	**89.0%**	301	kwdakkifqe aekffvsvgl pnmtkgfwen smltepgdgr kvvchptawd lg**kgdfr**ikm
Bat#14	XP_019522943.1	**89.0%**	301	kwdakkifqe aekffvsvgl pnmtkgfwen smltepgdgr kvvchptawd lg**kgdfr**ikm
Bat#15	XP_019522954.1	**89.0%**	301	kwdakkifqe aekffvsvgl pnmtkgfwen smltepgdgr kvvchptawd lg**kgdfr**ikm
Pan#1	XP_017505746.1	**91.0%**	301	twdanrifke aekffvsvgl pkmtqtfwen smltepgdgr kvvchptawd lg**khdfr**ikm
Pan#2	XP_017505752.1	**91.0%**	301	twdanrifke aekffvsvgl pkmtqtfwen smltepgdgr kvvchptawd lg**khdfr**ikm
Sna#1	XP_026530754.1	**75.0%**	361	ekkwtvdsif kaaehffisi glfnmtesfw knsmleepkd grkvvchpta wdmg**kedyr**i
Sna#2	XP_032082934.1	**74.0%**	321	tkkwtvnsif kaaeqfftsi glfpmtdnfw nnsmleepkd grkvvchpta wdmg**kkdyr**i

Whole molecule homology and Amino acid sequence alignment of the binding region of angiotensin converting enzyme 2 (ACE2) as receptor for SARS-CoV-2 spike glycoprotein and its phylogeny.

Whole molecule homology and the homologous binding region of Angiotensin Converting Enzyme 2 (ACE2) between human and other animal species including dogs, cats, tiger, bats, pangolins and snakes are indicated in figure. The key 5 amino acid residues KGDFR involved in the interaction with human SARS-CoV-2 spike glycoprotein are marked with the red bold words. Detailed information including protein accession numbers of ACE2 of other animal species can be found in the supplementary material.