Enfeksiyonlar ve İnsan

Haluk VAHABOĞLU

OTURUM PLANI

- Nasıl bir dünyada yaşıyoruz
- Pandemi ne zaman biter
- Gain-of-Function

Nasıl bir dünyada yaşıyoruz

Is the COVID-19 Pandemic an inevitable product of the "Publish-or-Perish" mentality that's turning both academia and popular journalism into factory farms whose primary goal is monetization – not the public good?

NE BİÇİM ‘SCIENCE’

RESEARCH ARTICLE | CORONAVIRUS

Impact of community masking on COVID-19: A cluster-randomized trial in Bangladesh

JASON ABALUCK, LAURA H. KWONG, ASHLEY STYCZYNSKI, ASHRAFUL HAQUE, MD. ALAMGIR KABIR, ELLEN BATES-JEFFERYS, EMILY CRAWFORD, JADE BENJAMIN-CHUNG, SHABIB RAIHAN, [...] AHMED MUSHFIQ MOBARAK +13 authors Authors Info & Affiliations

SCIENCE • 2 Dec 2021 • Vol 375, Issue 6577 • DOI: 10.1126/science.abi9069

The Bangladesh Mask study: a Bayesian perspective

Preprint · May 2022

DOI: 10.13140/RG.2.2.26189.92649

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1 author:

Norman Elliott Fenton
Queen Mary, University of London

covid infection. Given that the results of the study have been used explicitly to justify continuing or reintroducing aspects of mask mandates in the USA, UK and elsewhere, the study paper in Science needs to be corrected or withdrawn.

Editor's Choice

The curious case of the Danish mask study

BMJ 2020 ; 371 doi: https://doi.org/10.1136/bmj.m4586 (Published 26 November 2020)

A study of 6,000 Danes was set to reveal whether wearing a face mask actually reduces the risk of COVID-19. The only problem is leading medical journals are refusing to publish the data, and the study's lead author hinted it's because they're not "*brave enough*" to do it.

Annals of Internal Medicine®

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LATEST ISSUES IN THE CLINIC JOURNAL CLUB MULTIMEDIA CME / MOC AUTHORS / SUBMIT

Original Research | March 2021

Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers FREE

A Randomized Controlled Trial

Carl Heneghan & Tom Jefferson

Landmark Danish study finds no significant effect for facemask wearers

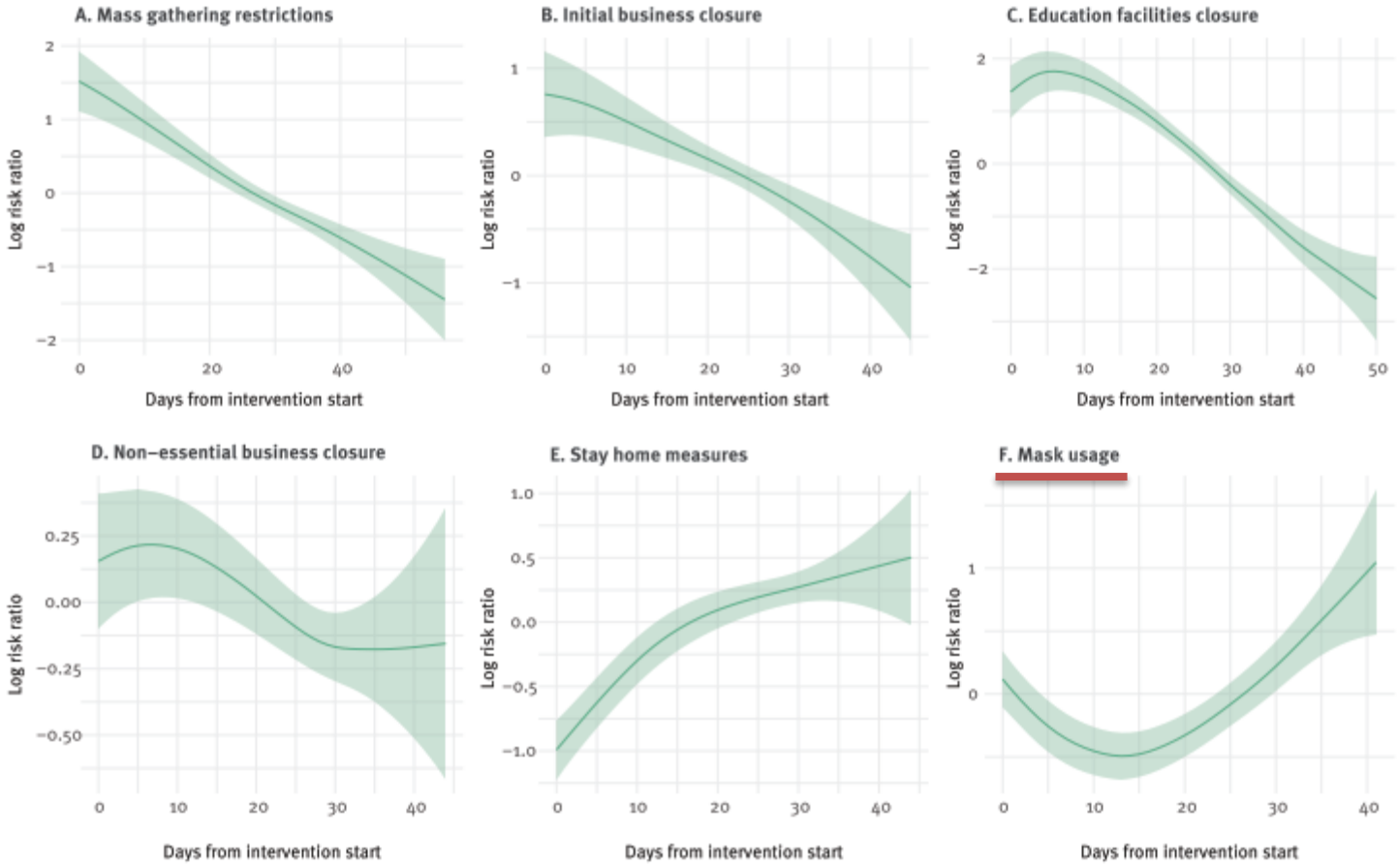
Impact of non-pharmaceutical interventions against COVID-19 in Europe in 2020: a quasi-experimental non-equivalent group and time series design study

Paul R Hunter[1,2] , Felipe J Colón-González[3,4,5] , Julii Brainard[1] , Steven Rushton[6]
1. Norwich Medical School, University of East Anglia, Norwich, United Kingdom
2. Department of Environmental Health, Tshwane University of Technology, Pretoria, South Africa
3. Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kin

impact. **Conclusions:** Our findings are that schools and some non-essential businesses operating 'as normal' as well as allowing mass gatherings were incompatible with suppressing disease spread. Closure of all businesses and stay at home orders are less likely to be required to keep disease incidence low. Our results help identify what were the most effective non-pharmaceutical interventions in this period.

FIGURE 2

Incidence rate ratios (cases) following implementation of country-level, non-pharmaceutical control measures and daily reported COVID-19 case numbers, 30 European countries, 2020



VİRAL SOLUNUM YOLU ENFEKSİYONLARINA KARŞI (DOĞAL/ADAPTİF) İMMÜNİTE

1. Banchereau J, Steinman RM. Dendritic cells and the control of immunity. Nature. 1998;392(6673):245-252. doi:10.1038/32588

2. Pilette C, Ouadrhiri Y, Godding V, Vaerman JP, Sibille Y. Lung mucosal immunity: Immunoglobulin-A revisited. Eur Respir J. 2001;18(3):571-588. doi:10.1183/09031936.01.00228801

3. Woodland DL. Cell-mediated immunity to respiratory virus infections. Curr Opin Immunol. 2003;15(4):430-435. doi:10.1016/S0952-7915(03)00067-0

4. Woodland DL, Hogan RJ, Zhong W. Cellular immunity and memory to respiratory virus infections. Immunol Res. 2001;24(1):53-67. doi:10.1385/IR:24:1:53

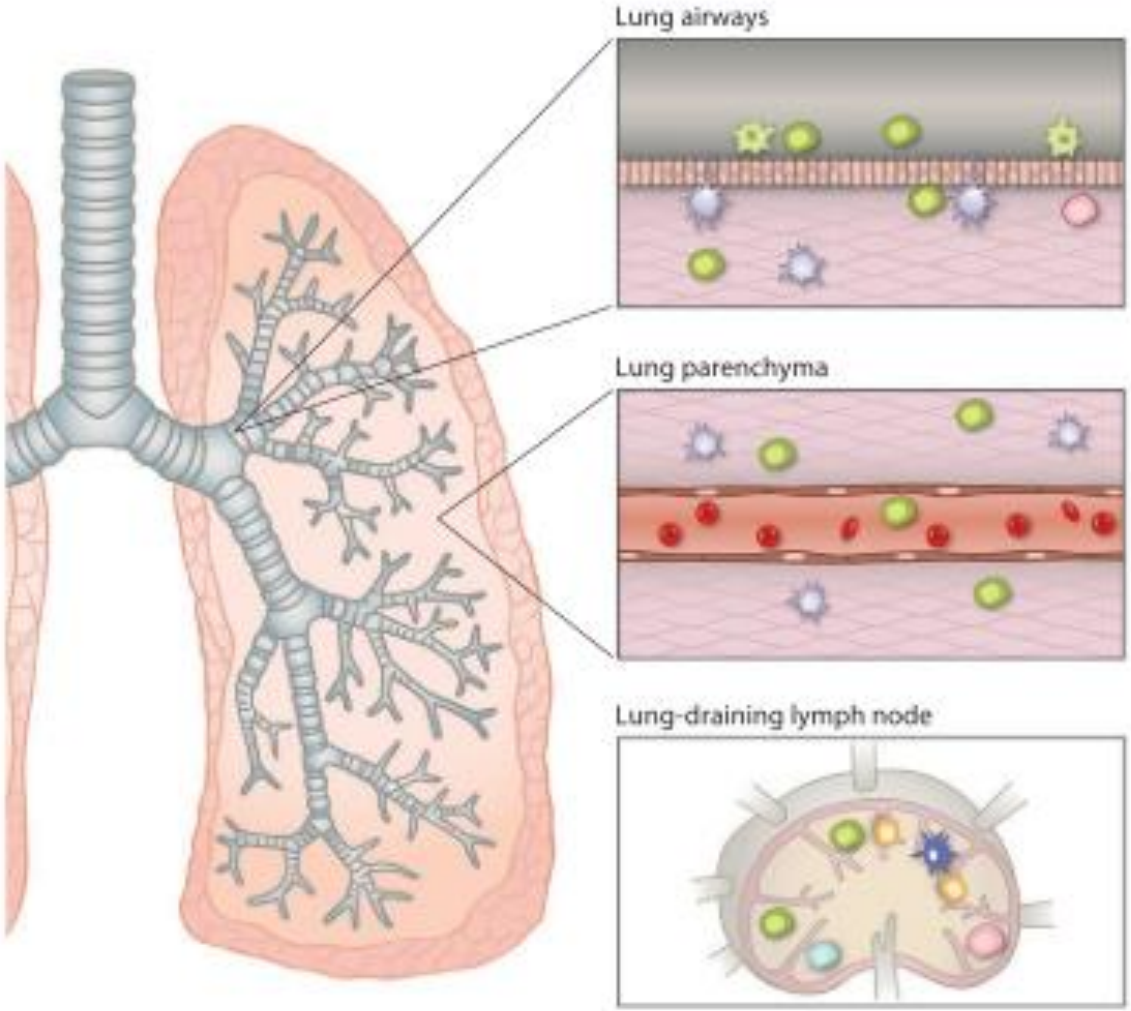
5. Kohlmeier JE, Woodland DL. Immunity to respiratory viruses. Annu Rev Immunol. 2009;27:61-82. doi:10.1146/annurev.immunol.021908.132625

6. Pabst R. The bronchus-associated-lymphoid tissue (BALT) an unique lymphoid organ in man and animals. Ann Anat. 2022;240:151833. doi:10.1016/j.aanat.2021.151833

Lung mucosal immunity: immunoglobulin-A revisited

C. Pilette, Y. Ouadrhiri, V. Godding, J-P. Vaerman, Y. Sibille

1. **Upper respiratory tract (nose, oropharynx, larynx)**
   Mechanical
   Complement Proteases Lactoferrin
   Secretory immunoglobulin (Ig-A and IgM)
2. **Lower respiratory tract (tracheobronchial tree)**
   Mucociliary clearance - Cough
   Bronchial-associated lymphoid tissue (BALT)
   Secretory IgA and IgM
3. **Lung parenchyma (alveoli and lung interstitium)**
   Surfactant products (SP-A, SP-B, SP-D)
   Phagocytic cellular mechanisms
   Resident alveolar macrophages


Lung airways
Lung parenchyma
Lung-draining lymph node
Respiratory dendritic cell
Alveolar macrophage
Red blood cell
Lymph node dendritic cell
Naive T cell
Naive B cell
Memory T cell
Virus-specific B cell

Immunity to Respiratory Viruses

Jacob E. Kohlmeier and David L. Woodland

Trudeau Institute, Saranac Lake, New York 12983; email: dwoodland@trudeauinstitute.org

Annu. Rev. Immunol. 2009. 27:61–82

Epithelial cells, as well as alveolar macrophages and **dendritic cells (DCs)**, continually sample the constituents of the airway lumen and detect the presence of an invading virus through **pattern-recognition receptors** (PRRs)

The recognition of pathogen-associated molecular patterns by these receptors initiates a cascade of signals that results in the production of cytokines and chemokines. The release of these inflammatory mediators into the surrounding environment alerts the innate immune system to the presence of infection and establishes a **localized antiviral state**

Contents lists available at ScienceDirect

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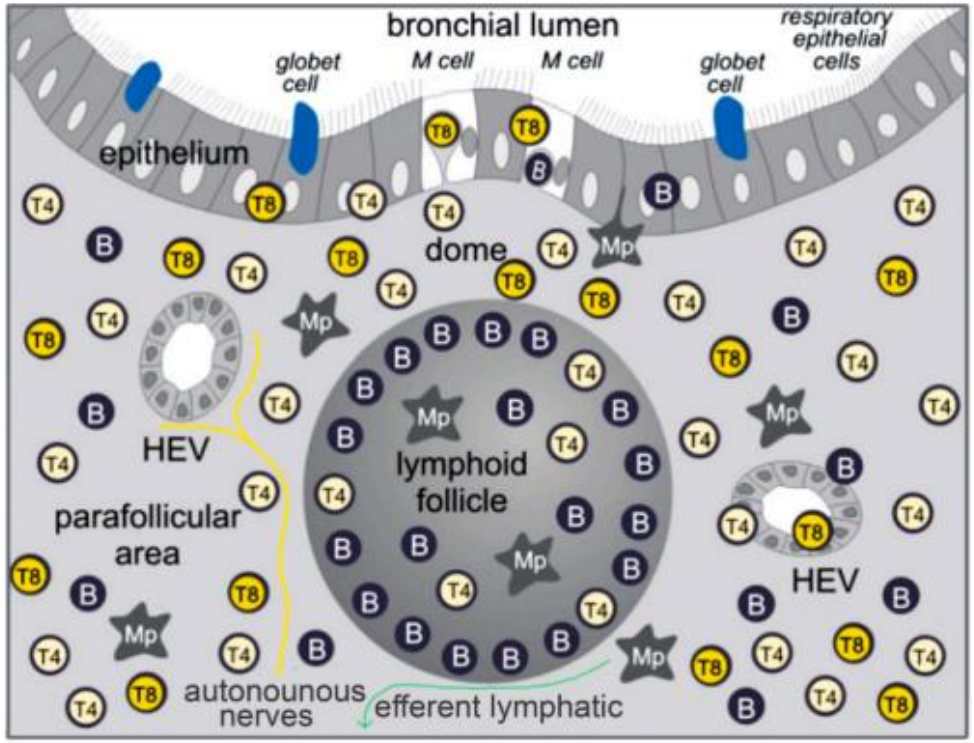
journal homepage: www.elsevier.com/locate/aanat

The bronchus-associated-lymphoid tissue (BALT) an unique lymphoid organ in man and animals

Reinhard Pabst*



Eur Respir J 2001; 18: 571–588
Printed in UK – all rights reserved

European Respiratory Journal
ISSN 0903-1936

SERIES "LUNG INFECTION AND LUNG IMMUNITY"
Edited by M. Spiteri and L.P. Nicod
Number 1 in this Series

Lung mucosal immunity: immunoglobulin-A revisited

C. Pilette, Y. Ouadrhiri, V. Godding, J-P. Vaerman, Y. Sibille

Lung mucosal immunity: immunoglobulin-A revisited. C. Pilette, Y. Ouadrhiri, V. Godding, J-P. Vaerman, Y. Sibille. ©ERS Journals Ltd 2001.

ABSTRACT: Mucosal defence mechanisms are critical in preventing colonization of the respiratory tract by pathogens and penetration of antigens through the epithelial barrier. Recent research has now illustrated the active contribution of the respiratory epithelium to the exclusion of microbes and particles, but also to the control of the inflammatory and immune responses in the airways and in the alveoli. Epithelial cells also mediate the active transport of polymeric immunoglobulin-A from the lamina propria to the airway lumen through the polymeric immunoglobulin receptor. The role of IgA in the defence of mucosal surfaces has now expanded from a limited role of scavenger of exogenous material to a broader protective function with potential applications in immunotherapy. In addition, the recent identification of receptors for IgA on the surface of blood leukocytes and alveolar macrophages provides an additional mechanism of interaction between the cellular and humoral immune systems at the level of the respiratory tract.

Eur Respir J 2001; 18: 571–588.

PLOS ONE

RESEARCH ARTICLE

Influenza vaccination in the elderly: 25 years follow-up of a randomized controlled trial. No impact on long-term mortality

Ruud Andreas Fritz Verhees[1☯*], **Carel Thijs**[2☯], **Ton Ambergen**[3☯], **Geert Jan Dinant**[1☯], **Johannes Andreas Knottnerus**[1☯]

1 Department of Family Medicine, School for Public Health and Primary Care (CAPHRI), Maastricht University, Maastricht, The Netherlands, **2** Department of Epidemiology, School for Public Health and Primary Care (CAPHRI), Maastricht University, Maastricht, The Netherlands, **3** Department of Methodology and Statistics, Maastricht University, Maastricht, The Netherlands

☯ These authors contributed equally to this work.
* ruud.verhees@maastrichtuniversity.nl, verhees@alumni.maastrichtuniversity.nl

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SNI: Infection

Editor
Ali Akhaddar, MD, IFAANS
Avicenne Military Hospital, Marrakech, Morocco

SNI
Open Access

Editorial

COVID UPDATE: What is the truth?

Russell L. Blaylock

Retired Neurosurgeon, Theoretical Neuroscience Research, LLC, Ridgeland, Mississippi, United States.

E-mail: *Russell L. Blaylock - Blay6307@gmail.com

essentially untested messenger RNA vaccines. For the first time in history medical treatment, protocols are not being formulated based on the experience of the physicians treating the largest number of patients successfully, but rather individuals and bureaucracies that have never treated a single patient—including Anthony Fauci, Bill Gates, EcoHealth Alliance, the CDC, WHO, state public health officers and hospital administrators.[23,38]

PANDEMİ

DSÖ Bülteni - 4 May 2009

“An influenza pandemic may occur when a new influenza virus appears against which the human population has no immunity.”

doi:10.2471/blt.11.086173

Published in final edited form as:
Rev Med Virol. 2011 September ; 21(5): 262–284. doi:10.1002/rmv.689.

Pandemic influenza: certain uncertainties

David M. Morens[*] and **Jeffery K. Taubenberger**
National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Date	Described	Reference
Ancient, undated	Mentioned by Hebrew writers	[205]
1194–1184 BC	Trojan war; 9-day epidemic; horses/dogs affected	[68,90,92,206]
713 BC	Host of Sennacherib, Assyrian epidemic in 185 000 men	[92]
430–425 BC	The "Plague of Athens" described by Thucydides	[13]
415 BC	Fatal epidemic in the Athenian army in Sicily	[3,5,207]
393 BC	Epidemic during the Carthaginian siege of Syracuse	[75]
212 BC	Epidemic during the Second Punic War	[208]
591–592 AD	Epidemic "extreme cough" over "the whole earth"	[71]

Table 2. **Descriptions of influenza outbreaks[a] that have carried the "pandemic" label**

Year	Virus	Nickname	Descriptions
1918	H1N1	Spanish flu	"devastating pandemic" (US CDC)[40]
			"severe" (US CDC)[41]
			"exceptional" (WHO)[42]
1957	H2N2	Asian flu	"comparatively mild" (WHO)[42]
			"substantial pandemic" (WHO)[17]
			"severe" (US CDC)[41]
			"moderate" (US HHS)[43]
1968	H3N2	Hong Kong flu	"moderate" (US CDC)[41]
			"huge economic and social disruption" (UK DoH)[44]
			"mild" (WHO)[45]
			"substantial pandemic" (WHO)[17]
			"Few people who lived through it even knew it occurred." (John Barry)[46]
1977	H1N1	Russian flu	"mild" (US CDC)[41]
			"benign pandemic" (WHO)[17]
2009	H1N1	Swine flu	"moderate" (WHO)[5,47]
			"largely reassuring clinical picture" (WHO)[48]

doi:10.2471/blt.11.086173

How Pandemics End

An infectious outbreak can conclude in more ways than one, historians say. But for whom does it end, and who gets to decide?

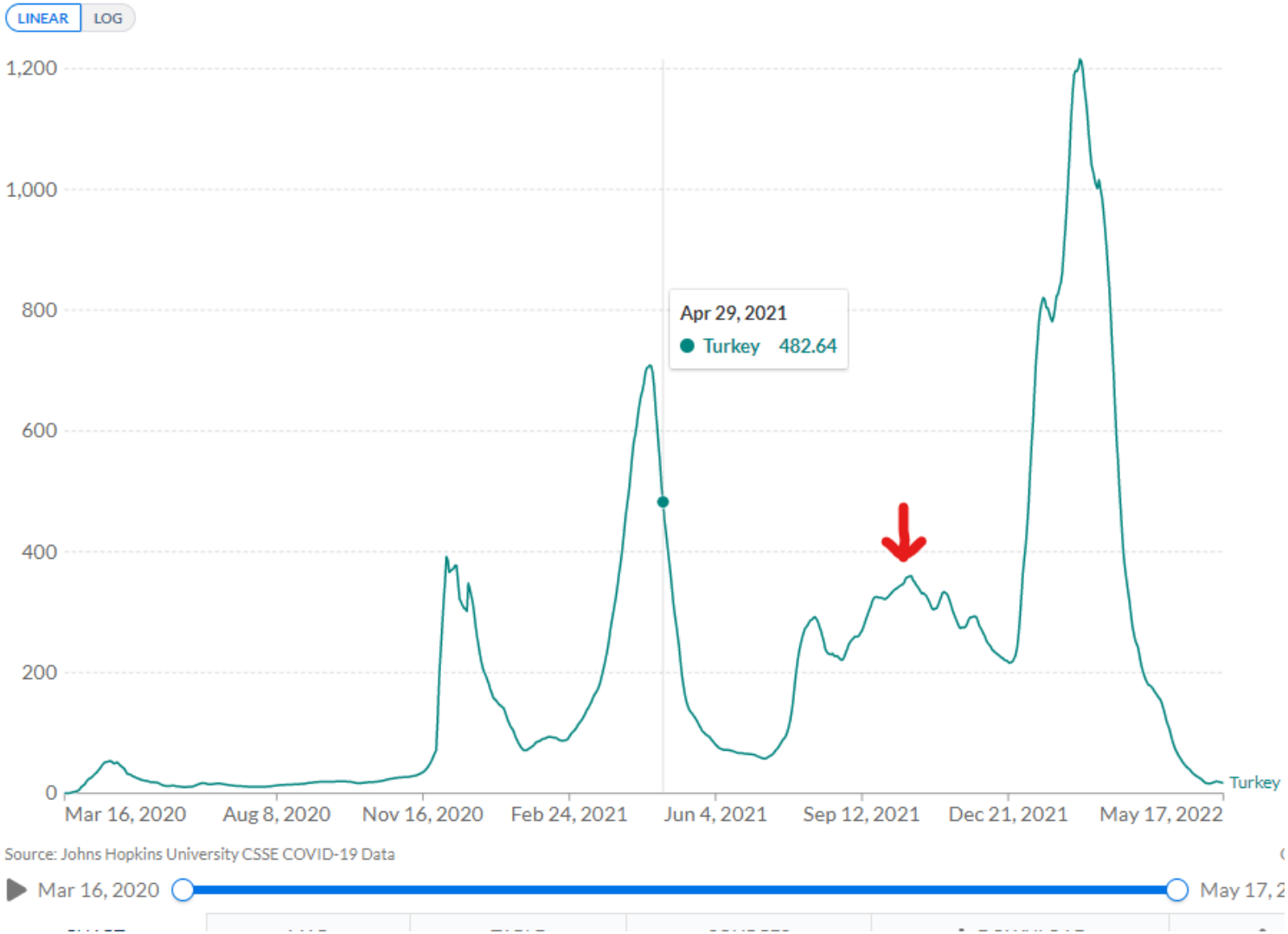
By Gina Kolata

- Published in the New York Times May 10, 2020, Updated May 14, 2020

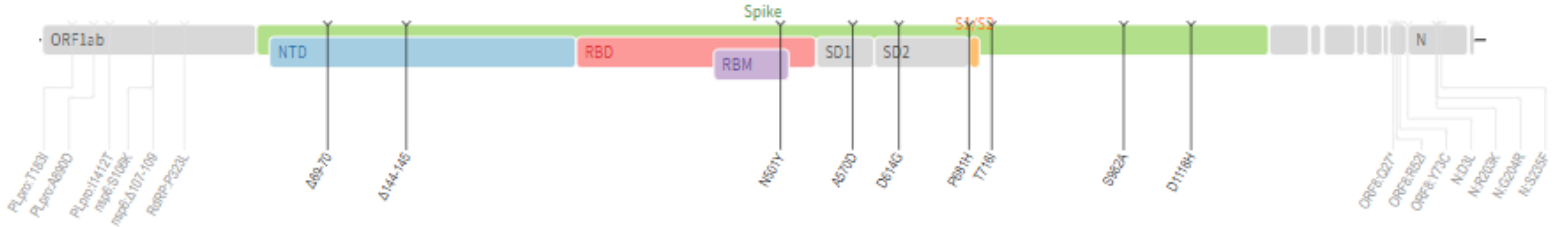
When will the Covid-19 pandemic end? And how?

According to historians, pandemics typically have two types of endings: the medical, which occurs when the incidence and death rates plummet, and the social, when the epidemic of fear about the disease wanes.

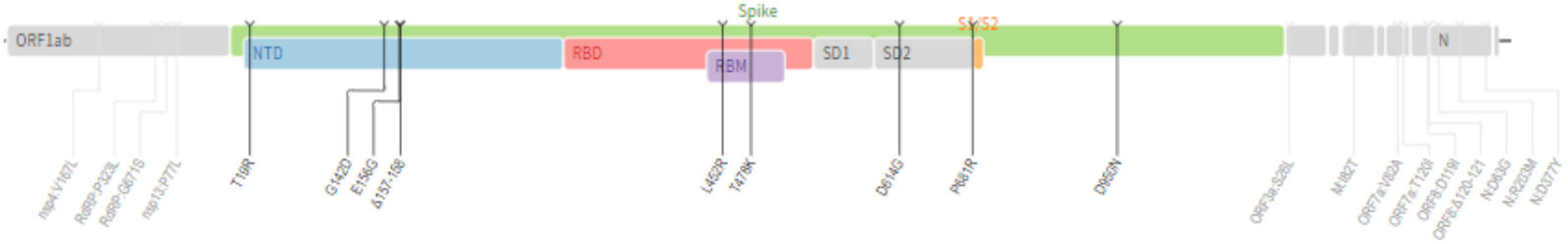
"When people ask, 'When will this end?,' they are asking about the social ending," said Dr. Jeremy Greene, a historian of medicine at Johns Hopkins.


LINEAR
LOG
1,200
1,000
800
600
400
200
0
Apr 29, 2021
Turkey 482.64
Turkey
Mar 16, 2020
Aug 8, 2020
Nov 16, 2020
Feb 24, 2021
Jun 4, 2021
Sep 12, 2021
Dec 21, 2021
May 17, 2022
Source: Johns Hopkins University CSSE COVID-19 Data
Mar 16, 2020
May 17, 2

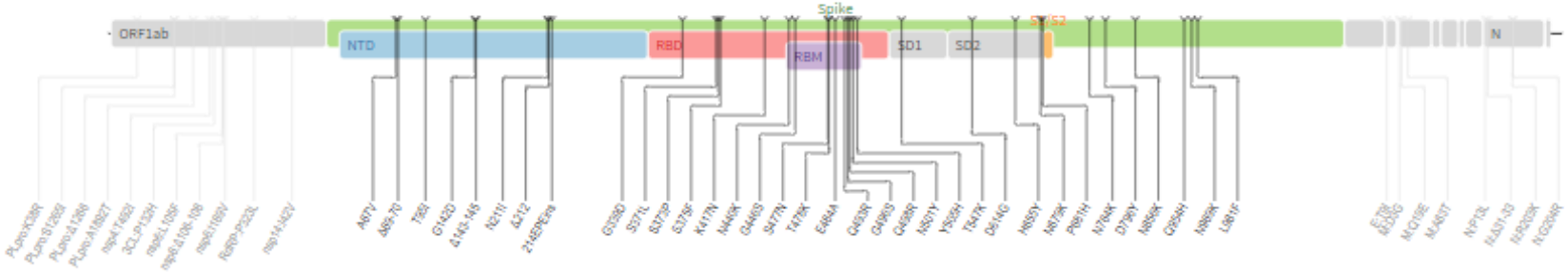
Alpha



Delta

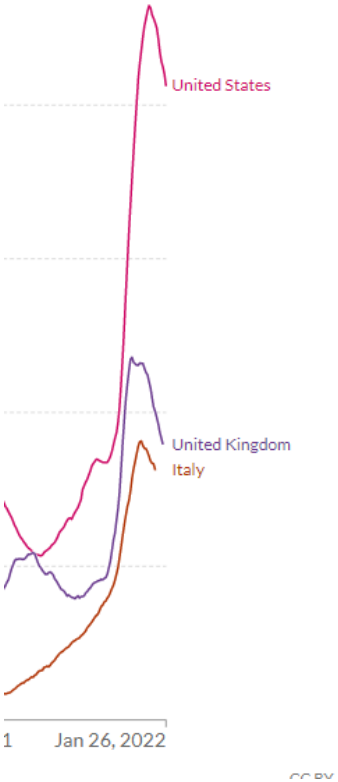


Omicron



Prof. Dr. Haluk VAHABOGLU @HalukVAHABOLU · Jan 29

omicron süratle yükselip süratle düşüyor. farklı ve yeni bir virüs gibi düşünmek lazım. oldukça hafif seyrediyor
Herhangi bir aşı işe yaramıyor, C19 geçirenler bile hastalanabiliyor ve hafif geçiriyor.
omicrona yeni bir soğuk algınlığı virüsü gözüyle bakmak lazım.. Pandemi bitti



Gain of function experiments aim to improve the ability of a pathogen to cause disease. "Select agents" are biological agents and toxins that have the potential to pose a severe threat to public health and safety.

The "government's decision to suspend all gain-of-function experiments on a variety of select agents" refers to the Obama administration's moratorium on gain-of-function research, officially called the 2014 U.S. Government Deliberative Process Research Funding Pause on Selected Gain-of-Function Research Involving Influenza, MERS and SARS Viruses.

Baric, Zhengli and their team acknowledged in their published study……that their work was allowed only because it was initiated before the 2014 funding pause on gain-of-function research involving SARS viruses, and also because the National Institutes of Health approved an exemption requested by the researchers.

https://www.organicconsumers.org/blog/dr-coronavirus-hunter-ralph-baric-preparing-us-pandemic-or-putting-us-peril-one?msclkid=25614e4bc85911eca06dcd9d33b4e5a3

Understanding the Risk of Bat Coronavirus Emergence

Project Number	Contact PI/Project Leader	Awardee Organization
1R01AI110964-01	DASZAK, PETER	ECOHEALTH ALLIANCE, INC.

Description

Abstract Text

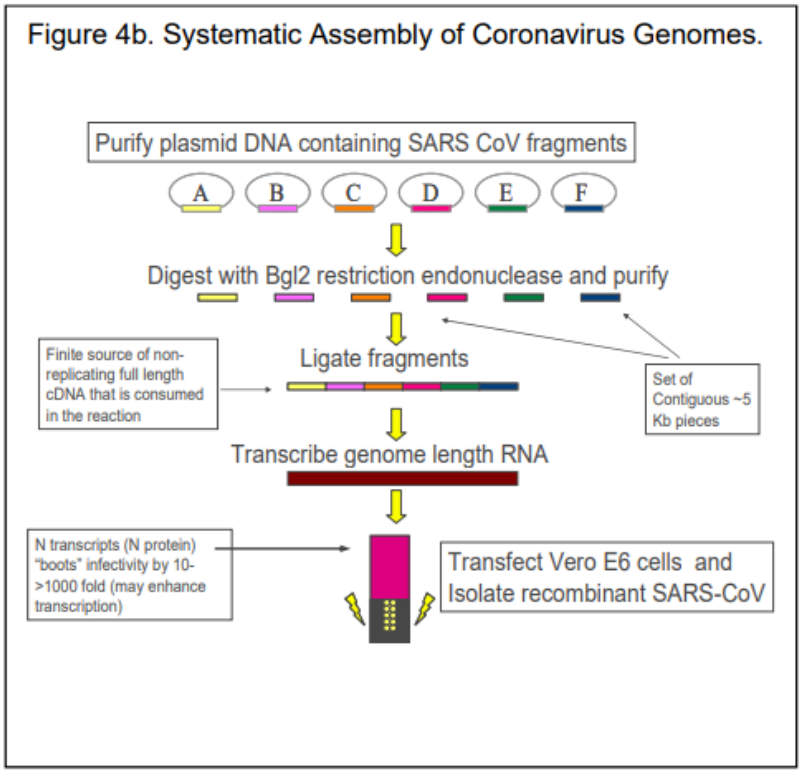
DESCRIPTION (provided by applicant): This project will examine the risk of future coronavirus (CoV) emergence from wildlife using investigations across the human-wildlife interface in China, molecular characterization of novel CoVs and host receptor binding d

Synthetic Viral Genomics: Risks and Benefits for Science and Society

Ralph S. Baric

University of North Carolina at Chapel Hill

https://dspace.mit.edu/bitstream/handle/1721.1/39652/Baric%20Synthetic%20Viral%20Genomics.pdf?sequence=1&origin=publication_detail

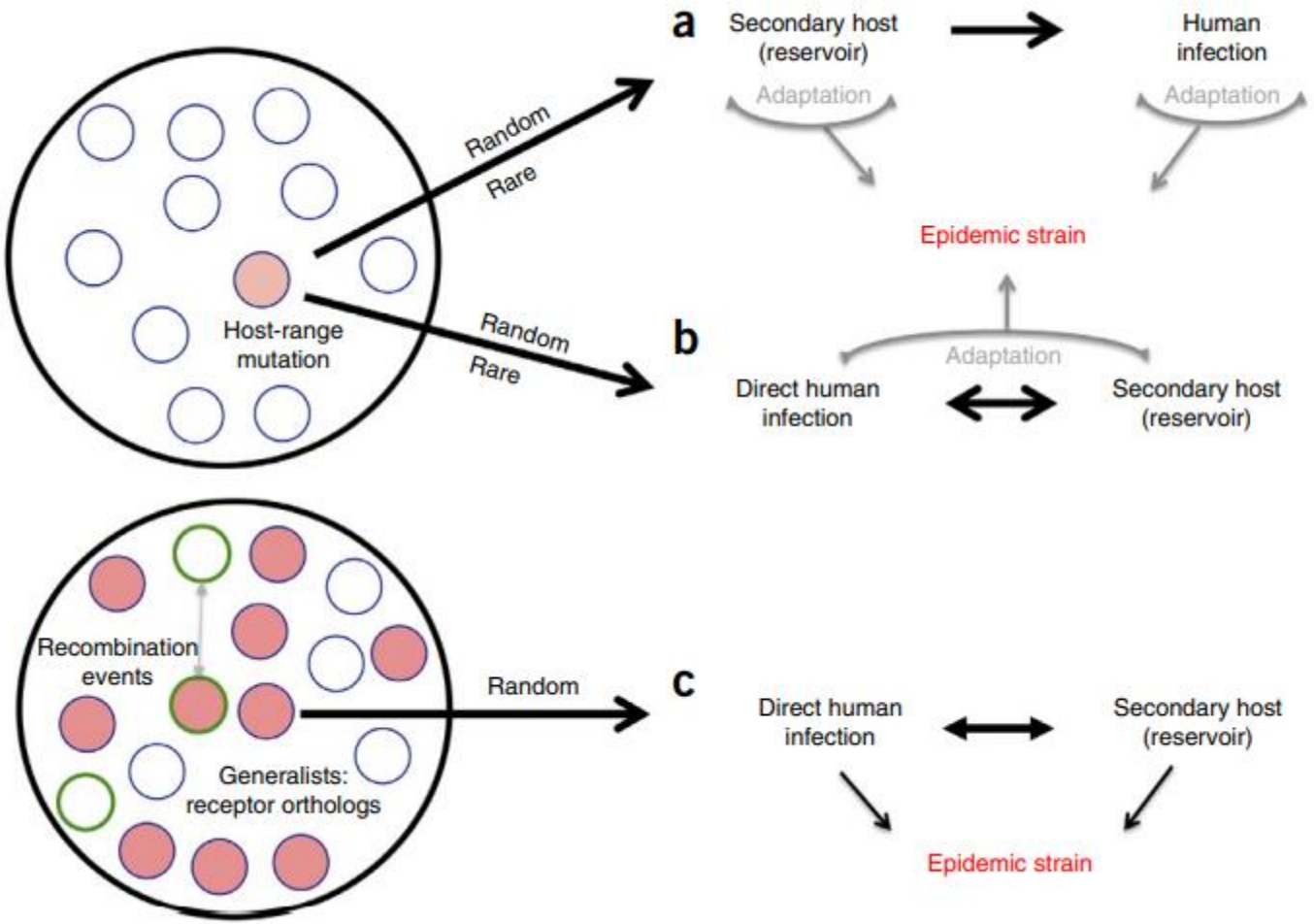


A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence

Vineet D Menachery[1], Boyd L Yount Jr[1], Kari Debbink[1,2], Sudhakar Agnihothram[3], Lisa E Gralinski[1], Jessica A Plante[1], Rachel L Graham[1], Trevor Scobey[1], Xing-Yi Ge[4], Eric F Donaldson[1], Scott H Randell[5,6], Antonio Lanzavecchia[7], Wayne A Marasco[8,9], Zhengli-Li Shi[4] & Ralph S Baric[1,2]

Nature Medicine, 2015; DOI: 10.1038/nm.3985

Baric is known as the Coronavirus Hunter. Zhengli's nickname is Bat Woman.



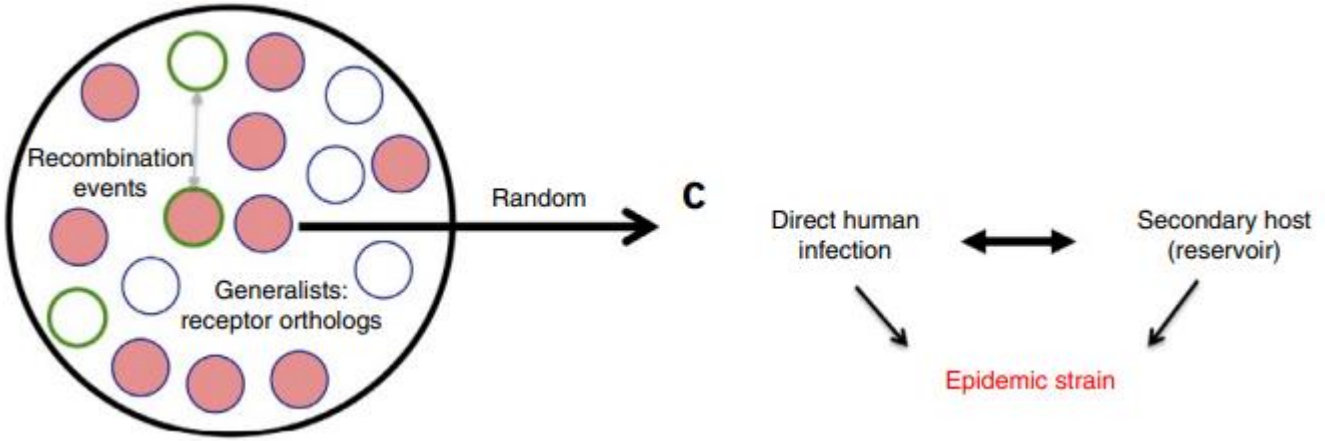
Nature Medicine, 2015; DOI: 10.1038/nm.3985

WHO's Six Pandemic Phases

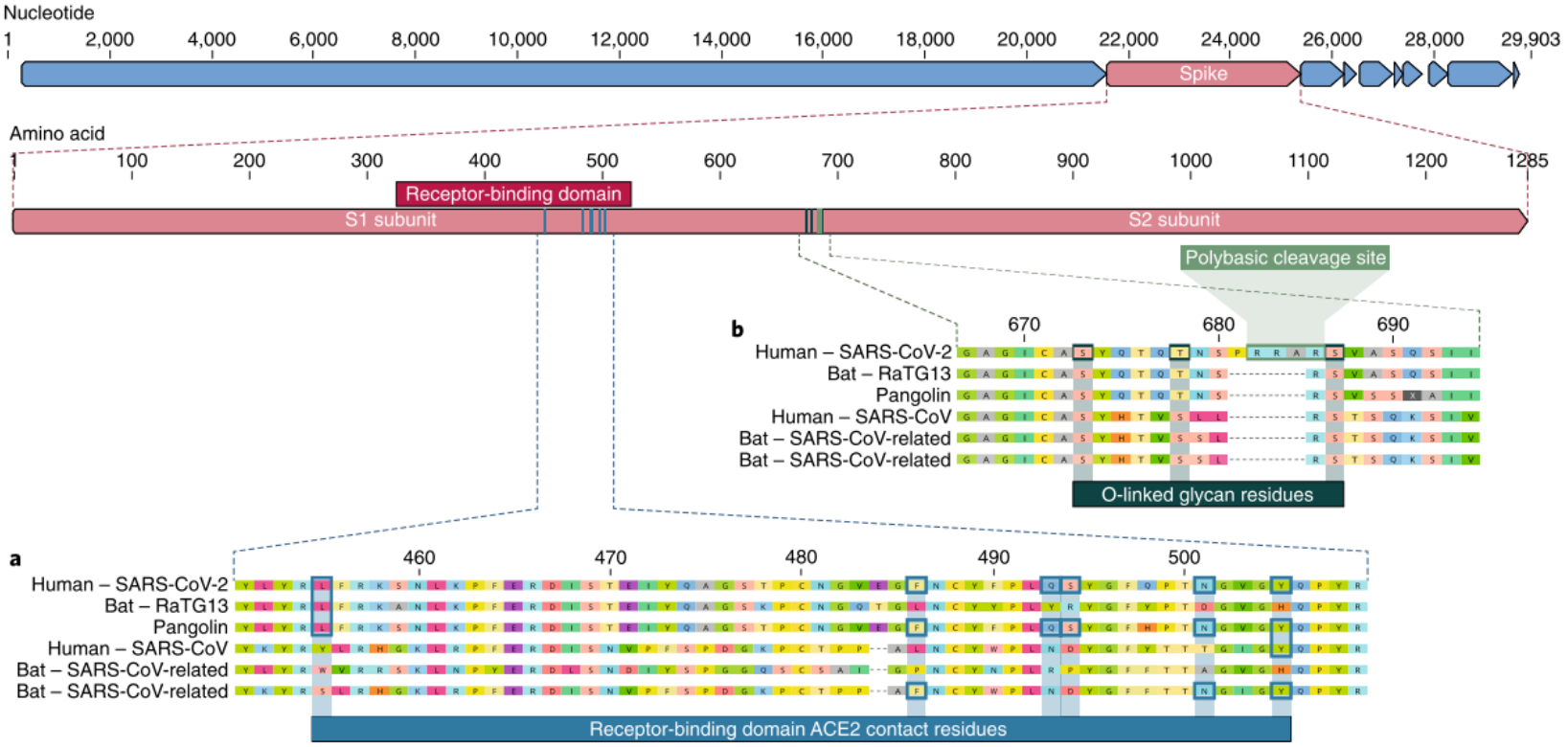
doi:10.1017/S0963180119001002

- Phase 1, the virus circulates only within animals and no human infection has been
- Phase 2, the virus circulates in wild and domesticated animals and human infection has been reported
- Phase 3, sporadic cases and small clusters of disease in humans have been reported

World Health Organization. *WHO Pandemic Phase Descriptions and Main Actions By Phase*; available at http://www.who.int/influenza/resources/documents/pandemic_phase_descriptions_and_actions.pdf (last accessed 11 Nov 2019).



This hypothesis is illustrated by the ability of a chimeric virus containing the SHC014 spike in a SARS-CoV backbone to cause robust infection in both human airway cultures and in mice without RBD adaptation.

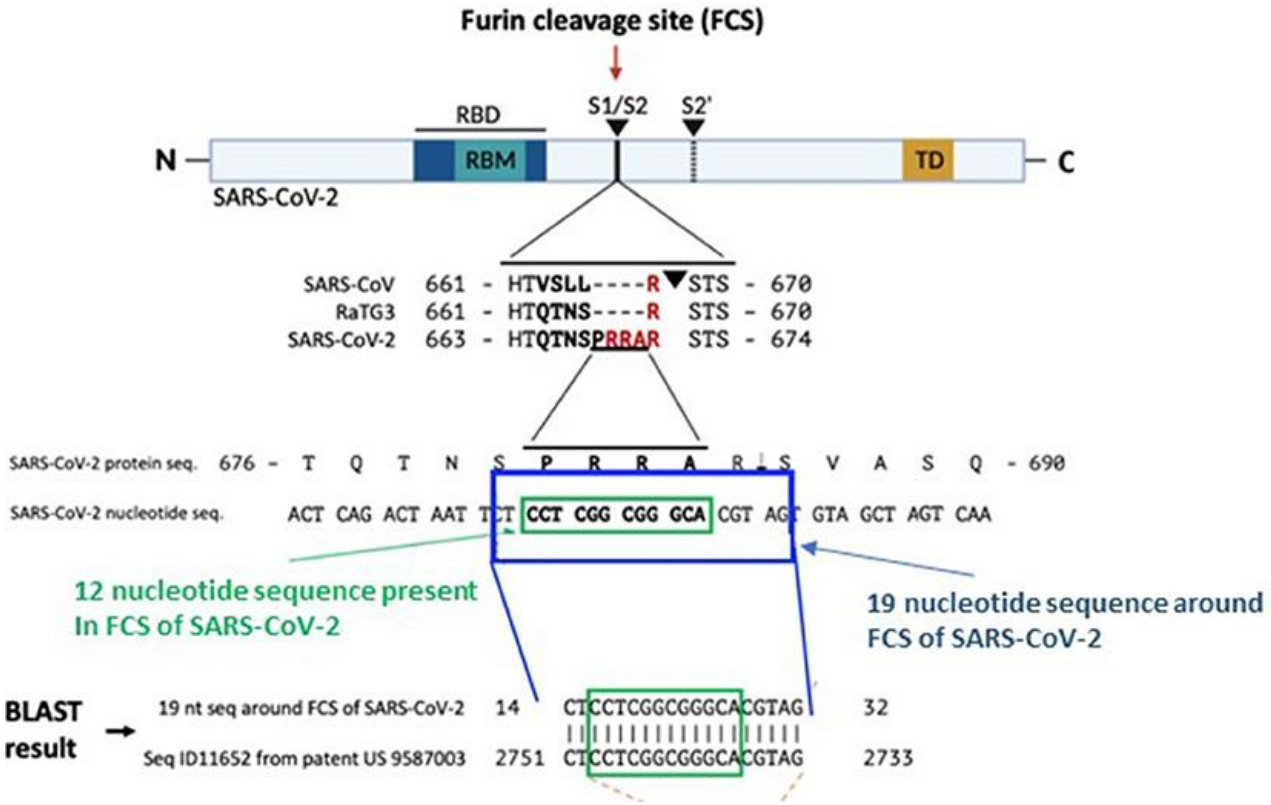


The genetic structure of SARS-CoV-2 does not rule out a laboratory origin

PERSPECTIVE article
Front Virol., 21 February 2022 | https://doi.org/10.3389/fviro.2022.834808

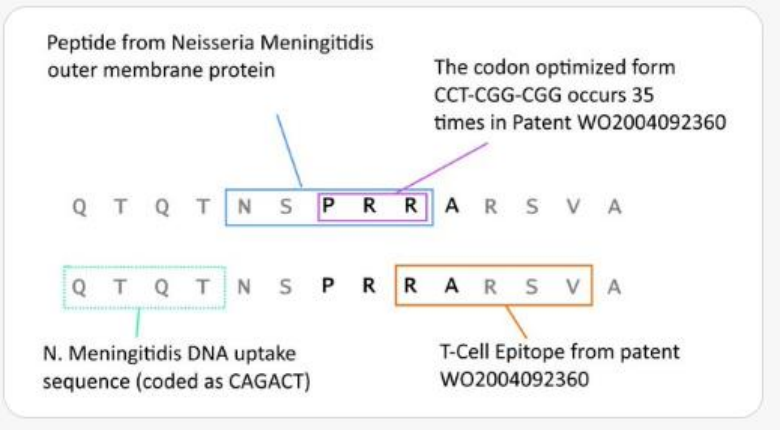
MSH3 Homology and Potential Recombination Link to SARS-CoV-2 Furin Cleavage Site

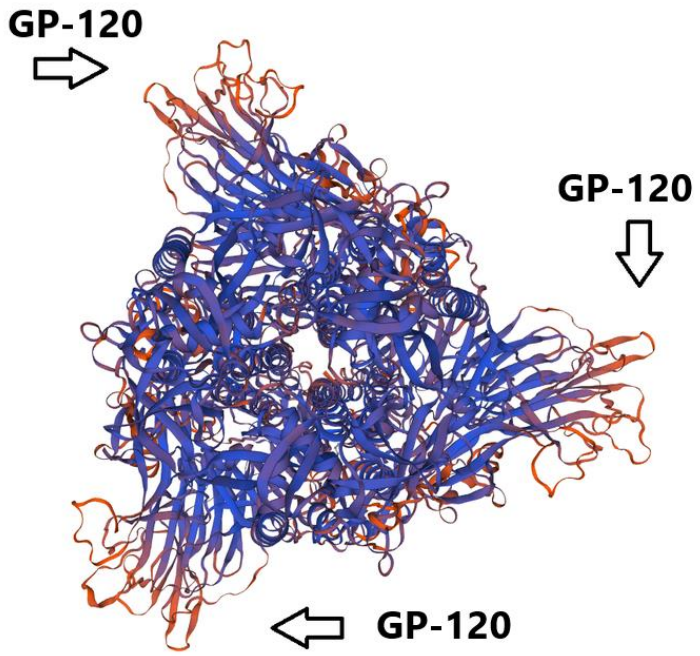
Balamurali K. Ambati[1], Akhil Varshney[2], Kenneth Lundstrom[3*], Giorgio Palù[4], Bruce D. Uhal[5], Vladimir N. Uversky[6] and Adam M. Brufsky[7]



The correlation between this SARS-CoV-2 sequence and the reverse complement of a proprietary mRNA sequence is of uncertain origin. Conventional biostatistical analysis indicates that the probability of this sequence randomly being present in a 30,000-nucleotide viral genome is 3.21×10^{-11} (Figure 2).

Motifs	Virus Glycoprotein	Motif Alignment	HIV protein and Variable region	HIV Genome Source Country/ subtype
Insert 1	2019- nCoV (GP) HIV1(GP120)	**71 76** TNGTKR TNGTKR **404 409**	gp120-V4	Thailand */ CRF01_AE
Insert 2	2019- nCoV (GP) HIV1(GP120)	**145 150** HKNNKS HKNNKS **462 467**	gp120-V5	Kenya*/ G
Insert 3	2019- nCoV (GP) HIV1(GP120)	**245 256** RSYL----TPGDSSSG RTYLFNETRGNSSSG **136 150**	gp120-V1	India*/C
Insert 4	2019- nCoV (Poly P) HIV1(gag)	**676 684** QTNS----------PRRA QTNSSILMQRSNFKG PRRA **366 384**	Gag	India*/C





HIV-1 gp120: A Target for Therapeutics and Vaccine Design

Authors: Cicala, Claudia; Nawaz, Fatima; Jelicic, Katija; Arthos, James; S. Fauci, Anthony
Source: Current Drug Targets, Volume 17, Number 1, 2016, pp. 122-135(14)

PROPOSAL: VOLUME I

DARPA – PREEMPT (HR001118S0017)

LEAD ORGANIZATION: EcoHealth Alliance (Other Nonprofit)

OTHER TEAM MEMBERS:

Duke NUS Medical School (Other Educational)

University of North Carolina (Other Educational)

Wuhan Institute of Virology (Other Educational)

USGS National Wildlife Health Center (Other Nonprofit)

Palo Alto Research Center (Large Business)

Project DEFUSE: Defusing the Threat of Bat-borne Coronaviruses

Principal Investigator and Technical Point of Contact
Peter Daszak, Ph.D.
EcoHealth Alliance

Administrative Point of Contact

Luke Hamel
EcoHealth Alliance

p. 13 *1 occurrence*

We will analyze all SARS-CoV § gene sequences for appropriately conserved proteolytic cleavage sites in 52 and for the presence of potential **furin** cleavage sites".

p. 41 *1 occurrence*

Computational prediction of **furin** cleavage ites by a hybrid method and understanding mechanism underlying diseases.

p. 13 *4 occurrences*

SARS- CoV with mismatches in proteolytic cleavage sits can be activated by exogenous trypsin or cathepsin L Where clear mismatches occur, we wil **introduce** appropriate human specific cleavage sites and evaluate growth potential in Vero cel and HAE cultures.

proteolytic cleavage sites, and if so, **introduce** these changes into the appropriate high abundant, low risk parental tain. linked gljcesyaon; Some gycosyaton events regulte SARS-CoV partic binding DC-SIGN/L-SIGN, alternative receptors for SARS-CoV entry into macrophages or monocytes".

https://www.documentcloud.org/documents/21066966-defuse-proposal

Statement in support of the scientists, public health professionals, and medical professionals of China combatting COVID-19

We are public health scientists who have closely followed the emergence of 2019 novel coronavirus disease (COVID-19) and are deeply concerned about its impact on global health and wellbeing. We have watched as the scientists, public health professionals, and medical professionals of China, in particular, have worked diligently and effectively to rapidly identify the pathogen behind this outbreak, put in place significant measures to reduce its impact, and share their results transparently with the global health community. This effort has been remarkable.

We sign this statement in solidarity with all scientists and health professionals in China who continue to save lives and protect global health during the challenge of the COVID-19 outbreak. We are all in this together, with our Chinese counterparts in the front [illegible] nothing but create fear, rumours, and prejudice that jeopardise our global collaboration in the fight against this virus. We support the call from the Director-General of WHO to promote scientific evidence and unity over misinformation and conjecture.[14] We want you, the science and health professionals of China, to know that we stand with you in your fight against this virus.

We invite others to join us in supporting the scientists, public health professionals, and medical professionals of Wuhan and across China. Stand with our colleagues on the frontline!

We speak in one voice. To add your support for this statement, sign our letter online. LM is editor of ProMED-mail. We declare no competing interests.

Charles Calisher, Dennis Carroll, Rita Colwell, Ronald B Corley, Peter Daszak, Christian Drosten, Luis Enjuanes, Jeremy Farrar, Hume Field, Josie Golding, Alexander Gorbalenya, Bart Haagmans, James M Hughes, William B Karesh, Gerald T Keusch, Sai Kit Lam, Juan Lubroth, John S Mackenzie, Larry Madoff, Jonna Mazet, Peter Palese, Stanley Perlman, Leo Poon, Bernard Roizman, Linda Saif, Kanta Subbarao, Mike Turner

The Wuhan Connection: What did Charité Professor Christian Drosten know about risky virus experiments in China? / dpa

Origin of the coronavirus

Drosten rows back: Dangerous experiments in Wuhan

At the beginning of the pandemic, Christian Drosten described the fact that the coronavirus could have come from a Chinese laboratory as a conspiracy theory. Now the Berlin star virologist admits: "Things were done in Wuhan that could be described as dangerous."

PERSPECTIVE

Use of Highly Pathogenic Avian Influenza A(H5N1) Gain-Of-Function Studies for Molecular-Based Surveillance and Pandemic Preparedness

C. Todd Davis, Li-Mei Chen, Claudia Pappas, James Stevens, Terrence M. Tumpey, Larisa V. Gubareva, Jacqueline M. Katz, Julie M. Villanueva, Ruben O. Donis, Nancy J. Cox

Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

(GOF). Influenza virus GOF studies have focused on several research areas: *in vitro* and/or *in vivo* replication in mammalian cell culture or animal hosts, adaptive mutations conferring changes in host susceptibility, alteration of receptor binding profiles and/or tropism for mammalian airway tissues, enhanced polymerase activity, changes in host antiviral response (e.g., cell signaling pathways), susceptibility to antiviral drugs, and pathogenesis and/or transmissibility in mammalian animal models. Such GOF exper-

lecular basis for avian versus mammalian influenza virus receptor binding (α2,3 versus α2,6 sialylated glycans) has been elucidated largely through GOF experiments, and some recent studies that identified specific HA mutations conferring a switch from avian to mammalian host receptor specificity also demonstrated the impact of these mutations on the ability of H5N1 virus to more