Dipartimento
Medicina Veterinaria
Produzioni Animali

SCUOLA DI
AGRARIA
E MEDICINA
VETERINARIA
2023

IL caffè
SCIENTIFICO

8 Febbraio 2023

SARS-CoV-2 negli animali: zoonosi e zoonosi inversa

Filomena Fiorito, PhD

Research and professional experience

- Dal Luglio 2022, Professore II fascia Malattie Infettive degli Animali Domestici 07/H3 - SSD VET/05, DMVPA, UNINA Malattie infettive ed epidemiologia applicata alle produzioni zootecniche
- 2019-2022, RTDB di Malattie Infettive degli Animali Domestici 07/H3 - SSD VET/05, DMVPA, UNINA
- 2015-2019, Borsista di Ricerca, Lab. Microinquinanti Organici Persistenti, IZS Mezzogiorno, Portici (NA)
- 2006-2015, Post-Doc Fellow, DMVPA, UNINA
- 2002-2005, PhD Student, in Biologia, Patologia ed Igiene Ambientale in Medicina Veterinaria, UNINA
- 2001-2002, Titolare di Borsa di Studio, Istituto di Cibernetica del C.N.R. di Arco Felice/Pozzuoli (NA)
- 1996-2000, Manufacturing Manager, nell'Industria Farmaceutica Splendore ALFA INTES, Casoria (NA)

Education

- 1995, Laurea in Chimica e Tecnologia Farmaceutiche, Università degli Studi di Roma La Sapienza, Roma;
- 1996, Laurea in Farmacia, Università degli Studi di Roma La Sapienza, Roma;
- 1998, Specializzazione in Farmacologia, DMVPA, UNINA
- 2005, Ph.D. in Biologia, Patologia ed Igiene Ambientale in Medicina Veterinaria (XVII° ciclo), DMVPA, UNINA

Research Interests

- Molecular processes involved in the replication of herpesviruses and coronaviruses, in the presence of environmental contaminants (dioxin) too.

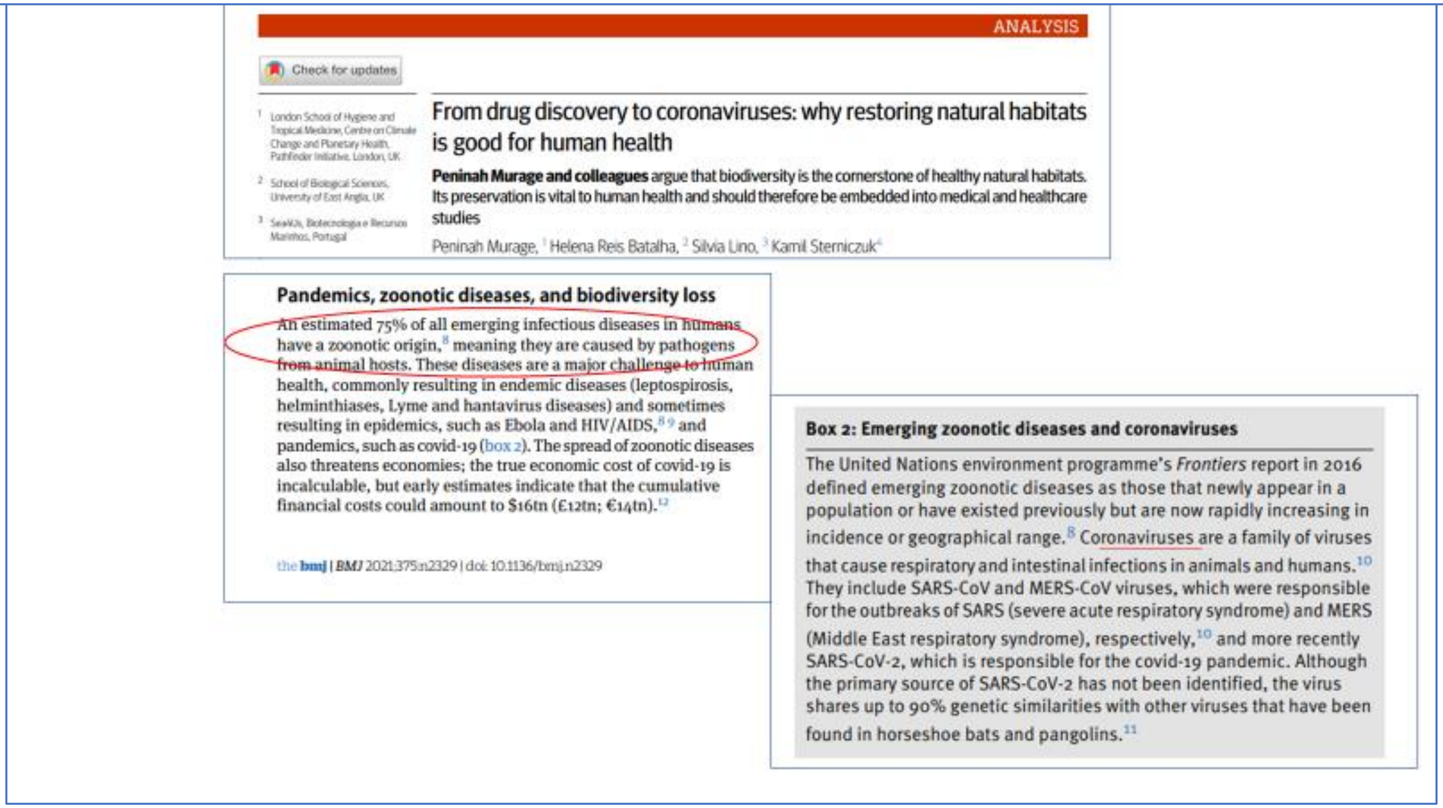
- Correlation between environmental pollutants and viruses in marine animals (bivalves and turtles).

- Surveillance of herpesviruses (BoHV-1, BuHV-1) and coronaviruses (BCoV; SARS-CoV-2) in animals.

- Moreover, she is currently studying the potential antivirals properties of synthetic (MG-132, CH-223191) and natural compounds (secondary fungal metabolites, extracts containing polyphenols and flavonoids) against herpesviruses and coronaviruses infections.

World Health Organization

- A zoonosis is any disease or infection that is naturally transmissible from vertebrate animals to humans
- There are over 200 known types of zoonoses
- Zoonoses comprise a large percentage of new and existing diseases in humans



ANALYSIS

Check for updates

From drug discovery to coronaviruses: why restoring natural habitats is good for human health

Peninah Murage and colleagues argue that biodiversity is the cornerstone of healthy natural habitats. Its preservation is vital to human health and should therefore be embedded into medical and healthcare studies

Peninah Murage,[1] Helena Reis Batalha,[2] Silvia Lino,[3] Kamil Sterniczuk[4]

[1] London School of Hygiene and Tropical Medicine, Centre on Climate Change and Planetary Health, Pathfinder Initiative, London, UK

[2] School of Biological Sciences, University of East Anglia, UK

[3] Sea4Us, Biotecnologia e Recursos Marinhos, Portugal

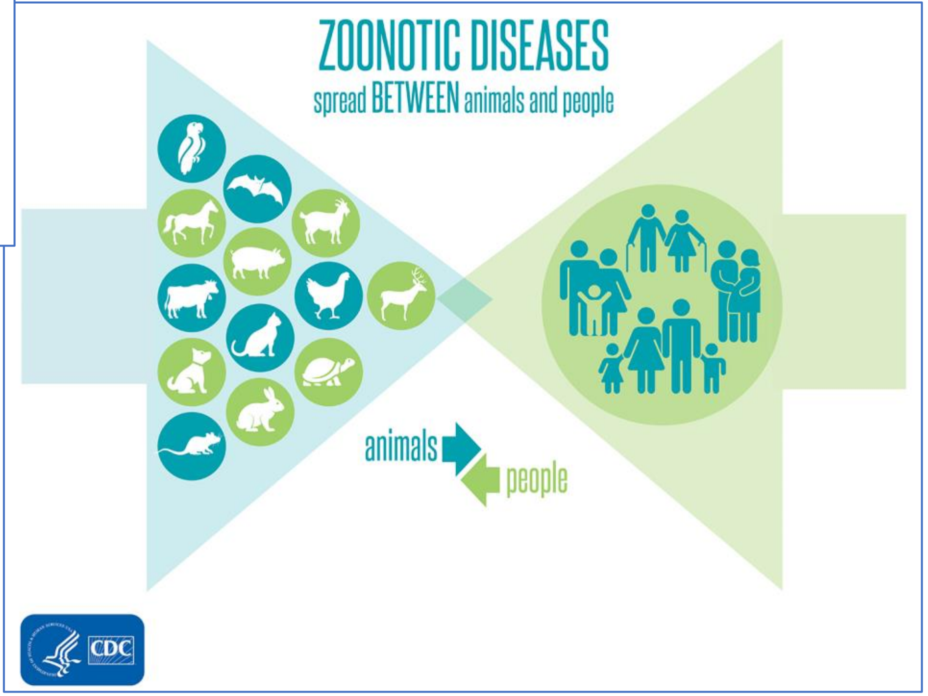
Pandemics, zoonotic diseases, and biodiversity loss

An estimated 75% of all emerging infectious diseases in humans have a zoonotic origin,[8] meaning they are caused by pathogens from animal hosts. These diseases are a major challenge to human health, commonly resulting in endemic diseases (leptospirosis, helminthiases, Lyme and hantavirus diseases) and sometimes resulting in epidemics, such as Ebola and HIV/AIDS,[8 9] and pandemics, such as covid-19 (box 2). The spread of zoonotic diseases also threatens economies; the true economic cost of covid-19 is incalculable, but early estimates indicate that the cumulative financial costs could amount to $16tn (£12tn; €14tn).[12]

the bmj | BMJ 2021;375:n2329 | doi: 10.1136/bmj.n2329

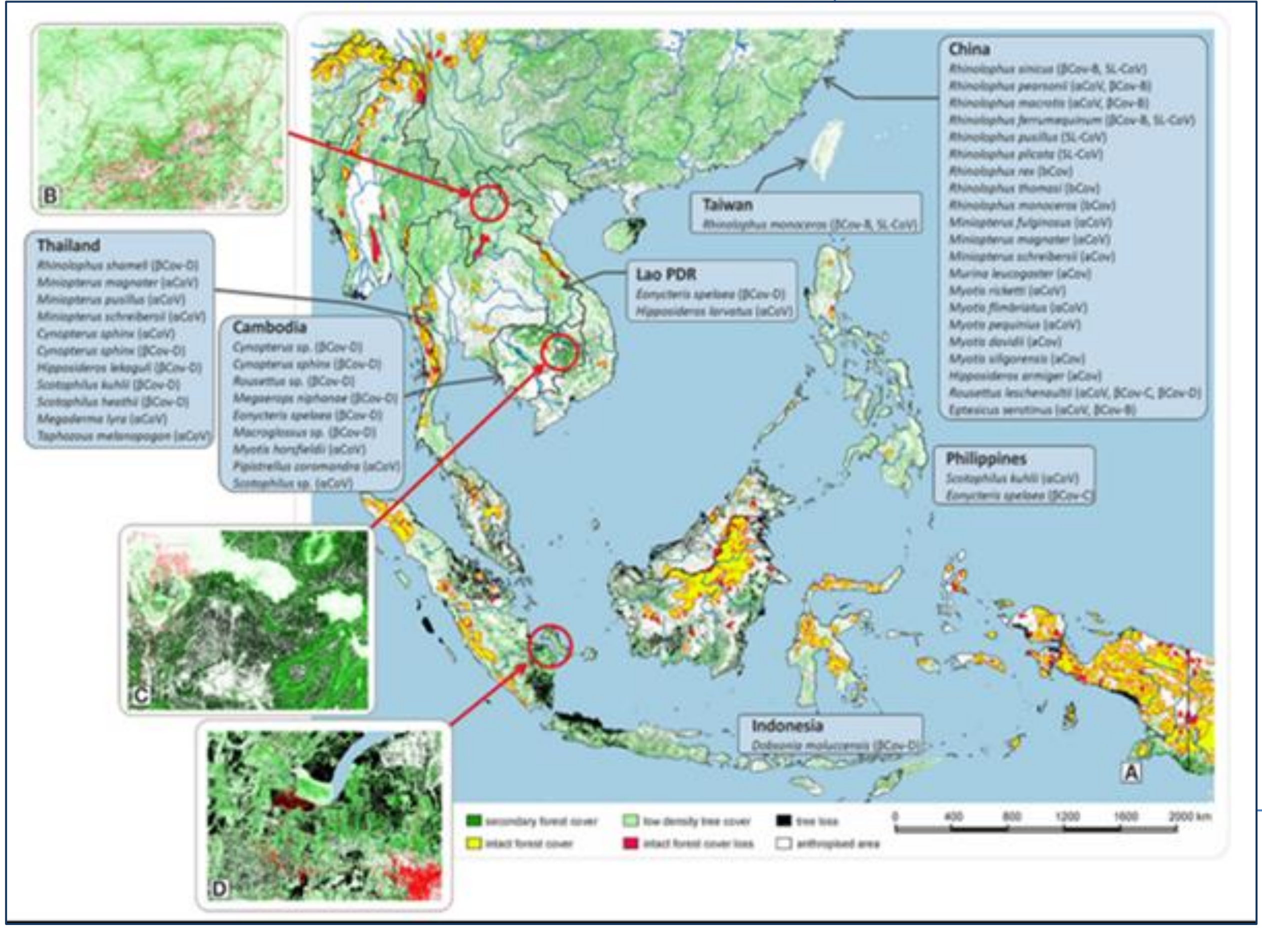
Box 2: Emerging zoonotic diseases and coronaviruses

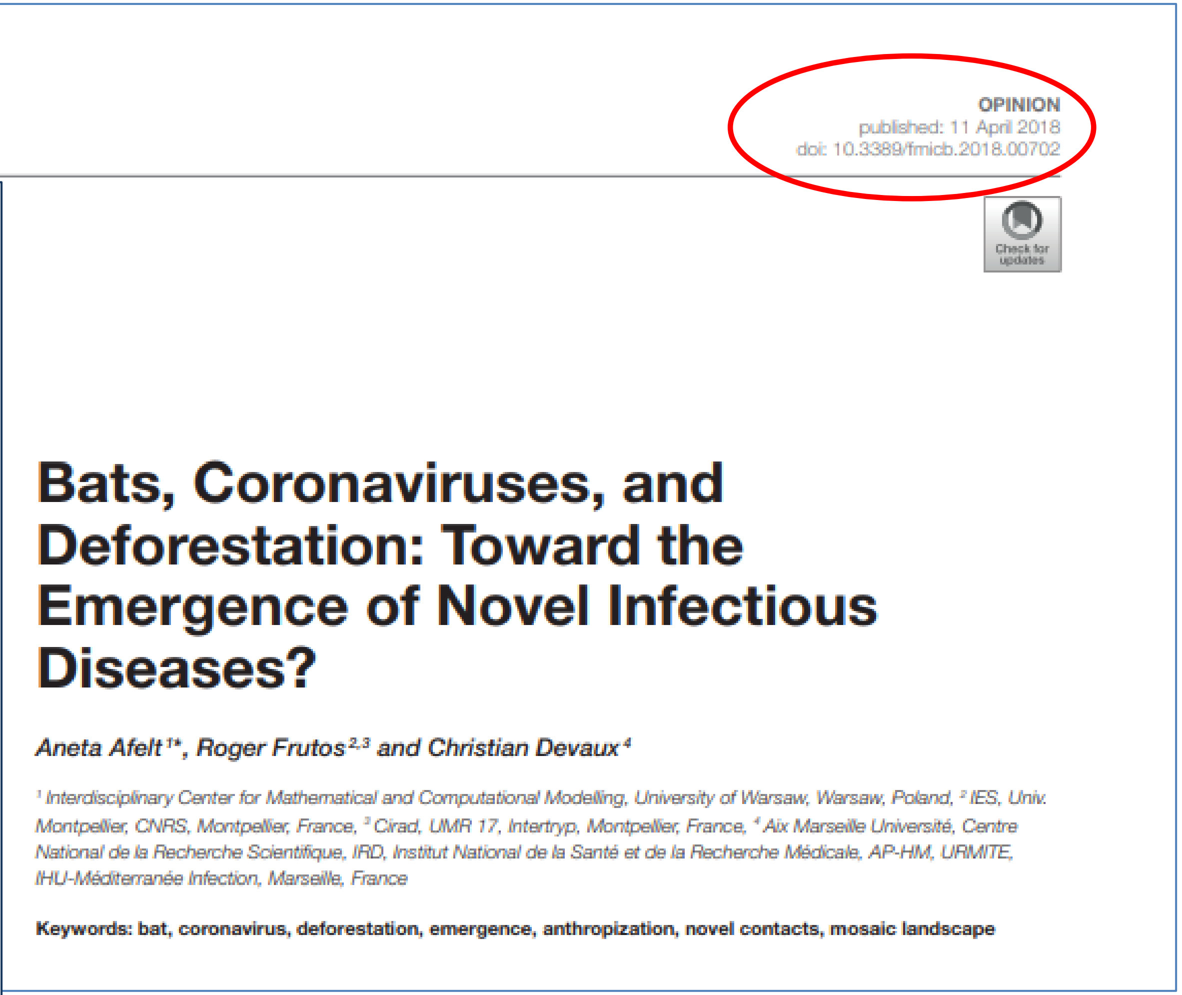
The United Nations environment programme's *Frontiers* report in 2016 defined emerging zoonotic diseases as those that newly appear in a population or have existed previously but are now rapidly increasing in incidence or geographical range.[8] Coronaviruses are a family of viruses that cause respiratory and intestinal infections in animals and humans.[10] They include SARS-CoV and MERS-CoV viruses, which were responsible for the outbreaks of SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome), respectively,[10] and more recently SARS-CoV-2, which is responsible for the covid-19 pandemic. Although the primary source of SARS-CoV-2 has not been identified, the virus shares up to 90% genetic similarities with other viruses that have been found in horseshoe bats and pangolins.[11]



Factors responsible for the emergence of novel viruses:

Anthropogenic factors: Climate change, Deforestation…




frontiers in Microbiology

OPINION
published: 11 April 2018
doi: 10.3389/fmicb.2018.00702

Bats, Coronaviruses, and Deforestation: Toward the Emergence of Novel Infectious Diseases?

Aneta Afelt[1], Roger Frutos[2,3] and Christian Devaux[4]*

[1] Interdisciplinary Center for Mathematical and Computational Modelling, University of Warsaw, Warsaw, Poland, [2] IES, Univ. Montpellier, CNRS, Montpellier, France, [3] Cirad, UMR 17, Intertryp, Montpellier, France, [4] Aix Marseille Université, Centre National de la Recherche Scientifique, IRD, Institut National de la Santé et de la Recherche Médicale, AP-HM, URMITE, IHU-Méditerranée Infection, Marseille, France

Keywords: bat, coronavirus, deforestation, emergence, anthropization, novel contacts, mosaic landscape

P.H. Brancalion, E.N. Broadbent, S. de-Miguel et al. *Perspectives in Ecology and Conservation 18 (2020) 243–246*

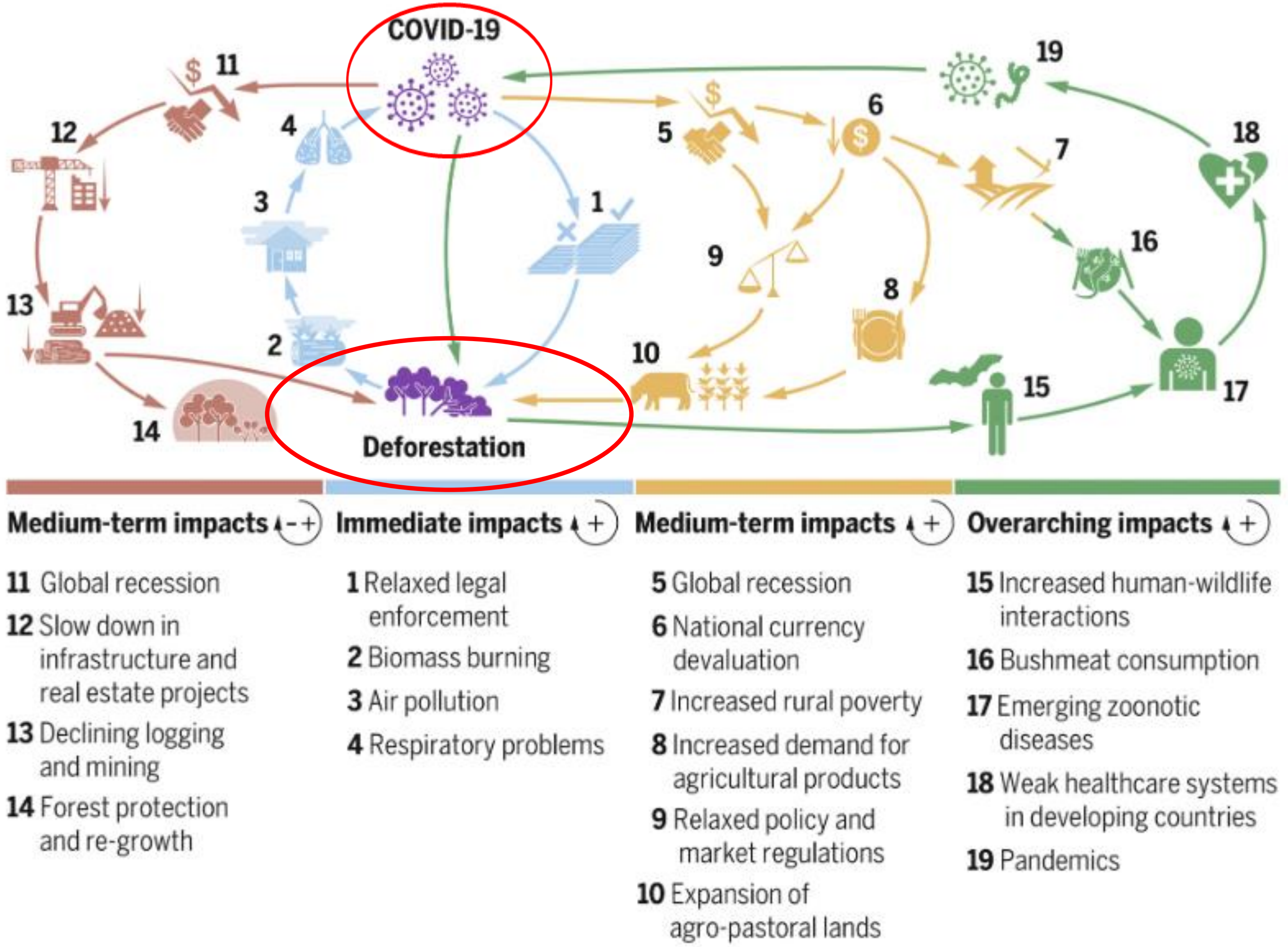


Fig. 1. Feedback loops between tropical deforestation and the COVID-19 pandemic. Zoonotic diseases, public health, economy, agriculture, and forests may all be reciprocally linked in complex positive and negative feedback loops with overarching consequences for nature and society.

Coronaviruses (CoVs): Generalità

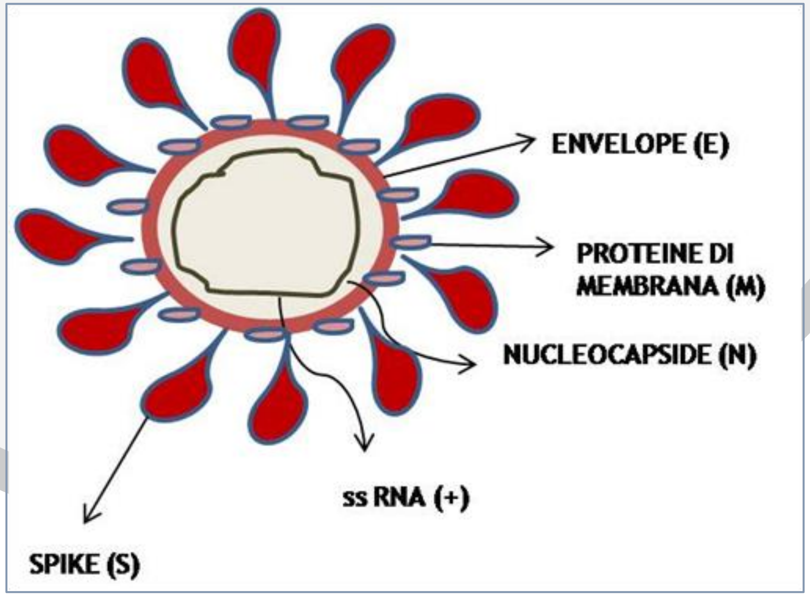
Classificazione

Famiglia - *Coronaviridae*

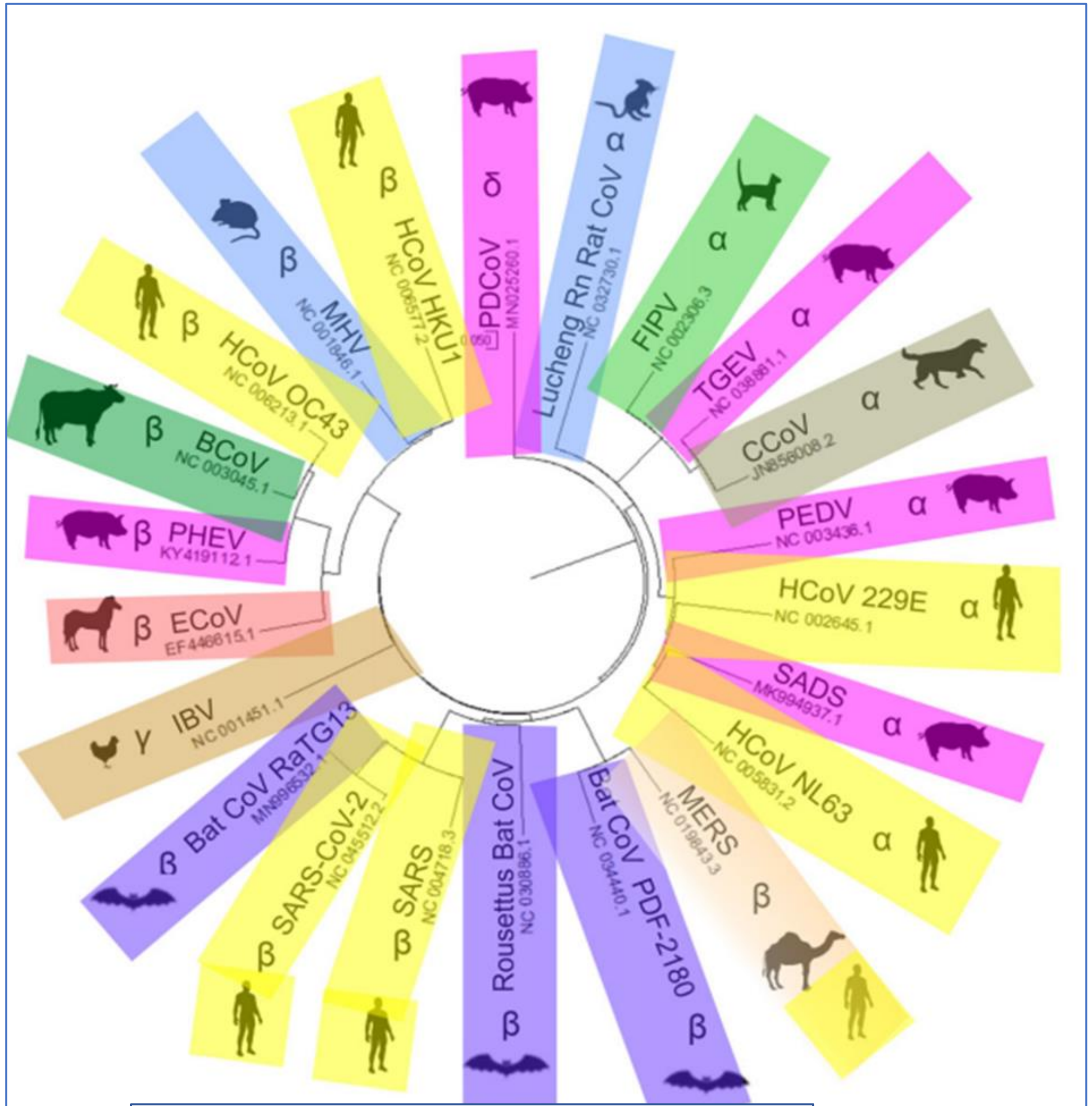
Sottofamiglia - *Coronavirinae*

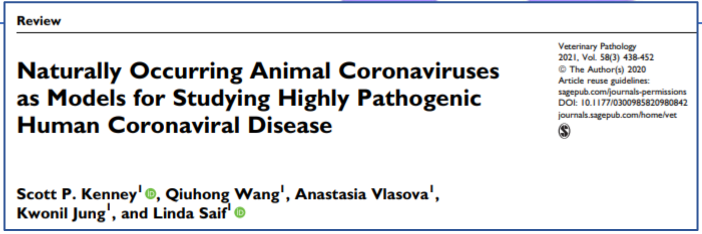
4 Generi **serbatoio**

Alfacoronaviruses
Betacoronavirus pipistrelli/roditori
Gammacoronavirus
Deltacoronavirus uccelli



ss(+)RNA virus





Review

Veterinary Pathology
2021, Vol. 58(3) 438-452
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DOI: 10.1177/0300985820980842
journals.sagepub.com/home/vet

Naturally Occurring Animal Coronaviruses as Models for Studying Highly Pathogenic Human Coronaviral Disease

Scott P. Kenney[1], Qiuhong Wang[1], Anastasia Vlasova[1],
Kwonil Jung[1], and Linda Saif[1]

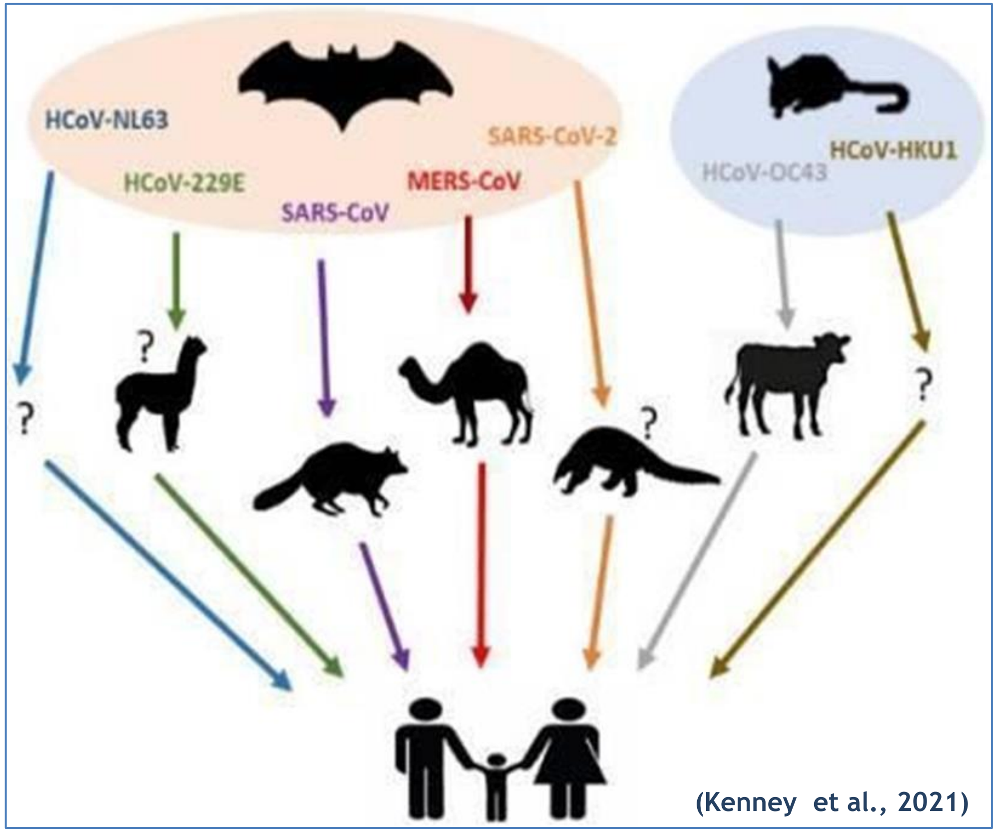
Human CoVs: α – β

SARS-CoV e MERS-CoV: ricombinazione e trasmissione interspecie

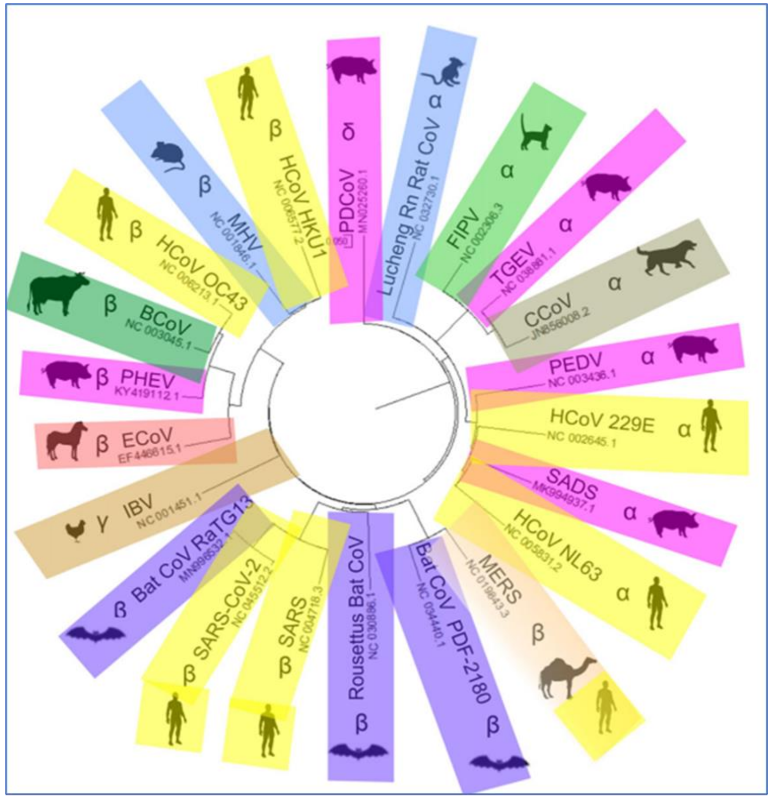
pipistrelli = serbatoi naturali di SARS-CoV e MERS-CoV

zibetti di palma, procioni, furetti, cammelli e dromedari = ospiti incidentali

→ hanno facilitato la diffusione di questi virus nell'uomo



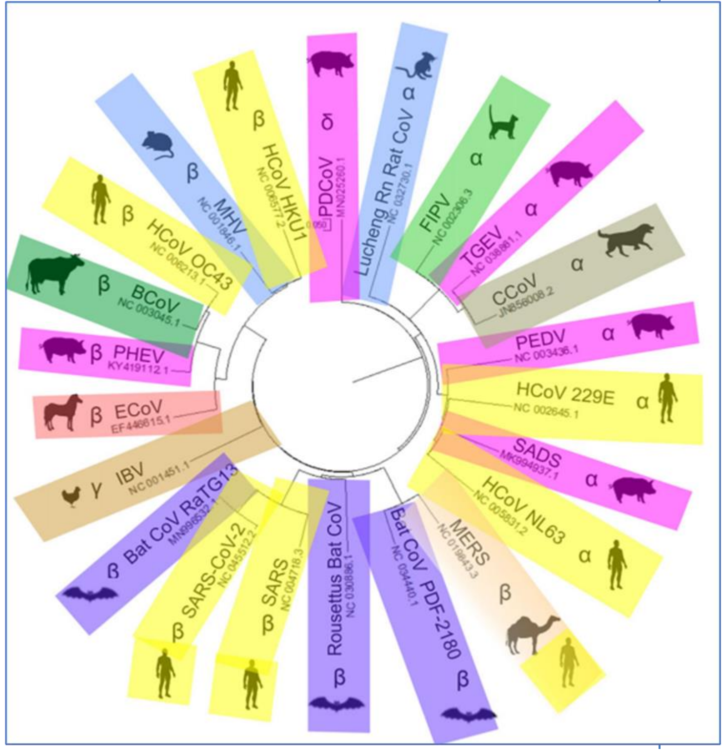
(Kenney et al., 2021)



(Kenney et al., 2021)

BatCoV - α/β

- ➢ Generalmente, no malattie manifeste
- ➢ Identità 96.2% SARS-CoV-2 e BatCoV RaTG13!



(Kenney et al., 2021)

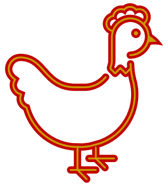
Mouse and Rat CoVs - β/α

The murine hepatitis virus (MHV) → important research model

Virus della bronchite infettiva (IBV): γ

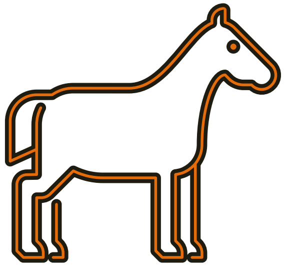
Patologia respiratoria; renale e riproduttiva

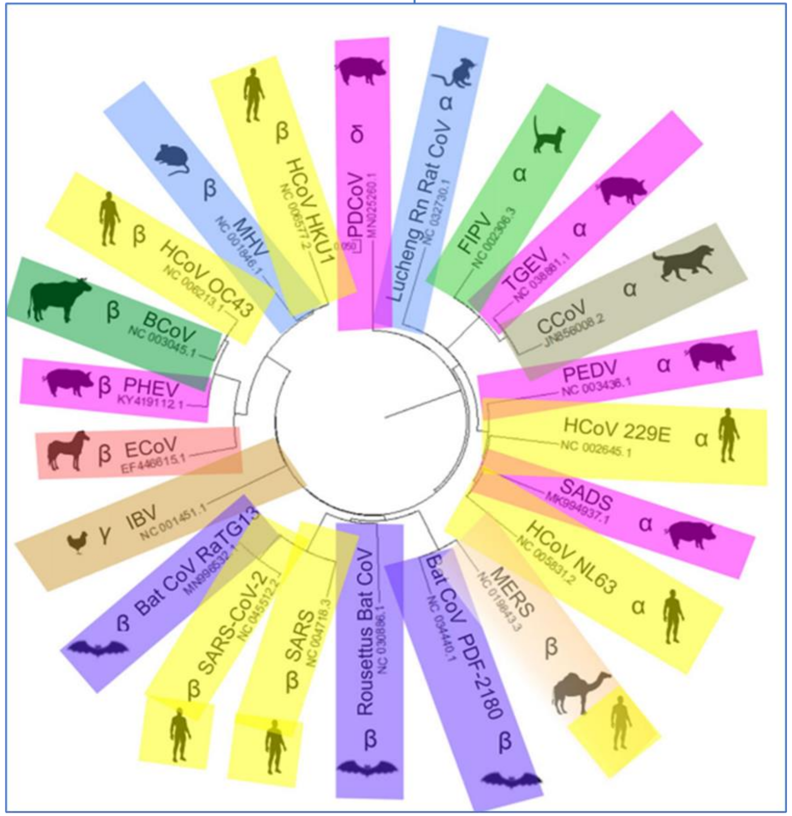
→ Notevoli danni economici



ECoV: β

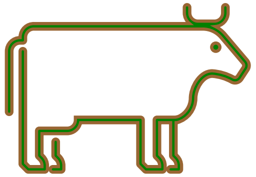
→ Enteriti nei puledri e negli adulti





(Kenney et al., 2021)

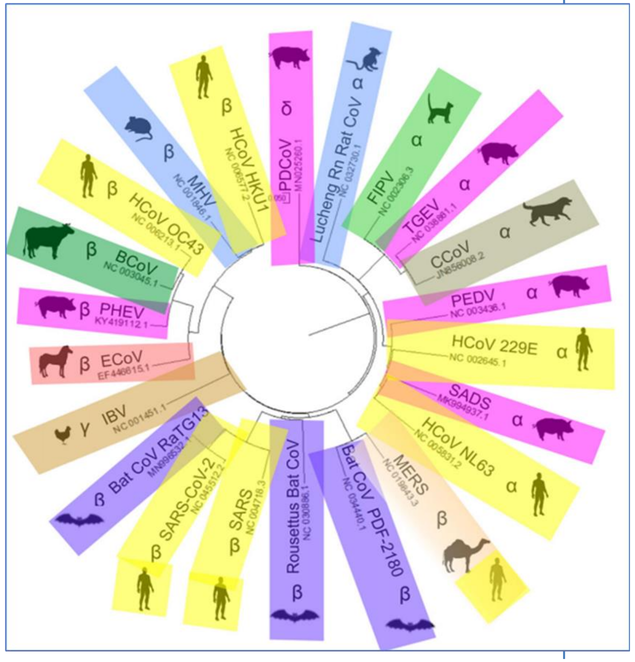
BCoV: β



- *diarrea del vitello*→(elevata mortalità)
- *dissenteria invernale*→ blocco lattazione;
- *infezioni respiratorie nei bovini di varie età*

BCoV-like → Superamento barriera di specie!

Pecore Capre Bufali - Lama Cervidi Dromedari



(Kenney et al., 2021)

Swine CoVs α – β – δ

AlfaCoVs

1) Virus della gastroenterite trasmissibile (TGEV)

(correlato a CCoV e FCoV)

→ Diarrea violenta ed elevata mortalità nei suinetti

2) Coronavirus respiratorio del suino (PRCoV)

3) Virus della diarrea endemica del suino (PEDV)

4) Coronavirus della sindrome della diarrea acuta (SADS-CoV)

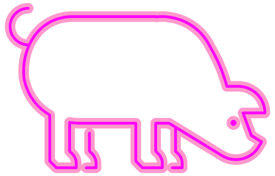
BetaCoVs

5) Virus dell'encefalomielite emoagglutinante suina (PHEV)

DeltaCoVs

6) Deltacoronavirus del suino (PDCoV) (recente)

→ danni economici gravi!

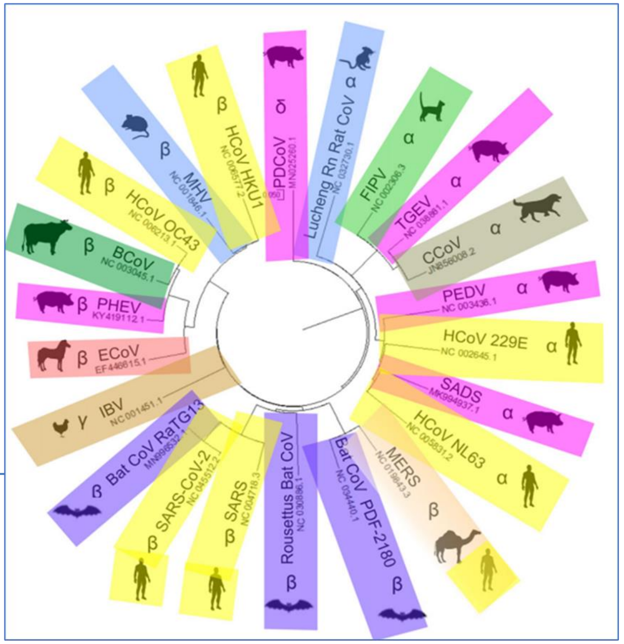


Virus Peritonite Infettiva Felina (**FIPV**) - α

Da FCoV enterico → mutazioni S → cambia tropismo:

enterocti → monociti/macrofagi <u>> virulenza → infezione sistemica</u>

FIPV → gravissima, letale



(Kenney et al., 2021)

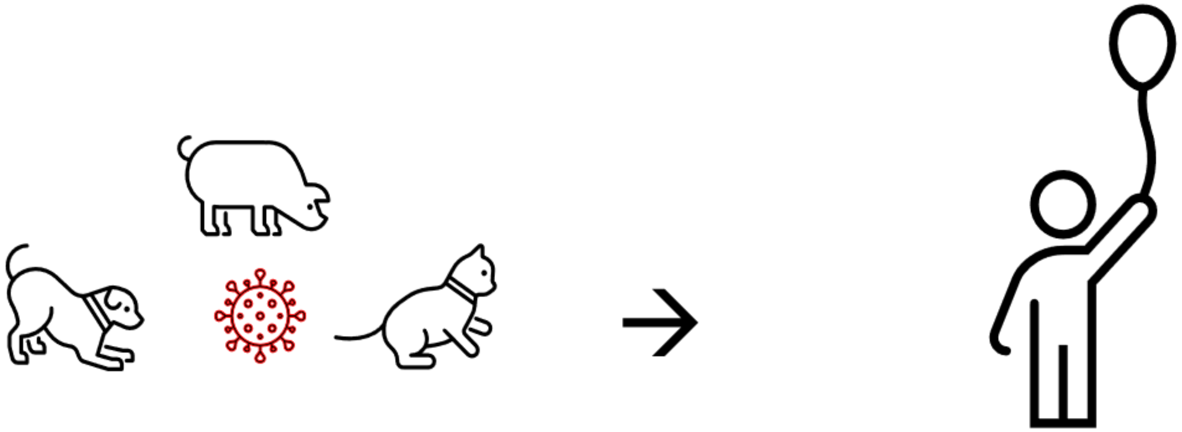
Canine CoV - α/β

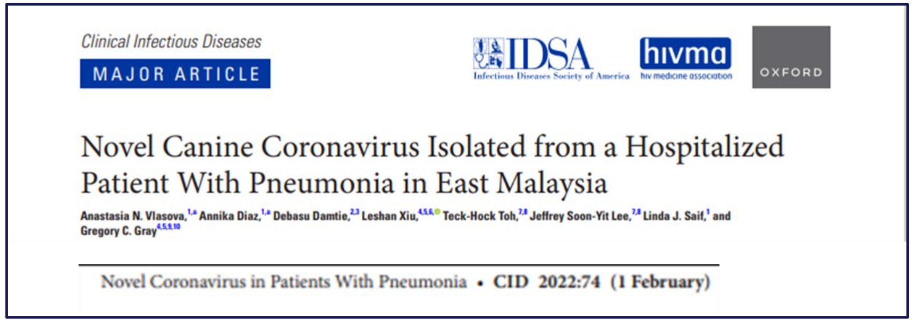
AlphaCoVs: CCoV → causes mild to enteric infectious. Genetic recombination (canine-feline-porcine) → pantropic biotypes → multi-systemic fatal infections in dogs.

BetaCoVs canine respiratory coronavirus → respiratory disease in dogs.

Recombinant CCoV strains: humans

→ CCoV-HuPn-2018 and HuCCoV_Z19, associated with acute respiratory illness, isolated from humans





Clinical Infectious Diseases

MAJOR ARTICLE

Novel Canine Coronavirus Isolated from a Hospitalized Patient With Pneumonia in East Malaysia

Anastasia N. Vlasova,[1,a] Annika Diaz,[1,a] Debasu Damtie,[2,3] Leshan Xiu,[4,5,6] Teck-Hock Toh,[7,8] Jeffrey Soon-Yit Lee,[7,8] Linda J. Saif,[1] and Gregory C. Gray[4,5,9,10]

Novel Coronavirus in Patients With Pneumonia • CID 2022:74 (1 February)

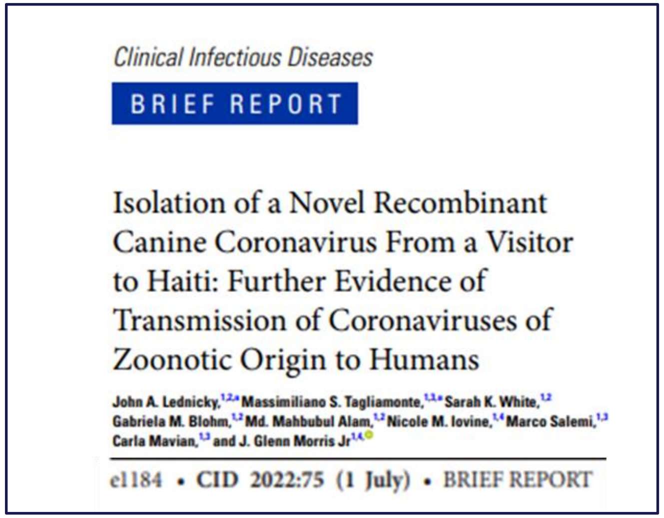
Emerging Microbes & Infections
2022, VOL. 11
https://doi.org/10.1080/22221751.2022.2040341

RESEARCH ARTICLE

OPEN ACCESS

Animal alphacoronaviruses found in human patients with acute respiratory illness in different countries.

Anastasia N. Vlasova[a], Teck-Hock Toh[b,c], Jeffrey Soon-Yit Lee[b,c], Yong Poovorawan[d], Phillip Davis[e], Marli S. P. Azevedo[f], John A. Lednicky[g,h], Linda J. Saif[a] and Gregory C. Gray[i]



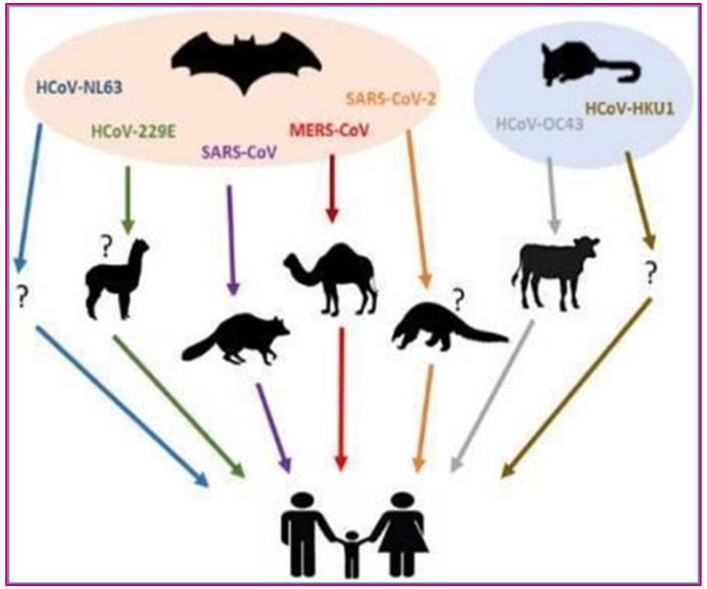
Clinical Infectious Diseases

BRIEF REPORT

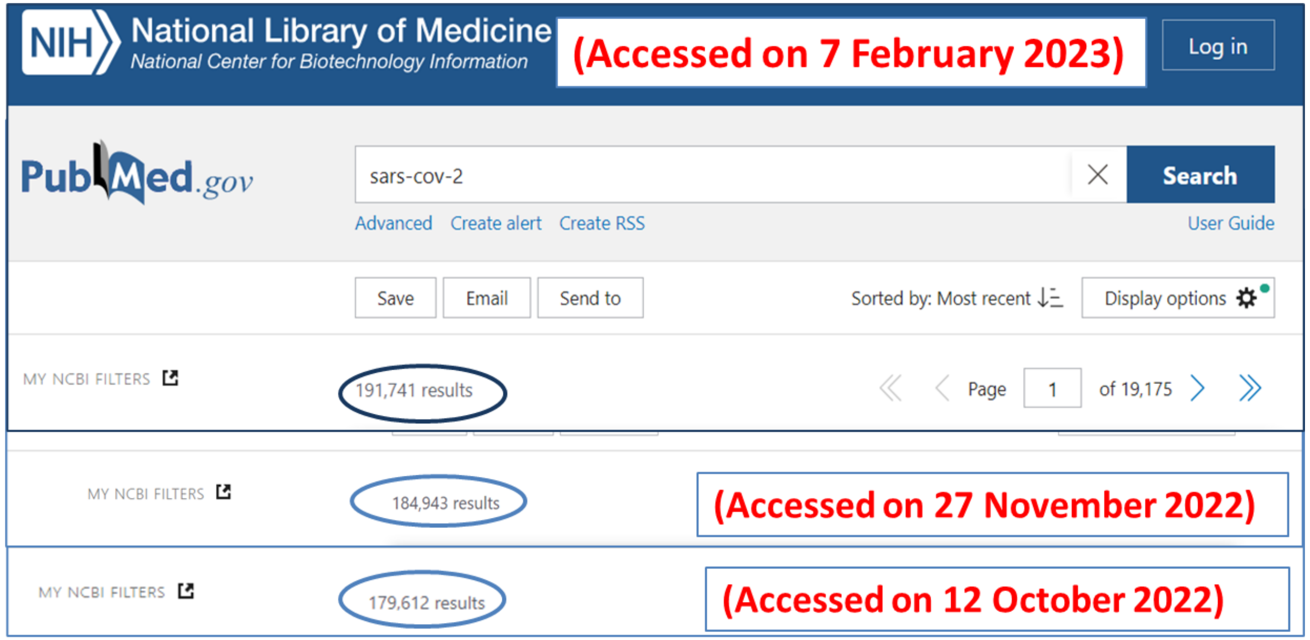
Isolation of a Novel Recombinant Canine Coronavirus From a Visitor to Haiti: Further Evidence of Transmission of Coronaviruses of Zoonotic Origin to Humans

John A. Lednicky,[1,2,a] Massimiliano S. Tagliamonte,[1,3,a] Sarah K. White,[1,2] Gabriela M. Blohm,[1,2] Md. Mahbubul Alam,[1,2] Nicole M. Iovine,[1,4] Marco Salemi,[1,3] Carla Mavian,[1,3] and J. Glenn Morris Jr[1,4]

e1184 • CID 2022:75 (1 July) • BRIEF REPORT



SARS-CoV-2



(Accessed on 7 February 2023)

sars-cov-2

Sorted by: Most recent

191,741 results

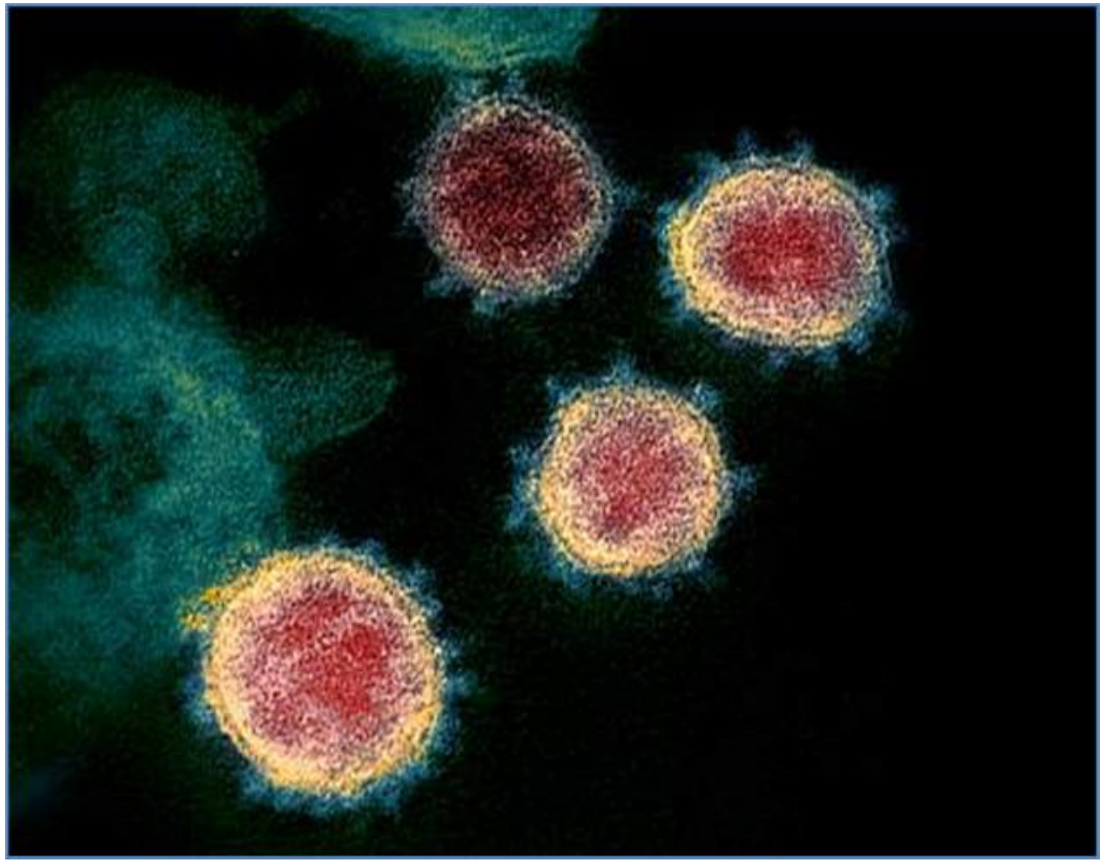
Page 1 of 19,175

184,943 results

(Accessed on 27 November 2022)

179,612 results

(Accessed on 12 October 2022)



(NIH.GOV)

Variants of concerns – (VOCs)

- **Increased transmissibility or virulence**
- **Decreased neutralization by antibodies**
- **Capacity to elude detection**
- **Reduction in therapeutic or vaccine efficiency**

Dati di sequenziamento periodo 19 dicembre 2022 – 29 gennaio 2023:

in Italia → 99,97% variante Omicron - 0,03% ricombinante Delta/Omicron

BA 5 (87,0%)

www.iss.it

Variante Omicron (Variante B.1.1.529) rilevata per la prima volta in Sud Africa il 24 novembre 2021.

Variante Delta (Variante VUI-21APR-01, nota anche come B.1.617) rilevata per la prima volta in India.

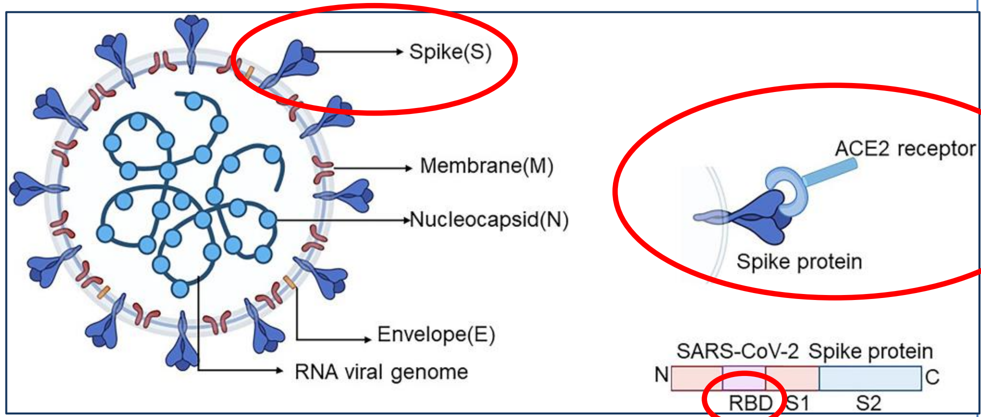
Variante Gamma (Variante P.1) con origine in Brasile.

Variante Beta (Variante 501Y.V2, nota anche come B.1.351) identificata in Sud Africa.

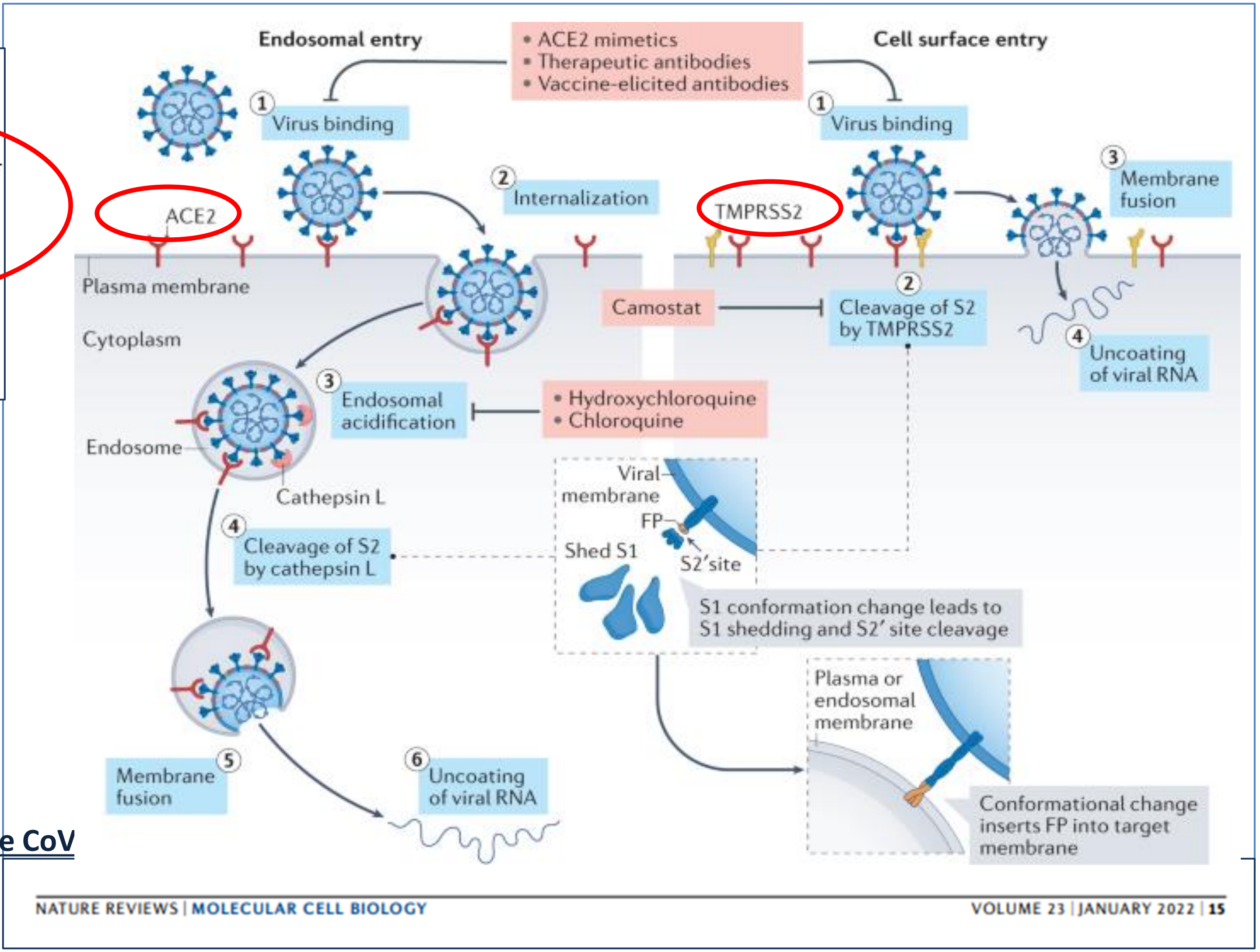
Variante Alfa (Variante VOC 202012/01, nota anche come B.1.1.7) identificata nel Regno Unito.

SARS-CoV-2: spike protein (S)-ACE2

The viral spike's RBD interacts with the ACE-2 receptor, involving TMPRSS2 → viral entry to host cells

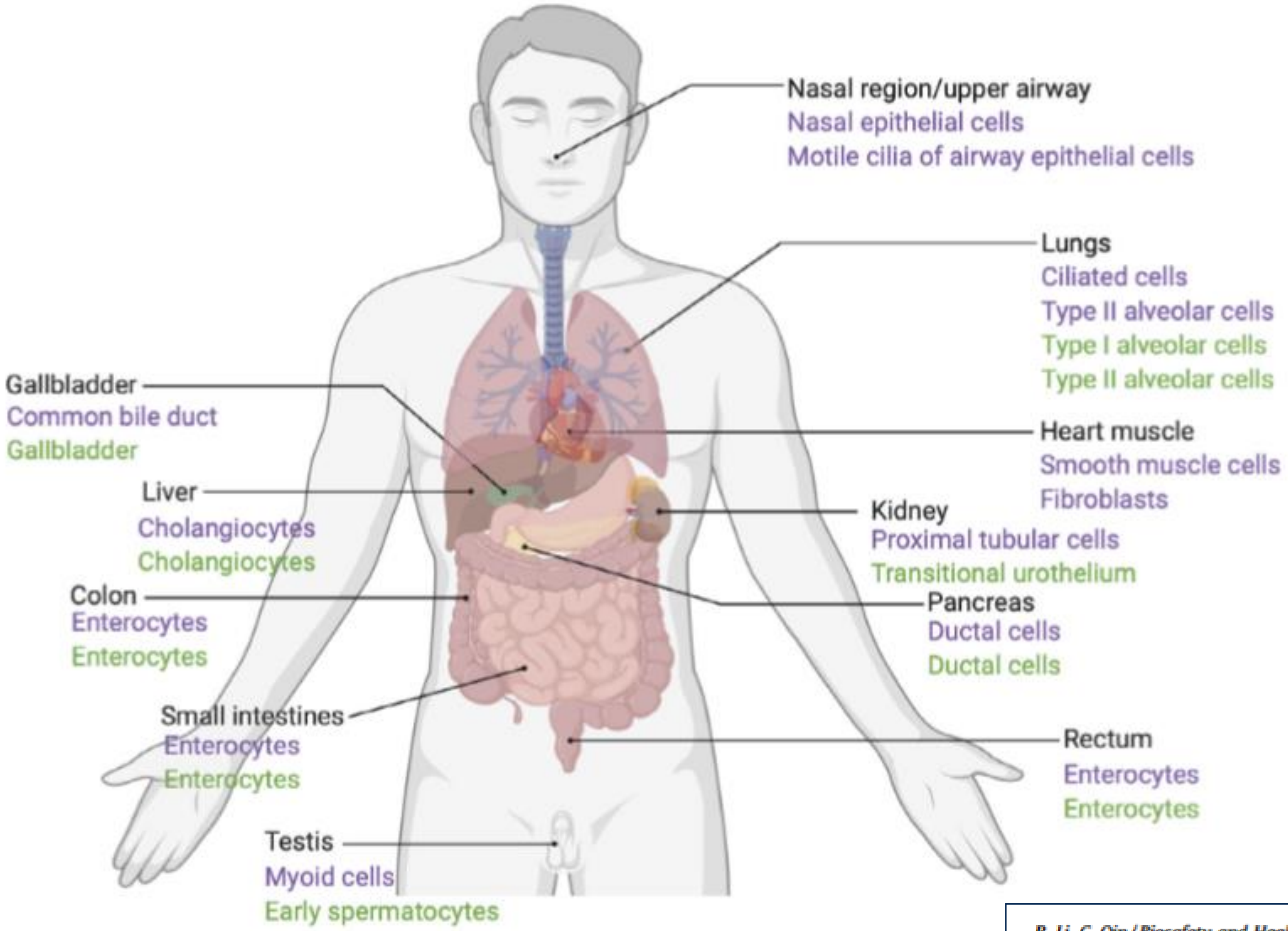


Front. Mol. Biosci., 22 April 2021
Sec. Structural Biology
Volume 8 - 2021 | https://doi.org/10.3389/fmolb.2021.671633



Receptor-binding domain (RBD) → the most variable region of the CoV
Angiotensin-converting enzyme 2 (ACE2)
Transmembrane serine protease 2 (TMPRSS2)

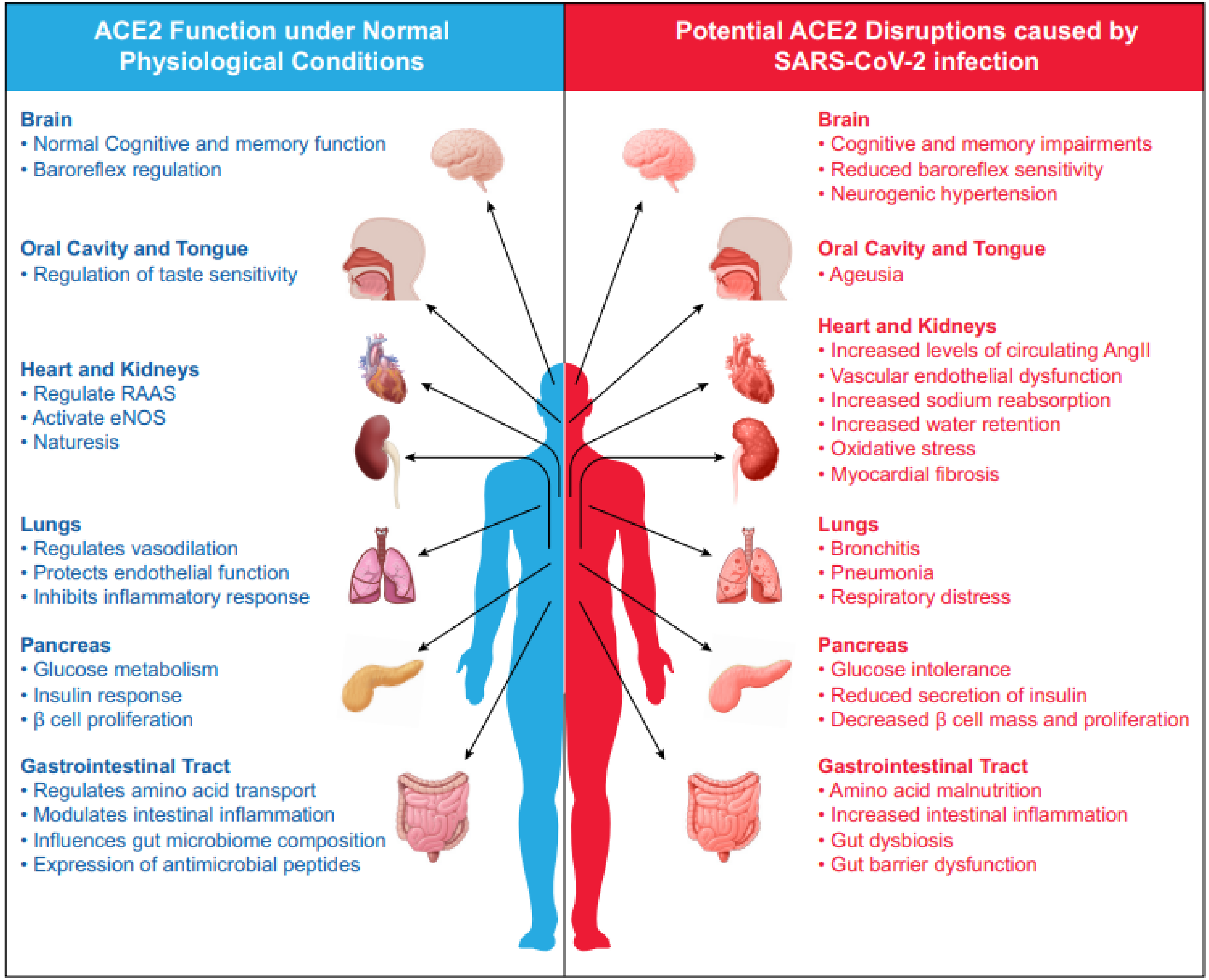
Expression pattern of ACE2 and TMPRSS2



Cell types expressing ACE2 →in purple.
Cell types expressing TMPRSS2 →in green.

R. Li, C. Qin / Biosafety and Health 3 (2021) 312–318

ACE2 (in human)



ACE2 Function under Normal Physiological Conditions

Brain
- Normal Cognitive and memory function
- Baroreflex regulation

Oral Cavity and Tongue
- Regulation of taste sensitivity

Heart and Kidneys
- Regulate RAAS
- Activate eNOS
- Naturesis

Lungs
- Regulates vasodilation
- Protects endothelial function
- Inhibits inflammatory response

Pancreas
- Glucose metabolism
- Insulin response
- β cell proliferation

Gastrointestinal Tract
- Regulates amino acid transport
- Modulates intestinal inflammation
- Influences gut microbiome composition
- Expression of antimicrobial peptides

Potential ACE2 Disruptions caused by SARS-CoV-2 infection

Brain
- Cognitive and memory impairments
- Reduced baroreflex sensitivity
- Neurogenic hypertension

Oral Cavity and Tongue
- Ageusia

Heart and Kidneys
- Increased levels of circulating AngII
- Vascular endothelial dysfunction
- Increased sodium reabsorption
- Increased water retention
- Oxidative stress
- Myocardial fibrosis

Lungs
- Bronchitis
- Pneumonia
- Respiratory distress

Pancreas
- Glucose intolerance
- Reduced secretion of insulin
- Decreased β cell mass and proliferation

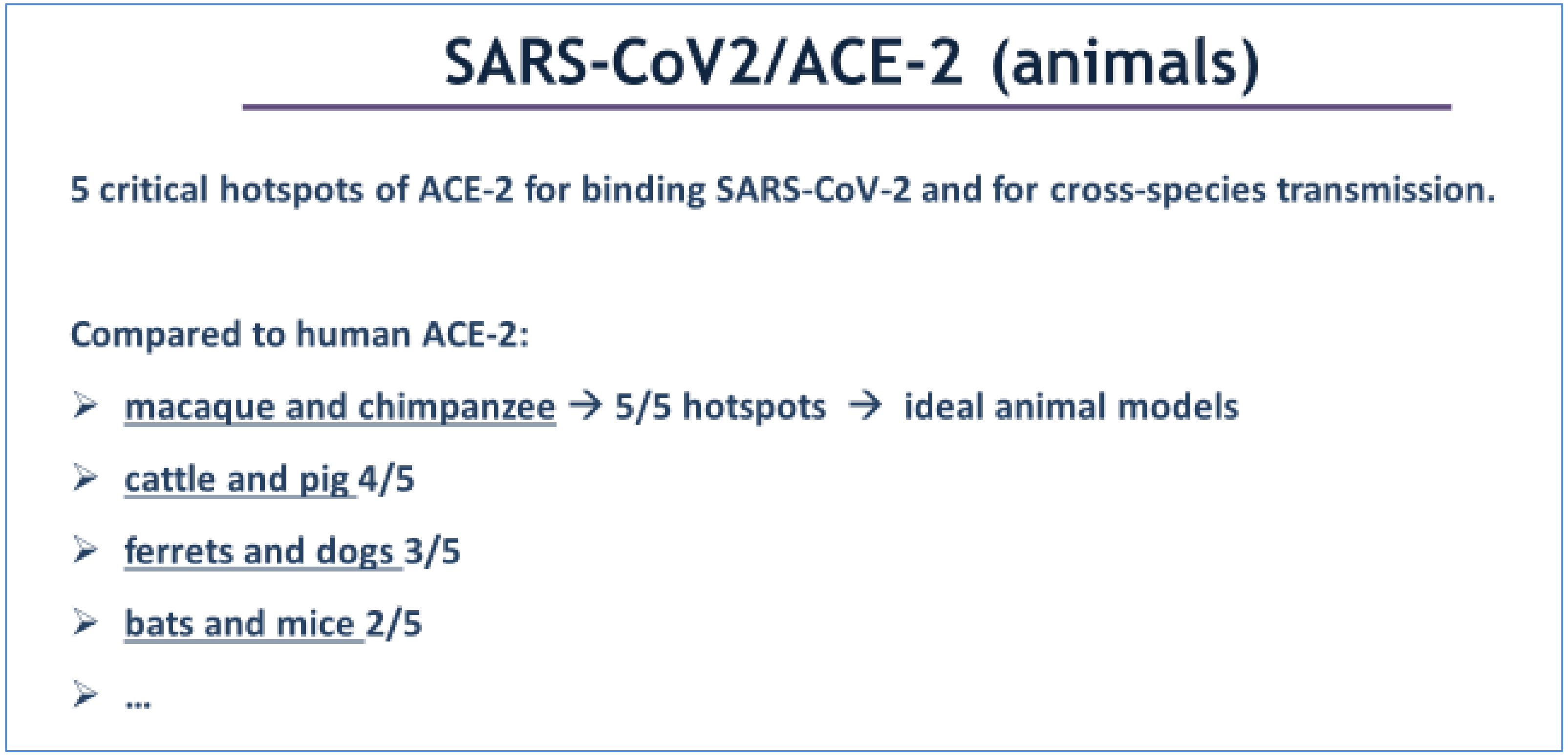
Gastrointestinal Tract
- Amino acid malnutrition
- Increased intestinal inflammation
- Gut dysbiosis
- Gut barrier dysfunction

Physiol Genomics 53: 51–60, 2021.

SARS-CoV2: Animal susceptibility

The critical step for a virus to infect an animal is its ability to enter the host cells.

SARS-CoV-2 entry into cells first requires the S protein on the surface of the virus to bind the host cell receptor.



SARS-CoV2/ACE-2 (animals)

5 critical hotspots of ACE-2 for binding SARS-CoV-2 and for cross-species transmission.

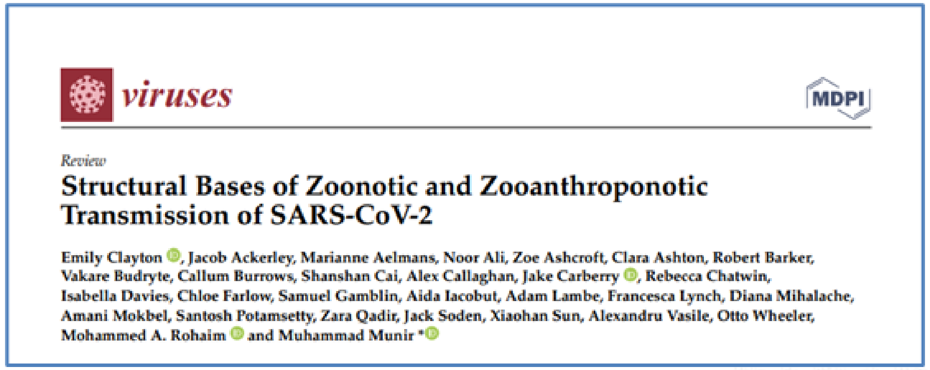
Compared to human ACE-2:

- macaque and chimpanzee → 5/5 hotspots → ideal animal models
- cattle and pig 4/5
- ferrets and dogs 3/5
- bats and mice 2/5
- …

SARS-CoV-2: spike-ACE2 (animals)

The susceptibility of animals to SARS-CoV-2 infection

→ by comparing ACE2 of animals and human.



viruses MDPI

Review

Structural Bases of Zoonotic and Zooanthroponotic Transmission of SARS-CoV-2

Emily Clayton, Jacob Ackerley, Marianne Aelmans, Noor Ali, Zoe Ashcroft, Clara Ashton, Robert Barker, Vakare Budryte, Callum Burrows, Shanshan Cai, Alex Callaghan, Jake Carberry, Rebecca Chatwin, Isabella Davies, Chloe Farlow, Samuel Gamblin, Aida Iacobut, Adam Lambe, Francesca Lynch, Diana Mihalache, Amani Mokbel, Santosh Potamsetty, Zara Qadir, Jack Soden, Xiaohan Sun, Alexandru Vasile, Otto Wheeler, Mohammed A. Rohaim and Muhammad Munir *

MÉDECINE TROPICALE ET SANTÉ INTERNATIONALE

ARTICLE ORIGINAL

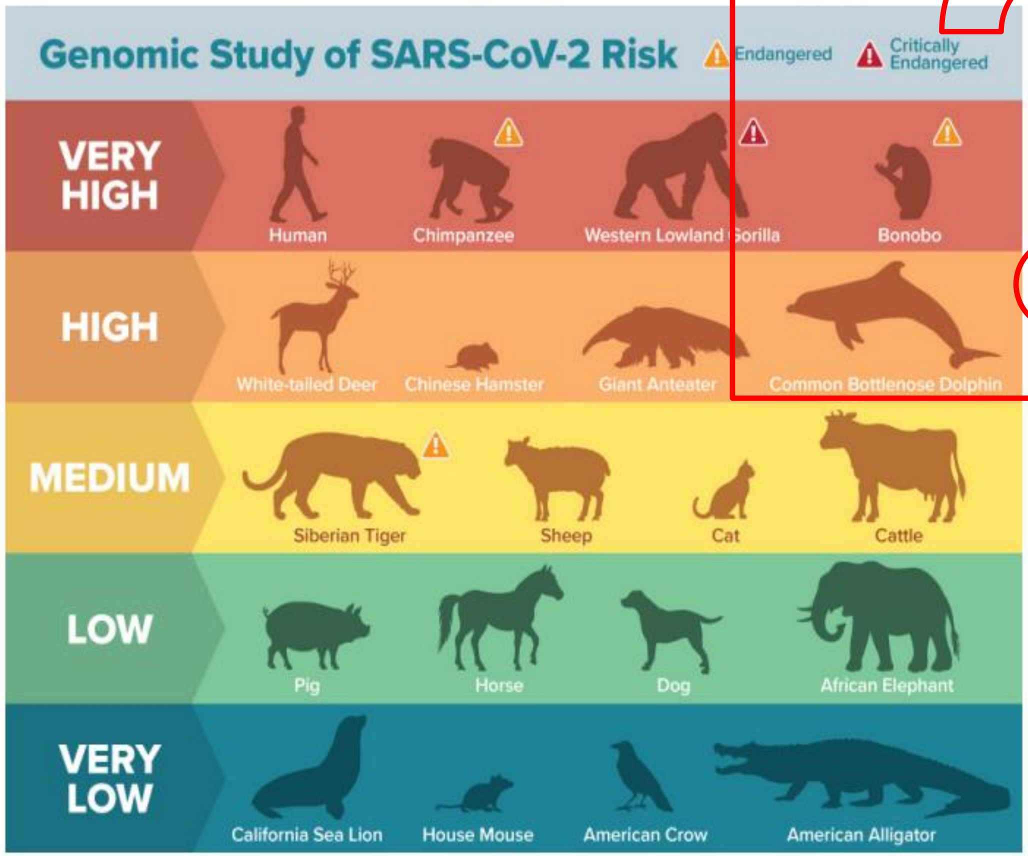
SANTÉ PUBLIQUE/PUBLIC HEALTH

LES DANGERS DU SARS-COV-2 POUR LES ÉCOSYSTÈMES AQUATIQUES

THE HAZARDS OF SARS-COV-2 FOR AQUATIC ECOSYSTEMS

Salma FERCHICHI, Naouel FATNASSI, Anissa DHAOUADI*, Hédia ATTIA EL HILI

Animal species' receptivity to SARS-CoV-2



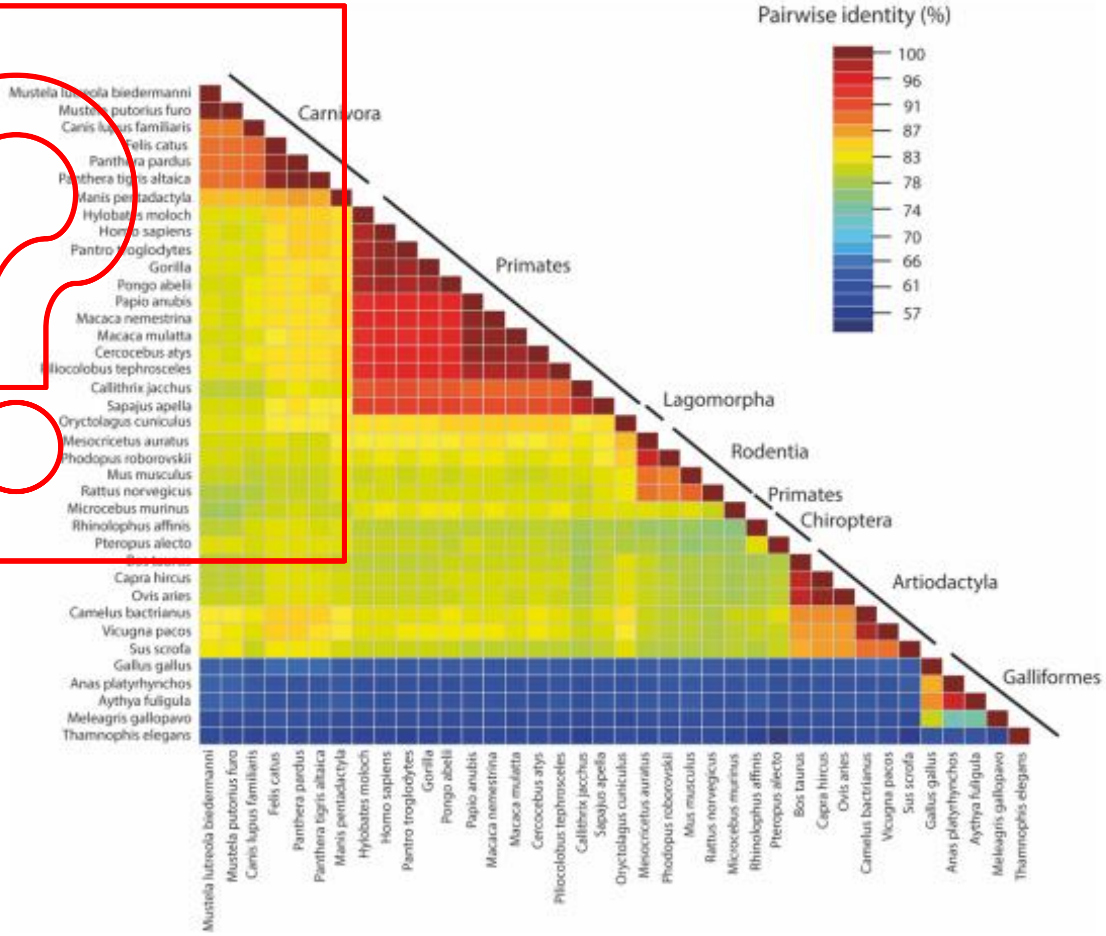


Figure 2. The pairwise identities plot of ACE2 protein sequences aligned by MAFFT and displayed by Sequence Demarcation Tool (SDT) software.

SARS-CoV2: Animal susceptibility

Binding affinity SARS-CoV-2---ACE-2 is not the only factor responsible for the differences in animal susceptibility

- **The binding energies between different animal receptors and the SARS-CoV-2 S protein differ;**
- **The ACE-2 receptor amino acid sequence varies with species → differing RBD-ACE-2 binding kinetics;**
- **The presence of multiple ACE-2 isoforms in animals → may activate/inhibit the binding RBD-ACE-2 → high/low susceptibility;**
- **The expression level of ACE2 also affects susceptibility.**

(Qiu et al., J Med Virol. 2022; 95, e28147)

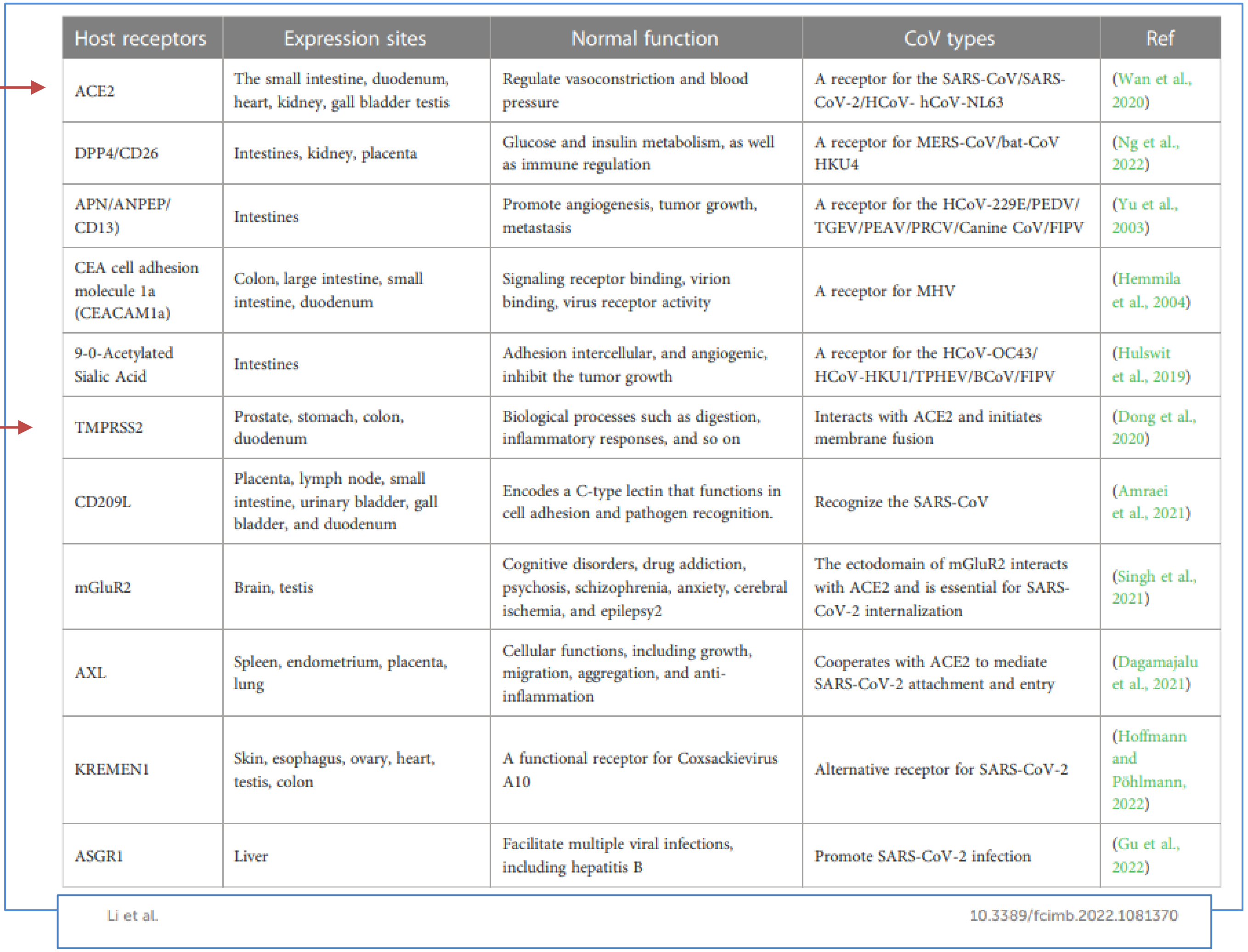
SARS-CoV2: (Animal susceptibility)

After the virus binds to the receptor, membrane fusion is also required, a process also mediated by the S protein.

- **Two cleavage events are involved, mainly involve two proteases, Furin and TMPRSS2, which are also important triggers for the entry of SARS-CoV-2 into cells;**
- **The cellular expression levels of Furin and TMPRSS2 may affect the infectivity of-SARS-CoV-2.**
- **Cells with high levels of Furin, TMPRSS2, and ACE2 co-expression may also be more susceptible to infection by SARS-CoV-2.**

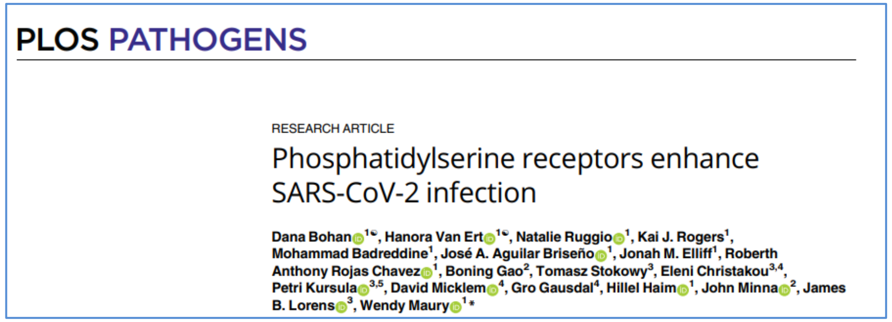
(Qiu et al., J Med Virol. 2022; 95, e28147)

Coronaviruses: receptors



Host receptors	Expression sites	Normal function	CoV types	Ref
ACE2	The small intestine, duodenum, heart, kidney, gall bladder testis	Regulate vasoconstriction and blood pressure	A receptor for the SARS-CoV/SARS-CoV-2/HCoV- hCoV-NL63	(Wan et al., 2020)
DPP4/CD26	Intestines, kidney, placenta	Glucose and insulin metabolism, as well as immune regulation	A receptor for MERS-CoV/bat-CoV HKU4	(Ng et al., 2022)
APN/ANPEP/CD13)	Intestines	Promote angiogenesis, tumor growth, metastasis	A receptor for the HCoV-229E/PEDV/TGEV/PEAV/PRCV/Canine CoV/FIPV	(Yu et al., 2003)
CEA cell adhesion molecule 1a (CEACAM1a)	Colon, large intestine, small intestine, duodenum	Signaling receptor binding, virion binding, virus receptor activity	A receptor for MHV	(Hemmila et al., 2004)
9-0-Acetylated Sialic Acid	Intestines	Adhesion intercellular, and angiogenic, inhibit the tumor growth	A receptor for the HCoV-OC43/HCoV-HKU1/TPHEV/BCoV/FIPV	(Hulswit et al., 2019)
TMPRSS2	Prostate, stomach, colon, duodenum	Biological processes such as digestion, inflammatory responses, and so on	Interacts with ACE2 and initiates membrane fusion	(Dong et al., 2020)
CD209L	Placenta, lymph node, small intestine, urinary bladder, gall bladder, and duodenum	Encodes a C-type lectin that functions in cell adhesion and pathogen recognition.	Recognize the SARS-CoV	(Amraei et al., 2021)
mGluR2	Brain, testis	Cognitive disorders, drug addiction, psychosis, schizophrenia, anxiety, cerebral ischemia, and epilepsy2	The ectodomain of mGluR2 interacts with ACE2 and is essential for SARS-CoV-2 internalization	(Singh et al., 2021)
AXL	Spleen, endometrium, placenta, lung	Cellular functions, including growth, migration, aggregation, and anti-inflammation	Cooperates with ACE2 to mediate SARS-CoV-2 attachment and entry	(Dagamajalu et al., 2021)
KREMEN1	Skin, esophagus, ovary, heart, testis, colon	A functional receptor for Coxsackievirus A10	Alternative receptor for SARS-CoV-2	(Hoffmann and Pöhlmann, 2022)
ASGR1	Liver	Facilitate multiple viral infections, including hepatitis B	Promote SARS-CoV-2 infection	(Gu et al., 2022)

Li et al. 10.3389/fcimb.2022.1081370



PLOS PATHOGENS

RESEARCH ARTICLE

Phosphatidylserine receptors enhance SARS-CoV-2 infection

Dana Bohan[1☯], Hanora Van Ert[1☯], Natalie Ruggio[1], Kai J. Rogers[1], Mohammad Badreddine[1], José A. Aguilar Briseño[1], Jonah M. Elliff[1], Roberth Anthony Rojas Chavez[1], Boning Gao[2], Tomasz Stokowy[3], Eleni Christakou[3,4], Petri Kursula[3,5], David Micklem[4], Gro Gausdal[4], Hillel Haim[1], John Minna[2], James B. Lorens[3], Wendy Maury[1*]

nature COMMUNICATIONS

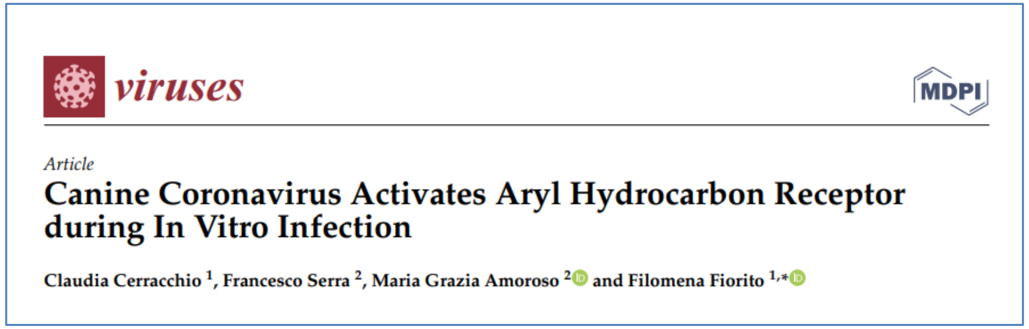
ARTICLE

Check for updates

https://doi.org/10.1038/s41467-021-25412-x OPEN

AHR signaling is induced by infection with coronaviruses

Federico Giovannoni[1,8], Zhaorong Li[1,8], Federico Remes-Lenicov[2], María E. Dávola[3], Mercedes Elizalde[2], Ana Paletta[2], Ali A. Ashkar[3], Karen L. Mossman[3], Andrea V. Dugour[4], Juan M. Figueroa[4], Andrea A. Barquero[5], Ana Ceballos[2], Cybele C. Garcia[6,9✉] & Francisco J. Quintana[1,7,9✉]



viruses MDPI

Article

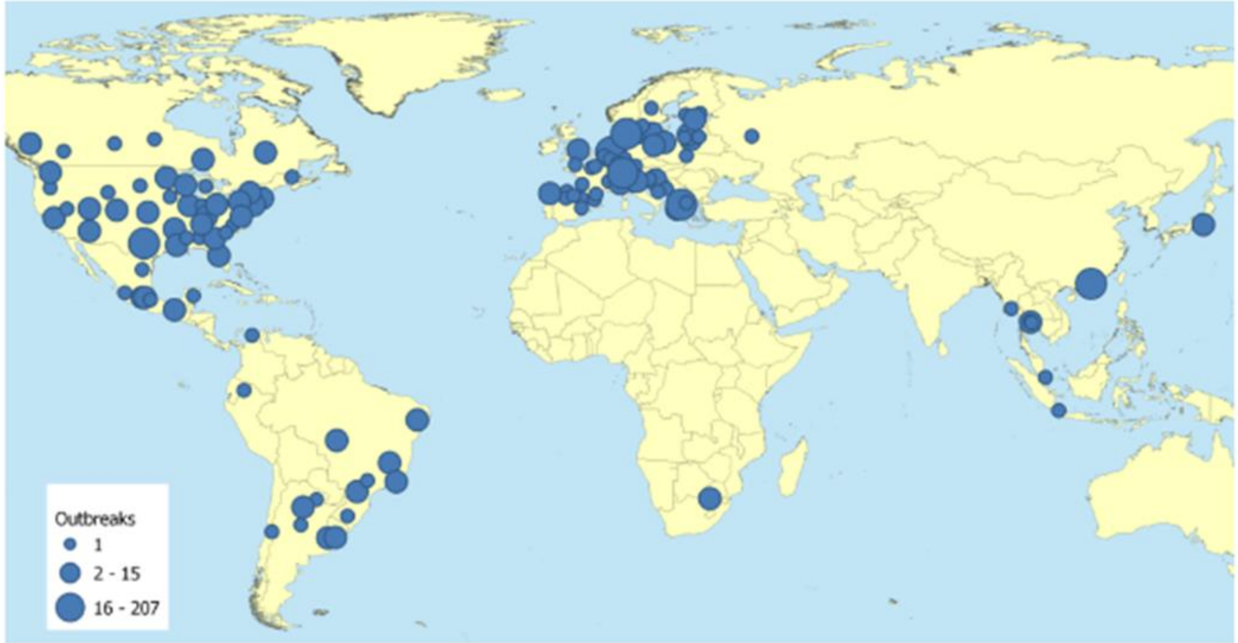
Canine Coronavirus Activates Aryl Hydrocarbon Receptor during In Vitro Infection

Claudia Cerracchio[1], Francesco Serra[2], Maria Grazia Amoroso[2] and Filomena Fiorito[1,*]

Map: cases of SARS-CoV-2 infection in animals reported to WOAH since March 2020

Global situation since the beginning of the pandemic

The worldwide geographical distribution of SARS-CoV-2 outbreaks in animals reported to WOAH is shown in Figure 1. The first case of SARS-CoV-2 in animals was officially reported to WOAH by Hong-Kong (SARC) on 29 February 2021 in a dog.



https://www.woah.org/
(accessed on 6 February 2023)

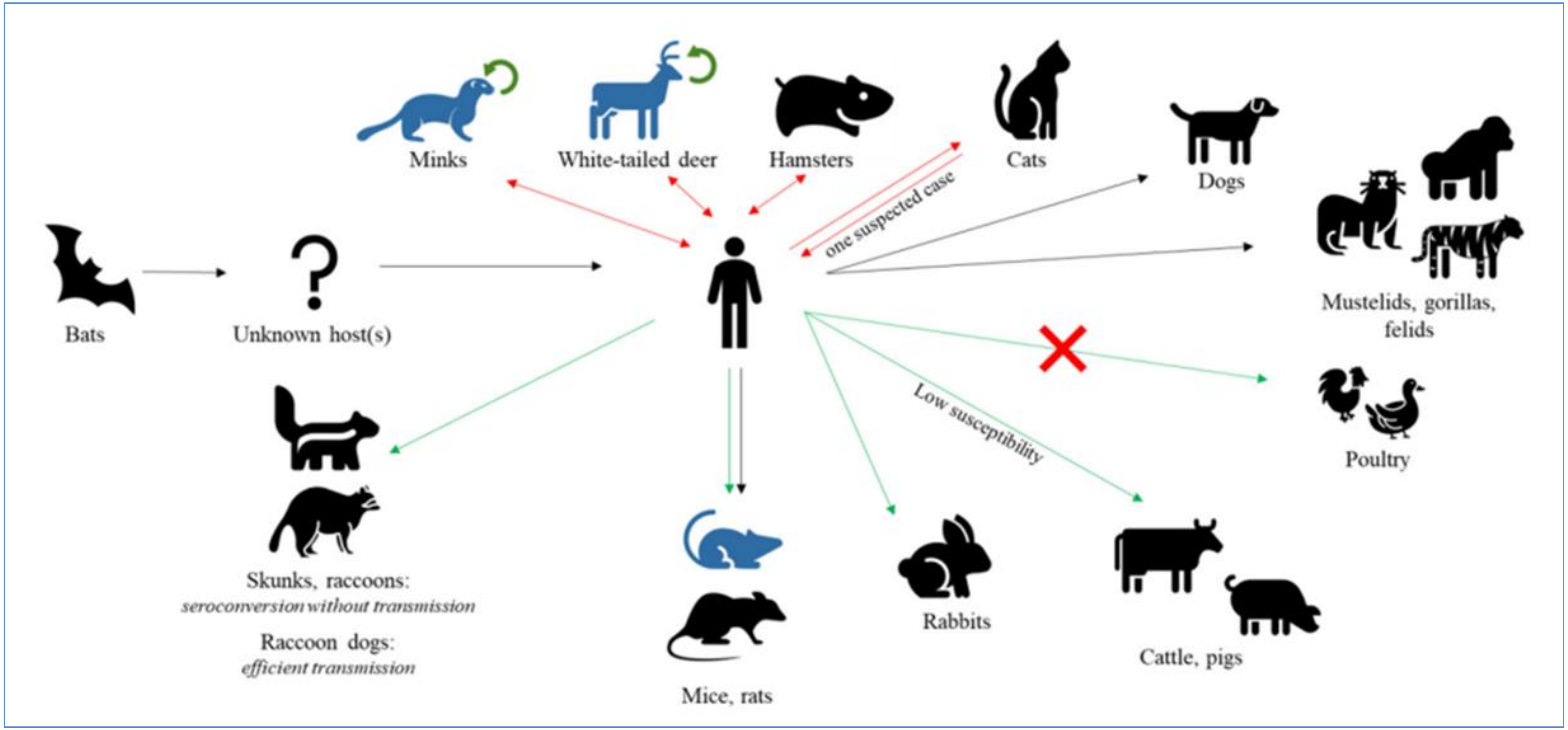
SARS-COV-2 IN ANIMALS – SITUATION REPORT 20 31/12/2022

Table 1. Number of outbreaks (n=699) reported worldwide, by species and region (as of 31 December 2022).

Region Species	Africa	Americas	Asia	Europe
Binturong		X		
Black-tailed marmoset		X		
Canada lynx		X		
Cat		X	X	X
Common squirrel monkey		X		
Dog		X	X	X
Eurasian lynx				X
Fishing cat		X		
Giant anteater		X		
Gorilla		X		X
Hamster			X	
Hippopotamus				X
Lion	X	X	X	X
Mandrill		X		
Mink		X		X
Mule deer		X		
Otter		X		
Pet ferret		X		X
Puma	X	X		
Red fox				X
Snow leopard		X		
South American coati		X		
Spotted hyena		X		
Tiger		X	X	X
West Indian manatee		X		
White-tailed deer		X		

26 species

SARS-CoV-2: mammalian hosts



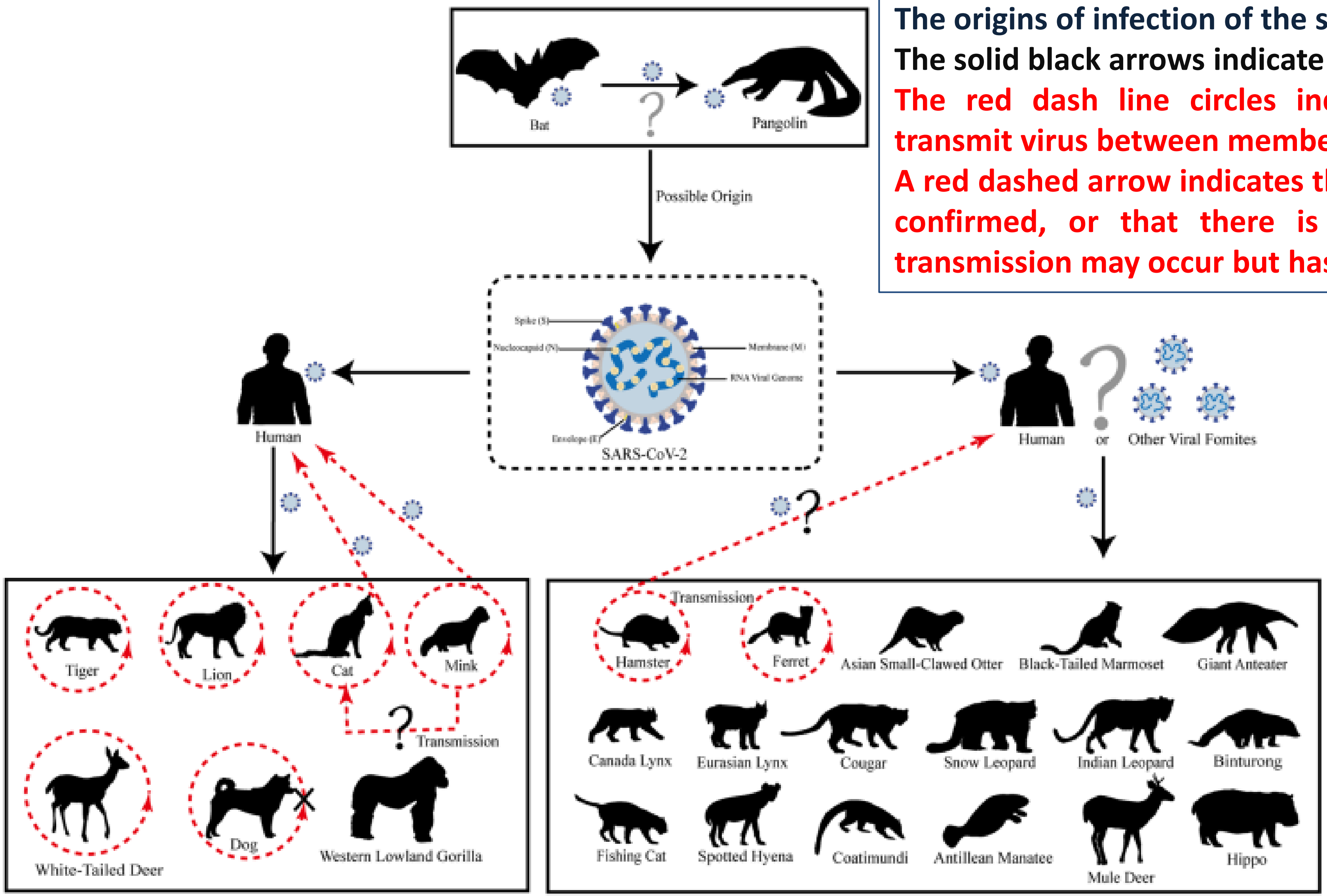
Reggiani et al., 2022

DOI 10.3389/fvets.2022.1085613

Black arrows = natural infections
Red double arrows = natural infections with demonstrated reverse spillover to humans
Green arrows = experimental infections
Green circular arrows = demonstrated intra-species circulation
Species with known adapted variants are indicated in blue

Possible sources of SARS-CoV-2 and animal species naturally infected with SARS-CoV-2

Species in the left box can be infected by positive humans.
The origins of infection of the species in the right box are not yet clear.
The solid black arrows indicate the transmission route of the virus.
The red dash line circles indicate that the infected animals can transmit virus between members of the same species.
A red dashed arrow indicates that cross-species transmission has been confirmed, or that there is research showing that cross-species transmission may occur but has not been confirmed.



(Qiu et al., J Med Virol. 2022; 95, e28147)

SARS-CoV2: bats

To date, two bat species, big brown bats (*Eptesicus fuscus*) and Egyptian fruit bats (*Rousettus aegyptiacus*), have been tested in the laboratory:

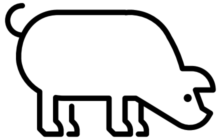
- Egyptian fruit bats → infected after exposure to inoculated animals
- None of the experimentally infected big brown bats shed virus or transmitted it
- Both species of bat did not develop clinical signs of disease

However, there are over 1,400 bat species worldwide and each species may respond differently to infection…

Low susceptibility to SARS-CoV-2 infection

rabbit

pig



Check for updates

Received: 15 June 2022 | Revised: 28 July 2022 | Accepted: 9 August 2022

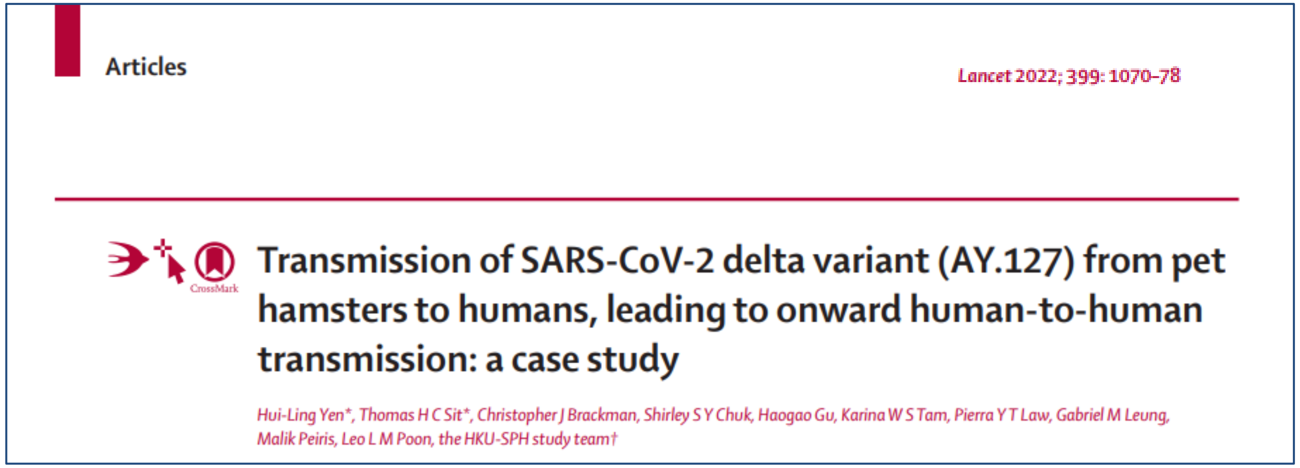
DOI: 10.1111/xen.12772

Xenotransplantation WILEY

REVIEW ARTICLE

SARS-CoV-2 does not infect pigs, but this has to be verified regularly

Tanja Opriessnig[1,2] | Yao-Wei Huang[3]

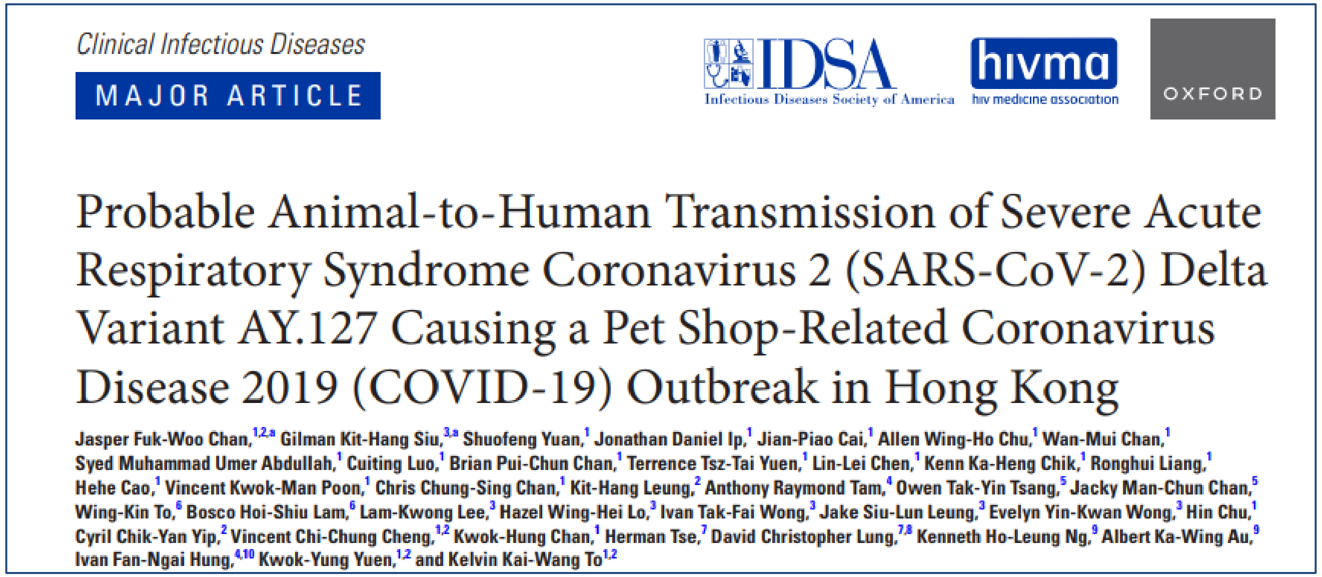


Articles

Lancet 2022; 399: 1070–78

Transmission of SARS-CoV-2 delta variant (AY.127) from pet hamsters to humans, leading to onward human-to-human transmission: a case study

Hui-Ling Yen, Thomas H C Sit*, Christopher J Brackman, Shirley S Y Chuk, Haogao Gu, Karina W S Tam, Pierra Y T Law, Gabriel M Leung, Malik Peiris, Leo L M Poon, the HKU-SPH study team†*



Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

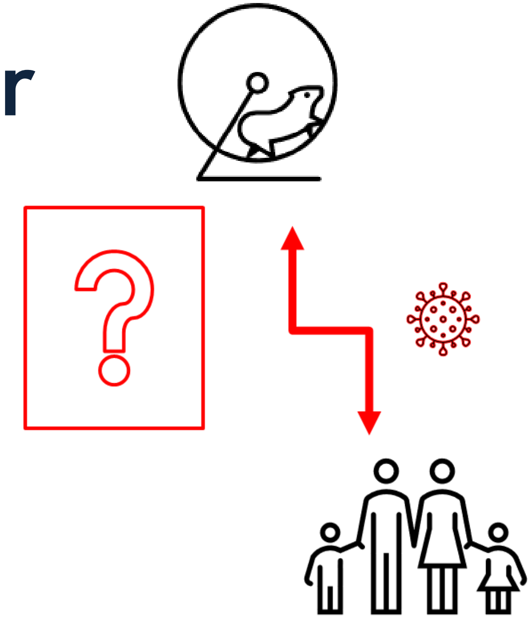
hivma hiv medicine association

OXFORD

Probable Animal-to-Human Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Delta Variant AY.127 Causing a Pet Shop-Related Coronavirus Disease 2019 (COVID-19) Outbreak in Hong Kong

Jasper Fuk-Woo Chan,[1,2,a] Gilman Kit-Hang Siu,[3,a] Shuofeng Yuan,[1] Jonathan Daniel Ip,[1] Jian-Piao Cai,[1] Allen Wing-Ho Chu,[1] Wan-Mui Chan,[1] Syed Muhammad Umer Abdullah,[1] Cuiting Luo,[1] Brian Pui-Chun Chan,[1] Terrence Tsz-Tai Yuen,[1] Lin-Lei Chen,[1] Kenn Ka-Heng Chik,[1] Ronghui Liang,[1] Hehe Cao,[1] Vincent Kwok-Man Poon,[1] Chris Chung-Sing Chan,[1] Kit-Hang Leung,[2] Anthony Raymond Tam,[4] Owen Tak-Yin Tsang,[5] Jacky Man-Chun Chan,[5] Wing-Kin To,[6] Bosco Hoi-Shiu Lam,[6] Lam-Kwong Lee,[3] Hazel Wing-Hei Lo,[3] Ivan Tak-Fai Wong,[3] Jake Siu-Lun Leung,[3] Evelyn Yin-Kwan Wong,[3] Hin Chu,[1] Cyril Chik-Yan Yip,[2] Vincent Chi-Chung Cheng,[1,2] Kwok-Hung Chan,[1] Herman Tse,[7] David Christopher Lung,[7,8] Kenneth Ho-Leung Ng,[9] Albert Ka-Wing Au,[9] Ivan Fan-Ngai Hung,[4,10] Kwok-Yung Yuen,[1,2] and Kelvin Kai-Wang To[1,2]

hamster



The origin of this case was associated with the SARS-CoV-2 δ variant AY.127 in Hong Kong, and an epidemiological investigation of these patients revealed that they were all associated with a local pet store.

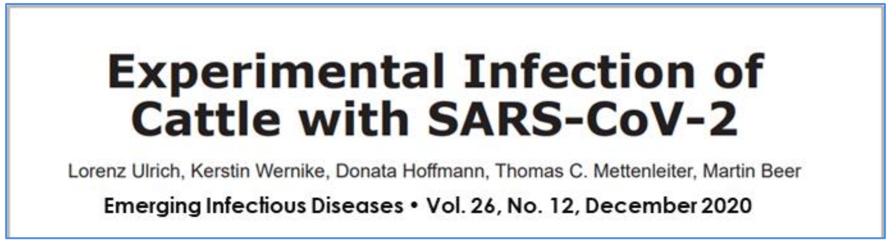
SARS-CoV-2-positive samples were found in environmental and hamster samples from pet stores. However, the hamsters were not exhibiting clinical signs.

SARS-CoV2: cattle

Experimental infection → low susceptibility to the virus (no transmission).

Viral RNA in only 2/6 inoculated animals, on day 3 after infection.

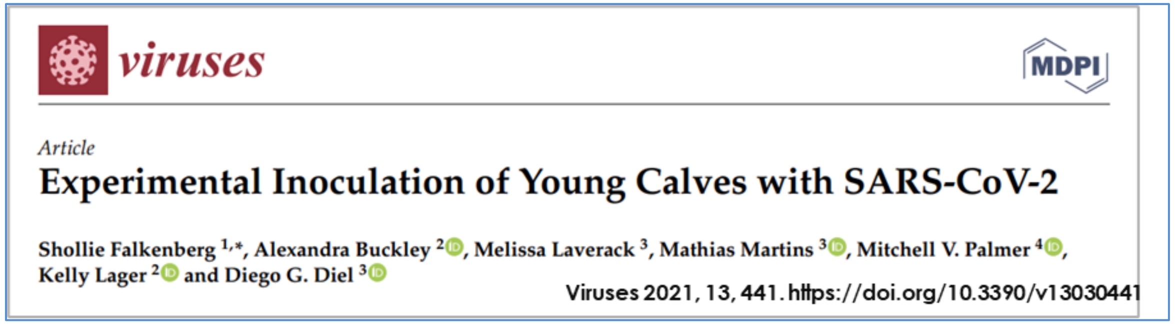
- High temperature and mild caught
- RNA Virus detection
- Antibody to SARS-CoV-2



Experimental Infection of Cattle with SARS-CoV-2

Lorenz Ulrich, Kerstin Wernike, Donata Hoffmann, Thomas C. Mettenleiter, Martin Beer

Emerging Infectious Diseases • Vol. 26, No. 12, December 2020



viruses MDPI

Article

Experimental Inoculation of Young Calves with SARS-CoV-2

Shollie Falkenberg [1,*], Alexandra Buckley [2], Melissa Laverack [3], Mathias Martins [3], Mitchell V. Palmer [4], Kelly Lager [2] and Diego G. Diel [3]

Viruses 2021, 13, 441. https://doi.org/10.3390/v13030441

SARS-CoV2: cattle

In April 2021, we investigated, for the presence of SARS-CoV-2 and BCoV, lactating cows on a farm at which 13/20 farmworkers in April 2020 had COVID-19-associated disease, and one of them had died.

The farm was located in Ariano Irpino, the first city in the Campania region to be locked down and declared a red zone in March 2020.

animals

MDPI

Article

First Description of Serological Evidence for SARS-CoV-2 in Lactating Cows

Filomena Fiorito [1], Valentina Iovane [2], Ugo Pagnini [1], Claudia Cerracchio [1], Sergio Brandi [3], Martina Levante [3], Luisa Marati [3], Gianmarco Ferrara [1], Virginio Tammaro [4], Esterina De Carlo [3,*], Giuseppe Iovane [1,*] and Giovanna Fusco [3]

The farm included heifers, beef cows, lactating cows.

To test also milk samples, we sampled only lactating cows.

The herd had never been vaccinated against BCoV.

Nasal and rectal swabs, serum and milk samples were analysed.

Results/1

All nasal and rectal swabs, as well as all milk samples → negative for SARS-CoV-2 RNA

The results on serum samples:

- 8/24 → negative for SARS-CoV-2 antibodies detection;
- 11/24 → antibodies for SARS-CoV-2 N
- 14/24 → antibodies for SARS-CoV-2 S
- 13/24 →developed SARS-COV-2-neutralising antibodies

All the samples → BCoV-negative (MTN≥4);

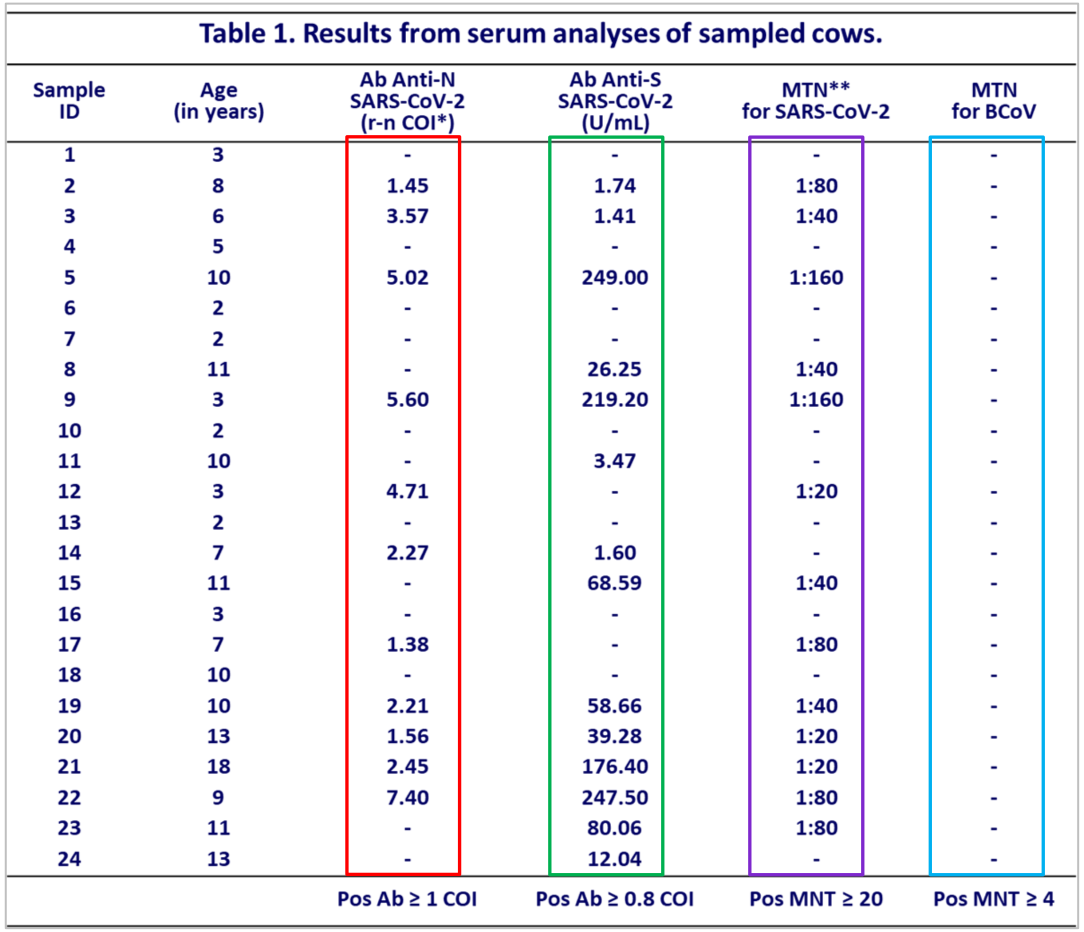


Table 1. Results from serum analyses of sampled cows.

Sample ID	Age (in years)	Ab Anti-N SARS-CoV-2 (r-n COI*)	Ab Anti-S SARS-CoV-2 (U/mL)	MTN** for SARS-CoV-2	MTN for BCoV
1	3	-	-	-	-
2	8	1.45	1.74	1:80	-
3	6	3.57	1.41	1:40	-
4	5	-	-	-	-
5	10	5.02	249.00	1:160	-
6	2	-	-	-	-
7	2	-	-	-	-
8	11	-	26.25	1:40	-
9	3	5.60	219.20	1:160	-
10	2	-	-	-	-
11	10	-	3.47	-	-
12	3	4.71	-	1:20	-
13	2	-	-	-	-
14	7	2.27	1.60	-	-
15	11	-	68.59	1:40	-
16	3	-	-	-	-
17	7	1.38	-	1:80	-
18	10	-	-	-	-
19	10	2.21	58.66	1:40	-
20	13	1.56	39.28	1:20	-
21	18	2.45	176.40	1:20	-
22	9	7.40	247.50	1:80	-
23	11	-	80.06	1:80	-
24	13	-	12.04	-	-
		Pos Ab ≥ 1 COI	Pos Ab ≥ 0.8 COI	Pos MNT ≥ 20	Pos MNT ≥ 4

*COI= Cut-off index; **MNT= microneutralization test.

None of the cows with neutralizing antibodies displayed fever, diarrhea and/or respiratory signs at the time of sampling

Results/2

Table 2. SARS-CoV-2 positivity (MTN) among cows divided into groups by possible risk factor (age and pregnancy status).

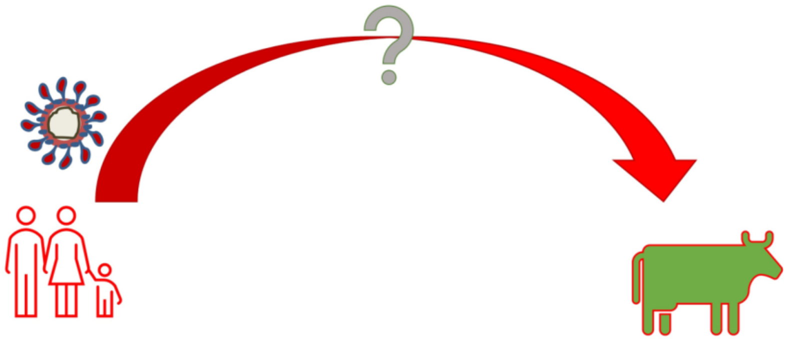
Age (years)	n. heads	Positivity for SARS-CoV-2	Positive pregnant cows
1-5	9	2/9 (22%, 95% CI -5-49)	1/6 (17%, 95% CI -13-47)
6-10	9	6/9 (67%, 95% CI 36-98)	3/6 (50%, 95% CI 10-90)
>10	6	5/6 (83%, 95% CI 53-113)	2/6 (33%, 95% CI -5-71)

The presence of SARS-CoV-2-neutralising antibodies and the age of the cows showed a significant relationship ($P < 0.05$).

- ➢ Comparison of the 1–5-year-old group to the >10-year-old group yielded a statistically significant two-sided p value ($P = 0.041$).
- ➢ No correlation with pregnancy status was detected.

Conclusions

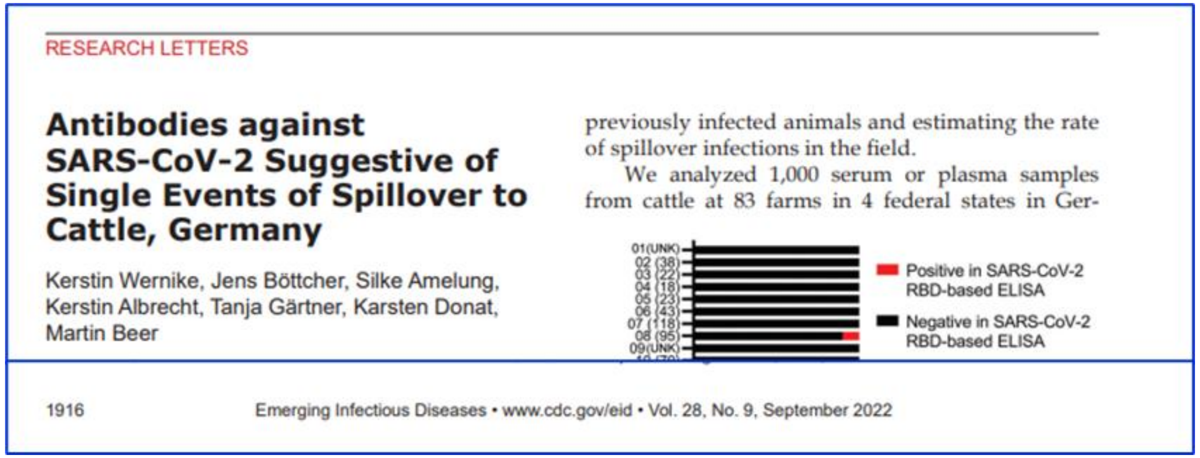
- ○ The first report of natural SARS-CoV-2 seroconversion in cattle
- ○ It may represent a case of reverse zoonosis
- ○ However, the role of cattle in SARS-CoV-2 infection seems to be negligible



Article

First Description of Serological Evidence for SARS-CoV-2 in Lactating Cows

Filomena Fiorito [1], Valentina Iovane [2], Ugo Pagnini [1], Claudia Cerracchio [1], Sergio Brandi [3], Martina Levante [3], Luisa Marati [3], Gianmarco Ferrara [1], Virginio Tammaro [4], Esterina De Carlo [3,*], Giuseppe Iovane [1,*] and Giovanna Fusco [3]



RESEARCH LETTERS

Antibodies against SARS-CoV-2 Suggestive of Single Events of Spillover to Cattle, Germany

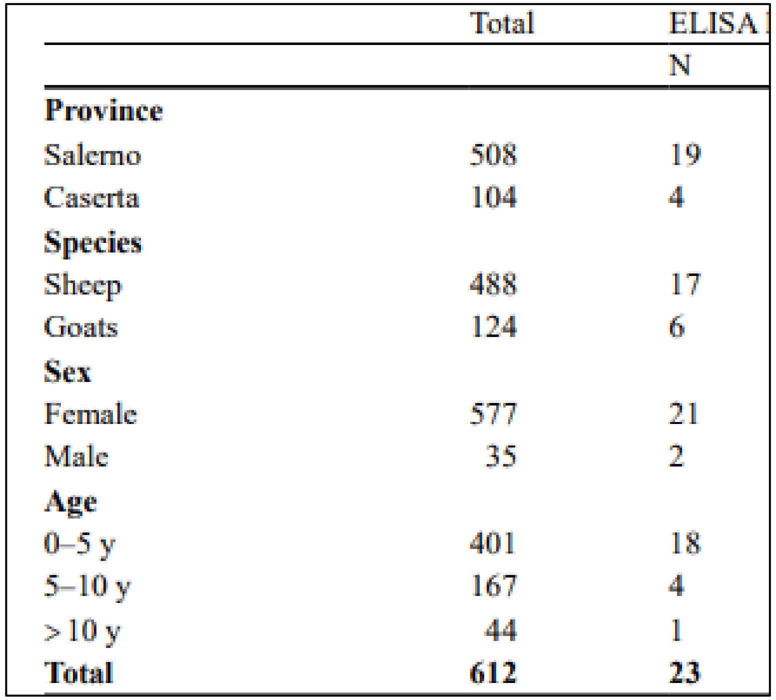
Kerstin Wernike, Jens Böttcher, Silke Amelung, Kerstin Albrecht, Tanja Gärtner, Karsten Donat, Martin Beer

previously infected animals and estimating the rate of spillover infections in the field.

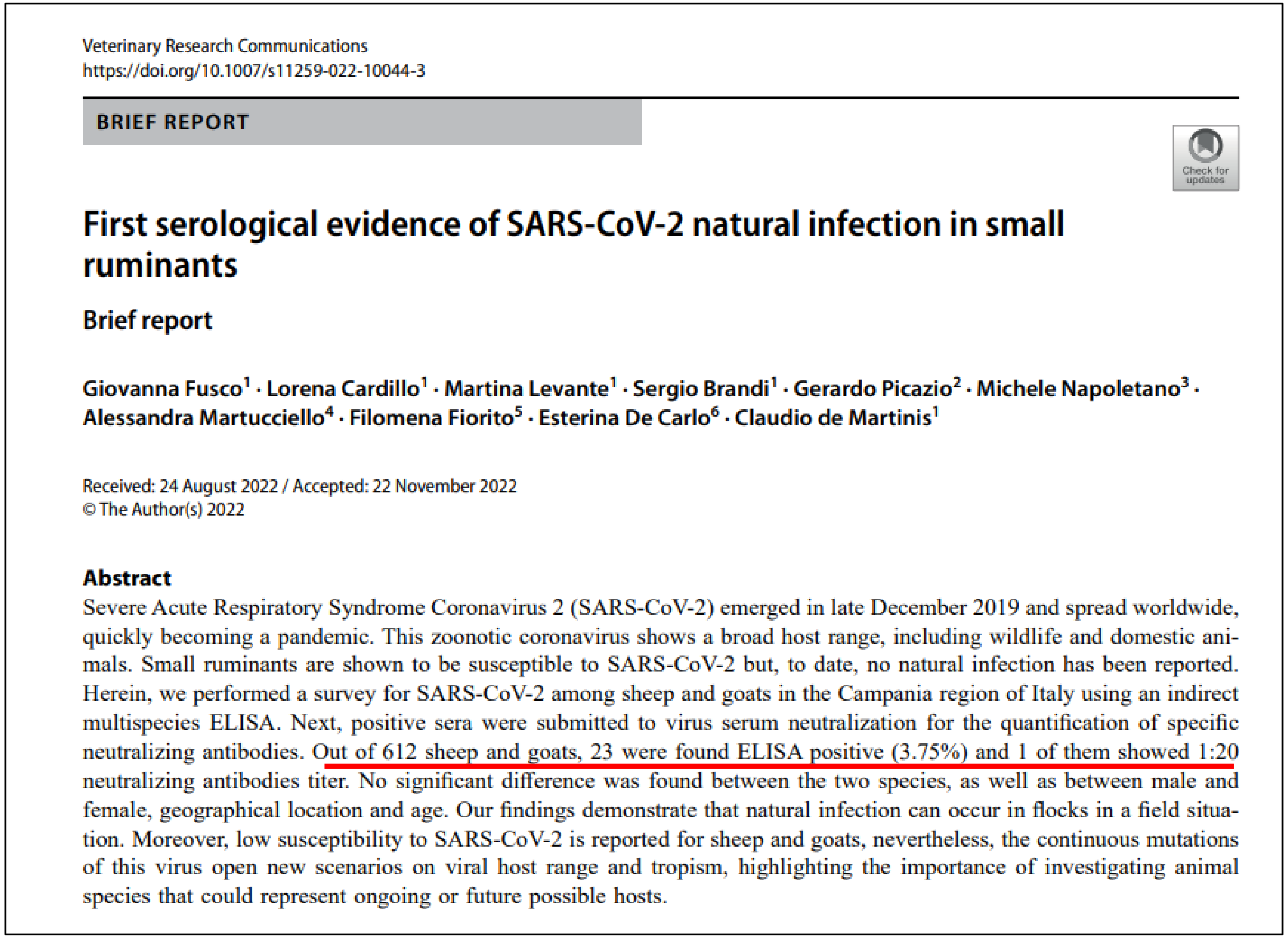
We analyzed 1,000 serum or plasma samples from cattle at 83 farms in 4 federal states in Ger-

1916 Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 28, No. 9, September 2022

SARS-CoV2: sheep and goats



	Total	ELISA
		N
Province		
Salerno	508	19
Caserta	104	4
Species		
Sheep	488	17
Goats	124	6
Sex		
Female	577	21
Male	35	2
Age		
0–5 y	401	18
5–10 y	167	4
> 10 y	44	1
Total	**612**	**23**



Veterinary Research Communications
https://doi.org/10.1007/s11259-022-10044-3

BRIEF REPORT

First serological evidence of SARS-CoV-2 natural infection in small ruminants

Brief report

Giovanna Fusco[1] · Lorena Cardillo[1] · Martina Levante[1] · Sergio Brandi[1] · Gerardo Picazio[2] · Michele Napoletano[3] · Alessandra Martucciello[4] · Filomena Fiorito[5] · Esterina De Carlo[6] · Claudio de Martinis[1]

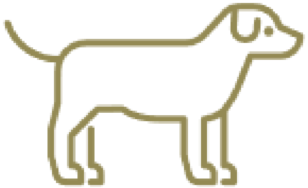
Received: 24 August 2022 / Accepted: 22 November 2022

Abstract

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) emerged in late December 2019 and spread worldwide, quickly becoming a pandemic. This zoonotic coronavirus shows a broad host range, including wildlife and domestic animals. Small ruminants are shown to be susceptible to SARS-CoV-2 but, to date, no natural infection has been reported. Herein, we performed a survey for SARS-CoV-2 among sheep and goats in the Campania region of Italy using an indirect multispecies ELISA. Next, positive sera were submitted to virus serum neutralization for the quantification of specific neutralizing antibodies. Out of 612 sheep and goats, 23 were found ELISA positive (3.75%) and 1 of them showed 1:20 neutralizing antibodies titer. No significant difference was found between the two species, as well as between male and female, geographical location and age. Our findings demonstrate that natural infection can occur in flocks in a field situation. Moreover, low susceptibility to SARS-CoV-2 is reported for sheep and goats, nevertheless, the continuous mutations of this virus open new scenarios on viral host range and tropism, highlighting the importance of investigating animal species that could represent ongoing or future possible hosts.

SARS-CoV2: dog

- Experimental studies (virus replication, but not shedding)
- Natural infections (*Canis lupus*) → low susceptibility to viral infections:
  - Mild respiratory signs, gastrointestinal signs, ocular signs, anorexia, lethargy, or asymptomatic
  - RNA Virus detection
  - Antibody to SARS-CoV-2



vaccines

MDPI

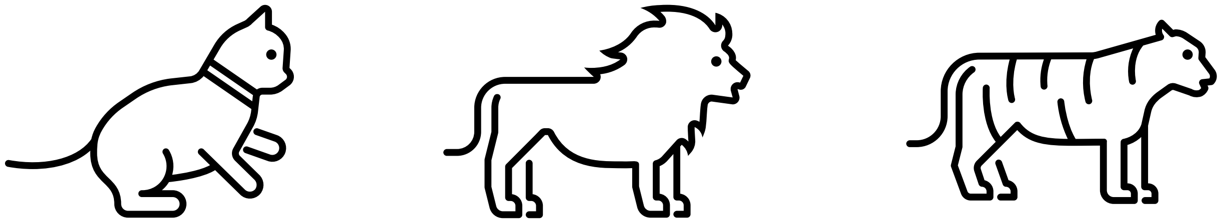
Article

A COVID-19 Vaccine for Dogs Prevents Reverse Zoonosis

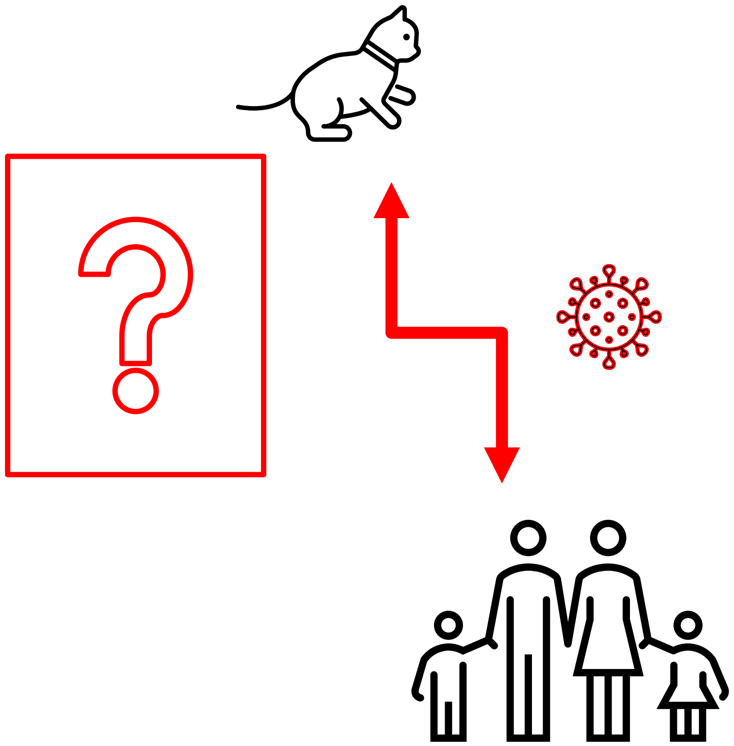
Eulhae Ga [1,2,†], Yongkwan Won [3,4,†], Jaehyun Hwang [1,2], Suyun Moon [1,2], Minju Yeom [5], Kwangsoo Lyoo [6], Daesub Song [5], Jeonghee Han [3,*] and Woonsung Na [1,2,*]

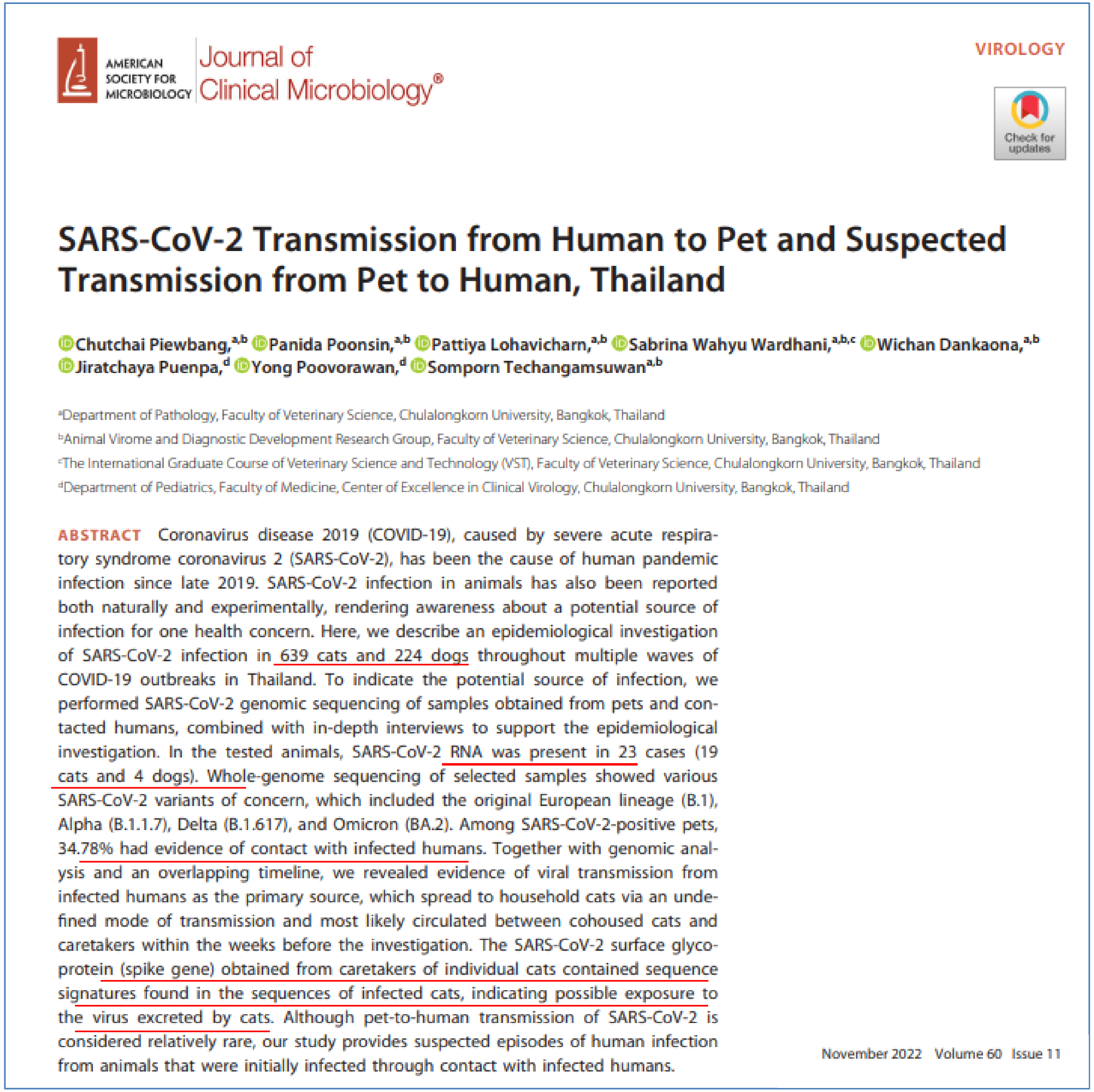
SARS-CoV2: Felidae

- Experimental studies (virus replication and shedding; young >> more susceptible to SARS-CoV-2 infections than adults)
- Natural infections (*Felis catus*) and in lions, tigers, snow leopards, cougars → high susceptibility to viral infections:
  - Mild respiratory signs, dyspnea, gastrointestinal signs, sneezing, clear ocular discharge, mild lethargy, anorexia, hypertrophic cardiomyopathy, thrombocytopenia, general symptoms or asymptomatic
  - RNA Virus detection
  - Antibody to SARS-CoV-2



SARS-CoV-2: cat





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Journal of Clinical Microbiology®

VIROLOGY

SARS-CoV-2 Transmission from Human to Pet and Suspected Transmission from Pet to Human, Thailand

Chutchai Piewbang,[a,b] Panida Poonsin,[a,b] Pattiya Lohavicharn,[a,b] Sabrina Wahyu Wardhani,[a,b,c] Wichan Dankaona,[a,b] Jiratchaya Puenpa,[d] Yong Poovorawan,[d] Somporn Techangamsuwan[a,b]

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[c]The International Graduate Course of Veterinary Science and Technology (VST), Faculty of Veterinary Science, Chulalongkorn University, Bangkok, Thailand
[d]Department of Pediatrics, Faculty of Medicine, Center of Excellence in Clinical Virology, Chulalongkorn University, Bangkok, Thailand

ABSTRACT Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been the cause of human pandemic infection since late 2019. SARS-CoV-2 infection in animals has also been reported both naturally and experimentally, rendering awareness about a potential source of infection for one health concern. Here, we describe an epidemiological investigation of SARS-CoV-2 infection in 639 cats and 224 dogs throughout multiple waves of COVID-19 outbreaks in Thailand. To indicate the potential source of infection, we performed SARS-CoV-2 genomic sequencing of samples obtained from pets and contacted humans, combined with in-depth interviews to support the epidemiological investigation. In the tested animals, SARS-CoV-2 RNA was present in 23 cases (19 cats and 4 dogs). Whole-genome sequencing of selected samples showed various SARS-CoV-2 variants of concern, which included the original European lineage (B.1), Alpha (B.1.1.7), Delta (B.1.617), and Omicron (BA.2). Among SARS-CoV-2-positive pets, 34.78% had evidence of contact with infected humans. Together with genomic analysis and an overlapping timeline, we revealed evidence of viral transmission from infected humans as the primary source, which spread to household cats via an undefined mode of transmission and most likely circulated between cohoused cats and caretakers within the weeks before the investigation. The SARS-CoV-2 surface glycoprotein (spike gene) obtained from caretakers of individual cats contained sequence signatures found in the sequences of infected cats, indicating possible exposure to the virus excreted by cats. Although pet-to-human transmission of SARS-CoV-2 is considered relatively rare, our study provides suspected episodes of human infection from animals that were initially infected through contact with infected humans.

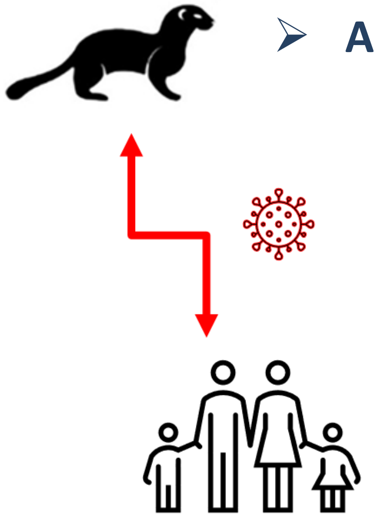
November 2022 Volume 60 Issue 11

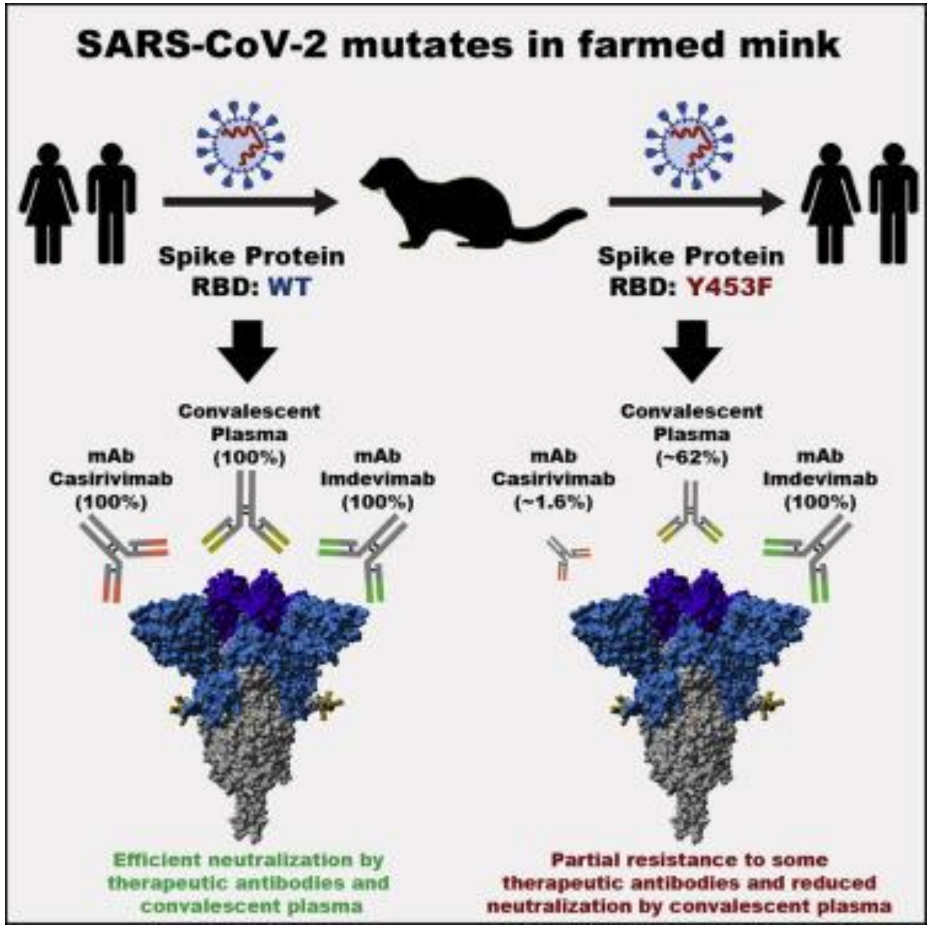
SARS-CoV2: mink

Minks have a high susceptibility to SARS-CoV-2 natural infection.

The virus appears to spread among minks and generate several new mutations, resulting in increased viral virulence.

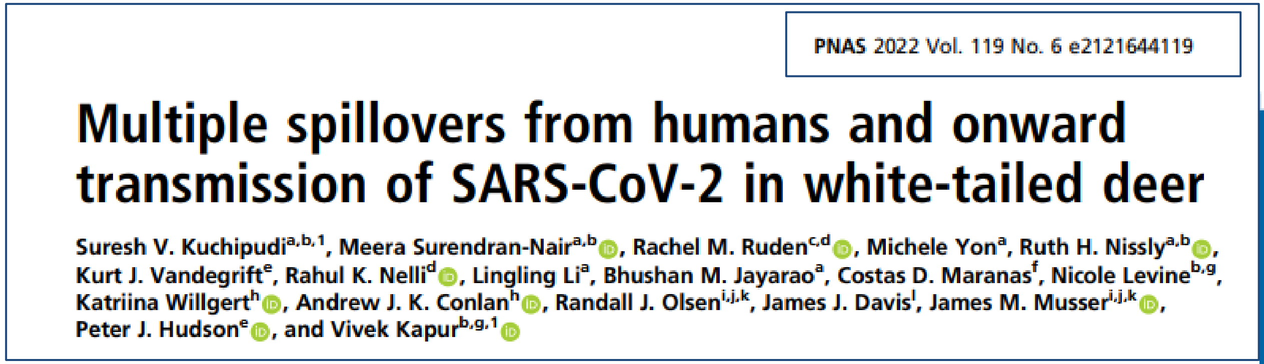
- Mild to severe respiratory signs (interstitial pneumonia), anorexia, death
- RNA Virus detection
- Antibody to SARS-CoV-2





Hoffmann et al., 2021

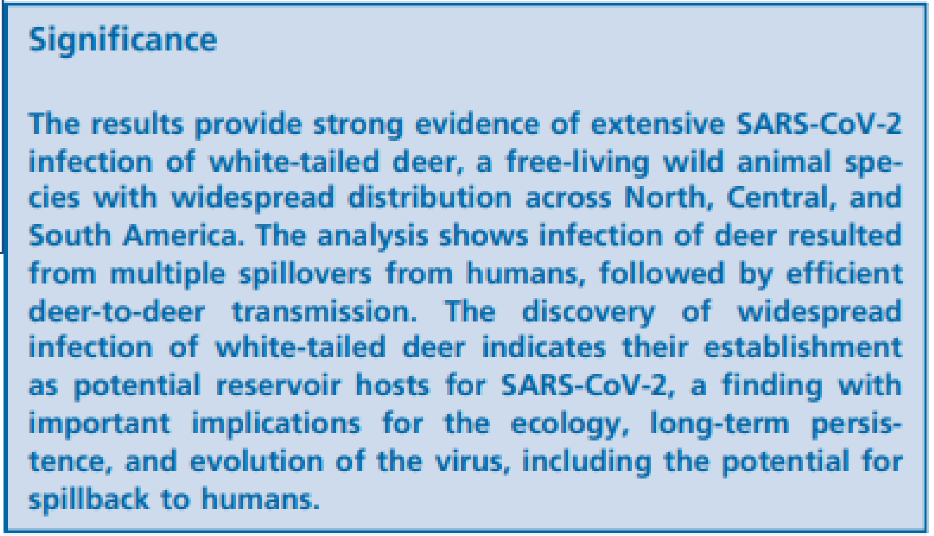
SARS-CoV2: white-tailed deer



PNAS 2022 Vol. 119 No. 6 e2121644119

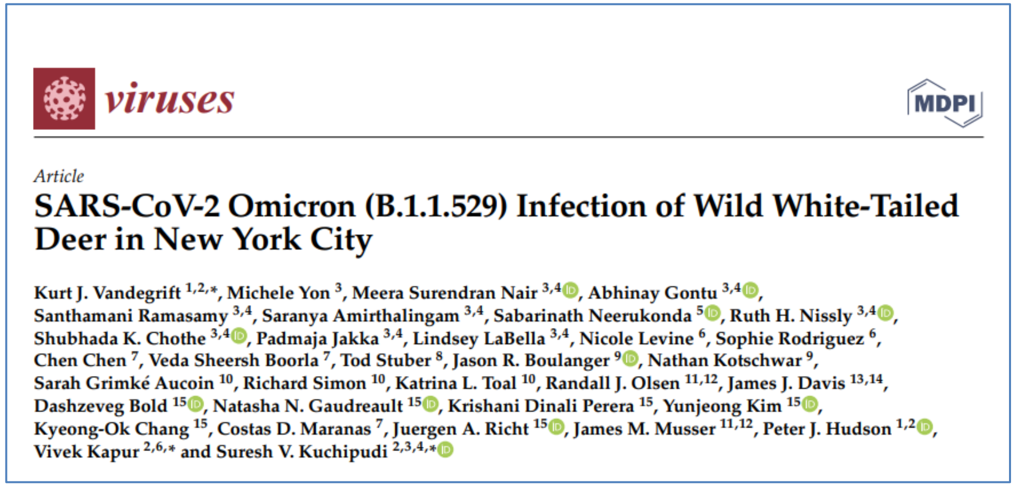
Multiple spillovers from humans and onward transmission of SARS-CoV-2 in white-tailed deer

Suresh V. Kuchipudi[a,b,1], Meera Surendran-Nair[a,b], Rachel M. Ruden[c,d], Michele Yon[a], Ruth H. Nissly[a,b], Kurt J. Vandegrift[e], Rahul K. Nelli[d], Lingling Li[a], Bhushan M. Jayarao[a], Costas D. Maranas[f], Nicole Levine[b,g], Katriina Willgert[h], Andrew J. K. Conlan[h], Randall J. Olsen[i,j,k], James J. Davis[l], James M. Musser[i,j,k], Peter J. Hudson[e], and Vivek Kapur[b,g,1]



Significance

The results provide strong evidence of extensive SARS-CoV-2 infection of white-tailed deer, a free-living wild animal species with widespread distribution across North, Central, and South America. The analysis shows infection of deer resulted from multiple spillovers from humans, followed by efficient deer-to-deer transmission. The discovery of widespread infection of white-tailed deer indicates their establishment as potential reservoir hosts for SARS-CoV-2, a finding with important implications for the ecology, long-term persistence, and evolution of the virus, including the potential for spillback to humans.

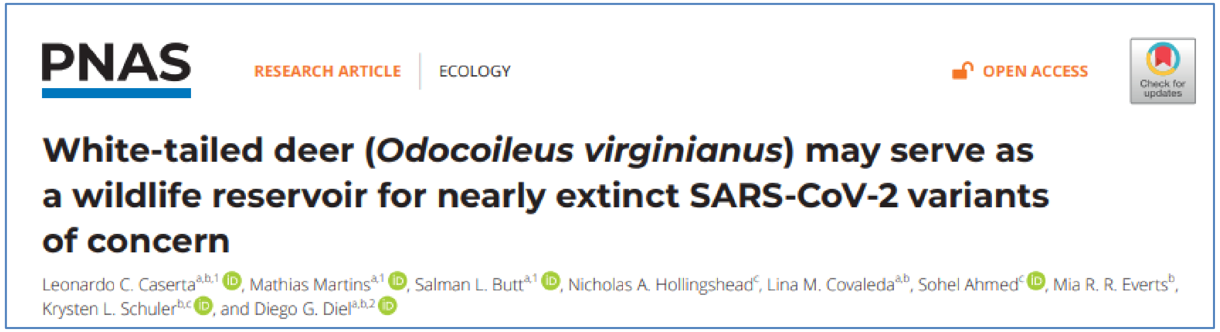


viruses MDPI

Article

SARS-CoV-2 Omicron (B.1.1.529) Infection of Wild White-Tailed Deer in New York City

Kurt J. Vandegrift [1,2,*], Michele Yon [3], Meera Surendran Nair [3,4], Abhinay Gontu [3,4], Santhamani Ramasamy [3,4], Saranya Amirthalingam [3,4], Sabarinath Neerukonda [5], Ruth H. Nissly [3,4], Shubhada K. Chothe [3,4], Padmaja Jakka [3,4], Lindsey LaBella [3,4], Nicole Levine [6], Sophie Rodriguez [6], Chen Chen [7], Veda Sheersh Boorla [7], Tod Stuber [8], Jason R. Boulanger [9], Nathan Kotschwar [9], Sarah Grimké Aucoin [10], Richard Simon [10], Katrina L. Toal [10], Randall J. Olsen [11,12], James J. Davis [13,14], Dashzeveg Bold [15], Natasha N. Gaudreault [15], Krishani Dinali Perera [15], Yunjeong Kim [15], Kyeong-Ok Chang [15], Costas D. Maranas [7], Juergen A. Richt [15], James M. Musser [11,12], Peter J. Hudson [1,2], Vivek Kapur [2,6,*] and Suresh V. Kuchipudi [2,3,4,*]

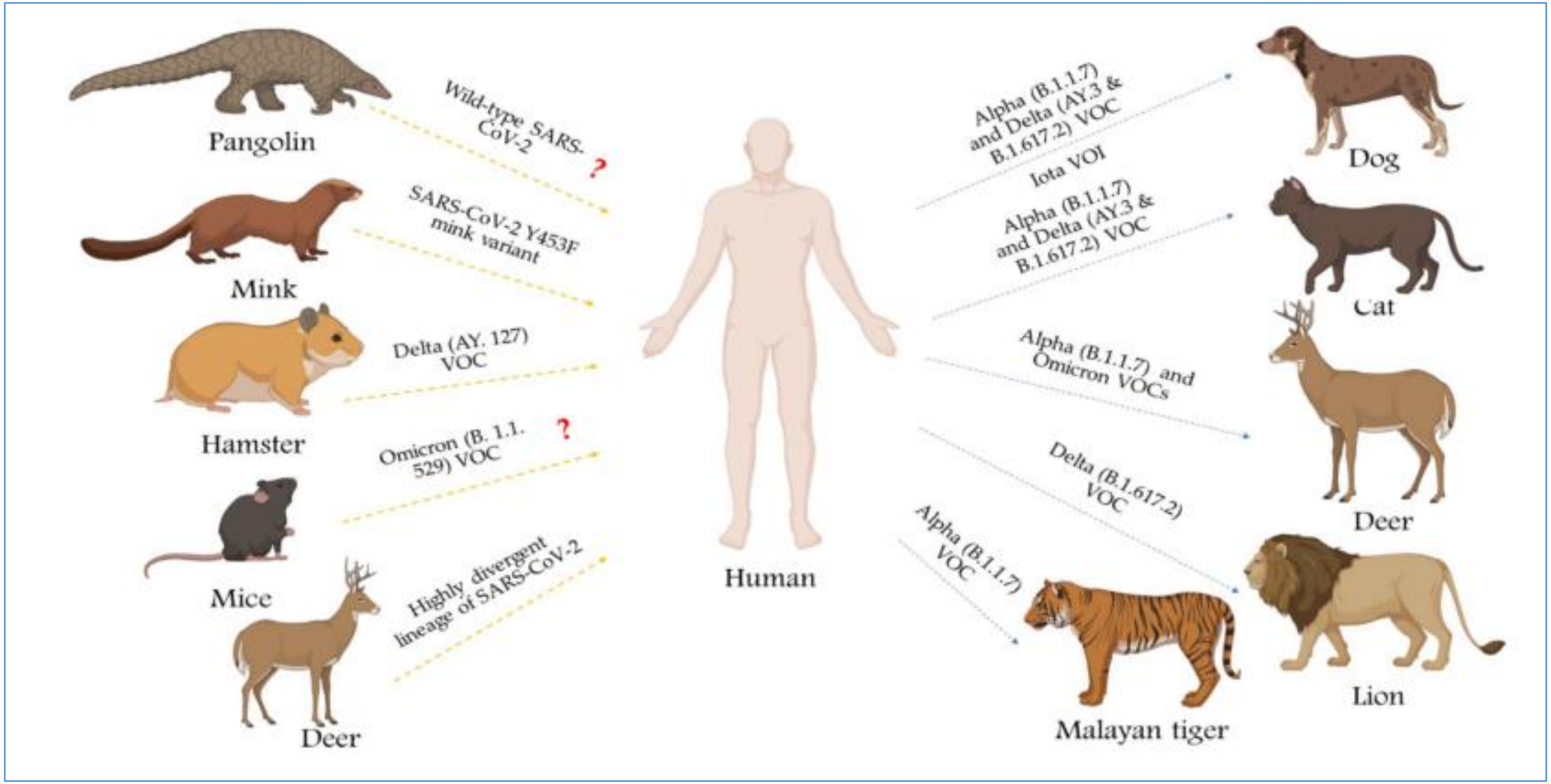


PNAS RESEARCH ARTICLE | ECOLOGY OPEN ACCESS

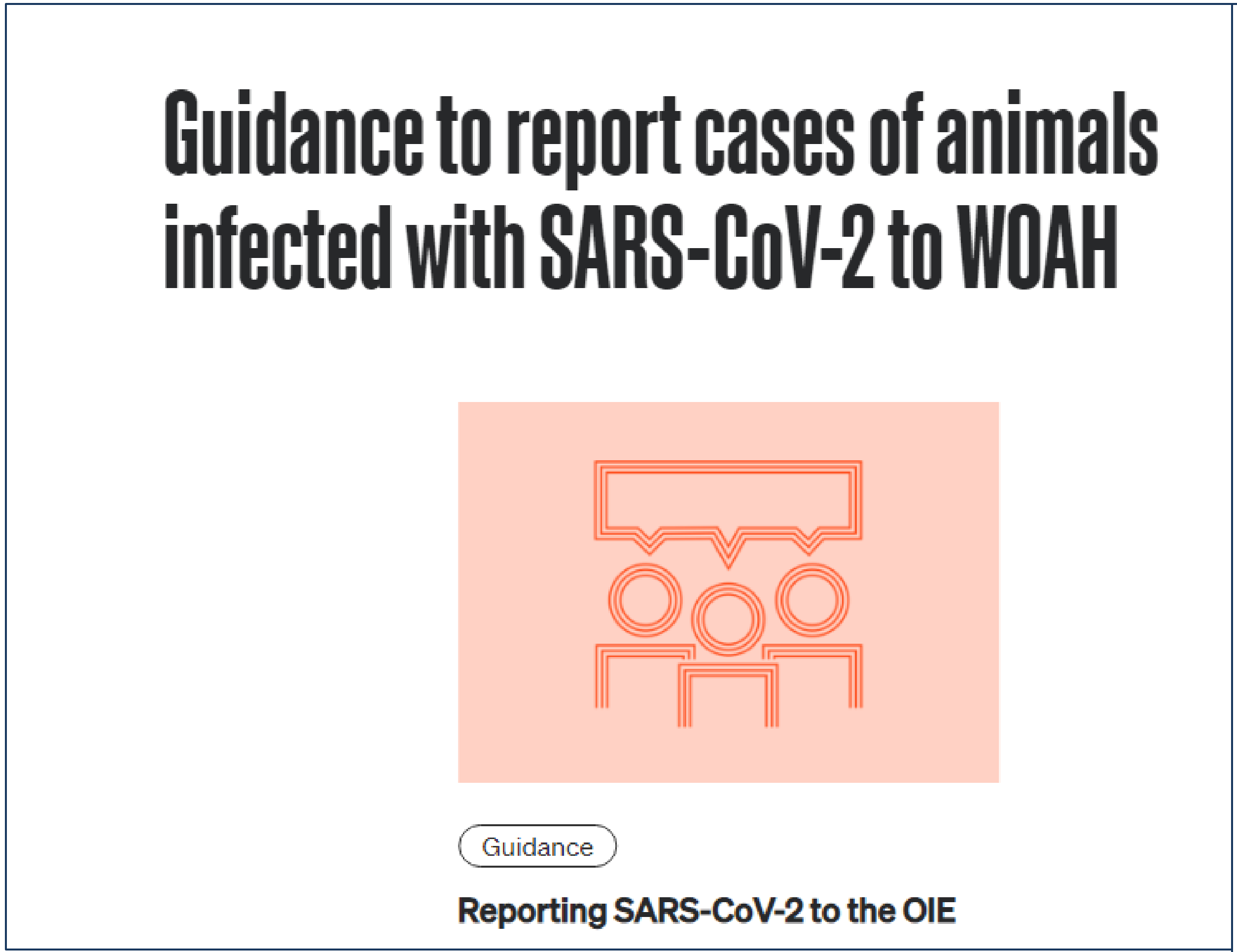
White-tailed deer (*Odocoileus virginianus*) may serve as a wildlife reservoir for nearly extinct SARS-CoV-2 variants of concern

Leonardo C. Caserta[a,b,1], Mathias Martins[a,1], Salman L. Butt[a,1], Nicholas A. Hollingshead[c], Lina M. Covaleda[a,b], Sohel Ahmed[c], Mia R. R. Everts[b], Krysten L. Schuler[b,c], and Diego G. Diel[a,b,2]

SARS-CoV-2 VOCs in animals



Saied and Metwally, 2022

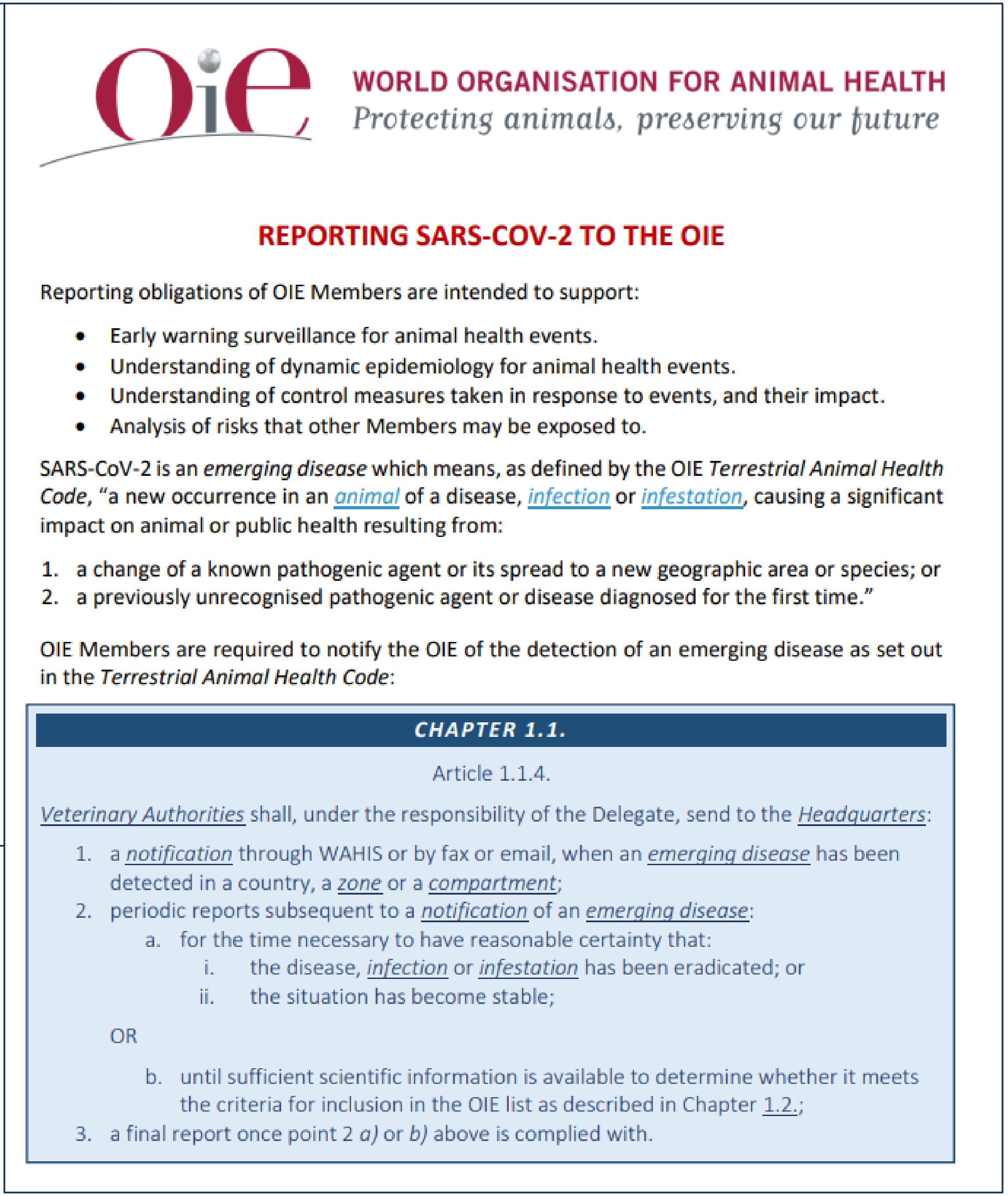


Guidance to report cases of animals infected with SARS-CoV-2 to WOAH

Guidance

Reporting SARS-CoV-2 to the OIE

[a-reporting-sars-cov-2-to-the-oie.pdf (woah.org)](a-reporting-sars-cov-2-to-the-oie.pdf)



WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future

REPORTING SARS-COV-2 TO THE OIE

Reporting obligations of OIE Members are intended to support:

- Early warning surveillance for animal health events.
- Understanding of dynamic epidemiology for animal health events.
- Understanding of control measures taken in response to events, and their impact.
- Analysis of risks that other Members may be exposed to.

SARS-CoV-2 is an *emerging disease* which means, as defined by the OIE *Terrestrial Animal Health Code*, "a new occurrence in an *animal* of a disease, *infection* or *infestation*, causing a significant impact on animal or public health resulting from:

1. a change of a known pathogenic agent or its spread to a new geographic area or species; or
2. a previously unrecognised pathogenic agent or disease diagnosed for the first time."

OIE Members are required to notify the OIE of the detection of an emerging disease as set out in the *Terrestrial Animal Health Code*:

CHAPTER 1.1.

Article 1.1.4.

Veterinary Authorities shall, under the responsibility of the Delegate, send to the *Headquarters*:

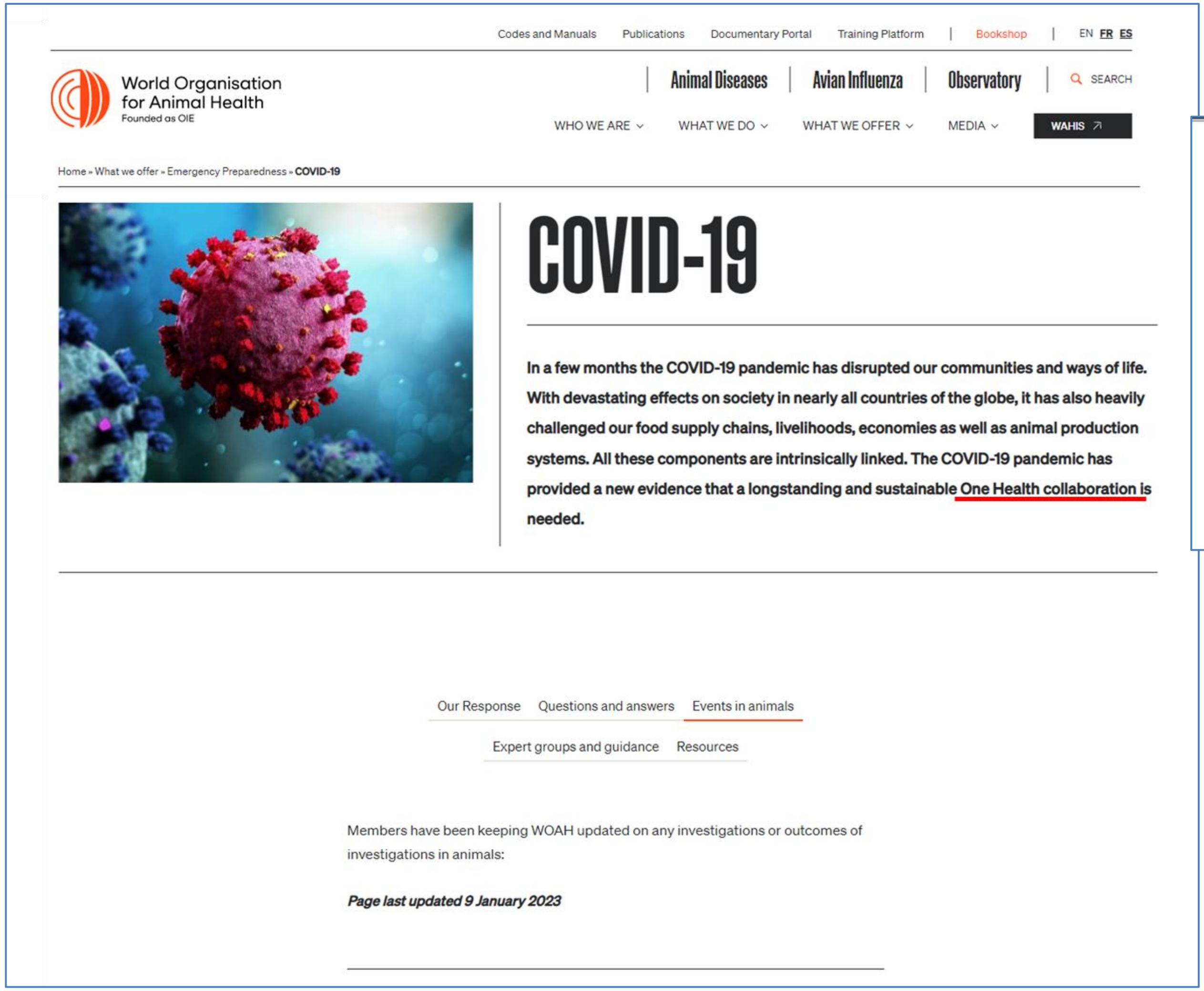
1. a *notification* through WAHIS or by fax or email, when an *emerging disease* has been detected in a country, a *zone* or a *compartment*;
2. periodic reports subsequent to a *notification* of an *emerging disease*:
    a. for the time necessary to have reasonable certainty that:
        i. the disease, *infection* or *infestation* has been eradicated; or
        ii. the situation has become stable;

    OR

    b. until sufficient scientific information is available to determine whether it meets the criteria for inclusion in the OIE list as described in Chapter 1.2.;
3. a final report once point 2 *a)* or *b)* above is complied with.

One Health Approach:

Mandatory or not mandatory?



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Animal Diseases | Avian Influenza | Observatory | SEARCH

WHO WE ARE WHAT WE DO WHAT WE OFFER MEDIA WAHIS

Home » What we offer » Emergency Preparedness » **COVID-19**

COVID-19

In a few months the COVID-19 pandemic has disrupted our communities and ways of life. With devastating effects on society in nearly all countries of the globe, it has also heavily challenged our food supply chains, livelihoods, economies as well as animal production systems. All these components are intrinsically linked. The COVID-19 pandemic has provided a new evidence that a longstanding and sustainable One Health collaboration is needed.

Our Response Questions and answers Events in animals

Expert groups and guidance Resources

Members have been keeping WOAH updated on any investigations or outcomes of investigations in animals:

Page last updated 9 January 2023

PNAS PERSPECTIVE OPEN ACCESS Check for updates

Pandemic origins and a One Health approach to preparedness and prevention: Solutions based on SARS-CoV-2 and other RNA viruses

Gerald T. Keusch[a,1], John H. Amuasi[b,c,d], Danielle E. Anderson[e], Peter Daszak[f], Isabella Eckerle[g,h], Hume Field[f,i], Marion Koopmans[j], Sai Kit Lam[k], Carlos G. Das Neves[l,m], Malik Peiris[n], Stanley Perlman[o], Supaporn Wacharapluesadee[p], Su Yadana[f], and Linda Saif[q,1]

Edited by Xiang Jin Meng, Virginia Polytechnic Institute and State University, Blacksburg, VA; received June 14, 2022; accepted August 18, 2022

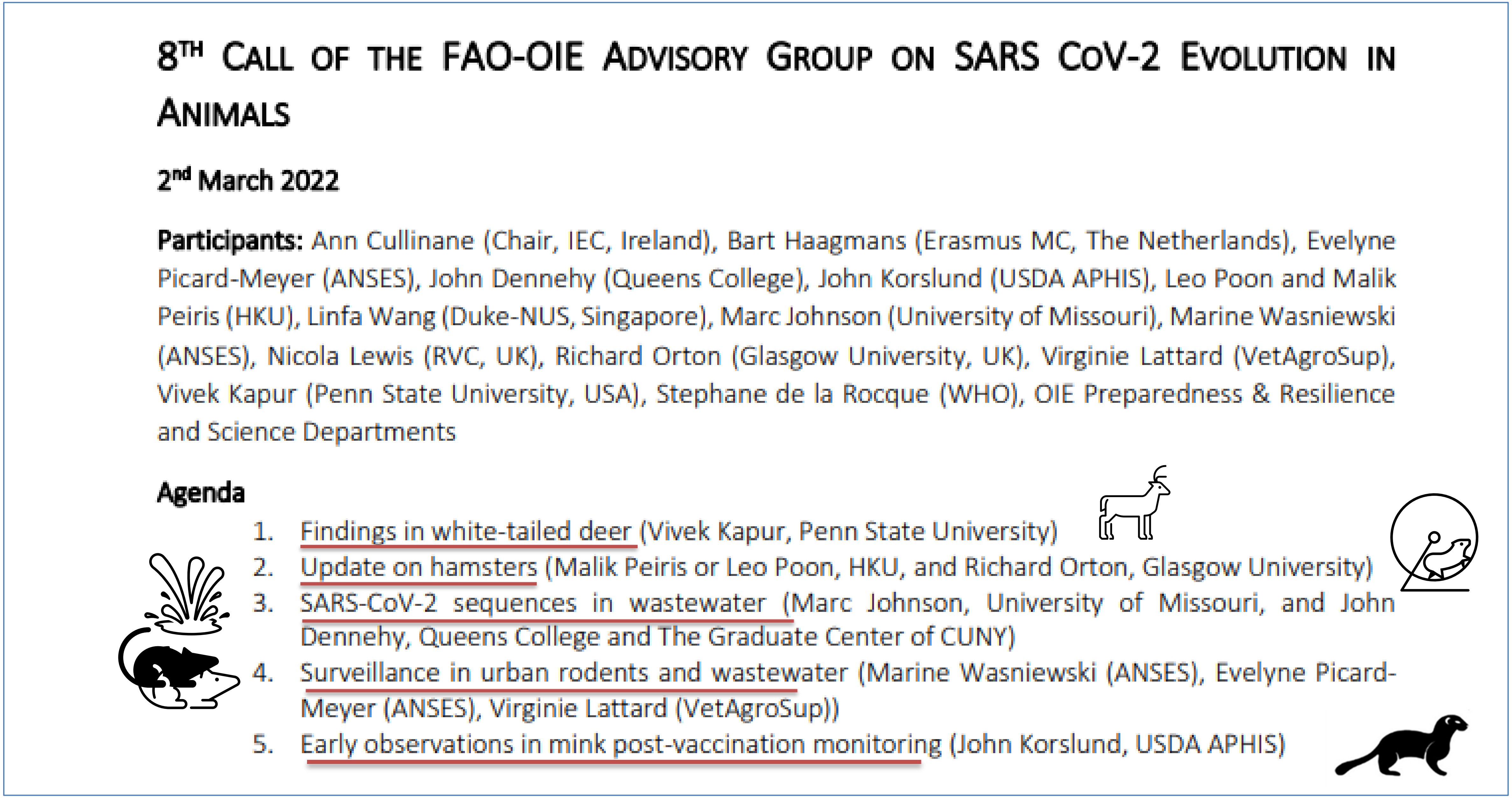
One health strategy!

SARS-CoV-2 in animals

Infected humans may produce very high viral load → increasing the chances of spillover to other animal species such as pet animals, farm animals, and wild animals inhabiting areas close to human community

⬇

Animal species must be tested → to prevent any spillovers!!!



8th Call of the FAO-OIE Advisory Group on SARS CoV-2 Evolution in Animals

2nd March 2022

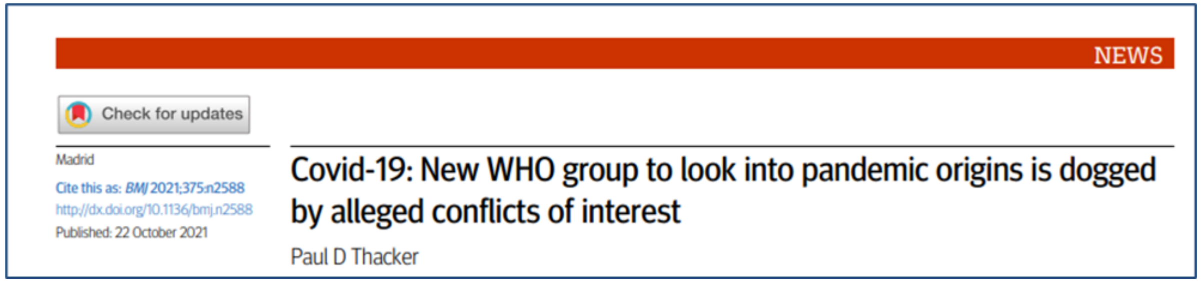
Participants: Ann Cullinane (Chair, IEC, Ireland), Bart Haagmans (Erasmus MC, The Netherlands), Evelyne Picard-Meyer (ANSES), John Dennehy (Queens College), John Korslund (USDA APHIS), Leo Poon and Malik Peiris (HKU), Linfa Wang (Duke-NUS, Singapore), Marc Johnson (University of Missouri), Marine Wasniewski (ANSES), Nicola Lewis (RVC, UK), Richard Orton (Glasgow University, UK), Virginie Lattard (VetAgroSup), Vivek Kapur (Penn State University, USA), Stephane de la Rocque (WHO), OIE Preparedness & Resilience and Science Departments

Agenda

1. Findings in white-tailed deer (Vivek Kapur, Penn State University)
2. Update on hamsters (Malik Peiris or Leo Poon, HKU, and Richard Orton, Glasgow University)
3. SARS-CoV-2 sequences in wastewater (Marc Johnson, University of Missouri, and John Dennehy, Queens College and The Graduate Center of CUNY)
4. Surveillance in urban rodents and wastewater (Marine Wasniewski (ANSES), Evelyne Picard-Meyer (ANSES), Virginie Lattard (VetAgroSup))
5. Early observations in mink post-vaccination monitoring (John Korslund, USDA APHIS)

SARS-CoV-2 origin

Viruses reach humans when they invade such ecosystems, including forests, and come into contact with the virus-bearing wildlife living there…


NEWS

Check for updates

Madrid

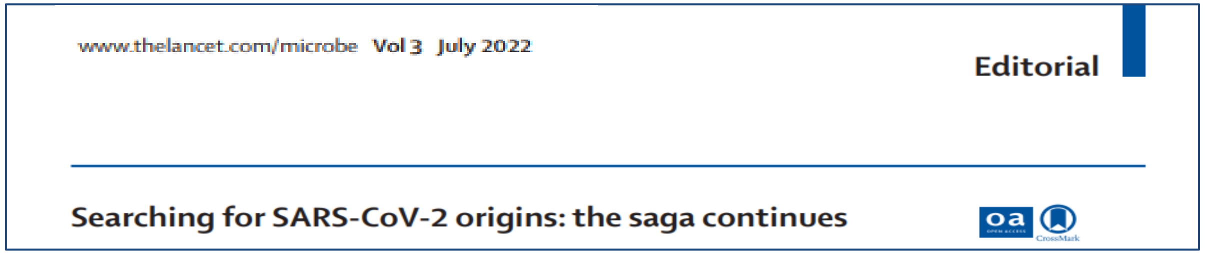
Cite this as: *BMJ* 2021;375:n2588

http://dx.doi.org/10.1136/bmj.n2588

Published: 22 October 2021

Covid-19: New WHO group to look into pandemic origins is dogged by alleged conflicts of interest

Paul D Thacker


www.thelancet.com/microbe Vol 3 July 2022

Editorial

Searching for SARS-CoV-2 origins: the saga continues

The Wuhan Institute of Virology carries out research on coronaviruses because these pathogens are endemic to the region where it's located.

THE COVID LAB-LEAK HYPOTHESIS: WHAT SCIENTISTS DO AND DON'T KNOW

Nature examines arguments that the coronavirus SARS-CoV-2 escaped from a lab in China, and the science behind them.

By Amy Maxmen & Smriti Mallapaty

Debate over the idea that the coronavirus SARS-CoV-2 emerged from a laboratory has escalated over the past few weeks, coinciding with the annual World Health Assembly, at which the World Health Organization (WHO) and officials from nearly 200 countries discussed the COVID-19 pandemic. After last year's assembly, the WHO agreed to sponsor the first phase of of Virology (WIV), located in the Chinese city where the first COVID-19 cases were reported. On 26 May, US President Joe Biden tasked the US Intelligence Community to join efforts to find SARS-CoV-2's origins, whatever they might be, and report back in 90 days.

Australia, the European Union and Japan have also called for a robust investigation into SARS-CoV-2's origins. The WHO has yet to reveal the next phase of its investigation. But China has asked that the probe examine other coun-

Nature looks at the key arguments that support a lab leak, and the extent to which research has answers.

There's not yet any substantial evidence for a lab leak. Why are scientists still considering it?

Scientists don't have enough evidence about the origins of SARS-CoV-2 to rule out the lab-leak hypothesis, or to prove the alternative – that the virus has a natural origin. Many


Opinion | Let's leave the covid origin mystery to scientists

…The not-quite-solved mystery of exactly where this virus came from and how it found its way into humans, on the other hand, is a scientific question best left to scientists…

By David Quammen,
January 23, 2023 The Washington Post

SARS-CoV-2 origin

May 19, 2022

PNAS ● OPINION

A call for an independent inquiry into the origin of the SARS-CoV-2 virus

Neil L. Harrison[a,b,1] and Jeffrey D. Sachs[c,1]

When it comes to deciphering the origins of COVID-19, much important information can be gleaned from US-based research institutions—information that has yet to be made available for independent, transparent, and scientific scrutiny. Image credit: Dave Cutler (artist).

Since the identification of theSARS-CoV-2 in Wuhan, China, in January 2020 (1), the origin of the virus has been a topic of intense scientific debate and public speculation. The two main hypotheses are that the virus emerged from human exposure to an infected animal ["zoonosis" (2)] or that it emerged in a research-related incident (3). The investigation into the origin of the virus has been made difficult by the lack of key evidence from the earliest days of the outbreak—there's no doubt that greater transparency on the part of Chinese authorities would be enormously helpful. Nevertheless, we argue here that there is much important information that can be gleaned from US-based research institutions, information not yet made available for independent, transparent, and scientific scrutiny.

The data available within the United States would explicitly include, but are not limited to, viral sequences gathered and held as part of the PREDICT project and other funded programs, as well as sequencing data and laboratory notebooks from US laboratories. We call on US government scientific agencies, most notably the NIH, to support a full, independent, and transparent investigation of the origins of SARS-CoV-2. This should take place, for example, within a tightly focused science-based bipartisan Congressional inquiry with full investigative powers, which would be able to ask important questions—but avoid misguided witch-hunts governed more by politics than by science.

Author contributions: N.L.H. and J.D.S. wrote the paper.

The authors declare no competing interest.

Any opinions, findings, conclusions, or recommendations expressed in this work are those of the authors and have not been endorsed by the National Academy of Sciences.

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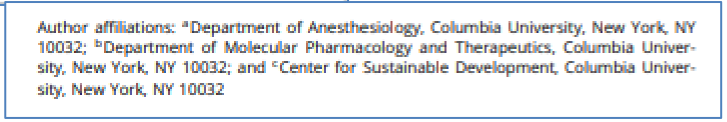
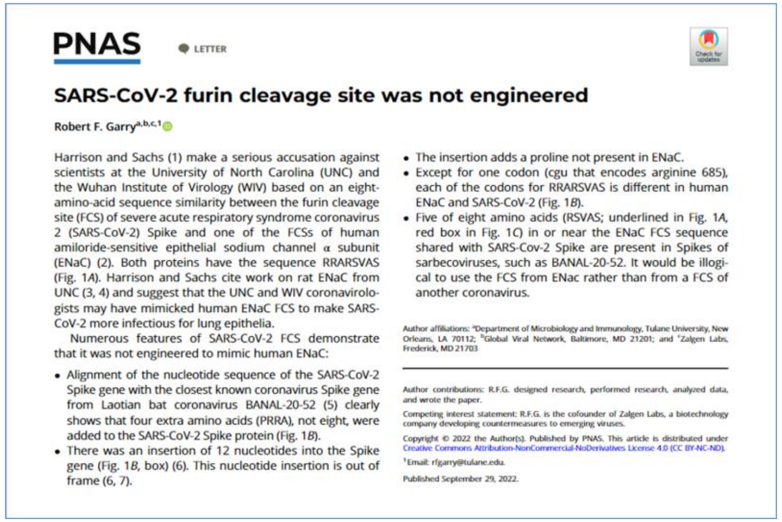
Published May 19, 2022.

PNAS 2022 Vol. 119 No. 21 e2202769119 https://doi.org/10.1073/pnas.2202769119 1 of 5



Author affiliations: [a]Department of Anesthesiology, Columbia University, New York, NY 10032; [b]Department of Molecular Pharmacology and Therapeutics, Columbia University, New York, NY 10032; and [c]Center for Sustainable Development, Columbia University, New York, NY 10032

September 29, 2022



PNAS ● LETTER

SARS-CoV-2 furin cleavage site was not engineered

Robert F. Garry[a,b,c,1]

Harrison and Sachs (1) make a serious accusation against scientists at the University of North Carolina (UNC) and the Wuhan Institute of Virology (WIV) based on an eight-amino-acid sequence similarity between the furin cleavage site (FCS) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Spike and one of the FCSs of human amiloride-sensitive epithelial sodium channel α subunit (ENaC) (2). Both proteins have the sequence RRARSVAS (Fig. 1*A*). Harrison and Sachs cite work on rat ENaC from UNC (3, 4) and suggest that the UNC and WIV coronavirologists may have mimicked human ENaC FCS to make SARS-CoV-2 more infectious for lung epithelia.

Numerous features of SARS-CoV-2 FCS demonstrate that it was not engineered to mimic human ENaC:

- Alignment of the nucleotide sequence of the SARS-CoV-2 Spike gene with the closest known coronavirus Spike gene from Laotian bat coronavirus BANAL-20-52 (5) clearly shows that four extra amino acids (PRRA), not eight, were added to the SARS-CoV-2 Spike protein (Fig. 1*B*).
- There was an insertion of 12 nucleotides into the Spike gene (Fig. 1*B*, box) (6). This nucleotide insertion is out of frame (6, 7).
- The insertion adds a proline not present in ENaC.
- Except for one codon (cgu that encodes arginine 685), each of the codons for RRARSVAS is different in human ENaC and SARS-CoV-2 (Fig. 1*B*).
- Five of eight amino acids (RSVAS; underlined in Fig. 1*A*, red box in Fig. 1*C*) in or near the ENaC FCS sequence shared with SARS-Cov-2 Spike are present in Spikes of sarbecoviruses, such as BANAL-20-52. It would be illogical to use the FCS from ENac rather than from a FCS of another coronavirus.

Author affiliations: [a]Department of Microbiology and Immunology, Tulane University, New Orleans, LA 70112; [b]Global Viral Network, Baltimore, MD 21201; and [c]Zalgen Labs, Frederick, MD 21703

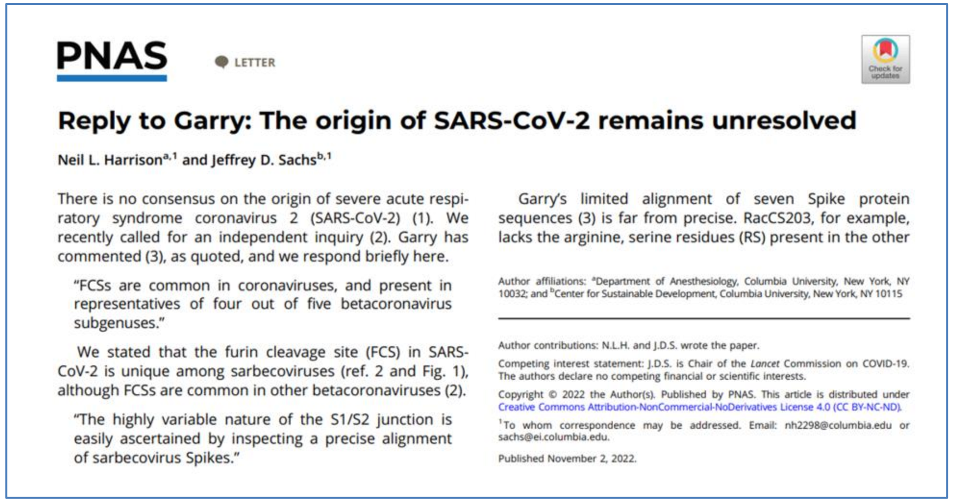
Author contributions: R.F.G. designed research, performed research, analyzed data, and wrote the paper.

Competing interest statement: R.F.G. is the cofounder of Zalgen Labs, a biotechnology company developing countermeasures to emerging viruses.

[1] Email: rfgarry@tulane.edu.

Published September 29, 2022.

November 2, 2022



PNAS ● LETTER

Reply to Garry: The origin of SARS-CoV-2 remains unresolved

Neil L. Harrison[a,1] and Jeffrey D. Sachs[b,1]

There is no consensus on the origin of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). We recently called for an independent inquiry (2). Garry has commented (3), as quoted, and we respond briefly here.

> "FCSs are common in coronaviruses, and present in representatives of four out of five betacoronavirus subgenuses."

We stated that the furin cleavage site (FCS) in SARS-CoV-2 is unique among sarbecoviruses (ref. 2 and Fig. 1), although FCSs are common in other betacoronaviruses (2).

> "The highly variable nature of the S1/S2 junction is easily ascertained by inspecting a precise alignment of sarbecovirus Spikes."

Garry's limited alignment of seven Spike protein sequences (3) is far from precise. RacCS203, for example, lacks the arginine, serine residues (RS) present in the other

Author affiliations: [a]Department of Anesthesiology, Columbia University, New York, NY 10032; and [b]Center for Sustainable Development, Columbia University, New York, NY 10115

Author contributions: N.L.H. and J.D.S. wrote the paper.

Competing interest statement: J.D.S. is Chair of the *Lancet* Commission on COVID-19. The authors declare no competing financial or scientific interests.

[1] To whom correspondence may be addressed. Email: nh2298@columbia.edu or sachs@ei.columbia.edu.

Published November 2, 2022.

November 11, 2022

The evidence remains clear: SARS-CoV-2 emerged via the wildlife trade

Robert F. Garry Authors Info & Affiliations

November 10, 2022 | 119 (47) e2214427119 | https://doi.org/10.1073/pnas.2214427119

SARS-CoV-2 origin

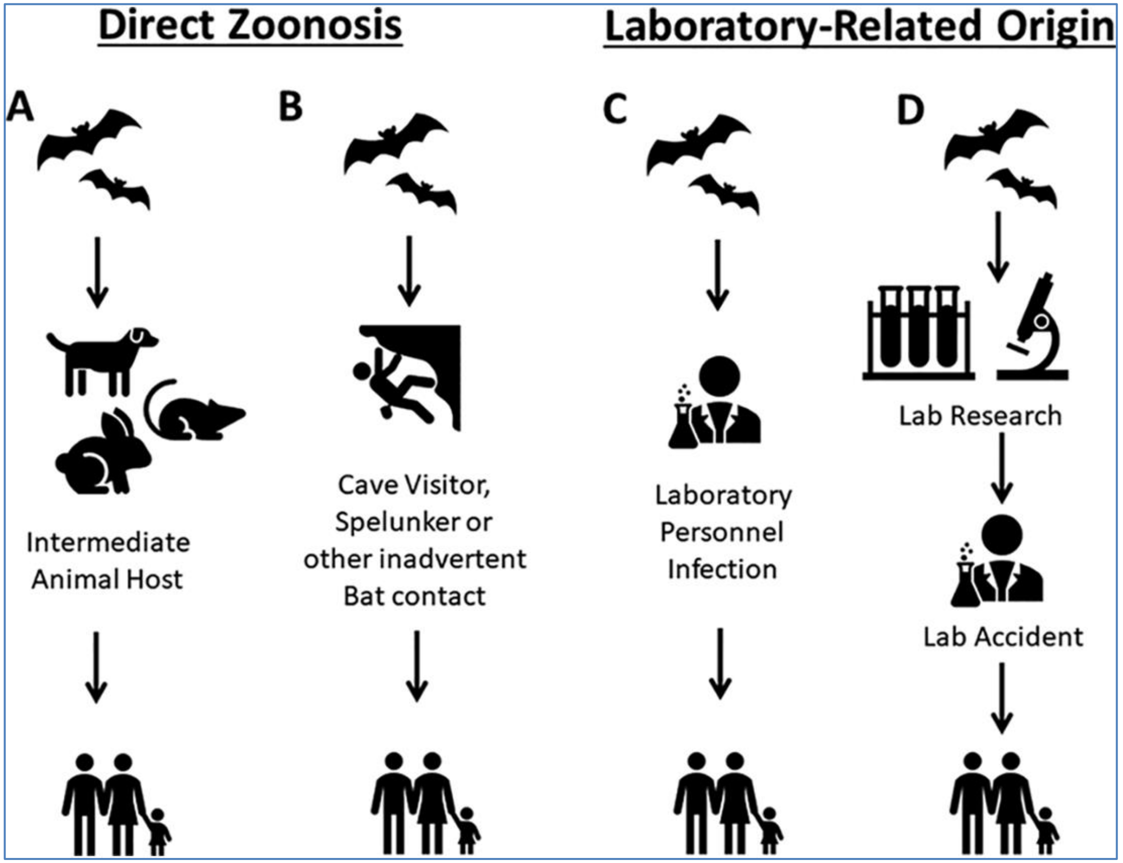
AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

EDITORIAL

Check for updates

Can Science Help Resolve the Controversy on the Origins of the SARS-CoV-2 Pandemic?

Arturo Casadevall,[a] Editor in Chief, *mBio*, and Chair of the Board of Governors, American Academy of Microbiology, **Susan R. Weiss,**[b] Governor, American Academy of Microbiology, **Michael J. Imperiale,**[c] Editor in Chief, *mSphere*, and Editorial Advisory Board, *mBio*



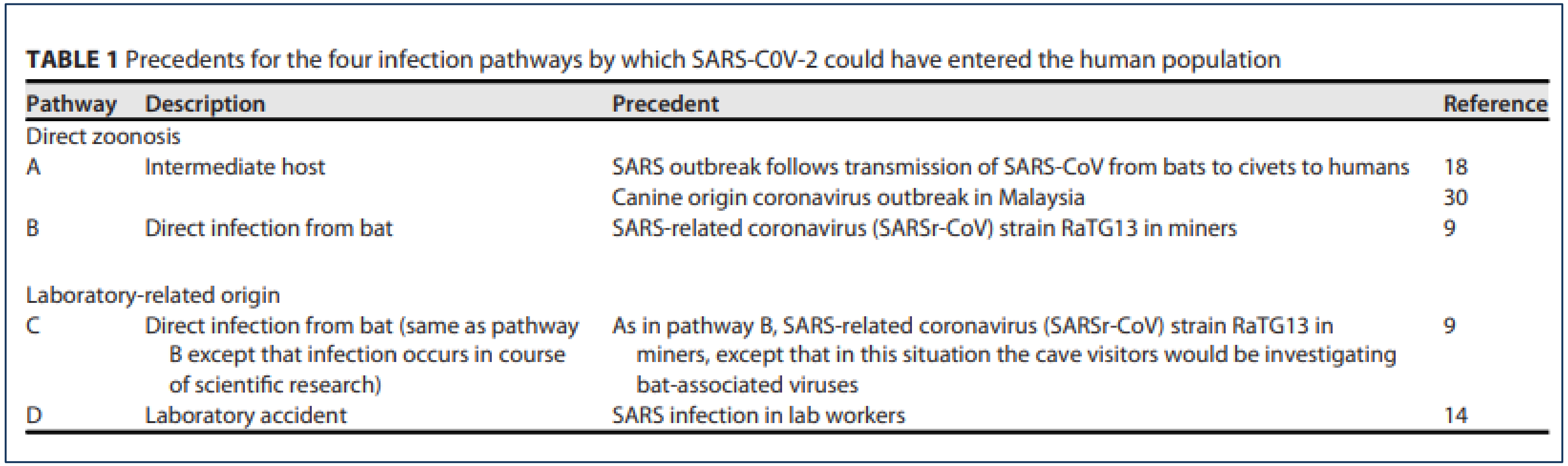


TABLE 1 Precedents for the four infection pathways by which SARS-C0V-2 could have entered the human population

Pathway	Description	Precedent	Reference
Direct zoonosis			
A	Intermediate host	SARS outbreak follows transmission of SARS-CoV from bats to civets to humans	18
		Canine origin coronavirus outbreak in Malaysia	30
B	Direct infection from bat	SARS-related coronavirus (SARSr-CoV) strain RaTG13 in miners	9
Laboratory-related origin			
C	Direct infection from bat (same as pathway B except that infection occurs in course of scientific research)	As in pathway B, SARS-related coronavirus (SARSr-CoV) strain RaTG13 in miners, except that in this situation the cave visitors would be investigating bat-associated viruses	9
D	Laboratory accident	SARS infection in lab workers	14

SARS-CoV-2: the early epicenter in Wuhan

RESEARCH

CORONAVIRUS

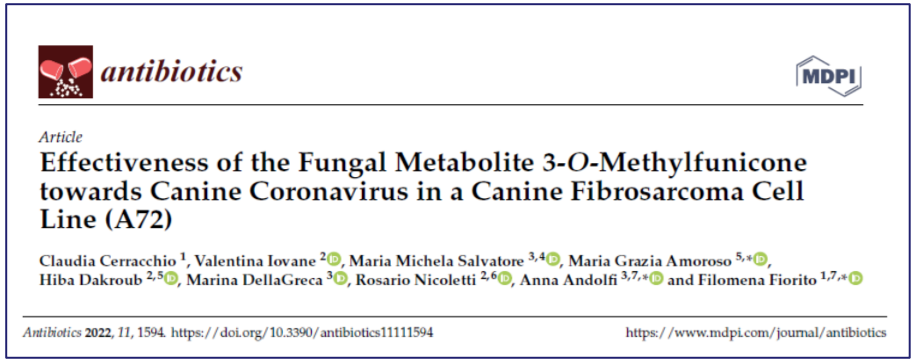
The Huanan Seafood Wholesale Market in Wuhan was the early epicenter of the COVID-19 pandemic

Michael Worobey[1]*, Joshua I. Levy[2], Lorena Malpica Serrano[1], Alexander Crits-Christoph[3], Jonathan E. Pekar[4,5], Stephen A. Goldstein[6], Angela L. Rasmussen[7,8], Moritz U. G. Kraemer[9], Chris Newman[10], Marion P. G. Koopmans[11,12], Marc A. Suchard[13,14,15], Joel O. Wertheim[16], Philippe Lemey[17,18], David L. Robertson[19], Robert F. Garry[18,20,21], Edward C. Holmes[22], Andrew Rambaut[23], Kristian G. Andersen[2,24]*

Worobey *et al.*, *Science* **377**, 951–959 (2022) 26 August 2022

Live SARS-CoV-2–susceptible mammals (red foxes, hog badgers, and common raccoon dogs), were sold live at the Huanan market up until in late 2019 and that within the market, SARS-CoV-2–positive environmental samples were spatially associated with vendors selling live mammals.

References



antibiotics

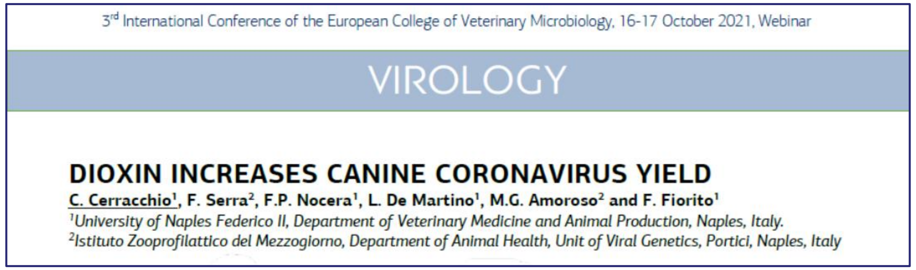
MDPI

Article

Effectiveness of the Fungal Metabolite 3-*O*-Methylfunicone towards Canine Coronavirus in a Canine Fibrosarcoma Cell Line (A72)

Claudia Cerracchio [1], Valentina Iovane [2], Maria Michela Salvatore [3,4], Maria Grazia Amoroso [5,*], Hiba Dakroub [2,5], Marina DellaGreca [3], Rosario Nicoletti [2,6], Anna Andolfi [3,7,*] and Filomena Fiorito [1,7,*]

Antibiotics **2022**, *11*, 1594. https://doi.org/10.3390/antibiotics11111594 https://www.mdpi.com/journal/antibiotics



3rd International Conference of the European College of Veterinary Microbiology, 16-17 October 2021, Webinar

VIROLOGY

DIOXIN INCREASES CANINE CORONAVIRUS YIELD

C. Cerracchio[1], F. Serra[2], F.P. Nocera[1], L. De Martino[1], M.G. Amoroso[2] and F. Fiorito[1]

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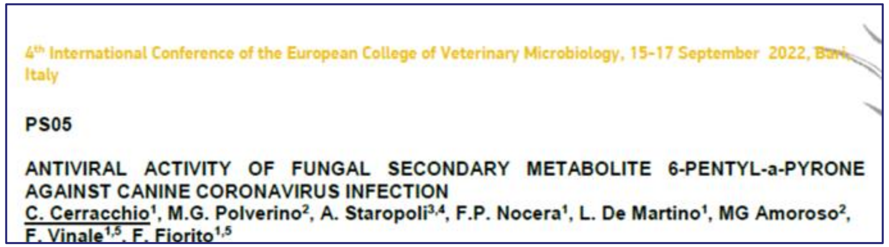
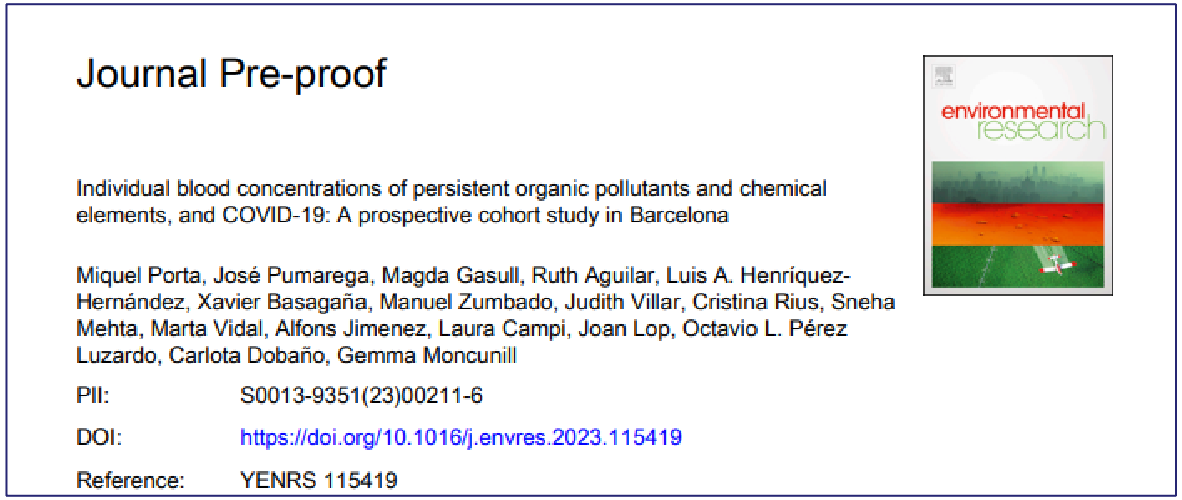


4th International Conference of the European College of Veterinary Microbiology, 15-17 September 2022, Bari, Italy

PS05

ANTIVIRAL ACTIVITY OF FUNGAL SECONDARY METABOLITE 6-PENTYL-a-PYRONE AGAINST CANINE CORONAVIRUS INFECTION

C. Cerracchio[1], M.G. Polverino[2], A. Staropoli[3,4], F.P. Nocera[1], L. De Martino[1], MG Amoroso[2], F. Vinale[1,5], F. Fiorito[1,5]



Journal Pre-proof

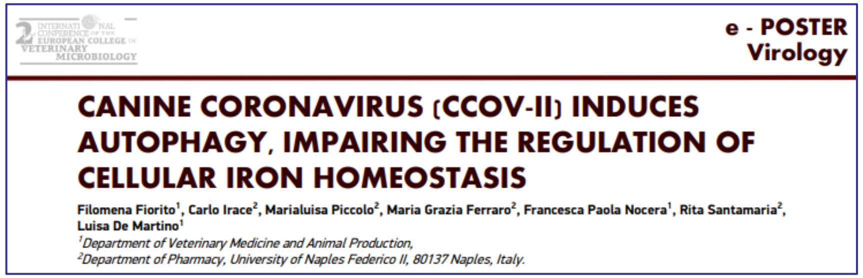
Individual blood concentrations of persistent organic pollutants and chemical elements, and COVID-19: A prospective cohort study in Barcelona

Miquel Porta, José Pumarega, Magda Gasull, Ruth Aguilar, Luis A. Henríquez-Hernández, Xavier Basagaña, Manuel Zumbado, Judith Villar, Cristina Rius, Sneha Mehta, Marta Vidal, Alfons Jimenez, Laura Campi, Joan Lop, Octavio L. Pérez Luzardo, Carlota Dobaño, Gemma Moncunill

PII: S0013-9351(23)00211-6

DOI: https://doi.org/10.1016/j.envres.2023.115419

Reference: YENRS 115419



2 INTERNATIONAL CONFERENCE OF THE EUROPEAN COLLEGE OF VETERINARY MICROBIOLOGY

e - POSTER
Virology

CANINE CORONAVIRUS (CCOV-II) INDUCES AUTOPHAGY, IMPAIRING THE REGULATION OF CELLULAR IRON HOMEOSTASIS

Filomena Fiorito[1], Carlo Irace[2], Marialuisa Piccolo[2], Maria Grazia Ferraro[2], Francesca Paola Nocera[1], Rita Santamaria[2], Luisa De Martino[1]

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Maria Grazia Ferraro
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Virginio Tammaro

22 Febbraio 2023 - Prof. Natascia Cocchia - Tumore mammario o infezione all’utero? È colpa mia... se solo le avessi fatto fare una cucciolata

SCUOLA DI AGRARIA E MEDICINA VETERINARIA 2023

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