SARS-CoV-2 & PASC/Long COVID through the prism of Gain-of-Function Research

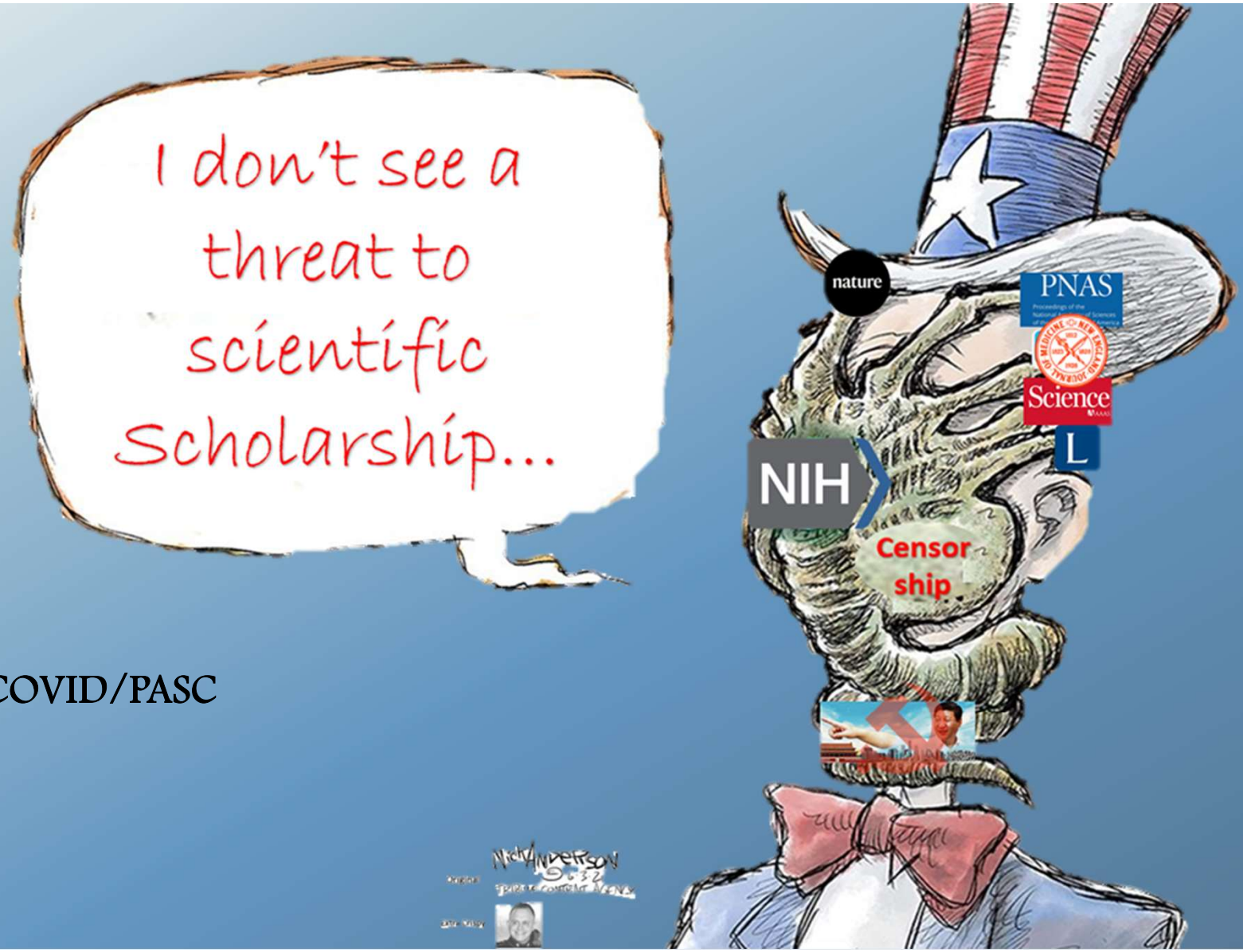
Charles Rixey

~ Outline ~

- **Censorship**

- What was censored, and why?

- Implications for Long COVID/PASC



Key moments in the early pandemic

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January-February 2020

1/11 – SARS-CoV-2 sequence released

1/13 – Moderna finishes vaccine sequence

1/27 – Anthony Fauci knows all about EHA

1/29 – Bill Gallaher announces the FCS

1/31 – *Pradhan et al* published

2/1 – Fauci/Farrar teleconference

2/2 – *Pradhan et al* retracted

2/3 – OSTP teleconference

Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag

Prashant Pradhan[$1,2], Ashutosh Kumar Pandey[$1], Akhilesh Mishra[$1], Parul Gupta[1], Praveen Kumar Tripathi[1], Manoj Balakrishnan Menon[1], James Gomes[1], Perumal Vivekanandan*[1]and Bishwajit Kundu*[1]

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Abstract:

We are currently witnessing a major epidemic caused by the 2019 novel coronavirus (2019-nCoV). The evolution of 2019-nCoV remains elusive. We found 4 insertions in the spike glycoprotein (S) which are unique to the 2019-nCoV and are not present in other coronaviruses. Importantly, amino acid residues in all the 4 inserts have identity or similarity to those in the HIV-1 gp120 or HIV-1 Gag. Interestingly, despite the inserts being discontinuous on the primary amino acid sequence, 3D-modelling of the 2019-nCoV suggests that they converge to constitute the receptor binding site. The finding of 4 unique inserts in the 2019-nCoV, all of which have identity /similarity to amino acid residues in key structural proteins of HIV-1 is unlikely to be fortuitous in nature. This work provides yet unknown insights on 2019-nCoV and sheds light on the evolution and pathogenicity of this virus with important implications for diagnosis of this virus.

Introduction

Coronaviruses (CoV) are single-stranded positive-sense RNA viruses that infect animals and humans. These are classified into 4 genera based on their host specificity: *Alphacoronavirus, Betacoronavirus, Deltacoronavirus and Gammacoronavirus* (Snijder et al., 2006). There are seven known types of CoVs that includes 229E and NL63 (Genus Alphacoronavirus), OC43, HKU1, MERS and SARS (Genus Betacoronavirus). While 229E, NL63, OC43, and HKU1 commonly infect humans, the SARS and MERS outbreak in 2002 and 2012 respectively occurred when the virus crossed-over from animals to humans causing significant mortality (J. Chan et al., n.d.; J. F. W. Chan et al., 2015). In December 2019, another outbreak of coronavirus was reported from Wuhan, China that also transmitted from animals to humans. This new virus has been temporarily termed as 2019-novel Coronavirus (2019-nCoV) by the World Health Organization (WHO) (J. F.-W. Chan et al., 2020; Zhu et al., 2020). While there are several hypotheses about the origin of 2019-nCoV, the source of this ongoing outbreak remains elusive.

The transmission patterns of 2019-nCoV is similar to patterns of transmission documented in the previous outbreaks including by bodily or aerosol contact with persons infected with the virus.
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Scientists involved in the construction of the natural-origin narrative:

- **2/1** The teleconference held by Fauci & Farrar to discuss suspicious parts of the viral genome
- **2/3** The teleconference held by Fauci & Droegemeier to discuss how to "combat misinformation"
- **2/4** The coordination between scientists to craft a pro-zoonosis paper as discuss

Co-authors of these key papers:

- **Prox** The Proximal origin of SARS-CoV-2
- **Lnc** The Lancet "Statement in support..."
- **Prox2** The Origins of SARS-CoV-2: A Critical Review
- **W1** Dissecting the early COVID-19 cases in Wuhan
- **WX** Evidence Against the Veracity of SARS-CoV-2 Genom… between Lineag
- **AO** The animal origin of SARS-CoV-2
- **W2** The Huanan market was the epicenter of SA… 2 emergence
- **W3** SARS-CoV-2 emergence very likely r… east two zoonotic events

2/1/2020 Teleconference

2/1 OPTIMALS	2/1	2/3	2/4	Prox	Lnc	Prox2	W1	WX	…	…
Pohlmann	1									
Schrier	1									
Fouchier	1									
Drosten	1				1					1
Vallance	1									
WIV										13
SCICOMM										32

The Approximals

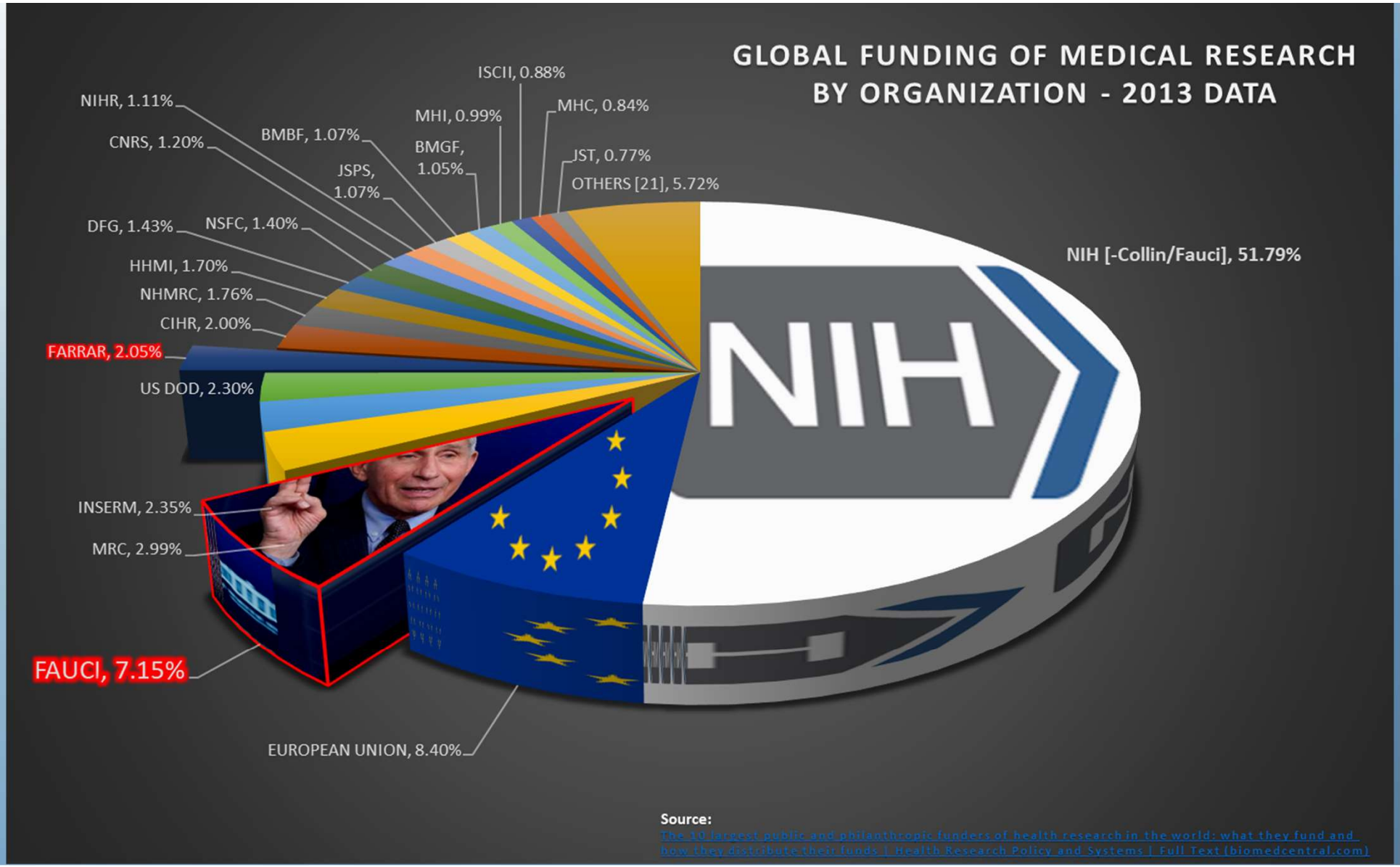
APPROXIMALS	2/1	2/3	2/4	Prox	Lnc	Prox2	W1	WX	AO	W2	W3	
Wertheim						1		1		1	1	4
Crits-Christoph						1				1	1	3
Pekar							1			1	1	3
Suchard							1			1	1	3
Goldstein						1				1		2
Rasmussen						1				1		2
Neil						1						1

The Proximals

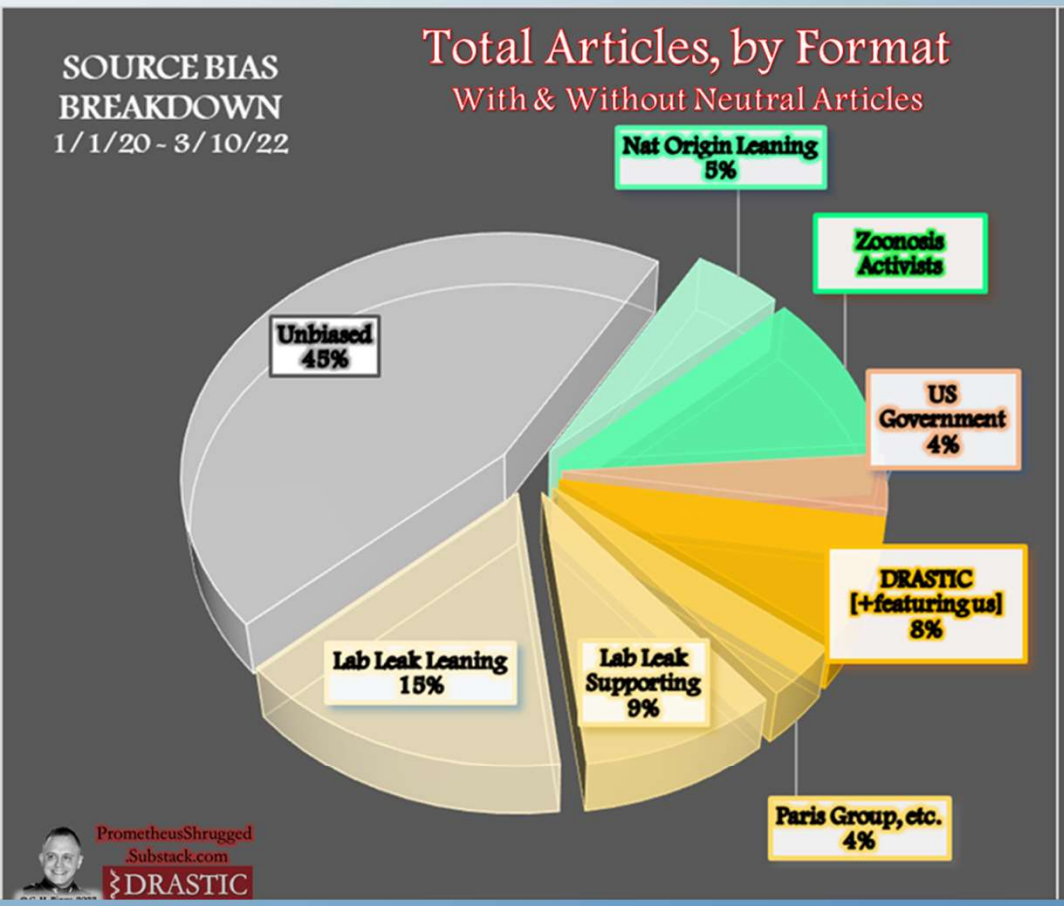
PROXIMALS	2/1	2/3	2/4	Prox	Lnc	Prox2	W1	WX	AO	W2	W3	#
Holmes	1	1	1	1		1				1	1	4
Andersen	1	1	1	1		1		1		1	1	5
Garry	1	1	1	1		1				1	1	4
Rambaut				1		1		1		1	1	5
Lipkin		1	1	1		1						2
[illegible]						1	1	1		1	1	5
[illegible]lins	1											
Fauci	1	1										
Farrar	1				1	1						2
Droegemeier		1										
Koopmans	1											

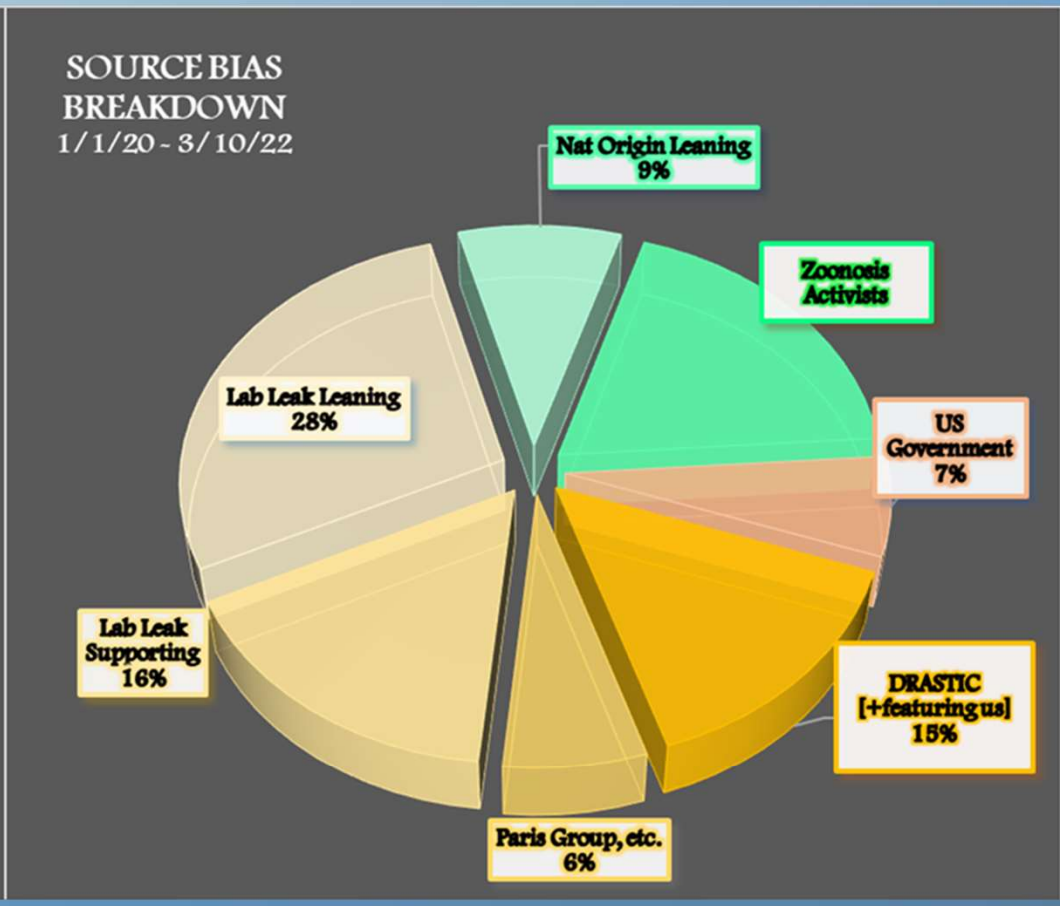
The Lanceteers

LANCETEERS	2/1	2/3	2/4	Prox	Lnc	Prox2	W1	WX	AO	W2	W3	
Daszak		1	1		1							1
Baric		1	1									
Weiss						1						1
Saif					1							1
Perlman		1	1		1							1
Karesh					1							1
Gronvall		1										
Mazet					1							1


GLOBAL FUNDING OF MEDICAL RESEARCH
BY ORGANIZATION - 2013 DATA
NIH [-Collin/Fauci], 51.79%
NIH
EUROPEAN UNION, 8.40%
FAUCI, 7.15%
FARRAR, 2.05%
NIHR, 1.11%
CNRS, 1.20%
BMBF, 1.07%
JSPS, 1.07%
BMGF, 1.05%
MHI, 0.99%
ISCII, 0.88%
MHC, 0.84%
JST, 0.77%
OTHERS [21], 5.72%
DFG, 1.43%
NSFC, 1.40%
HHMI, 1.70%
NHMRC, 1.76%
CIHR, 2.00%
US DOD, 2.30%
INSERM, 2.35%
MRC, 2.99%
Source:
The 10 largest public and philanthropic funders of health research in the world: what they fund and how they distribute their funds | Health Research Policy and Systems | Full Text (biomedcentral.com)

Fauci's 13% "Consensus"





Sources by Type & Perspective		Since 1/1/20	
D	DRASTIC [+coverage of]	0	0.0%
P	Paris Group, etc.	4	1.6%
S	Lab Leak Supporting	0	0.0%
L	Lab Leak Leaning	3	1.2%
U	Neutral/Unbiased	112	43.4%
N	Natural-Origin Leaning	26	10.1%
Z	Zoonosis Activists	113	43.8%
		258	

Since 1/1/20

Type	D	P	S	L	U	N	Z	#
journal	0	4	0	3	112	26	113	258

Publication	D	P	S	L	U	N	Z	#
Nature	0	0	0	0	16	15	22	53
Science	0	1	0	0	17	0	25	43
The Lancet	0	1	0	1	12	2	6	22
PNAS	0	1	0	2	8	1	5	17
New England Journal of Medicine	0	0	0	0	6	0	7	13
Nature Scientific Reports	0	0	0	0	10	0	2	12
Cell	0	0	0	0	4	0	6	10
Nature Medicine	0	0	0	0	4	1	5	10
Science Magazine; NAS	0	0	0	0	1	2	4	7
Nature Communications	0	0	0	0	3	0	2	5
Nature Scientific American	0	0	0	0	1	1	3	5
Nature Signal Transduction & Tar	0	0	0	0	0	0	5	5
The Lancet Infectious Diseases	0	0	0	0	3	0	2	5
Cell Research	0	0	0	0	0	0	3	3
Nature Cellular & Molecular Immu	0	0	0	0	0	0	3	3
Nature Microbiology	0	0	0	0	1	0	2	3
Nature Reviews Microbiology	0	0	0	0	2	0	1	3
Cell Current Biology	0	0	0	0	0	0	2	2
Cell Discovery	0	0	0	0	1	0	1	2
Cell Immunity	0	0	0	0	0	1	1	2
Cell iScience	0	0	0	0	2	0	0	2
Cell Reports	0	0	0	0	1	0	1	2
Nature Communications Biology	0	0	0	0	1	1	0	2
Nature Ecology & Evolution	0	0	0	0	1	1	0	2
Science Advances	0	0	0	0	2	0	0	2
Science Immunology	0	0	0	0	2	0	0	2
The Lancet Microbe	0	0	0	0	2	0	0	2
The Lancet Planetary Health	0	0	0	0	0	0	2	2
Cell & Bioscience	0	0	0	0	1	0	0	1
Cell Death & Differentiation	0	0	0	0	1	0	0	1
Cell Host & Microbe	0	0	0	0	1	0	0	1
Cell Med	0	0	0	0	0	0	1	1
Cell Molecular Biology	0	0	0	0	1	0	0	1
Cell The Innovation	0	0	0	0	0	1	0	1
Nature [Humanities & Social Scien	0	0	0	0	0	0	1	1
Nature Biotechnology	0	0	0	0	1	0	0	1
Nature Cell Death & Cell Different	0	0	0	0	1	0	0	1
Nature Cell Death Discovery	0	0	0	0	1	0	0	1
Nature Immunology	0	0	0	0	0	0	1	1
Nature Machine Intelligence	0	1	0	0	0	0	0	1
Nature Reviews Immunology	0	0	0	0	1	0	0	1
Nature Structural & MolecularBio	0	0	0	0	1	0	0	1
Science Communication	0	0	0	0	1	0	0	1
The Lancet Public Health	0	0	0	0	1	0	0	1
The Lancet Respiratory Medicine	0	0	0	0	1	0	0	1

Overall totals, with & without articles from the top 6 journals, as of 1/21/23

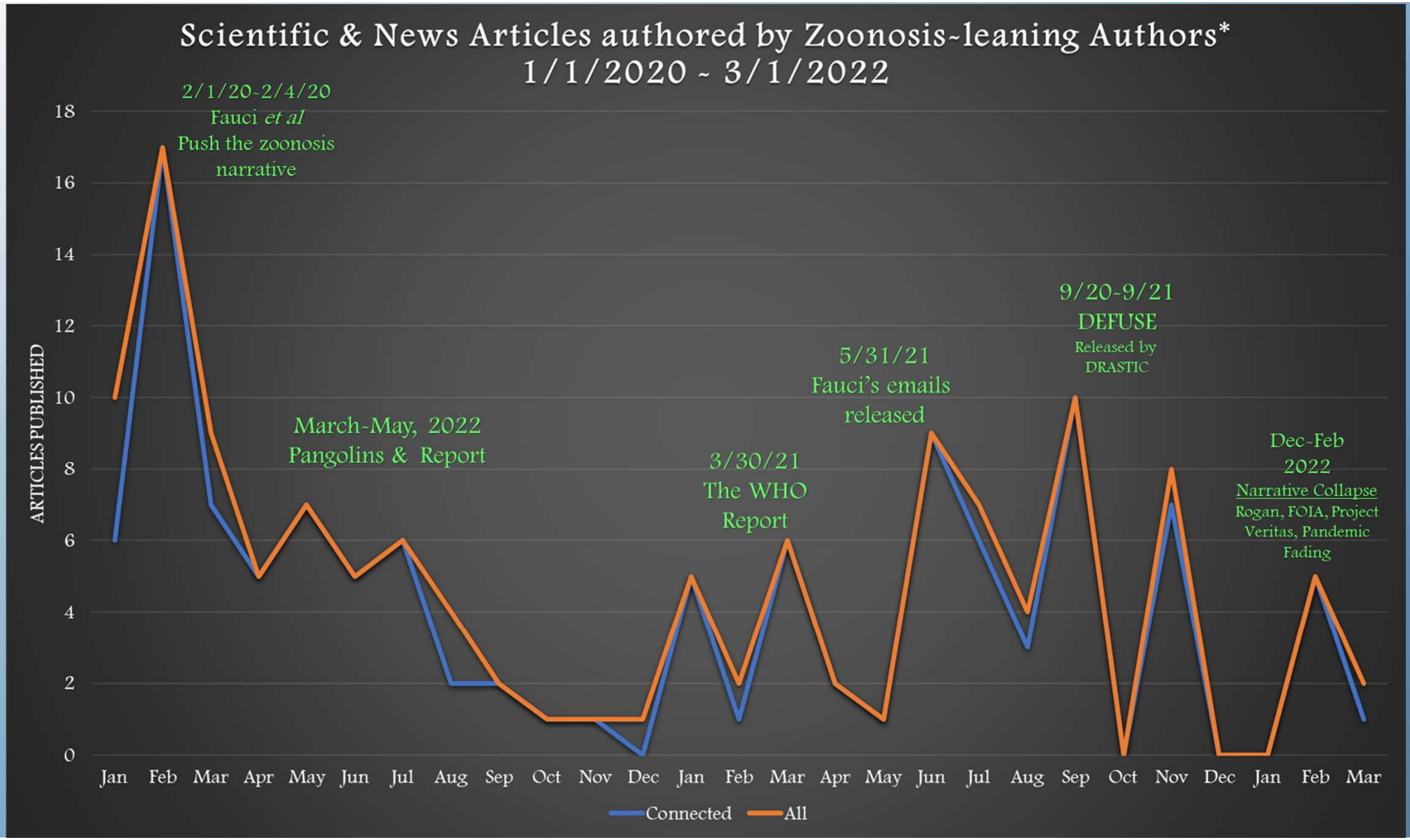
Journals	D	P	S	L	U	N	Z	#
Science	0	1	0	0	17	0	25	43
Other Science Journals	0	0	0	0	6	2	4	12
Nature	0	0	0	0	16	15	22	53
Other Nature Journals	0	1	0	0	28	4	25	58
The Lancet	0	1	0	1	12	2	6	22
Other Lancet Journals	0	0	0	0	7	0	4	11
Cell	0	0	0	0	4	0	6	10
Other Cell Journals	0	0	0	0	8	2	9	19
PNAS	0	1	0	2	8	1	5	17
NEJM	0	0	0	0	6	0	7	13
Totals	**0**	**4**	**0**	**3**	**112**	**26**	**113**	**258**
Top 6 Journals	0	3	0	3	63	18	71	158
Top 6 Specialty Journals	0	1	0	0	49	8	42	100

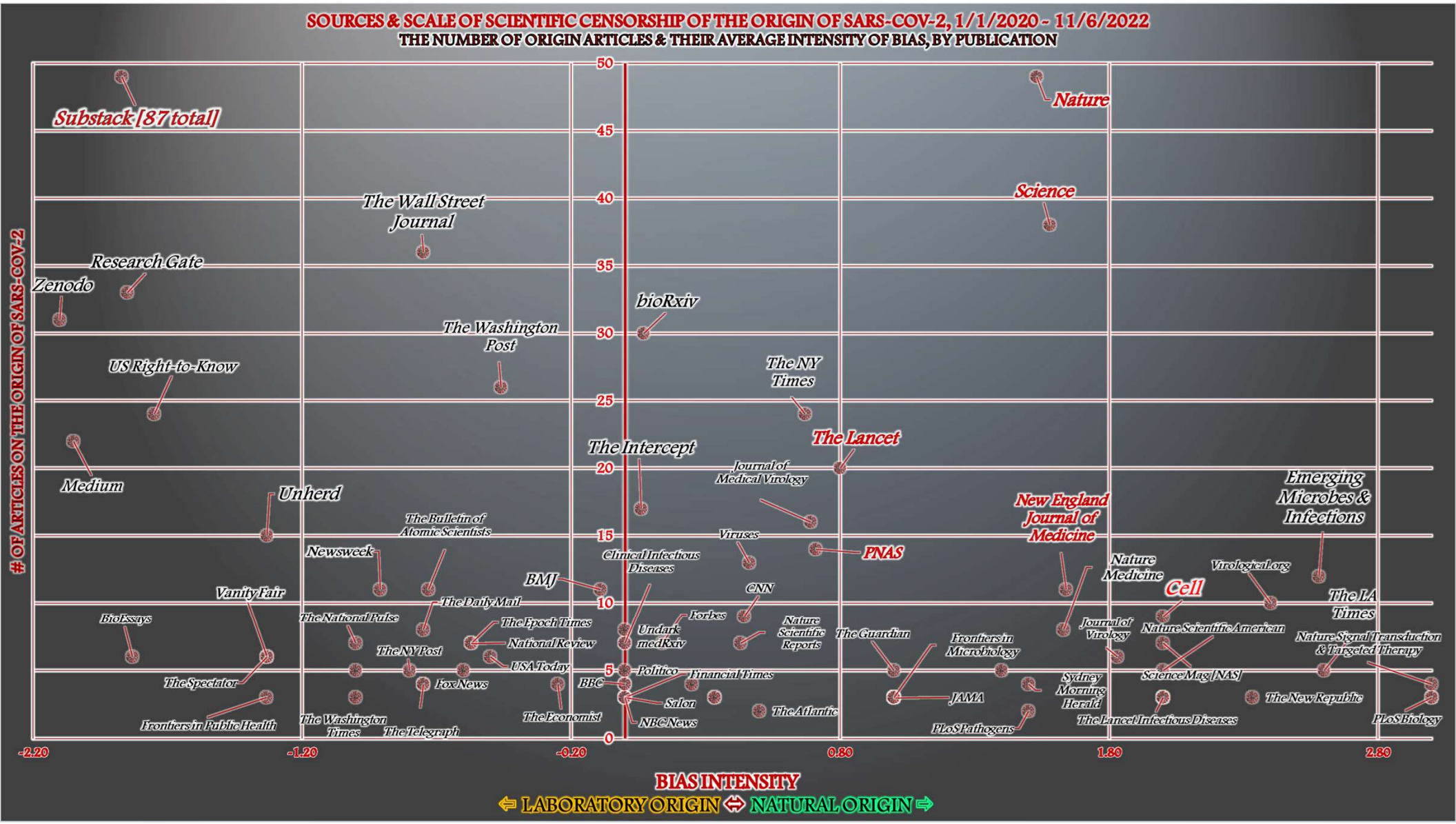
Combined	Main	Pub	All	L	U	Z	#
Nature	53	58	111	1	44	66	111
Science	43	12	55	1	23	31	55
The Lancet	22	11	33	2	19	12	33
NEJM	13	0	13	0	6	7	13
PNAS	17	0	17	3	8	6	17
Cell	10	19	29	0	12	17	29
Totals	158	100	258	7	112	139	258
				2.7%	43.4%	53.9%	

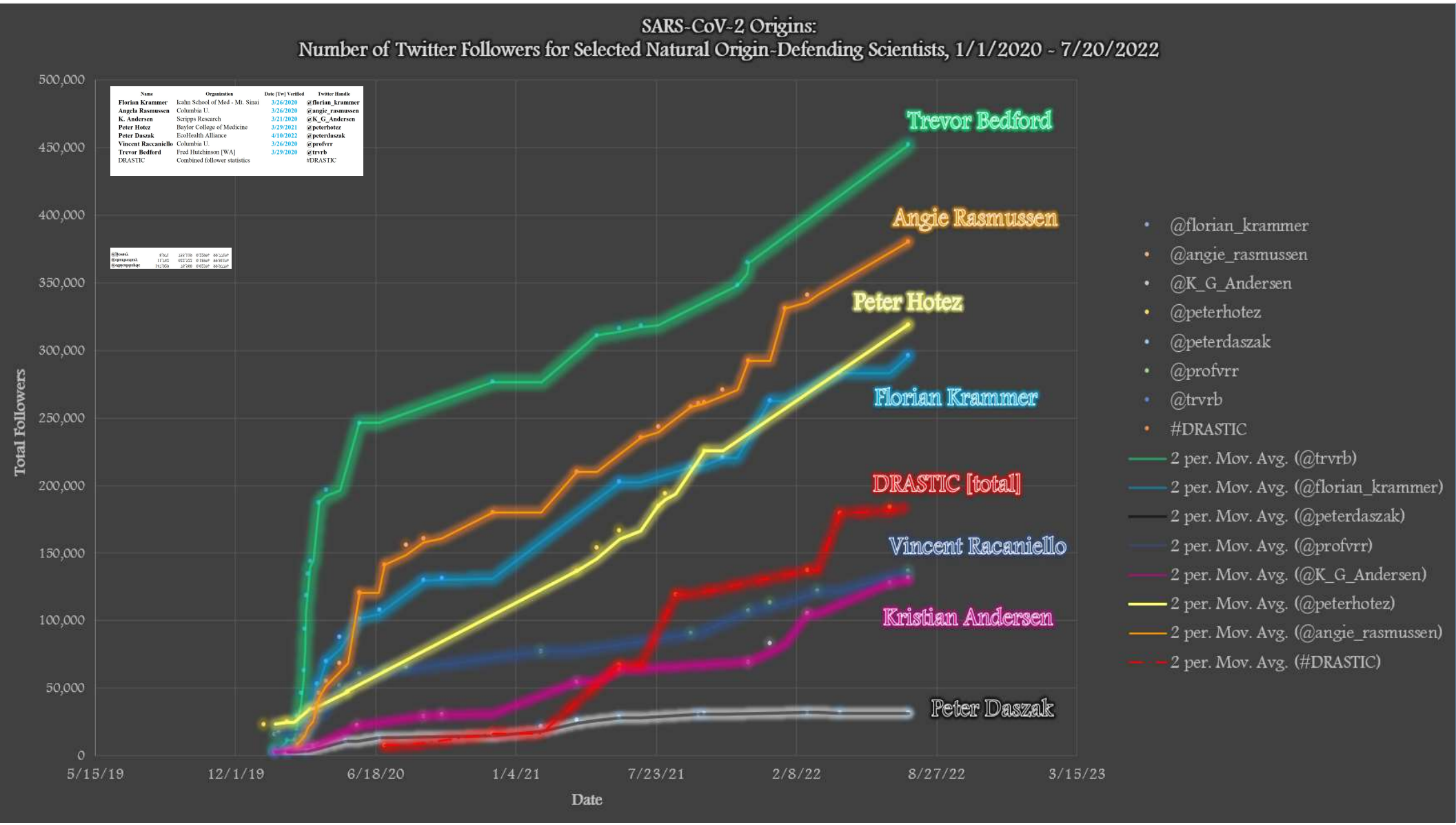
	L	U	Z
Nature	0.9%	39.6%	59.5%
Science	1.8%	41.8%	56.4%
The Lancet	6.1%	57.6%	36.4%
NEJM	0.0%	46.2%	53.8%
PNAS	17.6%	47.1%	35.3%
Cell	0.0%	41.4%	58.6%

	D	P	S	L	U	N	Z	
All Peer-Reviewed Journals	8	18	8	34	379	47	193	**687**
Top 6 Journals	0	4	0	3	112	26	113	**258**
All Except Top 6 Journals	8	14	8	31	267	21	80	**429**

	L	U	Z
All Peer-Reviewed Journals	9.9%	55.2%	28.1%
Top 6 Journals	2.7%	43.4%	53.9%
All Except Top 6 Journals	15.9%	62.2%	23.5%


Scientific & News Articles authored by Zoonosis-leaning Authors*
1/1/2020 - 3/1/2022
2/1/20-2/4/20
Fauci et al
Push the zoonosis narrative
March-May, 2022
Pangolins & Report
3/30/21
The WHO Report
5/31/21
Fauci's emails released
9/20-9/21
DEFUSE
Released by DRASTIC
Dec-Feb 2022
Narrative Collapse
Rogan, FOIA, Project Veritas, Pandemic Fading
ARTICLES PUBLISHED
0
2
4
6
8
10
12
14
16
18
Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar
Connected
All


SOURCES & SCALE OF SCIENTIFIC CENSORSHIP OF THE ORIGIN OF SARS-COV-2, 1/1/2020 ~ 11/6/2022
THE NUMBER OF ORIGIN ARTICLES & THEIR AVERAGE INTENSITY OF BIAS, BY PUBLICATION
OF ARTICLES ON THE ORIGIN OF SARS-COV-2
50
45
40
35
30
25
20
15
10
5
0
Substack [87 total]
Nature
Science
The Wall Street Journal
Research Gate
Zenodo
bioRxiv
The Washington Post
US Right-to-Know
The NY Times
The Lancet
The Intercept
Medium
Journal of Medical Virology
Emerging Microbes & Infections
Unherd
New England Journal of Medicine
The Bulletin of Atomic Scientists
Viruses
Newsweek
Clinical Infectious Diseases
PNAS
Nature Medicine
Virological.org
BMJ
CNN
Cell
Vanity Fair
The Daily Mail
The LA Times
Forbes
BioEssays
The National Pulse
Nature Scientific American
Undark
Nature Scientific Reports
The Guardian
Journal of Virology
Nature Signal Transduction & Targeted Therapy
The Epoch Times
medRxiv
Frontiers in Microbiology
National Review
The NY Post
Science Mag [NAS]
USA Today
Politico
Financial Times
The Spectator
Fox News
BBC
Sydney Morning Herald
The New Republic
JAMA
Salon
The Atlantic
Frontiers in Public Health
The Economist
NBC News
The Lancet Infectious Diseases
PLoS Biology
The Washington Times
The Telegraph
PLoS Pathogens
-2.20
-1.20
-0.20
0.80
1.80
2.80
BIAS INTENSITY
⇦ LABORATORY ORIGIN ⇔ NATURAL ORIGIN ⇨


SARS-CoV-2 Origins:
Number of Twitter Followers for Selected Natural Origin-Defending Scientists, 1/1/2020 - 7/20/2022
Name | Organization | Date [Tw] Verified | Twitter Handle
Florian Krammer | Icahn School of Med - Mt. Sinai | 3/26/2020 | @florian_krammer
Angela Rasmussen | Columbia U. | 3/26/2020 | @angie_rasmussen
K. Andersen | Scripps Research | 3/21/2020 | @K_G_Andersen
Peter Hotez | Baylor College of Medicine | 3/29/2021 | @peterhotez
Peter Daszak | EcoHealth Alliance | 4/10/2022 | @peterdaszak
Vincent Raccaniello | Columbia U. | 3/26/2020 | @profvrr
Trevor Bedford | Fred Hutchinson [WA] | 3/29/2020 | @trvrb
DRASTIC | Combined follower statistics | | #DRASTIC
Trevor Bedford
Angie Rasmussen
Peter Hotez
Florian Krammer
DRASTIC [total]
Vincent Racaniello
Kristian Andersen
Peter Daszak
Total Followers
500,000
450,000
400,000
350,000
300,000
250,000
200,000
150,000
100,000
50,000
0
5/15/19
12/1/19
6/18/20
1/4/21
7/23/21
2/8/22
8/27/22
3/15/23
Date
@florian_krammer
@angie_rasmussen
@K_G_Andersen
@peterhotez
@peterdaszak
@profvrr
@trvrb
#DRASTIC
2 per. Mov. Avg. (@trvrb)
2 per. Mov. Avg. (@florian_krammer)
2 per. Mov. Avg. (@peterdaszak)
2 per. Mov. Avg. (@profvrr)
2 per. Mov. Avg. (@K_G_Andersen)
2 per. Mov. Avg. (@peterhotez)
2 per. Mov. Avg. (@angie_rasmussen)
2 per. Mov. Avg. (#DRASTIC)

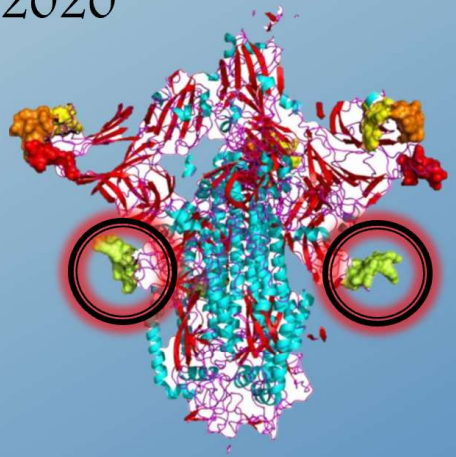
~ Outline ~

- Censorship
- What was censored, and why?
- Implications

2 specific elements of the SARS-CoV-2 genome

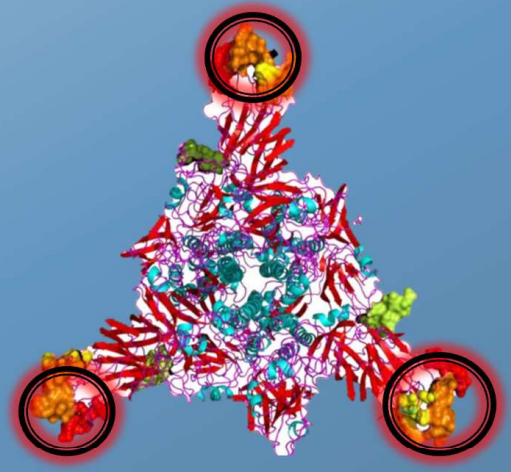
Furin Cleavage Site

- 1st announced in Chinese on 1/21/2020
- 1st announced in English on 1/29/2020



"HIV Inserts"

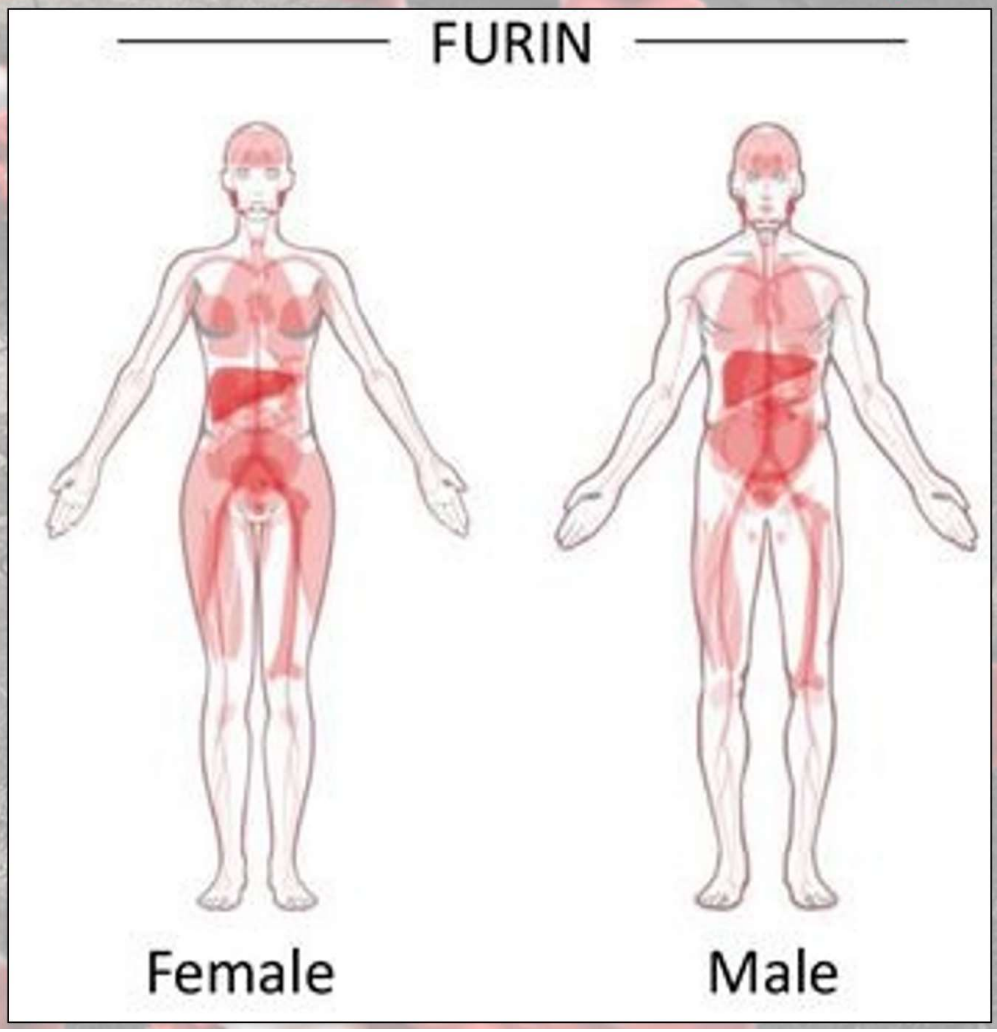
- 1st announced on 1/31/2020



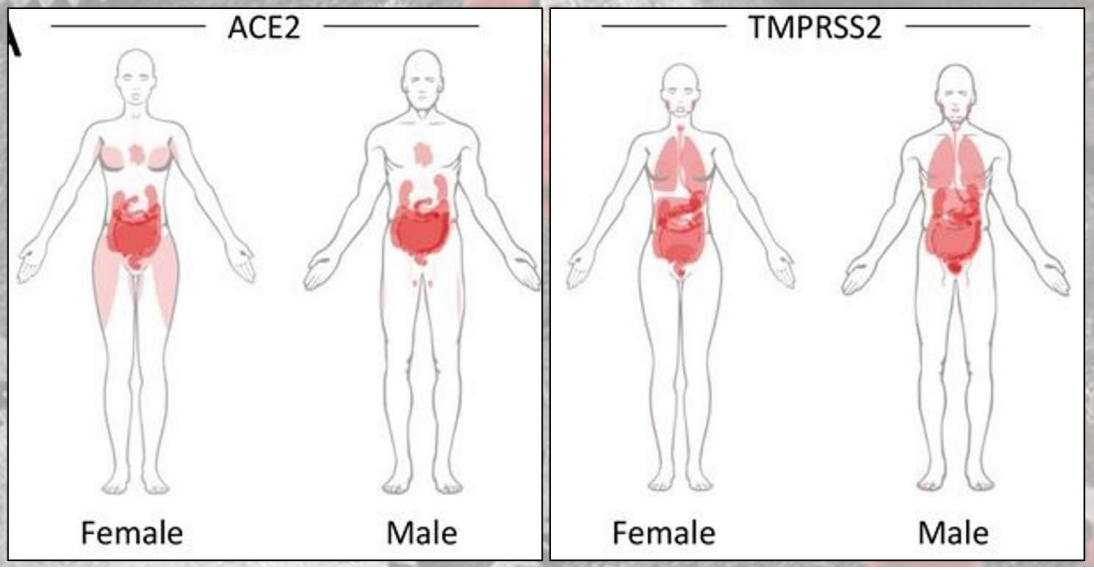
Insert 1 > TNGTKR
Insert 2 > HKNNKS
Insert 3 > RSYL- - - TPGDSSSG
Insert 4 > QTNSPRRA

Primary human cell receptors in…..

SARS-CoV-2



SARS-CoV



All articles published by the WIV, EHA or scientists involved in the 2/1 & 2/3 meetings:
[FCS mentions in **red**]

Date	Article
1/21	A furin cleavage site was discovered in the spike protein of the 2019 nCoV
1/21	An emerging CoV causing pneu. outbreak in Wuhan, China: calling for dev. therapeutic & prophylactic strategies
1/22	Emerging Viruses without Borders: The Wuhan Coronavirus
1/23	Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR
1/23	Complete genome characterization of an nCoV associated with severe human respiratory disease in Wuhan, China
1/23	Discovery of an nCoV associated with the recent pneumonia outbreak in humans and its potential bat origin
1/23	WHO Director-General's statement on the advice of the IHR Emergency Committee on Novel Coronavirus
1/24	A Novel Coronavirus from Patients with Pneumonia in China, 2019
1/24	Return of the Coronavirus: 2019-nCoV
1/24	A Novel Coronavirus Emerging in China — Key Questions for Impact Assessment
1/24	Another Decade, Another Coronavirus
1/28	Anti-Science kills: From Soviet embrace of Pseudoscience...
1/28	We Made the Coronavirus Epidemic - Daszak quotes
1/29	Analysis of Wuhan Coronavirus: Deja Vu - SARS-CoV-2 / nCoV-2019 Evolutionary History - Virological
1/30	Genomic characterization and epidemiology of 2019 nCoV: implications for virus origins and receptor binding
1/30	Origins of MERS-CoV, and lessons for 2019-nCoV
1/31	Analysis of Wuhan Coronavirus: Déjà Vu
1/31	Coronavirus (COVID-19): sharing research data | Wellcome
2/1	The continuing 2019-nCoV epidemic threat of novel CoV's to global health - The latest outbreak in Wuhan, China
2/1	A pneumonia outbreak associated with a new coronavirus of probable bat origin
2/3	Accelerated viral dynamics in bat cell lines, with implications for zoonotic emergence
2/3	Synergistic China–US Ecological Research is Essential for Global Emerging Infectious Disease Preparedness
2/4	HIV-1 did not contribute to the 2019-nCoV genome
2/4	Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro
2/7	NASEM Response to OSTP re Coronavirus February 6, 2020
2/11	Fusion mechanism of 2019-nCoV and fusion inhibitors targeting HR1 domain in spike protein
2/14	The First Disease X is Caused by a Highly Transmissible Acute Respiratory Syndrome Coronavirus
2/13	No credible evidence supporting claims of the laboratory engineering of SARS-CoV-2
2/16	The Proximal Origin of SARS-CoV-2 [pre-print on Virological.org]
2/17	Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes
2/19	Statement in support of the scientists, public health prof., and medical prof. of China combatting COVID-19
2/19	Is SARS-CoV-2 originated from laboratory? A rebuttal to the claim of formation via laboratory recombination
2/26	Escaping Pandora's Box — Another Novel Coronavirus
2/27	Coronavirus far more likely than Sars to bond to human cells due to HIV-like mutation, scientists say
3/1	2019-nCoV in context: lessons learned?
3/17	The Proximal Origin of SARS-CoV-2
3/17	The COVID-19 coronavirus epidemic has a natural origin, scientists say

6 Weeks & 33 papers

Fauci, Farrar, EHA, WIV, Drosten, Andersen *et al* waited >6 weeks to publish a paper about the FCS

-The element that made SARS-CoV-2 a pandemic-level virus

-The element that made SARS-CoV-2 so efficient at aerosol spread

-The element identified in a Chinese journal on 1/21/2020, & by Bill Gallaher on 1/29/2020

-They ALL stayed silent until the Narrative could be set by "Proximal Origin"

-At which point it was too late

Chapter 1: Sounds Like It Could Be Fun

Stéphane Bancel said in a December 17, 2020, interview with Antonio Regalado of *MIT Technology Review* that NIH and Moderna independently came "to the same design." This is apparently a reference to an explicit decision to leave intact the so-called furin-cleavage site, the spot where the spike protein normally gets split into two pieces by the furin enzyme. Graham could have made the spikes more durable by altering the furin-cleavage sequence, but he felt that cut, like a careful incision in a folded piece of origami, would provide the greater flexibility needed for a better immune response. He doubts that Moderna would have made the same counterintuitive call on its own.

"I would make sure I did NOT include that motif in that virus"

"If one is making viruses, intentionally, for use in manufacturing, and if I knew that there was a certain genetic motif that correlated with high transmissibility, I would make sure I did not include that motif in that virus; just as today, if there is a virus that has a polybasic cleavage site in HA which is associated with virulence we make sure - in fact we have a rule in our lab - we DO NOT make flu viruses with that motif there.

So, there is utility in knowing what are the bad actors genetically that you really don't want in your virus."

https://youtu.be/Aw-nR6-4kQQ?t=3111

P. Dormitzer, December 2014

Philip Dormitzer

Novartis, to 2015: Led H1N1 Vax Dev [fastest ever, pre-COVID]
Pfizer, 2015-2021: Led COVID-19 Vax Dev, through Comirnaty
GSK, 2021-present

In 26 HIV, SARS, MERS or SARS-CoV-2 vax prototypes [NIH/VRC or Pfizer] across 3 decades, the S1/S2 Furin Cleavage Site was retained unchanged **twice** – for the Moderna/Pfizer COVID-19 jabs.

None before or since.

SARS-CoV-2 Origins Research Reference Project - HIV & SARS [Last Updated 7/26/2022] - C. H. Rixey

Research Articles, News & Commentary		Source				Research Foci			
Date	Title	Author (s)	GF	Methods/Addtl Info	Vx	HI	SA	ME	SARS-CoV
5/1/1990	Mutational analysis of the human immunodeficiency virus type 1 env gene product proteolytic cleavage site (asm.org)	Valerie Bosch & Michael Pawlita		Changed FCS	Vaccine	HIV			
1/1/1991	Biological and immunological properties of human immunodeficiency virus type 1 envelope glycoprotein: analysis of proteins with truncations a	Patricia Earl et al	NIAID	No FCS [Primary & Secondary CS were removed/re	Vaccine	HIV			
1/15/2000	A Recombinant HIV-1 Envelope Glycoprotein Complex Stabilized by an Intermolecular Disulfide Bond between the gp120 and gp41 Subunits Is	Binley, James et al		No FCS [Disulfide bond replaces CS]	Vaccine	HIV			
12/15/2006	Phase 1 Safety and Immunogenicity Evaluation of a Multiclade HIV-1 DNA Candidate Vaccine	Barney Graham, John Mascola et al	VRC	No FCS, Multiclade/Conserved	Vaccine	HIV			
1/2/2014	Short Conserved Sequences of HIV-1 Are Highly Immunogenic and Shift Immunodominance	Otto Yang et al [UCLA]	UCLA	No FCS, Conserved Epitope, ~20%	Vaccine	HIV			
2/24/2016	Control of HIV-1 replication in vitro by vaccine-induced human CD8+ T cells through conserved subdominant Pol epitopes	Tina Ahmed et al	Oxford	No FCS, Chimaeric, Conserved, Alt. Clades	Vaccine	HIV			
4/1/2016	Novel Conserved-region T-cell Mosaic Vaccine With High Global HIV-1 Coverage Is Recognized by Protective Responses in Untreated Infecto	Bette Korber et al	LANL	No FCS, Removed AA's 364-389, Mosaic structure	Vaccine	HIV			
4/1/2016	Suppl figures5-v2.pptx [Novel Conserved Region]	Bette Korber et al	LANL	No FCS, Removed AA's 364-389, Mosaic structure	Vaccine	HIV			
8/29/2017	Immunogenicity and structures of a rationally designed prefusion MERS-CoV spike antigen	Kizzmekia Corbett, Barney Graham et al	VRC	Changed FCS [to ASVG], 2P	Vaccine	HIV		MERS	
11/21/2017	Structure-based design of native-like HIV-1 envelope trimers to silence non-neutralizing epitopes and eliminate CD4 binding	Daniel W. Kulp et al	Scripps	No FCS & replace it with a flexible 'linker'	Vaccine	HIV		MERS	
5/15/2018	HIV-1 Vaccines Based on Antibody Identification, B Cell Ontogeny, and Epitope Structure	Mascola, John & Kwong, Peter	VRC	No FCS, Prefusion	Vaccine	HIV			
5/24/2018	Codon optimization & improved delivery/ab regimen enhance the immune response against wild-type & drug-resistant HIV-1 rev-trans, preserv	AA Latanova et al	LANL	No FCS, Codon optimized, smaller conserved elemer	Vaccine	HIV			
10/25/2019	T cell-based strategies for HIV-1 vaccines	Bette Korber & Will Fischer	LANL	No FCS, 9 mosaic/conserved prototypes	Vaccine	HIV			
3/9/2020	Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein: Cell	Alexandra C. Walls et al		Changed FCS [removed 4 AA]	Vaccine				SARS-COV-2
3/16/2020	Don't rush to deploy COVID-19 vaccines and drugs without sufficient safety guarantees (nature.com)	Shibo Jiang	FUD	Changed FCS, 2P & Disulfide Bonds	Vaccine				SARS-COV-2
4/26/2020	Vaccines and Broadly Neutralizing Antibodies for HIV-1 Prevention	Bette Korber et al	LANL	No FCS, 4 mosaic/conserved prototypes	Vaccine	HIV			SARS-COV-2
6/2/2020	Biovacc-19: A candidate vaccine ...	Sorensen, Birger, Dalgleish, Angus & Sus	PG	Changed FCS; ~2 dozen pieces blended together	Vaccine	HIV			SARS-COV-2
8/4/2020	Structure-guided covalent stabilization of coronavirus spike glycoprotein trimers in the closed conformation	University of Washington team		Changed FCS, 2P	Vaccine		SARS	MERS	SARS-COV-2
8/5/2020	SARS-CoV-2 mRNA vaccine design enabled by prototype pathogen preparedness - PubMed (nih.gov)	Barney Graham et al	VRC	**Retained unchanged FCS, 2P**	Vaccine				SARS-COV-2
8/12/2020	Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults | Nature	Philip Dormitzer et al		**Retained unchanged FCS, 2P**	Vaccine				
10/26/2020	Inhibition of SARS-CoV-2 viral entry upon blocking N- and O-glycan elaboration | eLife (elifesciences.org)	Qi Yang et al		Changed FCS [RRAR switched out with SRAS]	Vaccine				SARS-COV-2
12/9/2020	Stabilized diverse HIV-1 envelope trimers for vaccine design	Wang, Qian et al	CHN	Changed FCS, disulfide bonds	Vaccine	HIV		MERS	SARS-COV-2
3/2/2021	Introduction of Two Prolines and Removal of the Polybasic Cleavage Site Lead to Higher Efficacy of a Recombinant Spike-Based SARS-CoV-2	Florian Krammer et al	NIAID	Changed FCS; 2P, disulfide bonds	Vaccine				SARS-COV-2
5/18/2021	Scalable live-attenuated SARS-CoV-2 vaccine candidate demonstrates preclinical safety and efficacy (pnas.org)		NIAID	No FCS, LAV, codon de-optimized	Vaccine				SARS-COV-2
12/9/2021	A multiclade env–gag VLP mRNA vaccine elicits tier-2 HIV-1-neutralizing antibodies and reduces the risk of heterologous SHIV infection in ma	Anthony Fauci, John Mascola et al	VRC	No FCS, Multiclade/Conserved	Vaccine	HIV			
3/2/2022	A highly immunogenic live-attenuated vaccine candidate prevents SARS-CoV-2 infection and transmission in hamsters (cell.com)	Xiao-Feng Li et al	CHN	No FCS, LAV	Vaccine				SARS-COV-2



Why did **A. Fauci**/**B. Graham**/**P. Dormitzer** keep the FCS unchanged in January 2020, for a **novel CoV jab**?

Why **haven't** they kept the FCS for **other prototypes since**?

The answer is critically important…

Collateral Damage

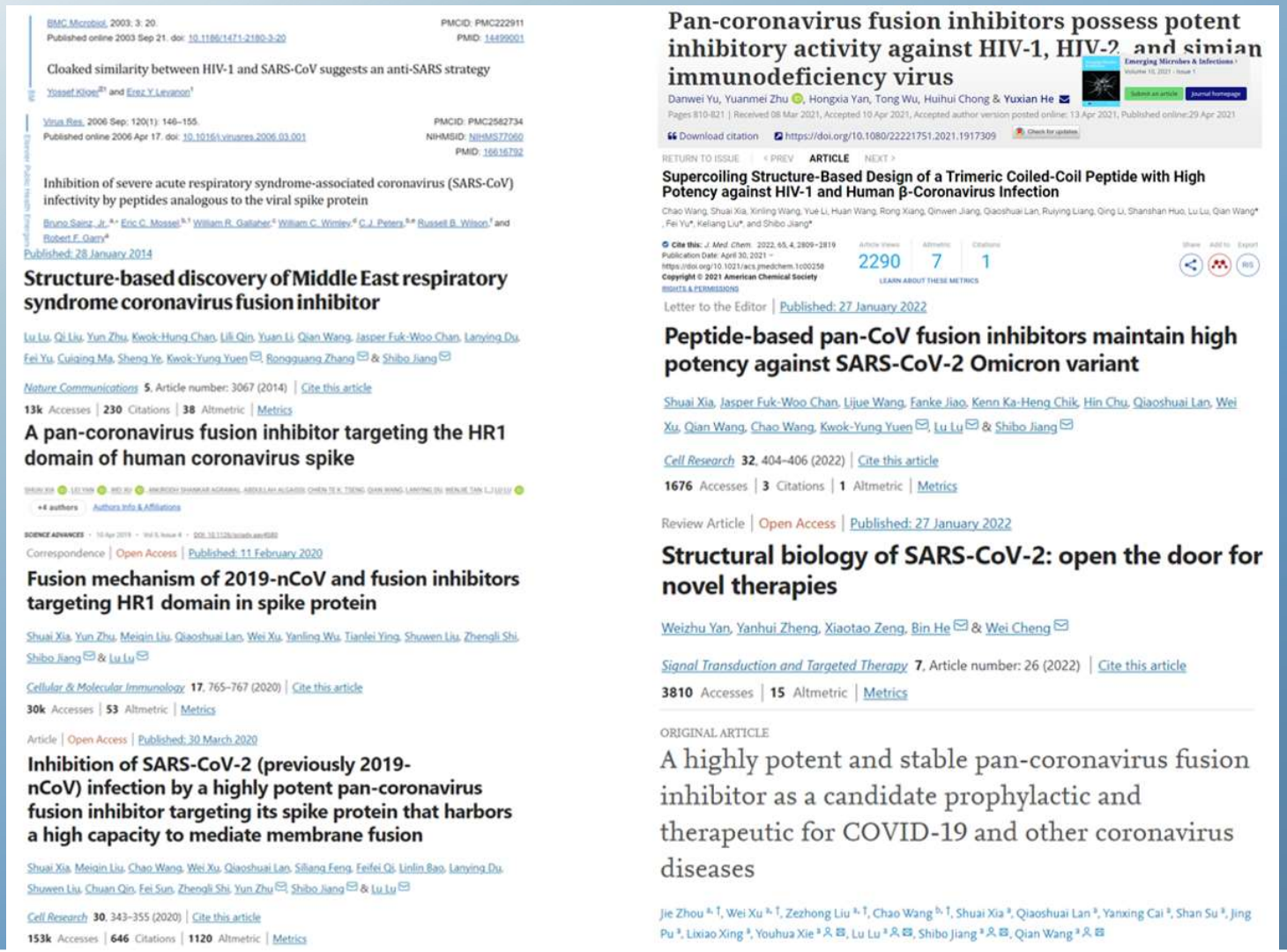
Top 20 COVID-19 Vaccine Manufacturers

Company	doses produced	% of Total
Pfizer BioNTech - Comirnaty	5,341,277,000	28.56%
Moderna - Spikevax	3,229,743,000	17.27%
AstraZeneca - Vaxzevria	2,142,294,000	11.45%
SII - Covishield	1,675,068,000	8.96%
Sinovac - CoronaVac	1,405,002,000	7.51%
Janssen - Ad26.COV 2-S	1,354,644,000	7.24%
Novavax-NUVAXOVID	927,553,000	4.96%
Beijing CNBG - BBIBP-CorV	852,614,000	4.56%
Bharat - Covaxin	384,400,000	2.06%
Shifa - COVIran Barakat	350,000,000	1.87%
Medicago - VLP	304,000,000	1.63%
Sanofi GSK - Vidprevtyn	302,880,000	1.62%
Gamaleya - Gam-Covid-Vac	270,116,000	1.44%
Curevac - CVnCoV	79,780,000	0.43%
CanSino - Convidecia	28,730,000	0.15%
Finlay - Soberana-02	26,200,000	0.14%
Vaxine-SpikoGen	18,000,000	0.10%
Gamaleya - Sputnik-Light	5,835,000	0.03%
Chumakov - Covi-Vac	3,012,000	0.02%
Valneva - VLA2001	2,232,000	0.01%
Total:	**18,703,380,000**	

from:

Immune response in COVID-19: what is next?		
Cell Death & Differentiation	Qing Li et al	5/17/2022

Peptide Fusion Inhibitors



BMC Microbiol. 2003; 3: 20.
Published online 2003 Sep 21. doi: 10.1186/1471-2180-3-20
PMCID: PMC222911
PMID: 14499001

Cloaked similarity between HIV-1 and SARS-CoV suggests an anti-SARS strategy

Yosset Kliger[21] and Erez Y Levanon[1]

Virus Res. 2006 Sep; 120(1): 146–155.
Published online 2006 Apr 17. doi: 10.1016/j.virusres.2006.03.001
PMCID: PMC2582734
NIHMSID: NIHMS77060
PMID: 16616792

Inhibition of severe acute respiratory syndrome-associated coronavirus (SARS-CoV) infectivity by peptides analogous to the viral spike protein

Bruno Sainz, Jr.,[a,*] Eric C. Mossel,[b,1] William R. Gallaher,[c] William C. Wimley,[d] C.J. Peters,[b,e] Russell B. Wilson,[f] and Robert F. Garry[a]

Published: 28 January 2014

Structure-based discovery of Middle East respiratory syndrome coronavirus fusion inhibitor

Lu Lu, Qi Liu, Yun Zhu, Kwok-Hung Chan, Lili Qin, Yuan Li, Qian Wang, Jasper Fuk-Woo Chan, Lanying Du, Fei Yu, Cuiqing Ma, Sheng Ye, Kwok-Yung Yuen ✉, Rongguang Zhang ✉ & Shibo Jiang ✉

Nature Communications **5**, Article number: 3067 (2014) | Cite this article

13k Accesses | **230** Citations | **38** Altmetric | Metrics

A pan-coronavirus fusion inhibitor targeting the HR1 domain of human coronavirus spike

+4 authors Authors Info & Affiliations

SCIENCE ADVANCES

Correspondence | Open Access | Published: 11 February 2020

Fusion mechanism of 2019-nCoV and fusion inhibitors targeting HR1 domain in spike protein

Shuai Xia, Yun Zhu, Meiqin Liu, Qiaoshuai Lan, Wei Xu, Yanling Wu, Tianlei Ying, Shuwen Liu, Zhengli Shi, Shibo Jiang ✉ & Lu Lu ✉

Cellular & Molecular Immunology **17**, 765–767 (2020) | Cite this article

30k Accesses | **53** Altmetric | Metrics

Article | Open Access | Published: 30 March 2020

Inhibition of SARS-CoV-2 (previously 2019-nCoV) infection by a highly potent pan-coronavirus fusion inhibitor targeting its spike protein that harbors a high capacity to mediate membrane fusion

Shuai Xia, Meiqin Liu, Chao Wang, Wei Xu, Qiaoshuai Lan, Siliang Feng, Feifei Qi, Linlin Bao, Lanying Du, Shuwen Liu, Chuan Qin, Fei Sun, Zhengli Shi, Yun Zhu ✉, Shibo Jiang ✉ & Lu Lu ✉

Cell Research **30**, 343–355 (2020) | Cite this article

153k Accesses | **646** Citations | **1120** Altmetric | Metrics

Pan-coronavirus fusion inhibitors possess potent inhibitory activity against HIV-1, HIV-2 and simian immunodeficiency virus

Danwei Yu, Yuanmei Zhu, Hongxia Yan, Tong Wu, Huihui Chong & Yuxian He ✉

Emerging Microbes & Infections

Pages 810-821 | Received 08 Mar 2021, Accepted 10 Apr 2021, Accepted author version posted online: 13 Apr 2021, Published online: 29 Apr 2021

Download citation https://doi.org/10.1080/22221751.2021.1917309

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Supercoiling Structure-Based Design of a Trimeric Coiled-Coil Peptide with High Potency against HIV-1 and Human β-Coronavirus Infection

Chao Wang, Shuai Xia, Xinling Wang, Yue Li, Huan Wang, Rong Xiang, Qinwen Jiang, Qiaoshuai Lan, Ruiying Liang, Qing Li, Shanshan Huo, Lu Lu, Qian Wang*, Fei Yu*, Keliang Liu*, and Shibo Jiang*

Cite this: *J. Med. Chem.* 2022, 65, 4, 2809−2819
Publication Date: April 30, 2021
https://doi.org/10.1021/acs.jmedchem.1c00256
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Article Views 2290 | Altmetric 7 | Citations 1
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Letter to the Editor | Published: 27 January 2022

Peptide-based pan-CoV fusion inhibitors maintain high potency against SARS-CoV-2 Omicron variant

Shuai Xia, Jasper Fuk-Woo Chan, Lijue Wang, Fanke Jiao, Kenn Ka-Heng Chik, Hin Chu, Qiaoshuai Lan, Wei Xu, Qian Wang, Chao Wang, Kwok-Yung Yuen ✉, Lu Lu ✉ & Shibo Jiang ✉

Cell Research **32**, 404–406 (2022) | Cite this article

1676 Accesses | **3** Citations | **1** Altmetric | Metrics

Review Article | Open Access | Published: 27 January 2022

Structural biology of SARS-CoV-2: open the door for novel therapies

Weizhu Yan, Yanhui Zheng, Xiaotao Zeng, Bin He ✉ & Wei Cheng ✉

Signal Transduction and Targeted Therapy **7**, Article number: 26 (2022) | Cite this article

3810 Accesses | **15** Altmetric | Metrics

ORIGINAL ARTICLE

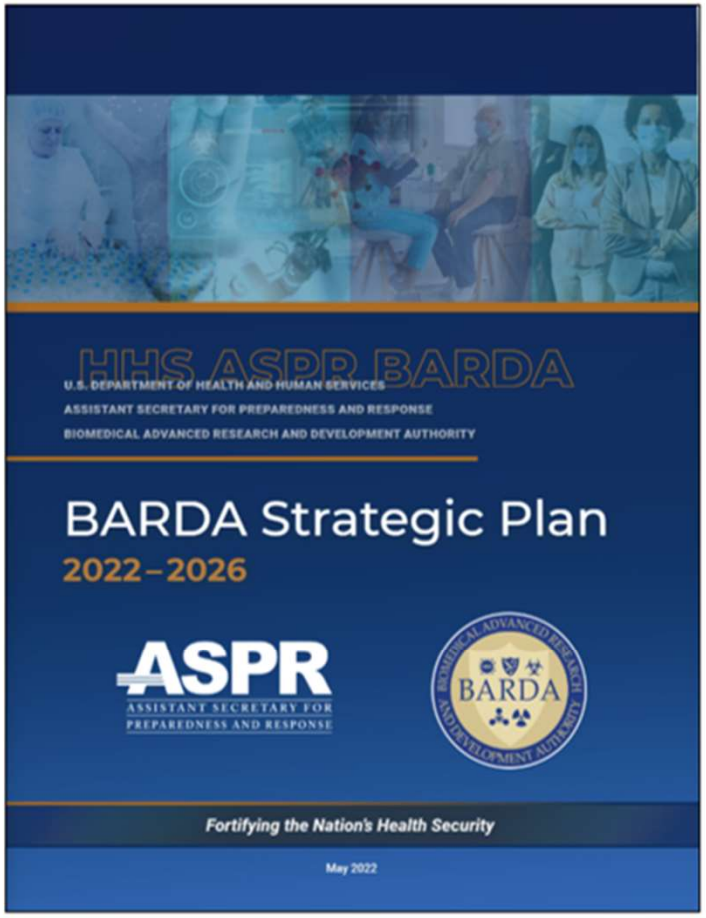
A highly potent and stable pan-coronavirus fusion inhibitor as a candidate prophylactic and therapeutic for COVID-19 and other coronavirus diseases

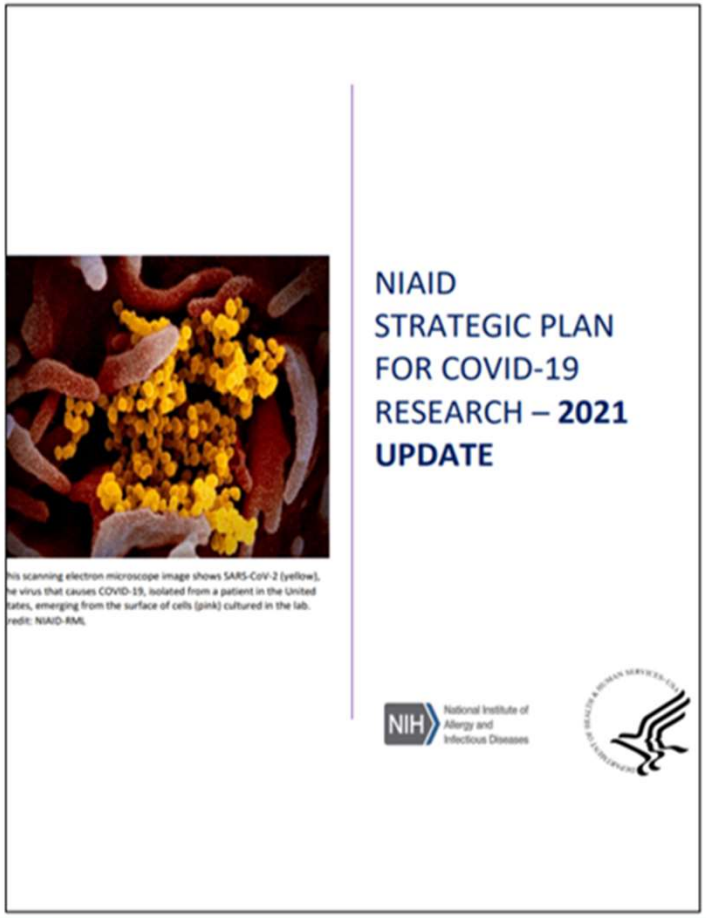
Jie Zhou[a,†], Wei Xu[a,†], Zezhong Liu[a,†], Chao Wang[b,†], Shuai Xia[a], Qiaoshuai Lan[a], Yanxing Cai[a], Shan Su[a], Jing Pu[a], Lixiao Xing[a], Youhua Xie[a] ✉, Lu Lu[a] ✉, Shibo Jiang[a] ✉, Qian Wang[a] ✉

SARS-CoV-2 Origins Research Reference Project - HIV & SARS [Last Updated 7/26/2022] - C. H. Rixey

Research Articles, News & Commentary		Source				Research Foci			
Date	Title	Author (s)	GR	Vx	F	HI	SA	ME	SARS-CoV
7/31/1987	Detection of a fusion peptide sequence in the transmembrane protein of human immunodeficiency virus	Gallaher, William	TUL		Fuz	HIV			
12/16/2002	Rational design of a CD4 mimic that inhibits HIV-1 entry and exposes cryptic neutralization epitopes	Vita, Claudio & Martin, Loic et al			Fuz	HIV			
4/8/2003	CoV as the causative agent of SARS	Peiris, JSM et al	CHN		Fuz		SARS		
5/1/2003	Model of the pre-insertion region of the spike (S2) fusion glycoprotein of the human SARS CoV: implications for antiviral ther	Gallaher, William & Garry, Robert	TUL		Fuz		SARS		
6/1/2003	Cloaked similarity between HIV-1 and SARS-CoV suggests an anti-SARS strategy	Yossef Kliger & Erez Levanon			Fuz	HIV	SARS		
5/1/2004	Structural similarity between HIV-1 gp41 and SARS-CoV S2 proteins suggests an analogous membrane fusion mechanism	Zhang, Xue Wu & Yap, Yee Leng	CHN		Fuz	HIV	SARS		
5/6/2004	HIV protease inhibitor nelfinavir inhibits replication of SARS-associated coronavirus - PMC (nih.gov)	Rongge Yang et al	CHN		Fuz	HIV	SARS		SARS-COV-2
4/12/2006	Inhibition of SARS-associated CoV infectivity by peptides analogous to the viral spike protein	Gallaher, William & Garry, Robert e	TUL		Fuz		SARS		
7/5/2006	Furin cleavage of the SARS CoV spike glycoprotein enhances cell–cell fusion but does not affect virion entry	Follis, Kathryn et al			Fuz		SARS		
1/1/2007	Combating the Threat of Pandemic Influenza: Drug Discovery Approaches - Chapter 7	George Gao	CHN		Fuz				
4/20/2007	Discovery and Optimization of a Natural HIV-1 Entry Inhibitor Targeting the gp41 Fusion Peptide	Pohlmann, Stefan & Jiang, Shibo et	PRX		Fuz	HIV			
5/1/2009	Structures and Mechanisms of Viral Membrane Fusion Proteins	White, Judith et al			Fuz	HIV	SARS		
12/1/2010	Peptide-based inhibitors of the HIV envelope protein and other class I viral fusion proteins	Pohlmann, Stefan et al	PRX		Fuz	HIV			
8/17/2011	Engineered Single Human CD4 Domains as Potent HIV-1 Inhibitors and Components of Vaccine Immunogens	Chen, Weizao et al	NIH	Vaccine	Fuz	HIV			
6/1/2012	Discovery of Critical Residues for Viral Entry and Inhibition through Structural Insight of HIV-1 Fusion Inhibitor CP621–652	Chong, Huihui et al	CHN		Fuz	HIV			
12/7/2012	A bivalent recombinant protein inactivates HIV-1 by targeting the gp41 prehairpin fusion intermediate induced by CD4 D1D2 c	Shibo Jiang et al	FUD		Fuz	HIV			
1/22/2013	HIV-1 Fusion Is Blocked through Binding of GB Virus C E2D Peptides to the HIV-1 gp41 Disulfide Loop	Shibo Jiang et al	FUD		Fuz	HIV			
9/25/2013	Structure of the fusion core and inhibition of fusion by a heptad repeat peptide derived from the S protein of MERS-CoV	George Gao et al	CHN		Fuz			MERS	
1/2/2015	Design of a highly potent HIV-1 fusion inhibitor targeting t...	Chong, Huihui et al	CHN		Fuz	HIV			
5/15/2016	Development of potent and long-acting HIV-1 fusion inhibitor...	Chong, Huihui et al	CHN		Fuz	HIV			
5/12/2017	A Lipopeptide HIV-1/2 Fusion Inhibitor with Highly Potent In Vitro, Ex Vivo, and In Vivo Antiviral Activity	Chong, Huihui et al	CHN		Fuz	HIV			
4/10/2019	A pan-CoV fusion inhibitor targeting the HR1 domain of human CoV spike	Xia, Shuai et al	CHN		Fuz				
2/1/2020	Analysis of Wuhan CoV: déjà vu [findings on 1/29, 1st edition on 2/1]	Gallaher, William & Gallaher, Andre	TUL		Fuz				SARS-COV-2
2/11/2020	Fusion mechanism of 2019-nCoV and fusion inhibitors targeting HR1 domain in spike protein	Shi, Zheng-Li et al	WIV		Fuz				SARS-COV-2
3/16/2020	Don't rush to deploy COVID-19 vaccines and drugs without sufficient safety guarantees (nature.com)	Shibo Jiang	FUD	Vaccine	Fuz				SARS-COV-2
3/30/2020	Inhibition of SARS-CoV-2 infection by a highly potent pan-CoV fusion inhibitor targeting its spike protein that harbors a high c	Shi, Zheng-Li et al	WIV		Fuz				SARS-COV-2
6/1/2020	CoV membrane fusion mechanism offers a potential target for antiviral development	Whitaker, Gary et al			Fuz				
7/1/2020	Design of Potent Membrane Fusion Inhibitors against SARS-CoV-2, an Emerging CoV with High Fusogenic Activity	Yuanmei Ju et al	CHN		Fuz				SARS-COV-2
10/26/2020	Inhibition of SARS-CoV-2 viral entry upon blocking N- and O-glycan elaboration | eLife (elifesciences.org)	Qi Yang et al		Vaccine	Fuz				SARS-COV-2
1/9/2021	Pan-CoV fusion inhibitors as the hope for today and tomorrow	Wang, Xinling et al	CHN		Fuz				
4/13/2021	Pan-CoV fusion inhibitors possess potent inhibitory activity against HIV-1, HIV-2, and SIV	Yu, Danwei et al	CHN		Fuz	HIV			
7/29/2021	Structural and functional basis for pan-CoV fusion inhibitors against SARS-CoV-2 and its variants with preclinical evaluation	Shibo Jiang et al	FUD		Fuz				SARS-COV-2
4/11/2022	CoV Entry Inhibitors	Xia, Shuai et al	CHN		Fuz				
4/13/2022	Peptide-Based HIV Entry Inhibitors	Shibo Jiang et al	FUD		Fuz	HIV			
6/9/2022	Conserved coronavirus proteins as targets of broad-spectrum antivirals - ScienceDirect	Ralph Baric et al	VRC		Fuz	HIV			SARS-COV-2

There's still no plan to research fusion inhibitors





NIAID Announces Antiviral Dru

May 18, 2022

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has awarded $577,000,000 to establish nine Antiviral Drug Discovery (AViDD) Centers for Pathogens of Pandemic Concern.

The AViDD centers will conduct innovative, multidisciplinary research to develop candidate COVID-19 antivirals, especially those that can be taken in an outpatient setting, as well as antivirals targeting specific viral families with high potential to cause a pandemic in the future. These include paramyxoviruses, bunyaviruses, togaviruses, filoviruses (including Ebola viruses and Marburg virus), picornaviruses (including enteroviruses and other cold-causing viruses), and flaviviruses (including the viruses that cause yellow fever, dengue and Zika). The awards are a part of the Antiviral Program for Pandemics (APP), an intensive research program designed to speed development of therapeutics for COVID-19. APP is led by NIAID, the National Center for Advancing Translational Sciences (NCATS) and the Office of Research Infrastructure Programs, all part of NIH; and the Biomedical Advanced Research and Development Authority (BARDA), part of HHS.

"The COVID-19 pandemic has highlighted the need for new antiviral drugs, especially those that could easily be taken by patients at home while their symptoms are still mild," sa on the structure and vulnerabilities of coronaviruses greatly accelerated our response to th antivirals will better prepare us for the next pandemic."

The AViDD award recipients are:

Center for Antiviral Medicines & Pandemic Preparedness
Principal Investigator: Sumit Chanda, Ph.D.
Institute: Scripps Research Institute, La Jolla, California

UTMB-Novartis Alliance for Pandemic Preparedness
Principal Investigator: Pei-Yong Shi, Ph.D.
Institute: The University of Texas Medical Branch, Galveston

Rapidly Emerging Antiviral Drug Development Initiative – AViDD Center
Principal Investigator: Ralph Baric, Ph.D.
Institute: The University of North Carolina at Chapel Hill

Development of Outpatient Antiviral Cocktails against SARS-CoV-2 and other Potential Pandemic RNA Viruses
Principal Investigator: Jeffrey Glenn, M.D., Ph.D.
Institute: Stanford University School of Medicine, Stanford, California

Antiviral Countermeasures Development Center
Principal Investigators: George Painter, Ph.D. and Richard Plemper, Ph.D.
Institutes: Emory University and Georgia State University, Atlanta

Metropolitan AntiViral Drug Accelerator
Principal Investigator: David Perlin, Ph.D.
Institute: Hackensack University Medical Center, Hackensack, New Jersey

QBI Coronavirus Research Group Pandemic Response Program
Principal Investigator: Nevan Krogan, Ph.D.
Institute: University of California, San Francisco

Midwest AViDD Center
Principal Investigator: Reuben Harris, Ph.D. + Fang Li
Institute: University of Minnesota, Minneapolis

AI-Driven Structure-Enabled Antiviral Platform
Principal Investigators: Ben Perry, Ph.D.; Alpha Lee, Ph.D.; John Chodera, Ph.D.
Institutes: Drugs for Neglected Diseases Initiative; PostEra; Sloan Kettering Institute and Memorial Sloan Kettering C

~ Outline ~

- Censorship
- What was censored, and why?
- Implications

SARS-CoV-2 Origins Research Reference Project - The Long & Winding Road - [Last Updated 11/29/2022] - C. H. Rixey

Research Articles, News & Commentary		Source		Labs/Organizations Involved										
Date	Title	Author (s)	Details	WIV	FUD	CHN	SING	CSIRO	EHA	UNC	VRC	NIH	OSTP	PRX	EU
1/15/2003	Differential N-Linked Glycosylation of HIV & Ebola Virus Envelope Glycoproteins Modulates Interactions with DC-SIGN and DC-SIGNI	Stefan Pohlmann et al	Inv. specifics of how N-linked glycosylation impacts DC-SIGN pathway usage											PRX	GRMY
4/8/2003	CoV as the causative agent of SARS	Peiris, JSM et al				CHN									
5/1/2003	Model of the pre-insertion region of the spike (S2) fusion glycoprotein of the human SARS CoV: implications for antiviral therapeutics	William Gallaher & Robert Garry	Initial highlighting of a pathway for exploiting fusion peptide homology between SARS/HIV										OSTP	PRX	
6/1/2003	Cloaked similarity between HIV-1 and SARS-CoV suggests an anti-SARS strategy	Yossef Kliger & Erez Levanon	Further work into the SARS-CoV/HIV fusion homology												
5/1/2004	Structural similarity between HIV-1 gp41 and SARS-CoV S2 proteins suggests an analogous membrane fusion mechanism	Zhang, Xue Wu & Yap, Yee Leng	Further work into the SARS-CoV/HIV fusion homology			CHN									
5/6/2004	HIV protease inhibitor nelfinavir inhibits replication of SARS-associated CoV's	Rongge Yang et al				CHN									GRMY
11/1/2004	DC-SIGN and DC-SIGNR interact with the glycoprotein of Marburg virus and the S protein of SARS CoV - PubMed (nih.gov)	Stefan Pohlmann et al	Confirmation of DC-SIGN pathway usage for SARS-CoV and Marburg											PRX	GRMY
11/2/2004	CD209L (L-SIGN) is a receptor for SARS-CoV	Scott Jeffers et al	Confirmation of L-SIGN pathway usage for SARS-CoV												
1/1/2005	Development of Mouse Hepatitis Virus and SARS-CoV Infectious cDNA Constructs	Ralph Baric & AC Sims	Creation of the first viable infectious clone constructs for SARS-CoV							UNC			OSTP		
3/25/2005	Different from the HIV Fusion Inhibitor C34, the Anti-HIV Drug Fuzeon (T-20) Inhibits HIV-1 Entry by Targeting Multiple Sites in gp41 a	Shibo Jiang et al	Further clarity into the interaction between the inhibitor Fuzeon and gp160 of HIV-1		FUD										
5/13/2005	Scorpion-toxin mimics of CD4 in complex with HIV gp120 crystal structures, molecular mimicry, and neutralization breadth	Peter Kwong et al									VRC				
9/16/2005	Structure of SARS CoV Spike Receptor-Binding Domain Complexed with Receptor	Michael Farzan & Fang Li	SARS-CoV RBD specifics of structure & interaction									MINN		PRX	
10/28/2005	Bats are Natural Reservoirs of SARS-like CoVs	Zheng-Li Shi & Peter Daszak et al		WIV					EHA				OSTP		
4/12/2006	Inhibition of SARS-associated CoV infectivity by peptides analogous to the viral spike protein	William Gallaher & Robert Garry et al										UTMB	OSTP	PRX	SCRIPPS
7/1/2006	Preparation of a Chimeric Armored RNA as a Versatile Calibrator for Multiple Virus Assays	Huang, Qiuying et al	HIV/CoV chimaeric construction and usage			CHN									
12/12/2006	Review of bats & SARS	Zheng-Li Shi & Peter Daszak et al		WIV		CHN		CSIRO	EHA				OSTP		
12/15/2006	Phase 1 Safety and Immunogenicity Evaluation of a Multiclade HIV-1 DNA Candidate Vaccine	Barney Graham, John Mascola et al	Multiclade/Conserved, avoidance of FCS in construction								VRC				
1/1/2007	Synthetic Viral Genomics: Risks & Benefits for Science & Society	Ralph Baric et al	Baric giving a fairly honest assessment of CoV bioweapon risks							UNC			OSTP		
1/12/2007	A mouse-adapted SARS-CoV causes disease and mortality in BALB/c mice	Ralph Baric et al	Creation of a SARS animal model							UNC		NIAID	OSTP		
6/27/2007	SARS CoV ORF6 Antagonizes STAT1 Function by Sequestering Nuclear Import Factors on the Rough Endoplasmic Reticulum/Golgi Me	Ralph Baric et al	ORF6 etc; Interferon evasion							UNC			OSTP		
9/28/2007	Combating the Threat of Pandemic Influenza: Drug Discovery Approaches - Chapter 7	George Gao				CHN									
11/1/2007	Specific Asparagine-Linked Glycosylation Sites Are Critical for DC-SIGN- and L-SIGN-Mediated SARS CoV Entry														
12/14/2007	Semen-Derived Amyloid Fibrils Drastically Enhance HIV Infection	Jan Munch et al										SCRIPPS			GRMY
2/15/2008	Difference in Receptor Usage between SARS (SARS) CoV and SARS-Like CoV of Bat Origin	Zheng-Li Shi, Wuze Ren et al	Interchanging RBD's between bat & human SARS viruses; HIV pseudoviruses	WIV				CSIRO							
11/26/2008	Synthetic recombinant bat SARS-like CoV is infectious in cultured cells and in mice	Ralph Baric et al	Building a consensus SARS-CoV-2-like CoV genome + the SARS-CoV RBD							UNC		VANDY	OSTP		
2/1/2010	Protease Cleavage Sites in HIV-1 gp120 Recognized by Antigen Processing Enzymes Are Conserved and Located at Receptor Binding Sit	Yu, Bin et al				CHN									
4/1/2010	Recombination, reservoirs, and the modular spike: mechanisms of CoV cross-species transmission	Ralph Baric et al								UNC			OSTP		
7/14/2010	TMPRSS2 and TMPRSS4 facilitate trypsin-independent spread of influenza virus in Caco-2 cells	Stefan Pohlmann et al												PRX	GRMY
12/1/2010	Peptide-based inhibitors of the HIV envelope protein and other class I viral fusion proteins	Stefan Pohlmann et al												PRX	GRMY
10/18/2011	Bat SARS-like CoV ORF3b homologues display different interferon antagonist activities	Zheng-Li Shi et al		WIV											
5/23/2012	A short segment of the HIV-1 gp120 V1/V2 region is a major determinant of resistance to V1/V2 neutralizing antibodies	John Mascola & Peter Kwong									VRC				
6/1/2012	Discovery of Critical Residues for Viral Entry and Inhibition through Structural Insight of HIV-1 Fusion Inhibitor CP621–652	Chong, Huihui et al				CHN									
7/15/2012	Extended Follow-up Confirms Early Vaccine-Enhanced Risk of HIV Acquisition and Demonstrates Waning Effect Over Time Among Parti	Duerr, Ann et al													
11/8/2012	Isolation of a Novel CoV from a Man with Pneumonia in Saudi Arabia	Ron Fouchier et al												PRX	
3/13/2013	Broad reception for CoV	Stanley Perlman & Tom Gallagher	Discovery of MERS-CoV										OSTP		
4/28/2013	Identification of Immunogenic Determinants of the Spike Protein of SARS-like CoV	Zheng-Li Shi et al	HIV pseudovirus work	WIV			SING								
5/1/2013	Analysis of Six Patients With Unknown Viruses	Li Xu	Master's thesis documenting the 6 Mojiang Miners cases	WIV		CHN									
11/11/2013	Simultaneous Expression of Displayed and Secreted Antibodies for Antibody Screen	Yuanoing Zhou, Shibo Jiang et al	Manipulation and use of FCS's to generate attached & soluble antibodies		FUD	CHN						NYBC			
11/28/2013	Isolation and characterization of a bat SARS-like CoV that uses the ACE2 receptor	Zheng-Li Shi et al	SHC014	WIV		CHN	SING	CSIRO	EHA			UC-D			
3/18/2014	Peptides derived from HIV-1 gp120 co-receptor binding domain form amyloid fibrils and enhance HIV-1 infection	Shibo Jiang et al	Learn to avoid EP1 & EP2 [HIV-1 enhancing peptides via amyloid fibrils]		FUD							NYBC			
9/17/2014	Effects of human anti-spike protein receptor binding domain antibodies on SARS CoV neutralization escape and fitness	Ralph Baric et al								UNC			OSTP		
7/15/2015	Imperfect Vaccination Can Enhance the Transmission of Highly Virulent Pathogens	Andrew Read et al													
8/14/2015	ADS-J1 Inhibits Semen-Derived Amyloid Fibril Formation and Blocks Fibril-Mediated Enhancement of HIV-1 Infection	Shibo Jiang et al	Jiang discovers a neutralizing agent for the fibrils that enhance HIV-1 infection		FUD	CHN									
11/9/2015	A SARS-like cluster of circulating bat CoVes shows potential for human emergence	Zheng-Li Shi et al	ZLS fiddles with WIV1, SHC, etc.	WIV					EHA	UNC		UTMB			
1/20/2016	SARS-like WIV1-CoV poised for human emergence	Ralph Baric et al	[SHC014]; Baric describes poor efficacy of SARS vaccine prototypes							UNC			OSTP		
1/22/2016	Coexistence of multiple CoVes in several bat colonies in an abandoned mineshaft	Zheng-Li Shi et al	RaBtCoV4991 discovery first discussed	WIV											
8/1/2016	TRR 60 - Collab. between the U. of Essen-Duisburg-Essen & certain Chinese institutions, incl. the Wuhan Institute of Virology	N/A	Outlining the WIV-Germany connection in HIV research	WIV		CHN								PRX	GRMY
2/1/2017	Discovery of a rich gene pool	Zheng-Li Shi et al	Highlighting dozens of SARS-like CoVs and their interesting properties	WIV			SING		EHA						
2/20/2017	Quaternary contact in the initial interaction of CD4 with the HIV-1 envelope trimer	Qingbo Liu, Peter Kwong et al									VRC				
4/1/2017	Reverse Genetic System of SARS-like CoV & Function Study of ORFX	Lei-Ping Zeng	Zheng-Li Shi - advised doctoral dissertation on reverse genetics & ORFX	WIV		CHN									
5/12/2017	A Lipopeptide HIV-1/2 Fusion Inhibitor with Highly Potent In Vitro, Ex Vivo, and In Vivo Antiviral Activity	Chong, Huihui et al				CHN									
5/16/2017	Efficient Reverse Genetic Systems for Rapid Genetic Manipulation of Emergent and Preemergent Infectious CoV	Ralph Baric et al	Self-explanatory							UNC			OSTP		
9/11/2017	Immunological Control of Viral Infections in Bats and the Emergence of Viruses Highly Pathogenic to Humans	Shountz, Tony et al	Arguing for pre-emptive suppression of SARS-like CoVs in bats					CSIRO				RML		PRX	
10/3/2017	A Degraded Fragment of HIV-1 Gp120 in Rat Hepatocytes Forms Fibrils and Enhances HIV-1 Infection	Shibo Jiang et al	Amyloid Fibrils can enhance HIV-1 infection		FUD	CHN						NYBC			
11/1/2017	RNA Pseudouridylation in Physiology and Medicine: For Better and for Worse	Marianna Penzo et al	Pseudouridine can be a potential trigger for cancer onset												
1/10/2018	Feline CoV: Insights into viral pathogenesis based on the spike protein structure and function - PMC (nih.gov)	Javier James & Gary Whittaker													
3/2/2018	Serological Evidence of Bat SARS-Related CoV Infection in Humans, China	Zheng-Li Shi & Peter Daszak et al	Used as 'evidence' of large-scale spillover of Bat-CoVs in SE China										OSTP		
3/16/2018	Bat-mouse bone marrow chimera: a novel animal model for dissecting the uniqueness of the bat immune system	Linfa Wang et al	"Batified" mice				SING								
3/27/2018	PREEMPT - DRASTIC's Analysis of the PREEMPT/DEFUSE Proposal	DRASTIC	FCS, DC-SIGN, Interferon, Batified Mice	WIV			SING		EHA	UNC		RML	OSTP		
4/4/2018	Fatal swine acute diarrhoea syndrome caused by an HKU2-related CoV of bat origin	Zheng-Li Shi & Peter Daszak et al	SADS-CoV analysis [potential ties to DC-SIGN efforts [see Sorenson et al]]	WIV		CHN	SING	[D. And]	EHA				OSTP		
4/15/2018	Novel Vaccine Technologies: Essential Components of an Adequate Response to Emerging Viral Diseases	Anthony Fauci, John Mascola & Barney Graham									VRC		OSTP	PRX	
4/27/2018	Shattuck Lecture Innovation for Pandemics	Bill Gates										BGMF			
5/24/2018	Codon optimization & improved delivery/jab regimen enhance the immune response against wild-type & drug-resistant HIV-1 rev-trans, pr	AA Latanova et al										LANL			
7/1/2018	Discovery of Novel Bat CoVes in South China that use the Same Receptor as MERS-CoV	Zheng-Li Shi et al		WIV					EHA			MINN			
9/1/2018	Bacterially expressed HIV-1 gp120 outer-domain fragment immunogens with improved stability and affinity for CD4-binding site neutralizin	Ujjwal Rathore et al													
9/12/2018	Genomic characterization and infectivity of a novel SARS-like coronavirus in Chinese bats	Dan Hu et al	Discovery of ZC45 & ZXC21			CHN									
9/26/2018	Lysosomal Proteases Are a Determinant of CoV Tropism	Ralph Baric, Fang Li et al								UNC		MINN	OSTP		
1/1/2019	EcoHealth Alliance NIH grant documents - 2014 & 2019	Peter Daszak et al		WIV		CHN			EHA	UNC		UC-D	OSTP	PRX	
1/4/2019	Mutations in the Spike Protein of MERS-CoV Transmitted in Korea Increase Resistance to Antibody-Mediated Neutralization	Drosten, Christian, Graham, Barney & Pohlmann, Stefan et al									VRC		OSTP	PRX	GRMY
4/10/2019	A pan-CoV fusion inhibitor targeting the HR1 domain of human CoV spike	Xia, Shuai et al			FUD	CHN						NYBC			
7/1/2019	Presentation of HIV-1 envelope glycoprotein trimers on diver…	Brouwer, Philip et al													AMST
10/25/2019	T cell-based strategies for HIV-1 vaccines	Bette Korber & Will Fischer										LANL			
12/11/2019	Molecular mechanism for antibody-dependent enhancement of CoV entry	Zheng-Li Shi et al	ZLS pointing out certain elements of CoV genomes that trigger ADE	WIV	FUD							MINN			
12/12/2019	NIH-Moderna-Confidential Agreements	National Institutes of Health								UNC	VRC		OSTP	PRX	
12/12/2019	Immune Monitoring Reveals Fusion Peptide Priming to Imprint Cross-Clade HIV-Neutralizing Responses with a Characteristic Early B Cell	John Mascola, Michael Worobey et al	A vaccine targeting the FP of HIV-1								VRC		OSTP	PRX	

CHINA	WIV FUD CHN
SINGAPORE & AUSTRALIA	SING CSIRO
USA - NIH	EHA UNC VRC NIH
2/1 & 2/3 TELE-CF [USA, UK, EU, AUS]	PRX OSTP
	EU

Exploration of antigenic determinants in spike glycoprotein of SARS-CoV2 and identification of five salient potential epitopes

Aditya Agrawal[1] · Rajat Varshney[2] · Mamta Pathak[1] · Shailesh Kumar Patel[1] · Vishal Rai[1] · Sourabh Sulabh[3] · Rohini Gupta[4] · Khushal Singh Solanki[1] · Ritu Varshney[5] · Ramadevi Nimmanapalli[2]

HIV Inserts in Pradhan et al

Table 1 List of predicted immunogenic epitopes of B cell for 2019-nCoV spike protein, their position, number of residues and scores on different IEDB scales (BepiPred, Emini accessibility prediction scale, Kolaskar and Tongaonkar antigenicity prediction scale and Parker hydrophillicity plot scale)

S. No	Peptide sequence (Epitope)	Position	No. of residues	BepiPred score (0.350)	Emini accessibility Score (1.000)	Kolaskar and Tongaonkar antigenicity Score (1.041)	Parker hydrophillicity plot Score (1.238)
1	KTQLPPAYTNS	21–32	12	1.185	2.868	1.016	1.675
#1	SGTNGTKRFDN#	71–81	11	1.262	3.464	0.899	4.818
#2	NKSWME	149–154	6	0.687	2.022	0.881	2.133
4	GKQGNF	181–186	6	0.934	1.229	0.927	3.483
#3	SYLTPG#	247–252	6	1.309	0.995	1.045	1.400
6	YQAGSTPCNGV	473–483	11	1.358	0.444	1.049	3.282
7	TVCGPKKSTN	523–532	10	1.121	1.170	1.020	4.080
8	RVYST*	634–638	5	0.554	1.426	1.068	2.060
#4	QTQTNSPRRARSV#	675–687	13	1.685	8.837	0.983	4.269
10	VEQDKNTQE	772–780	9	1.323	6.923	0.995	5.756
11	ILPDPSKPSKRS	805–816	12	2.291	4.690	1.019	2.850
12	QSAPH*	1054–1058	5	1.213	1.597	1.052	3.760
13	KNHTSPDVDLG	1157–1167	11	1.378	1.913	1.003	3.764

*Peptides revealed a higher score than threshold in all tools.

#Peptide epitopes possess novel inserts in spike protein.

HIV as Pseudovirus

Published: 01 September 1997

Multiply attenuated lentiviral vector achieves efficient gene delivery in vivo

Romain Zufferey, Dea Nagy, Ron J. Mandel, Luigi Naldini & Didier Trono

Nature Biotechnology **15**, 871–875(1997) | Cite this article

Abstract

Retroviral vectors derived from lentiviruses such as HIV-1 are promising tools for human gene therapy because they mediate the in vivo delivery and long-term expression of transgenes in nondividing tissues. We describe an HIV vector system in which the virulence genes *env*, *vif*, *vpr*, *vpu*, and *nef* have been deleted. This multiply attenuated vector conserved the ability to transduce growth-arrested cells and monocyte-derived macrophages in culture, and could efficiently deliver genes in vivo into adult neurons. These data demonstrate the potential of lentiviral vectors in human gene therapy.

9/1/1997

Geneva:
HIV =
Lentivirus

Gene Therapy (2000) 7, 20–23

www.nature.com/gt

MILLENNIUM REVIEW

Lentiviral vectors: turning a deadly foe into a therapeutic agent

D Trono
Department of Genetics and Microbiology, Faculty of Medicine, University of Geneva, CMU, 1 rue Michel-Servet, CH-1211 Geneva 4, Switzerland

The past 3 years have witnessed the spectacular irruption of lentiviral vectors into the limelight of the gene therapy scene. Owing to their ability to deliver transgenes in tissues that had long appeared irremediably refractory to stable genetic manipulation, lentivectors have opened fresh perspectives for the genetic treatment of a wide array of hereditary as well as acquired disorders, and a concrete proposal for their clinical use seems imminent. This article traces the path that has led to this rapid development and describes the current state of the art in the design and production of lentiviral vectors. The important question of biosafety is discussed. This system seems to have the edge over other gene delivery tools for particular targets, however, there remain several issues to be resolved before lentivectors make it to the bedside. Gene Therapy (2000) 7, 20–23.

Keywords: *lentiviral vectors; retroviral vectors; HIV; nondividing cells; in vivo gene delivery*

7/1/2000

Geneva:
HIV =
Lentivirus

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Biochemical and Biophysical Research Communications 313 (2004) 439–444
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Expression cloning of functional receptor used by SARS coronavirus

Peigang Wang,[1] Jian Chen,[1] Aihua Zheng,[1] Yuchun Nie, Xuanling Shi, Wei Wang, Guangwen Wang, Min Luo, Huijun Liu, Lei Tan, Xijun Song, Zai Wang, Xiaolei Yin, Xiuxia Qu, Xiaojing Wang, Tingting Qing, Mingxiao Ding,* and Hongkui Deng*

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Received 11 January 2004

1/28/2004

Beijing:
„Gain of Function"
SARS/HIV
Pseudovirus

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0022-538X/04/$08.00+0 DOI: 10.1128/JVI.78.19.10628–10635.2004

Retroviruses Pseudotyped with the Severe Acute Respiratory Syndrome Coronavirus Spike Protein Efficiently Infect Cells Expressing Angiotensin-Converting Enzyme 2

Michael J. Moore,[1] Tatyana Dorfman,[1] Wenhui Li,[1] Swee Kee Wong,[1] Yanhan Li,[2] Jens H. Kuhn,[1,3] James Coderre,[4] Natalya Vasilieva,[5] Zhongchao Han,[2] Thomas C. Greenough,[4] Michael Farzan,[1]* and Hyeryun Choe[5]*

Partners AIDS Research Center, Brigham and Women's Hospital, and Department of Medicine (Microbiology and Molecular Genetics),[1] and Perlmutter Laboratory, Children's Hospital, and Department of Pediatrics,[5] Harvard Medical School, Boston, and Program in Molecular Medicine, University of Massachusetts Medical School, Worcester,[4] Massachusetts; State Key Laboratory of Experimental Hematology, Institute of Hematology and Hospital of Blood Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin, China[2]; and Department of Biology, Chemistry, Pharmacy, Freie Universität Berlin, Berlin, Germany[3]

Received 3 February 2004/Accepted 28 May 2004

Infection of receptor-bearing cells by coronaviruses is mediated by their spike (S) proteins. The coronavirus (SARS-CoV) that causes severe acute respiratory syndrome (SARS) infects cells expressing the receptor angiotensin-converting enzyme 2 (ACE2). Here we show that codon optimization of the SARS-CoV S-protein gene substantially enhanced S-protein expression. We also found that two retroviruses, simian immunodeficiency virus (SIV) and murine leukemia virus, both expressing green fluorescent protein and pseudotyped with SARS-CoV S protein or S-protein variants, efficiently infected HEK293T cells stably expressing ACE2. Infection mediated by an S-protein variant whose cytoplasmic domain had been truncated and altered to include a fragment of the cytoplasmic tail of the human immunodeficiency virus type 1 envelope glycoprotein was, in both cases, substantially more efficient than that mediated by wild-type S protein. Using S-protein-pseudotyped SIV, we found that the enzymatic activity of ACE2 made no contribution to S-protein-mediated infection. Finally, we show that a soluble and catalytically inactive form of ACE2 potently blocked infection by S-protein-pseudotyped retrovirus and by SARS-CoV. These results permit studies of SARS-CoV entry inhibitors without the use of live virus and suggest a candidate therapy for SARS.

5/28/2004

Harvard, China & FU Berlin:
SARS/HIV Pseudovirus -
S-Protein truncated HIV 1 - deutlich effektiver bei ACE2 Bindung

T cell-based strategies for HIV-1 vaccines

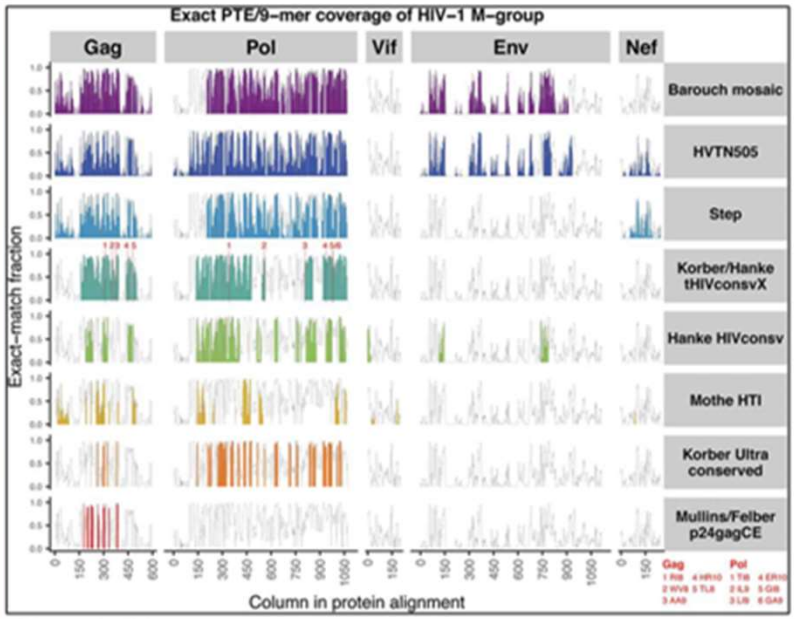
Bette Korber & Will Fischer

PUBLISHED ONLINE:
25 October 2019

https://doi.org/10.1080/21645515.2019.1666957

"Unlikely to be fortuitous…"

Bette Korber



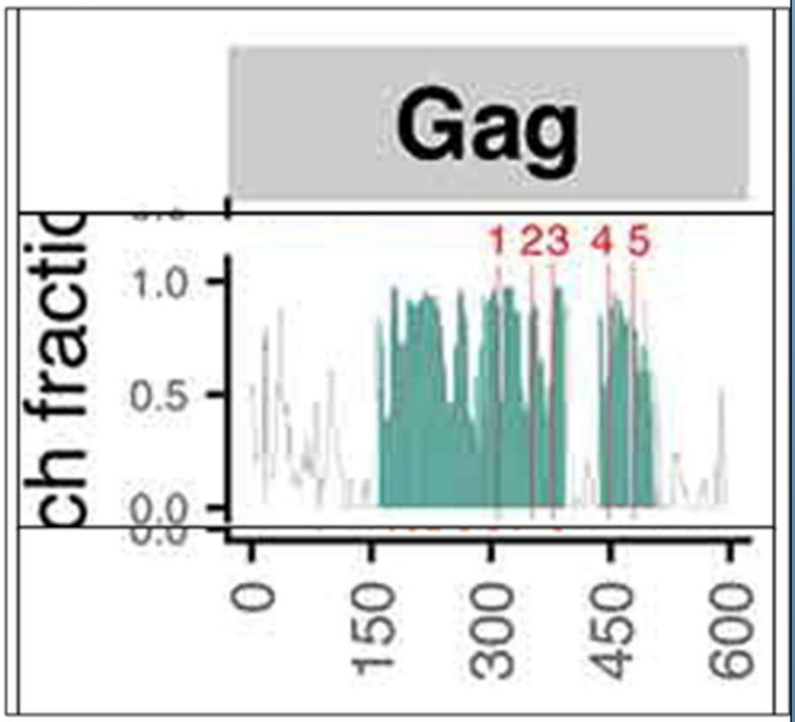


Figure 1 of 3

Figure 1. Exact 9-mer coverage of M group HIV by vaccine. For each graph, a position in the alignment marks the beginning of a 9-mer (a PTE); gray lines indicate the frequency in the HIV-1 M group alignment (see methods) of the most common form of 9-mer for sliding windows starting at positions 1–9, advancing to 2–10, then 3–11. For each 9-mer included in a vaccine, a colored bar indicates the summed frequencies of 9-mers that are present in (covered by) each vaccine. Brief descriptions of the vaccines: Barouch mosaic: two global mosaics for each of Gag and Pol, and Env;[37] these were the same inserts that were used in the MVA constructs in Barouch et al.[38] One of the Envs in the original vaccine[37] has been redesigned for stability and production reasons for use in the Adenovirus vector for the Imbokodo clinical trial.[38] HVTN505: natural HIV isolates: 1 each of Gag, Pol, and Nef, and 3 modified Envs (gp145). Step 2008: one Gag, Pol, and Nef protein, derived from natural HIV-1 B clade sequences.[39] Korber/Hanke tHIVconsvX 2015: 2 global mosaics spanning 6 highly conserved fragments of Gag and Pol.[19] Red numbers mark 5 epitopes in Gag and 6 in Pol that are included in this conserved vaccine that was subsequently found to be strongly associated with viral control *in vitro* and *in vivo* (the key to these epitopes is at bottom right).[40,41] Hanke HIVconsv 2007: 14 concatenated peptide fragments derived from different subtype consensus sequences (median length 40, range 27–130 amino acids (aa));[17] Mothe HTI 2015: 16 fragments (median length 22.5, range 11–78 aa), concatenated with three joining alanine residues, based on regions that were preferentially targeted by individuals with low viral loads, published as European Patent EP2620446A1;[25] Korber Ultra CE: 40 highly conserved peptides (median length 18, range 14–22 aa), selected based on contiguous HIV-1 M group 9-mer coverage >80%, designed using the Epigraph tools,[42] currently under study, and first published here; Mullins p24 CE: Two variants each, of 7 regions of Gag (median 18, range 12–24 aa), concatenated with 2–4 aa alanine-rich linkers.[43].

This is why the DOE leans lab origin –

They recognized unnaturally precise & unnaturally positioned HIV-like inserts within the SARS-CoV-2 Spike Genome

T cell-based strategies for HIV-1 vaccines

Bette Korber & Will Fischer

PUBLISHED ONLINE: 25 October 2019

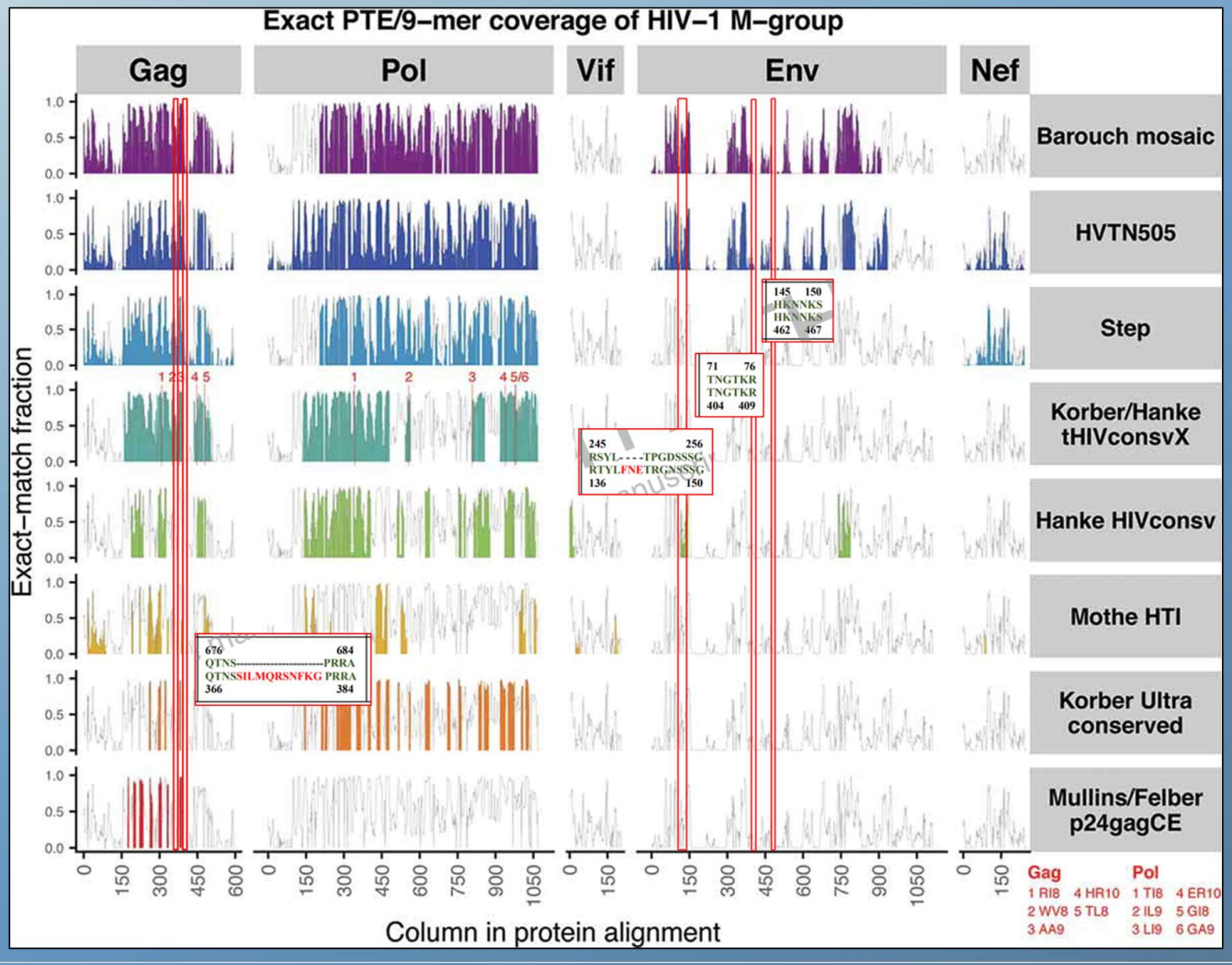
https://doi.org/10.1080/21645515.2019.1666957

Bette Korber

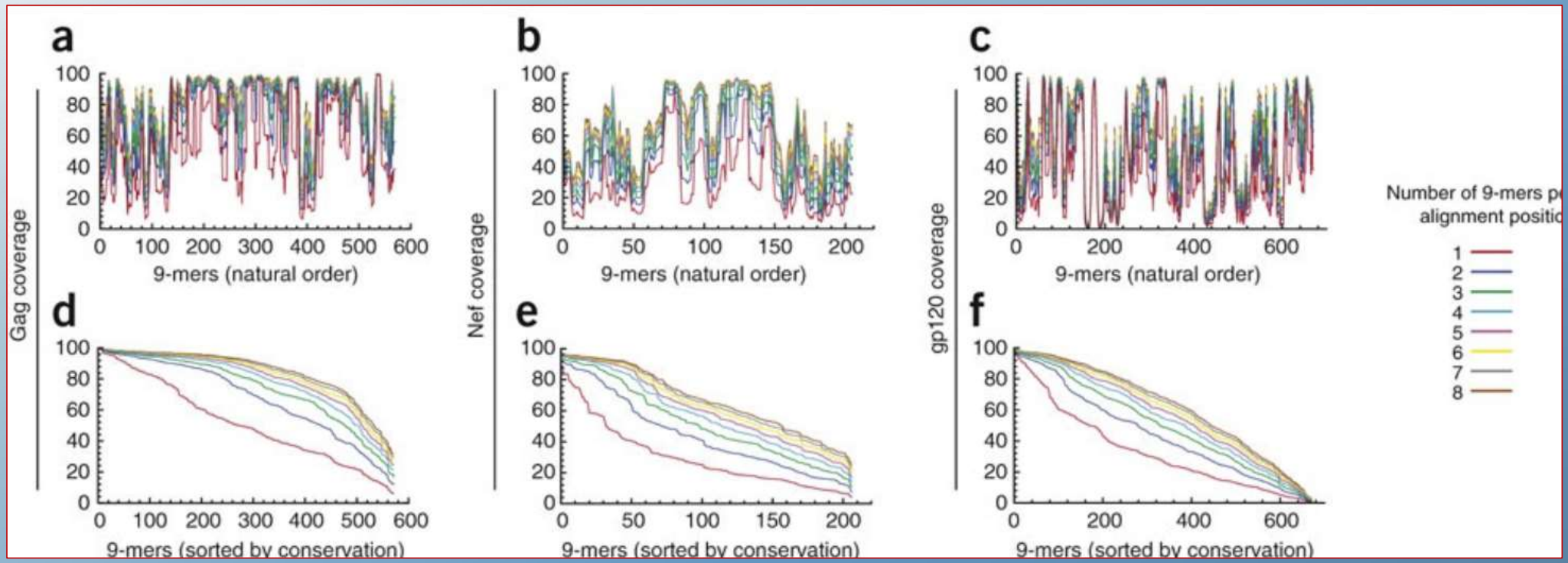
10/25/2019

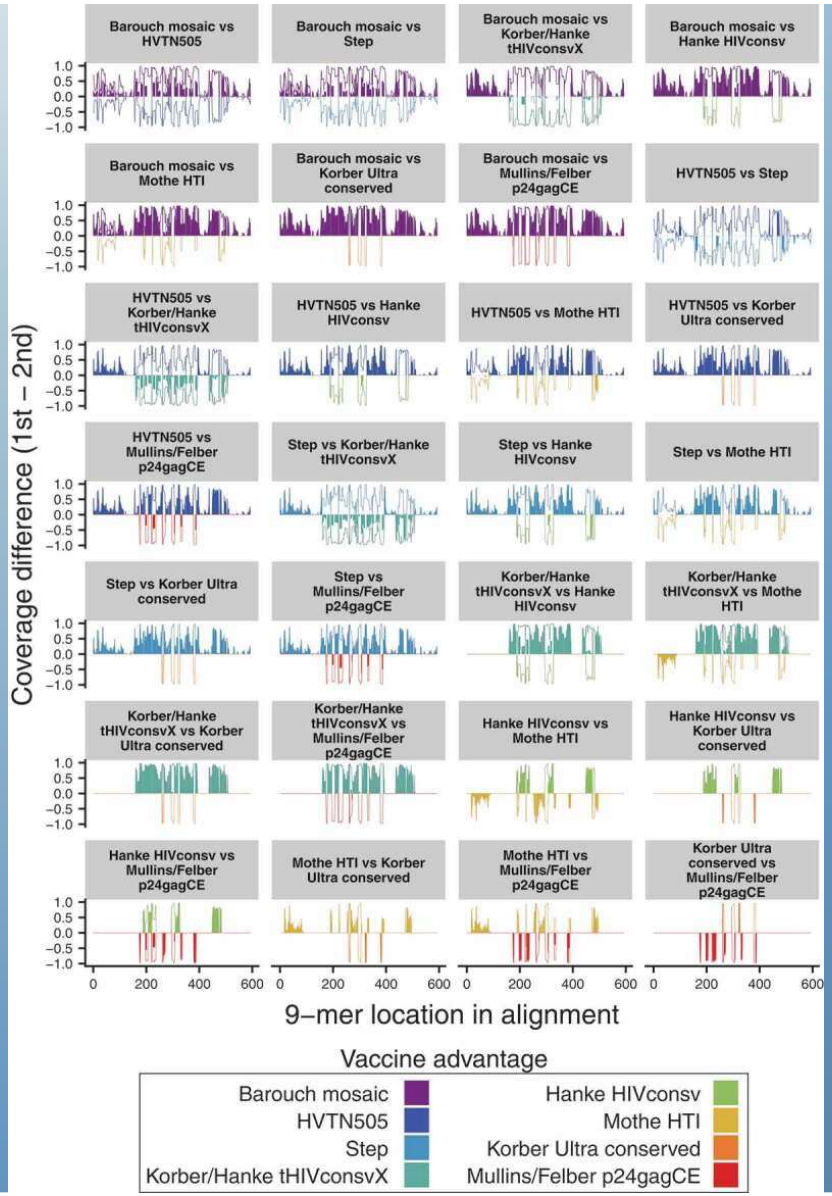
Motifs	Virus Glycoprotein	Motif Alignment
Insert 1	2019- nCoV (GP) HIV1(GP120)	71 76 TNGTKR TNGTKR 404 409
Insert 2	2019- nCoV (GP) HIV1(GP120)	145 150 HKNNKS HKNNKS 462 467
Insert 3	2019- nCoV (GP) HIV1(GP120)	245 256 RSYL----TPGDSSSG RTYLFNETRGNSSSG 136 150
Insert 4	2019- nCoV (Poly P) HIV1(gag)	676 684 QTNS----------PRRA QTNSSILMQRSNFKG PRRA 366 384

Table 1: Aligned sequences of 2019-nCoV and gp120 protein of HIV-1 with their positions in primary sequence of protein. All the inserts have a high density of positively charged residues. The deleted fragments in insert 3 and 4 increase the positive charge to surface area ratio. *please see Supp. Table 1 for accession numbers



Polyvalent vaccines for optimal coverage of potential T-cell...




Barouch mosaic vs HVTN505
Barouch mosaic vs Step
Barouch mosaic vs Korber/Hanke tHIVconsvX
Barouch mosaic vs Hanke HIVconsv
Barouch mosaic vs Mothe HTI
Barouch mosaic vs Korber Ultra conserved
Barouch mosaic vs Mullins/Felber p24gagCE
HVTN505 vs Step
HVTN505 vs Korber/Hanke tHIVconsvX
HVTN505 vs Hanke HIVconsv
HVTN505 vs Mothe HTI
HVTN505 vs Korber Ultra conserved
HVTN505 vs Mullins/Felber p24gagCE
Step vs Korber/Hanke tHIVconsvX
Step vs Hanke HIVconsv
Step vs Mothe HTI
Step vs Korber Ultra conserved
Step vs Mullins/Felber p24gagCE
Korber/Hanke tHIVconsvX vs Hanke HIVconsv
Korber/Hanke tHIVconsvX vs Mothe HTI
Korber/Hanke tHIVconsvX vs Korber Ultra conserved
Korber/Hanke tHIVconsvX vs Mullins/Felber p24gagCE
Hanke HIVconsv vs Mothe HTI
Hanke HIVconsv vs Korber Ultra conserved
Hanke HIVconsv vs Mullins/Felber p24gagCE
Mothe HTI vs Korber Ultra conserved
Mothe HTI vs Mullins/Felber p24gagCE
Korber Ultra conserved vs Mullins/Felber p24gagCE
Coverage difference (1st – 2nd)
1.0
0.5
0.0
−0.5
−1.0
0
200
400
600
9–mer location in alignment
Vaccine advantage
Barouch mosaic
HVTN505
Step
Korber/Hanke tHIVconsvX
Hanke HIVconsv
Mothe HTI
Korber Ultra conserved
Mullins/Felber p24gagCE


Mind the Gaps

The QTNSPRRA insert in SARS-CoV-2 corresponds to a part of the HIV-1 Gag Protein that is always removed in HIV-1 vaccine candidates

Bette Korber

This 2016 mosaic vax candidate specifically skips 364-390 – just like 2 dozen other HIV vax trials over 2 decades.

Molecular Therapy

Novel Conserved-region T-cell Mosaic Vaccine With High Global HIV-1 Coverage Is Recognized by Protective Responses in Untreated Infection

Beatrice Ondondo • Hayato Murakoshi • Genevieve Clutton • Sultan Abdul-Jawad • Edmund Gee • Hiroyuki Gatanaga • Shinichi Oka • Andrew J McMichael • Masafumi Takiguchi • Bette Korber • Tomáš Hanke

DOI: https://doi.org/10.1038/mt.2016.3

tPA leader sequence

MDAMKRGLCCVLLLCGAVFVSAR

Mosaic 1 Gag 1 (p24) 133-363

PIVQNLQGQMVHQAISPRTLNAWVKVIEEKAFSPEV
APGQMREPRGSDIAGTTSNLQEQIGWMTSNPPIPVG
NWMTDTLLVQNANPDCKTILRALGPGATLEEMMTAC

Mosaic 2 Gag 1 (p24) 133-363

PIVQNAQGQMVHQALSPRTLNAWVKVVEEKAFSPEV
PPGQMREPRGSDIAGTTSTLQEQIGWMTNNPPIPVG
NWMTETLLVQNANPDCKTILKALGPAATLEEMMTAC

Mosaic 1 Gag 2 391-459

KCFNCGKEGHIAKNCRAPRKRGCWKCGREGHQMKDC

Mosaic 2 Gag 2 391-459

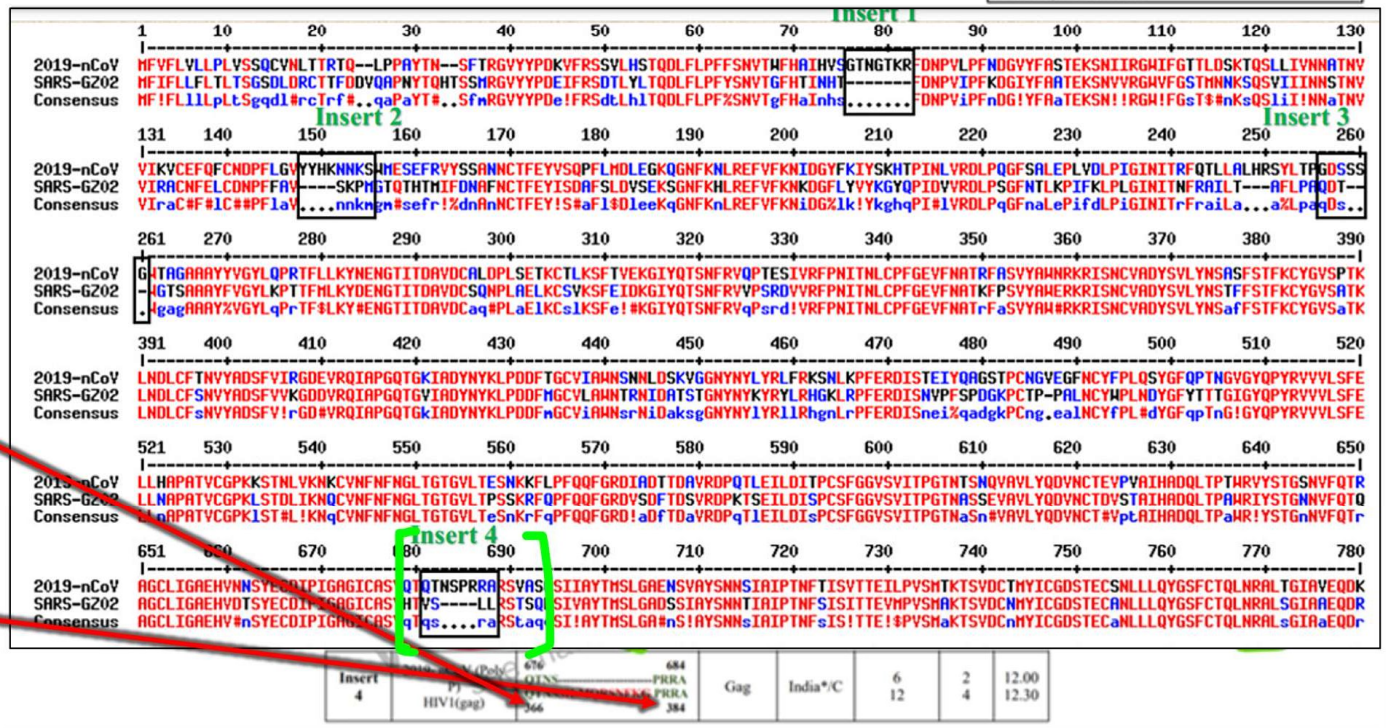
KCFNCGKEGHLARNCRAPRKKGCWKCGKEGHQMKDC

[Pradhan et al, 1/31/2020]

[i.e. the Watchmaker & intelligent design]

bioRxiv

Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag



ARTICLE | VOLUME 13, ISSUE 5, P755-768, MAY 2005 Download Full Issue

Scorpion-Toxin Mimics of CD4 in Complex with Human Immunodeficiency Virus gp120

Crystal Structures,Molecular Mimicry, and Neutralization Breadth

Chih-chin Huang • François Stricher • Loïc Martin • Julie M. Decker • Shahzad Majeed • Philippe Barthe • Wayne A. Hendrickson • James Robinson • Christian Roumestand • Joseph Sodroski • Richard Wyatt • George M. Shaw • Claudio Vita • Peter D. Kwong • Show less

Open Archive • DOI: https://doi.org/10.1016/j.str.2005.03.006

Mutations, Functional Elements & Antigenic Properties in the SARS-CoV-2 S Protein - Specifically, within the Receptor Binding Domain [RBD], N-Terminal Domain [NTD] Loops, & the HIV- Homologous Inserts identified by *Pradhan et al, Gallaher et al & Sorenson et al*

Inserts				C-19		Locations	HIV		Elements					Interactions [working]				
Pr*	SSD[2]	GI[6]	N-Lp[7]	Regn	AA	AA Sequence	AA	Regn	Details	Details	Glyc	SAg	PLD	CD4+	CD8+	B-cell	DC-SIGN	hACE2
		1	1	NTD	14-26	QCVNLTTRTQLPP				Ω								
1	1	2	2	NTD	71-76	TNGTKR	404-409	ENV	VL4		74-76			CD4+		B	N74	
1		2	2	NTD	67-81	AIHVSGTNGTKRFDN				Ω								
2		3	3	CTD	140-158	FLGVYYHKNNKSWMESEFR				Ω		*SAg*						
2	2	3	3	CTD	145-150	HKNNKS	462-467	ENV	VL5					CD4+		B	N149	
		4	4	CTD	178-180					Ω								
3	3	5	5	CTD	241-263	LLALHRSYLTPGDSSSGWTAGAA				Ω		*SAg*	Ω					
3	3	5		CTD	245-256	RSYL---TPGDSSSG	136-150	ENV	VL1			*SAg*		CD4+				

C-19		Locations	HIV		
Regn	AA	AA Sequence	AA	Regn	Details
NTD	14-26	QCVNLTTRTQLPP			
NTD	71-76	TNGTKR	404-409	ENV	VL4
NTD	67-81	AIHVSGTNGTKRFDN			
CTD	140-158	FLGVYYHKNNKSWMESEFR			
CTD	145-150	HKNNKS	462-467	ENV	VL5
CTD	178-180				
CTD	241-263	LLALHRSYLTPGDSSSGWTAGAA			
CTD	245-256	RSYL---TPGDSSSG	136-150	ENV	VL1

Table 3 Contact Surface Areas by Residue of gp120 for CD4, CD4M33, and F23 Complexes

	CD4/HXBc2 (821.8 Å²)			CD4/YU2 (874.1 Å²)			CD4M33/YU2(1) (527.6 Å²)			CD4M33/YU2(2) (543.1 Å²)			F23/YU2(1) (363.8 Å²)			F23/YU2(2) (398.0 Å²)		
YU2	Main	Side	Total	Main	Side	Total	Main	Side	Total	Main	Side	Total	Main	Side	Total	Main	Side	Total
123 T				0.0	4.1	4.1												
124 P	3.9	28.4	32.3	9.3	37.9	47.2	0.0	9.7	9.7	0.0	8.8	8.8	0.0	5.7	5.7	0.0	8.6	8.6
125 L	3.3	0.0	3.3	1.7	0.0	1.7												
126 C	17.9	28.0	45.9	15.8	29.8	45.5												
127 V	5.6	3.9	9.5	2.8	0.0	2.8												
128 G	2.8	0.0	2.8	15.0	0.0	15.0												
194 G				12.6	0.0	12.6												
196 C	0.0	6.9	6.9	0.0	20.1	20.1												
255 V							0.0	18.1	18.1	0.0	16.5	16.5						
256 S							8.2	0.0	8.2	7.4	0.0	7.4						
257 T	0.0	5.7	5.7	0.0	4.1	4.1	0.0	15.1	15.1	0.0	10.8	10.8	0.0	6.5	6.5	0.0	6.5	6.5
278 T	0.8	0.0	0.8															
279 N	2.0	16.3	18.3	0.0	15.6	15.6												
280 N	10.4	31.8	42.3	13.4	29.1	42.6	0.0	2.5	2.5	0.0	1.9	1.9	0.4	0.7	1.1	0.0	0.9	0.9
281 A	13.5	25.9	39.4	17.4	22.2	39.6	8.8	3.8	12.6	7.9	4.4	12.3	8.5	6.2	14.7	0.2	2.0	2.2
282 K	0.0	9.2	9.2	3.7	10.7	14.4												
283 T	1.4	14.7	16.1	3.2	13.2	16.4	0.0	0.2	0.2									
364 S	0.0	1.4	1.4				0.0	2.8	2.8	0.0	1.1	1.1				0.0	1.5	1.5
365 S	16.2	30.9	47.1	9.9	27.1	37.1	13.9	18.4	32.3	12.2	20.7	32.9	12.2	20.7	32.9	12.9	22.2	35.0
366 G	20.1	0.0	20.1	20.8	0.0	20.8	18.3	0.0	18.3	23.5	0.0	23.5	16.7	0.0	16.7	23.8	0.0	23.8
367 G	21.8	0.0	21.8	21.9	0.0	21.9	17.0	0.0	17.0	26.6	0.0	26.6	17.9	0.0	17.9	25.4	0.0	25.4
368 D	7.1	45.2	52.3	8.6	41.8	50.4	7.5	29.3	36.8	9.4	40.2	49.6	7.2	30.7	37.8	8.5	44.3	52.8
369 P																0.0	0.7	0.7
370 E	0.0	19.1	19.1	0.0	17.6	17.6	0.0	29.2	29.2	0.0	30.4	30.4	0.0	21.2	21.2	0.0	18.7	18.7
371 I	0.0	39.3	39.3	0.0	38.1	38.1	0.0	44.8	44.8	0.0	40.2	40.2	0.0	40.3	40.3	0.0	41.1	41.1
375 S							4.0	11.6	15.7	0.0	14.1	14.1						
376 F							10.7	0.0	10.7	13.0	0.0	13.0						
377 N							2.2	5.2	7.4	3.5	5.3	8.8						
382 F							0.0	19.4	19.4	0.0	23.1	23.1						
384 Y							0.0	9.0	9.0	0.0	7.4	7.4						
424 I							0.0	9.8	9.8	0.0	7.9	7.9						
425 N	6.5	20.3	26.8	7.7	24.0	31.6	9.7	11.4	21.1	11.3	11.1	22.4	6.6	9.0	15.5	5.5	9.9	15.4
426 M	13.8	0.0	13.8	12.7	0.0	12.7	15.3	0.0	15.3	15.4	0.0	15.4	14.8	0.0	14.8	13.9	0.0	13.9
427 W	18.2	12.3	30.5	15.5	10.2	25.7	20.2	22.0	42.2	17.2	22.1	39.3	16.4	9.3	25.6	19.2	8.3	27.5
428 Q	2.4	0.0	2.4	2.6	0.0	2.6	2.0	0.0	2.0	3.2	0.0	3.2	1.3	0.0	1.3	2.8	0.0	2.8
429 K	10.5	3.2	13.7	8.0	4.1	12.1	11.3	0.0	11.3	11.2	0.0	11.2	9.7	0.0	9.7	11.5	0.0	11.5
430 V	14.2	54.8	69.0	17.7	55.9	73.6	8.0	34.2	42.2	7.2	33.8	41.0	7.1	32.7	39.8	8.4	36.4	44.8
431 G	1.4	0.0	1.4	2.3	0.0	2.3	1.5	0.0	1.5	2.1	0.0	2.1	1.5	0.0	1.5	1.1	0.0	1.1
432 K	0.0	1.7	1.7	0.0	2.8	2.8												
455 T	0.0	12.8	12.8	1.8	8.3	10.0	0.0	3.1	3.1	0.0	2.8	2.8	0.0	0.2	0.2	0.0	0.9	0.9
456 R	7.0	0.0	7.0	3.8	0.0	3.8												
457 D	5.9	21.0	26.9	6.3	20.7	27.0	3.0	1.9	4.9	1.6	1.1	2.6	1.5	0.6	2.2	2.0	4.2	6.2
458 G	5.2	0.0	5.2	9.8	0.0	9.8	2.6	0.0	2.6				1.5	0.0	1.5			
459 G	29.2	0.0	29.2	11.8	0.0	11.8												
460 K	8.5	25.0	33.5	12.2	49.2	61.4												
461 D	1.7	0.0	1.7	1.1	8.5	9.6												
469 A	0.0	6.6	6.6	0.0	7.0	7.0										0.0	1.8	1.8
471 G	0.7	0.0	0.7	0.8	0.0	0.8												
472 G	22.4	0.0	22.4	17.6	0.0	17.6	5.1	0.0	5.1	6.5	0.0	6.5	6.7	0.0	6.7	6.2	0.0	6.2
473 G	23.5	0.0	23.5	23.2	0.0	23.2	25.5	0.0	25.5	26.1	0.0	26.1	21.4	0.0	21.4	21.1	0.0	21.1
474 D	12.7	26.2	38.9	5.4	27.3	32.7	7.5	13.6	21.1	10.1	13.0	23.1	9.9	12.3	22.2	8.0	13.6	21.6
475 M	0.0	7.0	7.0	0.0	6.1	6.1	0.0	10.5	10.5	0.2	11.0	11.2	0.0	6.3	6.3	0.0	6.1	6.1
476 R	0.0	3.8	3.8	0.0	3.4	3.4												
477 D	0.0	9.5	9.5	0.0	7.1	7.1												

"Main," "side," and "total" refer to the surface area of the main chain atoms, the surface area of the side chain atoms, and the total surface area for each gp120 residue specified. Residues are colored blue if they have a contact surface common to CD4, CD4M33, and F23, black if the contact is not conserved, and red if the contact is unique to both independent copies of CD4M33 in the $P2_1$ crystal.

Insert 3 [136-150] **deleted**

Insert 1 [404-409] **deleted**

Insert 2 [462-467] **deleted**

Open Access | Editor's Choice | Communication

Tetravalent Immunogen Assembled from Conserved Regions of HIV-1 and Delivered as mRNA Demonstrates Potent Preclinical T-Cell Immunogenicity and Breadth

by Nathifa Moyo [1], Edmund G. Wee [1], Bette Korber [2,3], Kapil Bahl [4], Samantha Falcone [4], Sunny Himansu [4], Adrianne L. Wong [5], Antu K. Dey [5], Mark Feinberg [5] and Tomáš Hanke [1,6,*]

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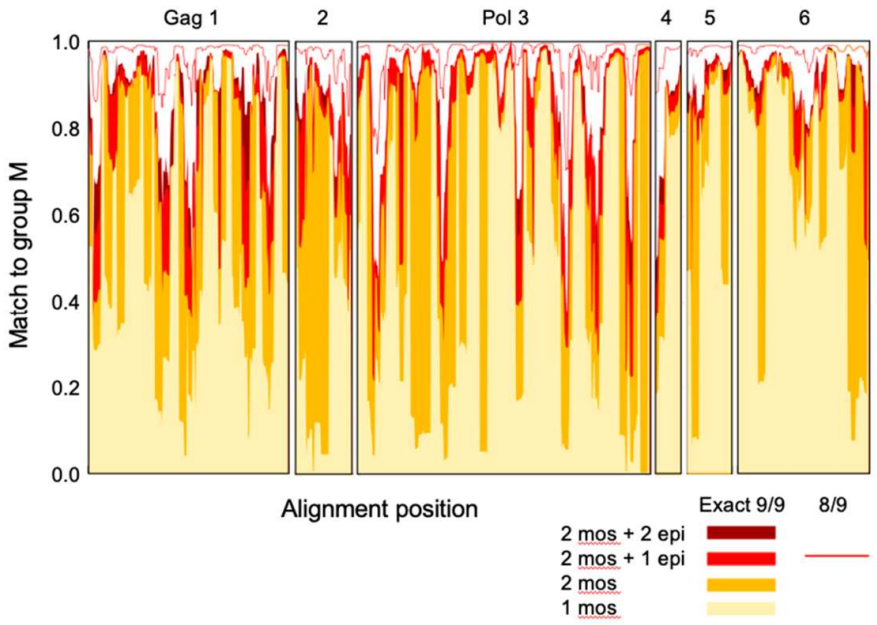
[2] Los Alamo National Laboratory, Theoretical Biology and Biophysics, Los Alamos, NM 87545, USA
[3] New Mexico Consortium, Los Alamos, NM 87545, USA
[4] Moderna Inc., Cambridge, MA 02139, USA
[5] International AIDS Vaccine Initiative-New York, New York, NY 10004, USA
[6] Joint Research Center for Human Retrovirus Infection, Kumamoto University, Kumamoto 860-0811, Japan
* Author to whom correspondence should be addressed.

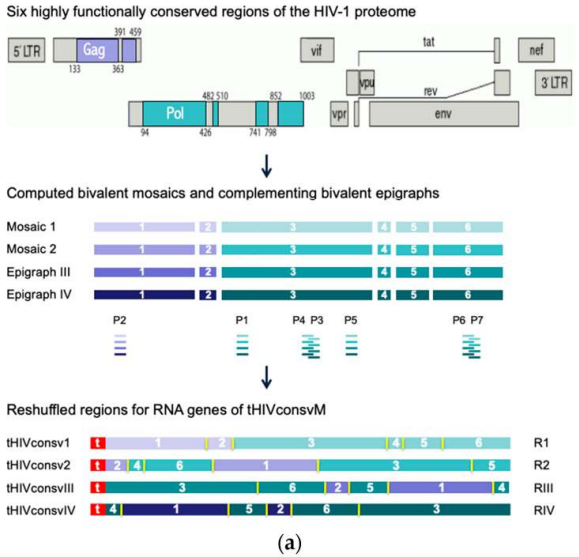
Vaccines **2020**, *8*(3), 360; **https://doi.org/10.3390/vaccines8030360**

Received: 5 June 2020 / Revised: 1 July 2020 / Accepted: 2 July 2020 / Published: 6 July 2020



(b)

Figure 1. The HIVconsvM vaccine design. (**a**) Curated full-length-protein amino acid sequences of HIV-1 present in the Los Alamos National Laboratory HIV Molecular Immunology Database (LANL-HMID) were used to compute first two mosaics (September 2013) and then sequentially two complementing epigraphs (September 2017; 4925 Gag and 2703 Pol sequences) [22,25]. The same dataset as used for mosaics was used to select 6 highly conserved regions of the HIV-1 proteome, which were reshuffled into unique orders to minimize the chance of inducing strong T-cell responses to potential non-HIV-1 neoepitopes irrelevant for protection [5], which might have been generated by two juxtaposed regions [11]. Mosaics 1 and 2, and epigraphs III and IV (color-coded) differ in approximately 1 amino acid per epitope and together maximize the match of the vaccines to globally circulating HIV-1 isolates of group M. Small 't' in front of the name indicates the presence of the human tissue plasminogen activator leader sequence [23]. The tetravalent immunogens were collectively called HIVconsvM and consisted of 4 mRNA molecules designated R1, R2, RIII or RIV. Pools P1 to P7 depicted under the regions indicate the approximate positions of the studied epitopes. (**b**) The 9-mer potential T-cell epitope coverage provided by the 6 vaccine regions is based on sliding window of 9 amino acids across the immunogen. Mosaics 1 and 2, being designed together, alternate the most common variants between themselves and the coverages of one (pale yellow) and both mosaics together (gold) are shown. The gain by adding epigraph III (red) and epigraphs IV (brown) into to the cocktail are also shown. Finally, the thin red line shows the fraction of 9-mers in each 9-mer window that matches 8/9 amino acids. Additionally, see **Figure S1**.



(a)

PLOS COMPUTATIONAL BIOLOGY

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

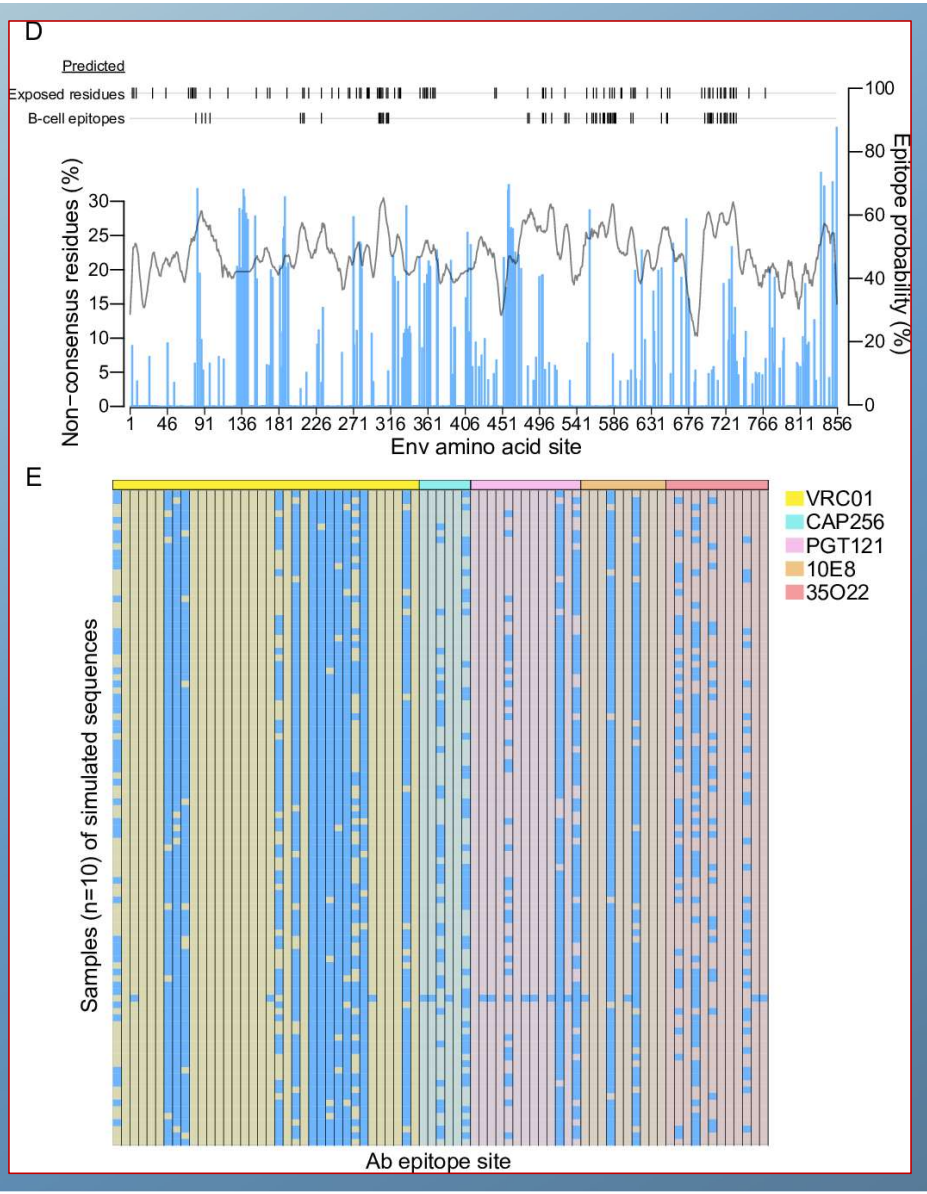
Optimal sequence-based design for multi-antigen HIV-1 vaccines using minimally distant antigens

Eric Lewitus, Jennifer Hoang, Yifan Li, Hongjun Bai, Morgane Rolland

Published: October 31, 2022 • https://doi.org/10.1371/journal.pcbi.1010624

Abstract

The immense global diversity of HIV-1 is a significant obstacle to developing a safe and effective vaccine. We recently showed that infections established with multiple founder variants are associated with the development of neutralization breadth years later. We propose a novel vaccine design strategy that integrates the variability observed in acute HIV-1 infections with multiple founder variants. We developed a probabilistic model to simulate this variability, yielding a set of sequences that present the minimal diversity seen in an infection with multiple founders. We applied this model to a subtype C consensus sequence for the Envelope (Env) (used as input) and showed that the simulated Env sequences mimic the mutational landscape of an infection with multiple founder variants, including diversity at antibody epitopes. The derived set of multi-founder-variant-like, minimally distant antigens is designed to be used as a vaccine cocktail specific to a HIV-1 subtype or circulating recombinant form and is expected to promote the development of broadly neutralizing antibodies.



Immunity

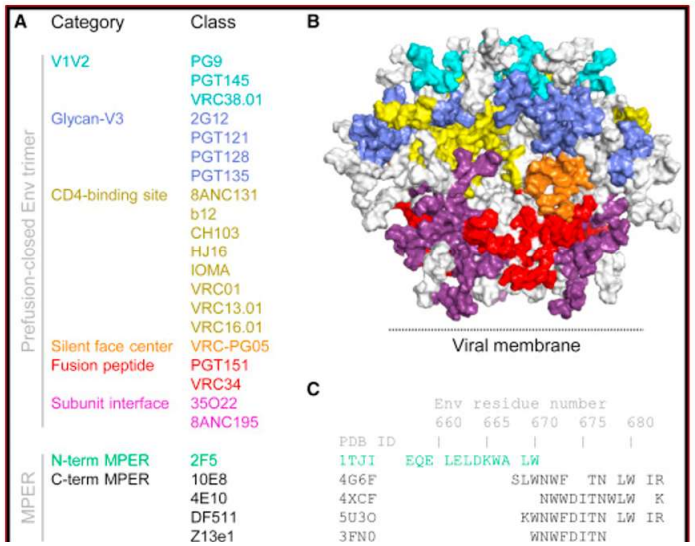
REVIEW | VOLUME 48, ISSUE 5, P855-871, MAY 15, 2018 Download Full Issue

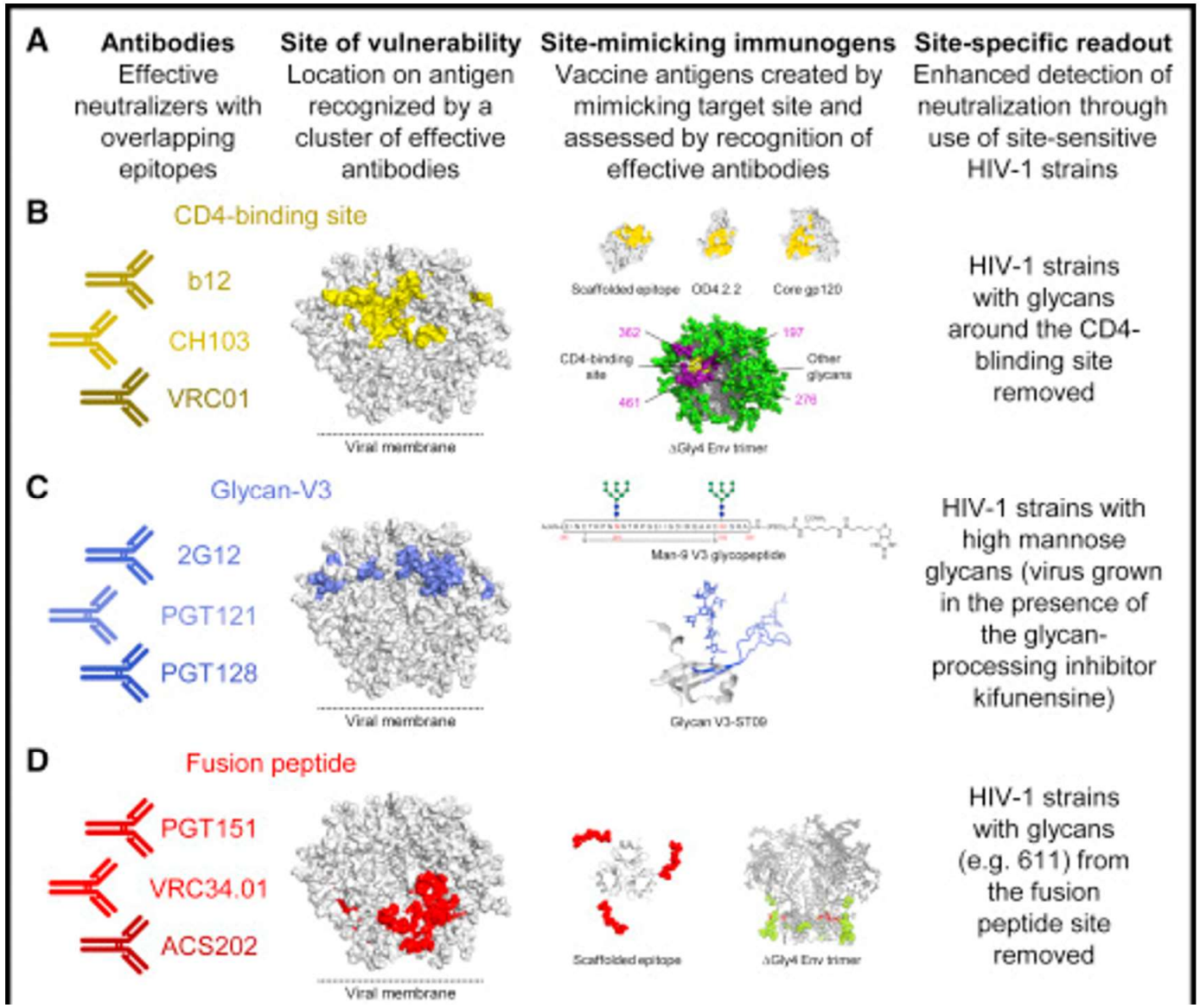
HIV-1 Vaccines Based on Antibody Identification, B Cell Ontogeny, and Epitope Structure

Peter D. Kwong • John R. Mascola

Open Archive • DOI: https://doi.org/10.1016/j.immuni.2018.04.029 • Check for updates

HIV-1 vaccine development has been stymied by an inability to induce broadly reactive neutralizing antibodies to the envelope (Env) trimer, the sole viral antigen on the virion surface. Antibodies isolated from HIV-1-infected donors, however, have been shown to recognize all major exposed regions of the prefusion-closed Env trimer, and an emerging understanding of the immunological and structural characteristics of these antibodies and the epitopes they recognize is enabling new approaches to vaccine design. Antibody lineage-based design creates immunogens that activate the naive ancestor-B cell of a target antibody lineage and that mature intermediate-B cells toward effective neutralization, with proof of principle achieved with select HIV-1-neutralizing antibody lineages in human-gene knock-in mouse models. Epitope-based vaccine design involves the engineering of sites of Env vulnerability as defined by the recognition of broadly neutralizing antibodies, with cross-reactive neutralizing antibodies elicited in animal models. Both epitope-based and antibody lineage-based HIV-1 vaccine approaches are being readied for human clinical trials.





Not just a Furin Cleavage Site….

Mutations, Functional Elements & Antigenic Properties in the SARS-CoV-2 S Protein - Specifically, within the Receptor Binding Domain [RBD], N-Terminal Domain [NTD] Loops, & the HIV- Homologous Inserts identified by *Pradhan et al, Gallaher et al & Sorenson et al*

Inserts				C-19		Locations	HIV		Elements				Interactions [working]				
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		1	1	NTD	14-26	QCVNLTTRTQLPP				Ω							
1	1	2	2	NTD	71-76	TNGTKR	404-409	ENV	VL4		74-76		CD4+		B	N74	
1		2	2	NTD	67-81	AIHVSGTNGTKRFDN				Ω							
2		3	3	CTD	140-158	FLGVYYHKNNKSWMESEFR				Ω							
2	2	3	3	CTD	145-150	HKNNKS	462-467	ENV	VL5				CD4+		B	N149	
		4	4	CTD	178-180					Ω							
3	3	5	5	CTD	241-263	LLALHRSYLTPGDSSSGWTAGAA				Ω		Ω					
3	3	5		CTD	245-256	RSYL---TPGDSSSG	136-150	ENV	VL1				CD4+				
					269-277	Ω						PLD		CD8+			
				Ω	274-294	LQPRTFLLKYNENGTITDAVD				Ω							
	4	6,7		RBD	414-506	QTGK.....GVGVY					414-506				Ω		10x
	5	7		RBD	473-510	IYQAGST..NGVGYQ						PLD			Ω		6x
					608-613	VAVLYQ						PLD					
					614	D to G											
4		8		FCS	674-680	QTQTNS	366-384	GAG		FCS			CD4+		Ω		
4	6	8		FCS	679-687	TNSPRRARSV	366-384	GAG		FCS/SEB			CD4+		Ω		
4		8		FCS	681-684	PRRA/	366-384	GAG		FCS			CD4+		Ω		
				FCS	685-689	/RSVAS	366-384	GAG		ENaC			CD4+		Ω		
				S2	689-697	SQSIIAYTM						PLD	CD4+				

[Killer T-Cell] [accrued mutations]

Mutations within or adjacent to HIV-homologous inserts within the SARS-CoV-2 S Protein, by variant

Ins	Strt	Stp	α	β	γ	δ	o1	o2
I1	14	26	0	0	3	1	0	5
I2	67	74	2	0	0	0	3	0
I3	143	149	1	0	0	1	4	1
I4	178	180	0	0	0	0	0	0
I5	241	252	0	3	0	0	0	0
I6	444	450	0	0	0	1	2	1
I7	474	488	0	1	1	1	3	3
I8	675	684	1	0	0	1	2	2
Inserts			4	4	4	5	14	12
Total			7	10	9	10	31	25
%			57%	40%	44%	50%	45%	48%

Inserts & Loops

Gallaher et al^ — *Gallaher et al - Spike protein mutations in novel SARS-CoV-2 'variants of concern' commonly occur in or near indels - Virological*

Pradhan et al* — *Pradhan et al - Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag*

Sorensen et al‡ — *Sorensen et al - Biovacc-19: A Candidate Vaccine for Covid-19 (SARS-CoV-2) Developed from Analysis of its General Method of Action for Infectivity*

NTD Loops^γ — *Evolutionary remodelling of N-terminal domain loops fine-tunes SARS-CoV-2 spike*

RBD — Consensus Receptor Binding Domain [RBD]

Antigens & Elements

Glyc — N-Linked Glycan sites of interest, as listed by Gallaher

SEB — *Superantigenic character of an insert unique to SARS-CoV-2 spike supported by skewed TCR repertoire in patients with hyperinflammation*

ENaC — SARS-CoV-2 strategically mimics **proteolytic activation of human ENaC**

PLD — ***Prion-like Domains*** *in Spike Protein of SARS-CoV-2 Differ across Its Variants and* ***Enable Changes in Affinity to ACE2***

Ω — ***Another*** PLD starts just after Insert #3, at AA 262-270 - also, just after the N5 Loop, and doubles as a Killer T-Cell epitope

Ω — *Emergence of immune escape at dominant SARS-CoV-2 killer T cell epitope*

Ω — **Immuno-dominant B cell epitopes** at 404-424, 439-451, 455-478, 483-493, 497-507, 673-691 [other epitopes outside of the inserts/RBD at 330-356, 370-395, 516-535]

Ω — Mutations in the residues of the NTD Loops of SARS-CoV-2 during the pandemic

Ω — **An immuno-suppressive domain in S1** with homology to HIV-1 & Ebola, etc, at AA 274-294 [Gallaher, in *déjà vu*]

Ω — The N4 Loop can utilize bilirubin to evade antiody immunity

Ω

Sorensen et al - The CoV-2 specific Cys538-Cys590 bridge brings in additional charge from 526-560, via the Cys391-Cys525 to positions right next to the RBM.

Sorensen et al - "We postulate that there are 2 charged domains on SADS that are likely to contribute to attachment receptor binding located in domains 330-360 and 540-560 respectively. Recollect that we have identified a simil

Difference in Receptor Usage between SARS-CoV & SARS-like CoV of Bat Origin [Interchanging RBD's between bat & human SARS viruses]

SARS-CoV-2 Spike Protein: AA 661 – 697

ECDIPIGAGICASYQTQTNSPRRA/RSVASQSIIAYTM

Superantigen SEB: 661 – 685

Furin Cleavage Site: 681 – 685

ENaC: ~ 686 – 689

Prion-Like Domain: 686 – 697

This isn't natural – 2 GOF elements in a row [SEB+FCS]

How Special is SARS-CoV-2?

No other sarbecovirus has a polybasic furin cleavage site
No other β-CoV has an SEB-analog sequence
No other coronavirus has higher human ACE2 affinity than SARS-CoV-2
No other coronavirus has a prion-like domain in its receptor-binding domain [RBD]
No other coronavirus contains prion-like domains in the spike protein
No other coronavirus has as many prion-like domains in its genome
No other coronavirus has an ENaC motif adjacent to an S1/S2 cleavage site
ORF6 & ORF10 contain amyloidogenic peptides; those two ORFs don't even exist in related CoVs in nature
No other coronavirus can transmit as efficiently via the aerosol route
No other viral spike protein interacts with 28 of 55 human tissues
ORF8 Protein of SARS-CoV-2 Mediates Immune Evasion through Potently Downregulating MHC-I - unlike SARS-CoV-1

Each of these traits would be ~~suspicious~~ special by themselves

Yes, but life finds a way….

Life doesn't find a way to turn a virus into a quantum Decepticon

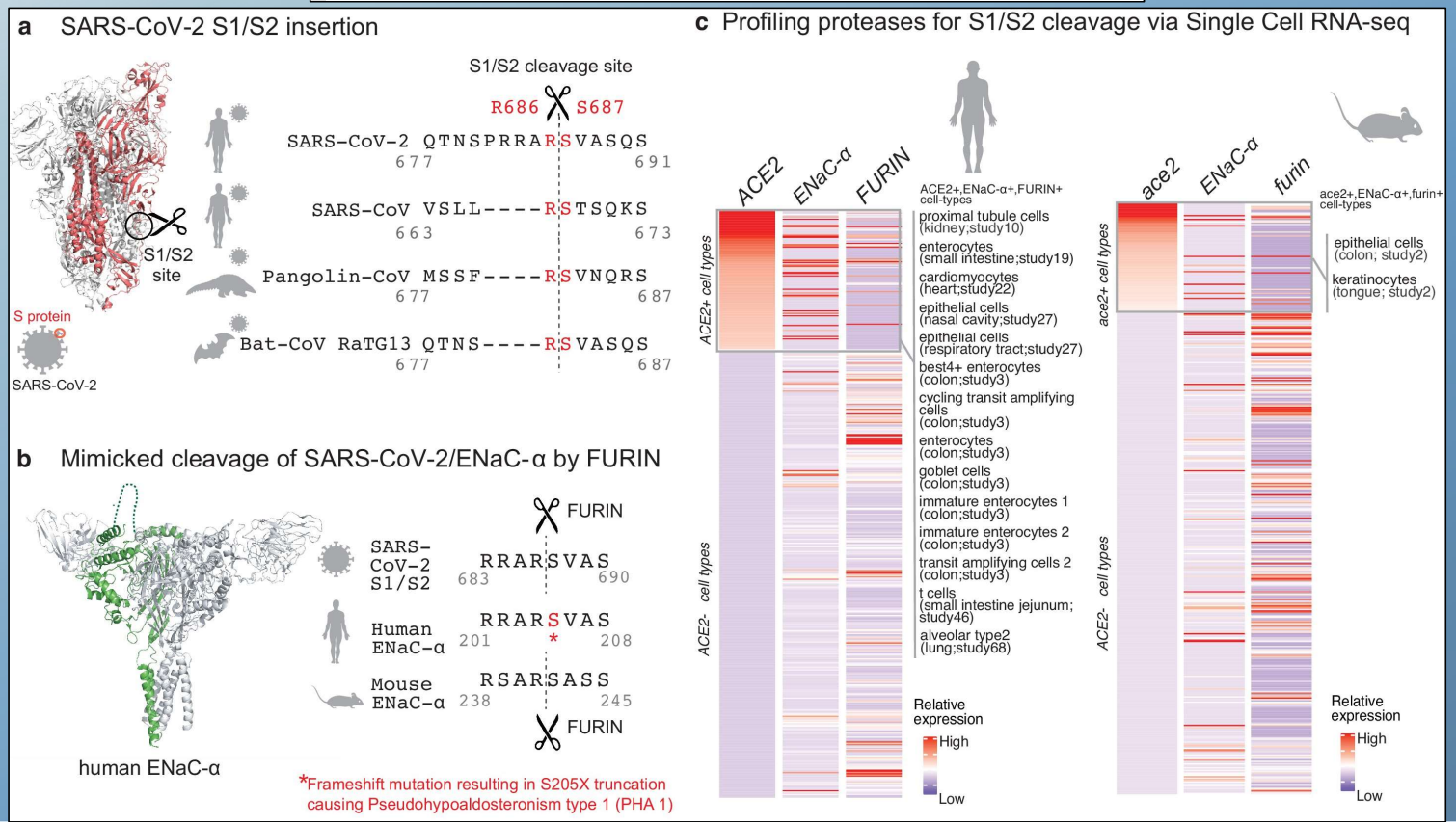
ECDIPIGAGICASYQTQTNSPRRA/RSVASQSIIAYTM

ENaC: ~ 686 – 689

Analysis of 8-mers of the human proteome

Request a detailed protocol

We enumerated 10,257,893 (10.26M) 8-mers from 20,350 reviewed uniprot reference sequences from human proteome (Proteome ID: UP000005640, as accessed on May 4th 2020). The previously identified SARS-CoV-2 8-mer 'RRARSVAS' was in fact found in ENaC-α protein (Uniprot ID: P37088; p-value ≈ $10.26M/20^8$ = 4E-4; chance of finding that particular 8-mer anywhere in the reference sequences).



ECDIPIGAGICASYQTQTNSPRRA/RSVASQSIIAYTM

Prion-Like Domain: 686 – 697

Peptide	Amino acid sequence[a]	MW (Da)[b]	pI	ThT kin	Congo Red	Ultrastructure
Spike192	FVFKNIDGYFKIYSKHTPIN	2431	9.4	+	+	fibril
Spike258	WTAGAAAYYVGYLQPRTFLLK	2389	9.5	-	+	fibril
Spike365	KKKGGGYSVLYNSASFSTFK	2169	10.0	-	+	amorphous
Spike532	NLVKNKCVNFNFNGLTGTGV	2139	9.3	+	+	amorphous
Spike601	GTNTSNQVAVLYQDVNCTEV	2155	3.7	+	+	fibril
Spike685	KKKRSVASQSIIAYTMSLGA	2139	10.5	-	-	ribbons
Spike1166	LGDISGINASVVNIQKEIDR	2141	4.6	+	+	fibril

SARS-CoV-2 S1, S2, human prion protein (note also AGAA/A/A sequences)

```
Prion Pr  :  QGGTHGQWNKPSKPKTNMKHVAGAAAAGAVVGGLGGYMLGSAMSRPLIHFGXDY
Spike S1  :  QTLLALHRSYLTPGDSSSGWTAGAAAY--YVGYLQ-PRTFLLKYNENGTITDAV
Spike S2  :  DEMIAQYTSALLAGTITSGWTFGAGAA------LQIPFAMQMAYRFNGIGVTQN

Prion Pr  :  QGGTHGQWNKPSKPKTNMKHVAGAAAAGAVVGGLGGYMLGSAMSRPLIHFGXDY
Spike S1  :  QTLLALHRSYLTPGDSSSGWTAGAAAY--YVGYLQ-PRTFLLKYNENGTITDAV
Spike S2  :  DEMIAQYTSALLAGTITSGWTFGAGAA------LQIPFAMQMAYRFNGIGVTQN
```

2023 DBP

ECDIPIGAGICASYQTQTNSPRRA/RSVASQSIIAYTM

Furin Cleavage Site: 681 – 685

Furin Cleavage Site

-Side note: Furin also plays a role in the pathogenesis of bacillus anthracis. [**anthrax**]
-Side note: Furin also plays a role in helping **Pseudomonas Aeruginosa** Exotoxin A get to the endoplasmic reticulum.
-Side note: Furin expression is **exacerbated** by Hypoxia, which fuels **cancer** & **amyloid** formation.
-Side note: GP120 is also a superantigen, that can cause ADE. [**SEB**]
-Side note: Guess what can cause IgG4 class-switching? – GP120 [***Pradhan et al* HIV inserts**]
-Side note: Guess what else can cause IgG4 class-switching? **Superantigens**

In other words, each of the elements "naturally" found within SARS-CoV-2's spike is exacerbated by furin expression – except for the superantigen, which triggers massive inflammation from the immune system – and each element adds to the cascade of effects that overwhelm your body, quickly [COVID-19, dying suddenly] or slowly [cancer, neurodegeneration]

In addition to **Furin**, each element also shares another common trait:

All of them are extensively tied to historical **biological weapons** development

& **ALL** of those elements were kept in the Spike protein of the two mRNA jabs*

[*After always being removed from vaccines, for decades]

Now you should turn to Anthony Fauci and ask

Why did he keep those elements in, this time?

Why did he intentionally hide their existence in the genome from the public?

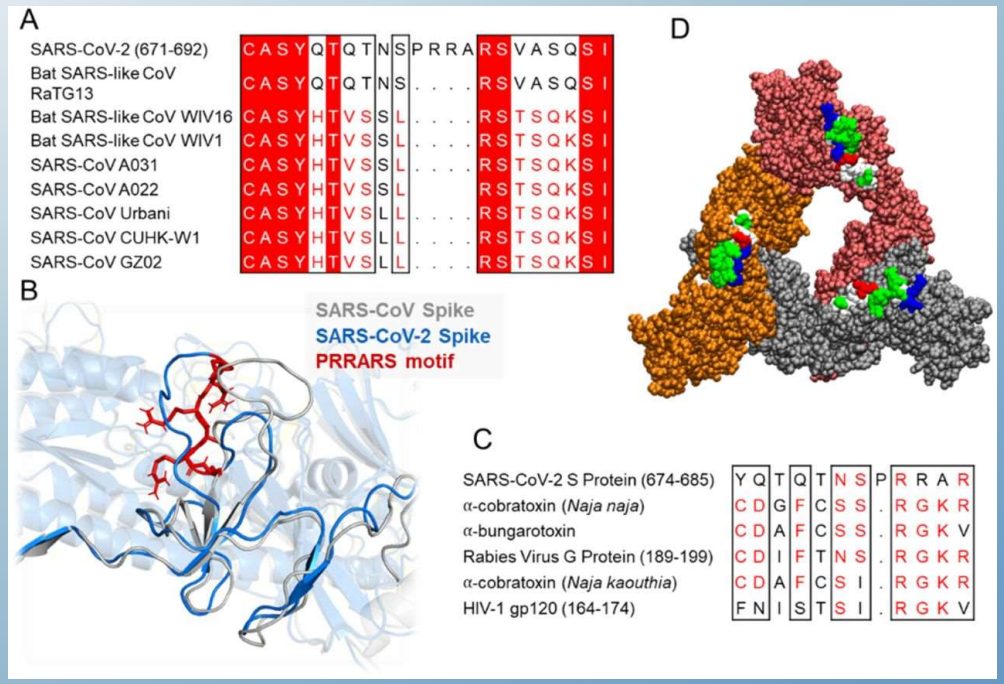
Why did he do so while understanding the dangerous risks [IgG4, etc]

And WHY would he keep the original Wuhan spike in the Bivalent booster?

ECDIPIGAGICASYQTQTNSPRRA/RSVASQSIIAYTM

Superantigen SEB: 661 – 685

SARS-CoV-2 spike
proposed superantigen



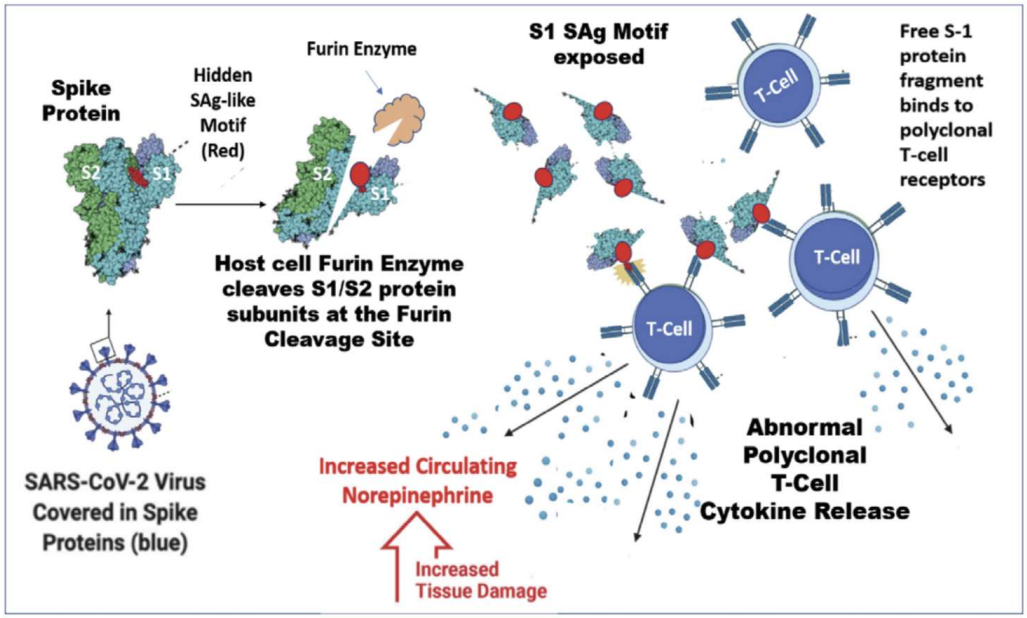


Figure 2. Conformation Changes in the Free-floating Fragment of the S1 Protein after Furin Cleavage of the SARS-CoV-2 Spike Protein

ECDIPIGAGICASYQTQTNSPRRA/RSVASQSIIAYTM

Superantigen SEB: 661 – 685

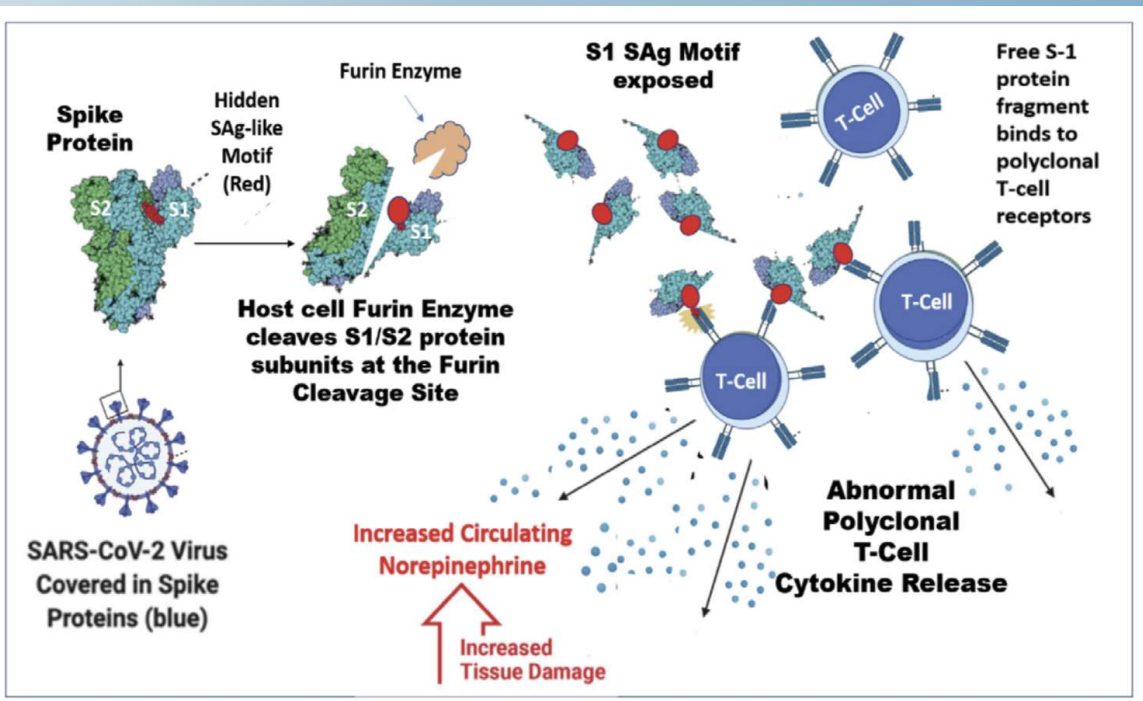
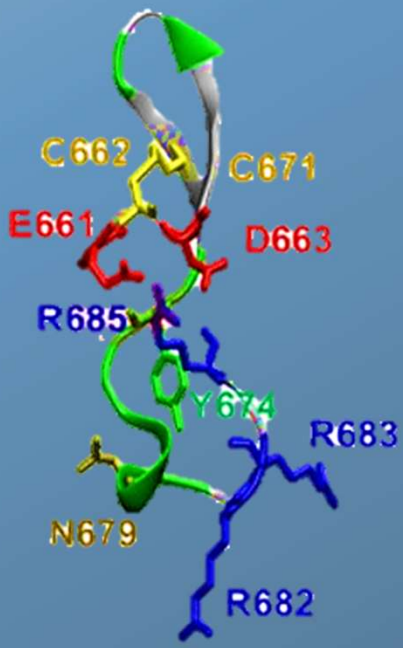


Figure 2. Conformation Changes in the Free-floating Fragment of the S1 Protein after Furin Cleavage of the SARS-CoV-2 Spike Protein

Journal of American Physicians and Surgeons Volume 27 Number 2 Summer 2022

SARS-CoV-2 spike proposed superantigen



Manipulation of Innate and Adaptive Immunity by Staphylococcal Superantigens

SAg	Grp	kDa	Emetic	Human Vβ Specificity	MHC-II	Associated Mobile Genetic Elements
SEA	III	27.1	+	1, 5, 6, 7, 9, 15, 16, 18, 21, 22, 24	α + β	ϕSa3n
SEB	II	28.3	+	1, 3, 6, 12, 13.2, 14, 15, 17, 20	α	SaPI
SEC	II	27.5	+	3, 12, 13.2, 14, 15, 17, 20	α	SaPI
SED	III	26.4	+	1, 3, 5, 8, 9, 12, 14	α + β	Plasmid (pIB485-like)
SEE	III	26.4	+	5, 6, 8, 9, 13.1, 16, 18, 21	α + β	Integrated Plasmid
SEG	II	27	+	3, 12, 13, 14, 15	α	vSAβ (egc)
SEH	III	25.2	+	Vα8, Vα10	β	ϕSa3mu
SEI	V	24.9	b	1, 5, 6, 23	β	vSAβ (egc)
SElJ	III	28.5	NK	8, 21	α + β	SaPI/ϕSa3n/Plasmid (pF5/pIB485-like)
SElK	V	26	-	1, 5, 6	β	SaPI
SElL	V	26	-	1, 5, 7, 16, 22, 23	α + β	SaPI
SElM	V	24.8	b	8, 9, 18, 21	α + β	vSAβ (egc)
SElN	III	26.1	b	7, 8, 9, 17	α + β	vSAβ (egc)
SElO	III	26.7	b	5, 7	α + β	vSAβ (egc)
SElP	III	27	b	5, 8, 16, 18, 21	α + β	ϕSa3n
SElQ	V	28	-	6, 21	α + β	SaPI/ϕSa3n
SER	II	27	+	3, 12, 14	α	Plasmid (pF5/pIB485-like)
SES	III	26.2	+	9, 16	α + β	Plasmid (pF5)
SET	I	22.6	b	NK	α	Plasmid (pF5)
SElU/U2	II	27.1	NK	13.2, 14	α	vSAβ (egc)
SElV	V	25	NK	6, 18, 21	α + β	vSAβ (egc)
SElW	III	27.3	NK	NK	NK	Chromosomal (Core genome)
SElX	I	19.3	NK	1, 6, 18, 21	NK	Chromosomal (Core genome)
SElY	I	22.5	+c	NK	NK	Chromosomal
SElZ	II	27	NK	NK	NK	Chromosomal
TSST-1	I	22	-		2 α	SaPI

Superantigen toxins

Staphylococcal SAg

- Staphylococcal enterotoxin A, B, C, D, E, G, H, I, J,(most studied A, B and TSST1)
- TSST-1 [staphylococcal enterotoxin F]
- Staphylococcal protein A (SpA) [B-cell Superantigen]

EB Virus

- HERV-K18 env

Peptostreptococcus magnus

- Protein L (B-cell SAg)

Streptococcal SAg

- Streptococcal pyrogenic exotoxins (SPE): SPE-A, SPE-B, SPE-C, SPE-D, SPE-F, SPE-G, SPE-H, SPE-J
- SMEZ
- Mitogenic factor (MF)
- SSA

HIV

- HIV-gp120 (B-cell SAg)

Mycoplasma arthritidis SAg

- MAM (mycoplasma arthritidis -derived Superantigen)

Human liver sialoprotein

- Protein Fv (B-cell SAg)

Yersinia pseudotuberculosis

- YPM

Immunomodulatory drugs useful for SAg-associated diseases

- Intravenous immunoglobulin (IVIg)
- Cyclosporin
- Pentoxyphylline (PF)
- Corticosteroids
- Thalidomide and its analogues
- Chinese herb: Baicalin
- STA-5236: A potent IL12/IL23 inhibitor
- TNF-α inhibitors: e.g. Adalimumab, Etanercept, Infliximab
- Monoclonal antibody and fusion protein: Alefacept, Efalizumab
- Vaccine
- Receptor antagonist: Genetically engineered proteins that interfere with binding of SAg to Vβ of TCR.

Factors affecting SAg-induced response

- MHC-II binding.
- Concomitant infection.
- Dose: low, high: dose lower than maximum, T-cell response and dose higher than that, produce different effect.
- Rechallenge: T-cell response to injected SAgs is very transient and more rapidly eliminated than primary response.
- Type of SAg, e.g. T cell, B cell.
- Host-immune status: during early stages of life with developing immune system there may be immune cell tolerance to SAg. In later stages with developed immune system produce specific immune response.

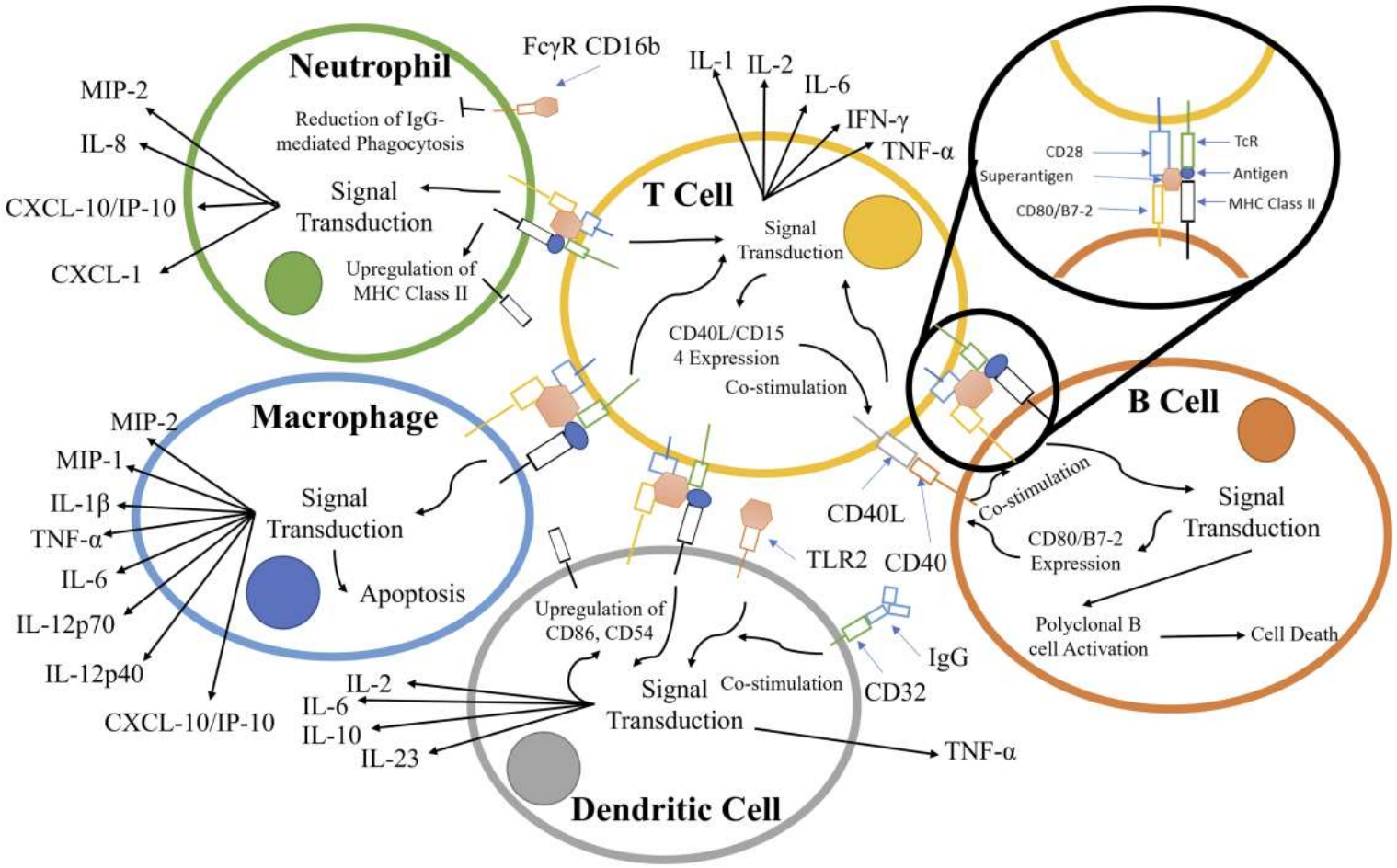


FIGURE 2 | Principal components involved in the superantigen activation of T-cells, B-cells, macrophages, and neutrophils. The interactions displayed are based on material from references (28–49). The responses contribute to and escalate the hyper-activation of T-cells and subsequent cytokine storm.

Emerg Infect Dis. 2020 Sep; 26(9): 2168–2171.
doi: 10.3201/eid2609.201806

PMCID: PMC7454081
PMID: 32568661

Persistence of Severe Acute Respiratory Syndrome Coronavirus 2 in Aerosol Suspensions

Alyssa C. Fears, William B. Klimstra, Paul Duprex, Amy Hartman, Scott C. Weaver, Kenneth S. Plante, Divya Mirchandani, Jessica Ann Plante, Patricia V. Aguilar, Diana Fernández, Aysegul Nalca, Aysegul Totura, David Dyer, Brian Kearney, Matthew Lackemeyer, J. Kyle Bohannon, Reed Johnson, Robert F. Garry, Doug S. Reed, [1] and Chad J. Roy[1]

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Conclusions

Go to: ▸

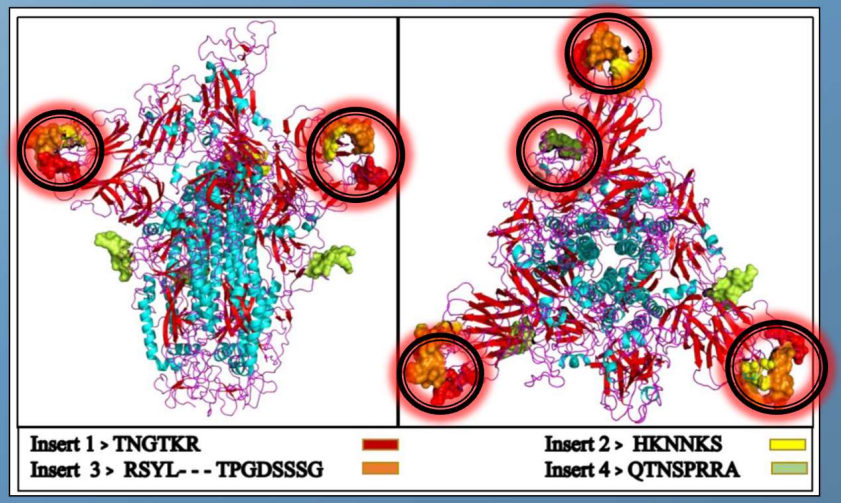
The comparison of short-term aerosol efficiencies of 3 coronaviruses showed SARS-CoV-2 approximates or exceeds the efficiency estimates of SARS-CoV and MERS-CoV. Some efficiency determinations for SARS-CoV-2 ranged to $-5.5^{\log 10}$ (Figure 1), a full log difference from MERS-CoV. The higher efficiencies across independent laboratories strengthens this observation. These data suggest that SARS-CoV-2 generally maintains infectivity at a respirable particle size over short distances, in contrast to either betacoronavirus. Aerosol suspension results suggest that SARS-CoV-2 persists longer than would be expected when generated as this size particle (2-μm mass median aerodynamic diameter). This finding is notable because decay and loss in the infectious fraction of airborne virus would be expected on the basis of prior susceptibility studies with other environmentally hardy viruses, such as monkeypox virus (5). A recent study (6) showing only a slight reduction of infectivity in aerosol suspensions with approximately similar particle sizes also suggested minimal effects on SARS-CoV-2 airborne degradation.

Collectively, these preliminary data suggest that SARS-CoV-2 is resilient in aerosol form and agree with conclusions reached in earlier studies of aerosol fitness (6). A clear limitation of the aerosol stability data is that we report only 1 measurement of the 16-h time point; future studies need to repeat these findings before any definitive conclusions are reached. Aerosol transmission of SARS-CoV-2 may be a more important exposure transmission pathway than previously considered (7). Our approach of quantitative measurement of infectivity of viral airborne efficiency augmented by assessment of virion morphology suggests that SARS-CoV-2 may be viable as an airborne pathogen. Humans produce aerosols continuously through normal respiration (8). Aerosol production increases during respiratory illnesses (9,10) and during louder-than-normal oration (11). A fraction of naturally generated aerosols falls within the size distribution used in our experimental studies (<5 μm), which leads us to conclude that SARS-CoV-2–infected persons may produce viral bioaerosols that remain infectious for long periods after production through human shedding and airborne transport. Accordingly, our study results provide a preliminary basis for broader recognition of the unique aerobiology of SARS-CoV-2, which might lead to tractable solutions and prevention interventions.

RSV – A "Tridemic" with Flu & COVID-19?

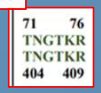
"HIV Inserts"

- 1st announced on 1/31/2020



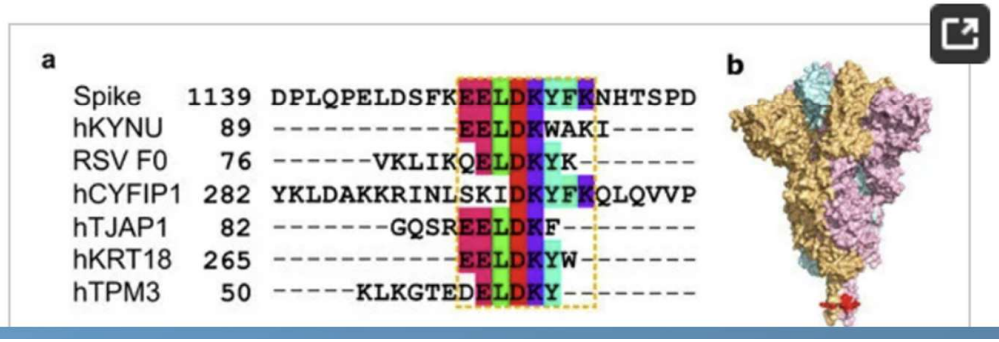
Potential autoimmunity resulting from molecular mimicry between SARS-CoV-2 Spike and human proteins

Motif	Protein	Species	RMSD	Z-Sco	EpiSco	PDB_cha
DPSKP	60S ribosomal protein L3	Human	0.1	-1.7	50	6LU8_B
LDKY	**Fusion Glycoprotein for RSV**	Human	0.12	-1.68	41.67	6EAE_F
DKYFK	Cytoplasmic interacting protein FMR1-1	Human	0.14	-1.66	35.71	4N78_A
LLQYG	Ankyrin 1	Human	0.2	-1.6	25	1N11_A
DPSKP	Alanine and proline-rich secreted protein apa pr	*Myco. tuberculosis*	0.21	-1.59	23.81	5ZXA_A
EELDK	Kynureninase	Human	0.22	-1.58	22.73	2HZP_A
EHVNN	Casein kinase 2 alpha isoform	Human	0.29	-1.51	17.24	2ZJW_A
LPDPS	BRCA1-A complex subunit BRE	Human	0.32	-1.48	15.62	6GVW_C
SFKEE	Small subunit processome component 20 homol	Human	0.32	-1.48	15.62	7MQA_SP
QLPPA	SMYD3 protein	Human	0.38	-1.42	13.16	5CCL_A
TQLPP	Thrombopoietin	Human	0.46	-1.34	10.87	1V7N_X
YSTGS	Argininosuccinate lyase	Human	0.48	-1.31	10.42	1K62_B
YSTGS	Argininosuccinate lyase	Human	0.48	-1.31	10.42	1K62_B
NLLLQ	DNA polymerase subunit gamma-1	Human	0.57	-1.22	8.77	5C51_A
GEVFN	Integrin beta 1	Human	0.63	-1.16	7.94	7NWL_B
FTVEKG	Pollen Allergen	*Phleum Pratense*	0.76	-1.03	7.89	1WHP_A
HAPAT	Activator of 90 kDa heat shock protein ATPase	Human	0.74	-1.05	6.76	7DME_A
IAARD	Talin	*mus musculus*	0.74	-1.05	6.76	6R9T_A
LPDPS	Semaphorin 7a	Human	0.84	-0.91	5.95	3NVQ_A
KNLRE	Toll-like receptor 8	Human	0.87	-0.92	5.75	6WML_D
GNCDV	Tryptophan-tRNA ligase	Human	0.91	-0.88	5.49	1O5T_A



RSV – A "Tridemic" with Flu & COVID-19?

intermolecular contacts are formed between charged-apolar, polar-apolar, and apolar-apolar residues (**Table S4**). In COVID-19, stronger antibody responses to the epitope containing the ELDKY motif have been recorded for severe (requiring hospitalization) vs. moderate cases, while fatal cases had a weaker response than surviving cases [**16**]. A synthetic epitope containing the ELDKY motif has also been shown to elicit antibody production following COVID-19 immunization [**70**]. Together with the 3D mimics identified here, these results suggest interesting possibilities for the ELDKY motif from the perspective of both protective immunity and an autoimmune response. First, while not an example of molecular mimicry but evolutionary conservation across beta-coronaviruses, prior exposure to an endemic cold-causing coronavirus (ex. HCoV-OC43) could result in the production of a broadly neutralizing antibody against an epitope containing the ELDKY motif that would be effective against SARS-CoV-2 infection, which could result in milder or asymptomatic infection. Further, a protective effect due to molecular mimicry is suggested by the 3D-mimic identified for the fusion F0 glycoprotein of RSV, a common virus that infects most children in the United States by the time they are 2 years old [**71**], where antibodies against the ELDKY-containing epitope in RSV may be effective in combatting SARS-CoV-2 infection. In contrast, the potential for an autoimmune response against this motif is suggested by its presence in both two human 3D- and AF-3D-mimics (**Figure 6**).



Collateral Damage – Hypoxia, Furin & Cancer

xii. Jean-Claude Perez & Luc Montagnier [who was awarded the 2008 Nobel Prize in Physiology or Medicine for his discovery of the HIV-1 virus in 1983] showed that the location of the PRRA insert within the SARS-CoV-2 genome ***was already an optimal cleavage site BEFORE this insertion***.[lxxv]

xiii. As oxygen levels decrease[lxxvi] [hypoxia] in the lungs, furin expression increases,[lxxvii] which can contribute to rapid declines in patient disposition as a snowball effect. This also plays a role in reducing the suppression of cancerous cells.[lxxviii]

xiv. Even mild hypoxia [~10% reduction] was enough to allow SARS-CoV-2 to pass through the Blood-Brain Barrier [BBB].[lxxix]

xv. The existence of many arginine residues within a small region that contains the FCS follows the pattern associated with the mechanism known as binding of cell penetrating peptides.[lxxx] The goal of building up a high cumulative positive charge[lxxxi] is to enhance cell affinity towards the virus.[lxxxii] SARS-CoV-2's ability to utilize the human sodium channel ENaC[lxxxiii] is unlikely to be fortuitous.

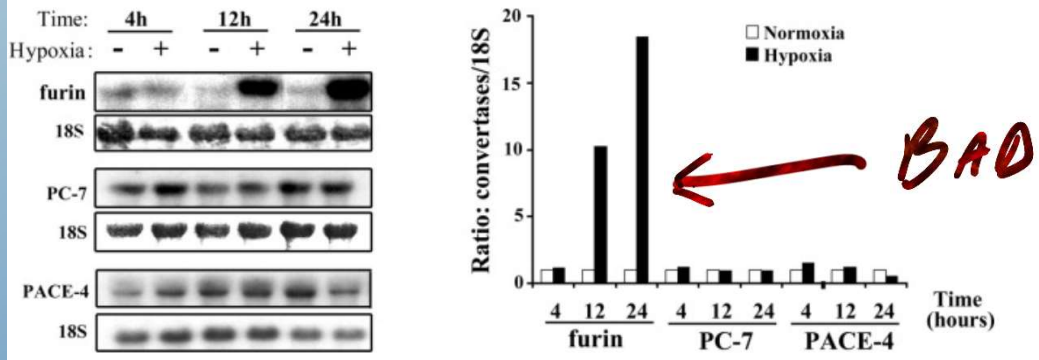


Fig. 1 **Expression of furin in hypoxic conditions.** Kinetics of *fur*, PACE-4, and PC7 mRNA accumulation. HepG2 cells were cultured in normoxia (21% O_2) or hypoxia (1% O_2) for various time periods as indicated. Total mRNA (5 µg/lane) was probed with specific furin, PACE-4, and PC7 rat riboprobes. A 18 S probe was used as an internal control. The autoradiogram and the densitometry ratio of each convertase/18 S (controls set to 1) are represented.

RESEARCH ARTICLE | APRIL 01 2006

HIV-1 Envelope Triggers Polyclonal Ig Class Switch Recombination through a CD40-Independent Mechanism Involving BAFF and C-Type Lectin Receptors[1] FREE

Bing He; Xugang Qiao; Per J. Klasse; April Chiu; Amy Chadburn; Daniel M. Knowles; John P. Moore; Andrea Cerutti

+ Author & Article Information

J Immunol (2006) 176 (7): 3931–3941.

https://doi.org/10.4049/jimmunol.176.7.3931 **Article history**

Paradoxically, hyperactivated B cells from HIV-1 viremic individuals respond poorly to T cell-dependent stimuli both in vivo and in vitro (4, 76). This humoral immunodeficiency is thought to stem from $CD4^+$ T cell depletion, GC disruption, CD40L down-regulation, and CD40 dysfunction (1, 66, 77). Protective T cell-dependent Ab responses could be further impaired by chronic activation of B cells by gp120 and gp120-induced BAFF. These T cell-independent stimuli would cause terminal differentiation and functional exhaustion, thereby lowering the number of B cell precursors available for the initiation of protective T cell-dependent Ab responses. In addition, nonspecific and low-affinity B cells polyclonally expanded by T cell-independent stimuli might compete with high-affinity B cells emerging from the T cell-dependent Ab pathway for survival factors and favorable anatomical niches. This competition would be particularly disadvantageous for B cells producing neutralizing Abs due to their physiologically low precursor frequency. Consistent with this point, early polyclonal hypergammaglobulinemia is inversely correlated with the initiation of virus-neutralizing Ab responses (78). In light of these considerations, administration of BAFF-blocking agents to individuals chronically infected by HIV-1 might not only attenuate the clinical manifestations of B cell hyperactivation disorders, but also improve the quality of Ab responses to HIV-1 infection, opportunistic pathogens, and vaccines.

Pre-exposure to mRNA-LNP inhibits adaptive immune responses and alters innate immune fitness in an inheritable fashion

Zhen Qin, Aurélie Bouteau, Christopher Herbst, Botond Z. Igyártó
doi: https://doi.org/10.1101/2022.03.16.484616
Now published in *PLOS Pathogens* doi: 10.1371/journal.ppat.1010830

ABSTRACT

Hundreds of millions of SARS-CoV-2 mRNA-LNP vaccine doses have already been administered to humans. However, we lack a comprehensive understanding of the immune effects of this platform. The mRNA-LNP-based SARS-CoV-2 vaccine is highly inflammatory, and its synthetic ionizable lipid component responsible for the induction of inflammation has a long *in vivo* half-life. Since chronic inflammation can lead to immune exhaustion and non-responsiveness, we sought to determine the effects of pre-exposure to the mRNA-LNP on adaptive immune responses and innate immune fitness. We found that pre-exposure to mRNA-LNPs or LNP alone led to long-term inhibition of the adaptive immune responses, which could be overcome using standard adjuvants. On the other hand, we report that after pre-exposure to mRNA-LNPs, the resistance of mice to heterologous infections with influenza virus increased while *Candida albicans* decreased. The diminished resistance to *Candida albicans* correlated with a general decrease in blood neutrophil percentages. Interestingly, mice pre-exposed to the mRNA-LNP platform can pass down the acquired immune traits to their offspring, providing better protection against influenza. In summary, the mRNA-LNP vaccine platform induces long-term unexpected immunological changes affecting both adaptive immune responses and heterologous protection against infections. Thus, our studies highlight the need for more research to determine this platform's true impact on human health.

They keep forgetting to mention the obvious answer…

New Results

This article has been withdrawn. Click here for details

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Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag

Prashant Pradhan, Ashutosh Kumar Pandey, Akhilesh Mishra, Parul Gupta, Praveen Kumar Tripathi, Manoj Balakrishnan Menon, James Gomes, Perumal Vivekanandan, Bishwajit Kundu

doi: https://doi.org/10.1101/2020.01.30.927871

Motifs	Virus Glycoprotein	Motif Alignment	HIV protein and Variable region	HIV Genome Source Country/ subtype	Number of Polar Residues	Total Charge	pI Value
Insert 1	2019- nCoV (GP) HIV1(GP120)	71 76 TNGTKR / TNGTKR 404 409	gp120-V4	Thailand* / CRF01_AE	5 / 5	2 / 2	11 / 11
Insert 2	2019- nCoV (GP) HIV1(GP120)	145 150 HKNNKS / HKNNKS 462 467	gp120-V5	Kenya* / G	6 / 6	2 / 2	10 / 10
Insert 3	2019- nCoV (GP) HIV1(GP120)	245 256 RSYL----TPGDSSSG / RTYL-NETPGAINSG 136 150	gp120-V1	India*/C	8 / 10	2 / 1	10.84 / 8.75
Insert 4	2019- nCoV (Polyp) HIV1(gag)	676 684 QTNS-------PRRA / QTANSAEAQRRNFRG PRRA 366 384	Gag	India*/C	6 / 12	2 / 4	12.00 / 12.30

Table 1: Aligned sequences of 2019-nCoV and gp120 protein of HIV-1 with their positions in primary sequence of protein. All the inserts have a high density of positively charged residues. The deleted fragments in insert 3 and 4 increase the positive charge to surface area ratio. *please see Supp. Table 1 for accession numbers

Furin Cleavage Site
+SEB-like SAg

Report | 1 September 2022 | OPEN ACCESS

Evolutionary remodelling of N-terminal domain loops fine-tunes SARS-CoV-2 spike

Diego Cantoni, Matthew J Murray, Mphatso D Kalemera, Samuel J Dicken, Lenka Stejskal, Georgina Brown, Spyros Lytras, Jonathon D Coey, James McKenna, Stephen Bridgett, David Simpson, Derek Fairley, Lucy G Thorne, Ann-Kathrin Reuschl, Calum Forrest, Maaroothen Ganeshalingham, Luke Muir, Machaela Palor, Lisa Jarvis, Brian Willett, Ultan F Power, Laura E McCoy, Clare Jolly, Greg J Towers, Katie J Doores, David L Robertson, Adrian J Shepherd, Matthew B Reeves, Connor G G Bamford, Joe Grove

thor information
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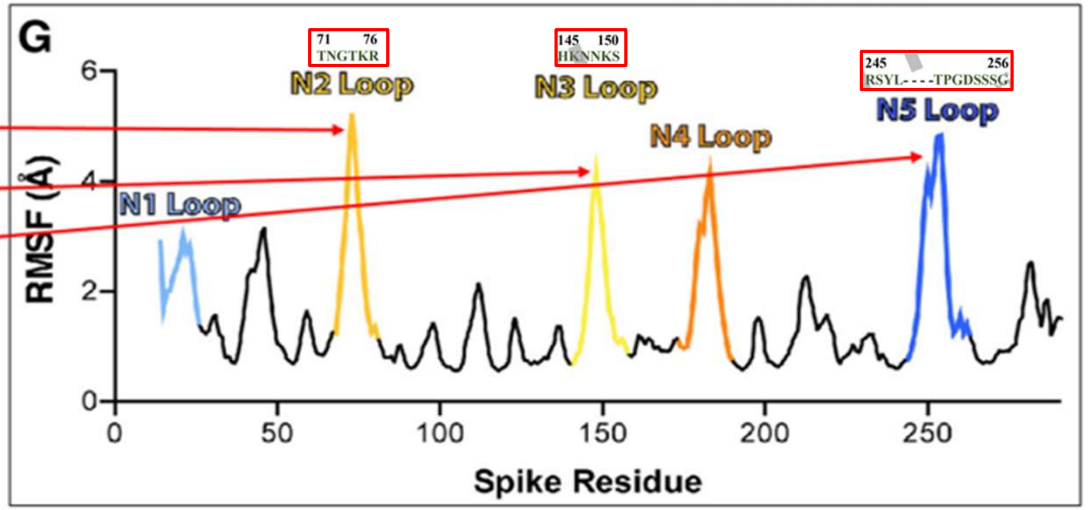
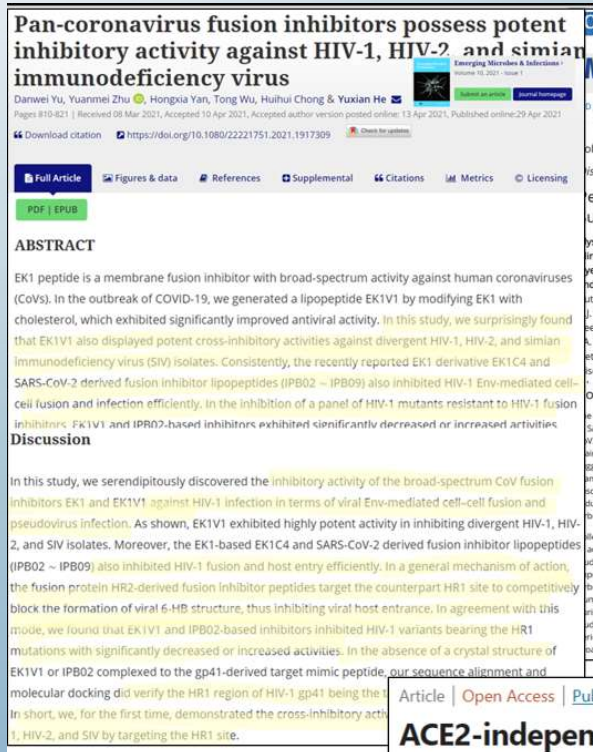


are absent (e.g. clade 5 has little/no N3 or N5 loops, clade 3 no N2 loop). This evokes a scenario in which NTD loops can be gained or lost through genetic insertion/deletion. Indeed, a recent study indicates that template switching by SARS-CoV-2 polymerase allows insertion of RNA sequence of viral and host origin at these sites (Peacock *et al*, 2021a, 2021b). However, our analyses suggest there is a potential limit on loop length. The N2, 3 and 5 loops of SARS-CoV-2 are amongst the longest observed thus far, suggestive of a functional ceiling on loop length. Notably, it is these loops that are becoming shorter in the majority of emergent variants.

Submucosal DCs are professional antigen-presenting cells with a potent capacity to capture luminal antigens by forming transepithelial dendrites (TEDs). Such antigen-bearings DCs migrate to the nearby lymph nodes, presenting foreign antigens to T cells and further initiating an effective adaptive immune response[20,21,22]. Paradoxically, submucosal DCs may sometimes be harnessed by viruses to help them overcome the epithelial barrier, serving as a "Trojan Horse" to evade antiviral immune responses and disseminate into the submucosal layer[23]. The infected DCs then migrate to the nearby lymph nodes and transmit the virus to T lymphocytes (productive or recessive infection)[24,25]. Typically, HIV is a DC-hijacking virus, and DCs might be conducive to its pathogenesis, a mechanism that promotes HIV transmission and infection of $CD4^+$ T cells and further dissemination into the body via the migration of T cells[26,27,28,29].

Collateral Damage



Pan-coronavirus fusion inhibitors possess potent inhibitory activity against HIV-1, HIV-2, and simian immunodeficiency virus

Danwei Yu, Yuanmei Zhu, Hongxia Yan, Tong Wu, Huihui Chong & Yuxian He

Pages 810-821 | Received 08 Mar 2021, Accepted 10 Apr 2021, Accepted author version posted online: 13 Apr 2021, Published online:29 Apr 2021

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ABSTRACT

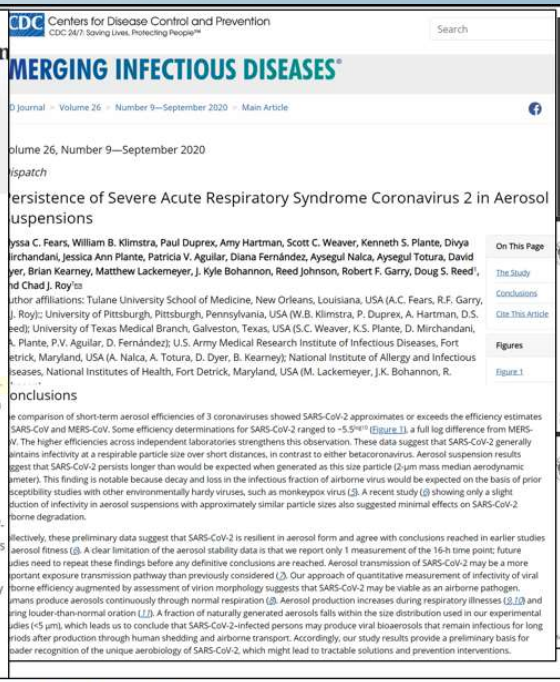
EK1 peptide is a membrane fusion inhibitor with broad-spectrum activity against human coronaviruses (CoVs). In the outbreak of COVID-19, we generated a lipopeptide EK1V1 by modifying EK1 with cholesterol, which exhibited significantly improved antiviral activity. In this study, we surprisingly found that EK1V1 also displayed potent cross-inhibitory activities against divergent HIV-1, HIV-2, and simian immunodeficiency virus (SIV) isolates. Consistently, the recently reported EK1 derivative EK1C4 and SARS-CoV-2 derived fusion inhibitor lipopeptides (IPB02 ~ IPB09) also inhibited HIV-1 Env-mediated cell–cell fusion and infection efficiently. In the inhibition of a panel of HIV-1 mutants resistant to HIV-1 fusion inhibitors, EK1V1 and IPB02-based inhibitors exhibited significantly decreased or increased activities

Discussion

In this study, we serendipitously discovered the inhibitory activity of the broad-spectrum CoV fusion inhibitors EK1 and EK1V1 against HIV-1 infection in terms of viral Env-mediated cell–cell fusion and pseudovirus infection. As shown, EK1V1 exhibited highly potent activity in inhibiting divergent HIV-1, HIV-2, and SIV isolates. Moreover, the EK1-based EK1C4 and SARS-CoV-2 derived fusion inhibitor lipopeptides (IPB02 ~ IPB09) also inhibited HIV-1 fusion and host entry efficiently. In a general mechanism of action, the fusion protein HR2-derived fusion inhibitor peptides target the counterpart HR1 site to competitively block the formation of viral 6-HB structure, thus inhibiting viral host entrance. In agreement with this mode, we found that EK1V1 and IPB02-based inhibitors inhibited HIV-1 variants bearing the HR1 mutations with significantly decreased or increased activities. In the absence of a crystal structure of EK1V1 or IPB02 complexed to the gp41-derived target mimic peptide, our sequence alignment and molecular docking did verify the HR1 region of HIV-1 gp41 being the t

In short, we, for the first time, demonstrated the cross-inhibitory acti

1, HIV-2, and SIV by targeting the HR1 site.



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MERGING INFECTIOUS DISEASES

Journal > Volume 26 > Number 9—September 2020 > Main Article

olume 26, Number 9—September 2020

ispatch

ersistence of Severe Acute Respiratory Syndrome Coronavirus 2 in Aerosol uspensions

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The Study

Conclusions

Cite This Article

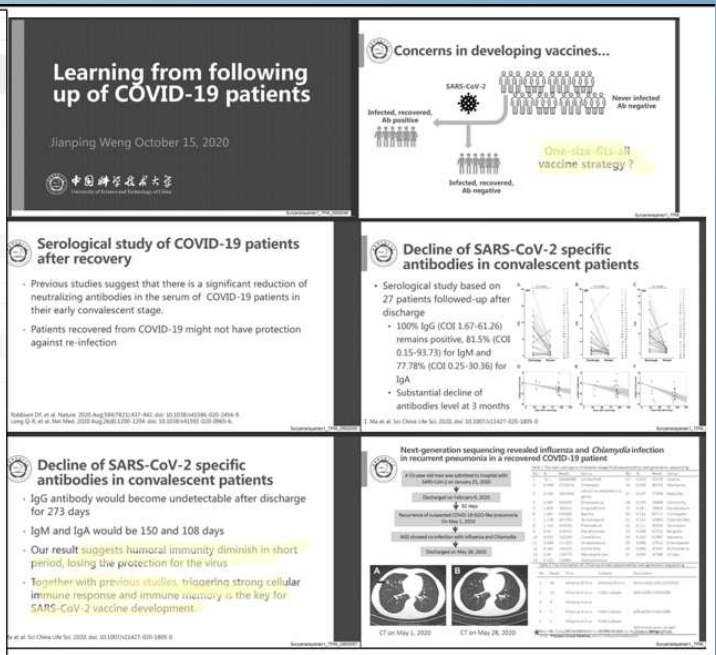
Figures

Figure 1

onclusions

e comparison of short-term aerosol efficiencies of 3 coronaviruses showed SARS-CoV-2 approximates or exceeds the efficiency estimates SARS-CoV and MERS-CoV. Some efficiency determinations for SARS-CoV-2 ranged to ~5.5[log10] (Figure 1), a full log difference from MERS-V. The higher efficiencies across independent laboratories strengthens this observation. These data suggest that SARS-CoV-2 generally ontains infectivity at a respirable particle size over short distances, in contrast to either betacoronavirus. Aerosol suspension results ggest that SARS-CoV-2 persists longer than would be expected when generated as this size particle (2-µm mass median aerodynamic ameter). This finding is notable because decay and loss in the infectious fraction of airborne virus would be expected on the basis of prior sceptibility studies with other environmentally hardy viruses, such as monkeypox virus (3). A recent study (4) showing only a slight duction of infectivity in aerosol suspensions with approximately similar particle sizes also suggested minimal effects on SARS-CoV-2 rborne degradation.

lectively, these preliminary data suggest that SARS-CoV-2 is resilient in aerosol form and agree with conclusions reached in earlier studies aerosol fitness (4). A clear limitation of the aerosol stability data is that we report only 1 measurement of the 16-h time point; future udies need to repeat these findings before any definitive conclusions are reached. Aerosol transmission of SARS-CoV-2 may be a more portant exposure transmission pathway than previously considered (7). Our approach of quantitative measurement of infectivity of viral rborne efficiency augmented by assessment of virion morphology suggests that SARS-CoV-2 may be viable as an airborne pathogen. umans produce aerosols continuously through normal respiration (8). Aerosol production increases during respiratory illnesses (9,10) and ering louder-than-normal oration (11). A fraction of naturally generated aerosols falls within the size distribution used in our experimental udies (<5 µm), which leads us to conclude that SARS-CoV-2–infected persons may produce viral bioaerosols that remain infectious for long riods after production through human shedding and airborne transport. Accordingly, our study results provide a preliminary basis for oader recognition of the unique aerobiology of SARS-CoV-2, which might lead to tractable solutions and prevention interventions.



Learning from following up of COVID-19 patients

Jianping Weng October 15, 2020

中国科学技术大学

Concerns in developing vaccines...

SARS-CoV-2

Infected, recovered, Ab positive

Never infected Ab negative

Infected, recovered, Ab negative

One-size-fits-all vaccine strategy ?

Serological study of COVID-19 patients after recovery

- Previous studies suggest that there is a significant reduction of neutralizing antibodies in the serum of COVID-19 patients in their early convalescent stage.
- Patients recovered from COVID-19 might not have protection against re-infection

Decline of SARS-CoV-2 specific antibodies in convalescent patients

- Serological study based on 27 patients followed-up after discharge
  - 100% IgG (COI 1.67-61.26) remains positive, 81.5% (COI 0.15-93.73) for IgM and 77.78% (COI 0.25-30.36) for IgA
  - Substantial decline of antibodies level at 3 months

Decline of SARS-CoV-2 specific antibodies in convalescent patients

- IgG antibody would become undetectable after discharge for 273 days
- IgM and IgA would be 150 and 108 days
- Our result suggests humoral immunity diminish in short period, losing the protection for the virus
- Together with previous studies, triggering strong cellular immune response and immune memory is the key for SARS-CoV-2 vaccine development.

Next-generation sequencing revealed influenza and *Chlamydia* infection in recurrent pneumonia in a recovered COVID-19 patient

CT on May 1, 2020

CT on May 28, 2020

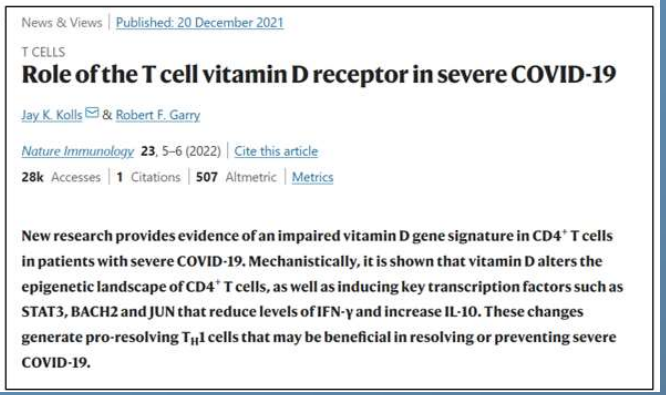
Article | Open Access | Published: 11 March 2022

ACE2-independent infection of T lymphocytes by SARS-CoV-2

Xu-Rui Shen, Rong Geng, Qian Li, Ying Chen, Shu-Fen Li, Qi Wang, Juan Min, Yong Yang, Bei Li, Ren-Di Jiang, Xi Wang, Xiao-Shuang Zheng, Yan Zhu, Jing-Kun Jia, Xing-Lou Yang, Mei-Qin Liu, Qian-Chun Gong, Yu-Lan Zhang, Zhen-Qiong Guan, Hui-Ling Li, Zhen-Hua Zheng, Zheng-Li Shi, Hui-Lan Zhang, Ke Peng & Peng Zhou

Signal Transduction and Targeted Therapy **7**, Article number: 83 (2022) | Cite this article

54k Accesses | **1** Citations | **3749** Altmetric | Metrics



News & Views | Published: 20 December 2021

T CELLS

Role of the T cell vitamin D receptor in severe COVID-19

Jay K. Kolls & Robert F. Garry

Nature Immunology **23**, 5–6 (2022) | Cite this article

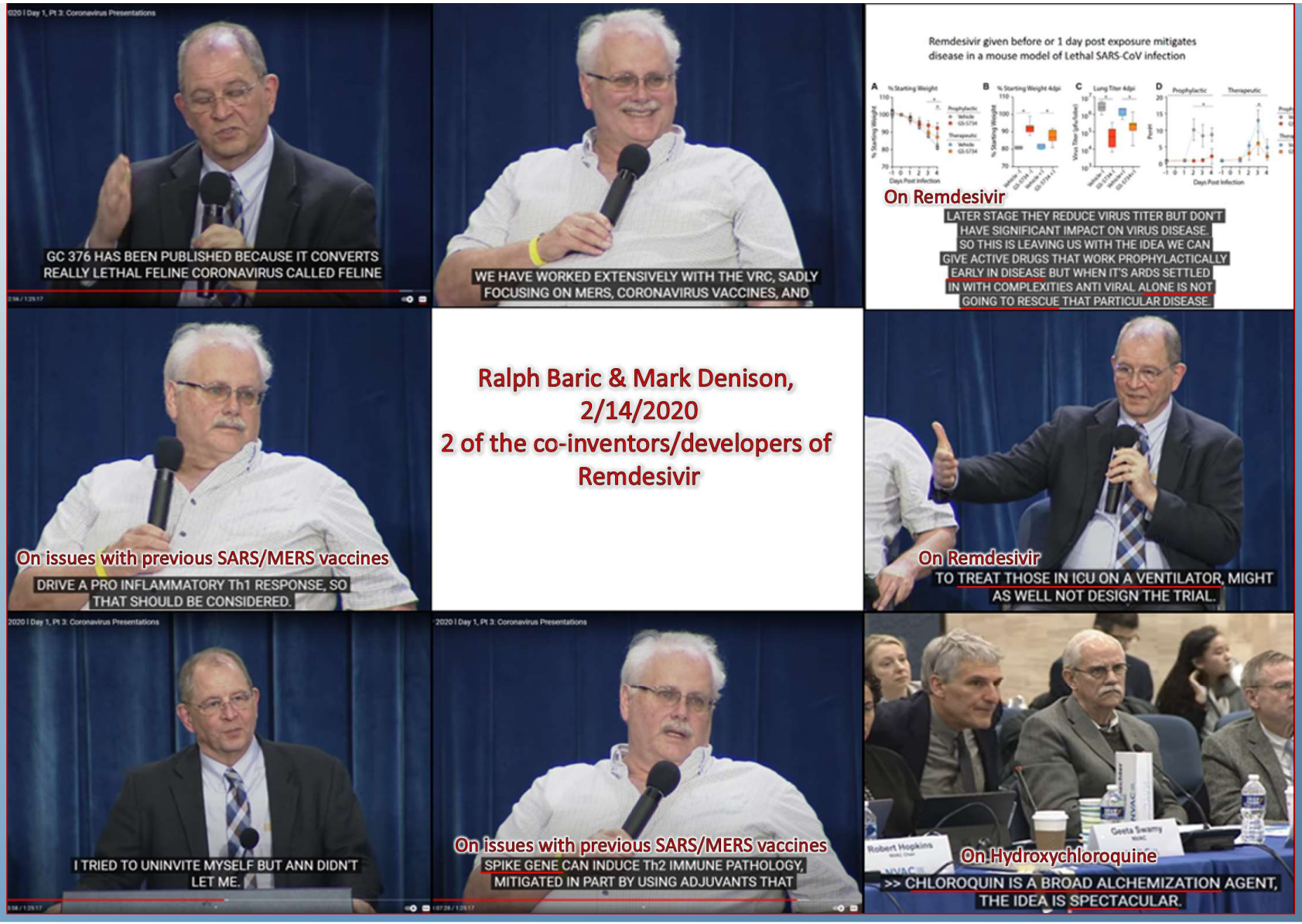
28k Accesses | **1** Citations | **507** Altmetric | Metrics

New research provides evidence of an impaired vitamin D gene signature in CD4$^+$ T cells in patients with severe COVID-19. Mechanistically, it is shown that vitamin D alters the epigenetic landscape of CD4$^+$ T cells, as well as inducing key transcription factors such as STAT3, BACH2 and JUN that reduce levels of IFN-γ and increase IL-10. These changes generate pro-resolving T_H1 cells that may be beneficial in resolving or preventing severe COVID-19.

Collateral Damage

% Excess Deaths (Non-COVID-19) by Age Group, Sex & Month (that week ended in)
England
Weeks Ending 27Mar20 - 18Nov22
Source Data:- Office for Health Improvement and Disparities

		0-24		25-49		50-64		65-74		75-84		85+	
Year	Month	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males
2020	3	-7.7%	-24.2%	-4.2%	2.5%	0.2%	-3.6%	-8.4%	-1.9%	-5.6%	-0.6%	-6.4%	-1.9%
2020	4	-5.2%	-20.8%	7.4%	0.4%	12.4%	16.1%	13.5%	18.2%	25.3%	25.9%	40.5%	36.1%
2020	5	-14.0%	-12.6%	-1.6%	-2.4%	3.8%	5.0%	-1.8%	-4.1%	-0.5%	-1.7%	10.9%	0.2%
2020	6	-22.4%	-21.0%	-7.9%	-7.4%	-5.8%	-2.4%	-3.3%	-8.0%	-8.6%	-10.6%	-11.3%	-13.2%
2020	7	-15.6%	-9.0%	0.9%	0.2%	-6.5%	2.6%	-3.1%	-4.8%	-7.0%	-7.4%	-9.2%	-13.9%
2020	8	-1.4%	-1.7%	2.5%	5.9%	2.4%	4.1%	-5.2%	-2.5%	-0.7%	-1.2%	-2.7%	-5.4%
2020	9	-0.7%	-15.8%	6.6%	6.2%	1.6%	5.8%	0.1%	2.4%	0.4%	-0.1%	-2.2%	-1.9%
2020	10	-22.4%	-12.0%	2.7%	7.6%	4.1%	3.9%	1.0%	-3.0%	-2.5%	-4.2%	-3.8%	-4.5%
2020	11	-10.1%	-6.5%	3.9%	5.1%	1.8%	6.1%	-7.2%	-2.9%	-8.1%	-7.0%	-7.2%	-10.7%
2020	12	-3.3%	-8.6%	5.5%	6.2%	-6.0%	3.1%	-10.3%	-11.0%	-14.9%	-16.1%	-14.9%	-17.7%
2021	1	-2.6%	-8.4%	0.4%	-11.0%	-10.4%	-6.3%	-17.0%	-16.4%	-19.9%	-23.0%	-22.8%	-26.7%
2021	2	-0.7%	4.6%	2.5%	-1.2%	-8.2%	-3.8%	-12.5%	-15.1%	-18.2%	-17.4%	-19.3%	-24.9%
2021	3	18.5%	-2.0%	-4.3%	5.3%	-7.7%	-3.3%	-13.3%	-14.2%	-18.1%	-20.7%	-22.3%	-25.2%
2021	4	-11.6%	-13.5%	2.7%	-4.9%	-5.7%	0.5%	-9.0%	-11.4%	-13.4%	-14.3%	-16.3%	-19.3%
2021	5	-7.8%	8.4%	2.6%	1.3%	-5.6%	3.2%	-10.1%	-7.4%	-8.8%	-7.4%	-10.0%	-10.4%
2021	6	10.1%	3.5%	-2.1%	4.9%	-0.8%	6.6%	-4.6%	-5.1%	-5.1%	-3.3%	-5.6%	-7.2%
2021	7	-8.4%	0.7%	2.4%	3.4%	7.1%	7.1%	0.2%	2.1%	0.6%	1.7%	-0.2%	-2.0%
2021	8	-8.9%	-4.4%	-0.2%	3.3%	6.0%	6.7%	5.4%	1.3%	2.6%	-0.1%	3.9%	1.2%
2021	9	-5.6%	-6.7%	6.8%	5.9%	8.4%	4.8%	7.9%	6.6%	6.0%	4.4%	4.1%	1.1%
2021	10	2.6%	5.9%	1.2%	12.0%	9.9%	10.2%	3.6%	3.3%	0.1%	0.9%	1.2%	-0.1%
2021	11	12.9%	9.8%	1.2%	3.4%	2.3%	9.2%	6.4%	6.4%	4.5%	0.7%	5.7%	0.1%
2021	12	3.3%	5.6%	-4.1%	2.9%	6.8%	6.9%	2.0%	1.9%	0.7%	-3.8%	0.4%	-3.7%
2022	1	-9.8%	-10.2%	-2.6%	-9.8%	-8.3%	-4.2%	-14.2%	-12.3%	-14.7%	-17.4%	-20.8%	-23.4%
2022	2	3.3%	14.8%	-2.9%	-4.4%	-3.7%	3.6%	-8.1%	-5.1%	-11.5%	-13.8%	-16.0%	-18.5%
2022	3	11.0%	8.3%	-6.2%	4.7%	-8.3%	3.4%	-7.4%	-6.2%	-9.2%	-12.0%	-14.7%	-15.2%
2022	4	-27.4%	-1.4%	-5.9%	-5.1%	-2.0%	-3.9%	-9.0%	-7.2%	-8.9%	-10.8%	-9.5%	-12.1%
2022	5	-9.3%	6.4%	5.4%	-4.8%	2.6%	8.9%	0.0%	1.7%	1.6%	2.3%	3.2%	1.4%
2022	6	14.5%	13.8%	14.8%	7.2%	17.4%	15.8%	8.1%	8.4%	9.5%	6.6%	7.9%	8.4%
2022	7	8.0%	5.5%	6.6%	8.5%	4.6%	11.0%	4.7%	5.5%	7.1%	2.8%	8.2%	6.9%
2022	8	9.7%	9.7%	-4.0%	10.7%	17.1%	12.5%	0.3%	7.2%	4.5%	5.6%	10.8%	4.1%
2022	9	-1.7%	11.2%	9.9%	8.2%	13.9%	17.0%	7.9%	5.2%	5.7%	6.6%	7.6%	7.5%
2022	10	3.9%	5.4%	16.9%	9.2%	11.8%	10.1%	7.4%	6.3%	6.4%	6.4%	9.1%	7.4%
2022	11	9.6%	2.2%	6.2%	11.3%	8.6%	14.3%	10.3%	9.0%	3.9%	1.8%	7.9%	3.9%


GC 376 HAS BEEN PUBLISHED BECAUSE IT CONVERTS REALLY LETHAL FELINE CORONAVIRUS CALLED FELINE
WE HAVE WORKED EXTENSIVELY WITH THE VRC, SADLY FOCUSING ON MERS, CORONAVIRUS VACCINES, AND
Remdesivir given before or 1 day post exposure mitigates disease in a mouse model of Lethal SARS-CoV infection
On Remdesivir
LATER STAGE THEY REDUCE VIRUS TITER BUT DON'T HAVE SIGNIFICANT IMPACT ON VIRUS DISEASE. SO THIS IS LEAVING US WITH THE IDEA WE CAN GIVE ACTIVE DRUGS THAT WORK PROPHYLACTICALLY EARLY IN DISEASE BUT WHEN IT'S ARDS SETTLED IN WITH COMPLEXITIES ANTI VIRAL ALONE IS NOT GOING TO RESCUE THAT PARTICULAR DISEASE.
On issues with previous SARS/MERS vaccines
DRIVE A PRO INFLAMMATORY Th1 RESPONSE, SO THAT SHOULD BE CONSIDERED.
Ralph Baric & Mark Denison,
2/14/2020
2 of the co-inventors/developers of
Remdesivir
On Remdesivir
TO TREAT THOSE IN ICU ON A VENTILATOR, MIGHT AS WELL NOT DESIGN THE TRIAL.
I TRIED TO UNINVITE MYSELF BUT ANN DIDN'T LET ME.
On issues with previous SARS/MERS vaccines
SPIKE GENE CAN INDUCE Th2 IMMUNE PATHOLOGY, MITIGATED IN PART BY USING ADJUVANTS THAT
On Hydroxychloroquine
>> CHLOROQUIN IS A BROAD ALCHEMIZATION AGENT, THE IDEA IS SPECTACULAR.

The EcoHealth Alliance DEFUSE Proposal

DRASTIC RESEARCH

Project DEFUSE

DARPA - PREEMPT (HR001118S0017)

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

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(f) 212-380-4465

Identifying Number: HR001118S0017-PREEMPT-PA-001
Award Instrument Requested: Grant
Places and Periods of Performance: 12/1/18 - 5/31/22; Palo Alto, CA; Kunming and Wuhan, China; Chapel Hill, NC, New York, NY; Singapore; Madison, WI
Total funds requested: $14,209,245
Proposal validity period: 6 months
Date proposal submitted: 3/27/18

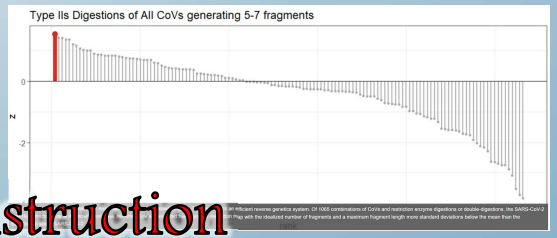
Documents made available by an anonymous source

Elements Of the DEFUSE proposal found within SARS-CoV-2

11. THE PROPOSAL SET A CLEAR PATHWAY FOR CHIMERIC VIRUS CONSTRUCTION

The use of known backbones is specified in the proposal:

> "*Synthesis of Chimeric Novel SARSr-CoV QS: We will commercially synthesize[2] SARSr-CoV S glycoprotein genes, designed for insertion into SHC014 or WIV16 molecular clone backbones (88% and 97% S-protein identity to epidemic SARS-Urbani). These are BSL-3, not select agents or subject to P3CO (they use bat SARSr-CoV backbones which are exempt) and are pathogenic to hACE2 transgenic mice*" (D1, p.8)

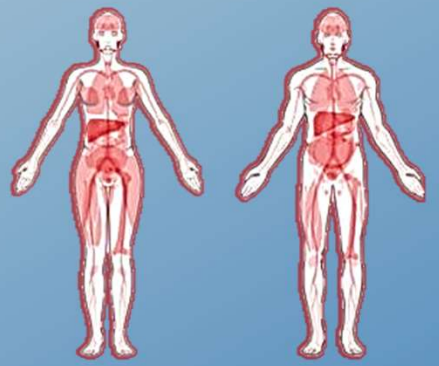


Chimaeric construction

16. THE PROPOSAL INCLUDES THE INTRODUCTION OF "HUMAN-SPECIFIC CLEAVAGE SITES"

Human protease-specific site insertion was proposed. The proposal does not specify exactly which protease, but does discuss Furin in the preceding text.

> "*We will analyze all SARSr-CoV S gene sequences for appropriately conserved proteolytic cleavage sites in S2 and for the presence of potential Furin cleavage sites[74,75]*".
>
> *SARSr-CoV S with mismatches in proteolytic cleavage sites can be activated by exogenous Trypsin or Cathepsin L.*
>
> *Where clear mismatches occur, we will introduce appropriate human-specific cleavage sites and evaluate growth potential in Vero cells and HAE cultures.*"
> (D1, p.13)



Human cleavage sites

18. THE PROPOSAL PLANNED TO RESEARCH ALTERNATE RECEPTORS TO ACE2

> "*To evaluate this, we will sequentially introduce clade 2 disrupting residues of SARS-CoV and SHCO14 and evaluate virus growth in Vero cells, non-permissive cells ectopically expressing DC-SIGN, and in human monocytes and macrophages anticipating reduced virus growth efficiency.*" (D1, p.13)

We note that while SARS-CoV was documented to use DC-SIGN as an attachment receptor (Marzi *et al.* 2004), L-SIGN and DC-SIGN act as entry receptors for SARS-CoV-2 (Amraei *et al.* 2020; Thépaut *et al.* 2021).

DC-SIGN

19. THE PROPOSAL PLANNED TO INTRODUCE "KEY RBD RESIDUES" INTO LOW RISK STRAINS TO TEST PATHOGENICITY IN HUMAN AIRWAY CELLS AND IN HACE2 MICE

> "*Low abundance micro-variations:*
> *We will structurally model and identify highly variable residue changes in the SARSr-CoV S RBD, use commercial gene blocks to introduce these changes singly and in combination into the S glycoprotein gene of the low risk, parental strain and test ACE2 receptor usage, growth in HAE and in-vivo pathogenesis*".
> (D1, p.13)

High ACE2 affinity

18 U.S. Code § 175 - Prohibitions with respect to biological weapons

U.S. Code | Notes

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(a) In General.—
Whoever knowingly develops, produces, stockpiles, transfers, acquires, retains, or possesses any biological agent, toxin, or delivery system for use as a weapon, or knowingly assists a foreign state or any organization to do so, or attempts, threatens, or conspires to do the same, shall be fined under this title or imprisoned for life or any term of years, or both. There is extraterritorial Federal jurisdiction over an offense under this section committed by or against a national of the United States.

(b) Additional Offense.—
Whoever knowingly possesses any biological agent, toxin, or delivery system of a type or in a quantity that, under the circumstances, is not reasonably justified by a prophylactic, protective, bona fide research, or other peaceful purpose, shall be fined under this title, imprisoned not more than 10 years, or both. In this subsection, the terms "biological agent" and "toxin" do not encompass any biological agent or toxin that is in its naturally occurring environment, if the biological agent or toxin has not been cultivated, collected, or otherwise extracted from its natural source.

(c) Definition.—
For purposes of this section, the term "for use as a weapon" includes the development, production, transfer, acquisition, retention, or possession of any biological agent, toxin, or delivery system for other than prophylactic, protective, bona fide research, or other peaceful purposes.

(Added Pub. L. 101–298, § 3(a), May 22, 1990, 104 Stat. 201; amended Pub. L. 104–132, title V, § 511(b)(1), Apr. 24, 1996, 110 Stat. 1284; Pub. L. 107–56, title VIII, § 817(1), Oct. 26, 2001, 115 Stat. 385; Pub. L. 107–188, title II, § 231(c)(1), June 12, 2002, 116 Stat. 661.)

In Summary …

- Scientific censorship
- What was censored, and why
- Ties to historical bioweapons research
- Implications for Long COVID/PASC

A COVID-19 Origin Project: The arc of Inquiry bends towards Enlightenment

A DRASTIC collection of references related to investigating the origin of SARS-CoV-2

Tab	Collections	Sources	Description	Last Upd.
1	Main / Censorship	1,928	A list of references regarding aspects of the SARS-CoV-2 origin debate, color-coded by the authors' perspective	11/29/2022
2	Links & Addtl Resources	-	Links to other recommended resources, FOIA repositories and other information	9/11/2022
3	Essential Key Articles	25	My list of the 25 most influential/important articles & findings related to the search for SARS-CoV-2's origin	9/11/2022
4	Key References	150	Significant articles, news stories & documents culled from the full list	1/12/2022
5	Key Videos	53	Significant episodes, livestreams, TV specials, etc.	9/11/2022
6	Pandemic Prep & Coverage	60	Key Videos on Preparedness, Early News Coverage & US Narrative Distractions	9/11/2022
7	Research Path to SARS-CoV-2	96	A list of key research articles which	11/29/2022
8	Evidence of Unnatural Origin	194	A [rough] working list of suspicious elements within, or characteristics of, the SARS-CoV-2 virus & the pandemic	11/29/2022
9	Significant Elements of the Spike	-	A breakdown of most of the siginficant features of the S1 portion of the SARS-CoV-2 spike protein	11/29/2022
10	Mutations within the RBD	-	A rough breakdown of the number & location of mutations within the S1 portion of the SARS-CoV-2 spike protein	11/29/2022
11	Article Breakdown by Month	-	A chart showing the volume of origin-related articles published by month, by bias of the author [s]	11/29/2022
12	Censorship Stats	-	Data from ~1,200 articles, categorized by the authors' perspectives/bias	4/2/2022
13	Cumulative bias ratings	-	Measuring the natural-lab leak leanings of major publishers, newspapers, etc.	11/2/2022
14	6 Narrative Waves	115	The 6 clear 'waves' of false-narrative protection, led by Fauci, the Proximals & the Lanceteers	4/2/2022
15	7th Narrative Wave	32	Chronicling 32 pro-zoonosis articles published over a few days in late July 2022 to support the market narrative	9/11/2022
16	Censorship Charts	-	6 images/graphics depicting various censorship figures/narrative methods	11/29/2022
17	Censorship Charts 2	-	6 more images/graphics depicting various censorship figures/narrative methods	11/29/2022
18	Proximal Origin Biblio. Edits	-	I list the references from the first & final drafts of "Proximal Origin of SARS-CoV-2" in parallel	11/29/2022
19	Censorship Timeline	48	[This page also available as a PDF with active links on Research Gate]	1/15/2022
20	Censorship [prev]	450	The original iteration of my censorship calculations from May 2021 [also found within this compiled PDF]	8/8/2021
21	Censorship-Top 6 [1st]	-	My original censorship analysis from May 15th, 2021	8/22/2021
22	Censorship-Top 6 [2nd]	117	All articles from the Main tab, for all of the Top 6 journals [click to read my article on this topic]	3/22/2022
23	Censorship - Top 6 [3rd]	262	All articles from the Main tab, for all of the Top 6 journals [Main & Subordinate Journals, & Select Others]	9/11/2022
24	Primary Sources	125	All FOIA collections, other government documents & similar primary source materials	6/1/2022
25	Key FOIA Timeline	34	[This page also available as a PDF with active links on Research Gate]	1/16/2022
26	Baric FOIA Guide	-	An overview of the contents & structure of US Right-to-Know's 83K pages of Ralph Baric FOIA documents	5/22/2021
27	Wuhan Outbreak	79	A list of references used for my Wuhan epidemiological analysis [the paper in progress now has 180]	7/2/2022
28	Most-Read Origin Articles	50	A list of the 50 most-read articles on the origin of the SARS-CoV-2 virus [all articles for which such data is public]	11/29/2022
29	Most-Watched Origin Videos	24	A list of the 24 most-viewed videos on the origin of the SARS-CoV-2 virus	9/11/2022
30	First lab-leaning articles	14	A list of the absolute earliest	11/29/2022
31	DRASTIC	77	Key written works by DRASTIC	11/29/2022
32	DRASTIC Findings	54	A list of DRASTIC's major discoveries, projects & achievements	5/14/2022
33	DRASTIC in the News	85	A list of articles discussing DRASTIC and our findings	11/29/2022
34	Lab Leak-Leaning	289	Written works by other lab-leak hypothesis proponents	4/2/2022
35	Natural Origin-Leaning	291	Proponents of a Zoonotic [Natural] Emergence of SARS-CoV-2	4/2/2022
36	Daszak EHA works	193	Articles published by Daszak withEH Alliance, looking at author relationships	5/27/2021
37	Daszak EHA-sorted	193	Articles published by Daszak with EH Alliance, looking at author relationships - sorted and counted	5/27/2021
38	HIV/SARS	504	Articles related to the FCS/HIV Inserts, as described in The Myth of the Blind Watchmaker	11/29/2022
39	HIV/SARS - Vaccine Research	96	HIV & Coronavirus Vaccine Research & Development	9/11/2022
40	HIV/SARS - Fusion Inhibitors	66	Class I Viral Fusion Peptide Inhibitor Research	9/11/2022
41	HIV/SARS - Chinese Research	84	Chinese Coronavirus Research	9/11/2022
42	Gain-of Function	404	Articles related to Gain-of-Function [GOF] research & the debates over its risks	1/15/2022
43	GOF Sorted	404	Articles related to Gain-of-Function [GOF] research & the debates over its risks, sorted between the two categories	1/16/2022
44	EHA Fed Contracts	-	A list of US federal contracts with EcoHealth Alliance under Peter Daszak [unhide for full 2002-2021]	8/22/2021
45	EHA Fed Grants	-	A list of US federal grants awarded to EcoHealth Alliance under Peter Daszak [unhide for full 2002-2021]	8/22/2021
46	NIH Grant Budget	-	The full grant budget for the National Institutes of Health, 2011-2020	8/22/2021
47	Global Funding	-	The Largest Global Public & Private Funders of Biomedical Research, 2013, By Share of World Total	1/16/2022
48	Top Articles (H-I)	-	COVID-19 articles amongst the Top 250 academic articles, by H-Index score	8/22/2021
49	Top Articles (Alt)	-	COVID-19 articles amongst the top 100 academic articles, by Altmetric score	8/22/2021

Tab 1 total References

1928

Sources by Type & Perspective	Since 20	Pre 20
US Gov Publications	36	21
DRASTIC	115	0
Paris Group, etc.	47	0
Lab Leak Supporting	120	0
Lab Leak Leaning	254	0
Neutral/Unbiased	708	150
Natural-Origin Leaning	97	12
Zoonosis Activists	266	102
	1643	285

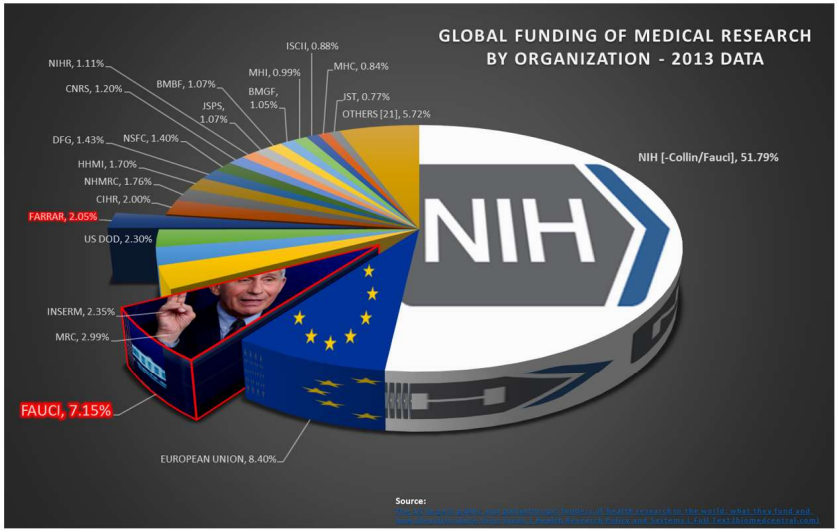
Complete List
Evidence of Unnatural Origin
Scientific Censorship
FOIA
Wuhan Outbreak
DRASTIC & Lab-Leaning
Natural-Origin Leaning
HIV-SARS Homology/Links
Gain-of-Function Research
Grant Funding of BioMed Research
Top Articles [Altmetric]

Updates			
Date	#	Refs	Tabs
5/14/2021	-	520	5
7/1/2021	1	598	7
8/13/2021	2	703	9
9/15/2021	3	798	9
10/14/2021	4	925	14
1/15/2022	5	1,036	24
5/14/2022	6	1,368	31
9/11/2022	7	1,684	40
11/29/2022	8	1,905	49

My other origin resources:

Prometheus Shrugged: Censorship & the Legacy of COVID-19 - Collects 173 pages of key emails from 94,00 6/17/2021
Manufactured Consensus: A chronology of sci. censorship within the context of the early COVID-19 pande 5/22/2021
The Ties that Bind: A Timeline of Key FOIA requests & other Primary Source Documents in the Investigati 1/9/2022
Linked Topical Bibliography - Wuhan's House of Cards: Proponents of COVID-19's natural-origin continue 2/28/2022
DRASTIC - An Analysis of Project DEFUSE 9/20/2021

https://prometheusshrugged.substack.com
https://drasticscience.com



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