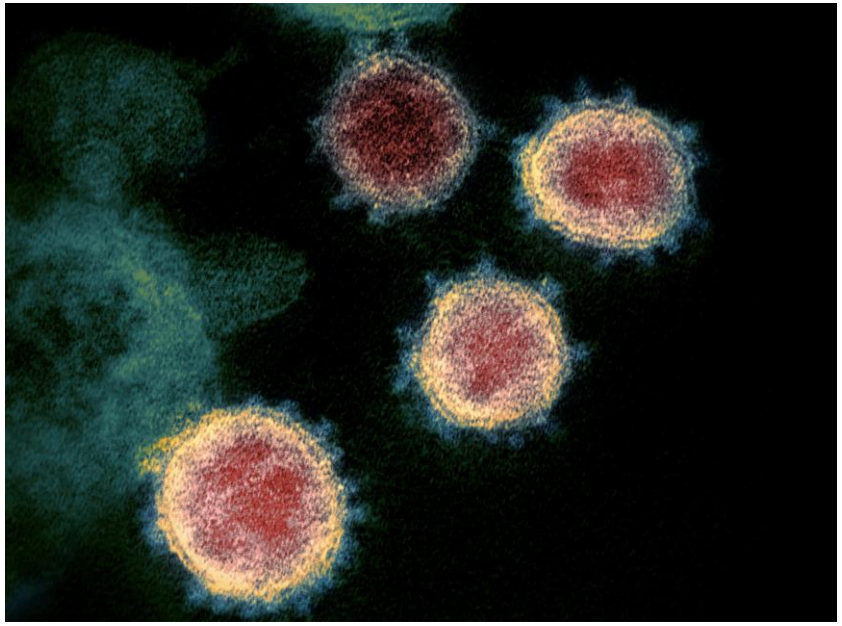


新型冠狀病毒知多少

馬偕兒童醫院　兒童感染科
主治醫師　黃瑽寧

DANIEL TSUNG-NING HUANG, M.D., PH.D.

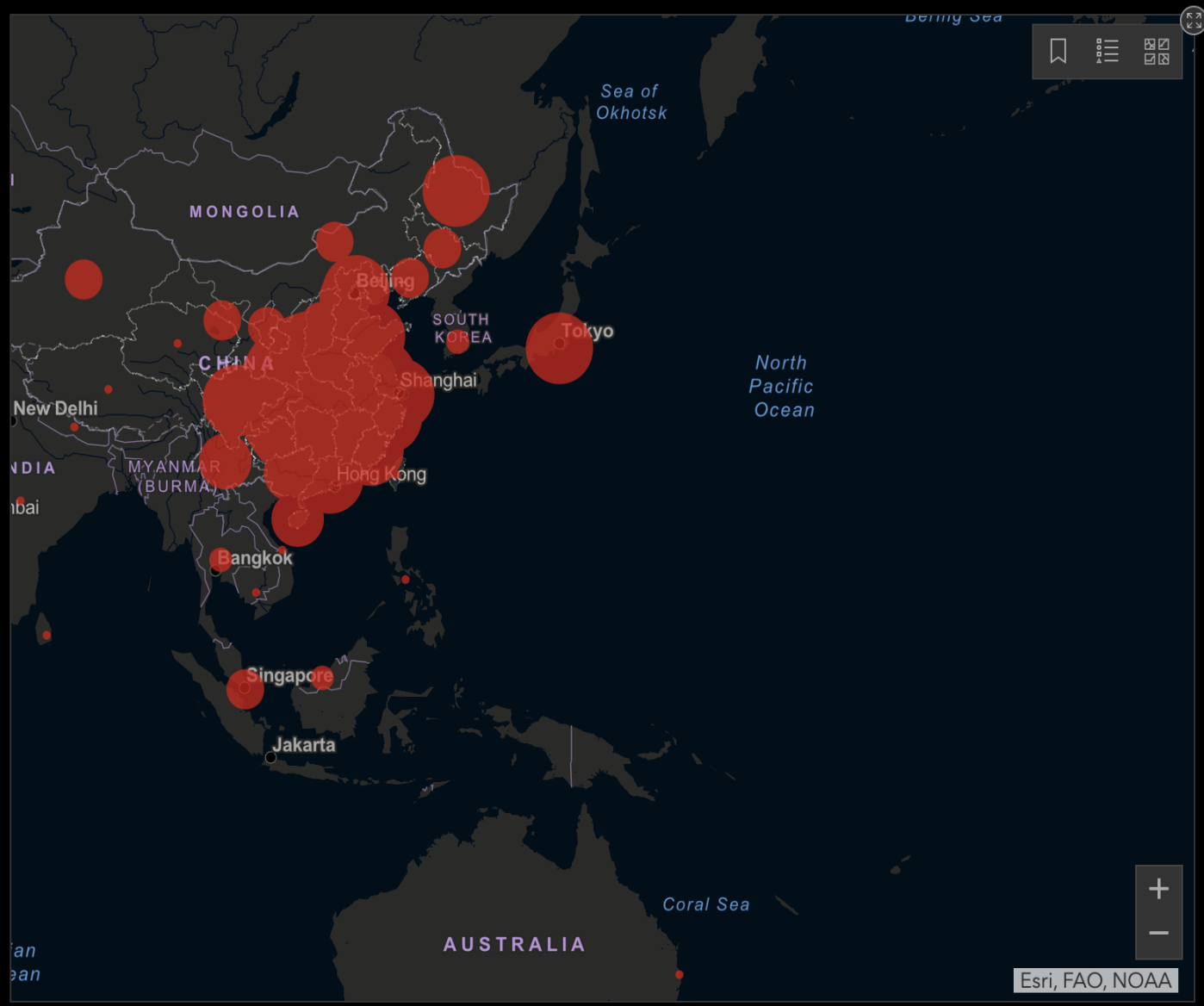
Coronavirus COVID-19 Global Cases by Johns Hopkins CSSE

Total Confirmed
69,186

Confirmed Cases by Country/Region
- 68,500 Mainland China
- 285 Others
- 72 Singapore
- 56 Hong Kong
- 43 Japan
- 33 Thailand
- 29 South Korea
- 22 Malaysia
- 18 Taiwan
- 16 Germany
- 16 Vietnam
- 15 Australia
- 15 US
- 12 France

Country/Region

Last Updated at (M/D/YYYY)
2/16/2020 11:13:07 上午



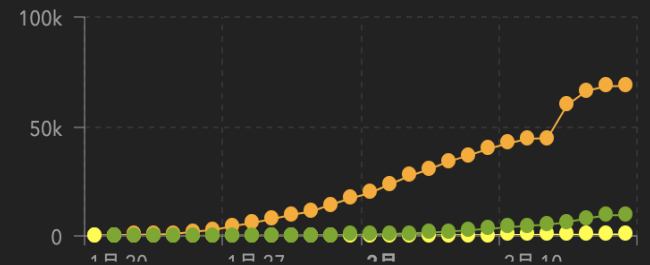
Mobile Version: Here. Visualization: JHU CSSE. Automation Support: Esri Living Atlas team.
Data sources: WHO, CDC, ECDC, NHC and DXY. Read more in this blog. Contact US.
Downloadable database: GitHub: Here. Feature layer: Here.
Point level: City level - US, Canada and Australia; Province level - China; Country level - other countries.

Total Deaths
1,669

- 1,596 deaths **Hubei** Mainland China
- 13 deaths **Henan** Mainland China
- 11 deaths **Heilongjiang** Mainland China
- 6 deaths **Anhui** Mainland China
- 5 deaths **Chongqing** Mainland China
- 4 deaths **Beijing** Mainland China
- 4 deaths **Hainan** Mainland China

Total Recovered
9,571

- 5,623 recovered **Hubei** Mainland China
- 437 recovered **Zhejiang** Mainland China
- 436 recovered **Guangdong** Mainland China
- 430 recovered **Hunan** Mainland China
- 402 recovered **Henan** Mainland China
- 242 recovered **Anhui** Mainland China
- 239 recovered **Jiangxi** Mainland China



Actual | Logarithmic | Daily Increase

COVID-19 CORONAVIRUS OUTBREAK

Last updated: February 16, 2020, 03:10 GMT

Cases – Deaths – Countries – Death Rate – Incubation – Age – Symptoms – Opinions

Coronavirus Cases:

69,269

view by country

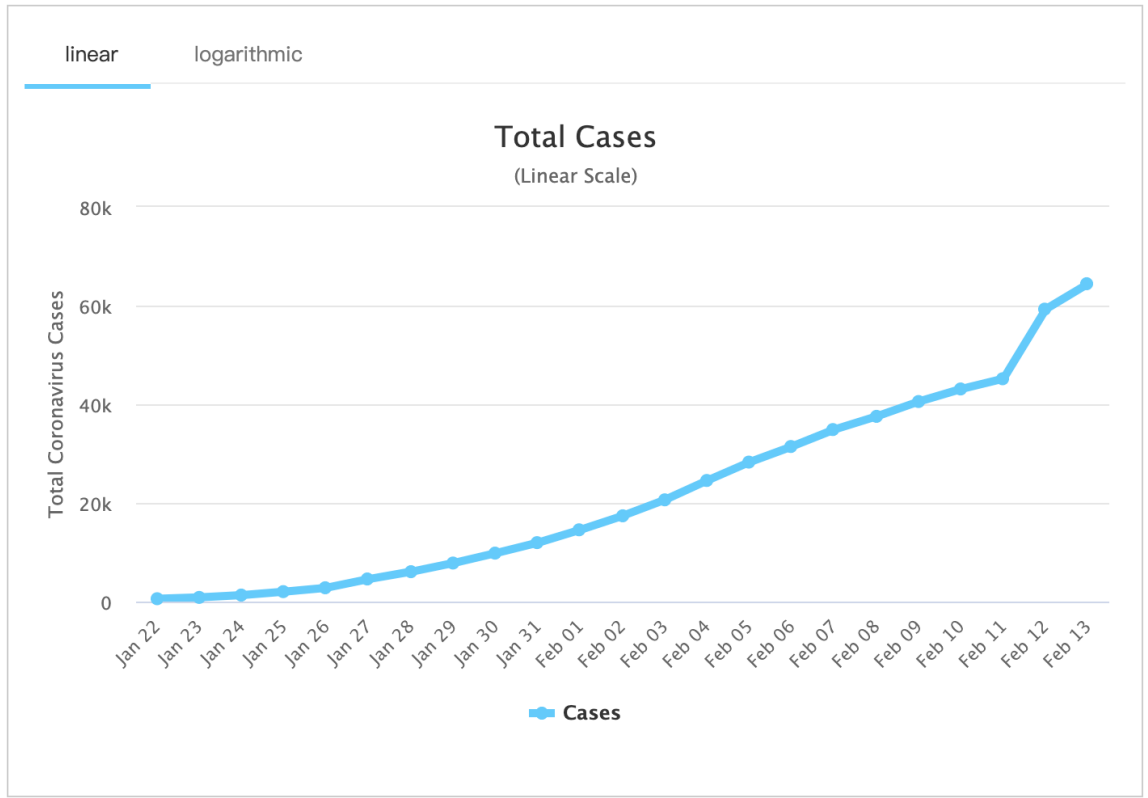
Deaths:

1,669

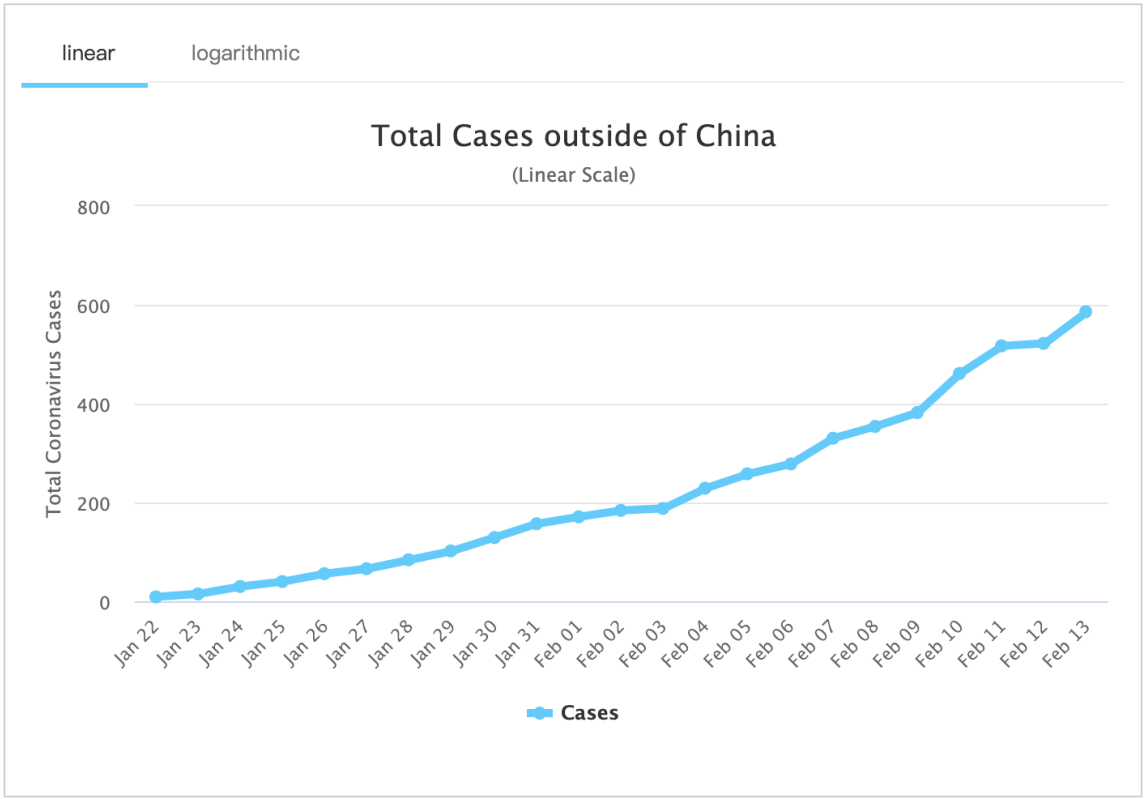
Recovered:

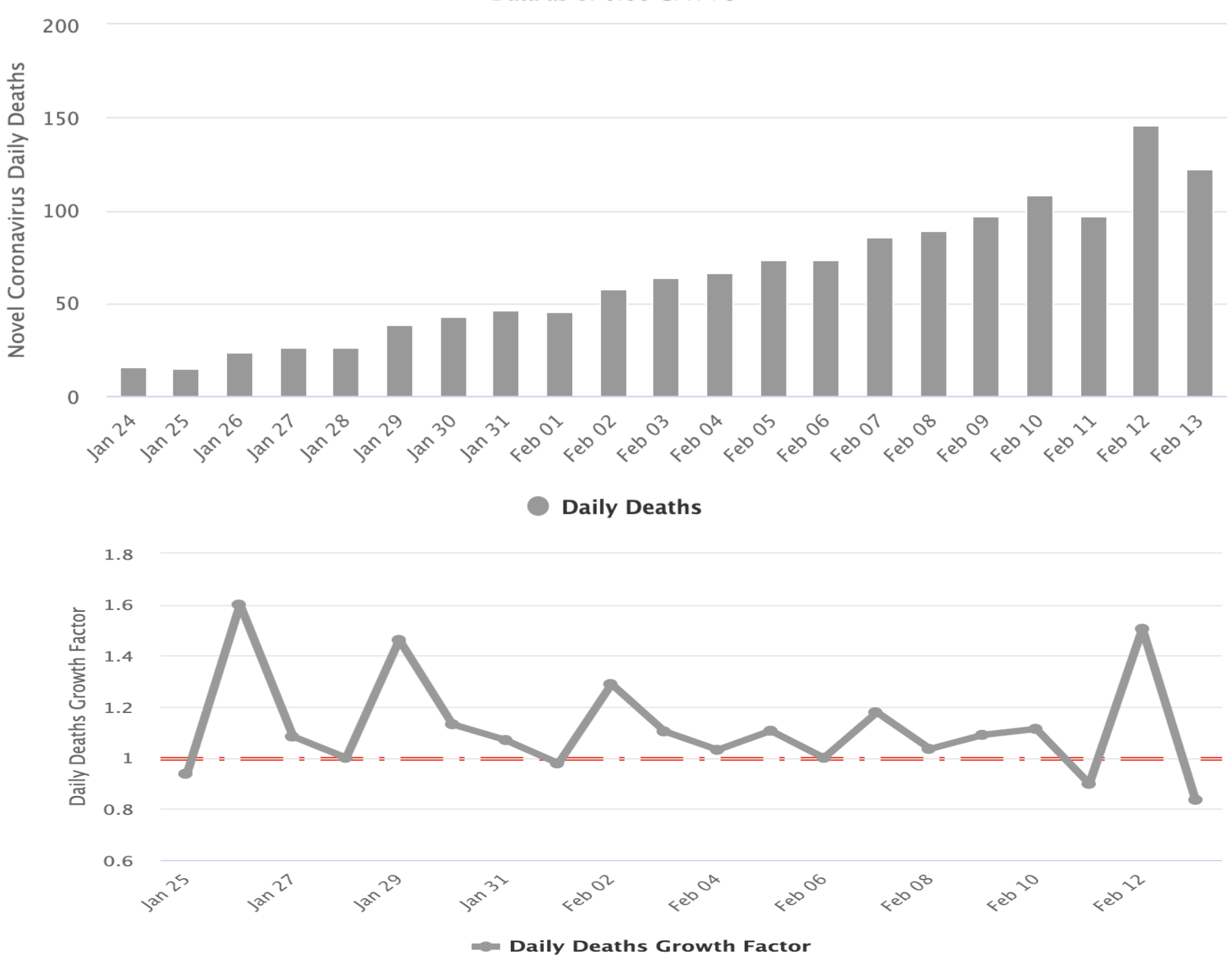
9,586

Total Cases (worldwide)

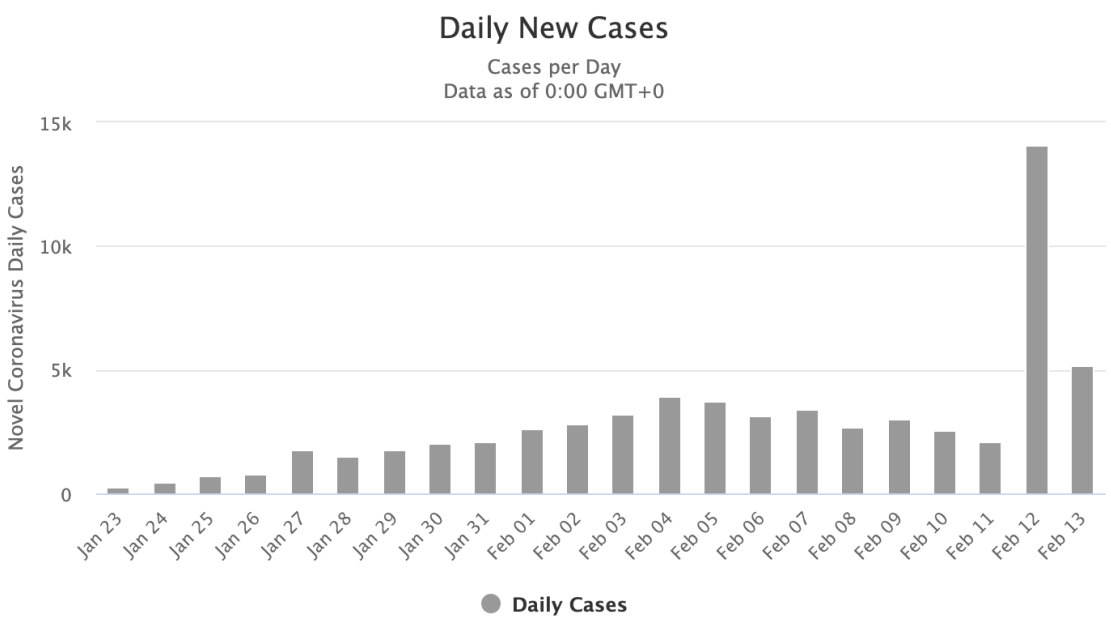


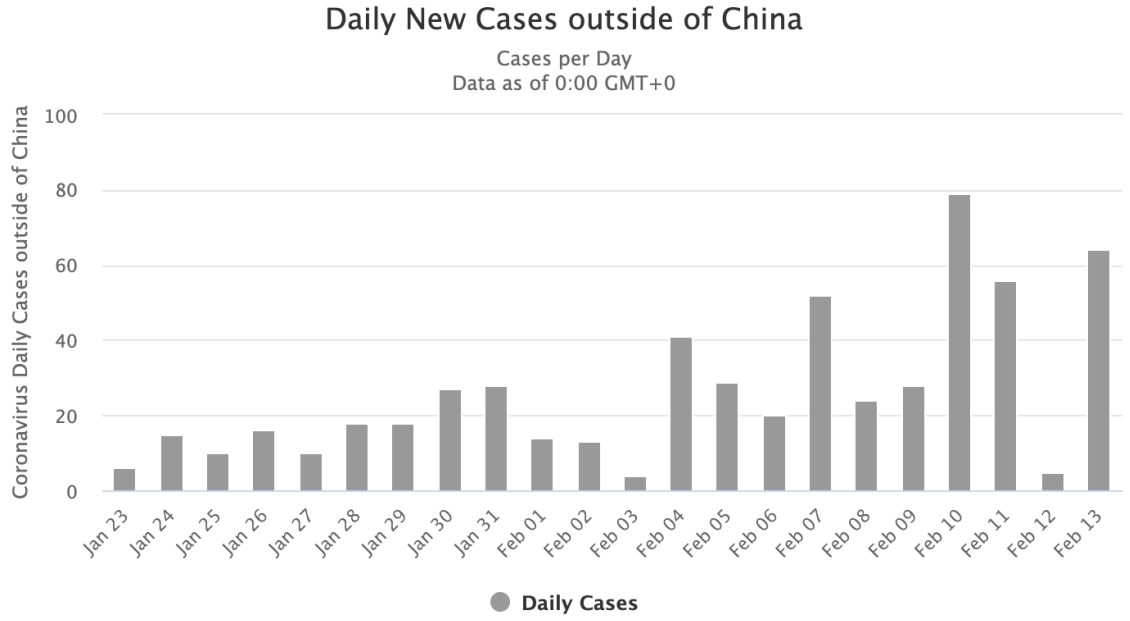
Total Cases excluding mainland China




Novel Coronavirus Daily Deaths
200
150
100
50
0
Jan 24
Jan 25
Jan 26
Jan 27
Jan 28
Jan 29
Jan 30
Jan 31
Feb 01
Feb 02
Feb 03
Feb 04
Feb 05
Feb 06
Feb 07
Feb 08
Feb 09
Feb 10
Feb 11
Feb 12
Feb 13
Daily Deaths
Daily Deaths Growth Factor
1.8
1.6
1.4
1.2
1
0.8
0.6
Jan 25
Jan 27
Jan 29
Jan 31
Feb 02
Feb 04
Feb 06
Feb 08
Feb 10
Feb 12
Daily Deaths Growth Factor

worldometer Coronavirus Population FAQ Contact





預測武漢肺炎未來趨勢：之前的統計數字大多已不適用。

Outline

1. Introduction to coronavirus (CoV)
2. Virology of SARS-CoV-2
3. Genomic epidemiology of SARS-CoV-2
4. Clinical manifestations of COVID19
5. Possible explanations for some crucial questions
6. Future perspectives

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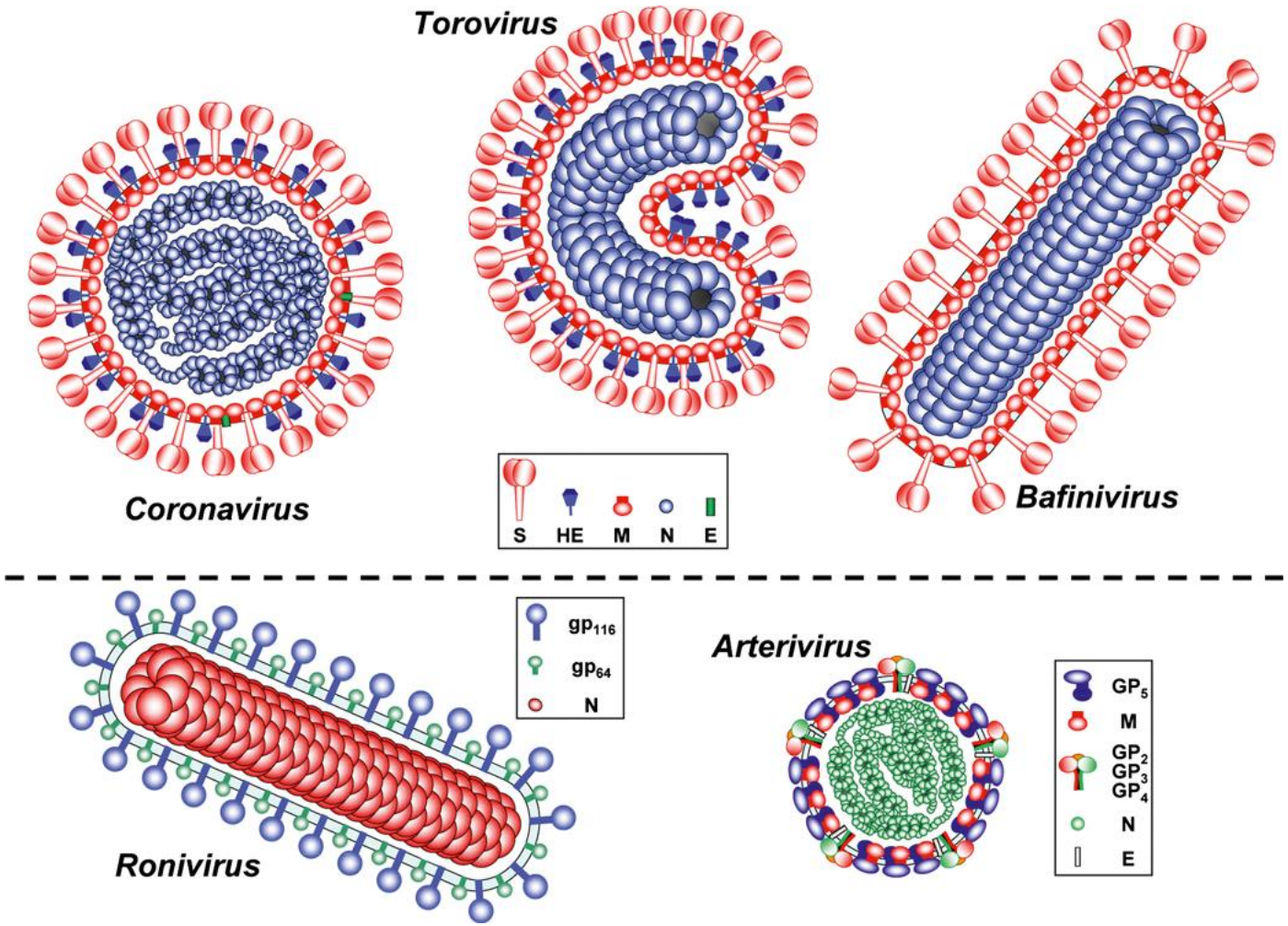
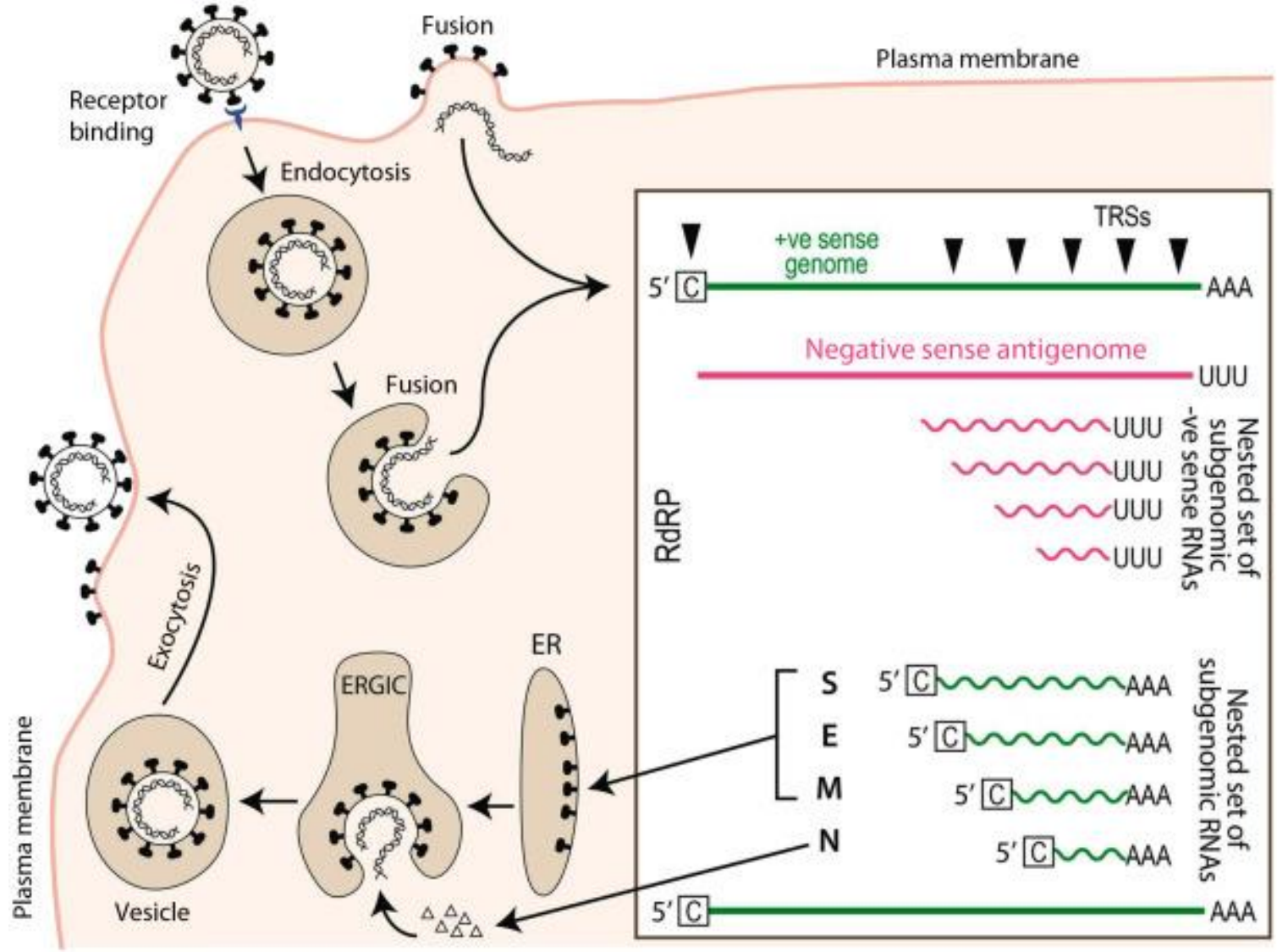
Nidovirales網巢病毒目

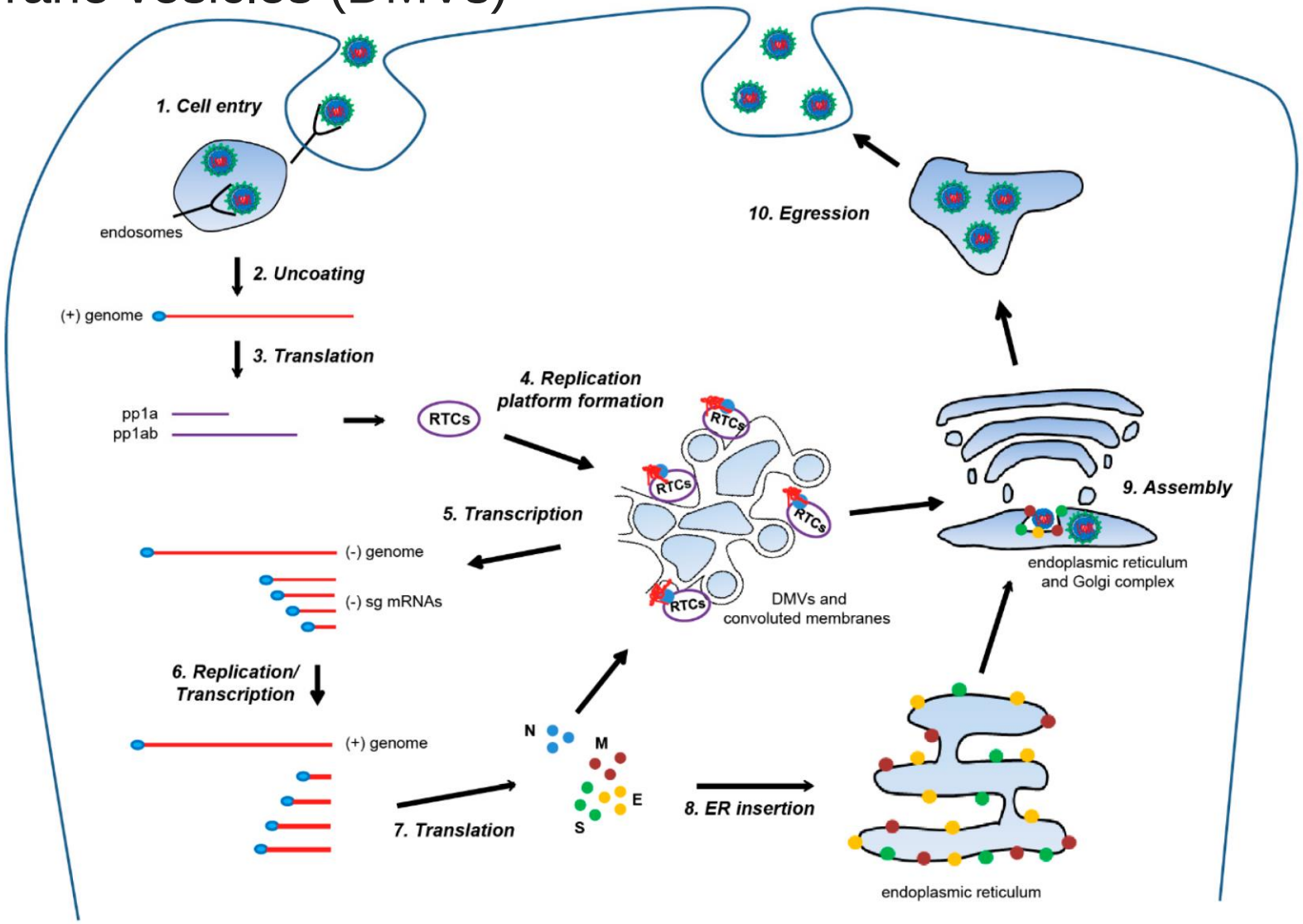


Nidovirales: produce a 3' co-terminal nested set of subgenomic mRNA's during infection.

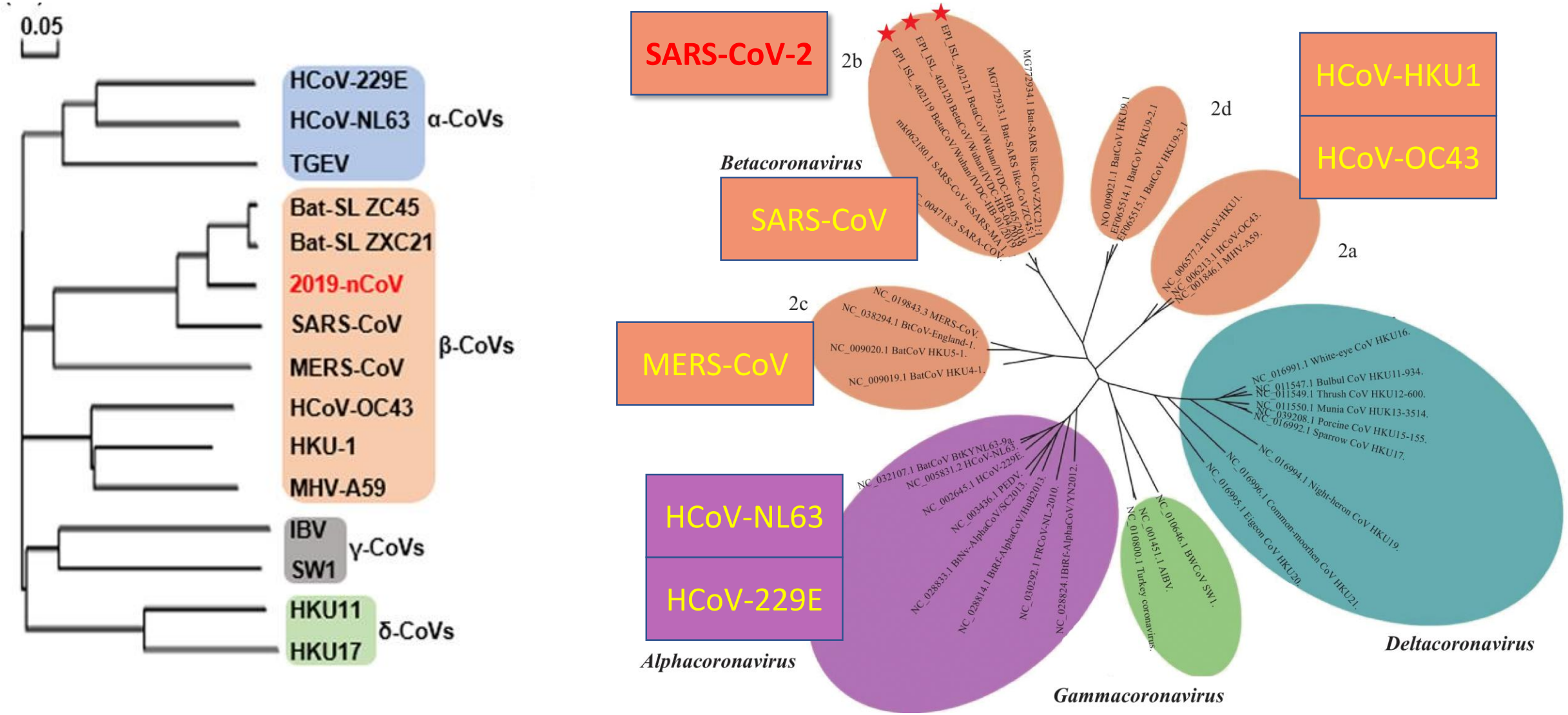


The first ORFs (ORF1a/b) of CoV, about two-thirds of the whole genome length, encode 16 nsps (nsp1-16).

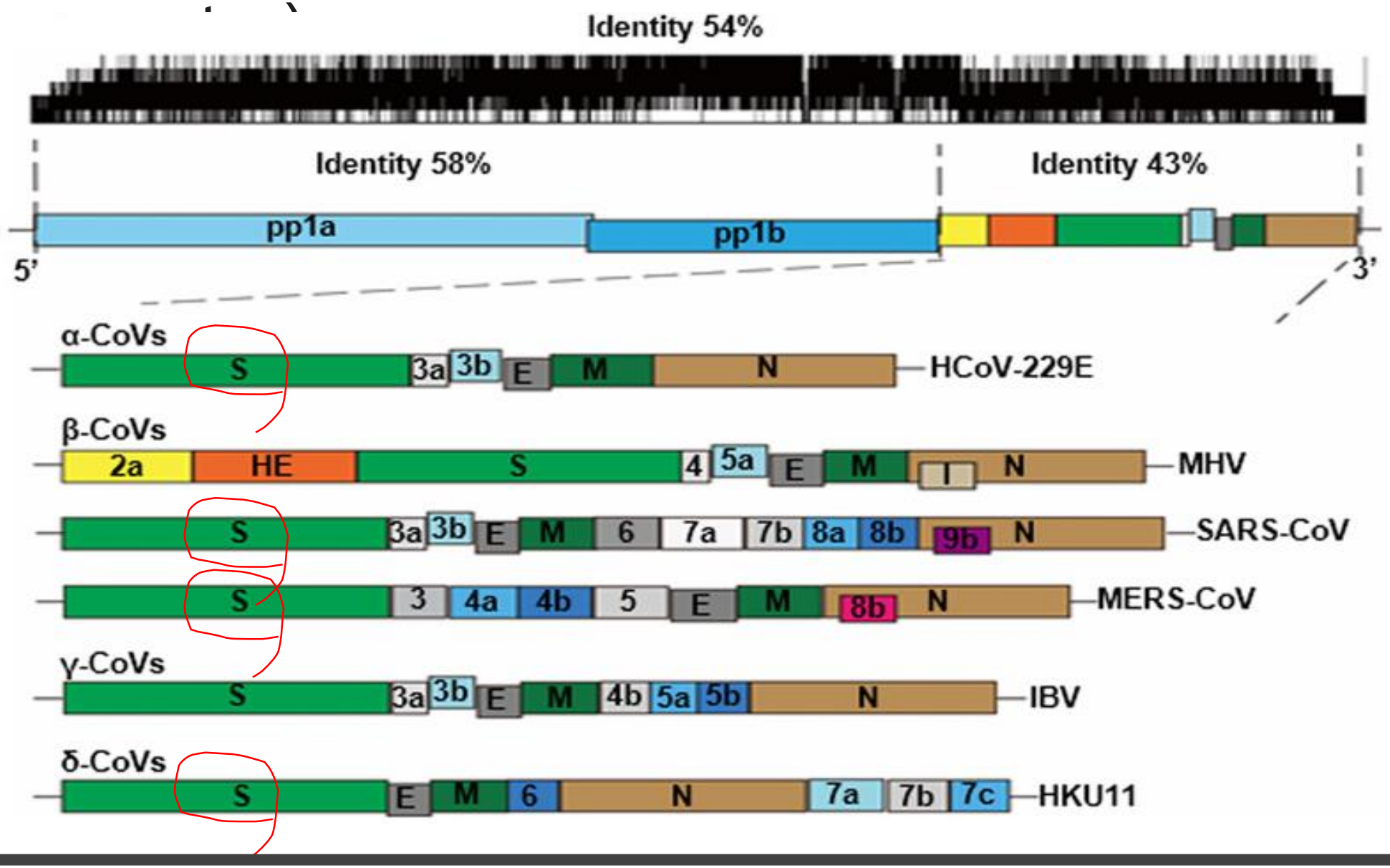
- Replication-transcription complexes (RTCs)
- Double membrane vesicles (DMVs)



Cong, Verlhac and Reggiori_Figure 2


0.05
HCoV-229E
HCoV-NL63
TGEV
α-CoVs
Bat-SL ZC45
Bat-SL ZXC21
2019-nCoV
SARS-CoV
MERS-CoV
HCoV-OC43
HKU-1
MHV-A59
β-CoVs
IBV
SW1
γ-CoVs
HKU11
HKU17
δ-CoVs
SARS-CoV-2
2b
Betacoronavirus
SARS-CoV
2d
HCoV-HKU1
HCoV-OC43
2a
2c
MERS-CoV
HCoV-NL63
HCoV-229E
Alphacoronavirus
Gammacoronavirus
Deltacoronavirus

S gene → spike protein (binds to host



Journal of Medical Virology, First published: 22 January 2020, DOI: (10.1002/jmv.25681)

Outline

1. Introduction to coronavirus (CoV)
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6. Future perspectives

A

	Strain	Complete genome (%)	Gene region (%)											
			1ab	1a	1b	S	3	E	M	7	8	10b	N	13	14
Nucleotide sequences	Bat-SL-CoVZC45	87·6	88·9	90·7	86·0	75·2	87·8	98·7	93·4	95·2	88·8	88·5	91·1	89·1	96·7
	Bat-SL-CoVZXC21	87·5	88·7	90·3	86·1	74·7	88·9	98·7	93·4	95·2	89·1	88·5	91·2	89·5	96·7
	SARS-CoVGZ02	79·0	79·5	75·4	86·3	72·7	75·6	93·5	85·1	74·5	82·1	..	88·1	..	..
Amino acid sequences	Bat-SL-CoVZC45	..	95·6	95·6	95·8	80·2	90·9	100·0	98·6	93·4	87·6	94·2	94·3	73·2	92·9
	Bat-SL-CoVZXC21	..	95·2	95·1	95·5	79·6	92·0	100·0	98·6	93·4	88·4	94·2	94·3	73·2	92·9
	SARS-CoVGZ02	..	86·2	80·5	95·6	76·2	73·1	94·7	90·1	68·9	85·2	..	90·3	..	..

B

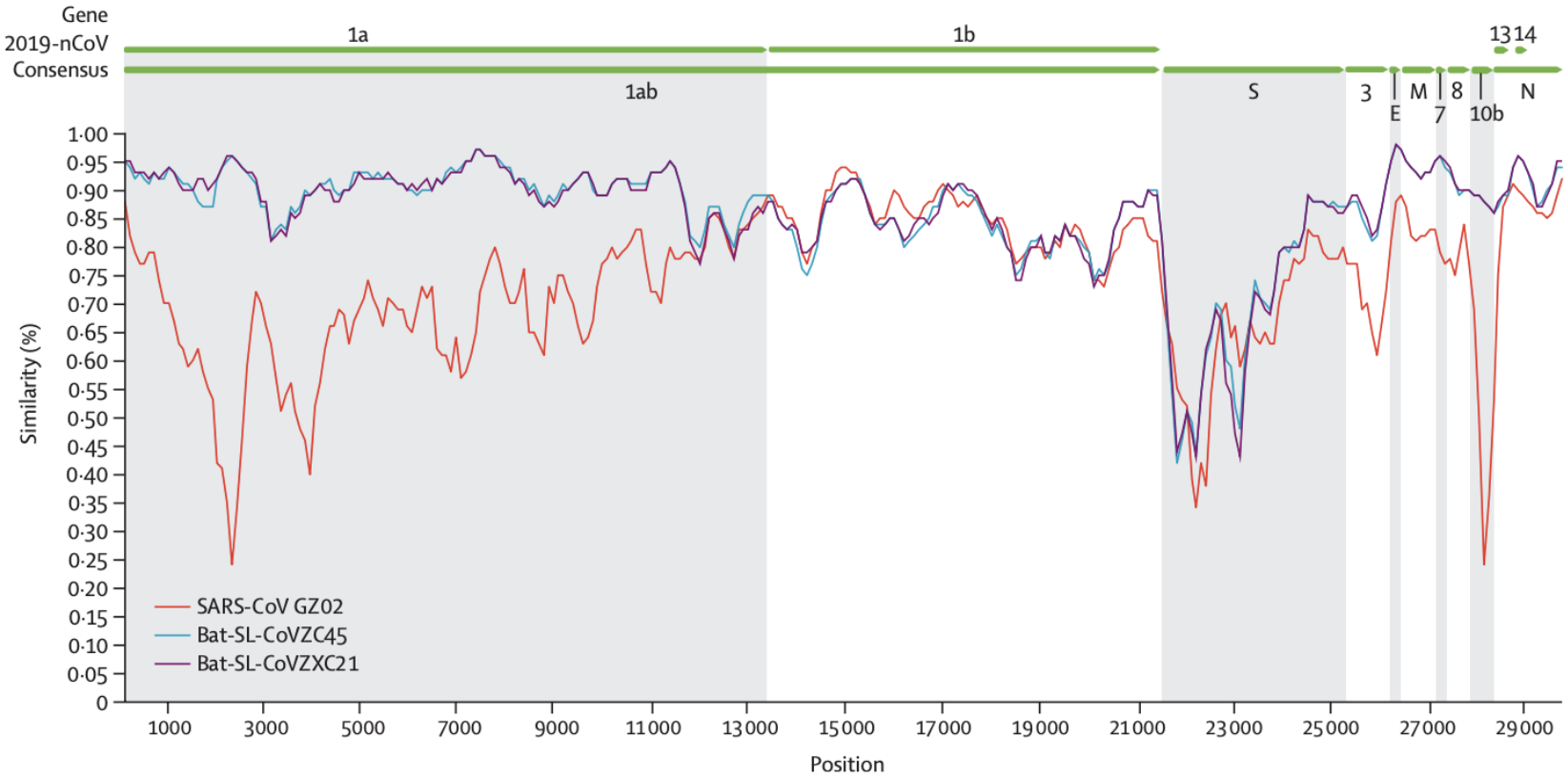
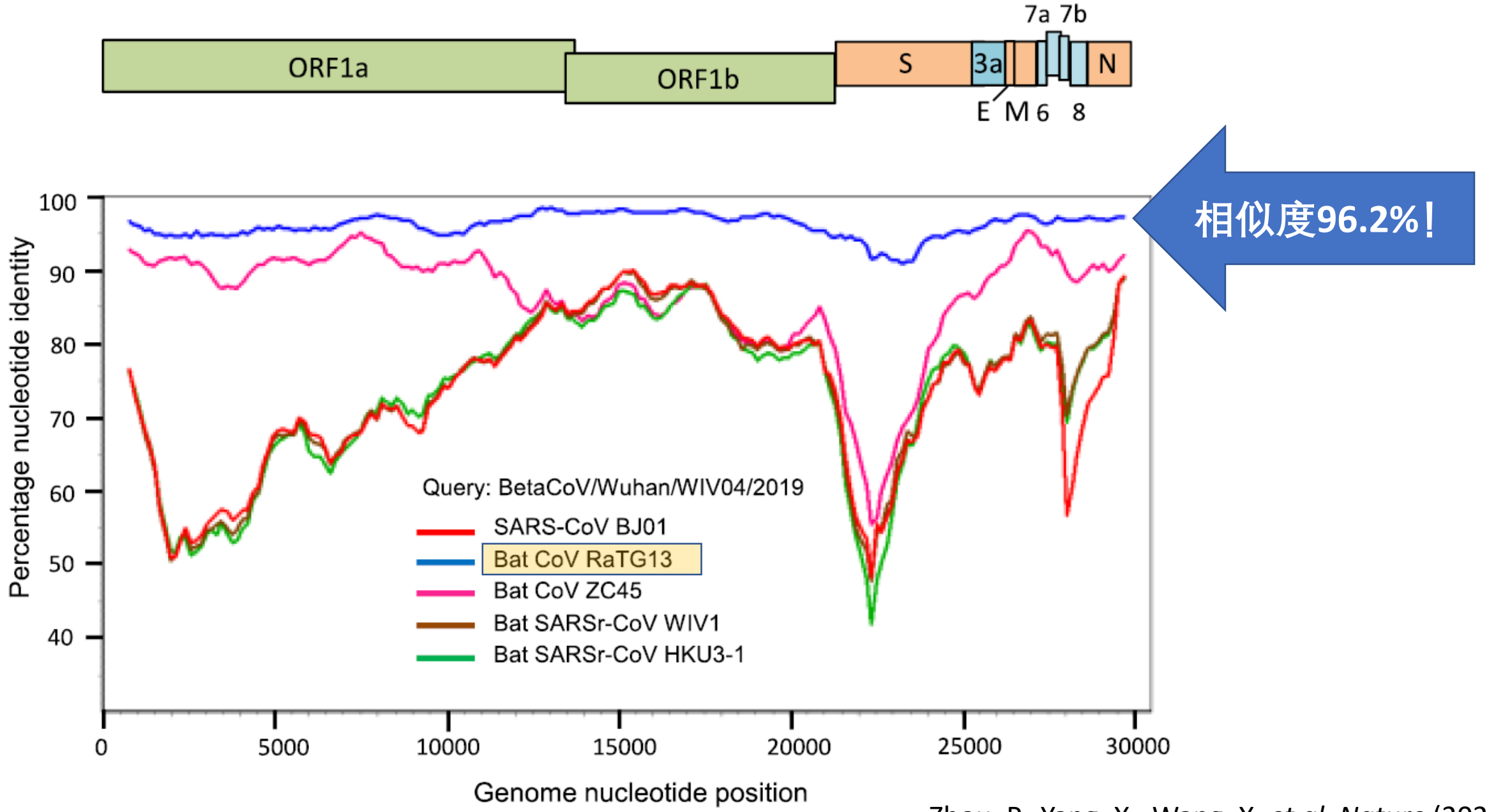
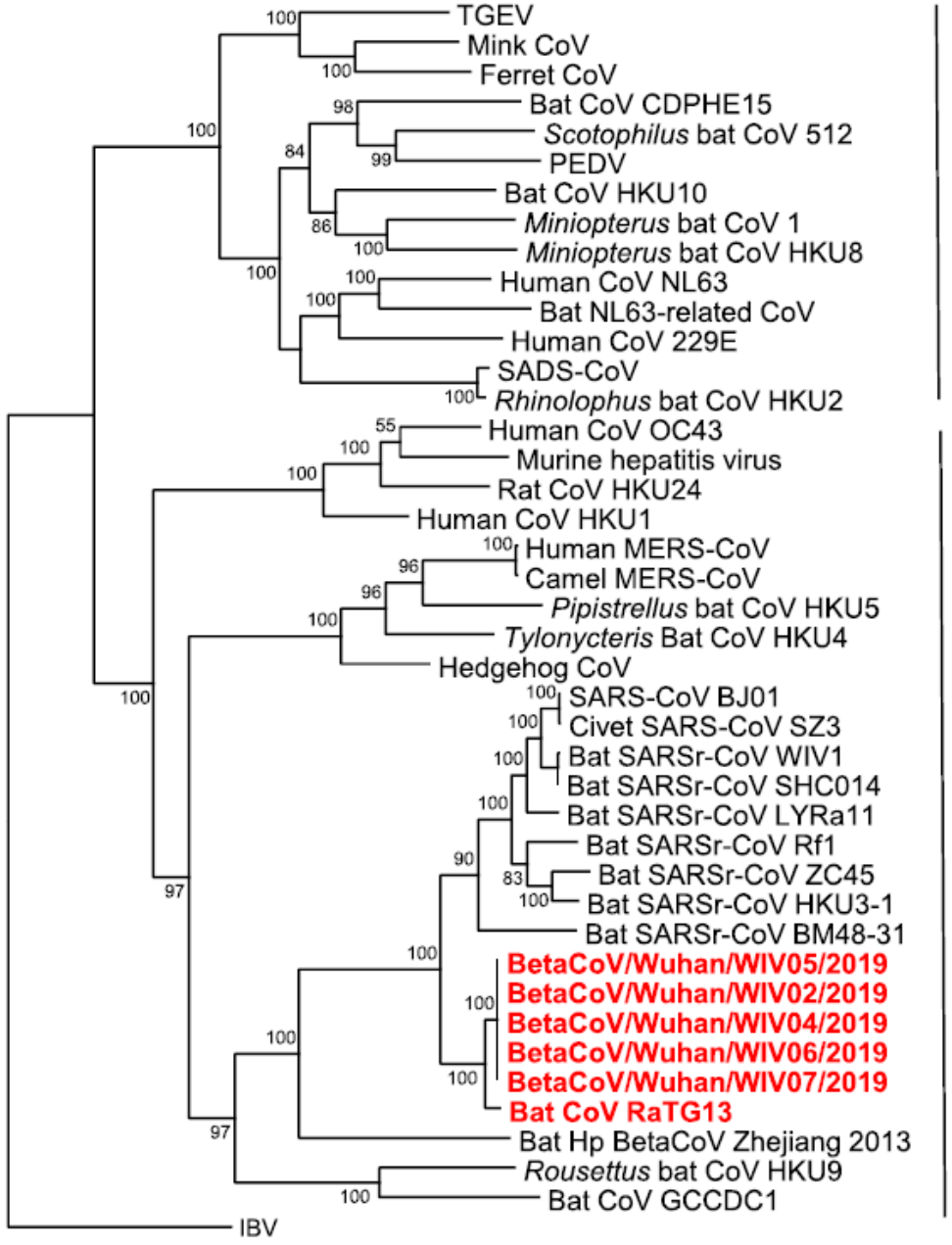


Figure 2: **Sequence identity between the consensus of 2019-nCoV and representative betacoronavirus genomes**

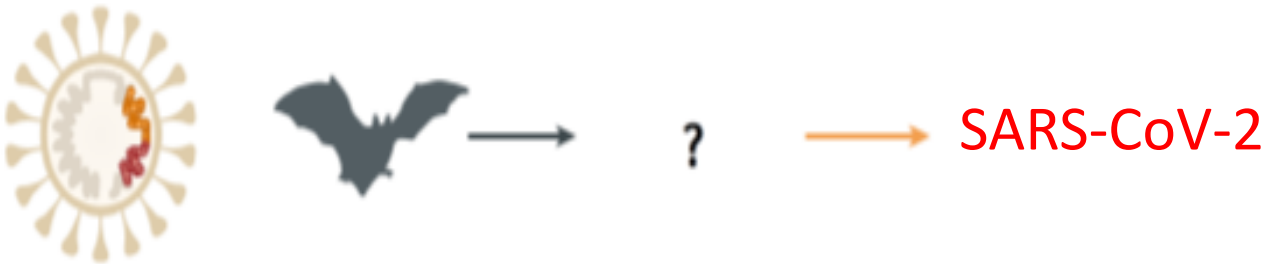
Lu R et al. *Lancet* 2020 Jan 30; [e-pub].



Zhou, P., Yang, X., Wang, X. *et al. Nature* (2020)



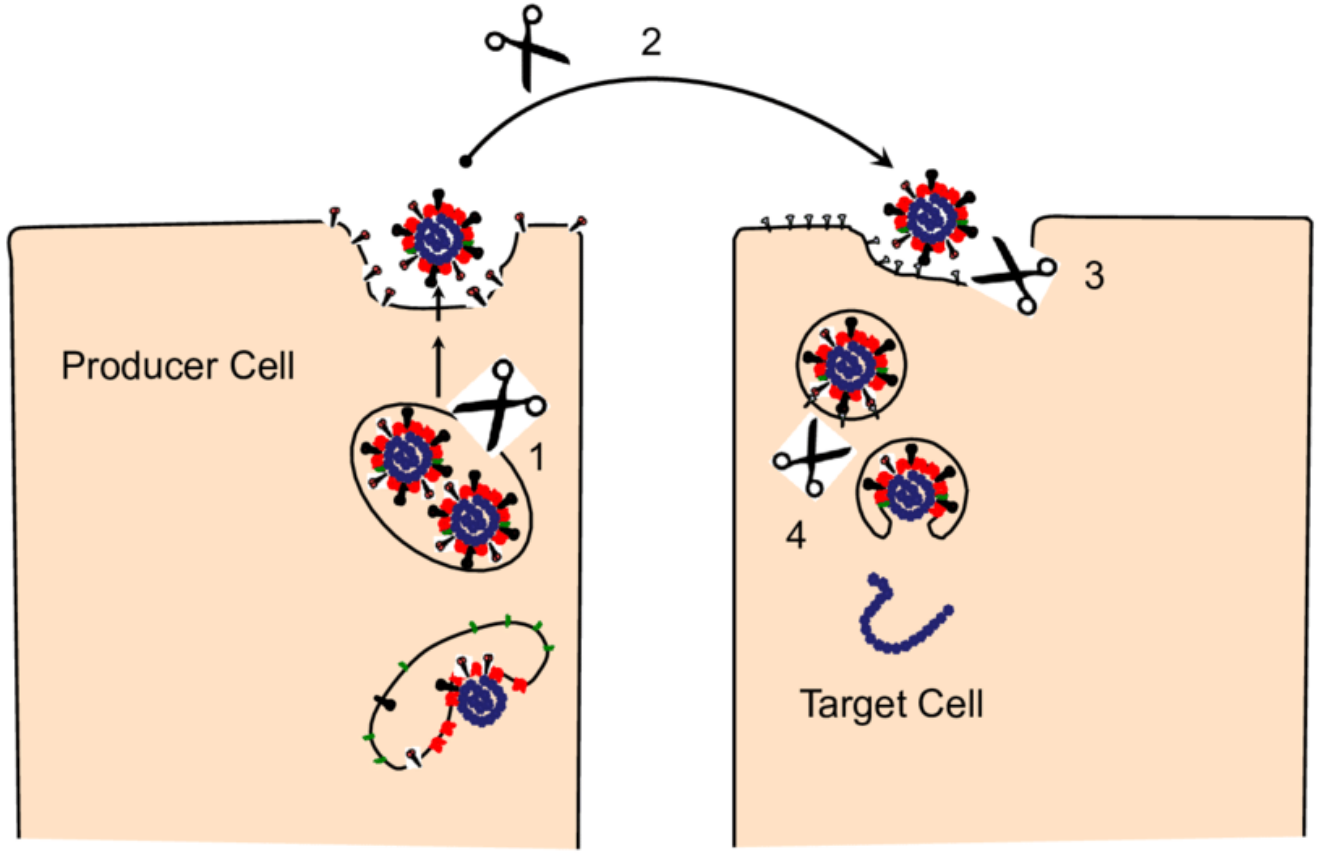
Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event.

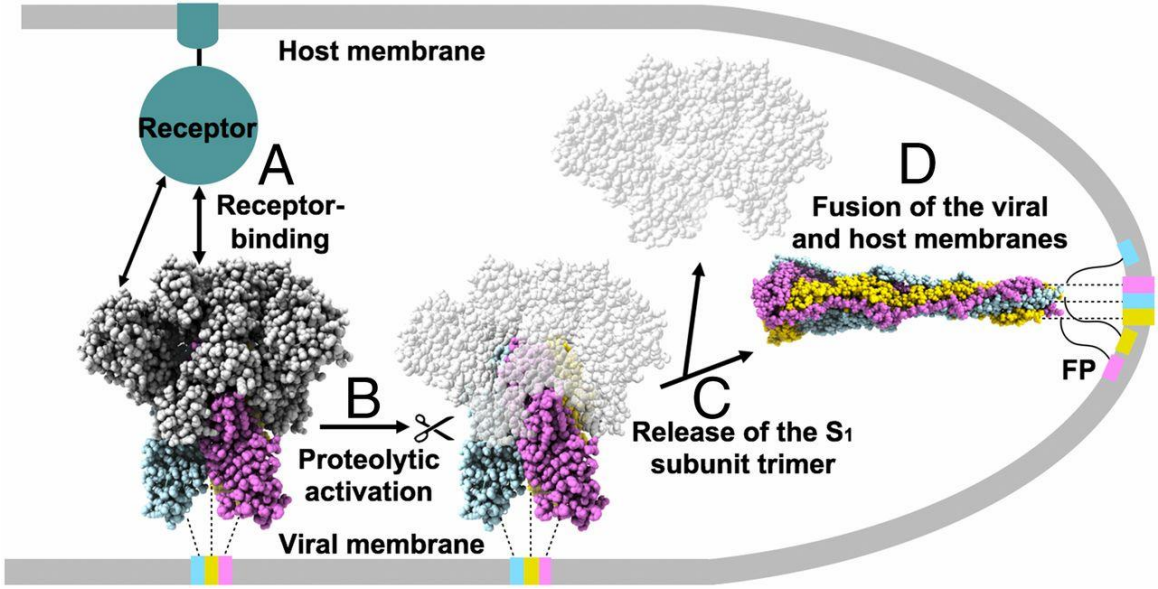


Extended Data Table 3 | Genomic comparison of 2019-nCoV WIV04 with SARS-CoVs and bat SARSr-CoVs

	Sequence identities with SARS-CoVs & bat SARSr-CoVs (nt/aa %)											
	Full-length genome	ORF1a	ORF1b	S	ORF3a	E	M	ORF6	ORF7a	ORF7b	ORF8	N
SARS-CoV GZ02	79.6	76.0/80.9	86.2/95.7	73.4/77.0	75.6/73.4	94.7/96.0	85.4/90.5	76.3/68.9	82.8/86.0	84.8/81.4	52.0/31.6	87.7/91.2
SARS-CoV BJ01	79.6	76.0/80.8	86.2/95.7	73.4/76.9	75.3/72.6	94.7/96.0	85.6/90.5	75.8/67.2	82.8/86.0	84.8/81.4	51.1/-	88.8/91.2
SARS-CoV Tor2	79.6	76.0/80.9	86.2/95.8	73.4/76.7	75.4/72.6	94.7/96.0	85.6/90.5	76.3/68.9	82.8/86.0	84.8/81.4	51.1/-	88.8/91.2
SARS-CoV SZ3	79.6	76.0/81.0	86.2/95.8	73.4/76.9	75.4/72.6	94.7/96.0	85.3/90.0	76.3/68.9	82.8/86.0	84.8/81.4	52.3/31.6	88.8/91.2
SARS-CoV PC4-227	79.5	76.0/80.8	86.1/95.6	73.4/76.7	75.5/72.6	94.7/96.0	85.1/90.0	75.8/68.9	82.8/86.0	84.8/81.4	52.3/-	88.5/90.7
Bat SARr-CoV RaTG13	96.2	96.0/98.0	97.3/99.3	93.1/97.7	96.3/97.8	99.6/100	95.5/99.6	98.4/100	95.6/97.5	99.2/97.7	97.0/95.0	96.9/99.0
Bat SARr-CoV WIV1	79.7	76.0/80.7	85.9/95.8	73.4/77.6	76.1/74.5	95.6/96.0	84.8/90.0	78.0/73.8	85.0/88.4	85.6/83.7	65.8/57.9	88.5/90.9
Bat SARSr-CoV WIV16	79.7	75.9/81.0	86.1/95.6	73.1/77.8	76.1/74.5	95.6/96.0	84.8/90.0	77.4/72.1	85.0/88.4	85.6/83.7	65.3/57.9	88.6/90.9
Bat SARSr-CoV SHC014	79.6	75.9/80.9	85.9/95.8	73.3/77.7	76.1/74.5	95.6/96.0	84.8/90.0	78.0/70.5	84.4/88.4	85.6/83.7	65.8/58.7	88.6/90.9
Bat SARSr-CoV Rs4231	79.7	76.0/81.0	86.2/95.8	72.9/77.5	75.8/74.1	94.3/94.7	84.4/90.0	76.9/67.2	85.0/88.4	85.6/83.7	65.3/57.9	88.8/91.4
Bat SARSr-CoV YNLF31C	79.0	75.7/80.6	85.8/95.7	71.4/75.5	75.0/71.2	94.3/96.0	84.7/89.6	76.9/70.5	83.1/87.6	86.4/83.7	50.3/31.3	88.3/90.5
Bat SARSr-CoV LYRa11	79.6	75.8/80.6	85.7/95.6	73.9/77.3	77.2/76.3	94.7/94.7	85.1/90.0	78.5/70.5	82.0/85.1	81.1/81.4	66.7/57.9	89.0/91.6
Bat SARSr-CoV ZC45	88.1	91.0/95.7	86.1/96.0	77.8/82.3	87.8/90.9	98.7/100	93.4/98.6	95.2/93.4	88.8/87.6	94.7/93.0	88.5/94.2	91.1/94.3
Bat SARSr-CoV ZXC21	88.0	90.9/95.7	86.2/95.8	77.1/81.7	88.9/92.0	98.7/100	93.4/98.6	95.2/93.4	89.1/88.4	95.5/93.0	88.5/94.2	91.2/94.3
Bat SARSr-CoV HuB2013	79.6	76.3/81.2	85.3/95.7	73.1/76.8	75.4/75.5	95.2/94.7	85.3/91.0	76.3/68.9	84.2/87.6	85.6/83.7	62.0/49.6	88.9/91.6
Bat SARSr-CoV GX2013	79.1	75.9/80.8	86.0/95.9	73.1/77.1	75.6/73.0	94.7/96.0	84.8/91.4	77.4/68.9	85.0/86.8	84.1/79.1	51.4/31.6	87.9/90.2
Bat SARSr-CoV SX2013	78.9	76.2/80.6	85.1/95.5	71.2/75.5	74.7/71.2	94.3/93.3	83.0/89.6	77.4/68.9	84.2/86.8	85.6/83.7	49.7/30.4	86.9/90.2
Bat SARSr-CoV SC2018	79.4	75.8/80.7	85.5/95.2	72.7/76.4	75.0/71.2	94.3/96.0	84.7/90.0	80.0/71.8	85.2/87.6	84.8/83.7	66.1/55.4	88.2/91.2
Bat SARSr-CoV Rs672	79.6	76.0/80.9	85.9/95.8	72.8/76.2	75.2/71.9	95.2/96.0	84.8/89.6	78.5/70.5	84.7/88.4	85.6/83.7	65.8/58.7	87.9/91.2
Bat SARSr-CoV Rp3	79.5	75.9/80.5	86.0/95.7	73.1/77.2	74.9/74.8	95.2/96.0	85.1/90.0	76.9/68.9	83.9/89.3	84.8/83.7	66.4/56.2	88.4/90.7
Bat SARSr-CoV Rf1	78.8	76.2/80.6	84.8/95.3	71.1/75.7	74.3/69.0	94.3/94.7	83.3/89.6	79.0/68.9	84.2/86.8	84.1/83.7	50.6/31.3	86.8/89.5
Bat SARSr-CoV HKU3-1	79.4	76.1/80.9	84.9/95.1	73.4/77.9	75.8/73.4	95.2/96.0	84.7/91.0	75.3/67.2	85.0/89.3	84.1/79.1	66.4/57.0	88.3/90.0

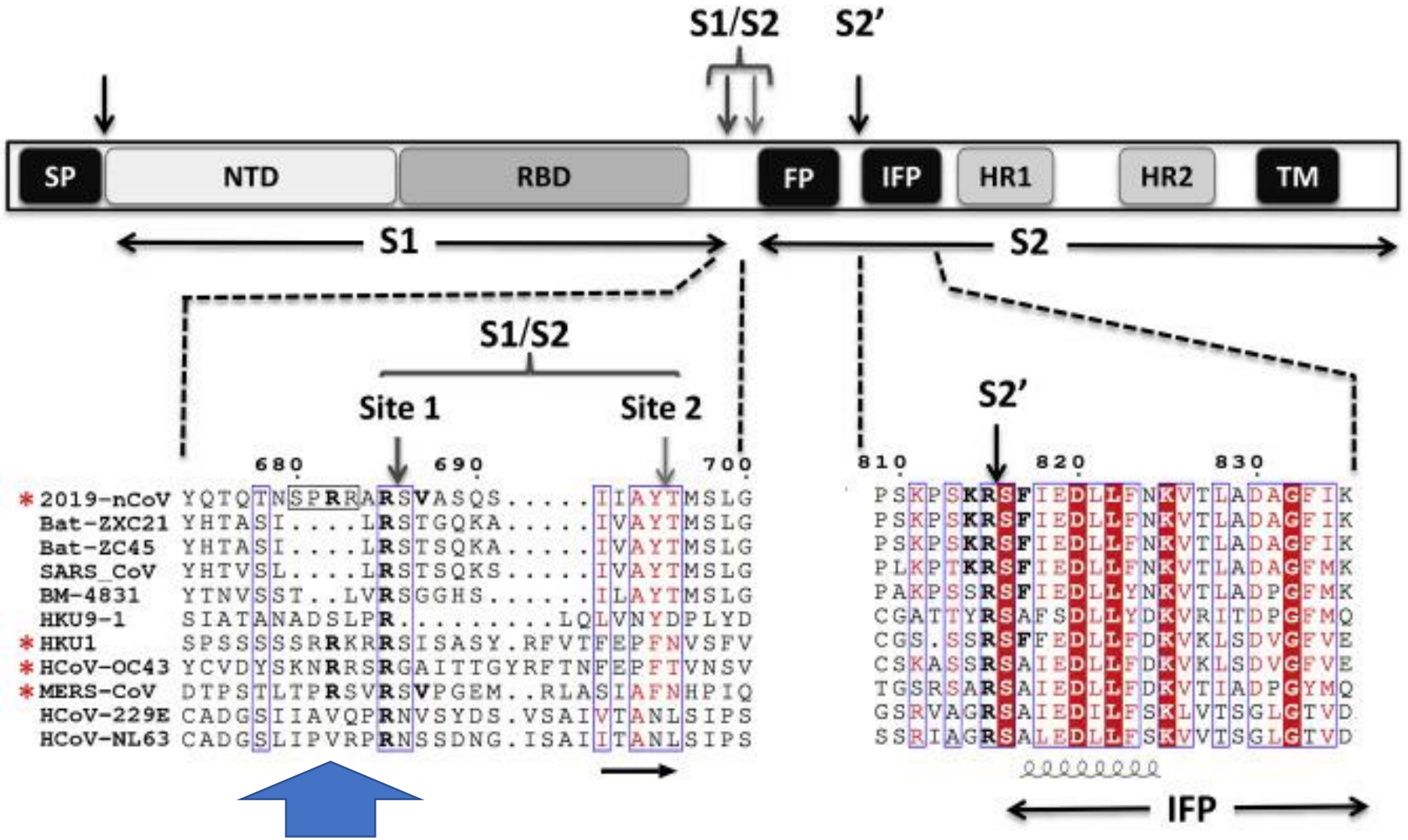
Class I viral fusion: influenza virus, coronavirus, and HIV-1





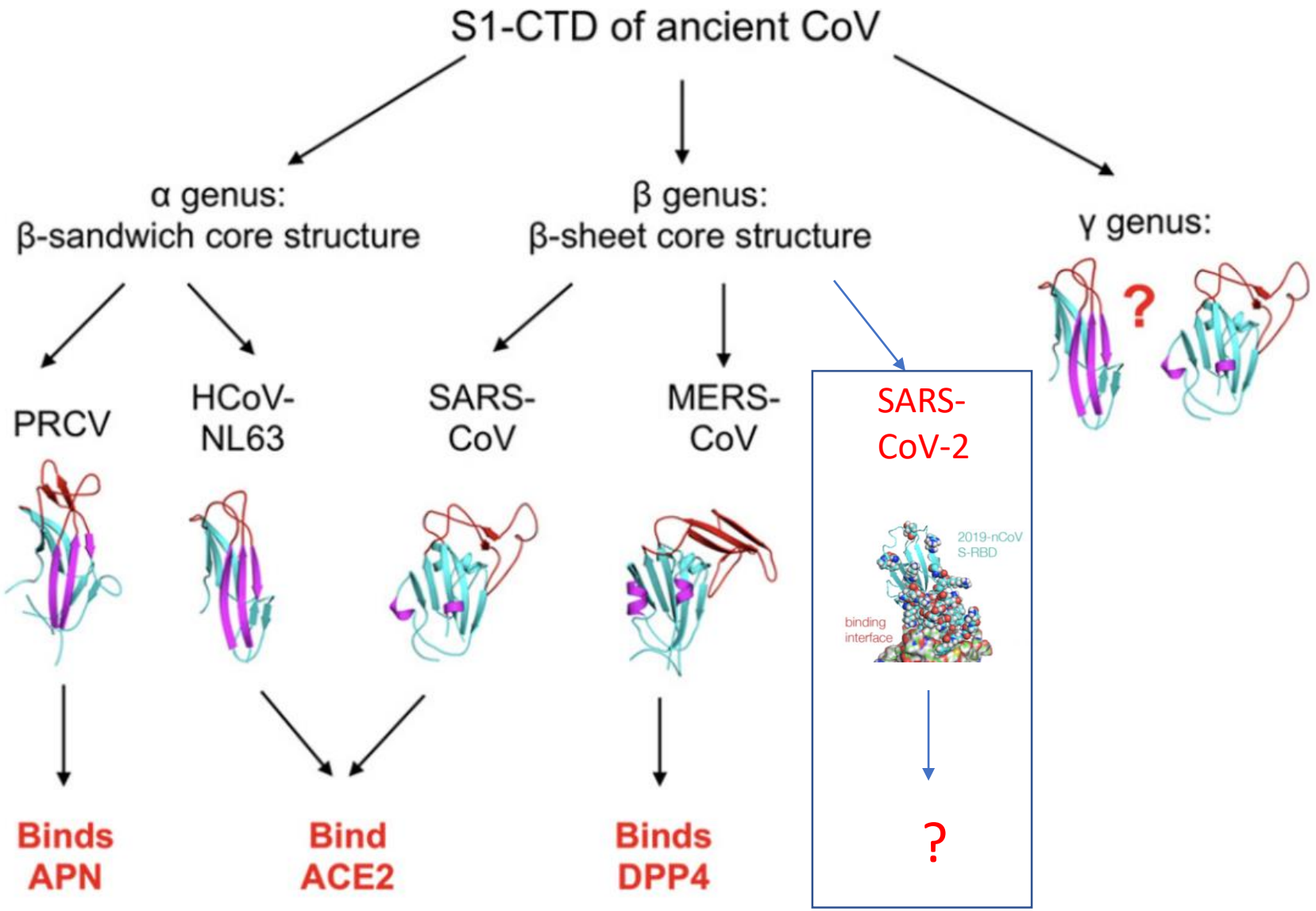
J Virol 94:e01774-19.

The S protein contains two functional domains: a receptor binding domain, and a second domain which contains sequences that mediate fusion of the viral and cell membranes.

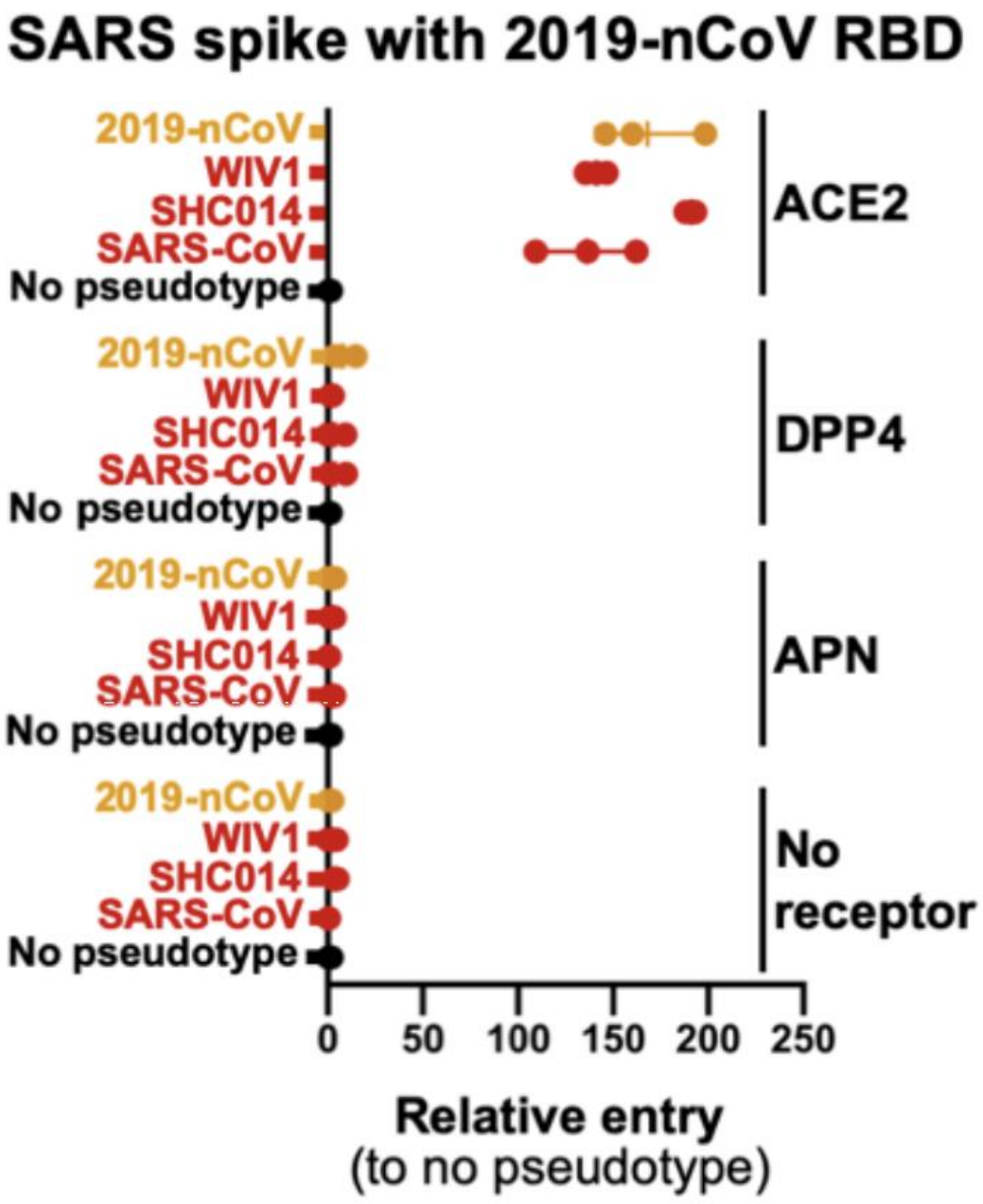


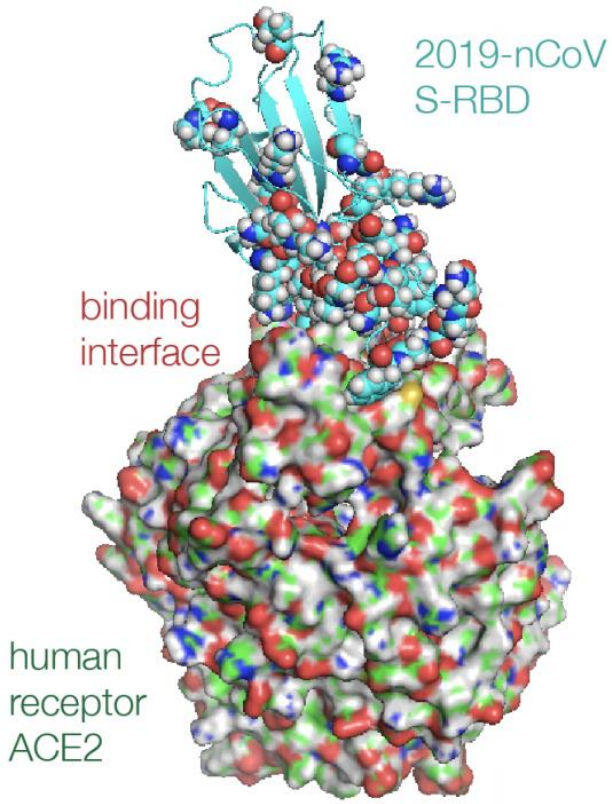
2019-nCoV S-protein sequence has a specific **furin-like cleavage site** absent in lineage b CoV including SARS-CoV sequences.

Antiviral Research Volume 176, April 2020

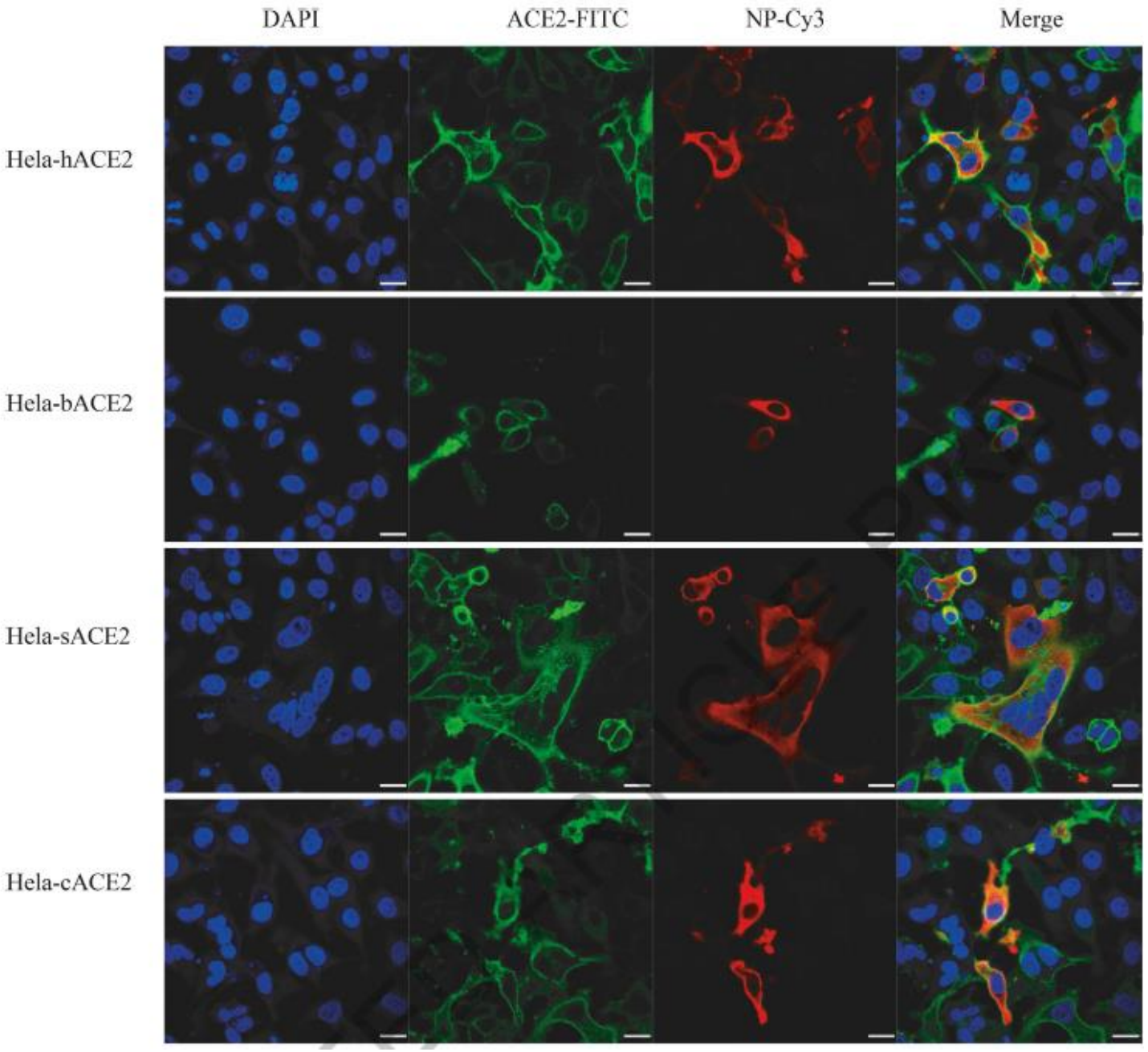


Journal of Virology Jan 2015, 89 (4) 1954-1964





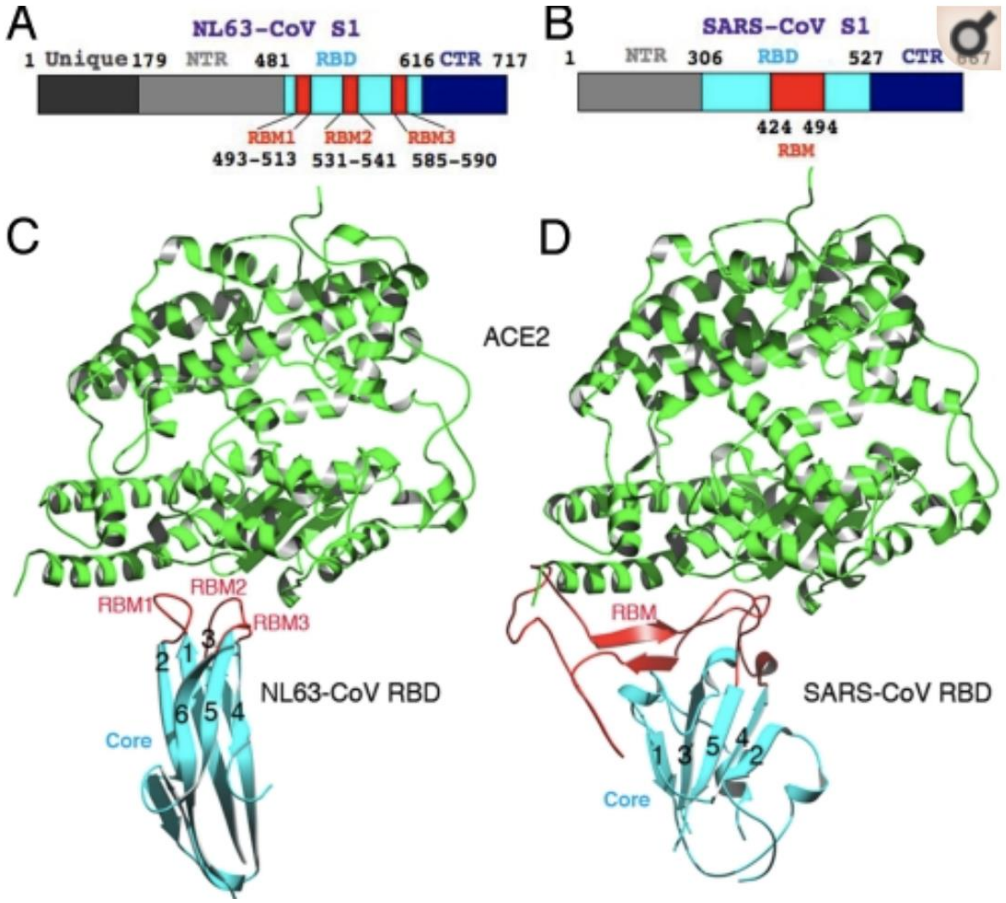
Functional assessment of cell entry and receptor usage for lineage B β-coronaviruses, including 2019-nCoV.

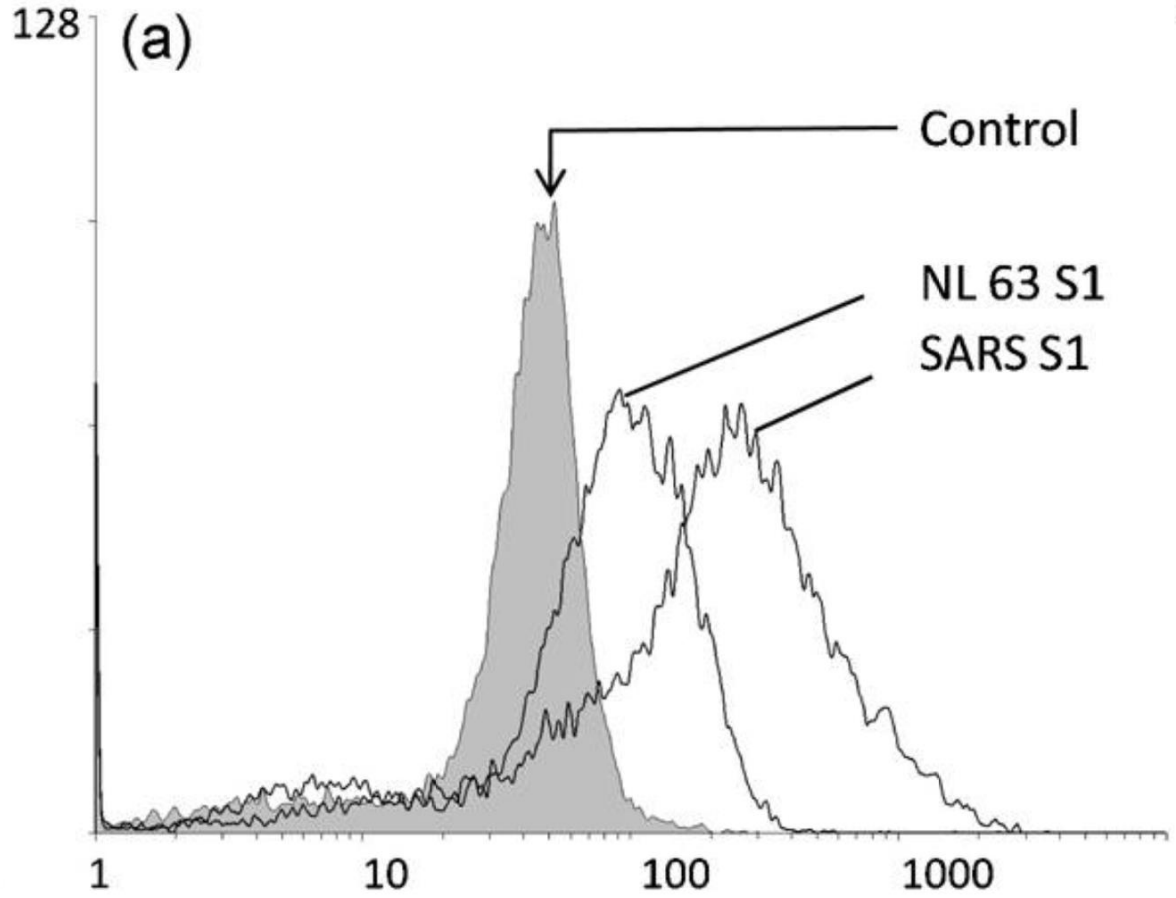


SARS-C0V-2 is able to use all but mouse ACE2 as an entry receptor (human, bat, swine, and civet), indicating which is likely the cell receptor of SARS-C0V-2.

Zhou, P., Yang, X., Wang, X. *et al. Nature* (2020).

A lower-affinity interaction with ACE-2 might partly explain the different pathological consequences of infection by SARS-CoV and NL63.





J Gen Virol. 2008 Nov; 89(Pt 11): 2741–2745.

Proc Natl Acad Sci U S A. 2009 Nov 24; 106(47): 19970–19974.

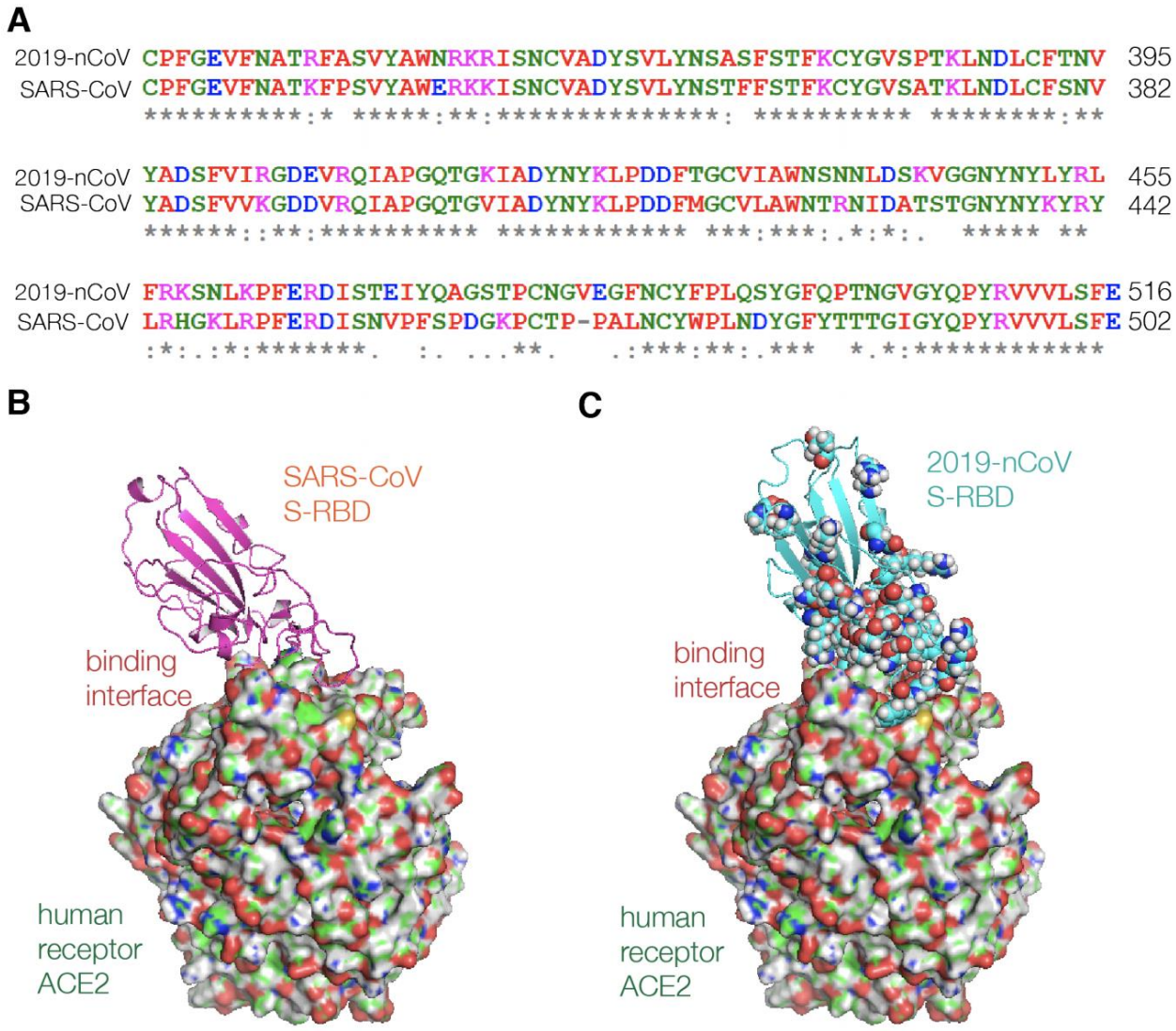
The binding strength of 2019-nCoV S-RBD vs. SARS-CoV S-RBD to ACE2:

- ~73% (Qiang Huang et al.)
- ~65% (Xu et al.)

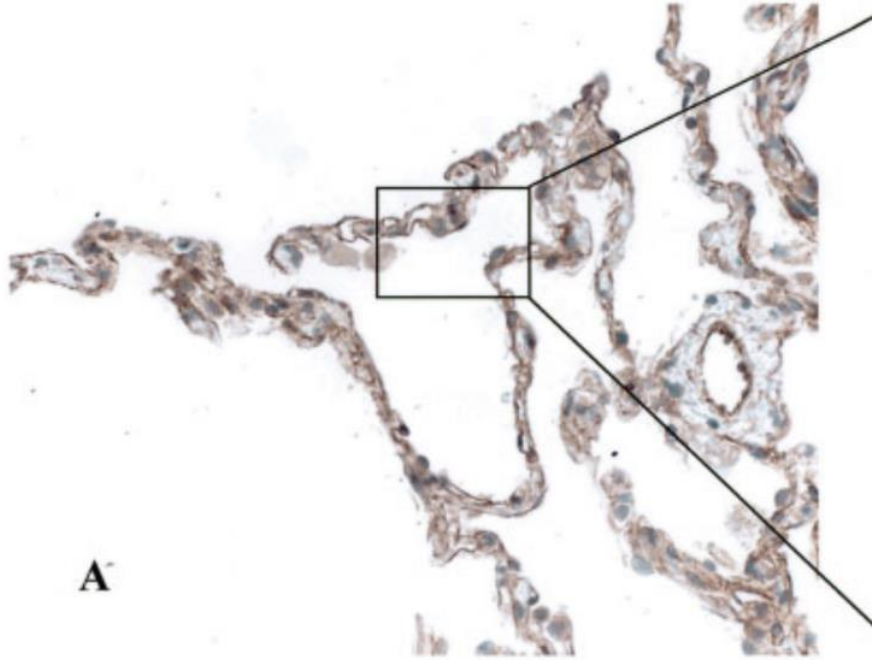
- 或許能解釋為什麼COVID19的症狀較SARS更偏輕症，和NL63類似。

$$\langle \Delta G^{SARS} \rangle \approx -36.6\ \text{kcal}\cdot\text{mol}^{-1}$$

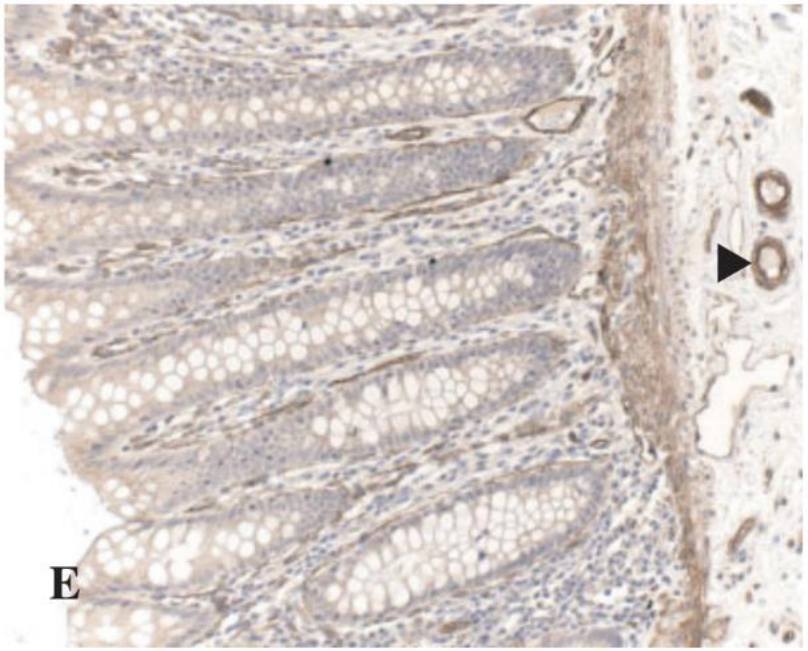
$$\langle \Delta G^{2019} \rangle \approx -27.2\ \text{kcal}\cdot\text{mol}^{-1}$$



ACE2不僅在肺部細胞存在，在腸胃道中的血管內皮細胞與平滑肌細胞也都存在。



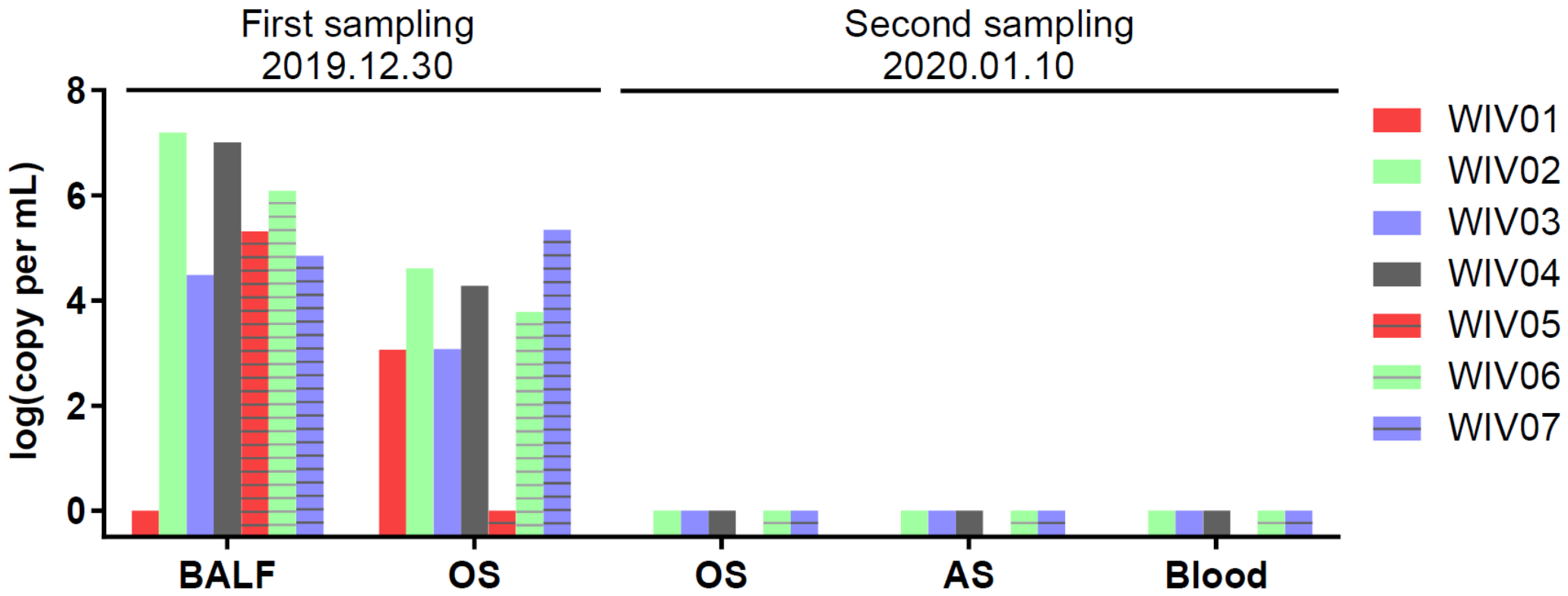
Positive staining for ACE2 is clearly present on alveolar epithelial cells and capillary endothelium.



In the colon, ACE2 staining is present in endothelium and vascular smooth muscle cells from the blood vessels (arrow-head) and in the muscular layers.

J Pathol 2004; 203: 631–637

在肛門拭子可找到病毒RNA，不等於可以糞口傳染



Molecular detection of 2019-nCoV in seven patients during two times of sampling.
BALF, bronchoalveolar lavage fluid; OS, oral swab; AS, anal swab.

Zhou, P., Yang, X., Wang, X. *et al.* *Nature* (2020).

ELSEVIER

Journal of Virological Methods 128 (2005) 156–161

www.elsevier.com/locate/jviromet

Concentration and detection of SARS coronavirus in sewage from Xiao Tang Shan Hospital and the 309th Hospital

X
Zhong
Wei
Fa

Journal of Clinical Virology 48 (2010) 27–30

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

ELSEVIER

Detection of human coronaviruses in children with acute gastroenteritis

Minna Risku

Enteric Involvement of Severe Acute Respiratory Syndrome–Associated Coronavirus Infection

WAI K. LEUNG,* KA–FAI TO,† PAUL K. S. CHAN,§ HENRY L. Y. CHAN,* ALAN K. L. WU,* NELSON LEE,* KWOK Y. YUEN,‖ and JOSEPH J. Y. SUNG*

Departments of *Medicine and Therapeutics, †Anatomical and Cellular Pathology, and §Microbiology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong; and ‖Department of Microbiology, University of Hong Kong, Hong Kong

THE LANCET

Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records

Huijun Chen, Juanjuan Guo*, Chen Wang*, Fan Luo, Xuechen Yu, Wei Zhang, Jiafu Li, Dongchi Zhao, Dan Xu, Qing Gong, Jing Liao, Huixia Yang, Wei Hou, Yuanzhen Zhang*

Amniotic fluid, cord blood, neonatal throat swab, and breastmilk samples from six patients were tested for SARS-CoV-2, and all samples tested negative for the virus.

→目前沒有證據顯示有垂直傳染的可能。

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1. Introduction to coronavirus (CoV)
2. Virology of SARS-CoV-2
3. Genomic epidemiology of SARS-CoV-2
4. Clinical manifestations of COVID19
5. Possible explanations for some crucial questions
6. Future perspectives

Genomic epidemiology of novel coronavirus (nCoV)

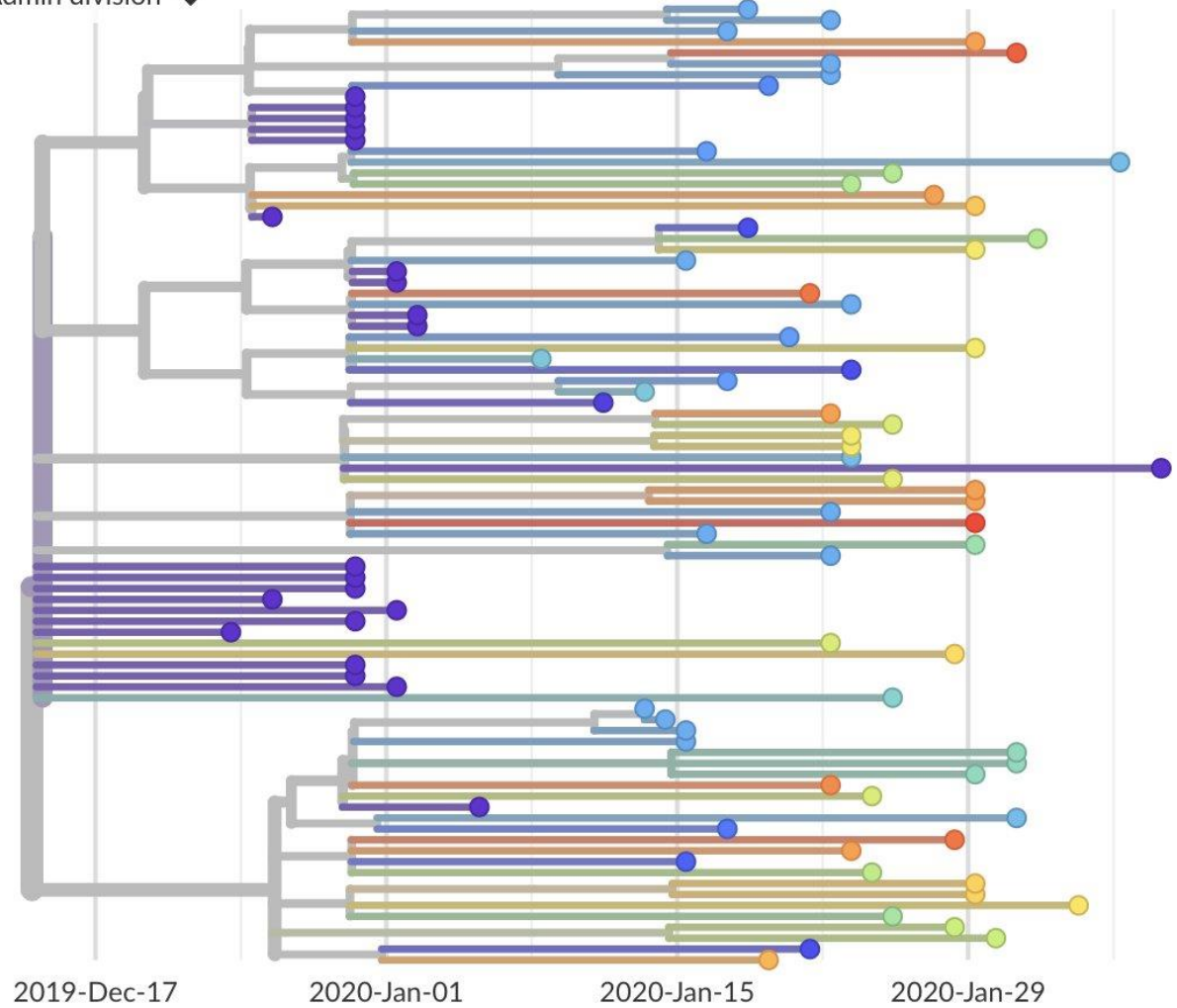
Built with github.com/nextstrain/ncov using data from GISAID.

Showing 89 of 89 genomes sampled between Dec 2019 and Feb 2020.

Phylogeny

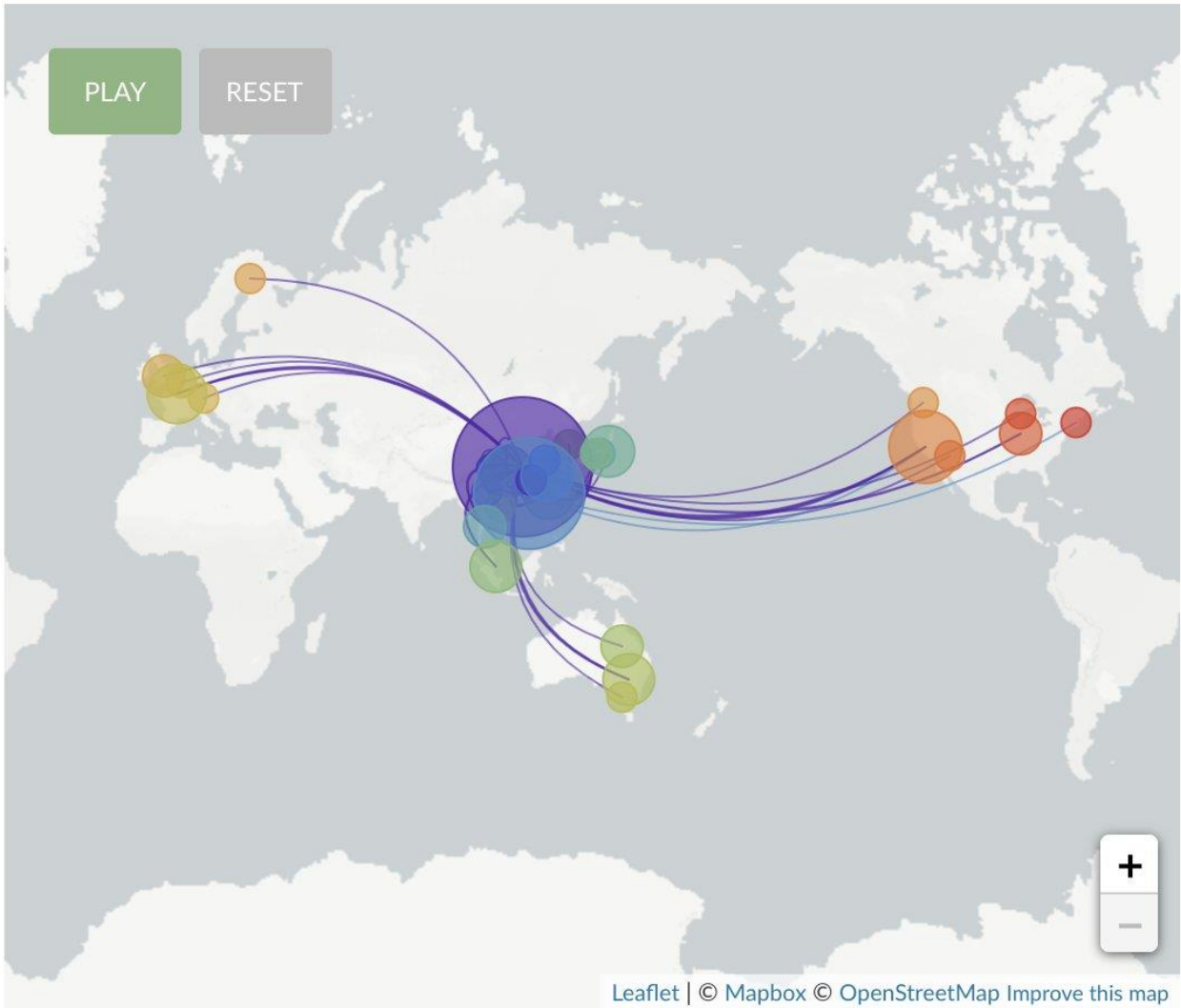
RESET LAYOUT

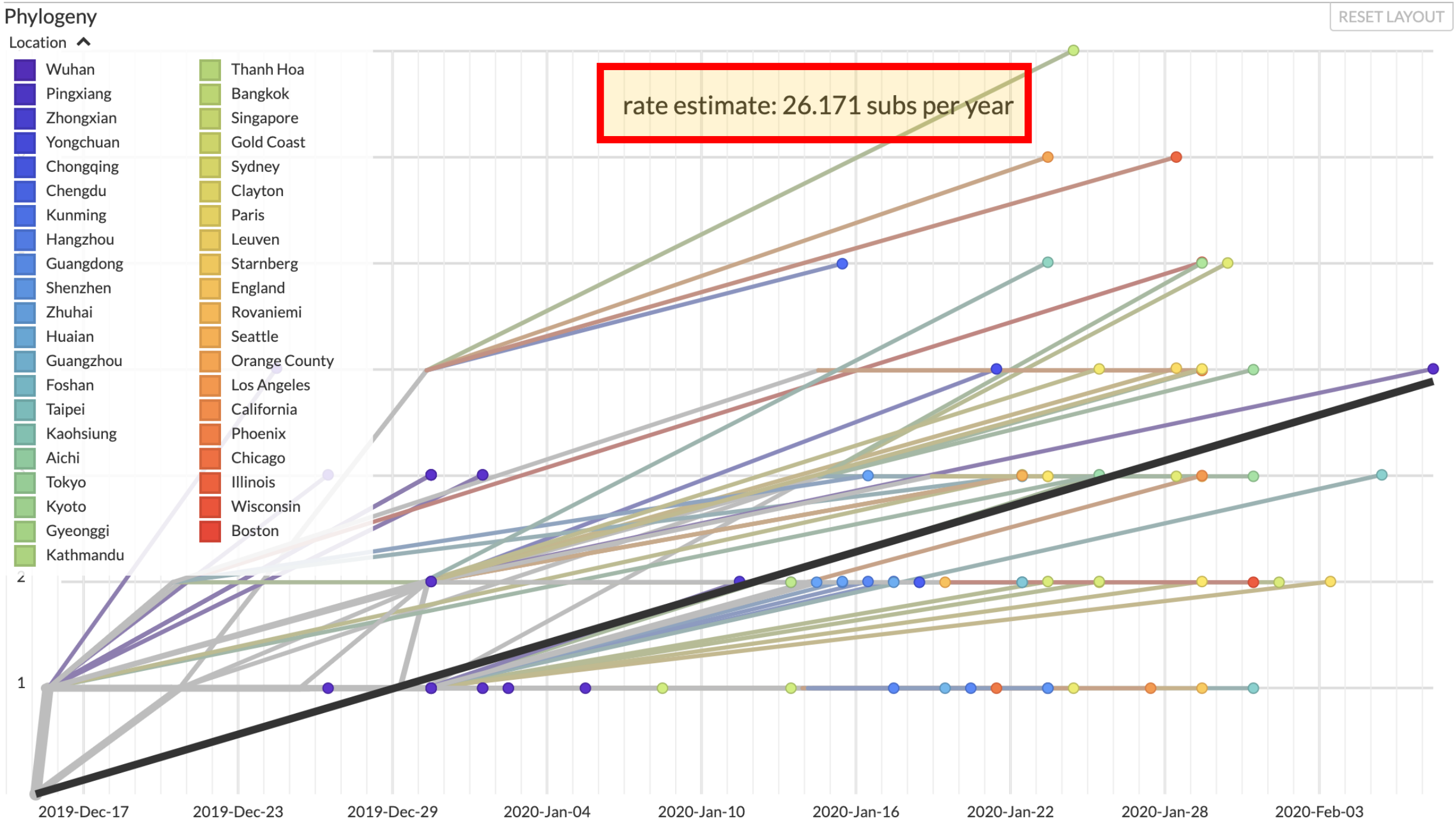
Admin division



Transmissions

RESET ZOOM



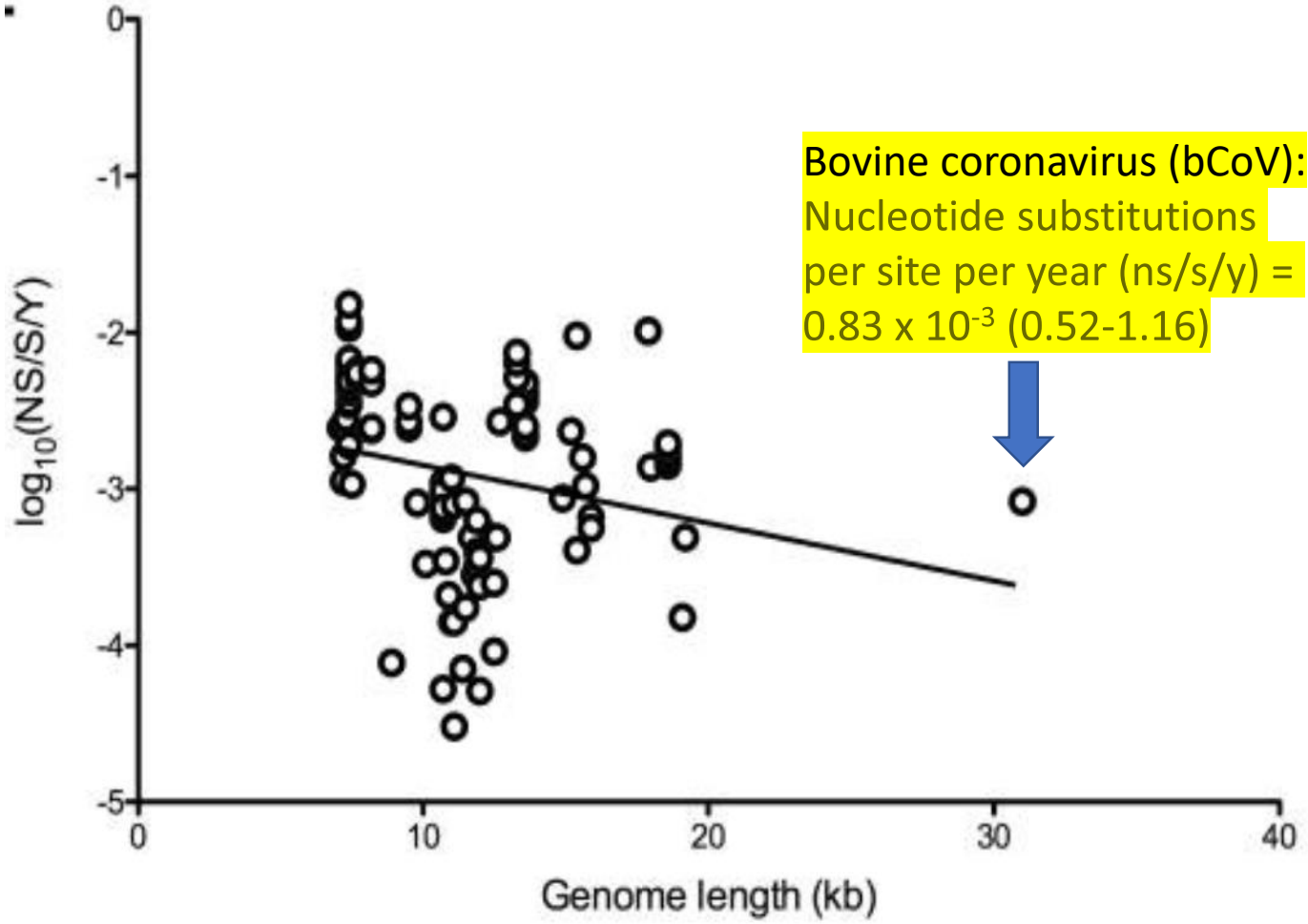

Phylogeny
RESET LAYOUT
Location
Wuhan
Pingxiang
Zhongxian
Yongchuan
Chongqing
Chengdu
Kunming
Hangzhou
Guangdong
Shenzhen
Zhuhai
Huaian
Guangzhou
Foshan
Taipei
Kaohsiung
Aichi
Tokyo
Kyoto
Gyeonggi
Kathmandu
Thanh Hoa
Bangkok
Singapore
Gold Coast
Sydney
Clayton
Paris
Leuven
Starnberg
England
Rovaniemi
Seattle
Orange County
Los Angeles
California
Phoenix
Chicago
Illinois
Wisconsin
Boston
rate estimate: 26.171 subs per year
2
1
2019-Dec-17
2019-Dec-23
2019-Dec-29
2020-Jan-04
2020-Jan-10
2020-Jan-16
2020-Jan-22
2020-Jan-28
2020-Feb-03

OPEN ACCESS Freely available online

PLOS | PATHOGENS

Cell Tropism Predicts Long-term Nucleotide Substitution Rates of Mammalian RNA Viruses

Allison L. Hicks, Siobain Duffy*

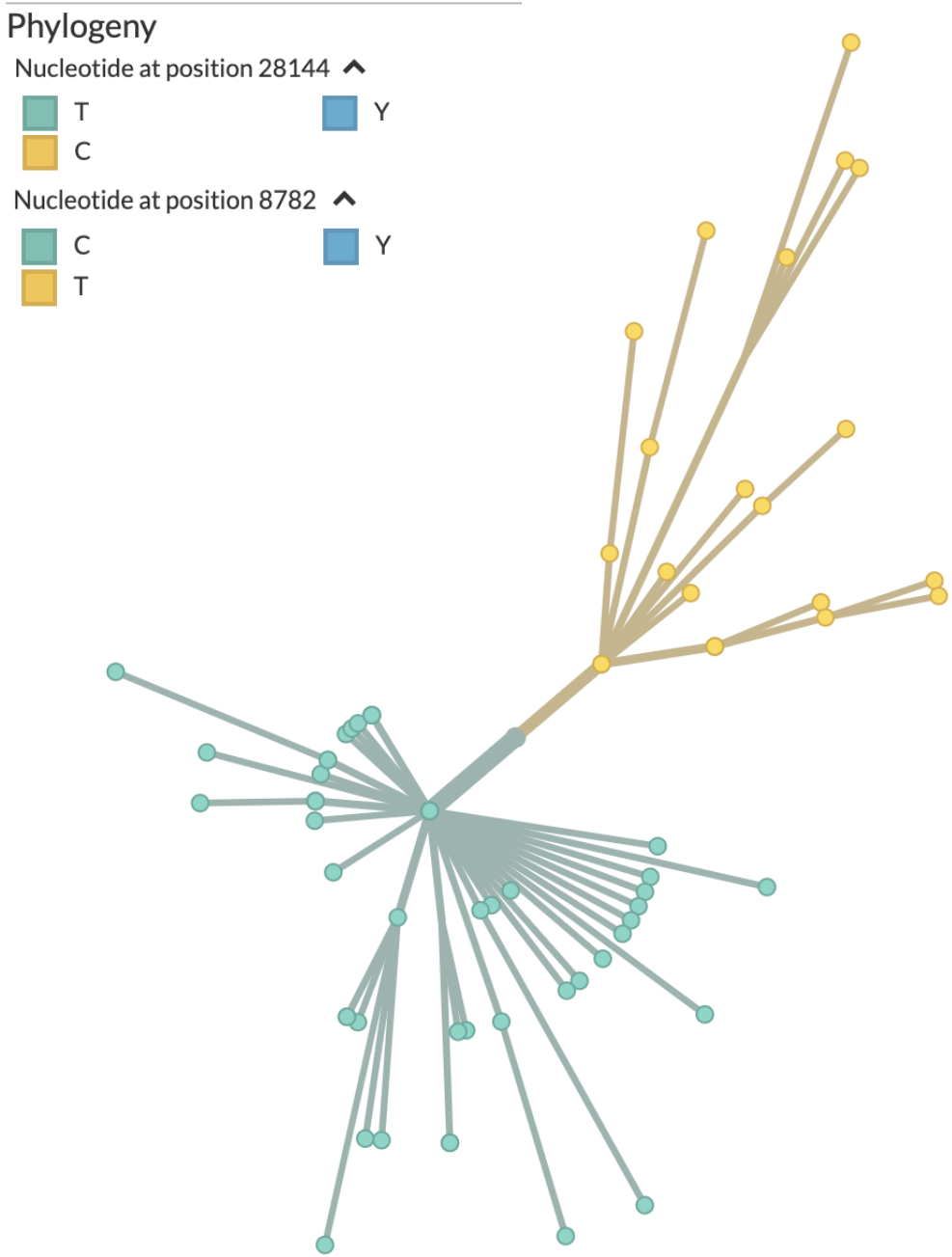


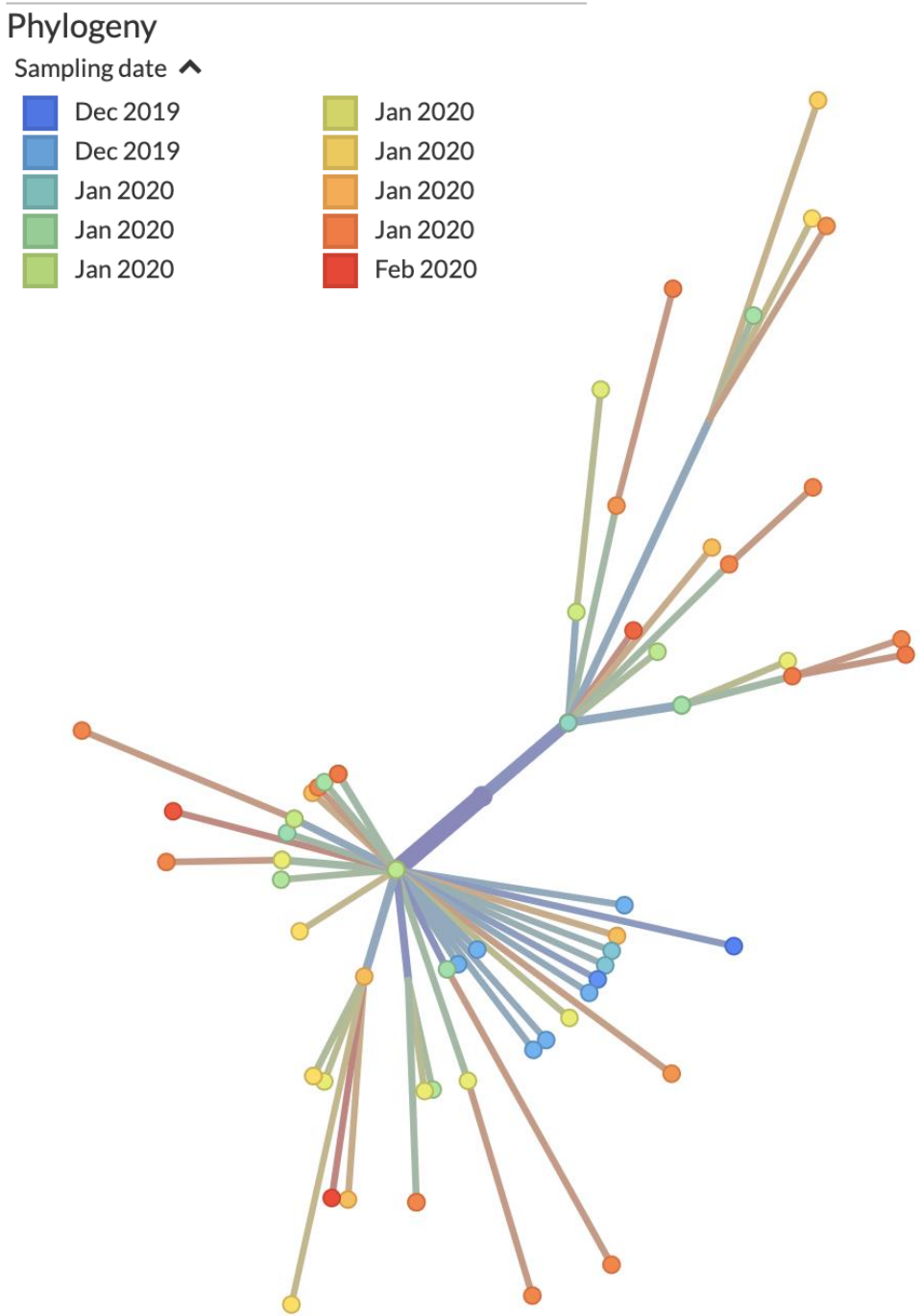
Bovine coronavirus (bCoV): Nucleotide substitutions per site per year (ns/s/y) = 0.83×10^{-3} (0.52-1.16)

$0.83 \times 10^{-3} \times 30000$
$= 24.9$ ns/s/y

和目前SARS-CoV-2的突變速度相近。

PLoS Pathog. 2014 Jan; 10(1): e1003838.


Phylogeny
Nucleotide at position 28144
T
Y
C
Nucleotide at position 8782
C
Y
T


Phylogeny
Sampling date
Dec 2019
Dec 2019
Jan 2020
Jan 2020
Jan 2020
Jan 2020
Jan 2020
Jan 2020
Jan 2020
Feb 2020

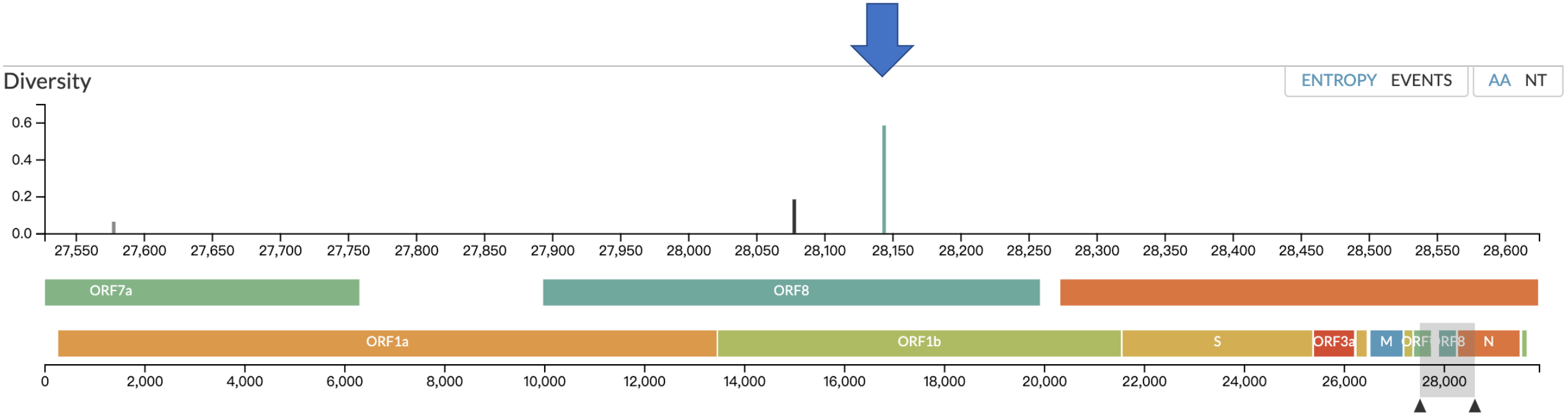
Phylogeny

Genotype at ORF8 site 84

L (Leucine)

S (Serine)

X



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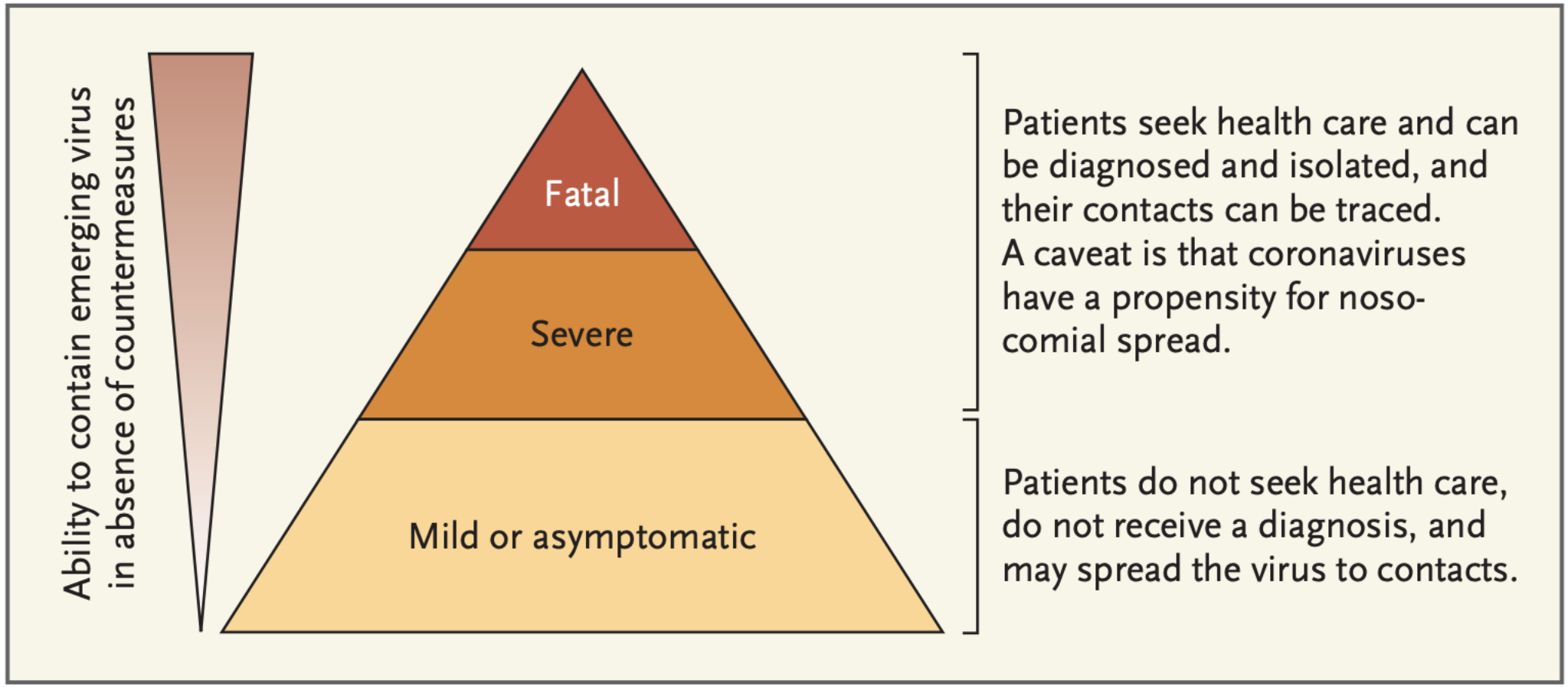


Figure 1. Surveillance Pyramid and Its Relation to Outbreak Containment.

The proportion of mild and asymptomatic cases versus severe and fatal cases is currently unknown for 2019-nCoV — a knowledge gap that hampers realistic assessment of the virus's epidemic potential and complicates the outbreak response.

華南市場41例新型冠狀病毒患者

患者背景	所有病人 (N=41)	重症ICU (N=13)	輕症非ICU (N=28)
	中位數 (四分位距) / 比例		
年齡 (歲)	49 (41-58)	49 (41-61)	49 (41-57.5)
男性	73%	85%	68%
體溫	70.6%	70%	71.4%
<37.3	2%	0%	4%
37.3-38.0	20%	23%	18%
> 38.0	78%	77%	78%
咳嗽	76%	85%	71%
有痰	28%	38%	23%
喘	55%	92%	37%
肌肉痠痛或疲倦	44%	54%	71%
共病症	32%	38%	29%

資料來源：Huang C, Wang Y, Li X, et al. Lancet 2020; published online Jan 24.

胸腔重症 蘇一峰醫師

武漢金銀潭醫院99例新型冠狀病毒患者

患者背景	所有病人 (N=99)	患者背景	所有病人 (N=99)
年齡 (平均，歲)	55.5 (21-82)	胸痛	2%
男性	68%	腹瀉	2%
發燒	83%	噁心嘔吐	1%
咳嗽	82%	慢性病	51%
喘	31%	心血管腦血管疾病	40%
發燒+咳嗽+喘	15%	消化道疾病	11%
肌肉痠痛	11%	內分泌疾病	13%
意識混亂	9%	癌症	1%
喉嚨痛	5%	神經系統	1%
流鼻水	4%	呼吸道	1%

資料來源：Chen N, et al. Lancet 2020; published online Jan 29.

胸腔重症 蘇一峰醫師

138 patients

Table 1. Baseline Characteristics of Patients Infected With 2019-nCoV

	No. (%)			
	Total (N = 138)	ICU (n = 36)	Non-ICU (n = 102)	*P* Value[a]
Age, median (IQR), y	56 (42-68)	66 (57-78)	51 (37-62)	<.001
Sex				
Female	63 (45.7)	14 (38.9)	51 (37-62)	.34
Male	75 (54.3)	22 (61.1)	53 (52.0)	
Huanan Seafood Wholesale Market exposure	12 (8.7)	5 (13.9)	7 (6.9)	.30
Infected				
Hospitalized patients	17 (12.3)	9 (25.0)	8 (7.8)	.02
Medical staff	40 (29)	1 (2.8)	39 (38.2)	<.001
Comorbidities	64 (46.4)	26 (72.2)	38 (37.3)	<.001
Hypertension	43 (31.2)	21 (58.3)	22 (21.6)	<.001
Cardiovascular disease	20 (14.5)	9 (25.0)	11 (10.8)	.04
Diabetes	14 (10.1)	8 (22.2)	6 (5.9)	.009
Malignancy	10 (7.2)	4 (11.1)	6 (5.9)	.29
Cerebrovascular disease	7 (5.1)	6 (16.7)	1 (1.0)	.001
COPD	4 (2.9)	3 (8.3)	1 (1.0)	.054
Chronic kidney disease	4 (2.9)	2 (5.6)	2 (2.0)	.28
Chronic liver disease	4 (2.9)	0	4 (3.9)	.57
HIV infection	2 (1.4)	0	2 (2.0)	>.99
Signs and symptoms				
Fever	136 (98.6)	36 (100)	100 (98.0)	>.99
Fatigue	96 (69.6)	29 (80.6)	67 (65.7)	.10
Dry cough	82 (59.4)	21 (58.3)	61 (59.8)	.88
Anorexia	55 (39.9)	24 (66.7)	31 (30.4)	<.001
Myalgia	48 (34.8)	12 (33.3)	36 (35.3)	.83
Dyspnea	43 (31.2)	23 (63.9)	20 (19.6)	<.001
Expectoration	37 (26.8)	8 (22.2)	29 (28.4)	.35
Pharyngalgia	24 (17.4)	12 (33.3)	12 (11.8)	.003
Diarrhea	14 (10.1)	6 (16.7)	8 (7.8)	.20
Nausea	14 (10.1)	4 (11.1)	10 (9.8)	>.99
Dizziness	13 (9.4)	8 (22.2)	5 (4.9)	.007
Headache	9 (6.5)	3 (8.3)	6 (5.9)	.70
Vomiting	5 (3.6)	3 (8.3)	2 (2.0)	.13
Abdominal pain	3 (2.2)	3 (8.3)	0 (0)	.02
Onset of symptom to, median (IQR), d				
Hospital admission	7.0 (4.0-8.0)	8.0 (4.5-10.0)	6.0 (3.0-7.0)	.009
Dyspnea	5.0 (1.0-10.0)	6.5 (3.0-10.8)	2.5 (0.0-7.3)	.02
ARDS	8.0 (6.0-12.0)	8.0 (6.0-12.0)	8.0 (6.3-11.3)	.97
Heart rate, median (IQR), bpm	88 (78-97)	89 (81-101)	86 (77-96)	.14
Respiratory rate, median (IQR)	20 (19-21)	20 (16-25)	20 (19-21)	.57
Mean arterial pressure, median (IQR), mm Hg	90 (84-97)	91 (78-96)	90 (85-98)	.33

Abbreviations: ARDS, acute respiratory distress syndrome; bpm, beats per minute; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IQR, interquartile range; 2019-nCoV, 2019 novel coronavirus.

[a] *P* values indicate differences between ICU and non-ICU patients. *P* < .05 was considered statistically significant.

JAMA. 2020 Feb 7.

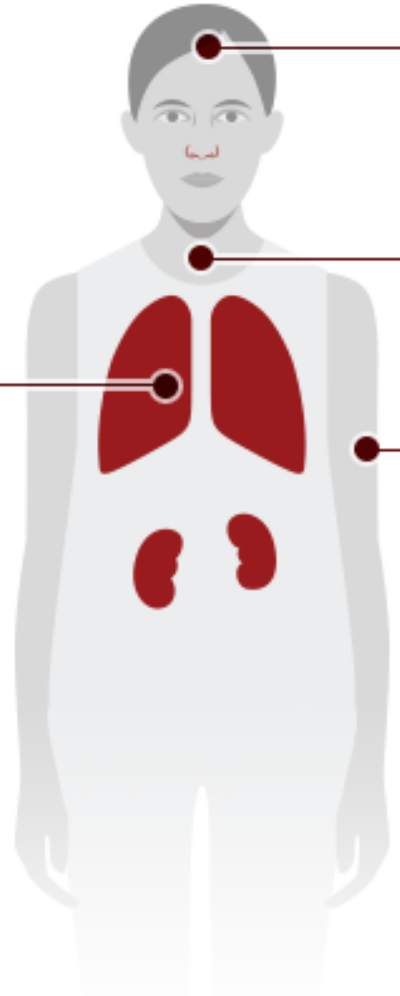
1,099例新型冠狀病毒急性呼吸道疾病

患者背景	所有病人	患者背景	所有病人
	1099		1099
年齡 (中位數、歲)	47	咳嗽	67.7%
男性	58.2%	痰	33.4%
住院前發燒	43.1%	疲勞	38.1%
住院前體溫>38	21.4%	喘	18.6%
住院後發燒	87.9%	噁心嘔吐	5%
結膜充血	0.8%	腹瀉	3.7%
鼻充血	4.8%	肌肉痠痛關節痛	14.8%
頭痛	13.6%	發冷	11.4%
喉嚨痛	13.9%	咳血	0.9%
喉嚨充血	1.7%	紅疹	0.2%

資料來源：Zhong NS, et al. medRxiv preprint first posted online Feb. 9, 2020.

胸腔重症 蘇一峰醫師

Symptoms of China coronavirus



Headache

Cough

Shortness of breath
breathing difficulties

Muscle pain

Fever &
tiredness

Virus seems to start
with a **fever**,
followed by a **dry cough**
and then, after a week,
leads to **shortness of breath**
and some patients
needing hospital treatment

World Health Organization (WHO)
@WHO

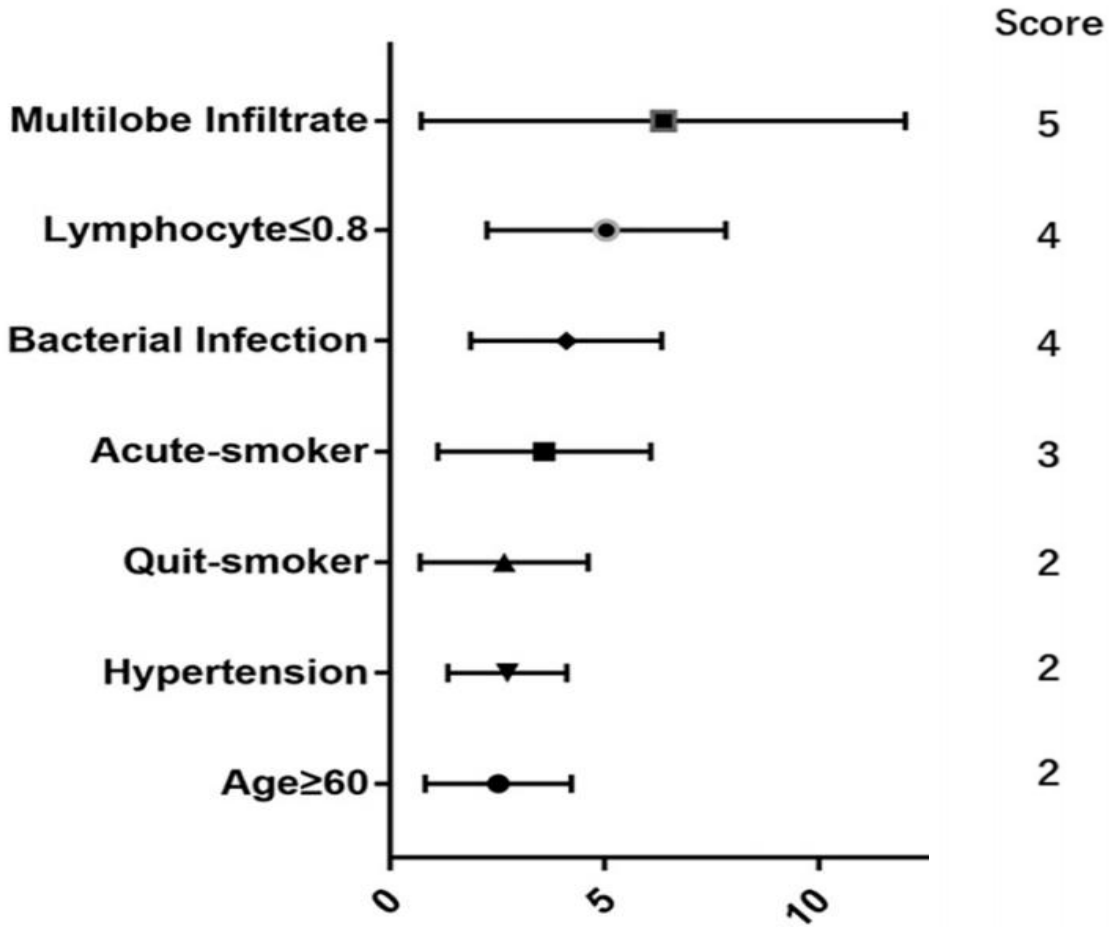
- 82% develop mild symptoms
- 15% develop severe symptoms
- 3% become critically ill

Source: WHO

BBC

MuLBSTA Score

Multilobular infiltration, hypo-Lymphocytosis, Bacterial coinfection, Smoking history, hyper-Tension and Age



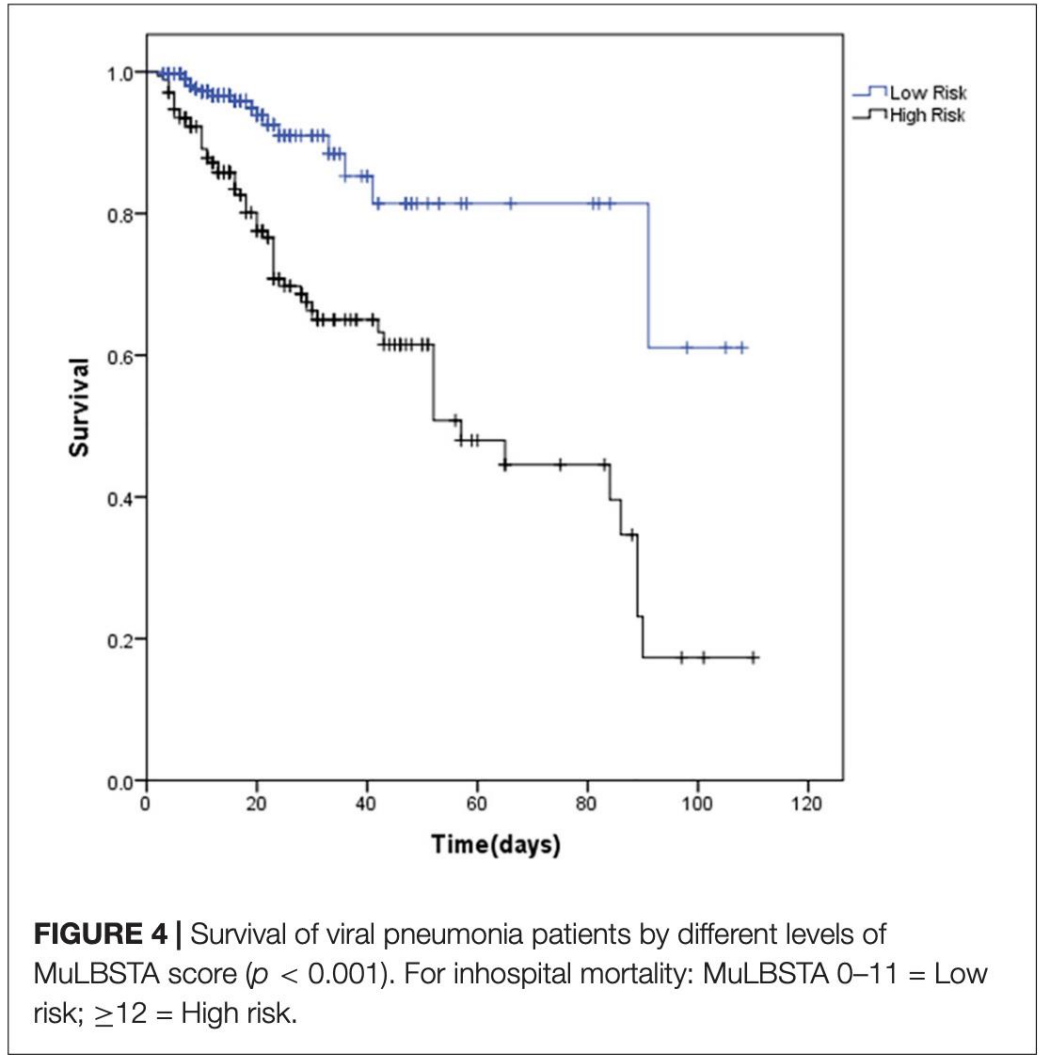


FIGURE 4 | Survival of viral pneumonia patients by different levels of MuLBSTA score ($p < 0.001$). For inhospital mortality: MuLBSTA 0–11 = Low risk; ≥12 = High risk.

Front. Microbiol., 03 December 2019

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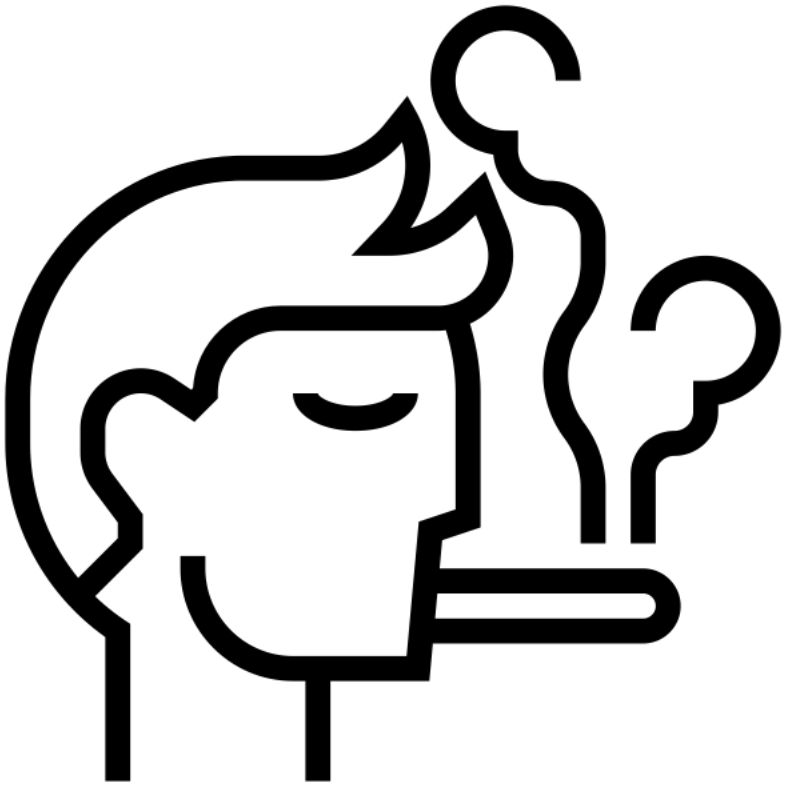
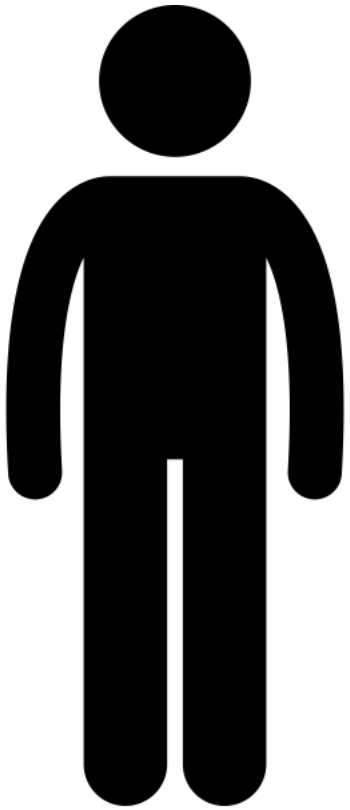
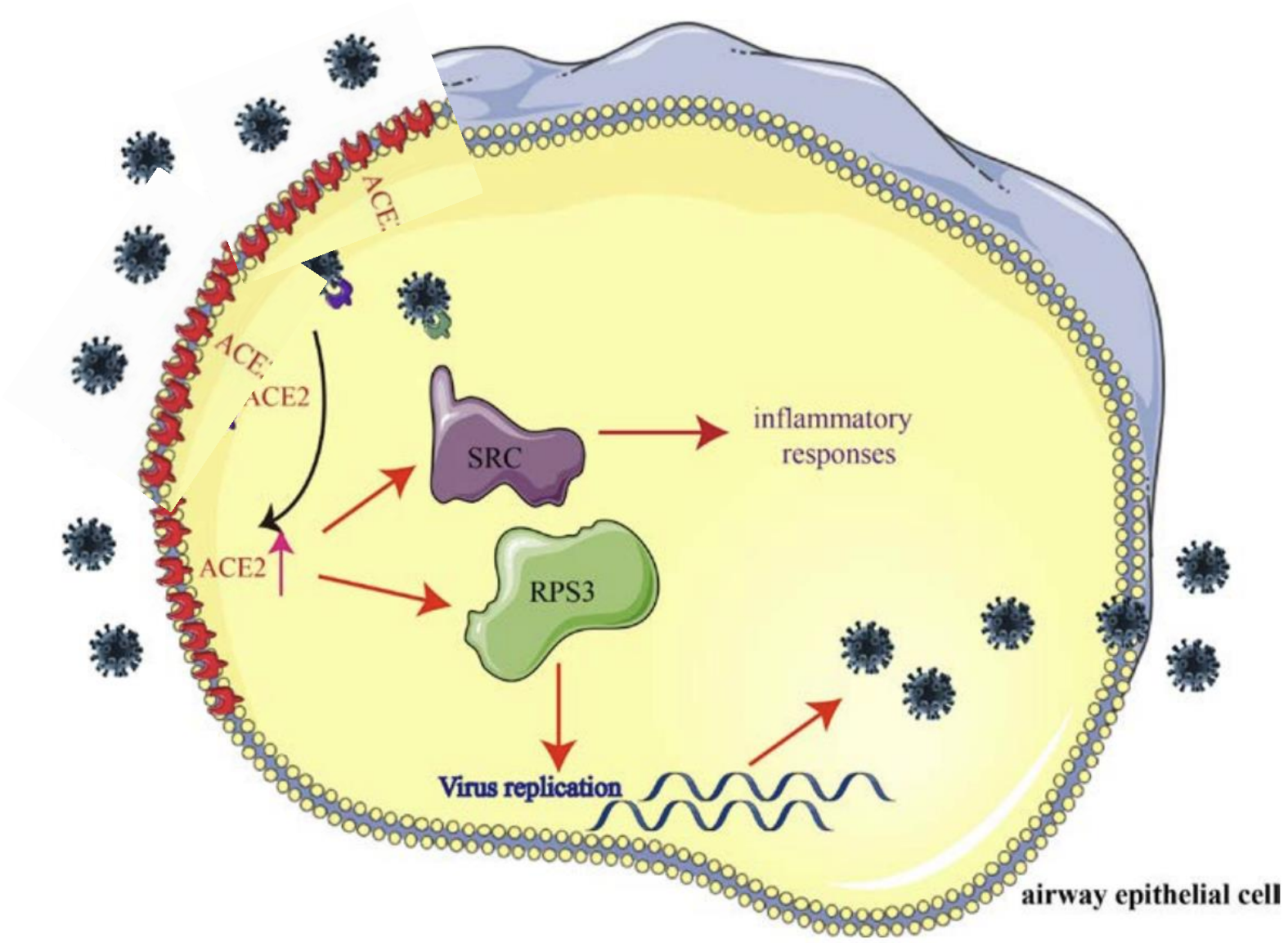


Smoking history



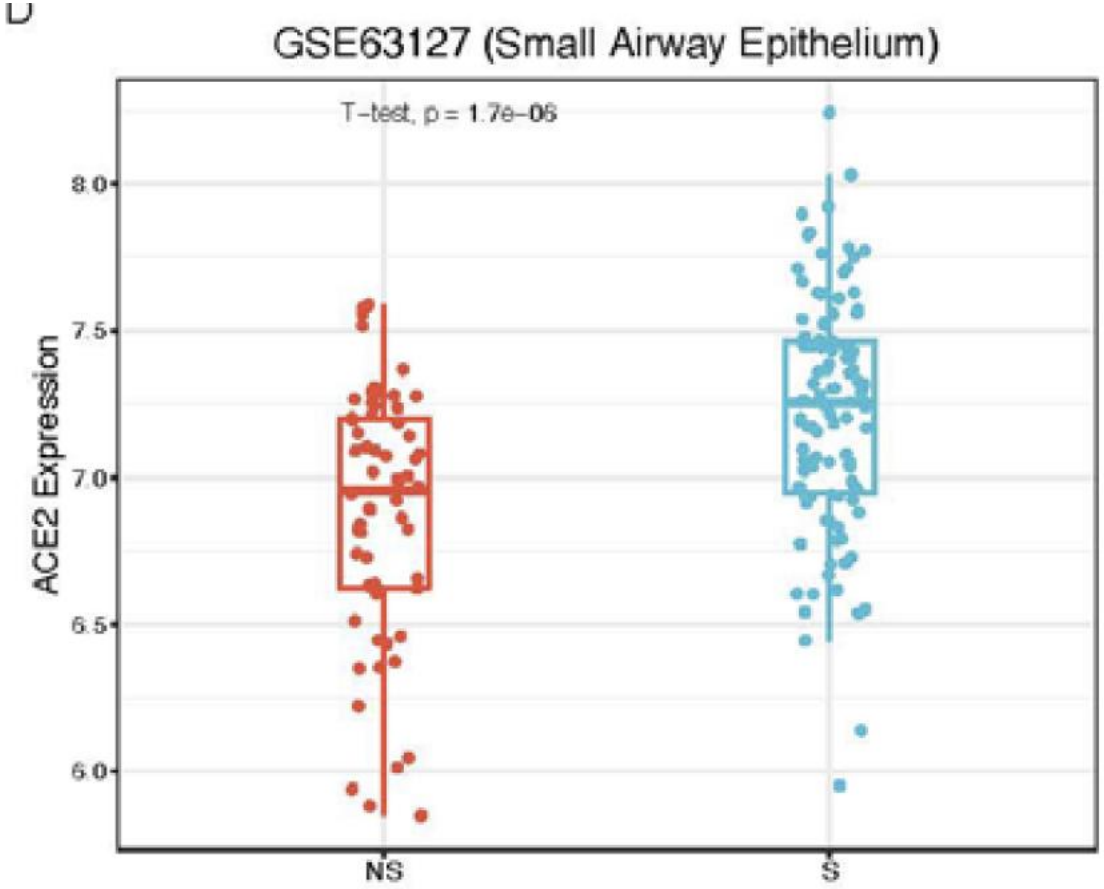
Male gender

Mild symptoms in children



Nat Med. 2005 Aug;11(8):875-9.

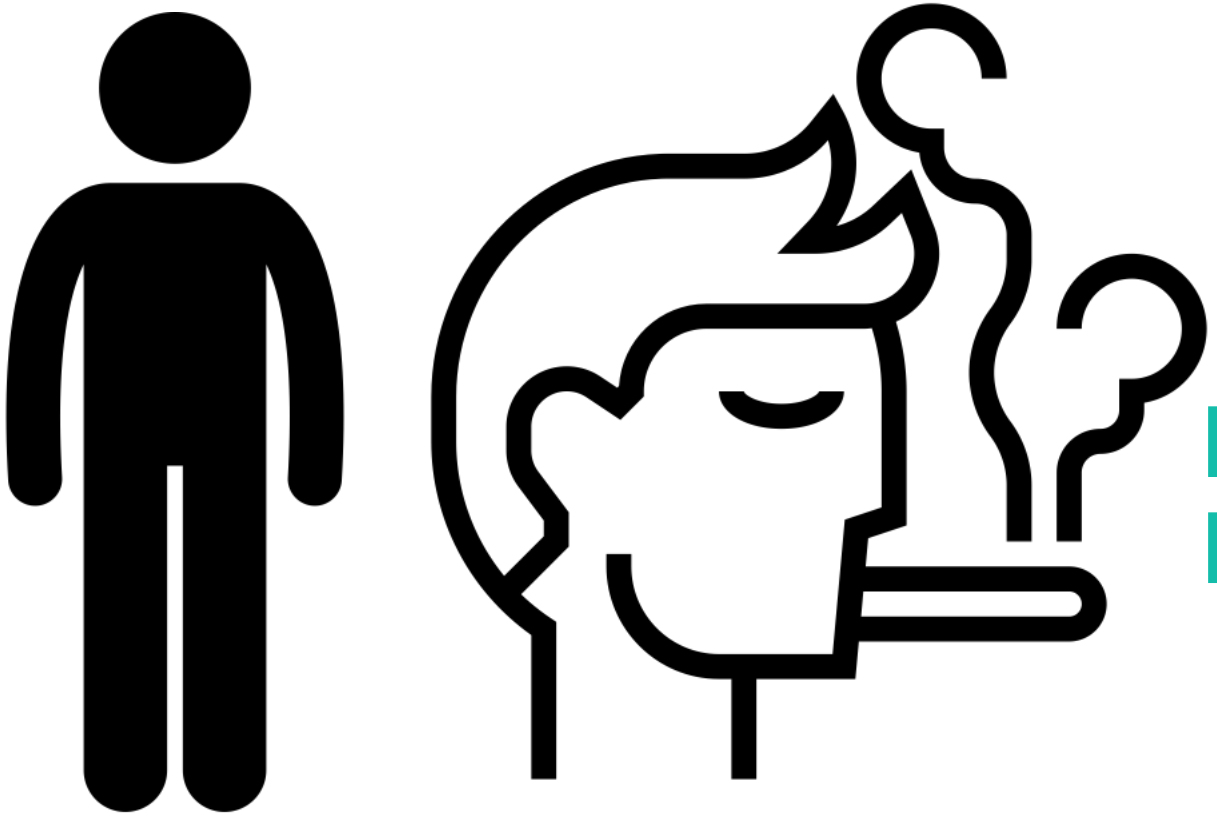
Significantly higher ACE2 gene expression in smokers compared to non-smokers.



Variable	Beta	P-value
Platform: RNA-seq	-5.940	<2e-16
Race: Caucasian	0.088	0.359
Age: >60	-0.012	0.900
Gender: Male	0.105	0.352
Smoking: Smoker	0.313	**0.008**

Xiang He et al. 2020 medRxiv preprint.

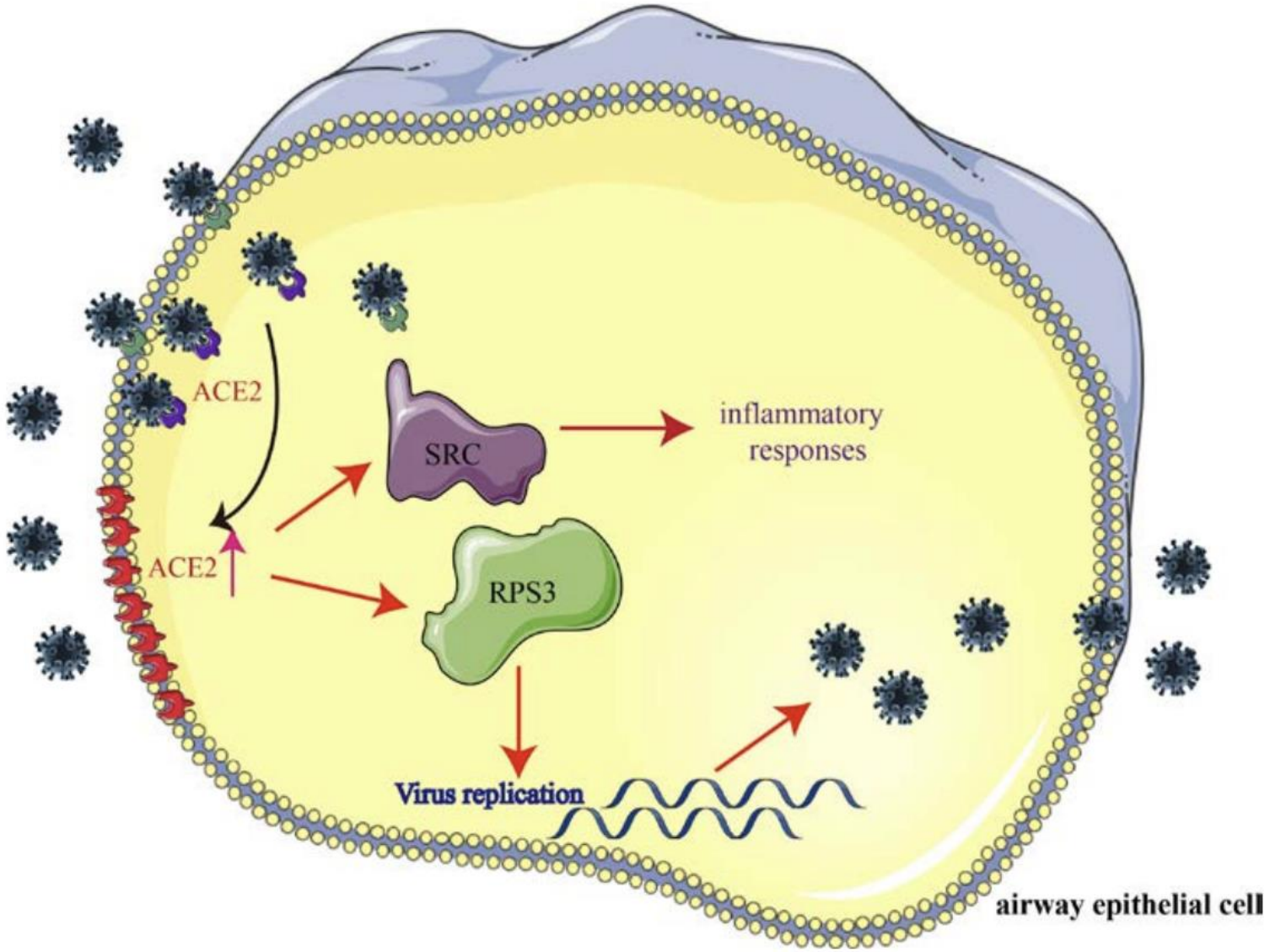
Cai, G. et al. *Preprints* **2020**

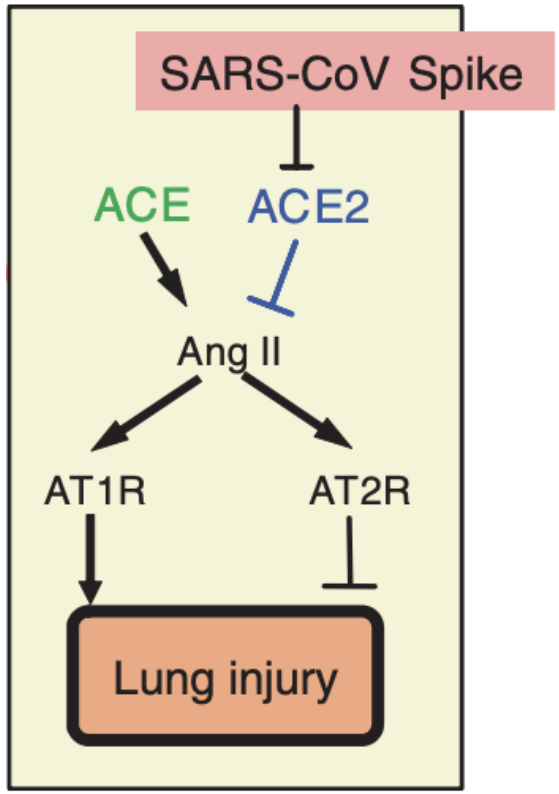


Male gender

Smoking history

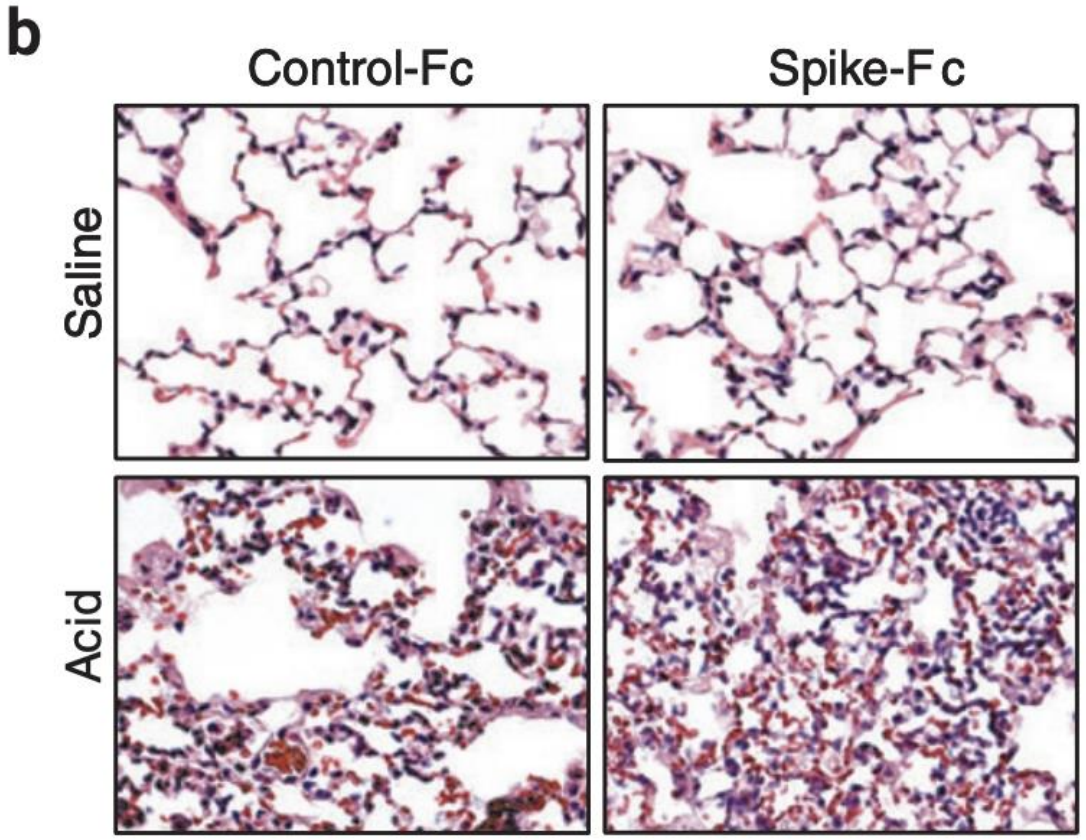
= 48%

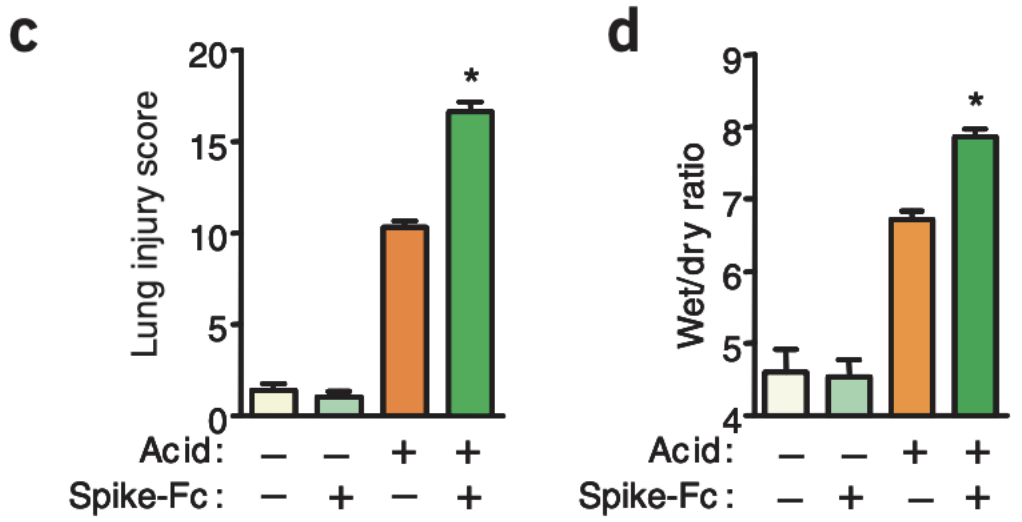




Nat Med. 2005 Aug;11(8):875-9.

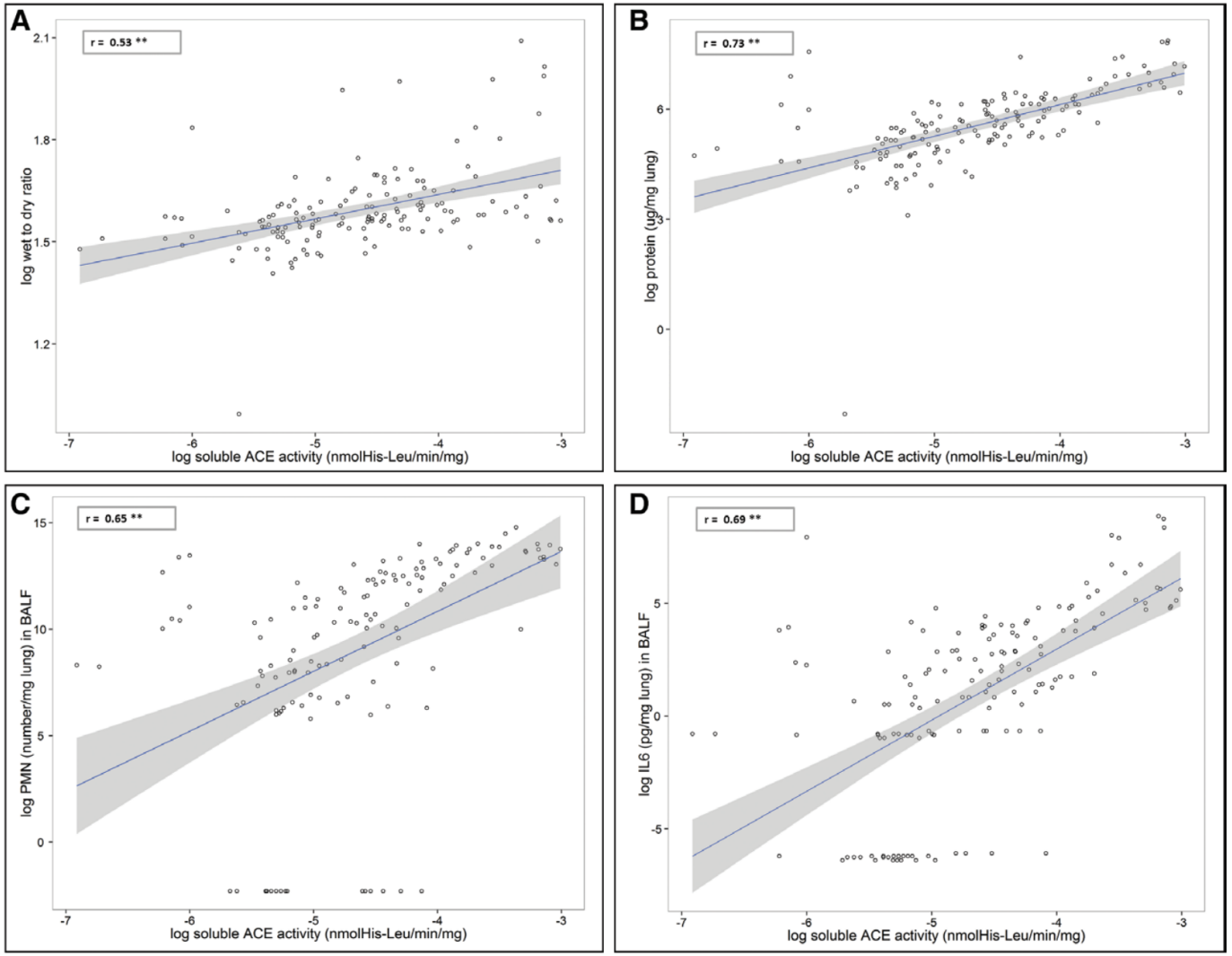
The SARS-CoV Spike protein enhances the severity of acute lung injury.





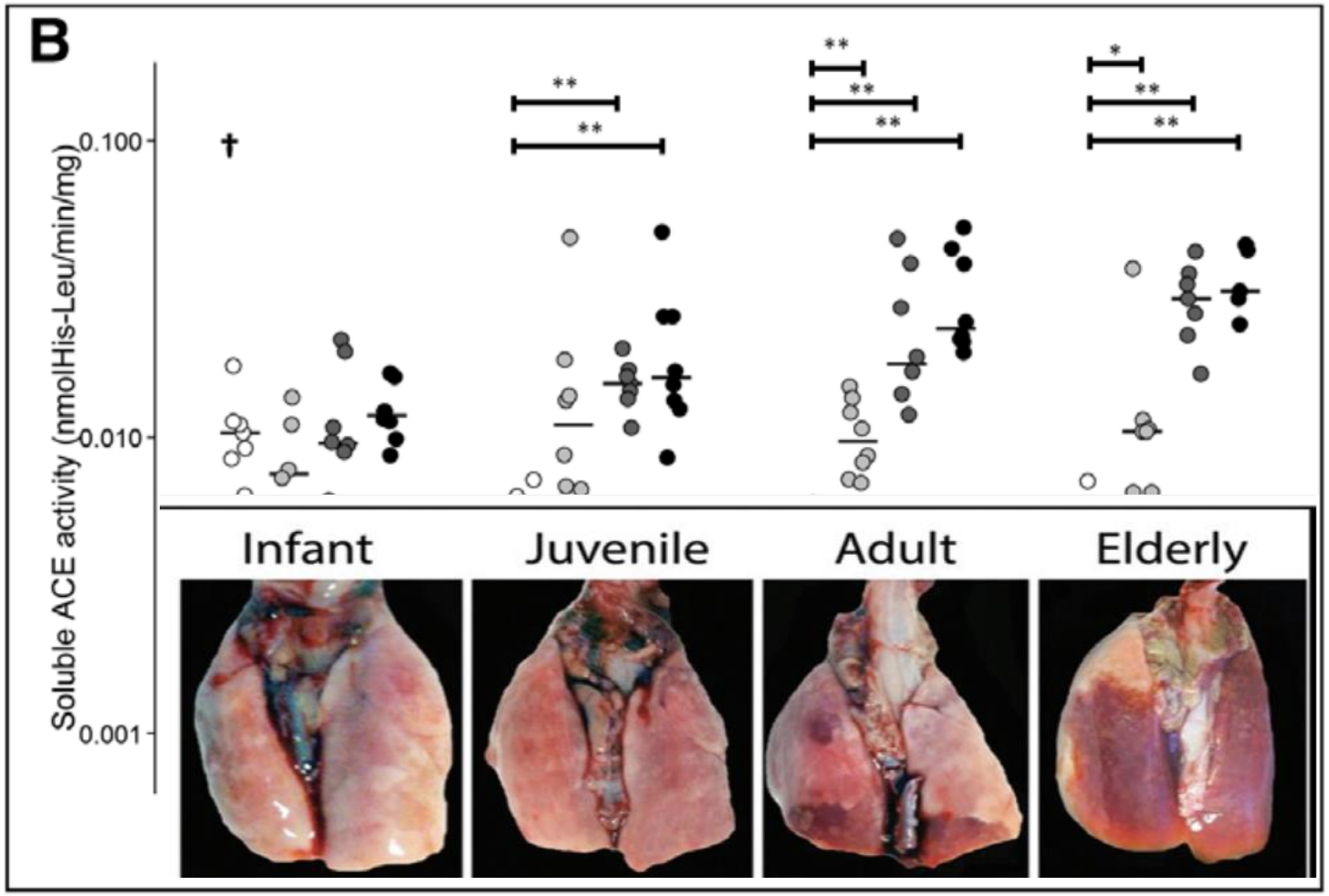
Nat Med. 2005 Aug;11(8):875-9.

Correlation between soluble ACE activity and lung injury and inflammation.



Crit Care Med. 2016 Dec;44(12):e1226-e1235.

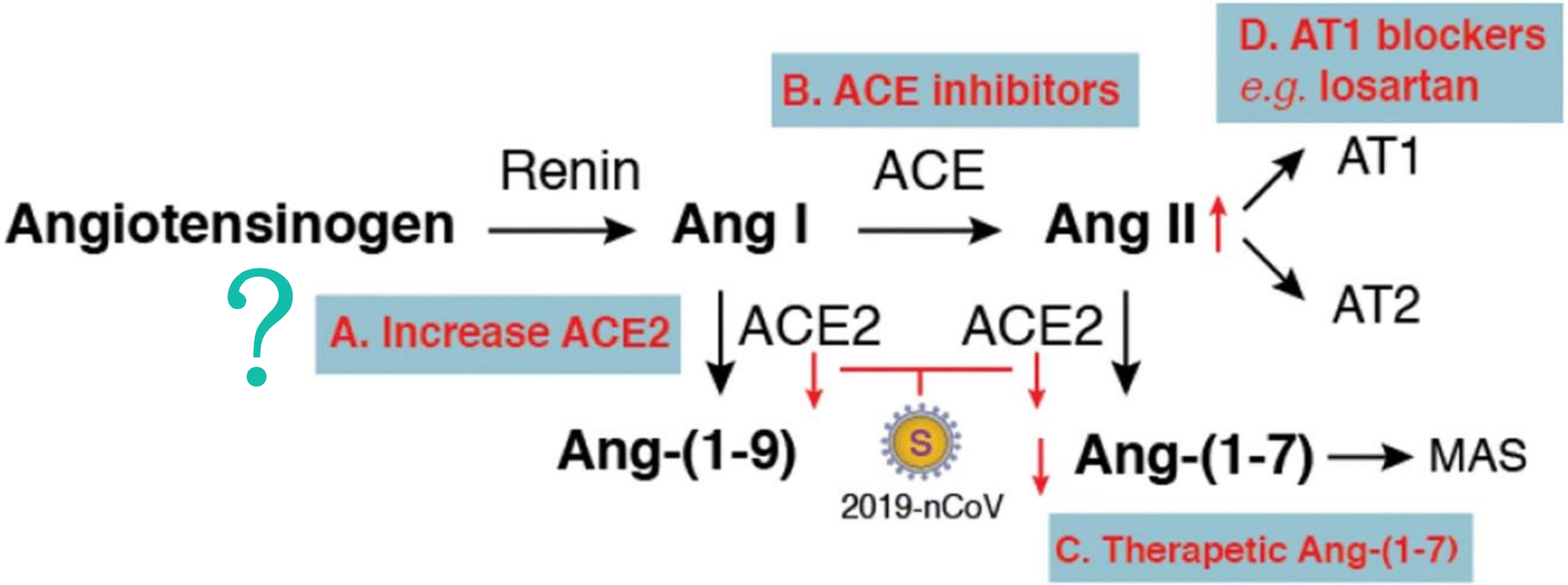
Age Is Associated With Differences in the ACE Activity in Response to Injury in Mice



Crit Care Med. 2016 Dec;44(12):e1226-e1235.

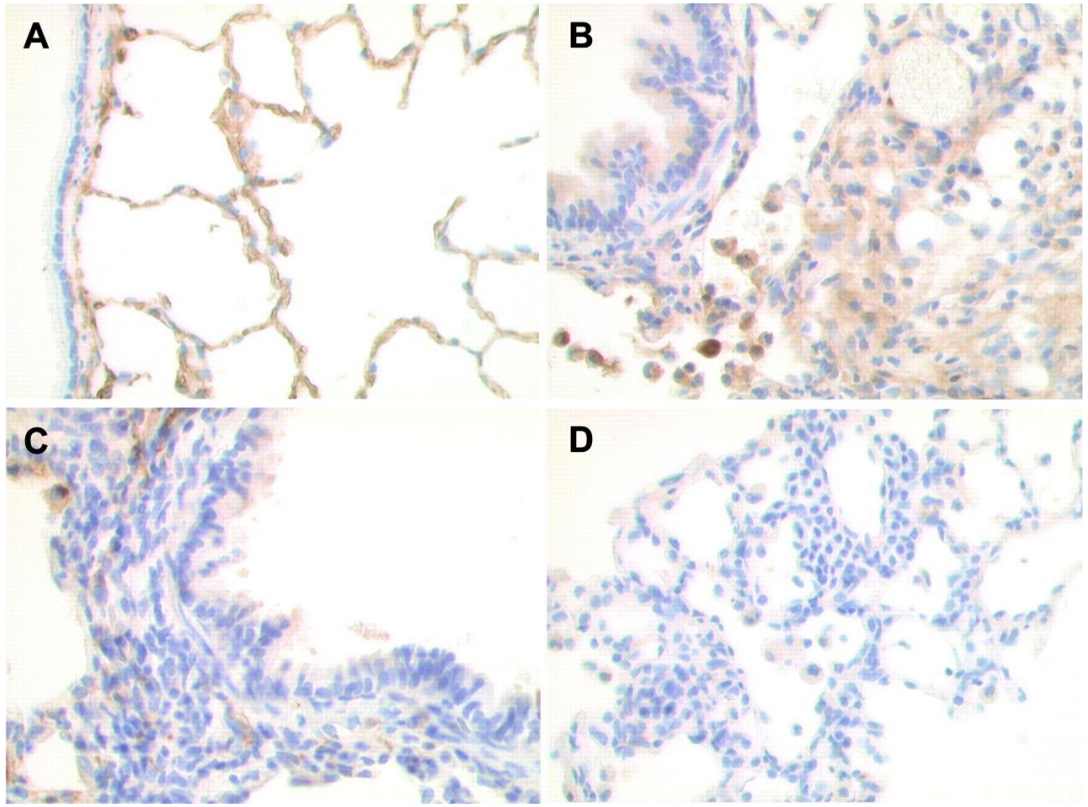
Mild symptoms in Children?

Potential therapeutics for 2019-nCoV-induced lung injury based on balancing the renin–angiotensin system (RAS).

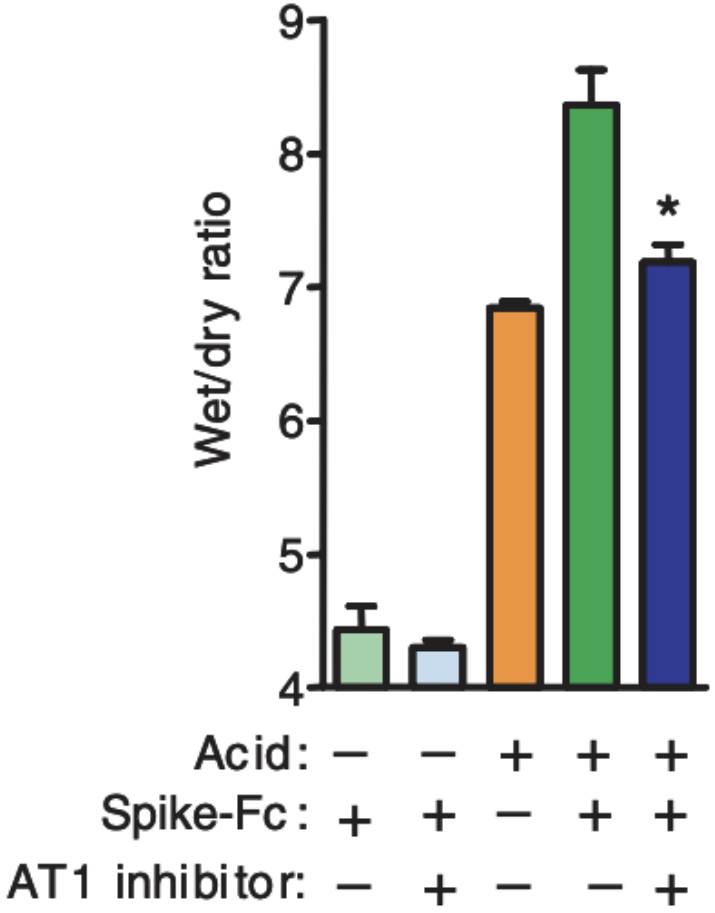


Virologica Sinica (2020)

TGF-β immunohistochemistry in bleomycin-induced lung injury:
A: saline alone; *B*: saline + bleomycin;
C: losartan + bleomycin;
D: ramipril + bleomycin.



Wet to dry weight ratios of lungs of acid and Spike(S1190)-challenged mice in the presence or absence of losartan (15 mg/kg).

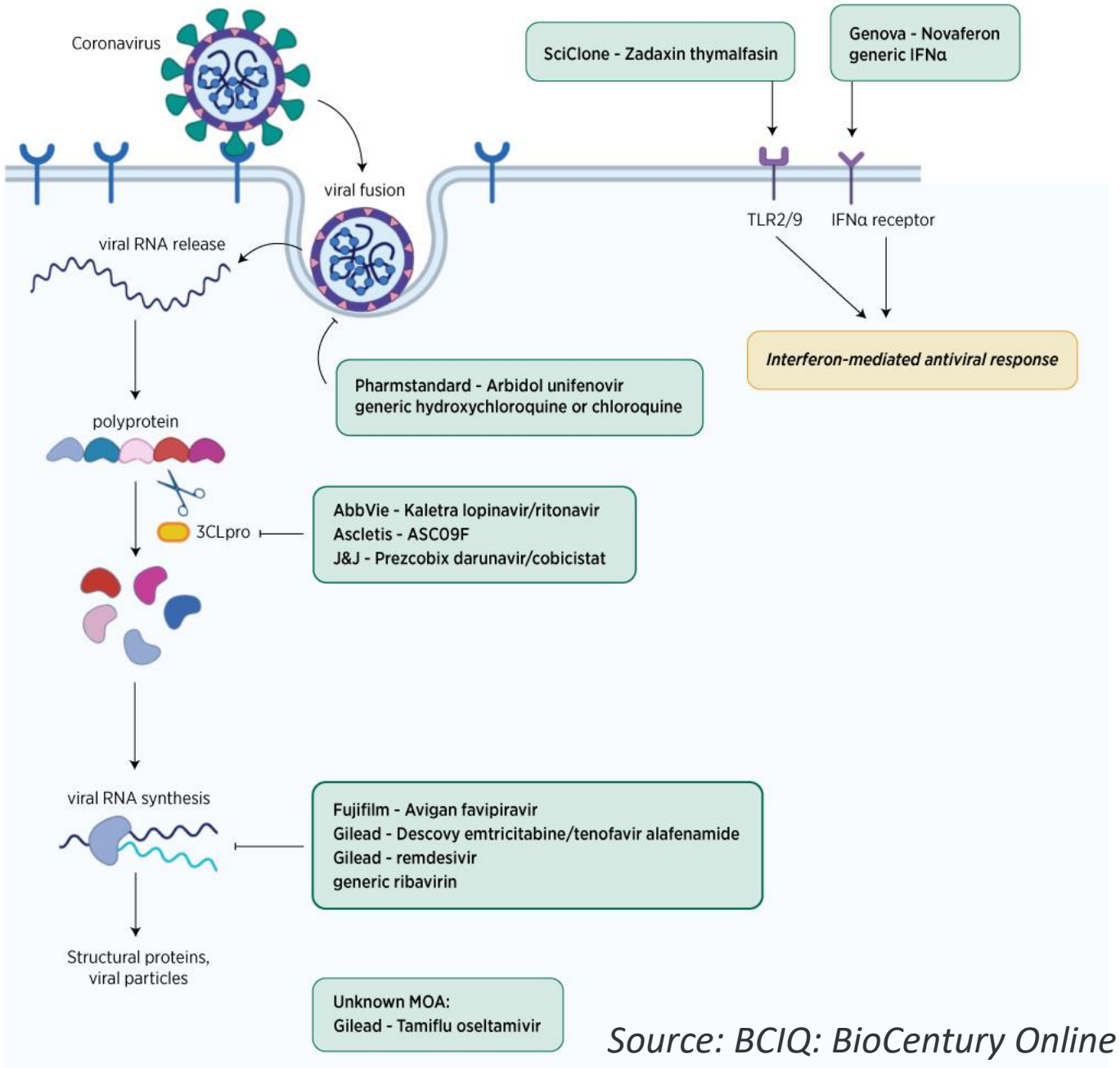


AMERICAN JOURNAL of PHYSIOLOGY
Lung Cellular and Molecular Physiology
DOI: (10.1152/ajplung.00313.2002)

Nat Med. 2005 Aug;11(8):875-9.

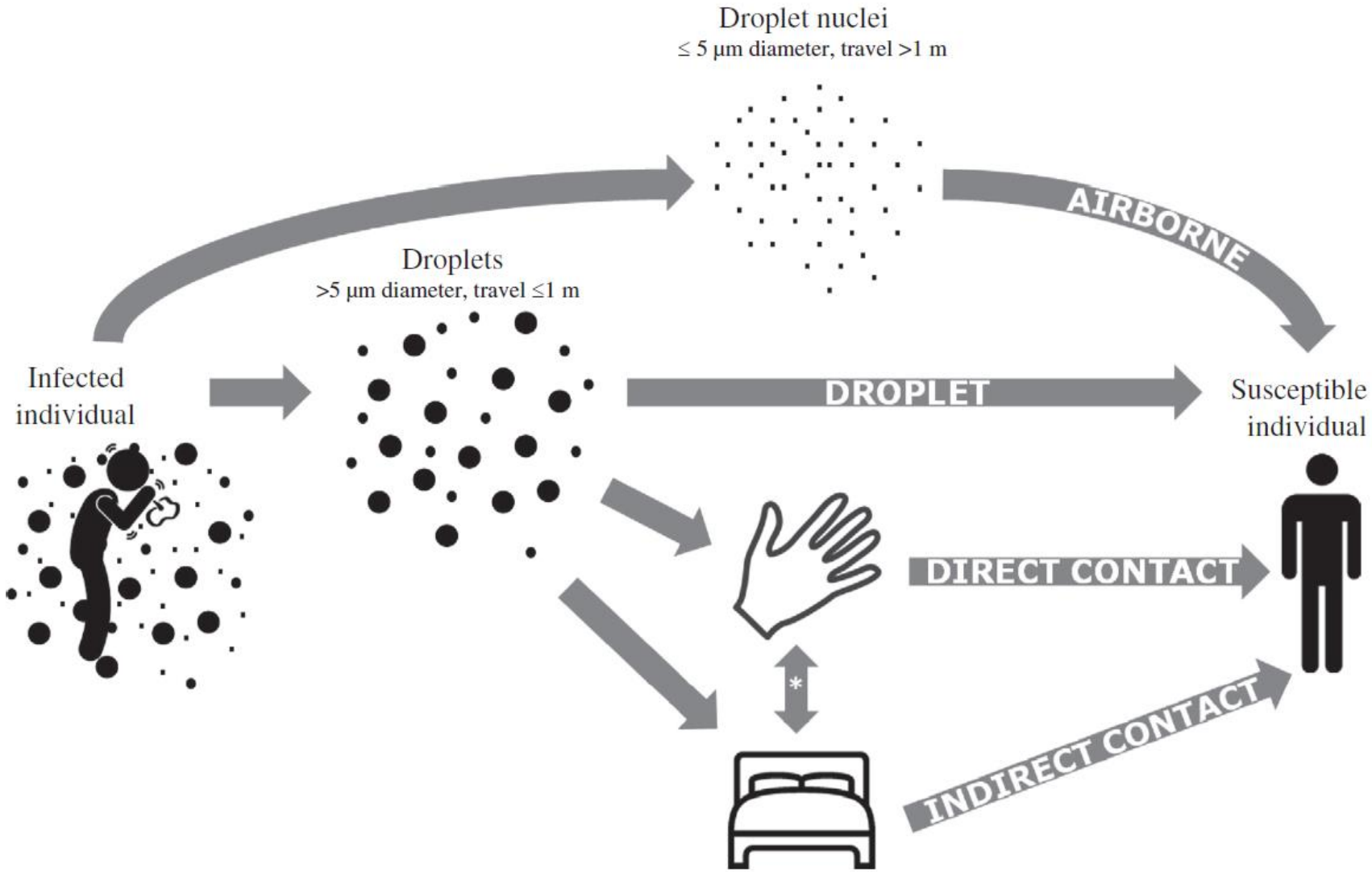
Outline

1. Introduction to coronavirus (CoV)
2. Virology of SARS-CoV-2
3. Genomic epidemiology of SARS-CoV-2
4. Clinical manifestations of COVID19
5. Possible explanations for some crucial questions
6. Future perspectives



- Lopinavir/Ritonavir (200mg+50mg/tablet) 2# PO BID
- Interferon-β1b 0.25 mg SC QOD5
- Remdesivir ?
- Chloroquine ?

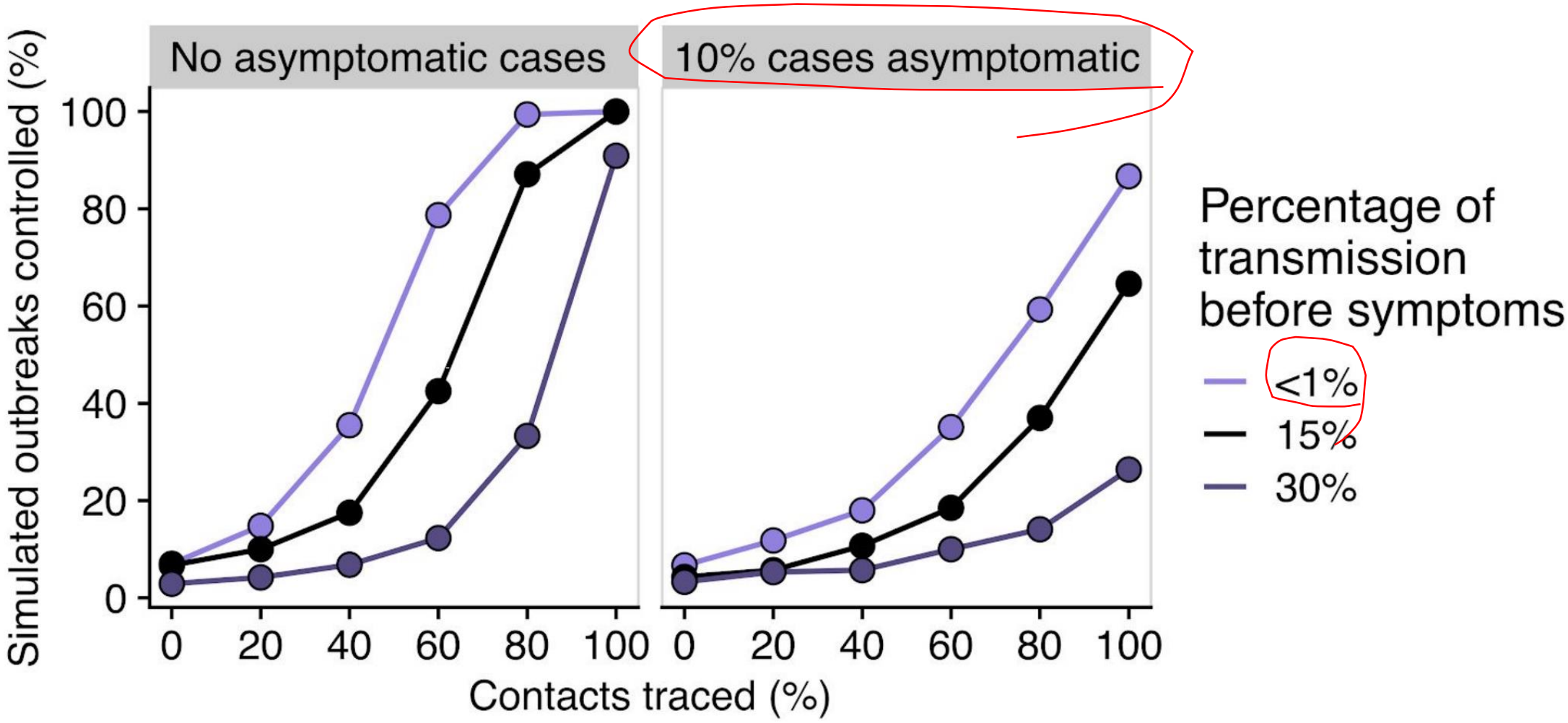
Source: BCIQ: BioCentury Online Intelligence, company websites, scientific literature



* Transmission routes involving a combination of hand & surface = indirect contact.

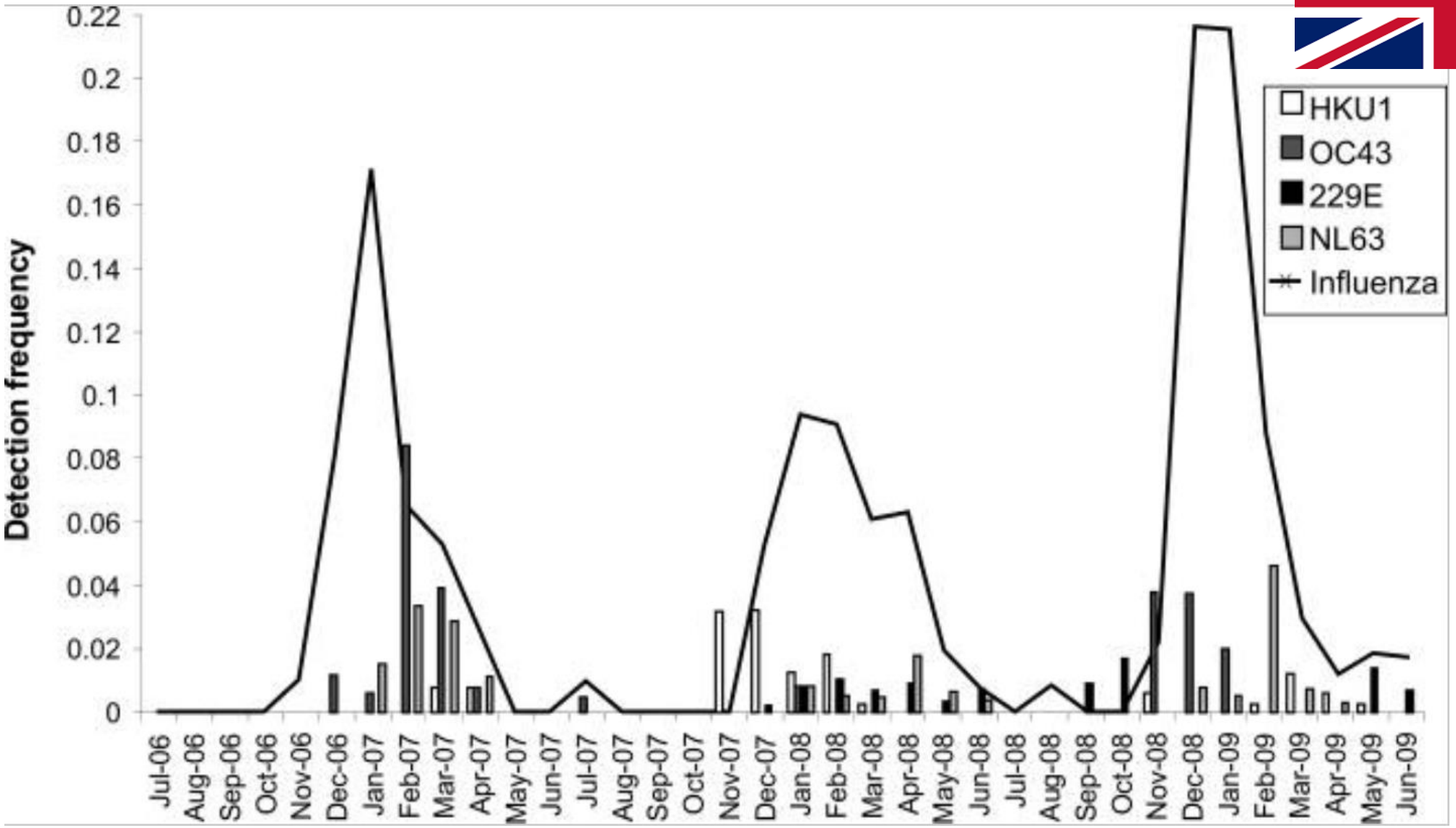
Journal of Hospital Infection Volume 92, Issue 3, March 2016, Pages 235-250

Contact tracing and case isolation alone is unlikely to control a new outbreak of 2019-nCov within three months.



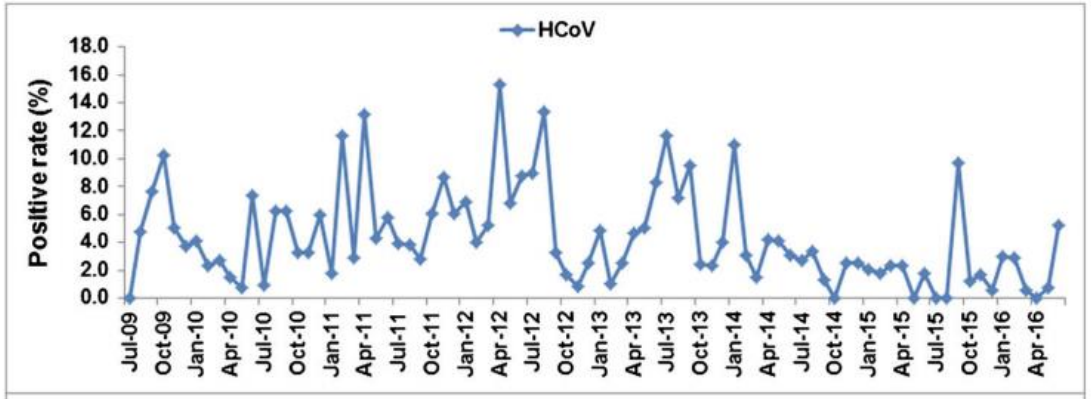
Joel Hellewell et al. preprint (2020)

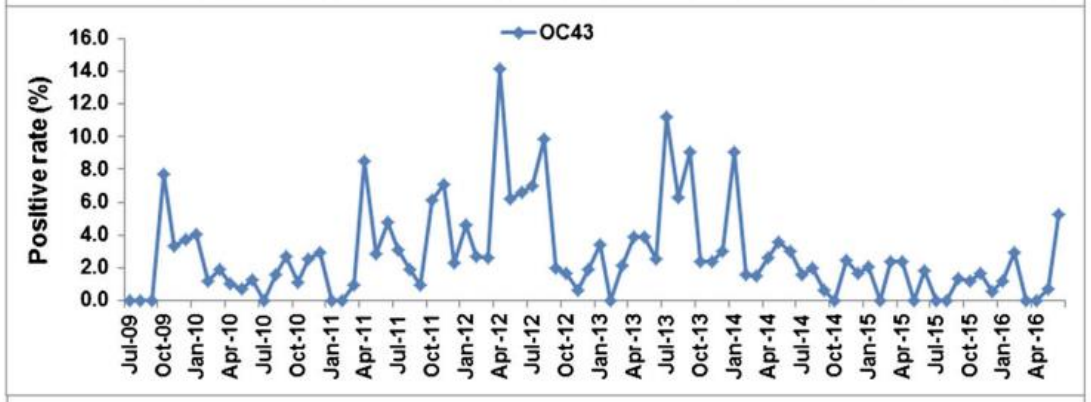
Seasonality of human coronaviruses: United Kingdom

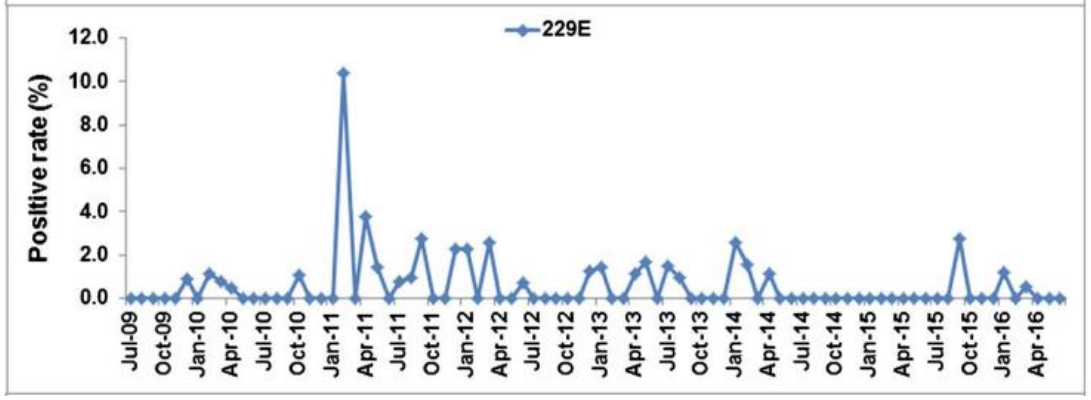


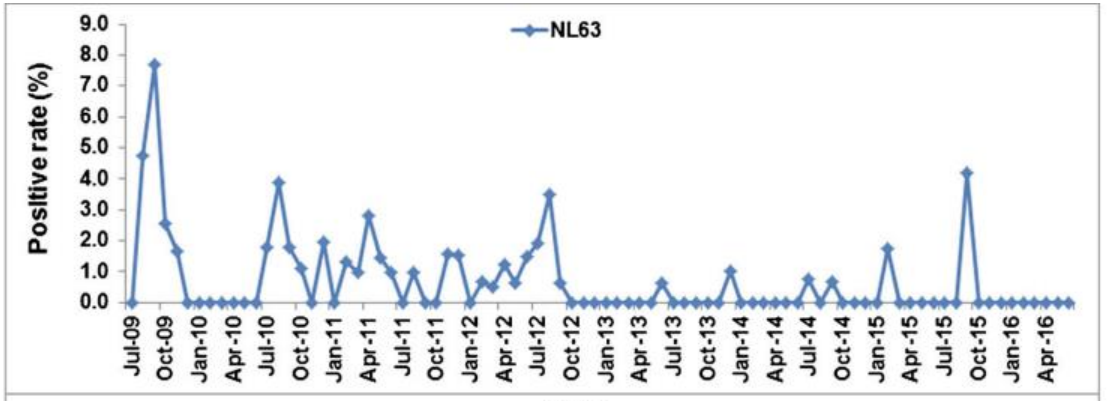
J Clin Microbiol. 2010 Aug;48(8):2940-7.

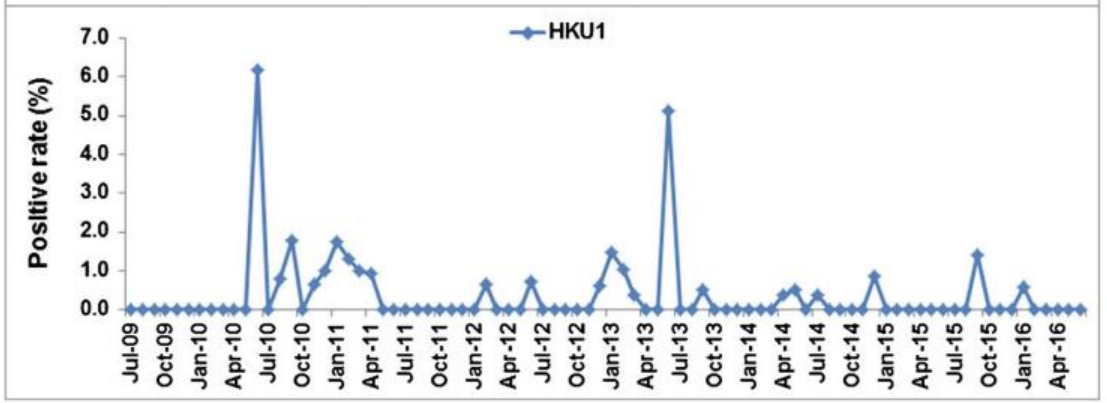
Seasonality of human coronaviruses: 廣州市









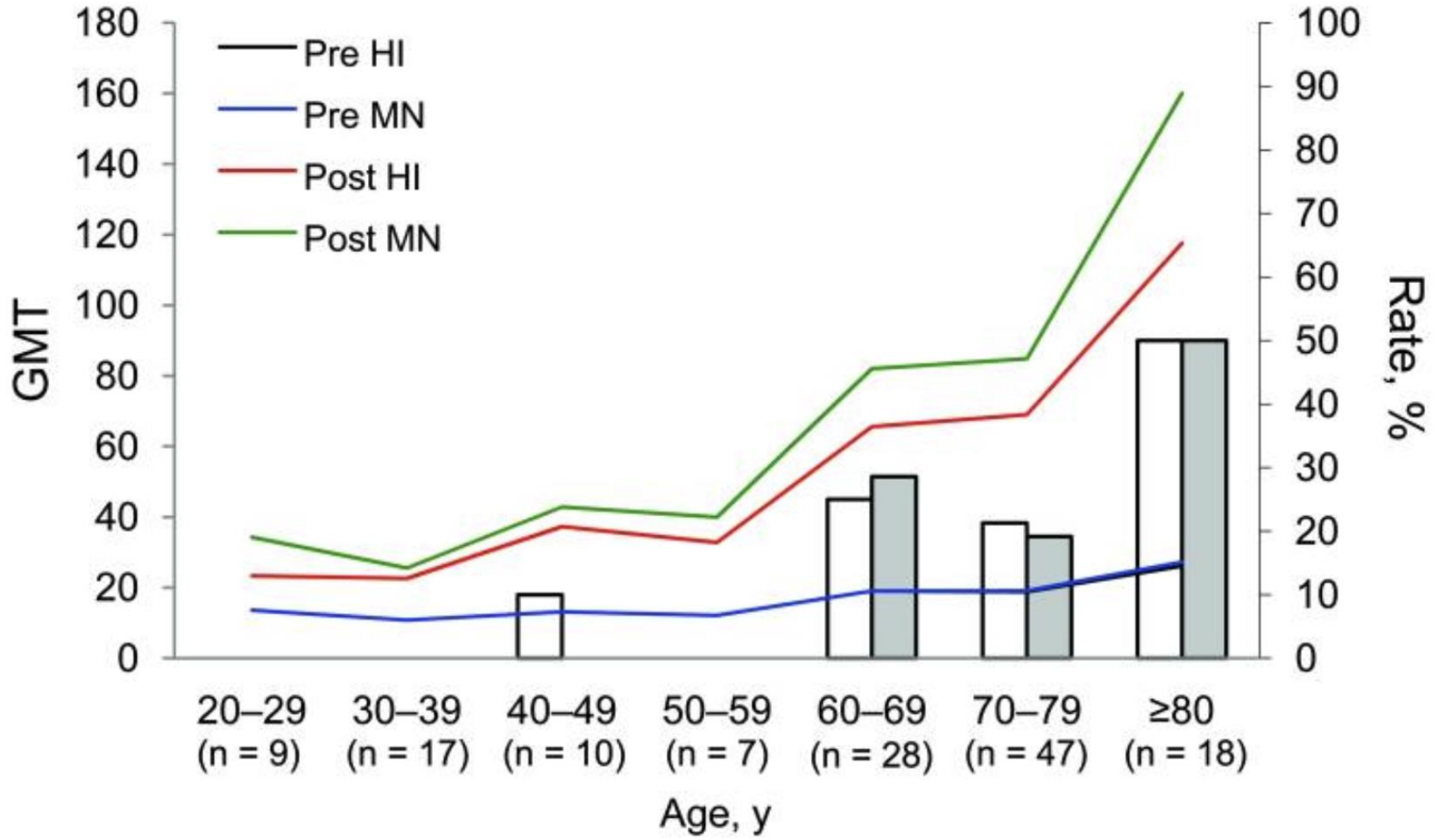


Eur J Clin Microbiol Infect Dis. 2018; 37(2): 363–369.

2019新型冠狀病毒與其他傳染病比較

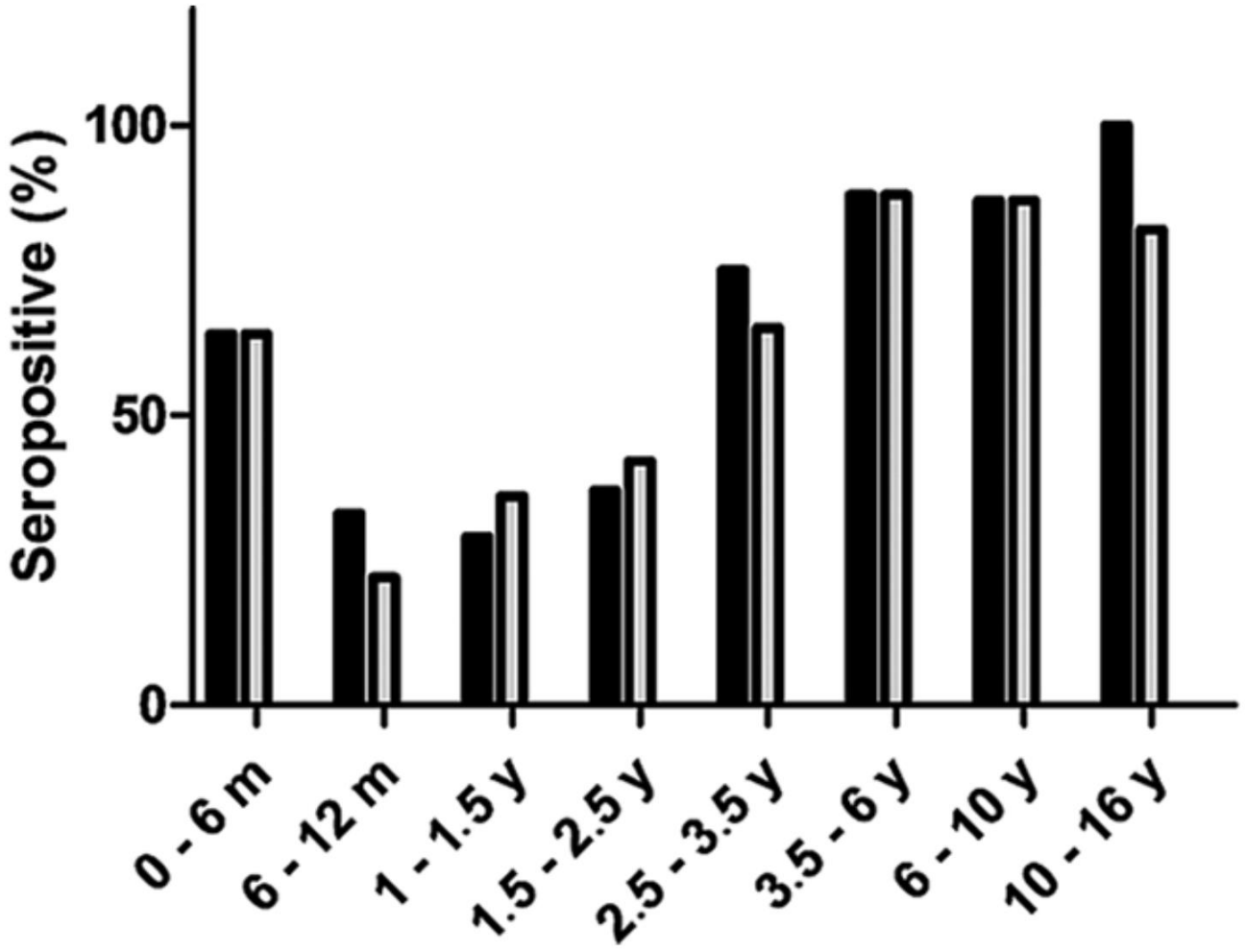
親子天下 資料來源：How Bad Will theCoronavirus Outbreak Get? Here Are 6 Key Factors 文字整理：黃瑽寧 製表：廖婕伶

Serologic Status for Pandemic (H1N1) 2009 Virus, Taiwan

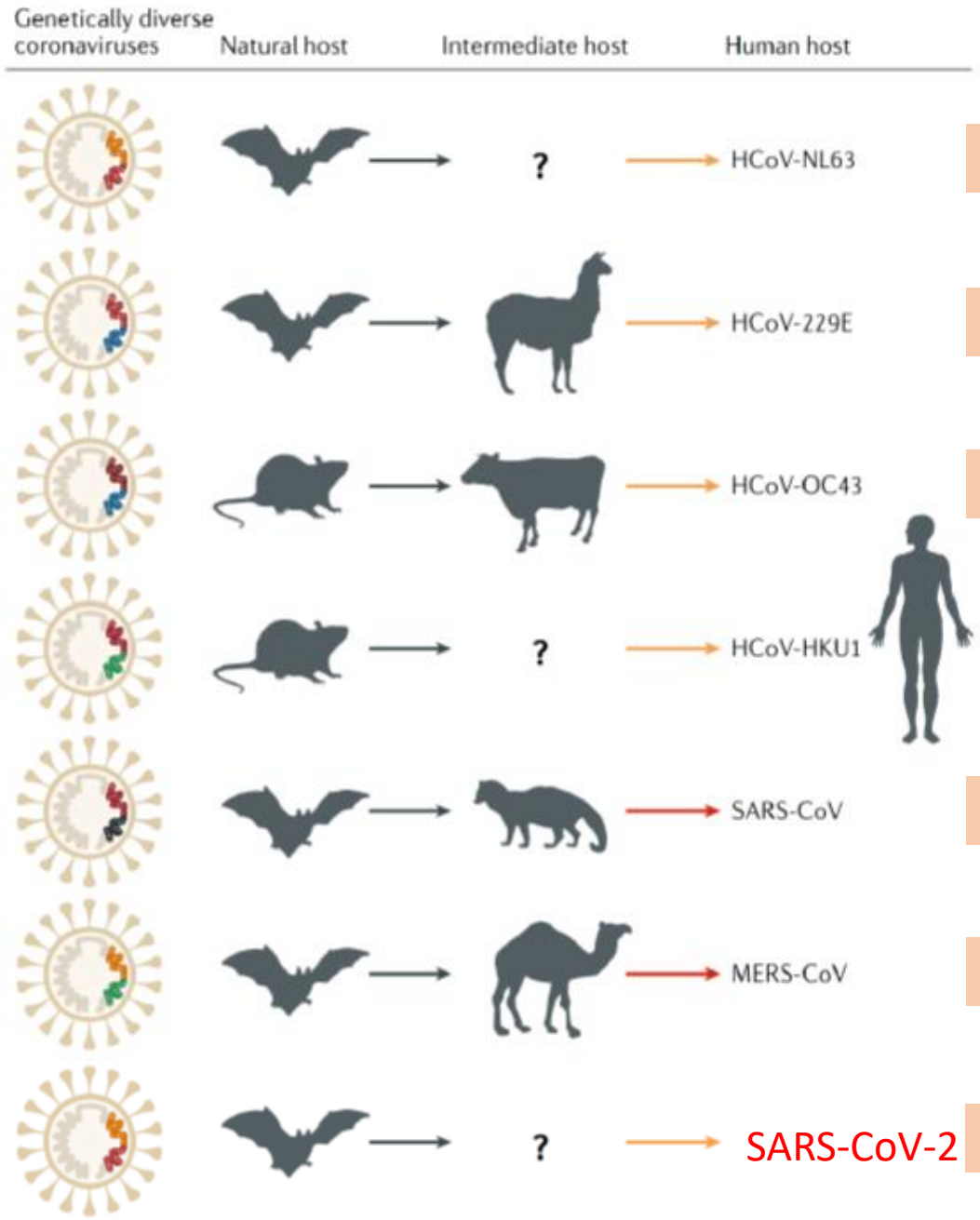


Emerg Infect Dis. 2011 Jan; 17(1): 76–78.

Percentages of HCoV-NL63- and HCoV-229E-seropositive results in different age groups.



J Clin Microbiol. 2008 Jul; 46(7): 2368–2373.



~800 years ago

~200 years ago

~100 years ago

~18 years ago

~ 8 years ago

NOW

已有的事，後必再有，
日光之下並無新事。
（聖經傳道書1:9）

聞子由瘦（宋·蘇軾）

五日一見花豬肉，十日一遇黃雞粥。
土人頓頓食藷芋，薦以薰鼠**燒蝙蝠**。

- 宋朝三百餘年間，發生大規模疫病近四十次；1075年「南方大疫，兩浙無貧富皆病，死者十有五六」；1131年浙江大疫；1142、1146、1151、1156年臨安幾乎是接連暴發疫情。

THANK YOU FOR LISTENING!