800 1222·2022 ANNI
Università degli Studi di Padova
DMM DIPARTIMENTO DI MEDICINA MOLECOLARE

Current Knowledge about SARS-CoV-2

Giorgio Palù, MD, FESCMID

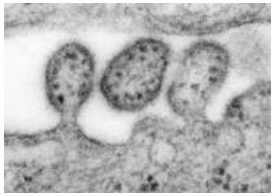
Emeritus Professor, Padua University

Professor of Neurosciences and of Science and Technology, Temple Univesrsity, Philadelphia

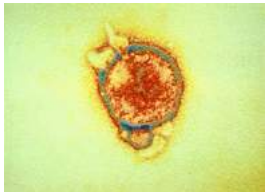
SIV ISV SOCIETA'ITALIANA DI VIROLOGIA
ITALIAN SOCIETY FOR VIROLOGY

EUROPEAN SOCIETY for VIROLOGY

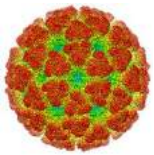
Emerging and re-emerging deadly viral infections during the last decades



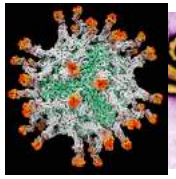
Lassa



Nipah/Hendra

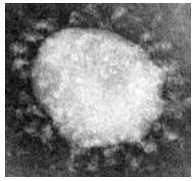


CHIKV

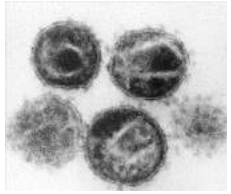


Polio

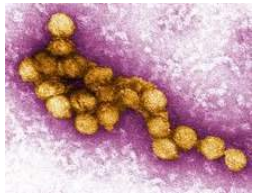
Ebola



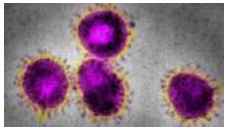
SARS-CoV-2



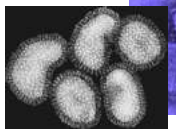
HIV



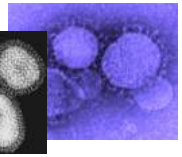
WNV



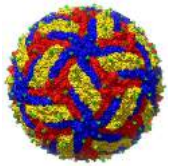
SARS



H1N1v



MERS



ZIKV

1980 1990 2000 2010 2020

Direct and indirect costs of zoonotic diseases estimated to exceed US$ 220 bllion in the last decade alone

https://wwwnc.cdc.gov – http://documents.worldbank.org

DMM
Dipartimento di Medicina Molecolare
Università di Padova

ABOUT ANIMAL-HUMAN INTERFACE









LIVE MARKETS IN CHINA

JUMP OF THE SPECIES BARRIER

Drivers of emergence of zoonotic and vector-borne viruses

Modified from Martina et al. Curr Opin Virol 2017

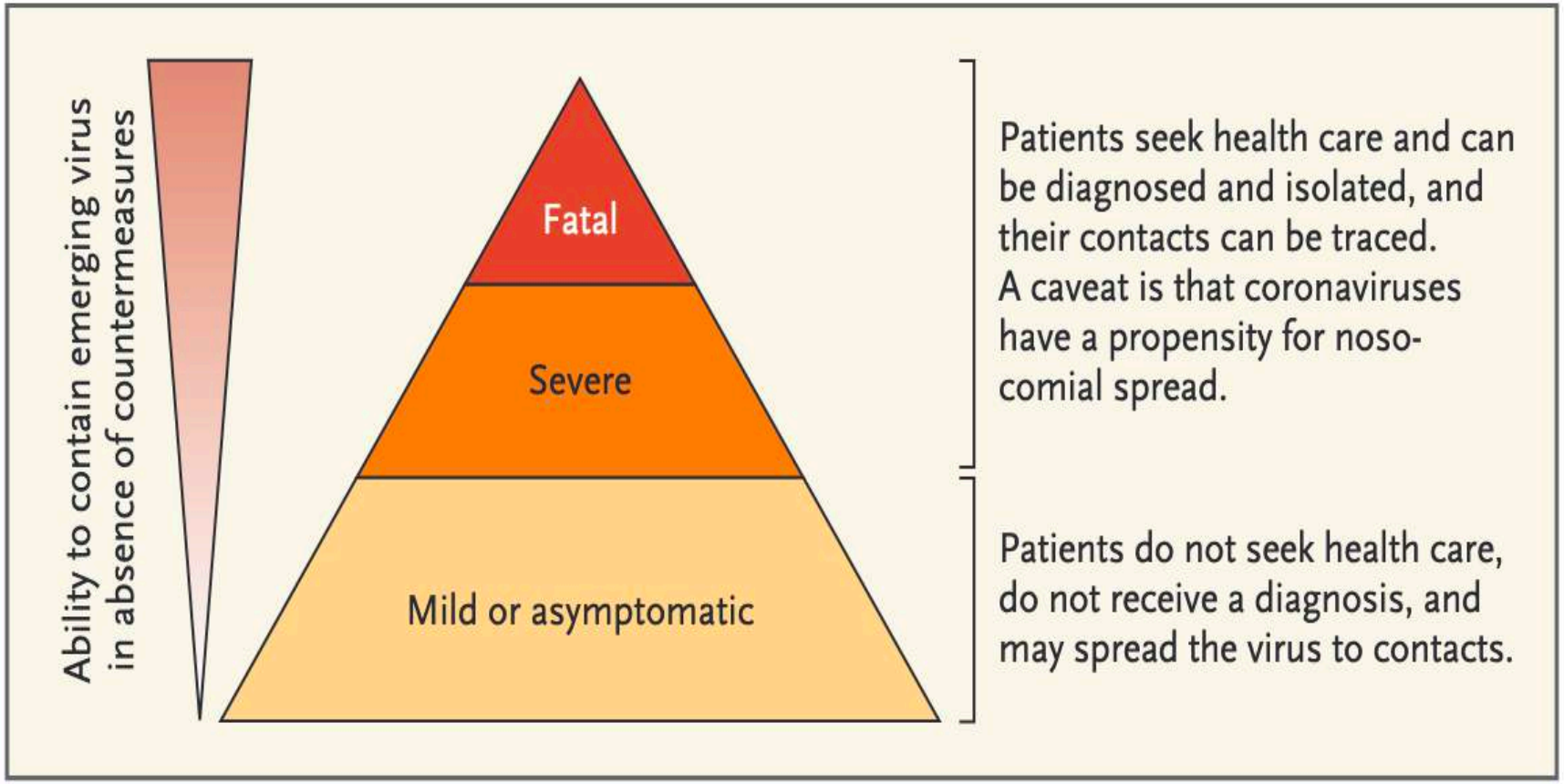
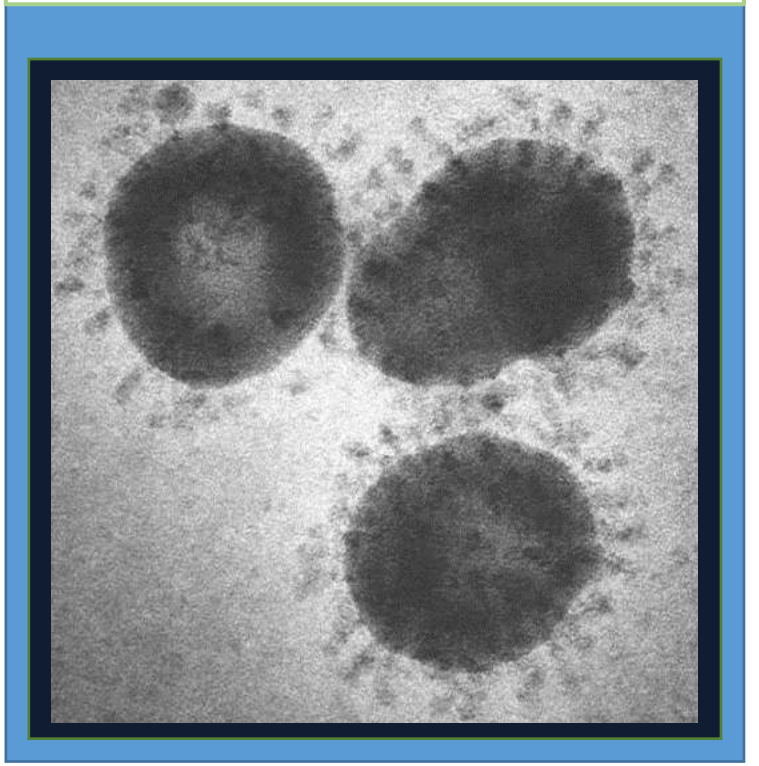


Figure 1. Surveillance Pyramid and Its Relation to Outbreak Containment.

Coronavirus Classification

- **Family:** ***Coronaviridae,***
- **Subfam.:** ***Coronovirinae,***
- **Genera:** ***Alphacoronavirus***
  Betacoronavirus
  Gammacoronavirus
  Deltacoronavirus

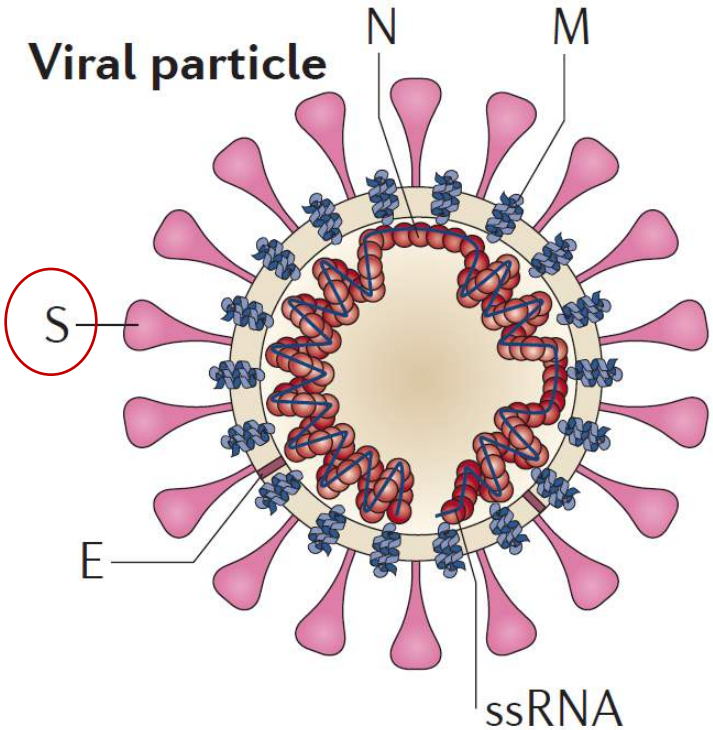
TEM of CoV

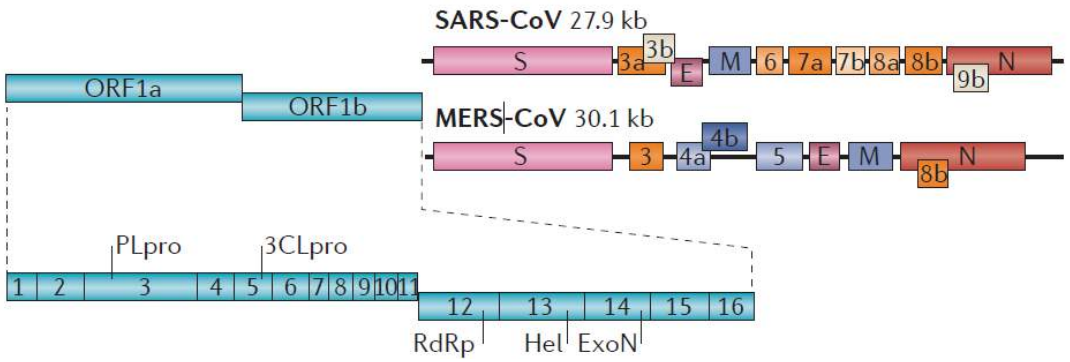


100 -160 nm

Coronavirus Structure

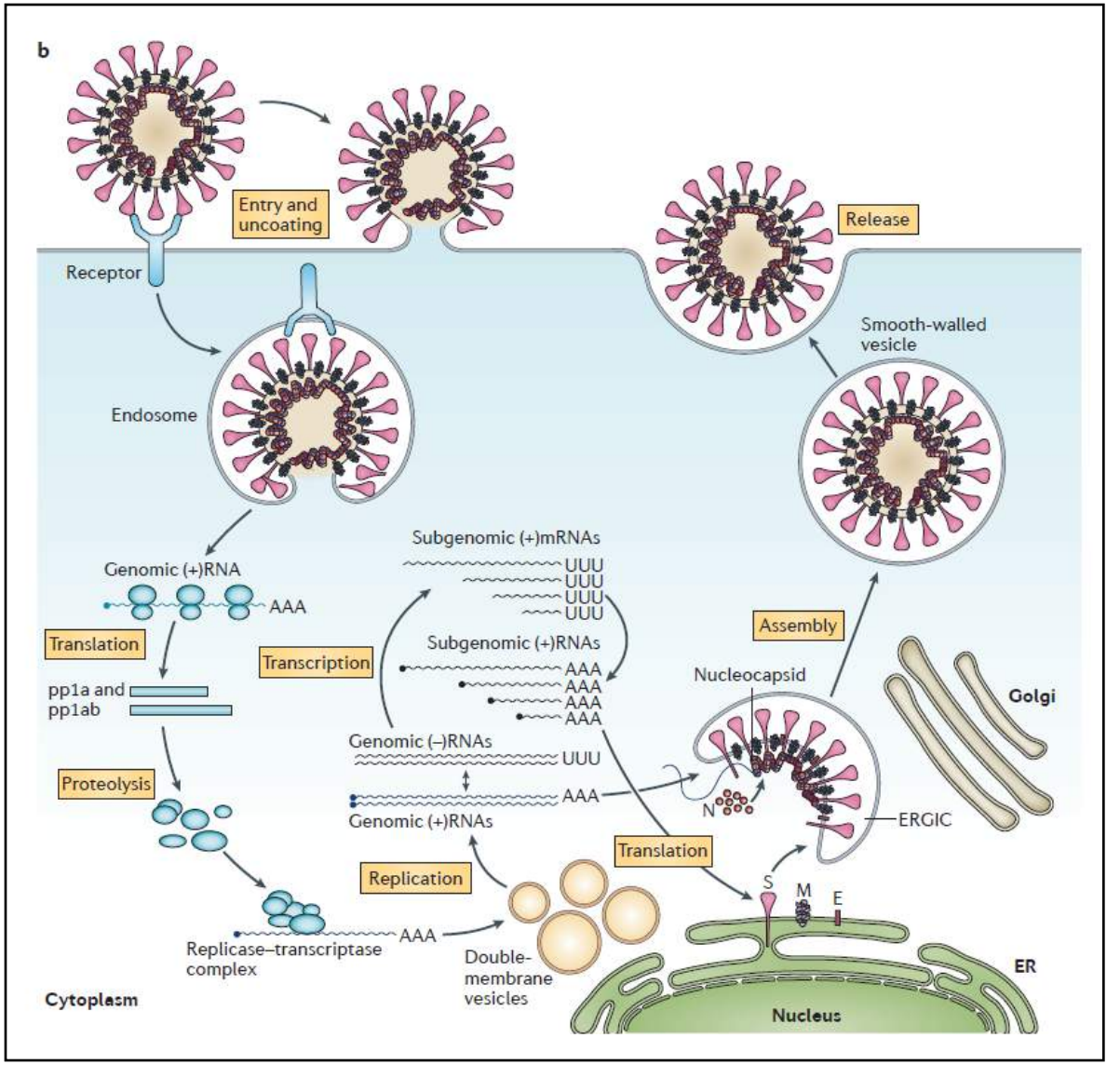
- **Virus dotati di envelope con 3 proteine di superficie**
- **Genoma ssRNA+ di grandi dimensioni (≈30kb)**





De Wit et al., Nat Rev Microbiol 2016; 14: 523-534.

Coronavirus Replicative Cycle



De Wit et al., Nat Rev Microbiol 2016; 14: 523-534.

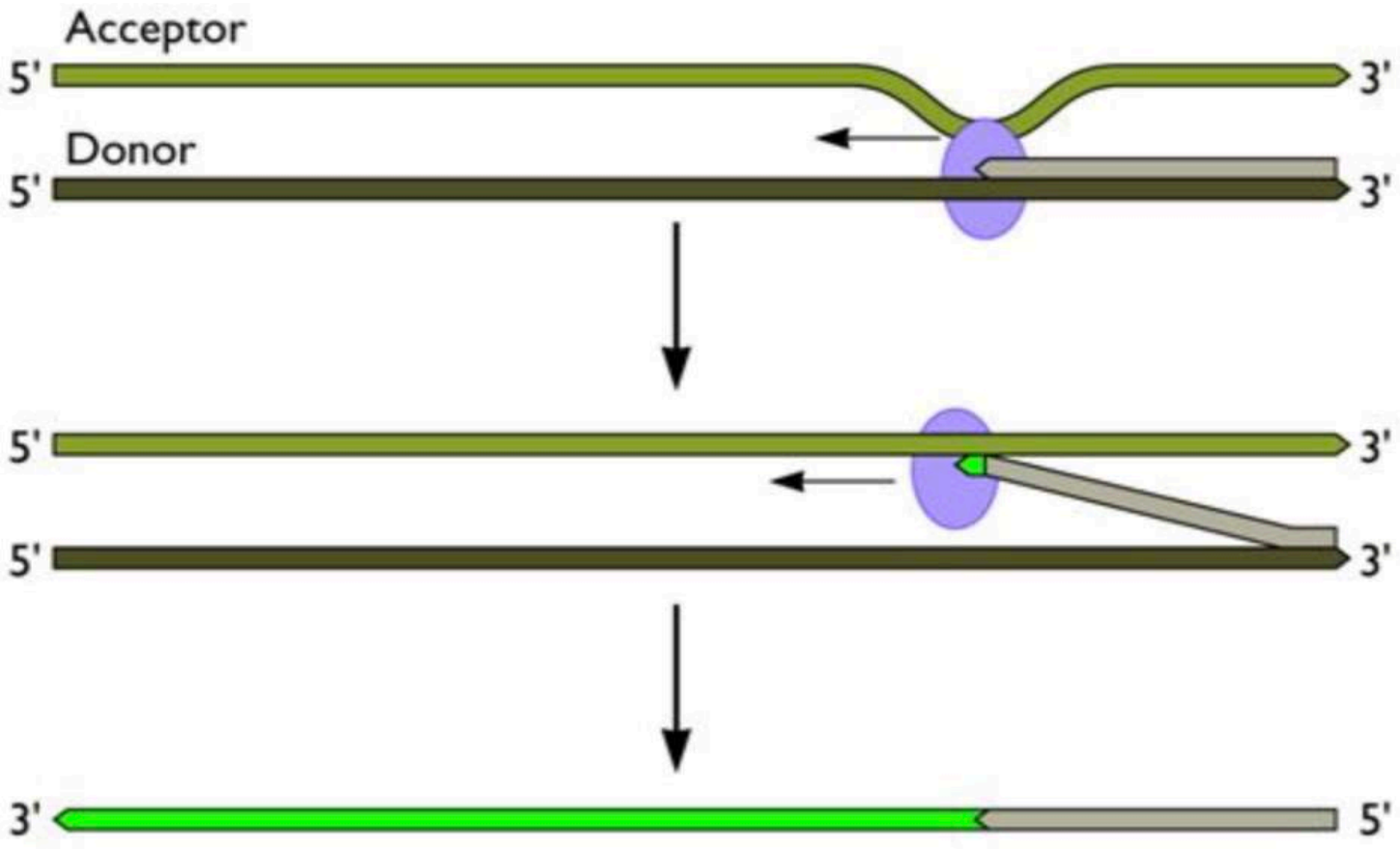
The 16 nonstructural proteins of coronaviruses and their functions

nsps	Functions
nsp1	Cellular mRNA degradation, inhibiting IFN signaling
nsp2	Unknown
nsp3	PLP, polypeptides cleaving, blocking host innate immune response, promoting cytokine expression
nsp4	DMV formation
nsp5	$3CL^{pro}$, M^{pro}, polypeptides cleaving, inhibiting IFN signaling
nsp6	Restricting autophagosome expansion, DMV formation
nsp7	Cofactor with nsp8 and nsp12
nsp8	Cofactor with nsp7 and nsp12, primase
nsp9	Dimerization and RNA binding
nsp10	Scaffold protein for nsp14 and nsp16
nsp11	Unknown
nsp12	Primer dependent RdRp
nsp13	RNA helicase, 5′ triphosphatase
nsp14	Exoribonuclease, N7-MTase
nsp15	Endoribonuclease, evasion of dsRNA sensors
nsp16	2′-O-MTase; avoiding MDA5 recognition, negatively regulating innate immunity

Abbreviations: $3CL^{pro}$, chymotrypsin-like protease; DMV, double-membrane vesicle; dsRNA, double-stranded RNA interferon; mRNA, messenger RNA; M^{pro}, main protease.

J Med Virol. 2020;92:418–423.

RNA Recombination by Copy Choice



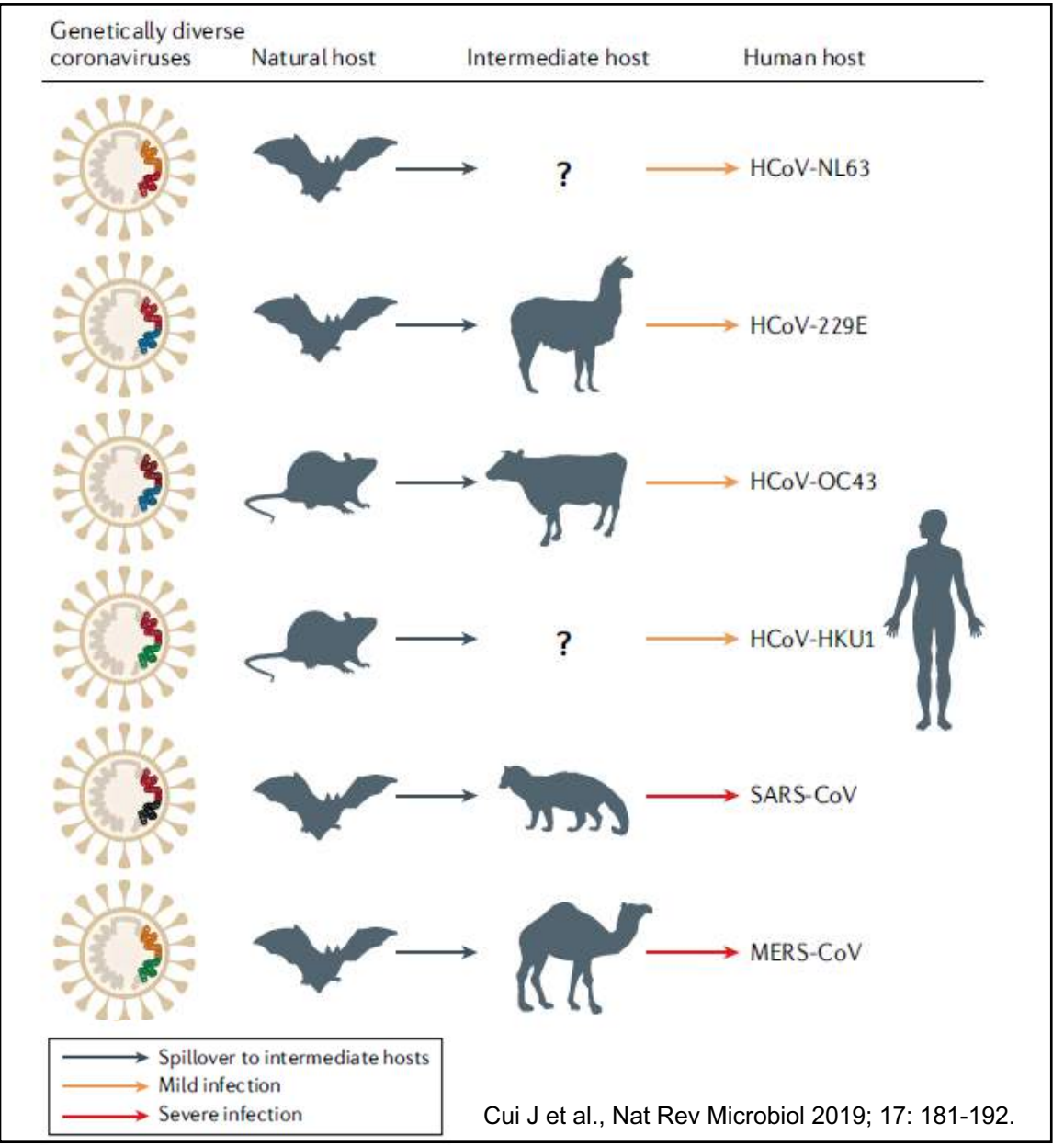
Human Coronaviruses (up to December 19)

Genus	Virus	Disease
Alphacoronavirus	HCoV-NL63*	Mild respiratory tract infections
	HCoV-229E	Mild respiratory tract infections
Betacoronavirus	HCoV-OC43	Mild respiratory tract infections
	HCoV-HKU1*	Mild respiratory tract infections and pneumonia
	SARS-CoV	Severe acute respiratory syndrome
	MERS-CoV	Severe acute respiratory syndrome

Salata C & Palù G. Path and Dis 2020

DMM Dipartimento di Medicina Molecolare Università di Padova

Origin of human coronaviruses

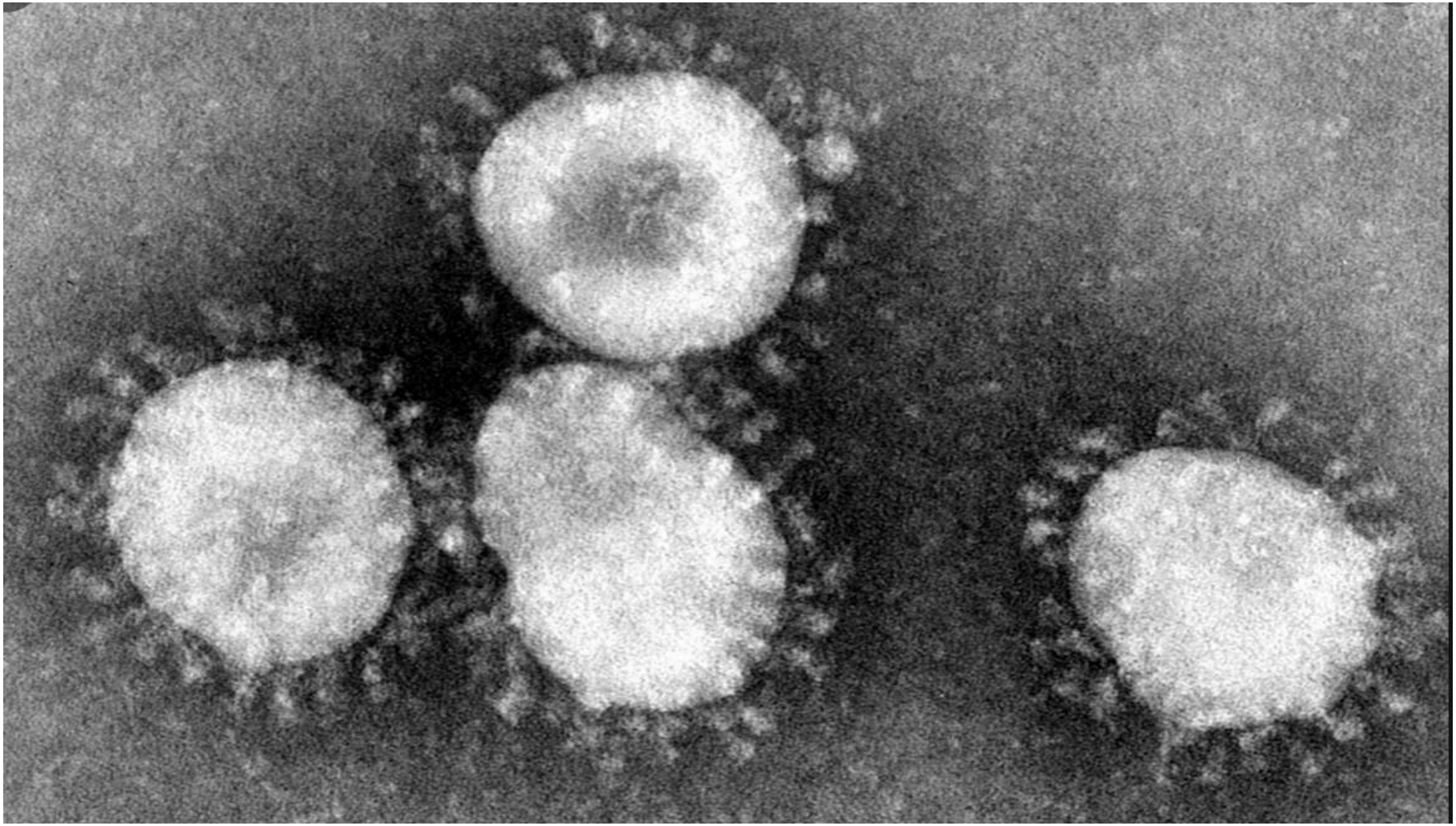


Cui J et al., Nat Rev Microbiol 2019; 17: 181-192.

Coronavirus infections are zoonotic in origin

THE VIRUS SPREADERS

SARS-CoV-2 as the cause of Covid-19



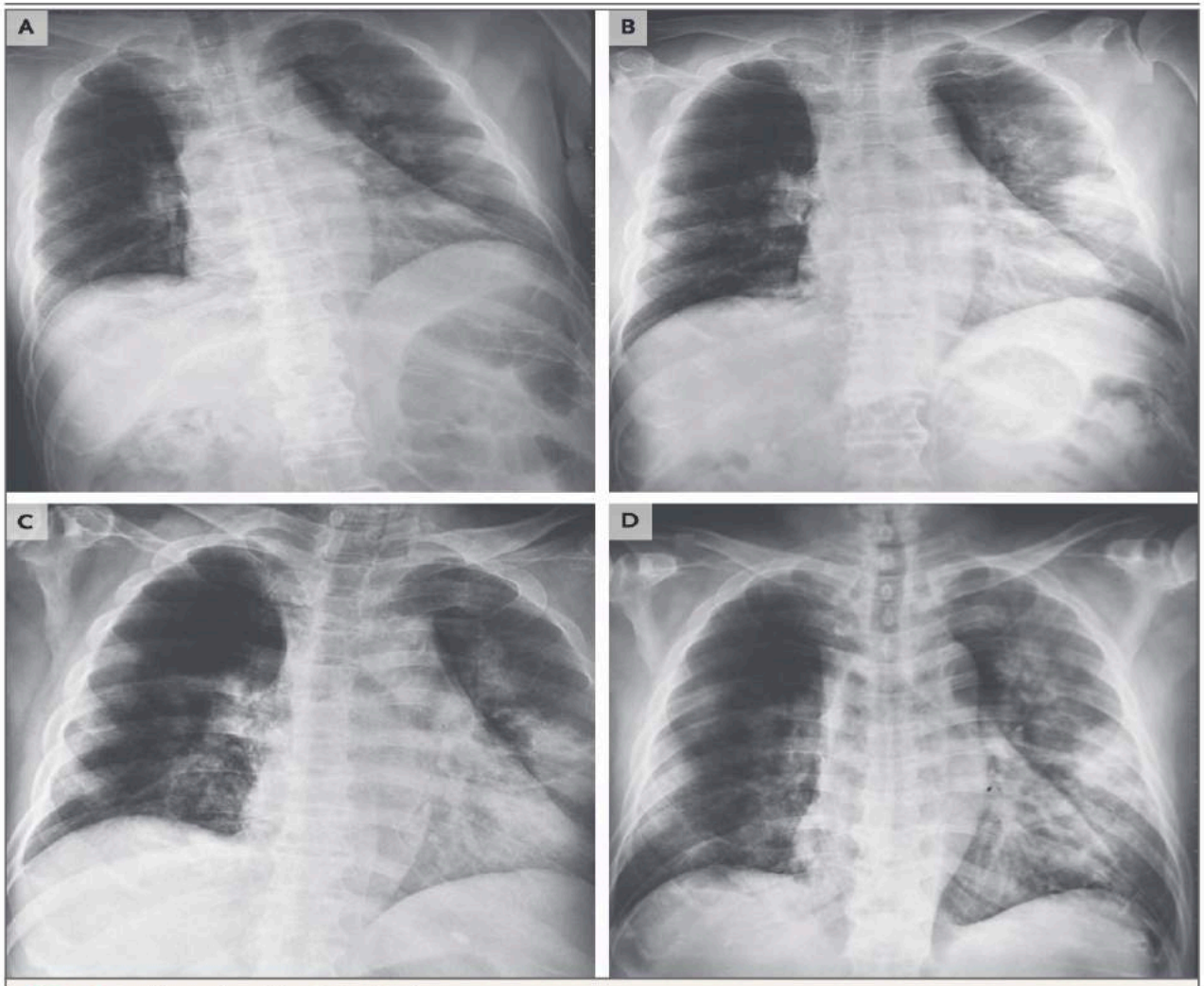


Figure 1. Radiographs of the Father's Chest.
Shown are chest radiographs obtained at admission (Panel A) and on day 3 (Panel B), day 5 (Panel C), and day 6 (Panel D) after admission.

COVID-19 SYMPTOMS

MOST COMMON SYMPTONS

- Fever
- Dry cough
- fatigue

LESS COMMOM SYMPTOMS

- Ailment, pain
- Sore throat
- Diarrhea
- Conjunctivitis
- Headache
- Anosmia, dysgeusia
- Skin eruptions, discolored feet and hands fingers

SEVERE SYMPTOMS

- Dyspnea and breathe shortage
- Chest pain and oppression
- Difficulty in speaking and moving

DMM Dipartimento di Medicina Molecolare Università di Padova

Source: who.int/health-topics/coronavirus

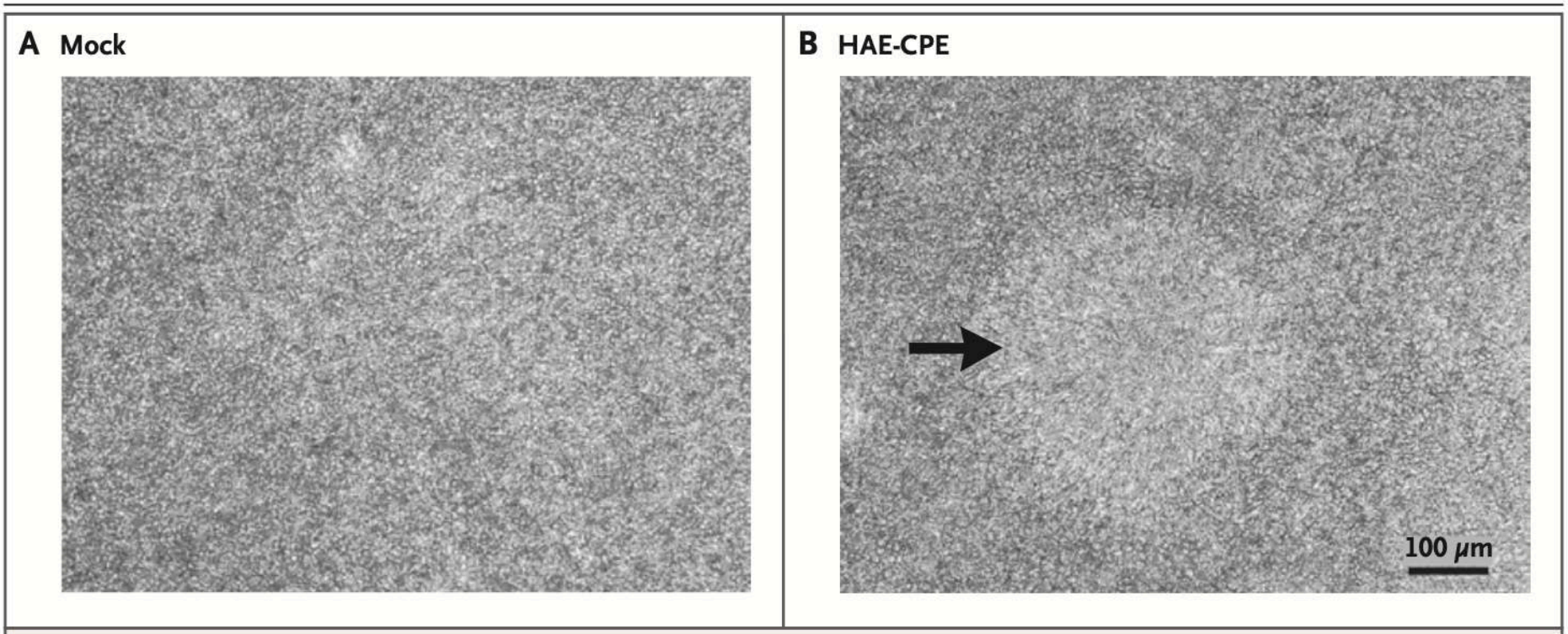
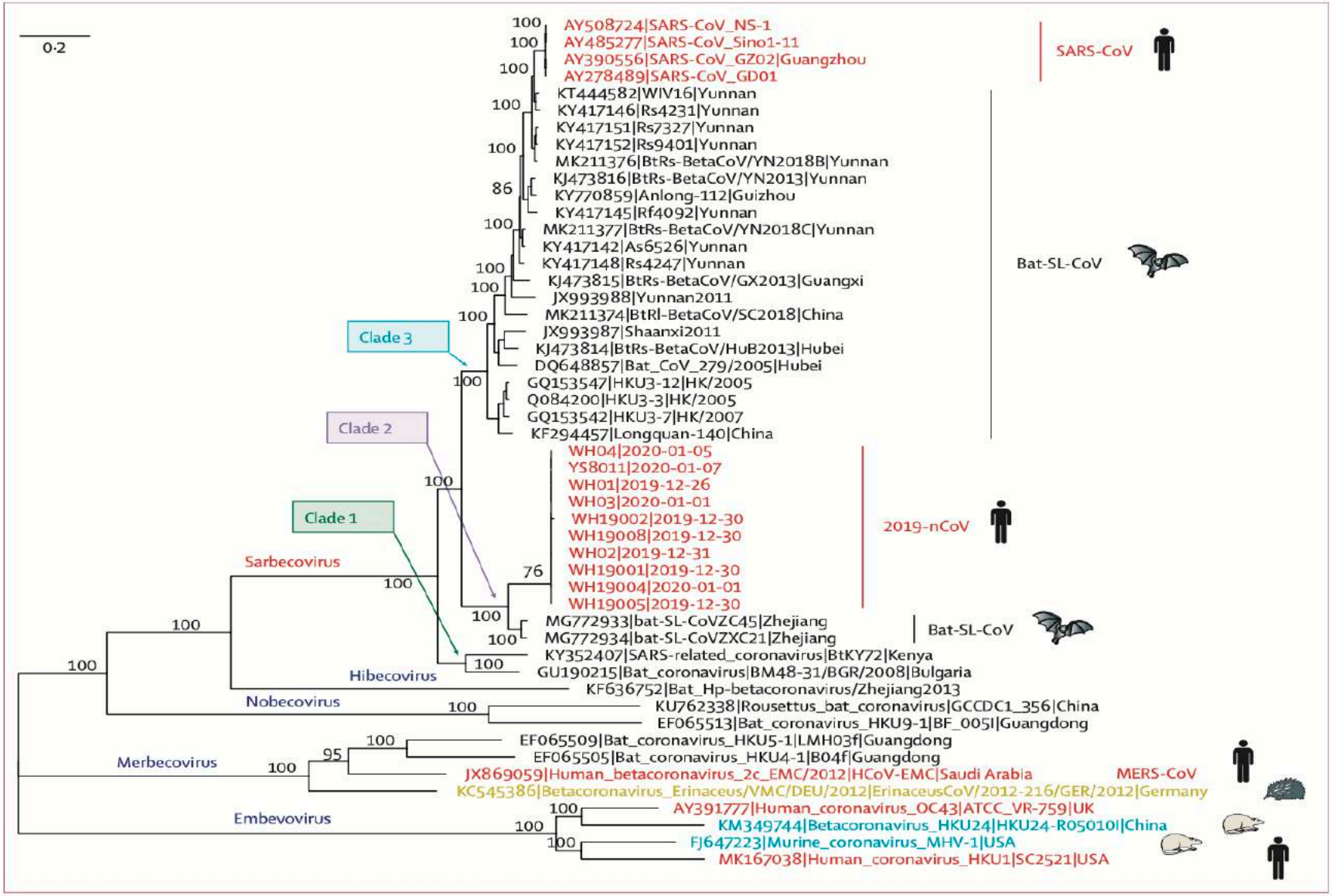
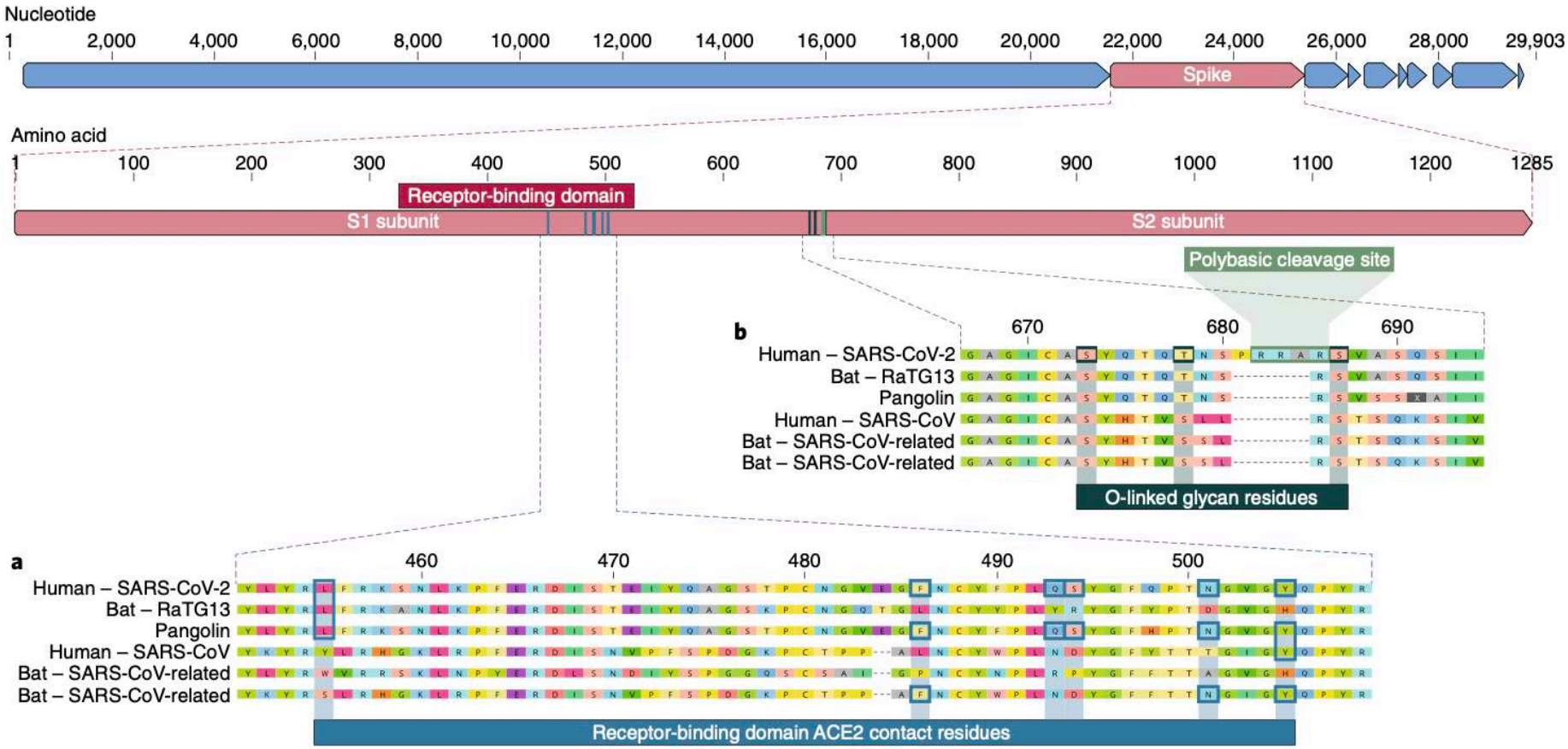


Figure 2. Cytopathic Effects in Human Airway Epithelial Cell Cultures after Inoculation with 2019-nCoV.


0·2
AY508724|SARS-CoV_NS-1
AY485277|SARS-CoV_Sino1-11
AY390556|SARS-CoV_GZ02|Guangzhou
AY278489|SARS-CoV_GD01
SARS-CoV
KT444582|WIV16|Yunnan
KY417146|Rs4231|Yunnan
KY417151|Rs7327|Yunnan
KY417152|Rs9401|Yunnan
MK211376|BtRs-BetaCoV/YN2018B|Yunnan
KJ473816|BtRs-BetaCoV/YN2013|Yunnan
KY770859|Anlong-112|Guizhou
KY417145|Rf4092|Yunnan
MK211377|BtRs-BetaCoV/YN2018C|Yunnan
KY417142|As6526|Yunnan
KY417148|Rs4247|Yunnan
KJ473815|BtRs-BetaCoV/GX2013|Guangxi
JX993988|Yunnan2011
MK211374|BtRl-BetaCoV/SC2018|China
JX993987|Shaanxi2011
KJ473814|BtRs-BetaCoV/HuB2013|Hubei
DQ648857|Bat_CoV_279/2005|Hubei
GQ153547|HKU3-12|HK/2005
Q084200|HKU3-3|HK/2005
GQ153542|HKU3-7|HK/2007
KF294457|Longquan-140|China
Bat-SL-CoV
Clade 3
Clade 2
Clade 1
WH04|2020-01-05
YS8011|2020-01-07
WH01|2019-12-26
WH03|2020-01-01
WH19002|2019-12-30
WH19008|2019-12-30
WH02|2019-12-31
WH19001|2019-12-30
WH19004|2020-01-01
WH19005|2019-12-30
2019-nCoV
Sarbecovirus
MG772933|bat-SL-CoVZC45|Zhejiang
MG772934|bat-SL-CoVZXC21|Zhejiang
Bat-SL-CoV
KY352407|SARS-related_coronavirus|BtKY72|Kenya
GU190215|Bat_coronavirus|BM48-31/BGR/2008|Bulgaria
Hibecovirus
KF636752|Bat_Hp-betacoronavirus/Zhejiang2013
Nobecovirus
KU762338|Rousettus_bat_coronavirus|GCCDC1_356|China
EF065513|Bat_coronavirus_HKU9-1|BF_005I|Guangdong
EF065509|Bat_coronavirus_HKU5-1|LMH03f|Guangdong
EF065505|Bat_coronavirus_HKU4-1|B04f|Guangdong
Merbecovirus
JX869059|Human_betacoronavirus_2c_EMC/2012|HCoV-EMC|Saudi Arabia
MERS-CoV
KC545386|Betacoronavirus_Erinaceus/VMC/DEU/2012|ErinaceusCoV/2012-216/GER/2012|Germany
AY391777|Human_coronavirus_OC43|ATCC_VR-759|UK
KM349744|Betacoronavirus_HKU24|HKU24-R05010I|China
FJ647223|Murine_coronavirus_MHV-1|USA
MK167038|Human_coronavirus_HKU1|SC2521|USA
Embevovirus

Features of the spike protein in human SARS-CoV-2 and related coronaviruses



About the virus origin?

- Molecular data suggest an **origin from bats** and that human infection occurred through **an intermediate host**

- Studies on bats have shown that the majority of CoVs **can not utilize human receptors** therefore implying a recombination event in an intermediate host as a necessary step

- For these reasons it is of utmost importance the study of **animal virome** and to adopt an active virus surveillance at the **human-animal interface**

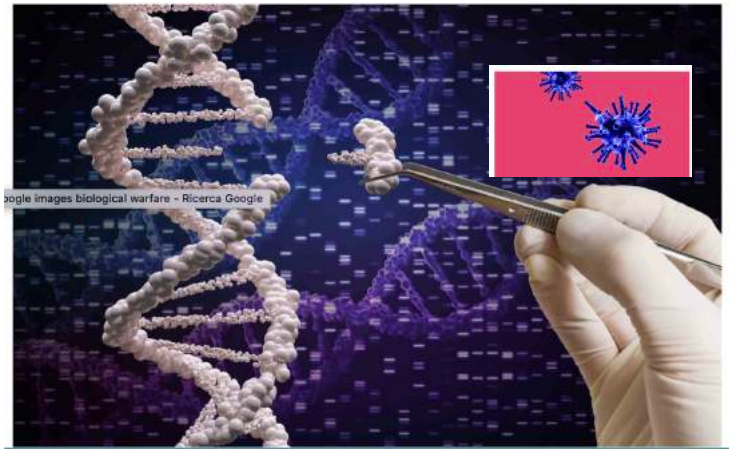
How is the virus spreading?

<u>A likely intermediate host</u>:

Pangolin

CoV isolatees were identified with only 90-92% sequence homology with SARS-CoV-2 ???

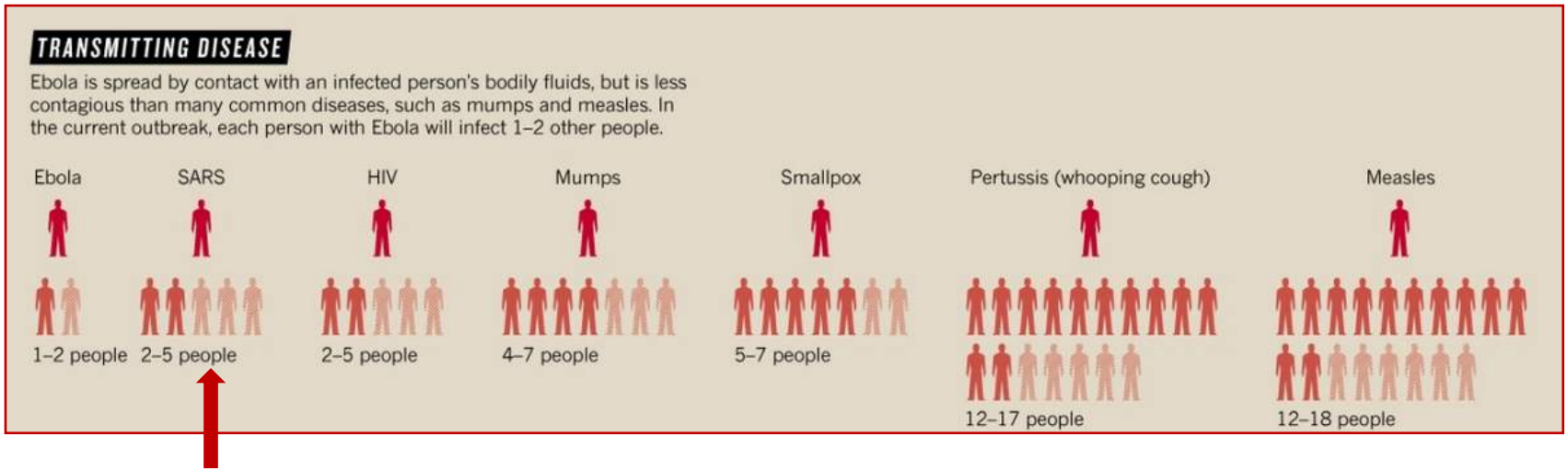
THE BIOLOGICAL WARFARE?



About virus transmission

Person to person:

- **Announced by Chinese authorities (cases unrelated to live market)**
- **Confirmed in imported cases**
- **Reproduction number R_0 2.2 (superspreader)**

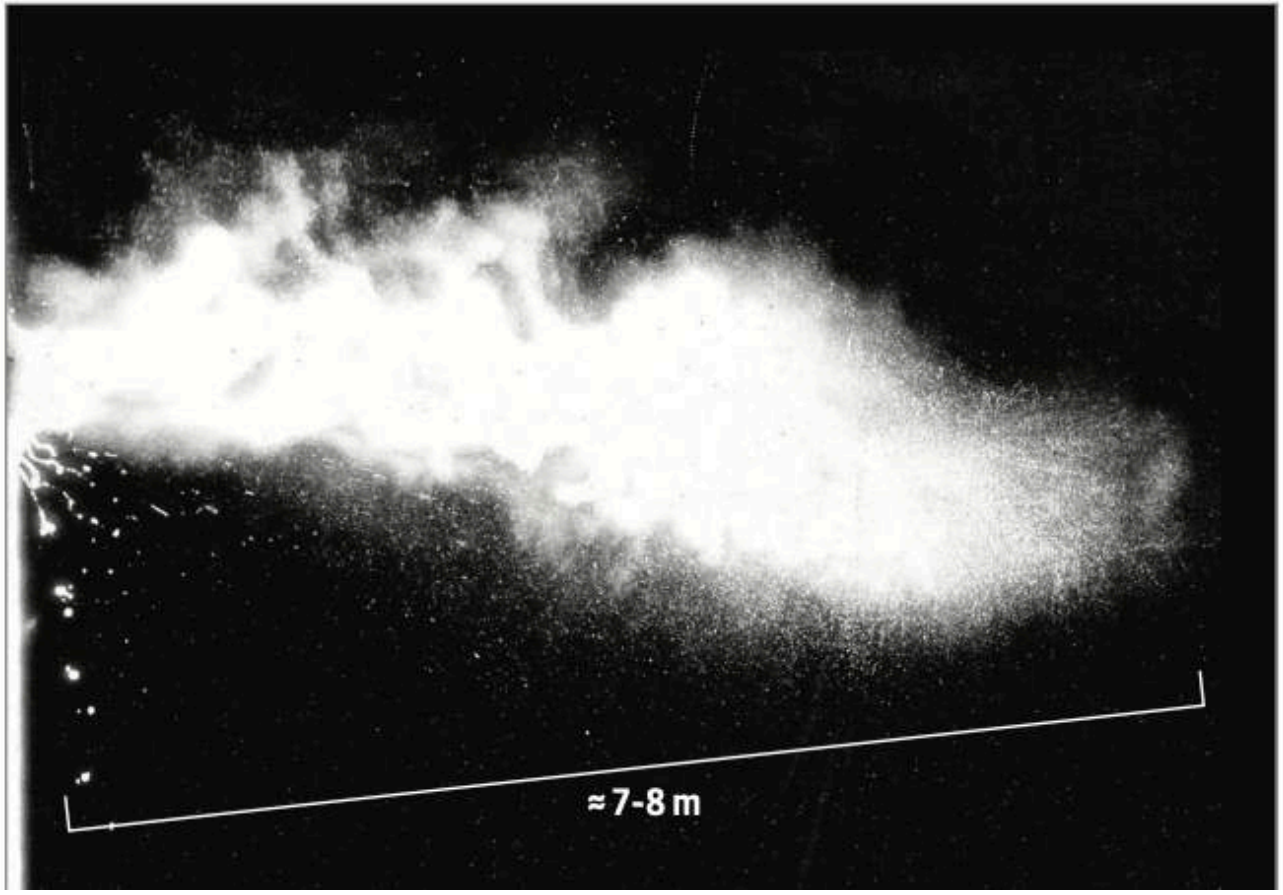


JAMA Insights

Turbulent Gas Clouds and Respiratory Pathogen Emissions
Potential Implications for Reducing Transmission of COVID-19

Lydia Bourouiba, PhD

Figure. Multiphase Turbulent Gas Cloud From a Human Sneeze

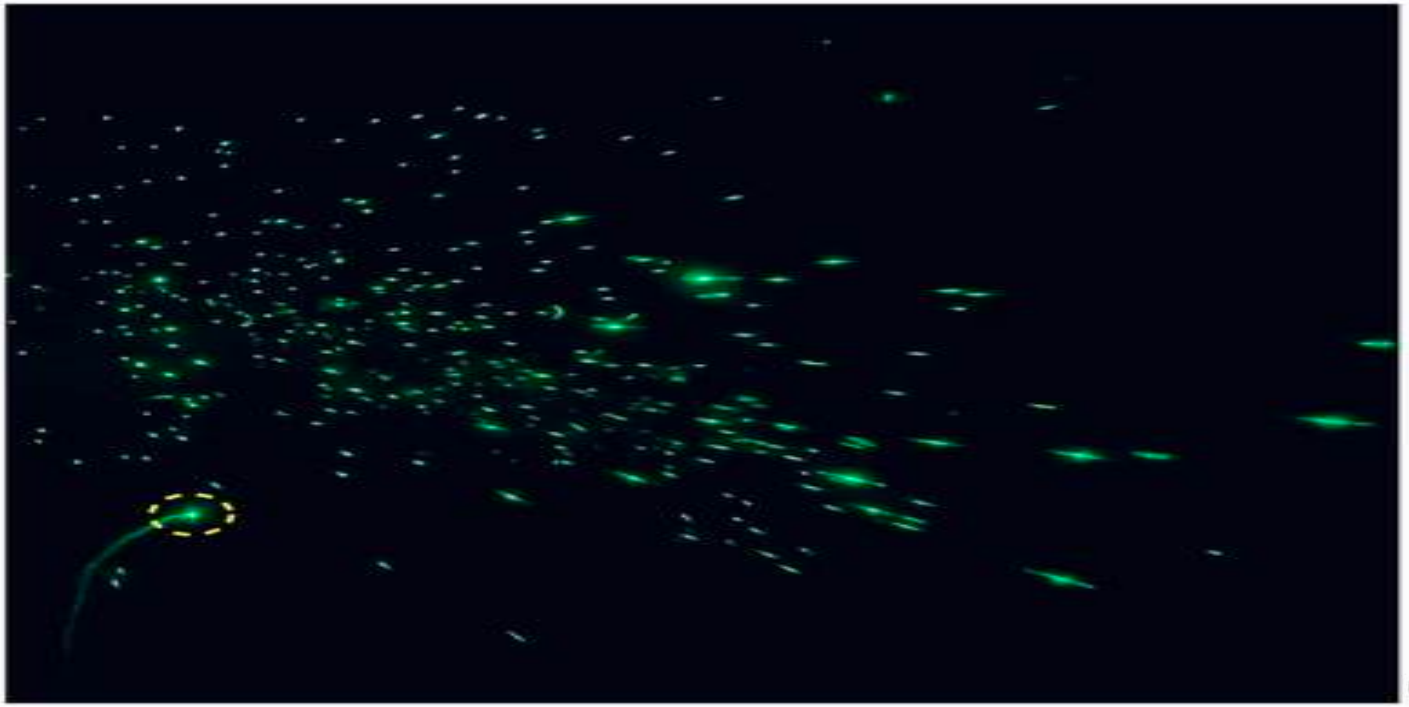


The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Visualizing Speech-Generated Oral Fluid Droplets with Laser Light Scattering

Anfinrud P et al, April 17, 2020



Cite as: K. A. Prather *et al.*, *Science* 10.1126/science.abc6197 (2020).

Reducing transmission of SARS-CoV-2

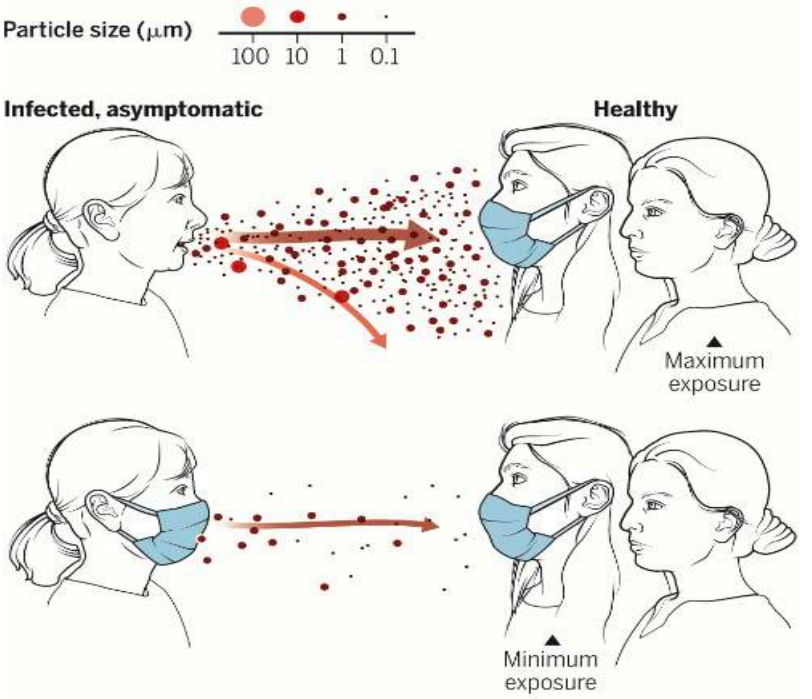
Kimberly A. Prather[1], Chia C. Wang,[2,3] Robert T. Schooley[4]

[1]Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA 92037, USA. [2]Department of Chemistry, National Sun Yat-sen University, Kaohsiung, Taiwan 804, Republic of China. [3]Aerosol Science Research Center, National Sun Yat-Sen University, Kaohsiung, Taiwan 804, Republic of China. [4]Department of Medicine, Division of Infectious Diseases and Global Public Health, School of Medicine, University of California San Diego, La Jolla, CA 92093, USA. Email: kprather@ucsd.edu

Masks and testing are necessary to combat asymptomatic spread in aerosols and droplets

Masks reduce airborne transmission

Infectious aerosol particles can be released during breathing and speaking by asymptomatic infected individuals. No masking maximizes exposure, whereas universal masking results in the least exposure.



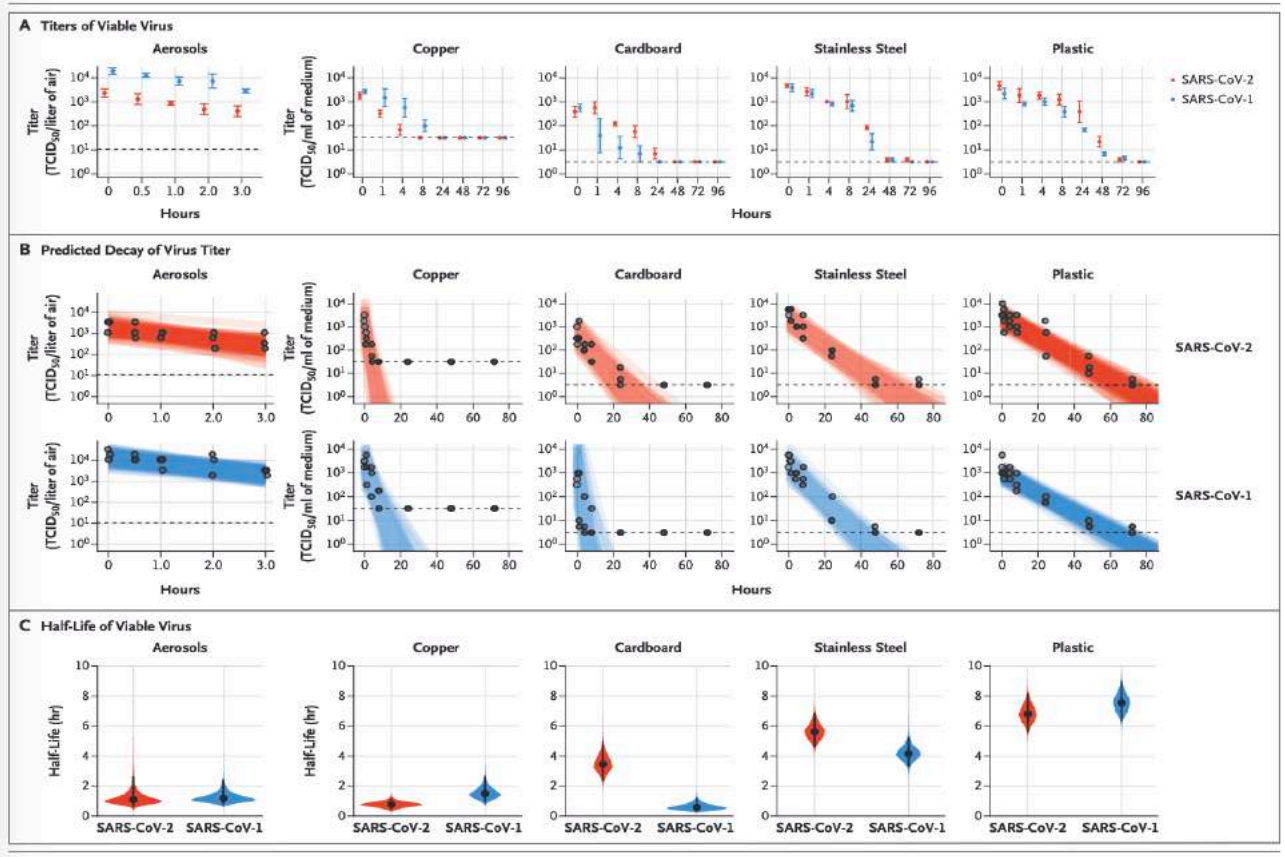
GRAPHIC: V. ALTOUNIAN/*SCIENCE*

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

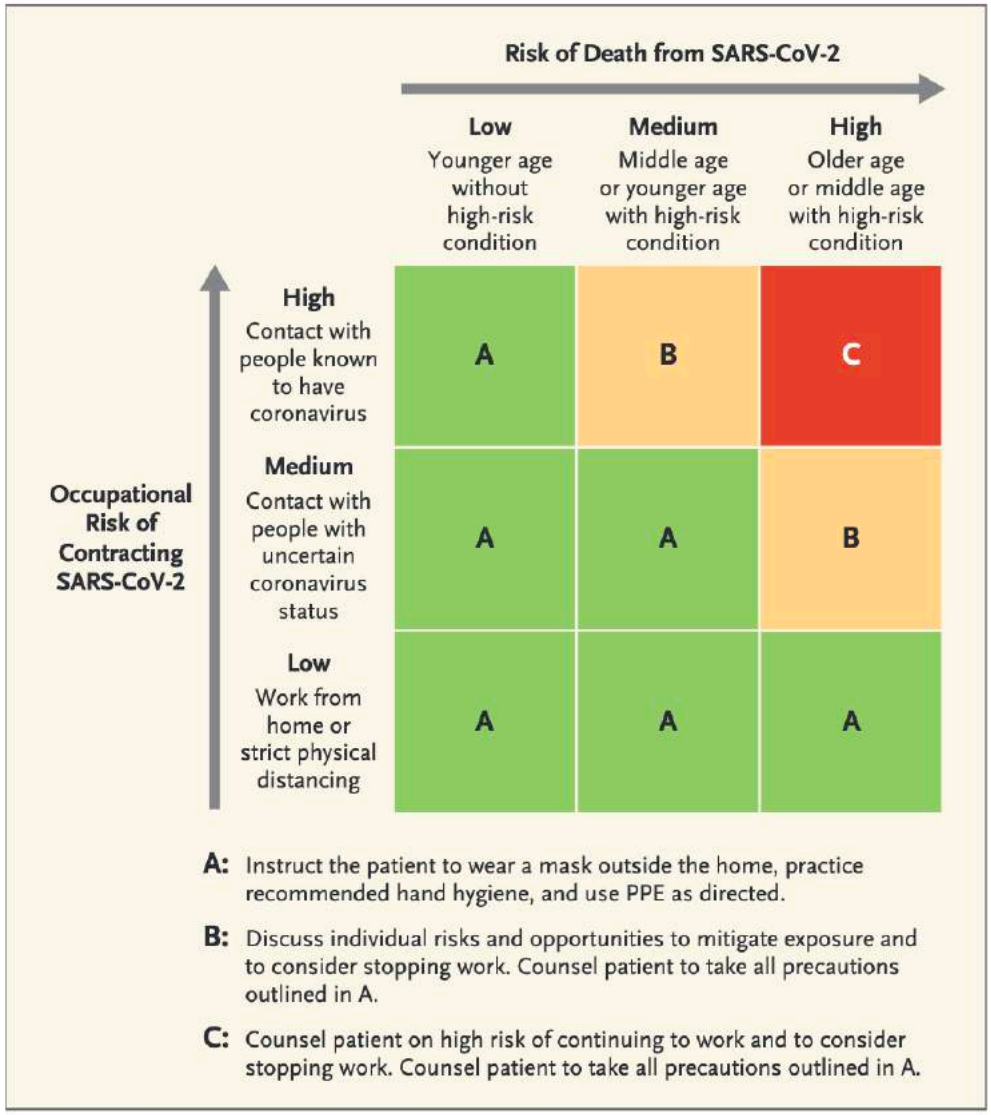
Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1

Van Doremalen N. et al, April 17, 2020



"Is It Safe for Me to Go to Work?" Risk Stratification for Workers during the Covid-19 Pandemic

Marc R. Larochelle, M.D., M.P.H.



Proposed Framework for Counseling Patients about Working during the Pandemic.

NEJM May 30, 2020

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany

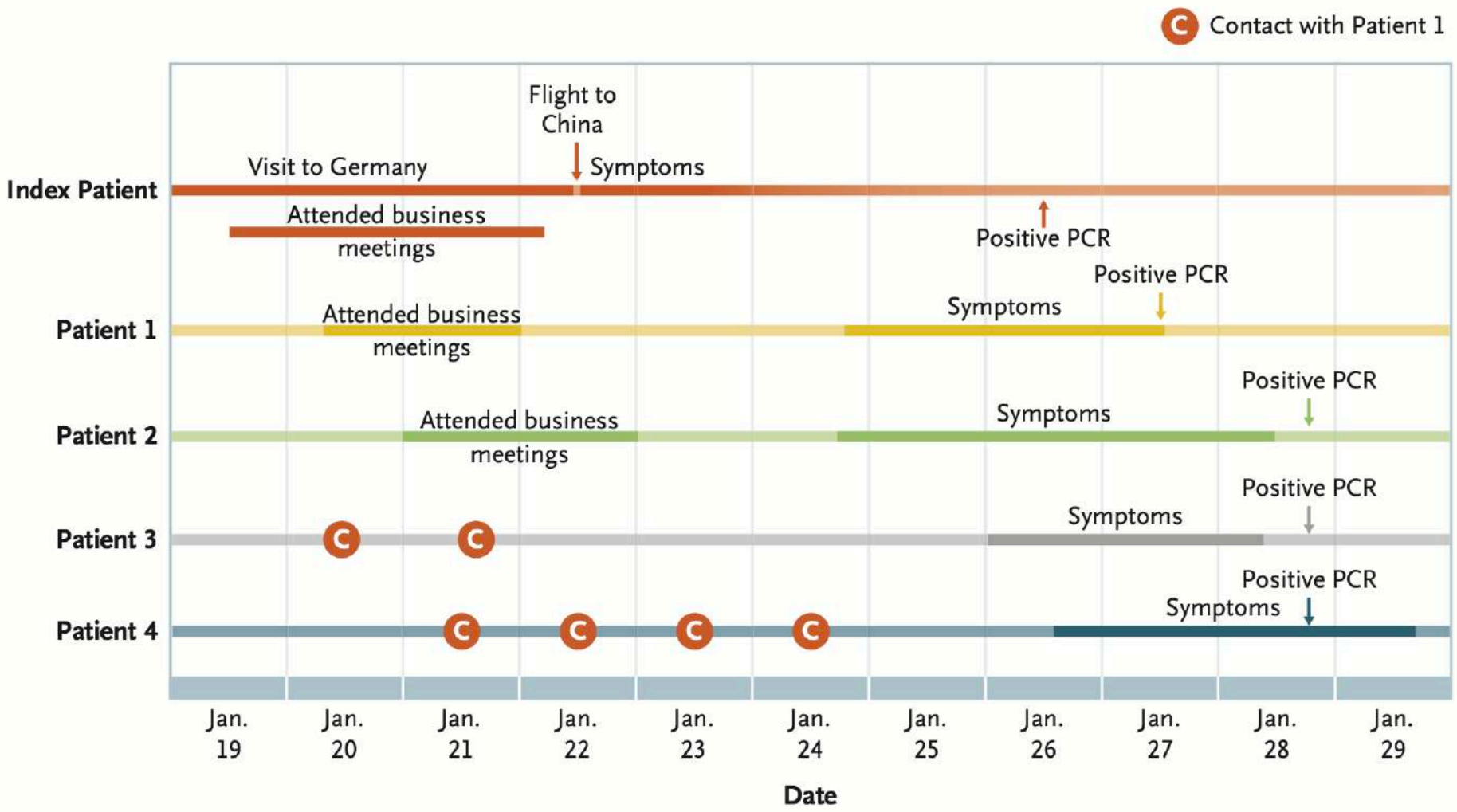
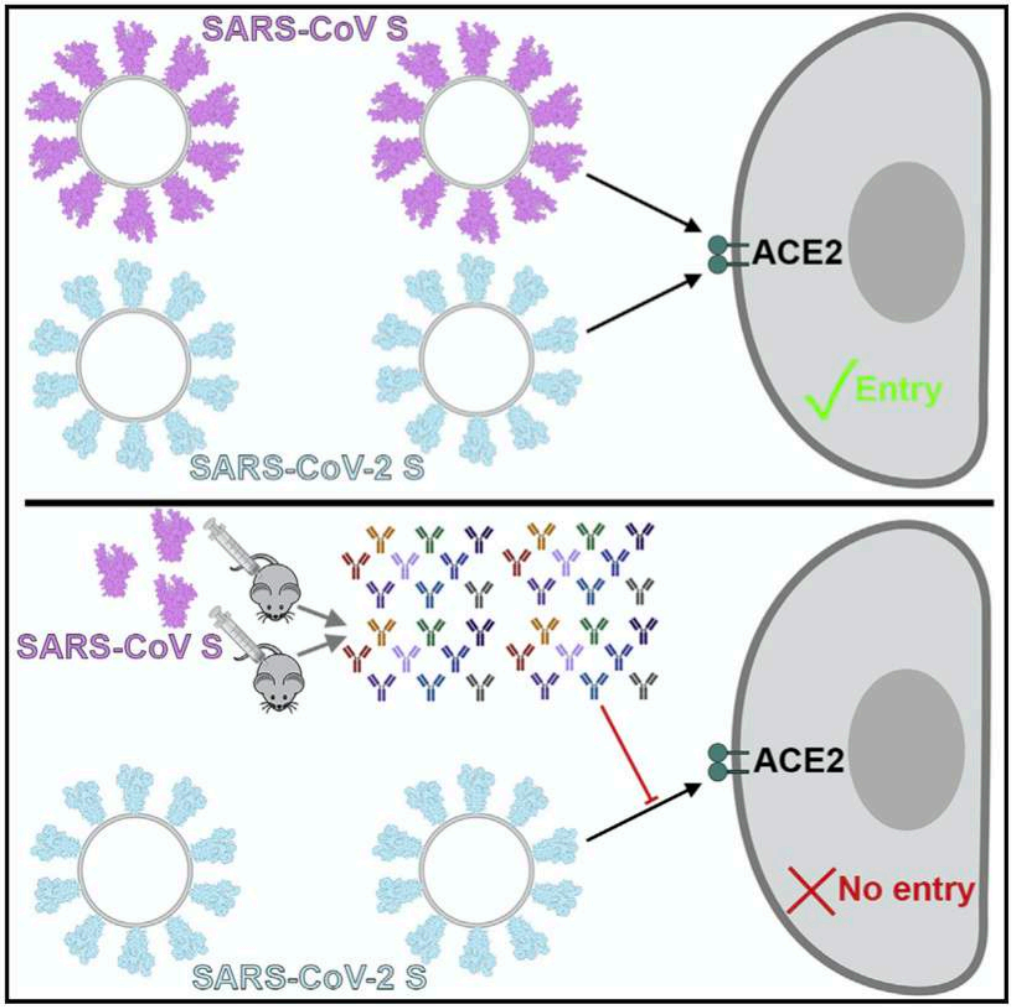


Figure 1. **Timeline of Exposure to Index Patient with Asymptomatic 2019-CoV Infection in Germany.**

Cell

Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein

Graphical Abstract



Authors

Alexandra C. Walls, Young-Jun Park, M. Alejandra Tortorici, Abigail Wall, Andrew T. McGuire, David Veesler

Correspondence

dveesler@uw.edu

In Brief

SARS-CoV-2, a newly emerged pathogen spreading worldwide, binds with high affinity to human ACE2 and uses it as an entry receptor to invade target cells. Cryo-EM structures of the SARS-CoV-2 spike glycoprotein in two distinct conformations, along with inhibition of spike-mediated entry by SARS-CoV polyclonal antibodies, provide a blueprint for the design of vaccines and therapeutics.

Cell

Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein

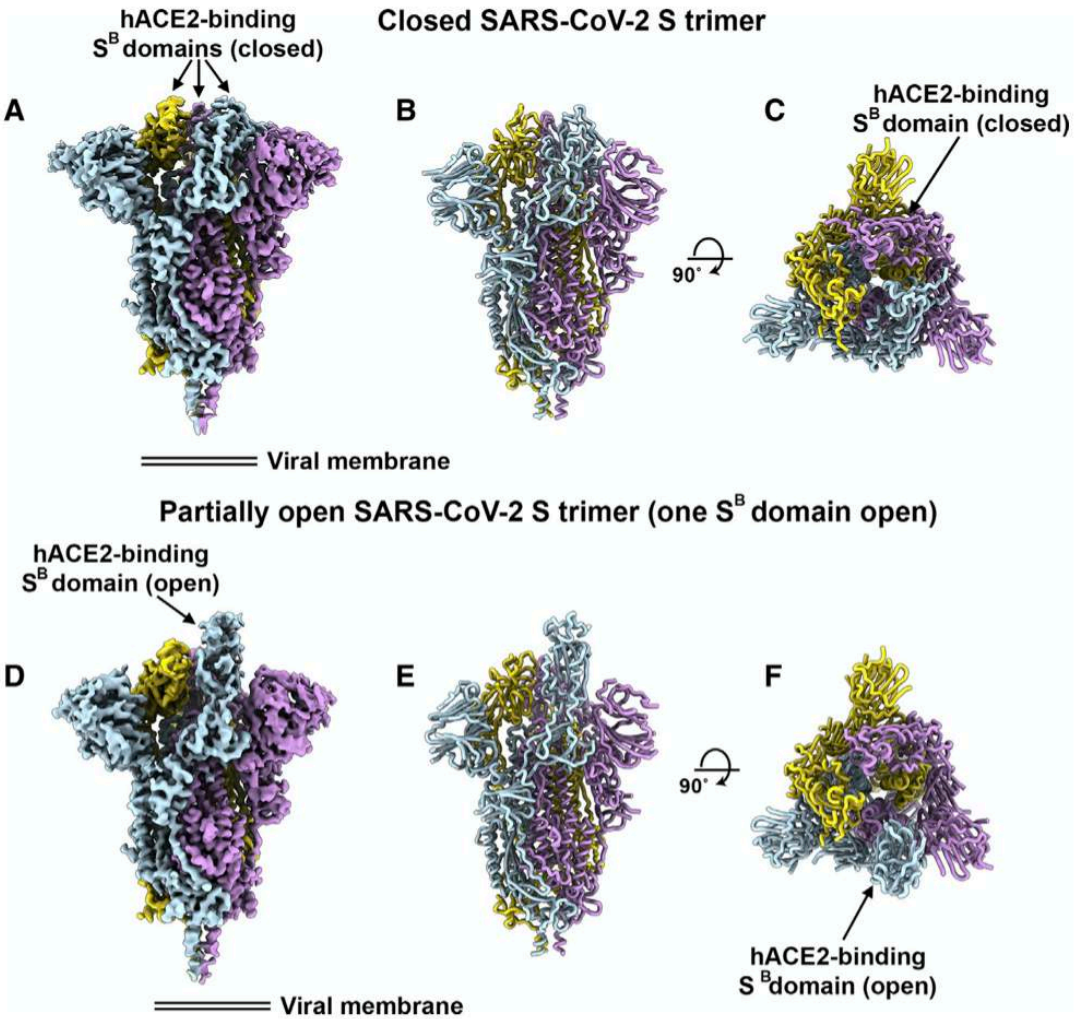


Figure 3. Cryo-EM Structures of the SARS-CoV-2 S Glycoprotein

(A) Closed SARS-CoV-2 S trimer unsharpened cryo-EM map.

(B and C) Two orthogonal views from the side (B) and top (C) of the atomic model of the closed SARS-CoV-2 S trimer.

(D) Partially open SARS-CoV-2 S trimer unsharpened cryo-EM map (one S^B domain is open).

(E-F) Two orthogonal views from the side (E) and top (F) of the atomic model of the closed SARS-CoV-2 S trimer. The glycans were omitted for clarity. See also Figures S1 and S2.

Cell

Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein

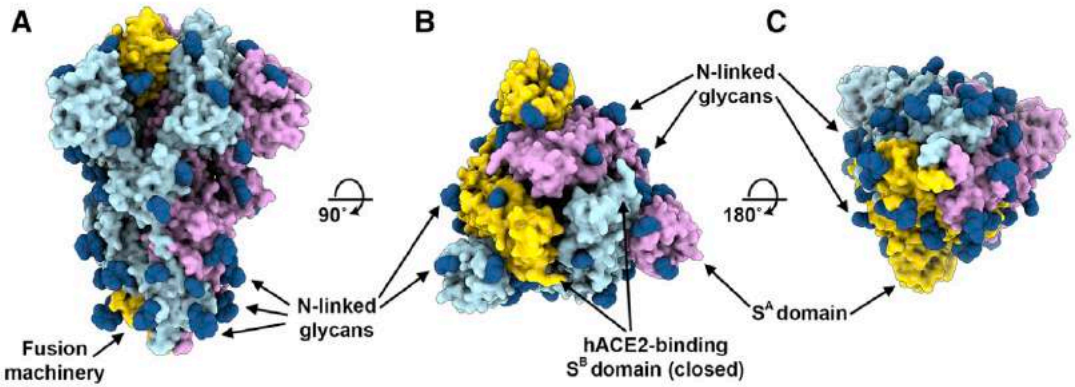


Figure 4. Organization of the SARS-CoV-2 S N-Linked Glycans

(A–C) Ribbon diagrams of the SARS-CoV-2 S closed structure rendered as a surface with glycans resolved in the cryo-EM map rendered as dark blue spheres. See also Table 2 and Data S1.

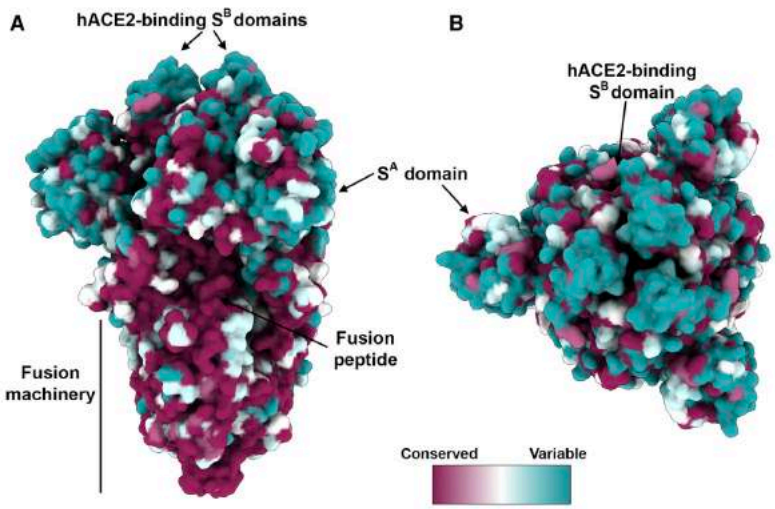


Figure 5. SARS-CoV S Elicits Antibodies Neutralizing SARS-CoV-2 S-Mediated Entry into Host Cells

(A and B) Sequence conservation of sarbecovirus S glycoproteins plotted on the SARS-CoV-2 S structure viewed from the side (A) and top (B). The sequence alignment was generated using 48 SARS-CoV-2 S sequences obtained from GISAID in addition to the sequences listed in Data S1.

(C) Entry of SARS-CoV-2 S-MLV and SARS-CoV S-MLV is potently inhibited by four SARS-CoV S mouse polyclonal immune plasma.

CORONAVIRUS

Science 367: 1260-1263, 2020

Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation

Daniel Wrapp[1]*, Nianshuang Wang[1]*, Kizzmekia S. Corbett[2], Jory A. Goldsmith[1], Ching-Lin Hsieh[1], Olubukola Abiona[2], Barney S. Graham[2], Jason S. McLellan[1]†

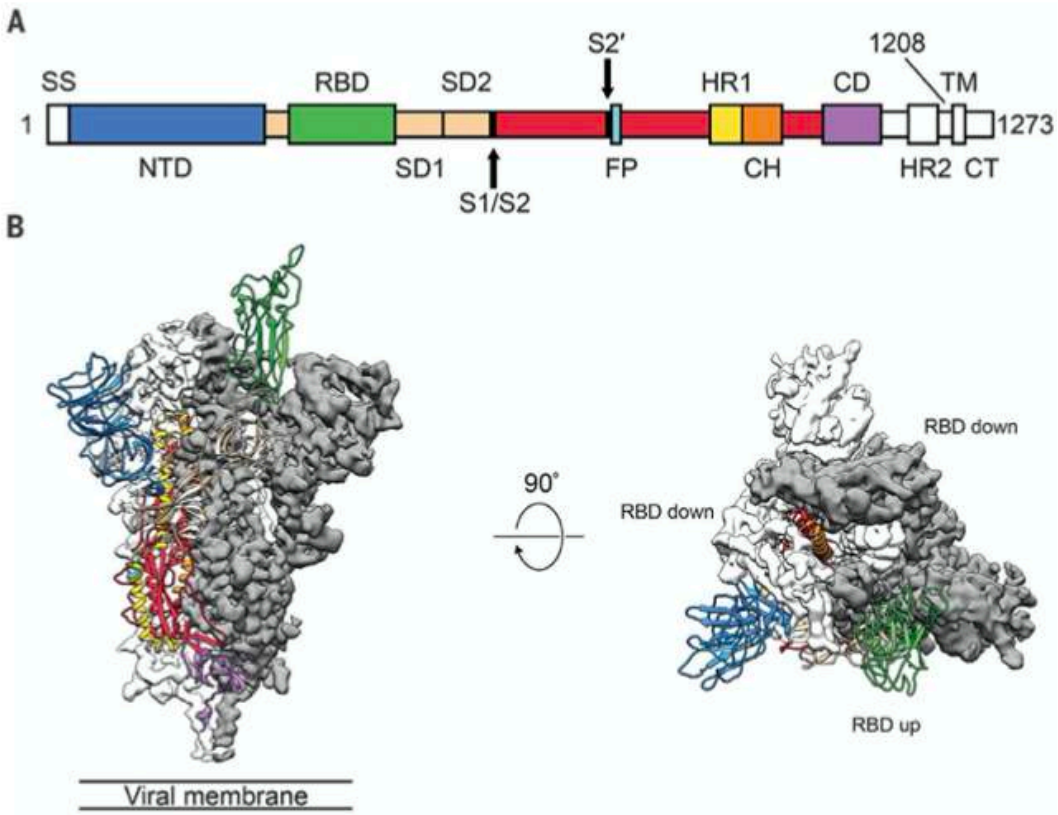


Fig. 1. Structure of 2019-nCoV S in the prefusion conformation. (**A**) Schematic of 2019-nCoV S primary structure colored by domain. Domains that were excluded from the ectodomain expression construct or could not be visualized in the final map are colored white. SS, signal sequence; S2′, S2′ protease cleavage site; FP, fusion peptide; HR1, heptad repeat 1; CH, central helix; CD, connector domain; HR2, heptad repeat 2; TM, transmembrane domain; CT, cytoplasmic tail. Arrows denote protease cleavage sites. (**B**) Side and top views of the prefusion structure of the 2019-nCoV S protein with a single RBD in the up conformation. The two RBD down protomers are showr as cryo-EM density in either white or gray and the RBD up protomer is shown in ribbons colored corresponding to the schematic in (A).

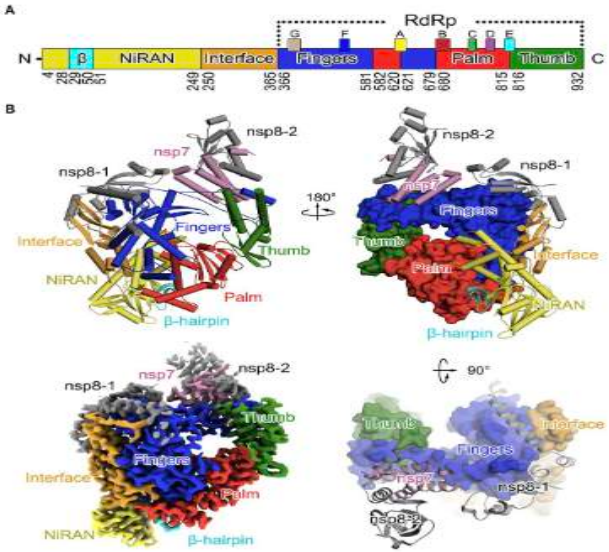
Science

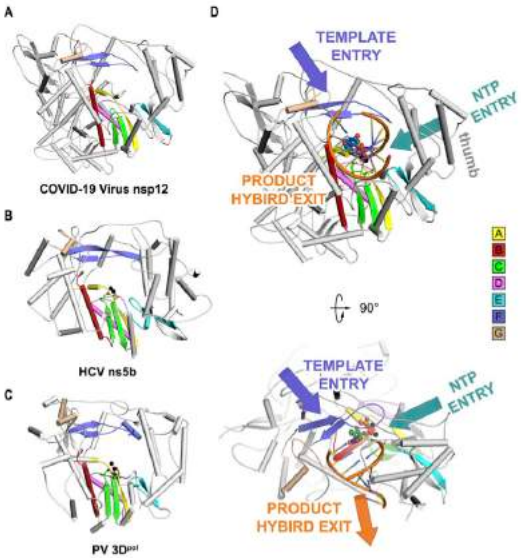
REPORTS

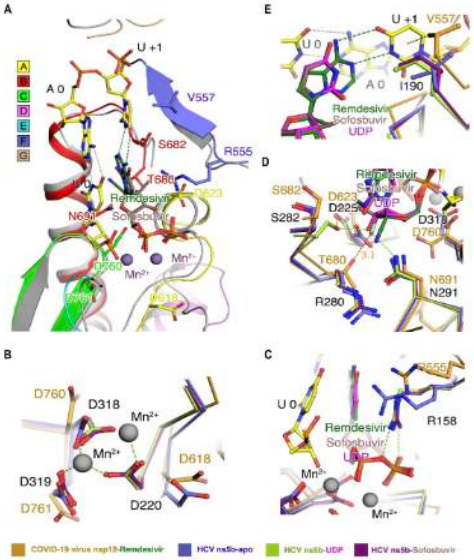
Cite as: Y. Gao *et al.*, *Science* 10.1126/science.abb7498 (2020).

Structure of the RNA-dependent RNA polymerase from COVID-19 virus

Yan Gao[1,2]*, Liming Yan[1]*, Yucen Huang[1]*, Fengjiang Liu[2]*, Yao Zhao[2], Lin Cao[3], Tao Wang[1], Qianqian Sun[2], Zhenhua Ming[4], Lianqi Zhang[1], Ji Ge[1], Litao Zheng[1], Ying Zhang[1], Haofeng Wang[2,5], Yan Zhu[2], Chen Zhu[2], Tianyu Hu[2], Tian Hua[2], Bing Zhang[2], Xiuna Yang[2], Jun Li[2], Haitao Yang[2], Zhijie Liu[2], Wenqing Xu[2], Luke W. Guddat[6], Quan Wang[2]†, Zhiyong Lou[1]†, Zihe Rao[1,2,3,7]†







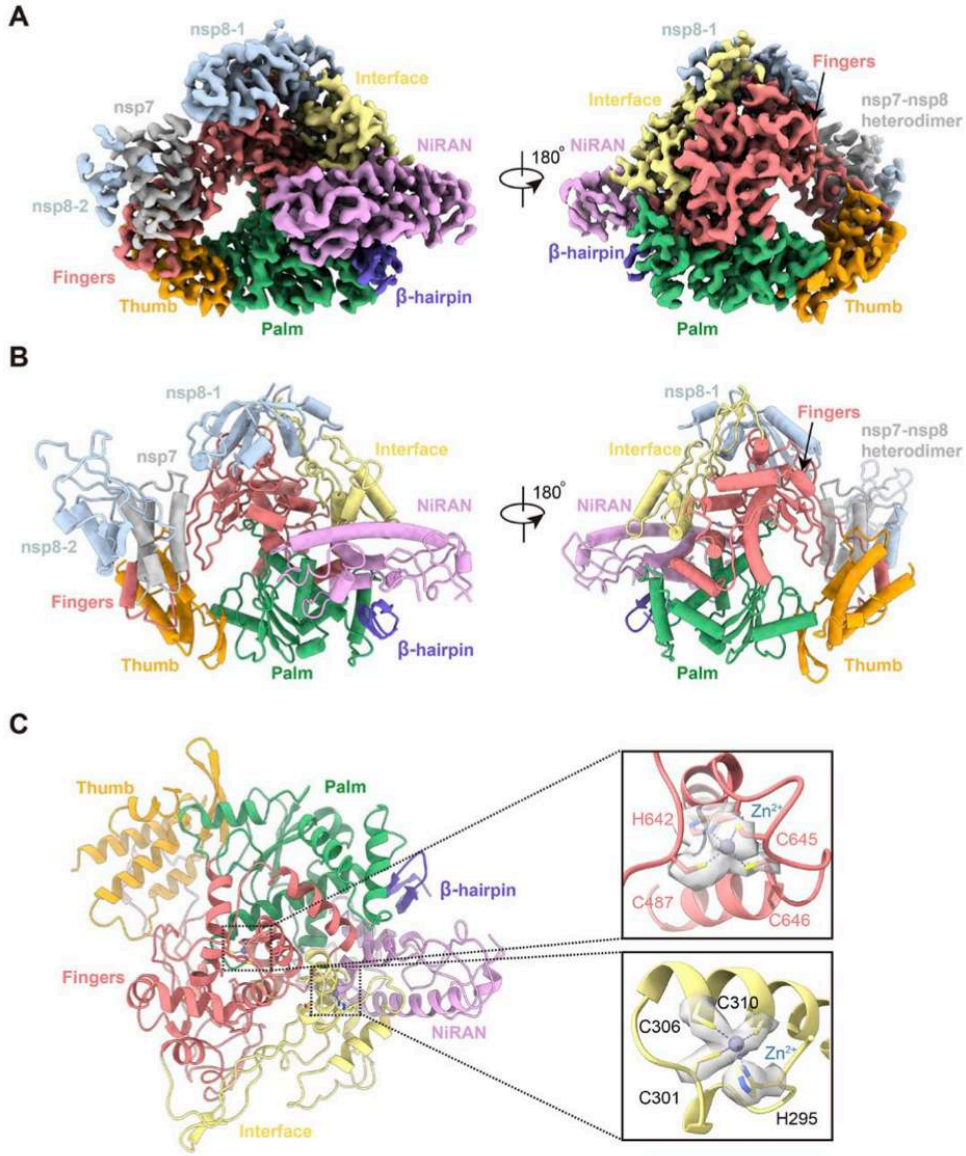


Fig. 2. Cryo-EM Structure of the apo nsp12-nsp-7-nsp8 RdRp complex. (A and B) Two views of cryo-EM map (A) and structure (B) of the apo nsp12-nsp7-nsp8 complex. The color scheme is according to Fig. 1A and is used throughout the paper. (C) The conserved zinc binding motifs are highlighted in the apo structure rendered in ribbon. The coordinate details of the zinc-binding residues are shown in stick with the EM map in gray surface.

Cite as: W. Yin *et al.*, *Science*
10.1126/science.abc1560 (2020).

Structural basis for inhibition of the RNA-dependent RNA polymerase from SARS-CoV-2 by remdesivir

Wanchao Yin[1,2*], Chunyou Mao[2*], Xiaodong Luan[3,4,5*], Dan-Dan Shen[2*], Qingya Shen[2*], Haixia Su[1,6*], Xiaoxi Wang[1], Fulai Zhou[1], Wenfeng Zhao[1], Minqi Gao[7], Shenghai Chang[8,9], Yuan-Chao Xie[1], Guanghui Tian[1], He-Wei Jiang[10], Sheng-Ce Tao[10], Jingshan Shen[1,6], Yi Jiang[1,6], Hualiang Jiang[1,6], Yechun Xu[1,6]†, Shuyang Zhang[4,5,3]†, Yan Zhang[2,11]†, H. Eric Xu[1,6]†

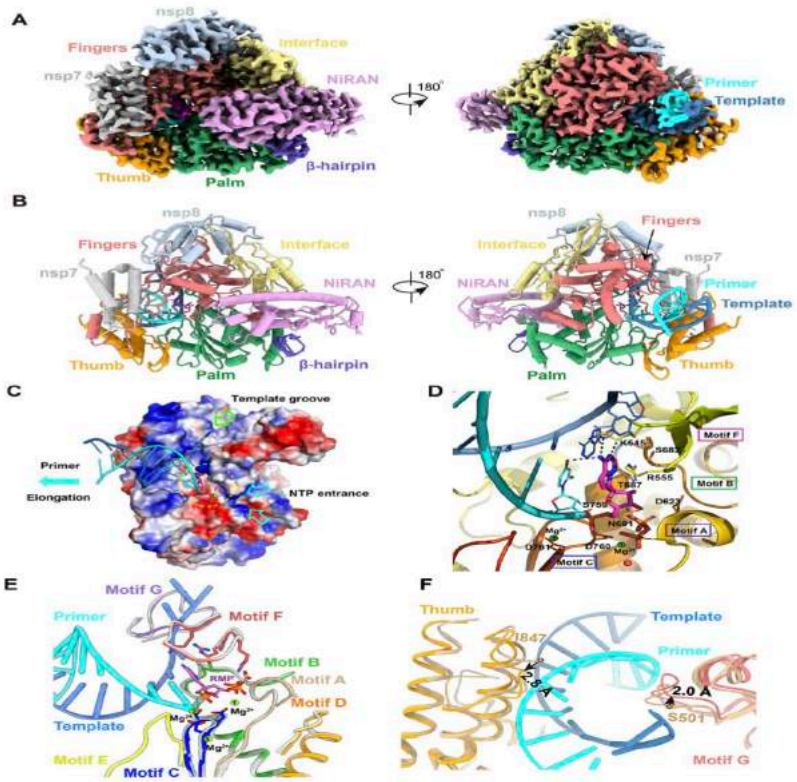
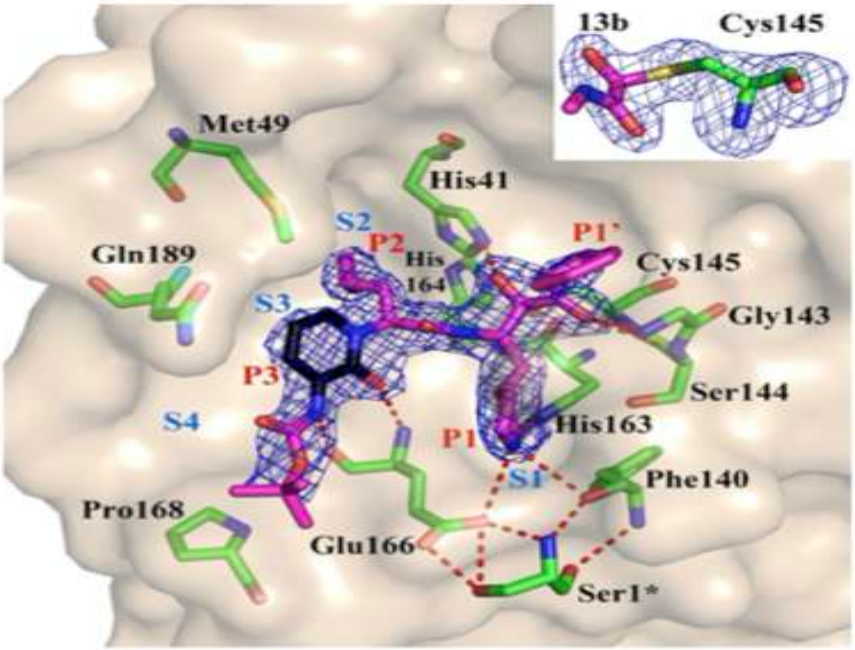


Fig. 3. Cryo-EM Structure of the Remdesivir and RNA bound RdRp complex. (A and B)

Cite as: L. Zhang *et al.*, *Science*
10.1126/science.abb3405 (2020).

Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved α-ketoamide inhibitors

Linlin Zhang[1,2], Daizong Lin[1,3], Xinyuanyuan Sun[1,2], Ute Curth[4], Christian Drosten[5], Lucie Sauerhering[6,7], Stephan Becker[6,7], Katharina Rox[8,9], Rolf Hilgenfeld[1,2]*



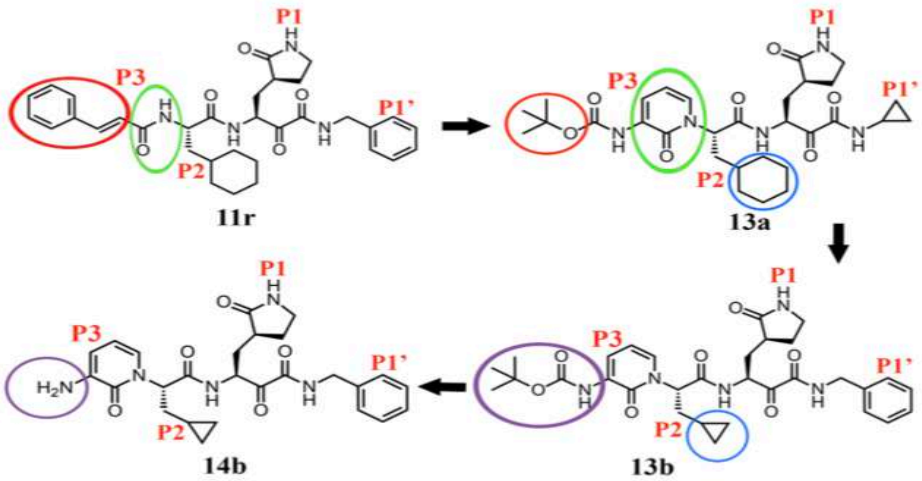


Fig. 1. Chemical structures of α-ketoamide inhibitors 11r, 13a, 13b, and 14b. Colored circles highlight the modifications from one development step to the next (see text).

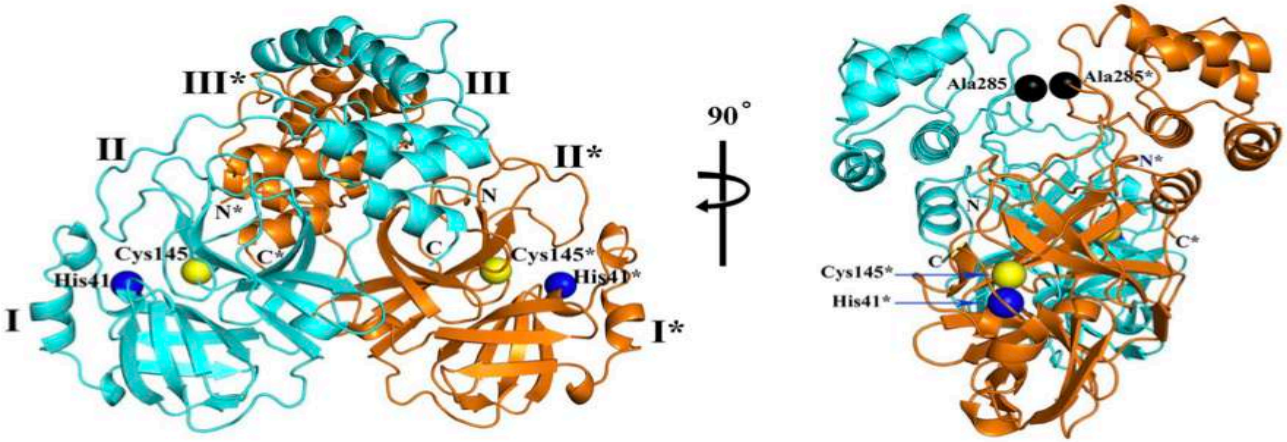


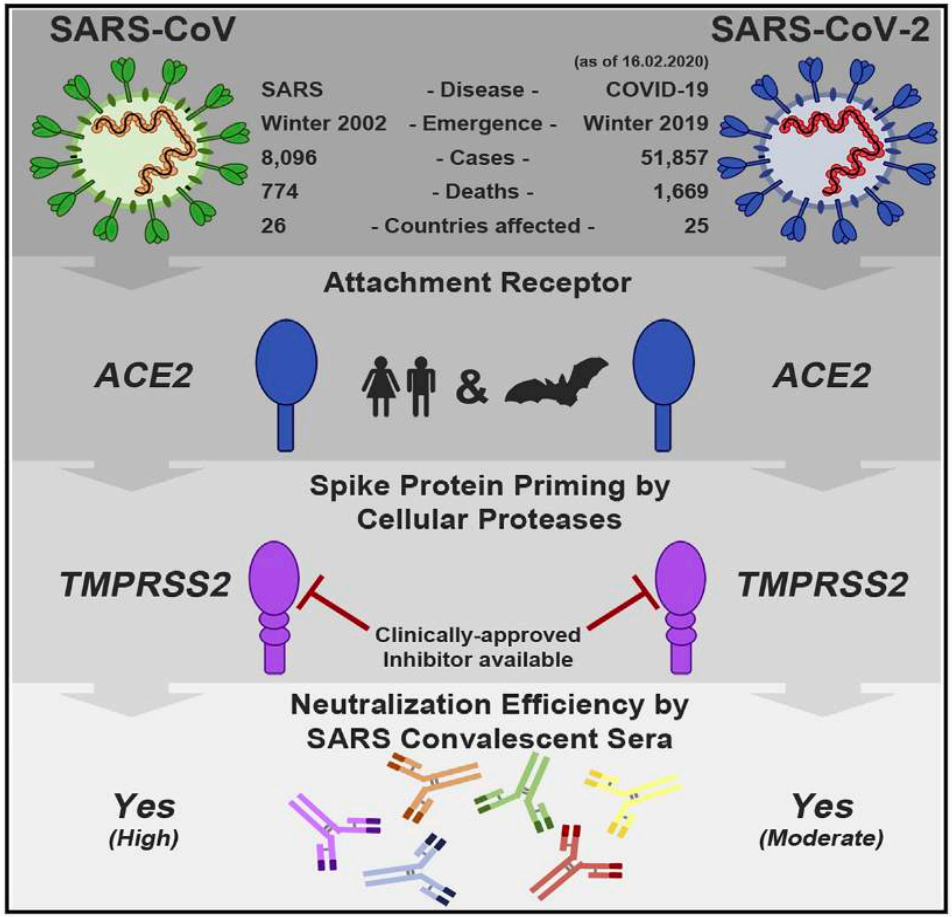
Fig. 2. Three-dimensional structure of SARS-CoV-2 M^{pro}, in two different views. One protomer of the dimer is shown in light blue, the other one in orange. Domains are labeled by Roman numbers. Amino-acid residues of the catalytic site are indicated as yellow and blue spheres, for Cys^{145} and His^{41}, respectively. (An asterisk marks a residue from protomer B (orange)). Black spheres indicate the positions of Ala^{285} of each of the two domains III (see text). Chain termini are labeled N and C for molecule A (light blue) and N* and C* for molecule B (orange).

Article

Cell

SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor

Graphical Abstract



Authors

Markus Hoffmann, Hannah Kleine-Weber, Simon Schroeder, ..., Marcel A. Müller, Christian Drosten, Stefan Pöhlmann

Correspondence

mhoffmann@dpz.eu (M.H.),
spoehlmann@dpz.eu (S.P.)

In Brief

The emerging SARS-coronavirus 2 (SARS-CoV-2) threatens public health. Hoffmann and coworkers show that SARS-CoV-2 infection depends on the host cell factors ACE2 and TMPRSS2 and can be blocked by a clinically proven protease inhibitor. These findings might help to establish options for prevention and treatment.

Please cite this article in press as: Hirano and Murakami, COVID-19: A New Virus, but a Familiar Receptor and Cytokine Release Syndrome, Immunity (2020), https://doi.org/10.1016/j.immuni.2020.04.003

Immunity
Preview

CellPress

COVID-19: A New Virus, but a Familiar Receptor and Cytokine Release Syndrome

Toshio Hirano[1,2,*] and Masaaki Murakami[2]
[1]Headquarters, National Institutes for Quantum and Radiological Science and Technology, Chiba, 263-8555, Japan
[2]Division of Molecular Psychoimmunology, Institute for Genetic Medicine and Graduate School of Medicine, Hokkaido University, Sapporo 060-0815, Japan
*Correspondence: hirano.toshio@qst.go.jp
https://doi.org/10.1016/j.immuni.2020.04.003

Zhou et al. (*Nature*) and Hoffmann et al. (*Cell*) identify ACE2 as a SARS-CoV-2 receptor, and the latter show its entry mechanism depends on cellular serine protease TMPRSS2. These results may explain proinflammatory cytokine release via the associated angiotestin II pathway and a possible therapeutic target via the IL-6-STAT3 axis.

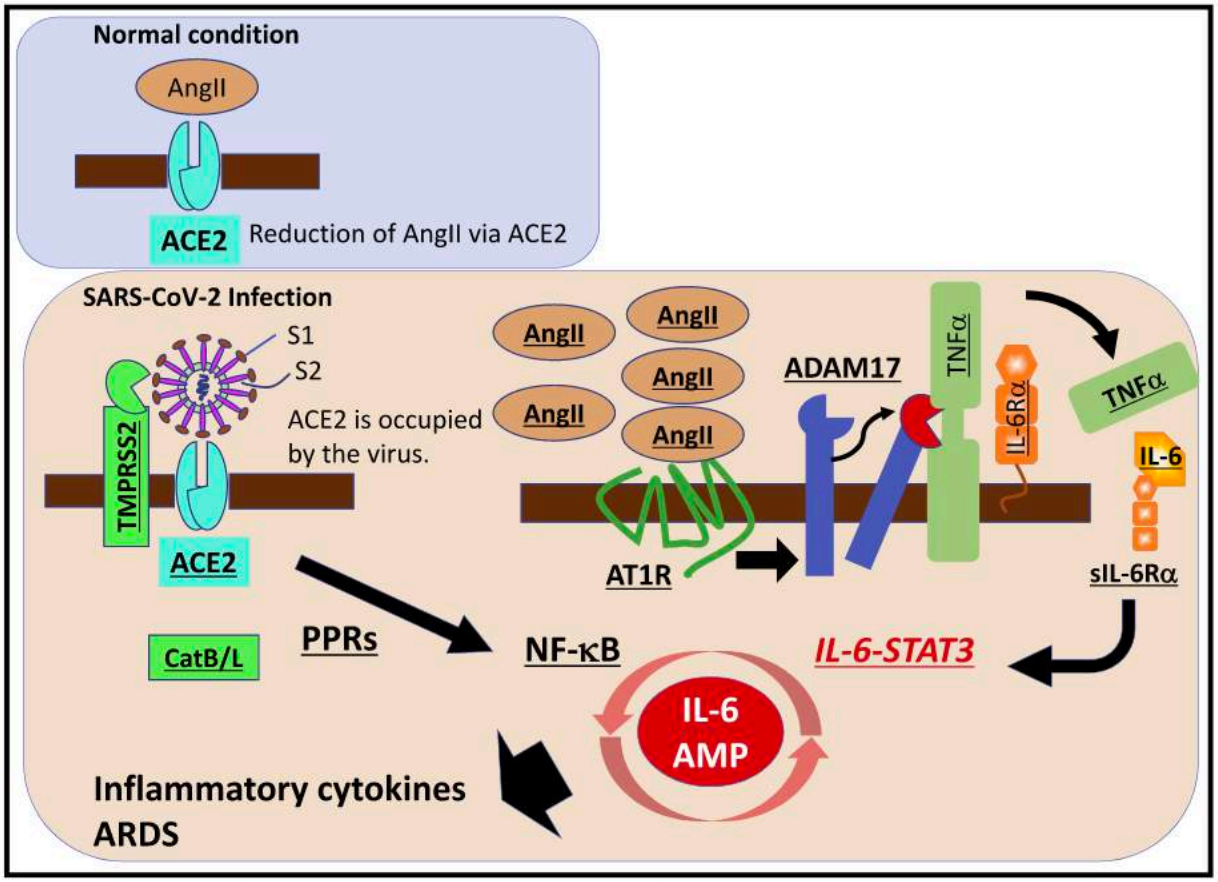


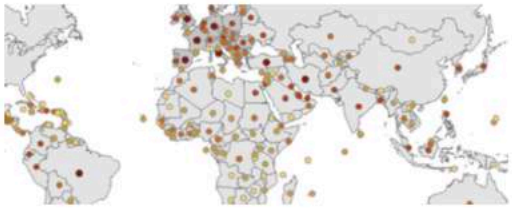
Figure 1. Possible therapeutic targets for COVID-19, a cytokine release syndrome.
SARS-CoV-2 uses angiotensin converting enzyme II (ACE2) and transmembrane serine protease 2 (TMPRSS2) as cell entry receptors, followed by a cytokine-related syndrome, ARDS, which is induced by the hyper-activation of the transcription factor NF-κB, most likely in nonimmune cells including lung epithelial cells. ACE2 molecules on the cell surface are occupied by SARS-CoV-2. Angiotensin 2 (AngII) then increases in the serum due to a reduction of ACE2-mediated degradation. SARS-CoV-2 itself activates NF-κB via pattern recognition receptors (PPRs), and the accumulated AngII induces inflammatory cytokines including TNFα and IL-6-soluble (s)IL-6R via disintegrin and metalloprotease 17 (ADAM17), followed by activation of the IL-6 amplifier (IL-6 AMP), which describes enhanced NF-κB activation machinery via the coactivation of NF-κB and transcription factor STAT3. The molecules underlined indicate possible therapeutic targets for COVID-19, which is a cytokine release syndrome (CRS).

Situation update 29 May 2020, dataset collected 6:00-10:00 CET

5 776 934 cases Worldwide

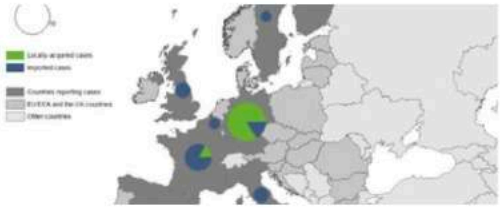
360 089 deaths Whereof 163 515 deaths in the EU/EEA and UK

1 384 703 cases in the EU/EEA and the UK.



Interactive situation dashboard

Interactive map with the latest available data on COVID-19 >



Situation update for the EU/EEA and the UK

Situation update, map and case count >

Situation update worldwide

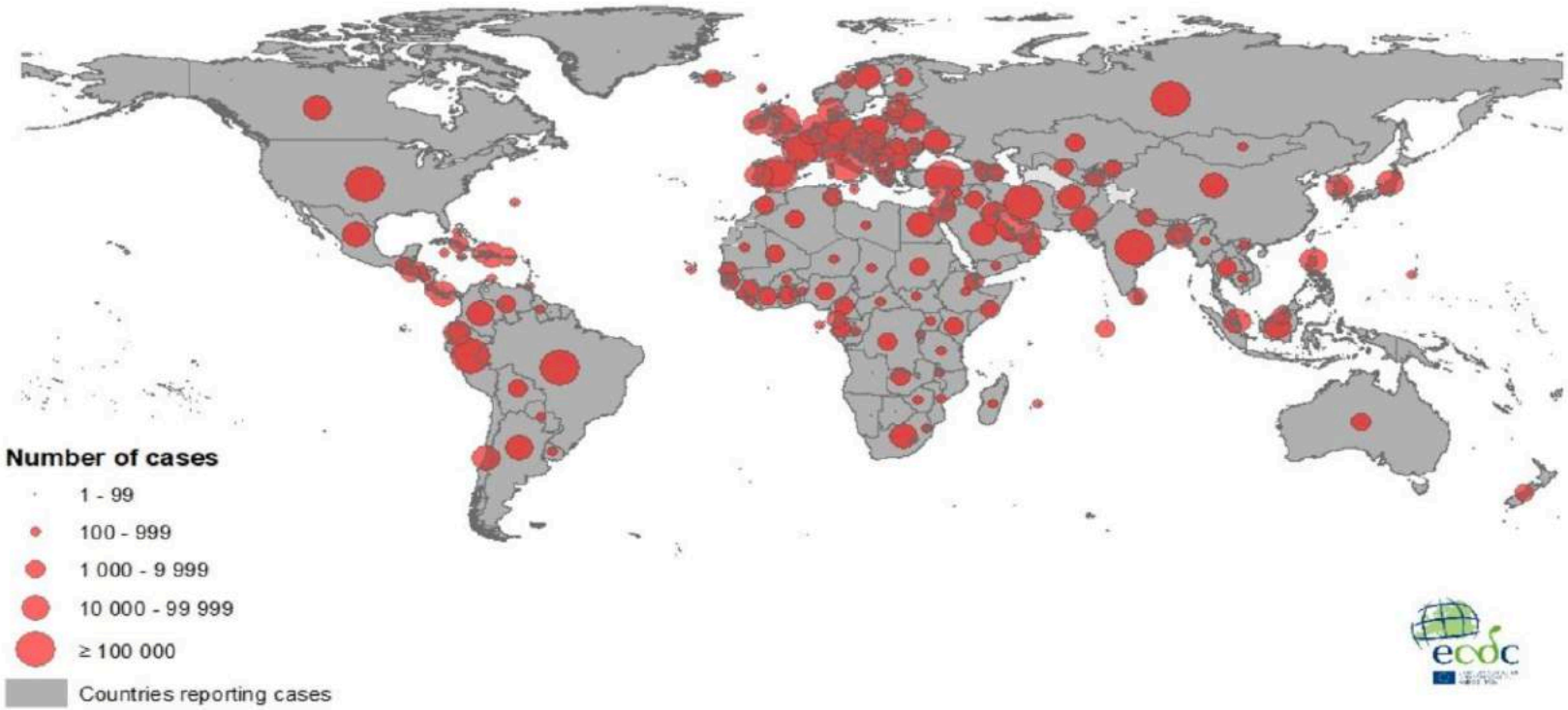
Situation update, map and case count >

Geographic distribution of COVID-19 in the EU/EEA and the UK, as of 29 May 2020

Date of production: 29/05/2020

The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union.

Geographic distribution of COVID-19 cases worldwide, as of 29 May 2020

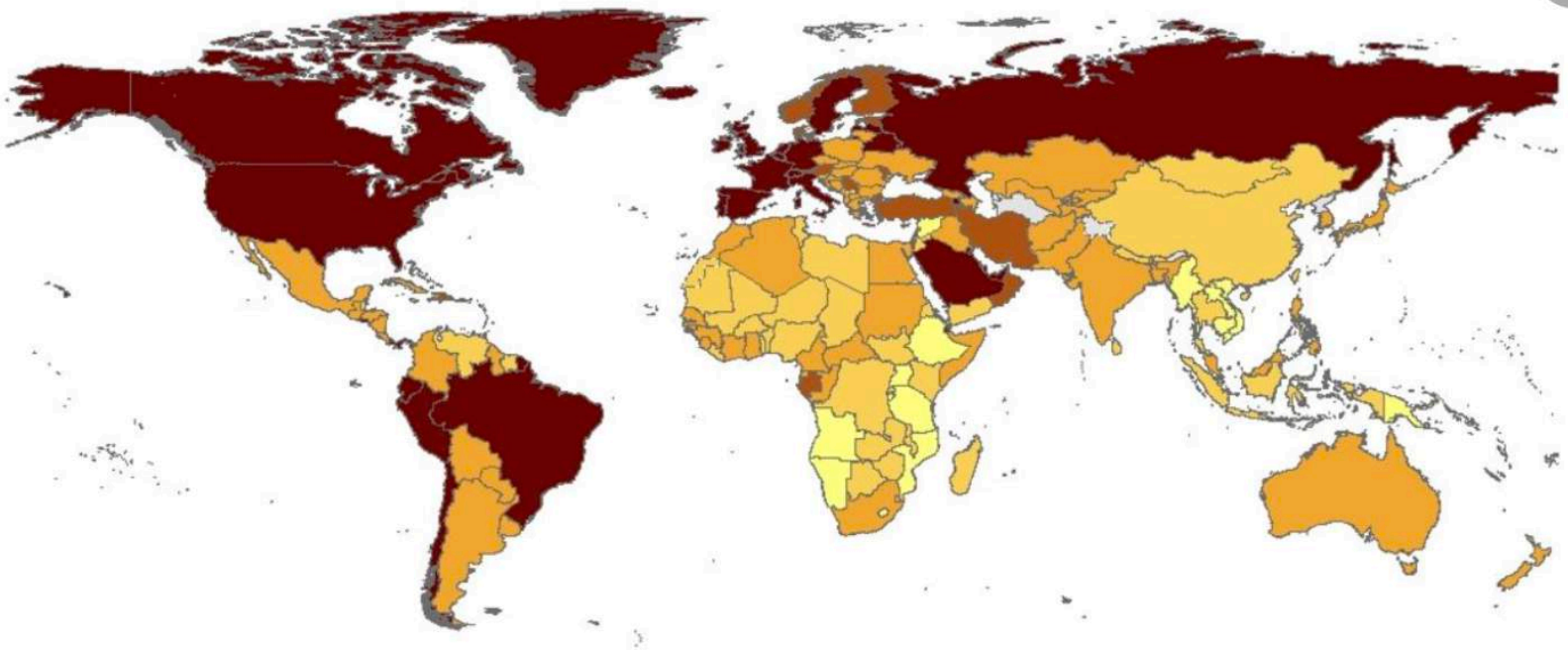


Date of production: 29/05/2020

The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union.

Geographical distribution of COVID-19 cases - worldwide

Geographic distribution of cumulative number of reported COVID-19 cases per 100 000 population, worldwide, as of 29 May 2020



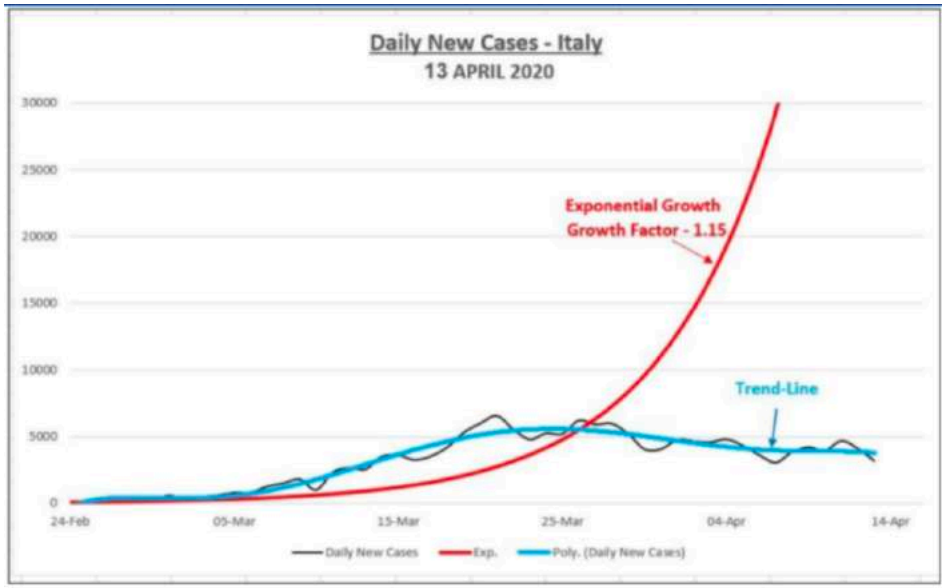
Cumulative number of reported COVID-19 cases per 100 000

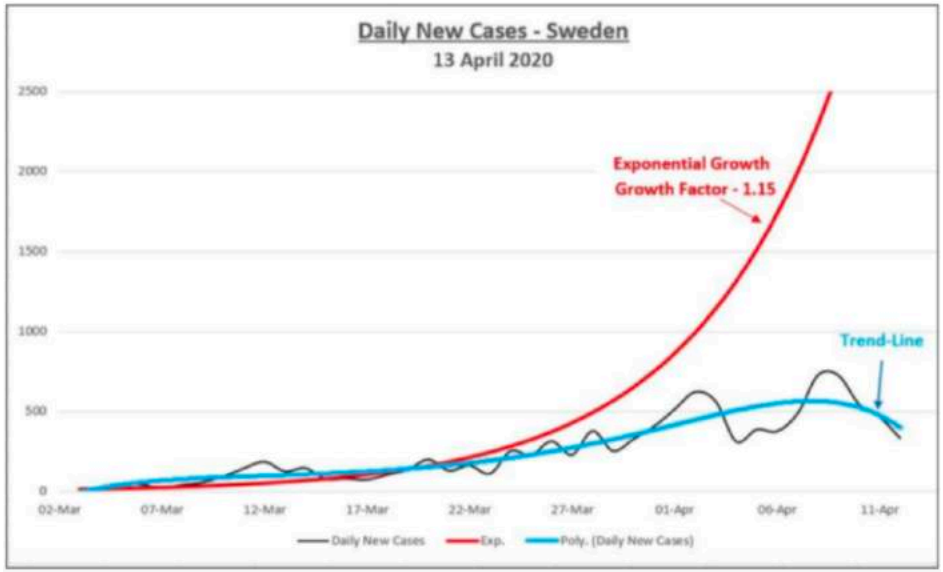
- < 1.0
- 1.0 - 9.9
- 10.0 - 99.9
- 100.0 - 199.9
- ≥ 200.0
- Countries and territories without cases reported

Date of production: 29/05/2020

The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union.

Geographic distribution of cumulative number of reported COVID-19 cases per 100 000 population, worldwide


Daily New Cases - Italy
13 APRIL 2020
30000
25000
20000
15000
10000
5000
0
24-Feb
05-Mar
15-Mar
25-Mar
04-Apr
14-Apr
Exponential Growth
Growth Factor - 1.15
Trend-Line
Daily New Cases
Exp.
Poly. (Daily New Cases)


Daily New Cases - Sweden
13 April 2020
2500
2000
1500
1000
500
0
02-Mar
07-Mar
12-Mar
17-Mar
22-Mar
27-Mar
01-Apr
06-Apr
11-Apr
Exponential Growth
Growth Factor - 1.15
Trend-Line
Daily New Cases
Exp.
Poly. (Daily New Cases)

RESEARCH

Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR

Victor M Corman[1], Olfert Landt[2], Marco Kaiser[2], Richard Molenkamp[3], Adam Meijer[4], Daniel KW Chu[5], Tobias Bleicker[1], Sebastian Brünink[1], Julia Schneider[1], Marie Luisa Schmidt[1], Daphne GJC Mulders[3], Bart L Haagmans[3], Bas van der Veer[4], Sharon van den Brink[4], Lisa Wijsman[4], Gabriel Goderski[4], Jean-Louis Romette[6], Joanna Ellis[7], Maria Zambon[7], Malik Peiris[5], Herman Goossens[8], Chantal Reusken[4], Marion PG Koopmans[3], Christian Drosten[1]

1. Charité – Universitätsmedizin Berlin Institute of Virology, Berlin, Germany and German Centre for Infection Research (DZIF), Berlin, Germany
2. Tib-Molbiol, Berlin, Germany
3. Department of Viroscience, Erasmus MC, Rotterdam, the Netherlands
4. National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
5. University of Hong Kong, Hong Kong, China
6. Universite d Aix-Marseille, Marseille, France
7. Public Health England, London, United Kingdom
8. Department of Medical Microbiology, Vaccine and Infectious Diseases Institute, University of Antwerp, Antwerp, Belgium

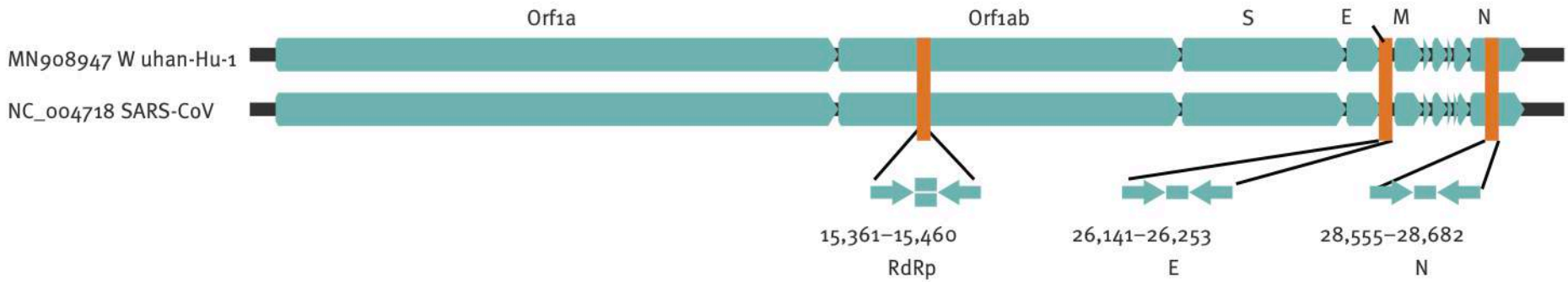
Correspondence: Christian Drosten (christian.drosten@charite.de)

Citation style for this article:
Corman Victor M, Landt Olfert, Kaiser Marco, Molenkamp Richard, Meijer Adam, Chu Daniel KW, Bleicker Tobias, Brünink Sebastian, Schneider Julia, Schmidt Marie Luisa, Mulders Daphne GJC, Haagmans Bart L, van der Veer Bas, van den Brink Sharon, Wijsman Lisa, Goderski Gabriel, Romette Jean-Louis, Ellis Joanna, Zambon Maria, Peiris Malik, Goossens Herman, Reusken Chantal, Koopmans Marion PG, Drosten Christian. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020;25(3):pii=2000045. https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045

Article submitted on 21 Jan 2020 / accepted on 22 Jan 2020 / published on 23 Jan 2020

FIGURE 1

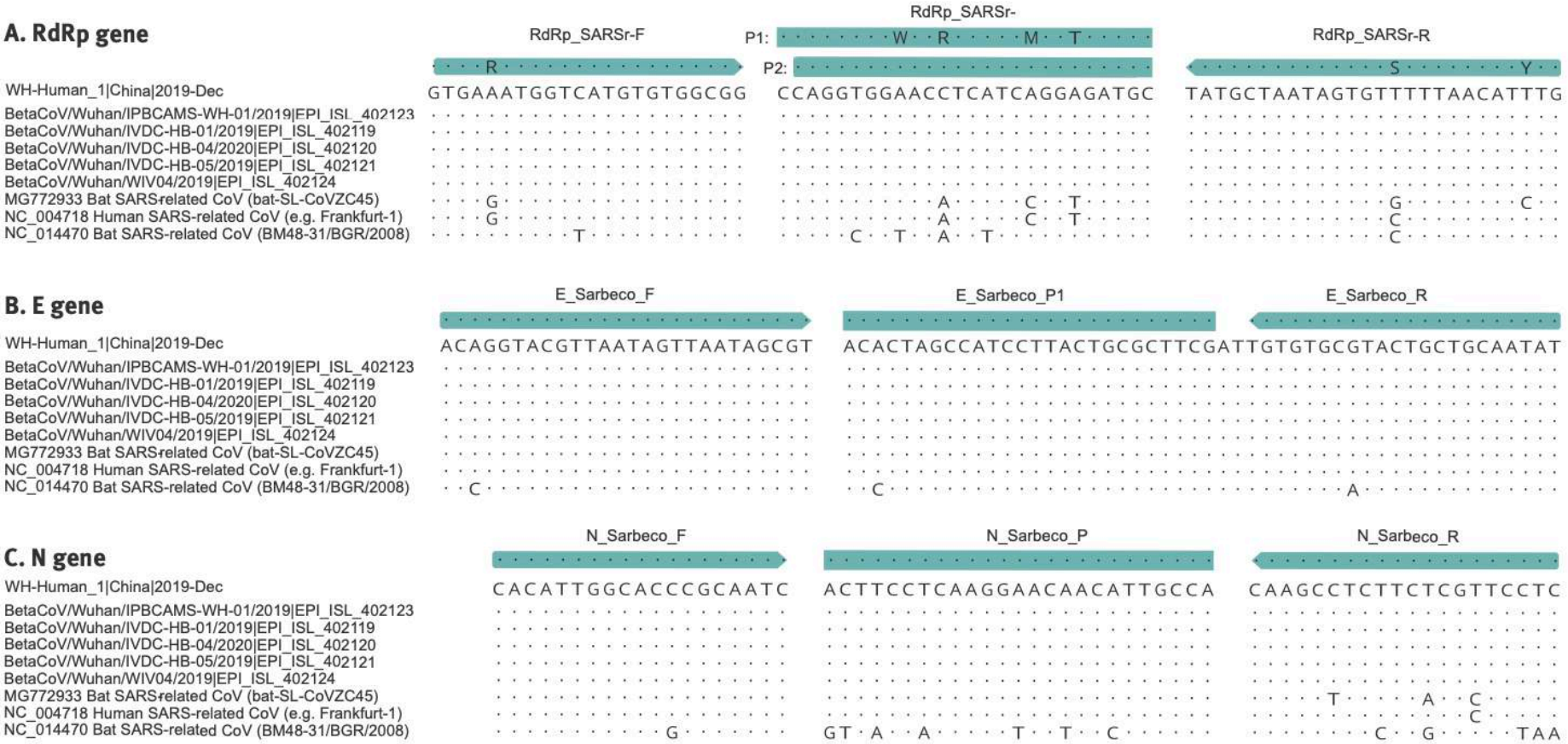
Relative positions of amplicon targets on the SARS coronavirus and the 2019 novel coronavirus genome



E: envelope protein gene; M: membrane protein gene; N: nucleocapsid protein gene; ORF: open reading frame; RdRp: RNA-dependent RNA polymerase gene; S: spike protein gene.

FIGURE 2

Partial alignments of oligonucleotide binding regions, SARS-related coronaviruses (n = 9)



Science

PERSPECTIVES

Cite as: F. Krammer, V. Simon, *Science* 10.1126/science.abc1227 (2020).

Serology assays to manage COVID-19

Florian Krammer[1] and Viviana Simon[1,2,3]

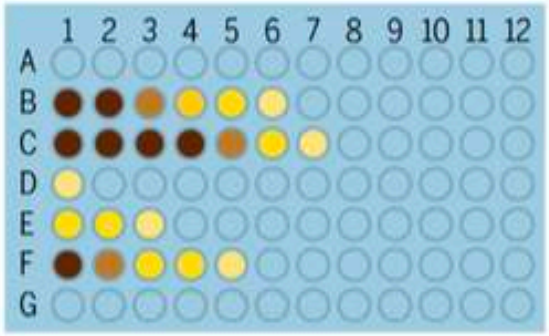
[1]Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [2]Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [3]Global Health Emerging Pathogens Institute, Icahn School of Medicine at Mount Sinai, NY, USA. Email: florian.krammer@mssm.edu; viviana.simon@mssm.edu

Measurement of antibodies to SARS-CoV-2 will improve disease management if used correctly

Quantitative and binary readouts in serology assays

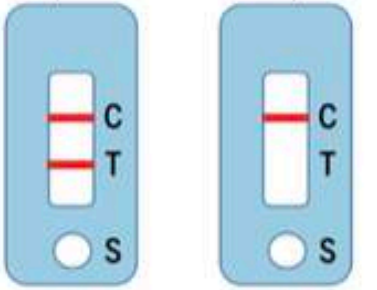
Quantitative and binary serology tests can provide important information about infection.

Quantitative assays [e.g., enzyme-linked immunosorbent assay (ELISA)]



Titers	Protected?
Negative	No
Titer 1:12,150	Yes
Titer 1:36,450	Yes
Titer 1:50	No
Titer 1:450	No
Titer 1:4050	Yes
Negative	No

Assay with binary result (e.g., lateral flow assay)



Result	Quantitative titer	Yes or no
Linked to protection?	A quantitative titer can be linked to protection	A positive result can be loosely associated with protection
Could predict protection duration?	Yes	No
Scalability	Moderate	High
Ease of use	Performed in specialized laboratories	Easy to use, even as point-of-care test

Antigens: Who is using what?

	Nucleocapsid	"Spike"	S1	S2
DiaSorin			✓	✓
Roche	✓			
Abbott	✓			
OCD		✓		
Euroimmun			✓	
Bio-Rad	✓			
Snibe	?	?		

Information on Siemens and Beckman pending

SARS-CoV-2 seroprevalence in Veneto Region

M. Plebani, A. Padoan…..& G. Palù (submitted)

Table 1: Structures in which Healthcare workers were enrolled, total number and percentages of positive tests with 95% confidence intervals (CI).

	Total number of tests	Percentage (%) of positive tests	95% CI of the percentage
University-Hospital of Padova	3246	3.4%	2.8-4.0%
Hospital S. Antony of Padova	446	2.7%	1.4%-4.7%
Istituto Oncologico Veneto, Unit of Padova	649	4.9%	3.4-6.9%
Istituto Oncologico Veneto, Unit of Castelfranco	307	2.6%	1.1%-5.7%
University-Hospital of Verona	2984	6.1%	5.3%-7.0%
Hospital of Vicenza	608	5.6%	3.9%-7.7%
Others hospitals	45	2.2%	0.1-11.8%

Table 2: Total number and percentages of positive tests with 95% confidence intervals (CI), subdivided by age classes.

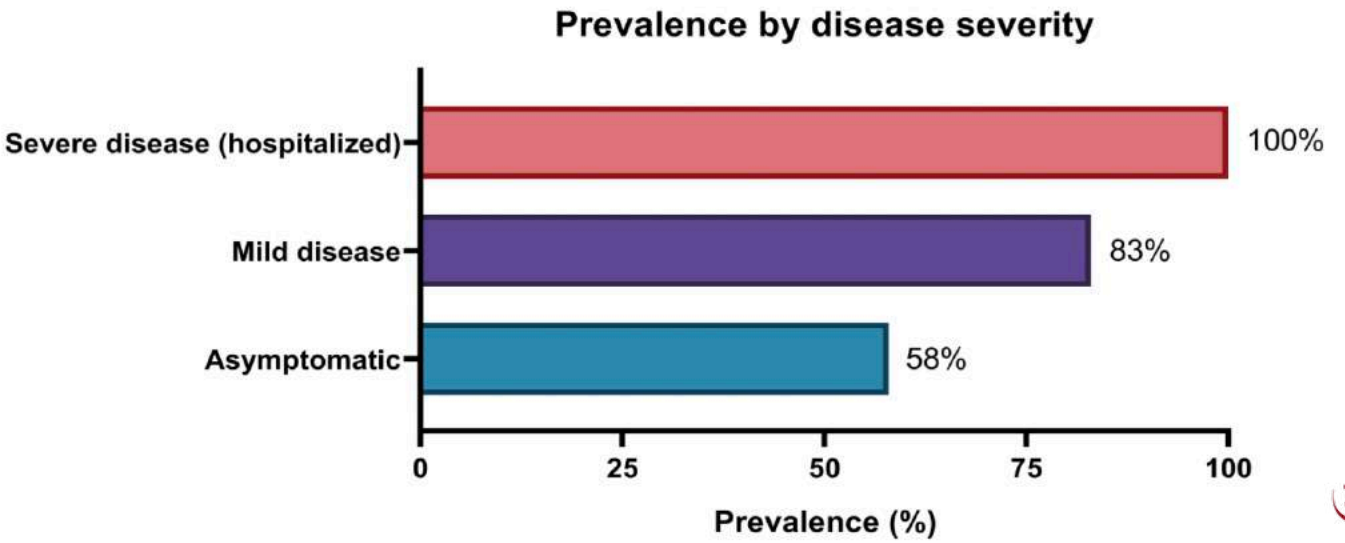
Age classes (yrs)	Total number of tests	Percentage (%) of positive tests	Percentage 95% CI
< 30 yrs	1512	4.1%	3.2-5.2%
30-39 yrs	1826	3.5%	2.7%-4.4%
40-49 yrs	1962	4.4%	3.6%-5.4%
50-59 yrs	2389	6.0%	5.1%-7.1%
> 60 yrs	596	3.7%	2.3-5.5%

SARS-CoV-2 seroprevalence in Veneto Region

M. Plebani, A. Padoan…..& G. Palù (submitted)

Table 3: Total number and percentages of positive tests with 95% confidence intervals (CI), subdivided by the different health care figures

Healthcare figures	Total number of tests	Percentage (%) of positive tests	Percentage 95% CI
Physicians	2337	3.6%	2.8%-4.4%
Nurses	3230	4.7%	4.0-5.5%
Healthcare assistants	1040	6.0%	4.6%-7.6%
Others	1678	4.8%	3.8%5.9%



Current Drugs for the treatmnet of COVID-19

Targeting the pathogenic mechanism

inflammation: prednisone antiocox-2,IL6R tocilizumab;
singnaling: Jak/Stat ruxolitinib & tofacitinib;
coagulation:low mw heparin

Targeting the Host

late endosome + proteases:Hydroxichloroquine, Carmostat mesylate, Trasylol-aprotinine

Repurposed drugs

energy & ion metabolism: Niclosamide, Ivermectine

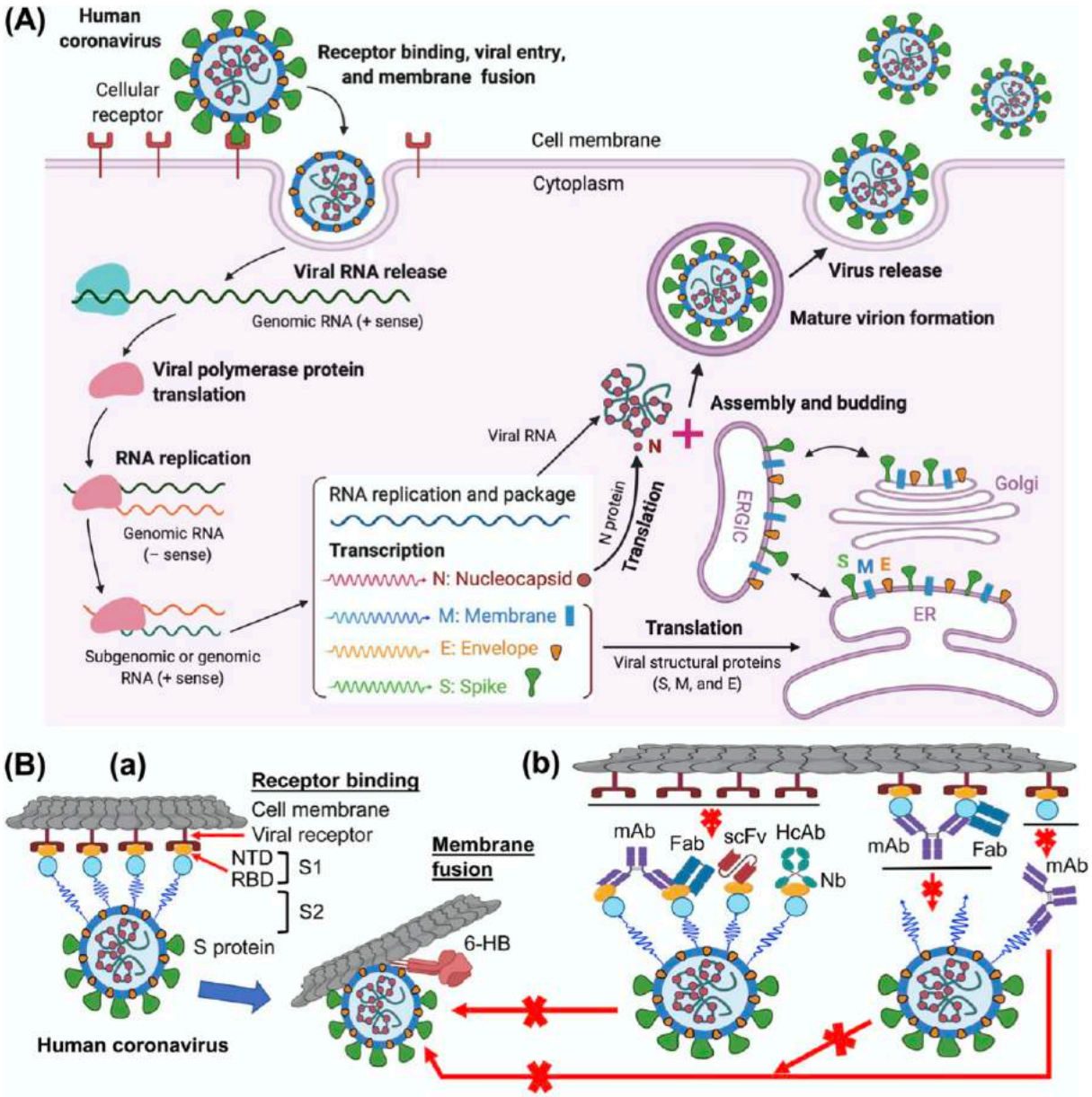
Antivirals (off label)

remdesivir, facvipiravir, arbidol/limifenovir, anti-HIV protease

Anti-SARS-CoV-2 drugs

a series of Mabs; structure-based: deoxycytidine analogues, antiprotease

CellPress
REVIEWS



ABOUT VACCINES AND PLATFORMS

1. Inactivated-killed (Chinese recepie)
2. Live-attenuated (?)
3. Recombinant protein-based
4. RNA-based (Moderna)
5. DNA-based (Inovio)
6. Vector-based (IRBM-Oxford)

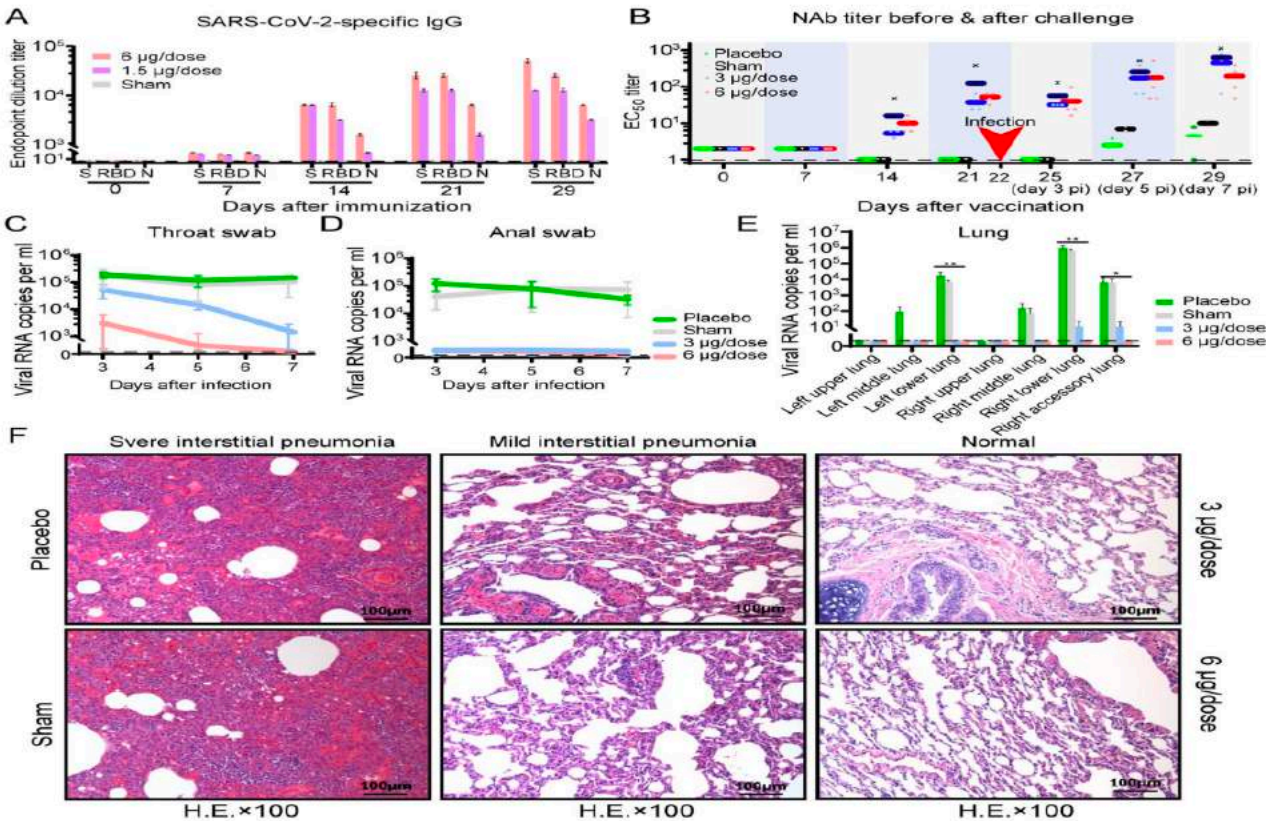
Science

REPORTS

Cite as: Q. Gao *et al.*, *Science* 10.1126/science.abc1932 (2020).

Development of an inactivated vaccine candidate for SARS-CoV-2

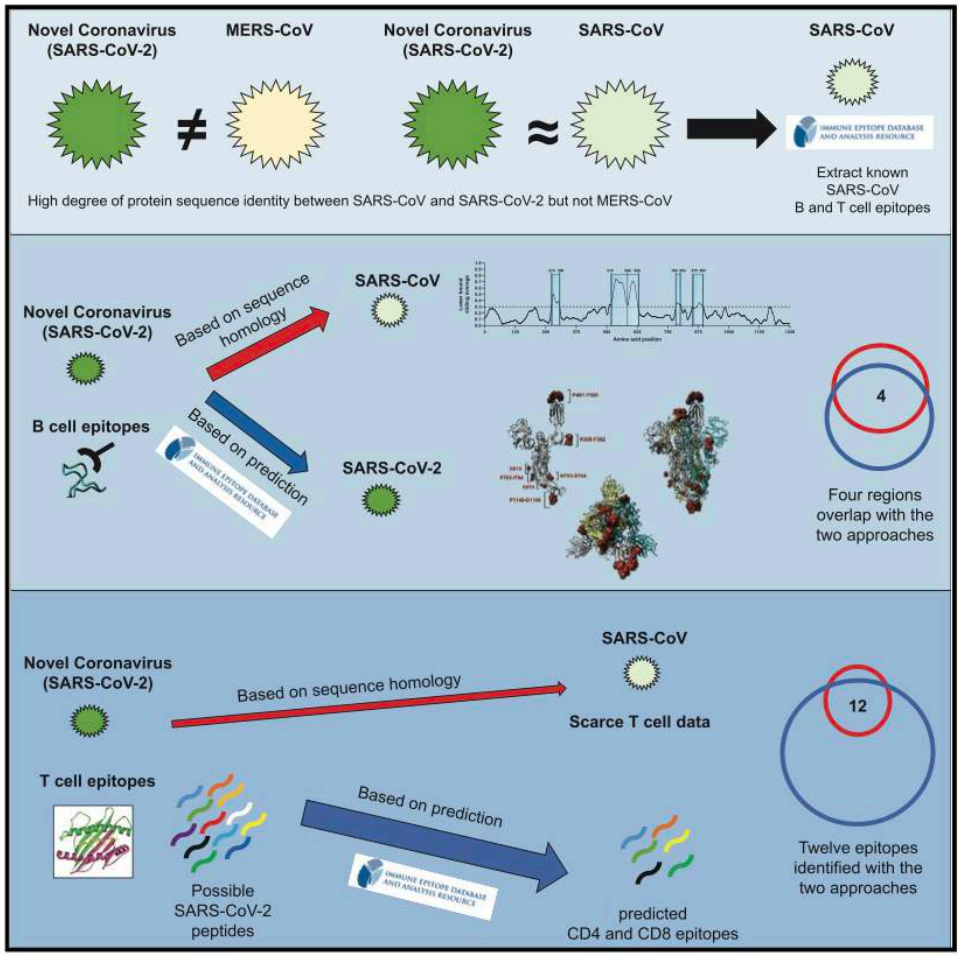
Qiang Gao[1]*, Linlin Bao[2]*, Haiyan Mao[3]*, Lin Wang[1]*, Kangwei Xu[4]*, Minnan Yang[5]*, Yajing Li[1], Ling Zhu[5], Nan Wang[5], Zhe Lv[5], Hong Gao[2], Xiaoqin Ge[1], Biao Kan[6], Yaling Hu[1], Jiangning Liu[2], Fang Cai[1], Deyu Jiang[1], Yanhui Yin[1], Chengfeng Qin[7], Jing Li[1], Xuejie Gong[1], Xiuyu Lou[3], Wen Shi[3], Dongdong Wu[1], Hengming Zhang[1], Lang Zhu[1], Wei Deng[2], Yurong Li[1], Jinxing Lu[6]†, Changgui Li[4]†, Xiangxi Wang[5]†, Weidong Yin[1]†, Yanjun Zhang[3]†, Chuan Qin[2]†



Cell Host & Microbe

A Sequence Homology and Bioinformatic Approach Can Predict Candidate Targets for Immune Responses to SARS-CoV-2

Graphical Abstract



Authors

Alba Grifoni, John Sidney, Yun Zhang, Richard H. Scheuermann, Bjoern Peters, Alessandro Sette

Correspondence

alex@lji.org

In Brief

Grifoni et al. identify potential targets for immune responses to the 2019 novel coronavirus (SARS-CoV-2) by sequence homology with closely related SARS-CoV and by *a priori* epitope prediction using bioinformatics approaches. This analysis provides essential information for understanding human immune responses to this virus and for evaluating diagnostic and vaccine candidates.

Immunity
CellPress

Report

Detection of SARS-CoV-2-Specific Humoral and Cellular Immunity in COVID-19 Convalescent Individuals

Ling Ni,[1,2,9] Fang Ye,[3,9] Meng-Li Cheng,[4,9] Yu Feng,[1] Yong-Qiang Deng,[4] Hui Zhao,[4] Peng Wei,[1] Jiwan Ge,[5] Mengting Gou,[1] Xiaoli Li,[1] Lin Sun,[1] Tianshu Cao,[4] Pengzhi Wang,[1] Chao Zhou,[4] Rongrong Zhang,[4] Peng Liang,[6] Han Guo,[7] Xinquan Wang,[5] Cheng-Feng Qin,[4,*] Fang Chen,[6,*] and Chen Dong[1,2,8,10,*]

Immunity
Report
CellPress

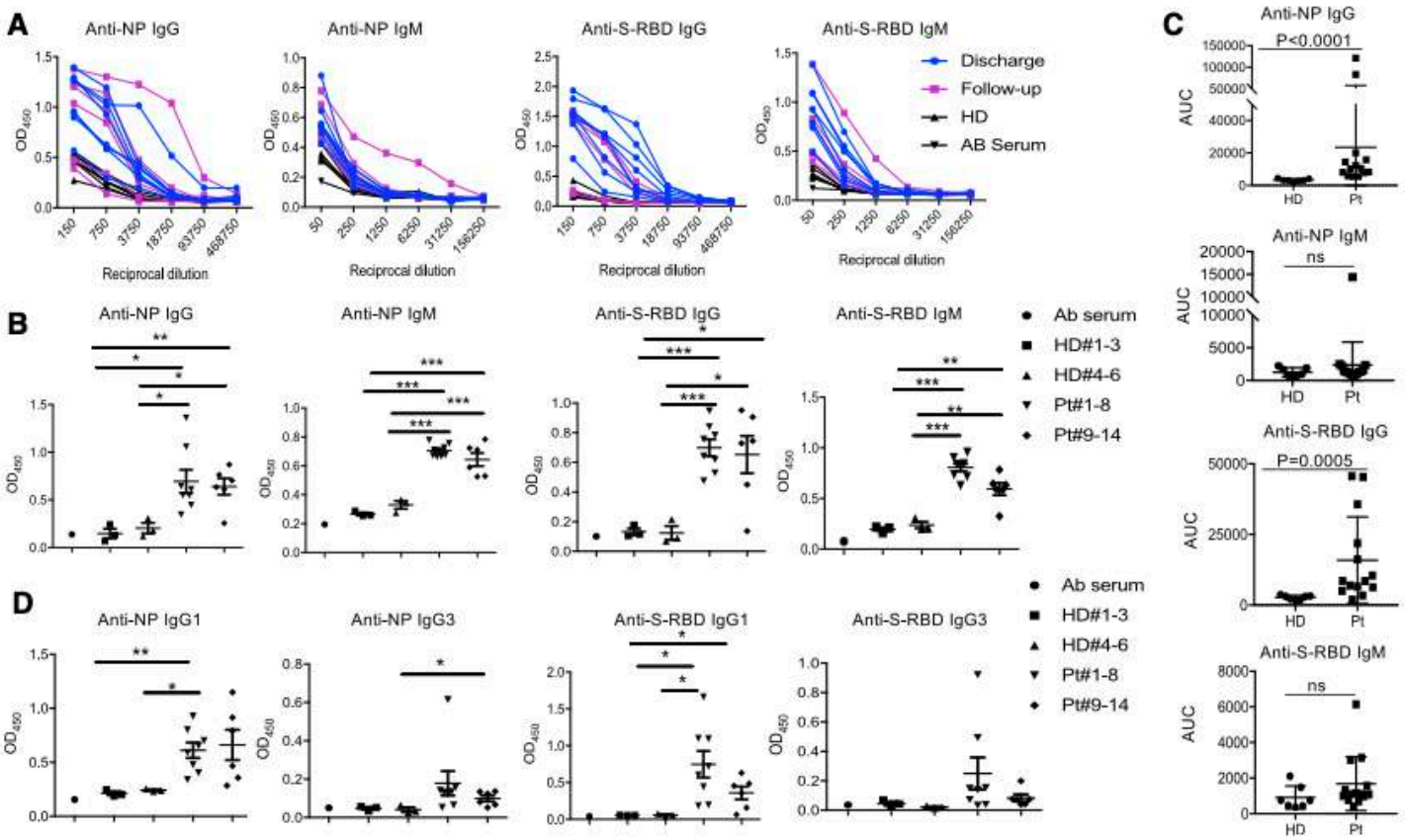


Figure 1. SARS-CoV-2 NP- and S-RBD-Specific Antibodies in COVID-19 Convalescent Individuals

Immunity
Report
CellPress

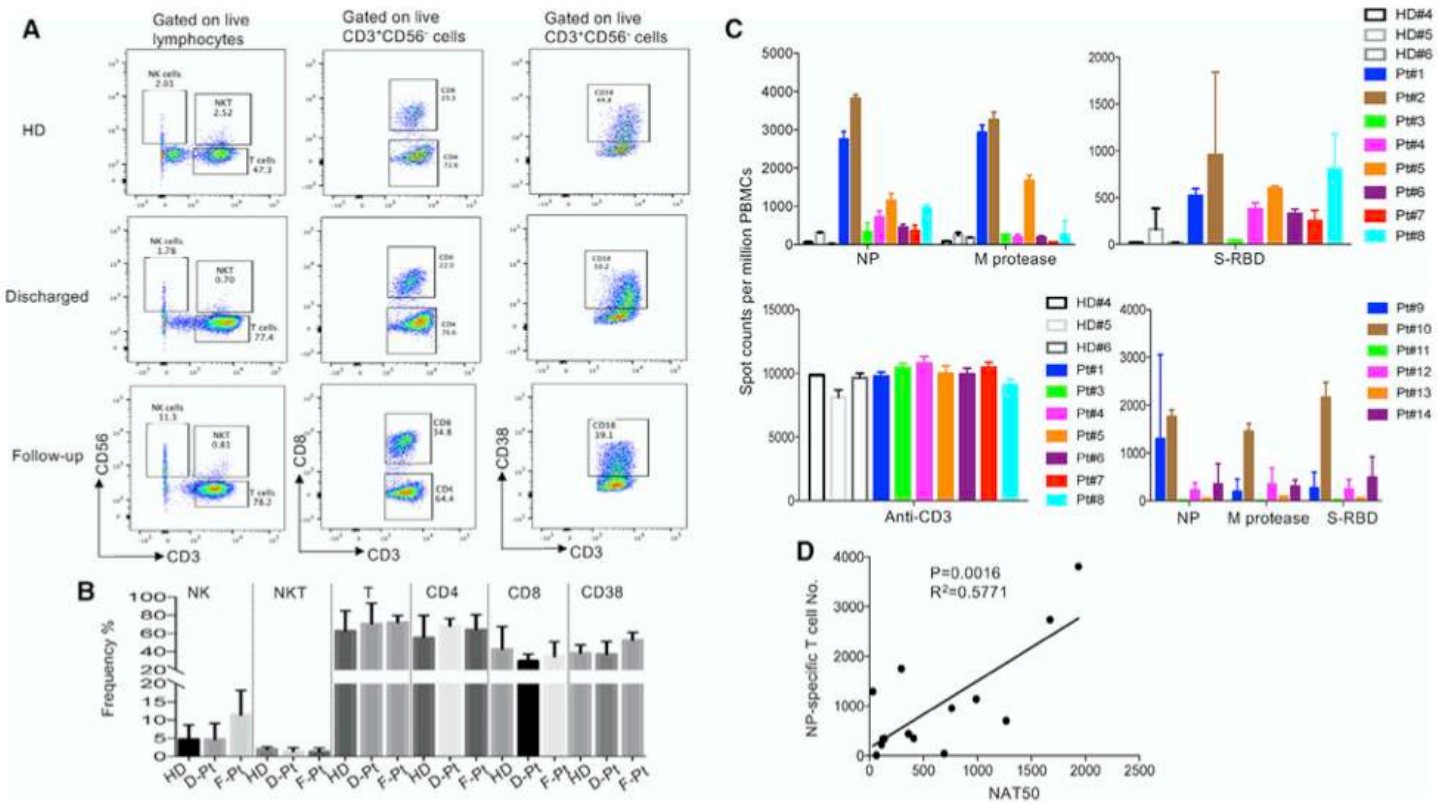
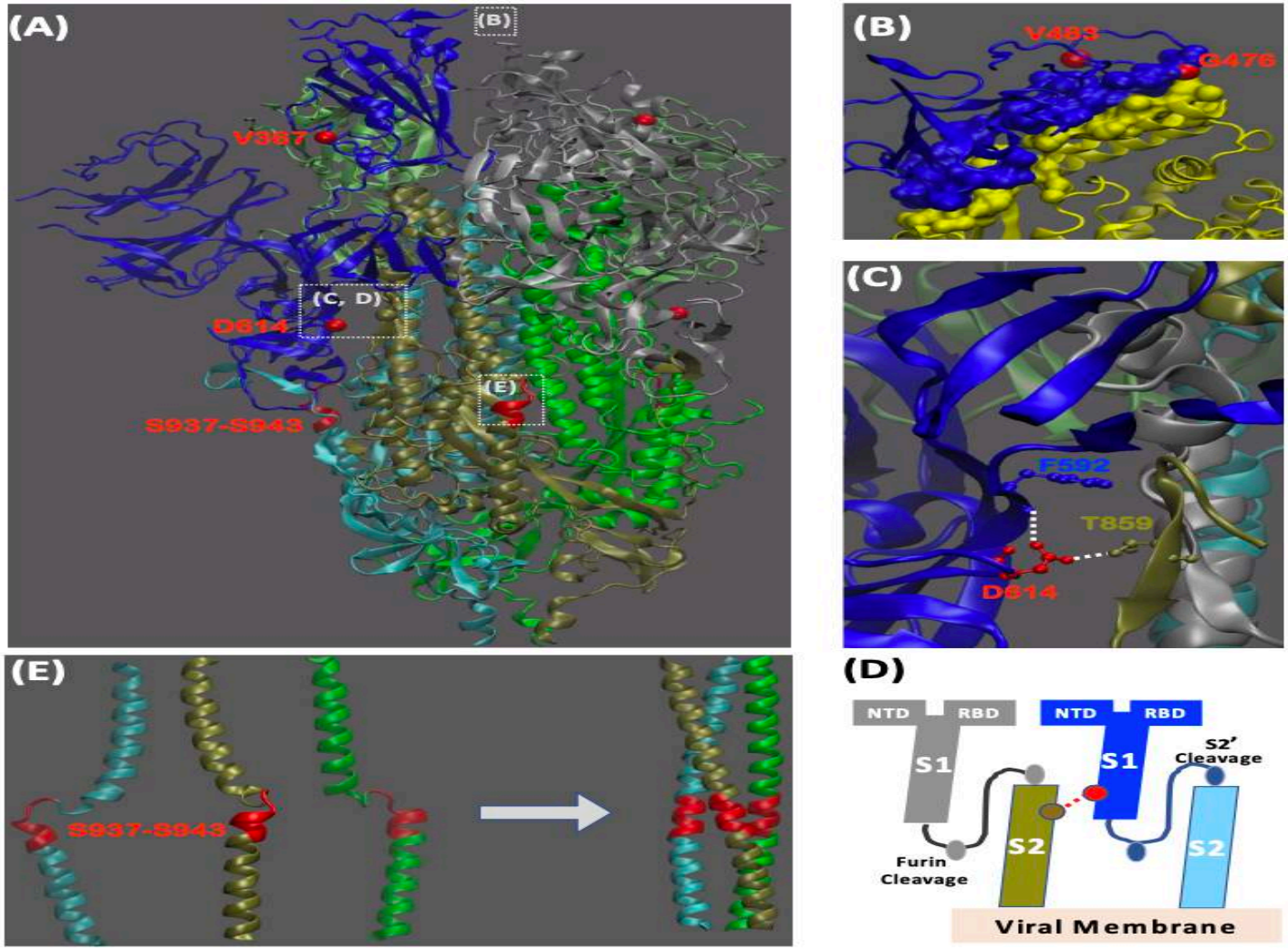


Figure 3. T cell Responses to Recombinant SARS-CoV-2 Proteins in COVID-19 Convalescent Individuals

Structural mapping key mutation sites in the spike protein



Potential scenarios

Three possible evolutions can be envisaged:

1) Virus will be contained and disappear from human species being confined in the animal reservoir (SARS).
2) Virus will be contained but will cause sporadic re-emerging infections as with MERS and avian flu.
3) Virus will become seasonal, endogenous to our species (like Flu and other human CoVs) by reducing its virulence.

Salata C & Palù G. Path and Dis 2020