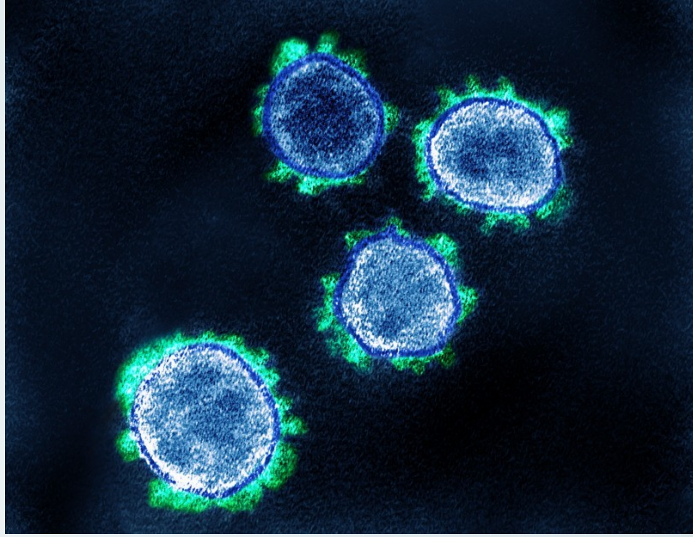
Pandemia da COVID-19
luci ed ombre

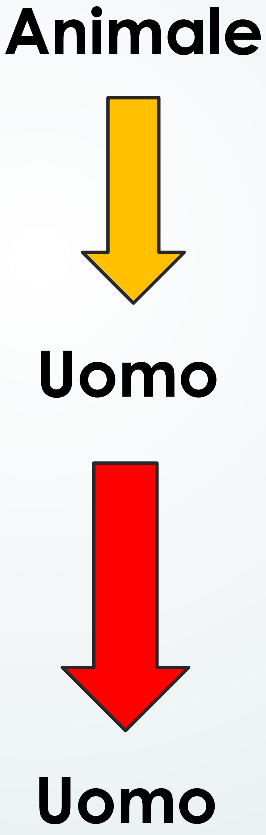
Prof. Pietro Castellino

Dipartimento di Medicina Clinica e Sperimentale

Università di Catania

Infezioni Virali :
il salto di specie





Animale

Uomo

Uomo

Possibile

Virus Ebola

Altissima Infettività
Altissima Letalità

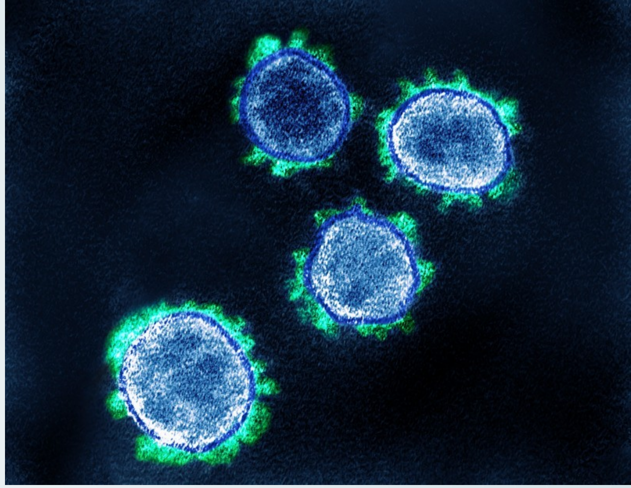
Trasmissione cutanea

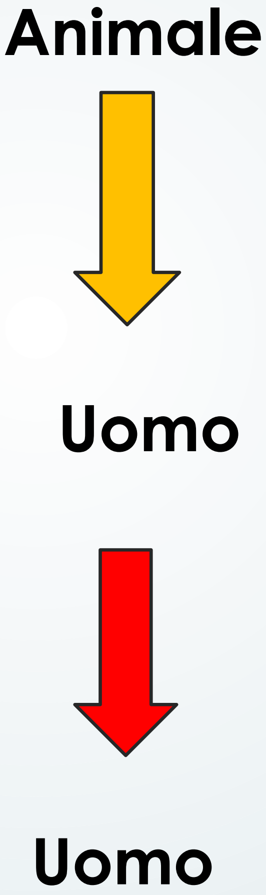
Molto Raro
SARS, MERS, Influenza Suina

Bassa Infettività
Alta Letalità

Trasmissione respiratoria
Scarsa diffusione

SARS COV 2:
il salto di specie





Animale

Uomo

Uomo

Come è Avvenuto?

Virus influenzali H5 e H7

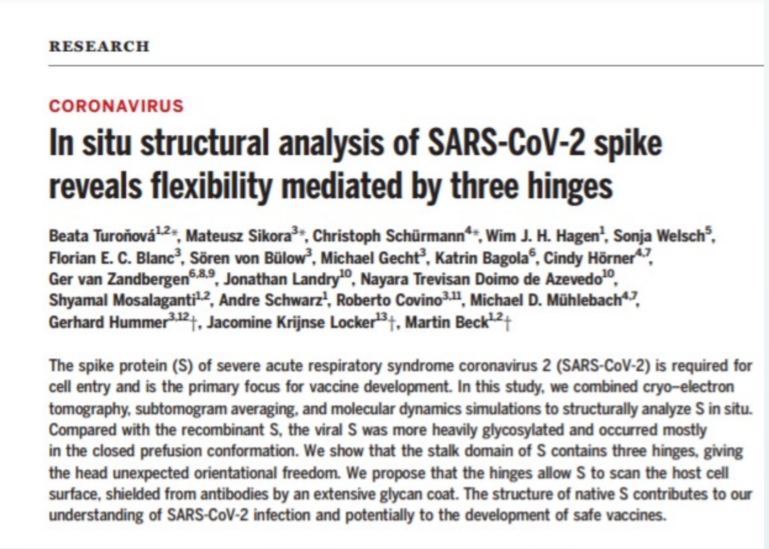
Passaggio interumano
mai riportato

Diffusione rapidissima

Alta Infettività
Bassa Letalità

Trasmissione
Respiratoria / altro?

Il recettore



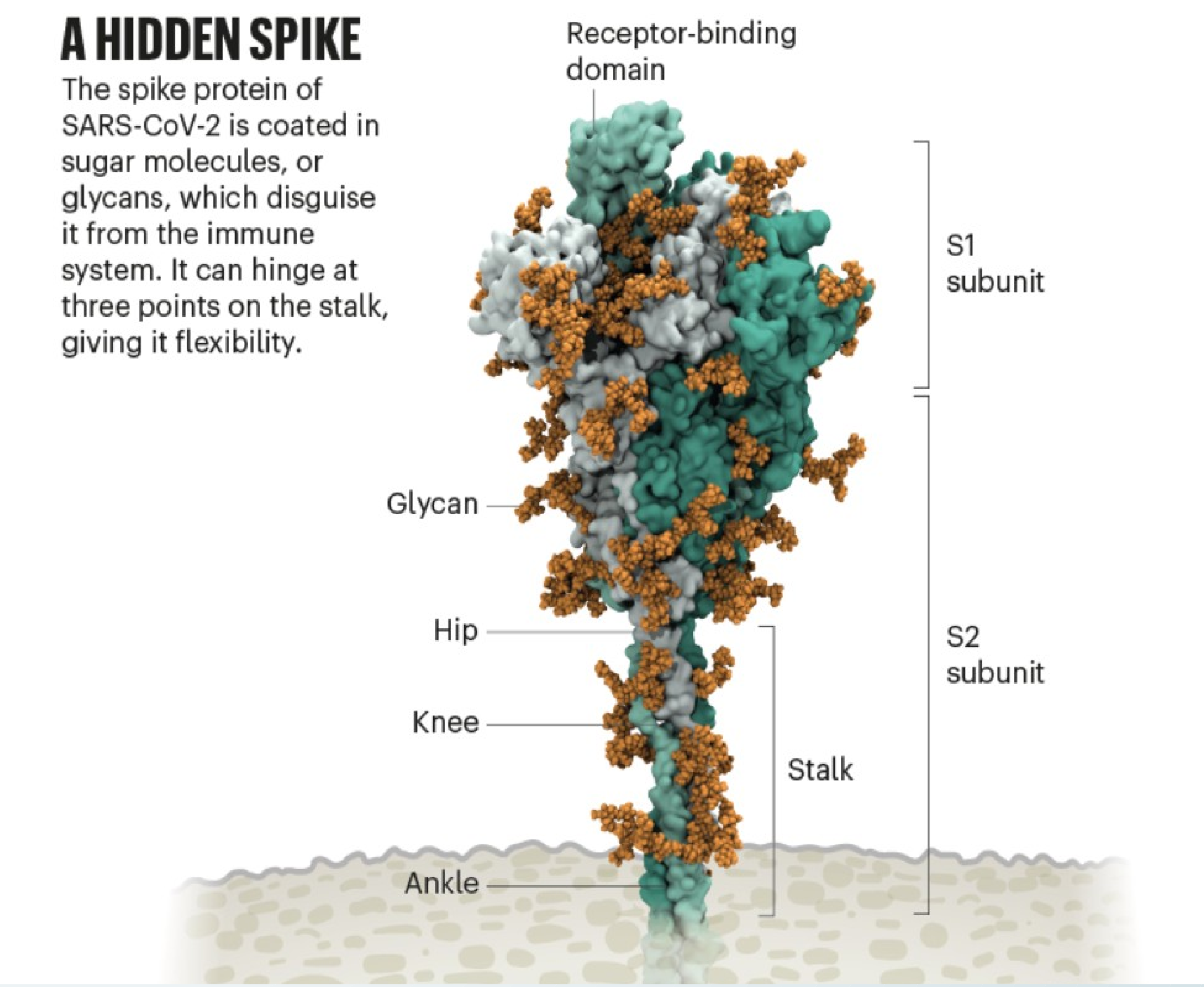
RESEARCH

CORONAVIRUS

In situ structural analysis of SARS-CoV-2 spike reveals flexibility mediated by three hinges

Beata Turoňová[1,2]*, Mateusz Sikora[3]*, Christoph Schürmann[4]*, Wim J. H. Hagen[1], Sonja Welsch[5], Florian E. C. Blanc[3], Sören von Bülow[3], Michael Gecht[3], Katrin Bagola[6], Cindy Hörner[4,7], Ger van Zandbergen[6,8,9], Jonathan Landry[10], Nayara Trevisan Doimo de Azevedo[10], Shyamal Mosalaganti[1,2], Andre Schwarz[1], Roberto Covino[3,11], Michael D. Mühlebach[4,7], Gerhard Hummer[3,12]†, Jacomine Krijnse Locker[13]†, Martin Beck[1,2]†

The spike protein (S) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is required for cell entry and is the primary focus for vaccine development. In this study, we combined cryo–electron tomography, subtomogram averaging, and molecular dynamics simulations to structurally analyze S in situ. Compared with the recombinant S, the viral S was more heavily glycosylated and occurred mostly in the closed prefusion conformation. We show that the stalk domain of S contains three hinges, giving the head unexpected orientational freedom. We propose that the hinges allow S to scan the host cell surface, shielded from antibodies by an extensive glycan coat. The structure of native S contributes to our understanding of SARS-CoV-2 infection and potentially to the development of safe vaccines.



A HIDDEN SPIKE

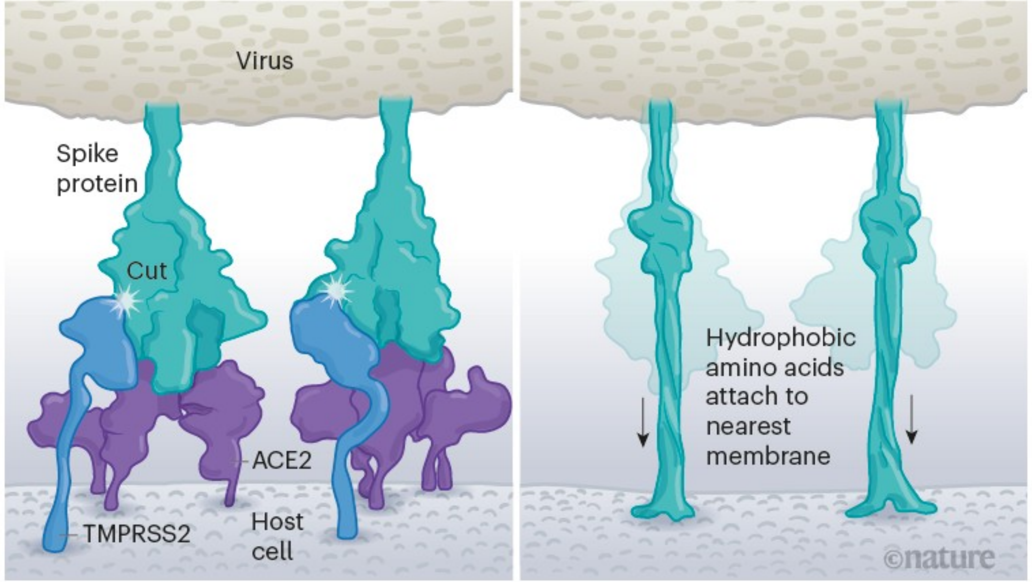
The spike protein of SARS-CoV-2 is coated in sugar molecules, or glycans, which disguise it from the immune system. It can hinge at three points on the stalk, giving it flexibility.

La subunità S1 viene separata dalla S2 da una proteasi di membrana TMPRSS2

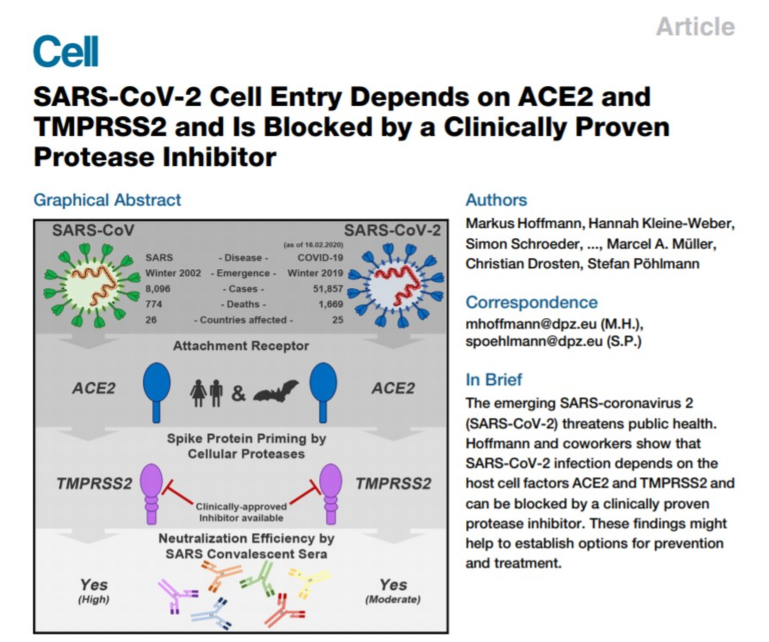
La sub unità S2 permette la fusione
Delle membrane virali e dell’ ospite

VIRAL ENTRY UP CLOSE

Virus and host-cell membranes fuse after the TMPRSS2 enzyme cuts a SARS-CoV-2 spike protein. This exposes hydrophobic amino acids in the spike that rapidly embed themselves into the nearest membrane — that of the host cell.


Virus
Spike protein
Cut
ACE2
TMPRSS2
Host cell
Hydrophobic amino acids attach to nearest membrane
©nature

Source: Janet Iwasa, Univ. Utah; Graphic: Nik Spencer/*Nature*



Cell

Article

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

Graphical Abstract

SARS-CoV
SARS-CoV-2
(as of 16.02.2020)
SARS - Disease - COVID-19
Winter 2002 - Emergence - Winter 2019
8,096 - Cases - 51,857
774 - Deaths - 1,669
26 - Countries affected - 25
Attachment Receptor
ACE2
&
ACE2
Spike Protein Priming by Cellular Proteases
TMPRSS2
Clinically-approved Inhibitor available
TMPRSS2
Neutralization Efficiency by SARS Convalescent Sera
Yes (High)
Yes (Moderate)

Authors

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

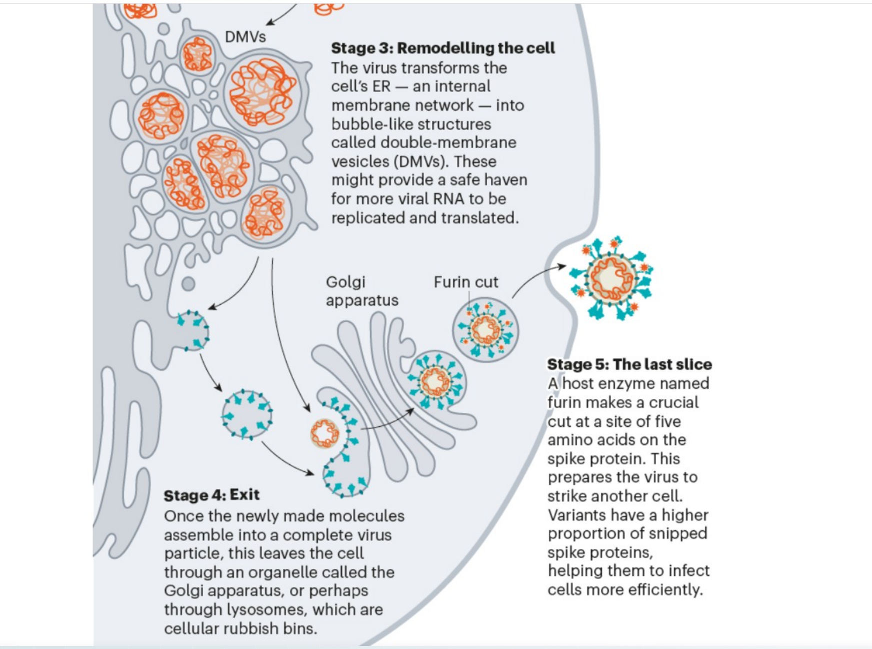
Correspondence

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

In Brief

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

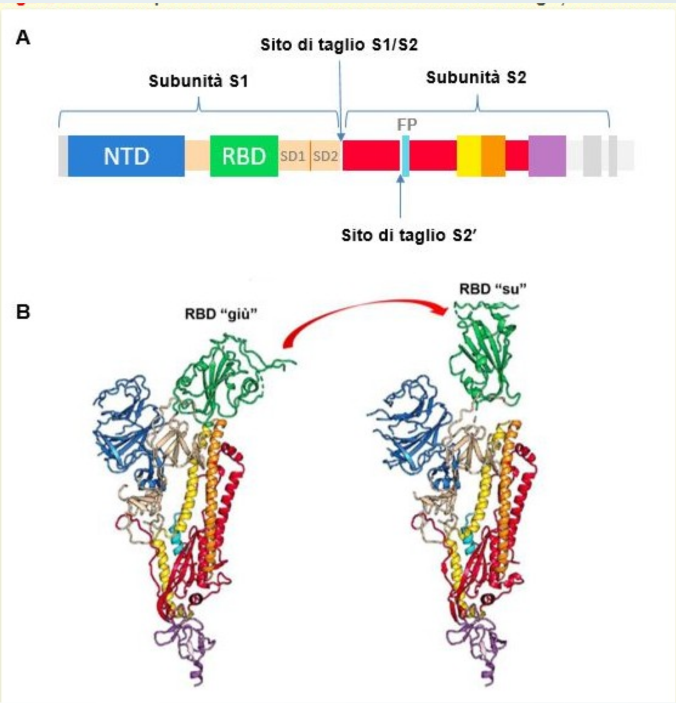
La proteina spike presenta un sito di clivaggio per la proteasi FURINA

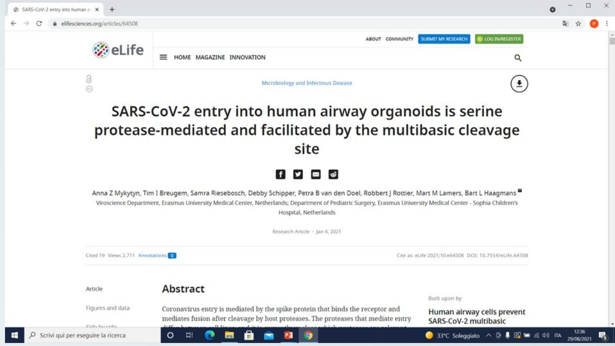

DMVs
Golgi apparatus
Furin cut

Stage 3: Remodelling the cell
The virus transforms the cell's ER — an internal membrane network — into bubble-like structures called double-membrane vesicles (DMVs). These might provide a safe haven for more viral RNA to be replicated and translated.

Stage 4: Exit
Once the newly made molecules assemble into a complete virus particle, this leaves the cell through an organelle called the Golgi apparatus, or perhaps through lysosomes, which are cellular rubbish bins.

Stage 5: The last slice
A host enzyme named furin makes a crucial cut at a site of five amino acids on the spike protein. This prepares the virus to strike another cell. Variants have a higher proportion of snipped spike proteins, helping them to infect cells more efficiently.


A
Sito di taglio S1/S2
Subunità S1
Subunità S2
FP
NTD
RBD
SD1
SD2
Sito di taglio S2'
B
RBD "giù"
RBD "su"


SARS-CoV-2 entry into human a
elifesciences.org/articles/64508
eLife
ABOUT
COMMUNITY
SUBMIT MY RESEARCH
LOG IN/REGISTER
HOME
MAGAZINE
INNOVATION
Scrivi qui per eseguire la ricerca
33°C Soleggiato
ITA
12:36
29/08/2021

Microbiology and Infectious Disease

SARS-CoV-2 entry into human airway organoids is serine protease-mediated and facilitated by the multibasic cleavage site

Anna Z Mykytyn, Tim I Breugem, Samra Riesebosch, Debby Schipper, Petra B van den Doel, Robbert J Rottier, Mart M Lamers, Bart L Haagmans
Viroscience Department, Erasmus University Medical Center, Netherlands; Department of Pediatric Surgery, Erasmus University Medical Center - Sophia Children's Hospital, Netherlands

Research Article · Jan 4, 2021

Cited 19 Views 2,711 Annotations 0

Cite as: eLife 2021;10:e64508 DOI: 10.7554/eLife.64508

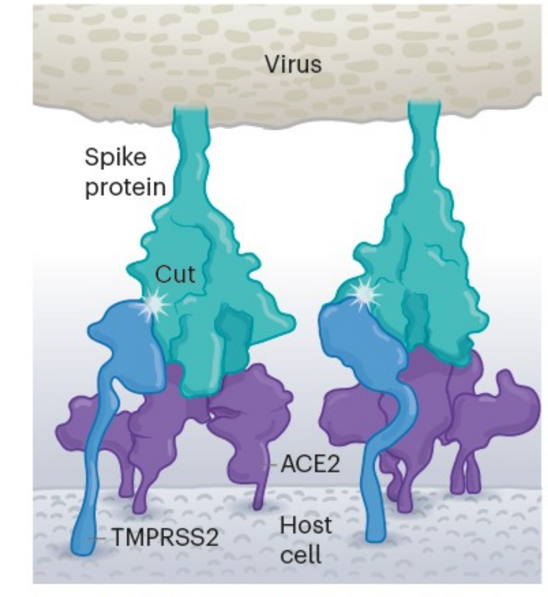
Article
Figures and data

Abstract

Coronavirus entry is mediated by the spike protein that binds the receptor and mediates fusion after cleavage by host proteases. The proteases that mediate entry

Built upon by

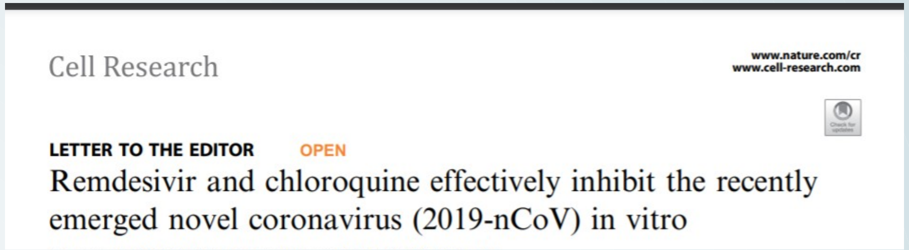
Human airway cells prevent SARS-CoV-2 multibasic


Virus
Spike protein
Cut
ACE2
TMPRSS2
Host cell

Sito di clivaggio della furina (un enzima proteolitico) che è presente tra la subunità 1 (S1) e la subunità 2 (S2) della Spike (S) di Sars-CoV-2.

Si tratta 4 residui amino-acidici, Prra (prolina-arginina-arginina-alanina), corrispondenti appunto a 12 nucleotidi (quindi 4 codoni, CCT-CGG-CGG-GCA), inseriti in una posizione strategica tra la serina 680 e l'arginina 681 della proteina Spike.

L’ ingresso nella cellula può avvenire anche per endocitosi

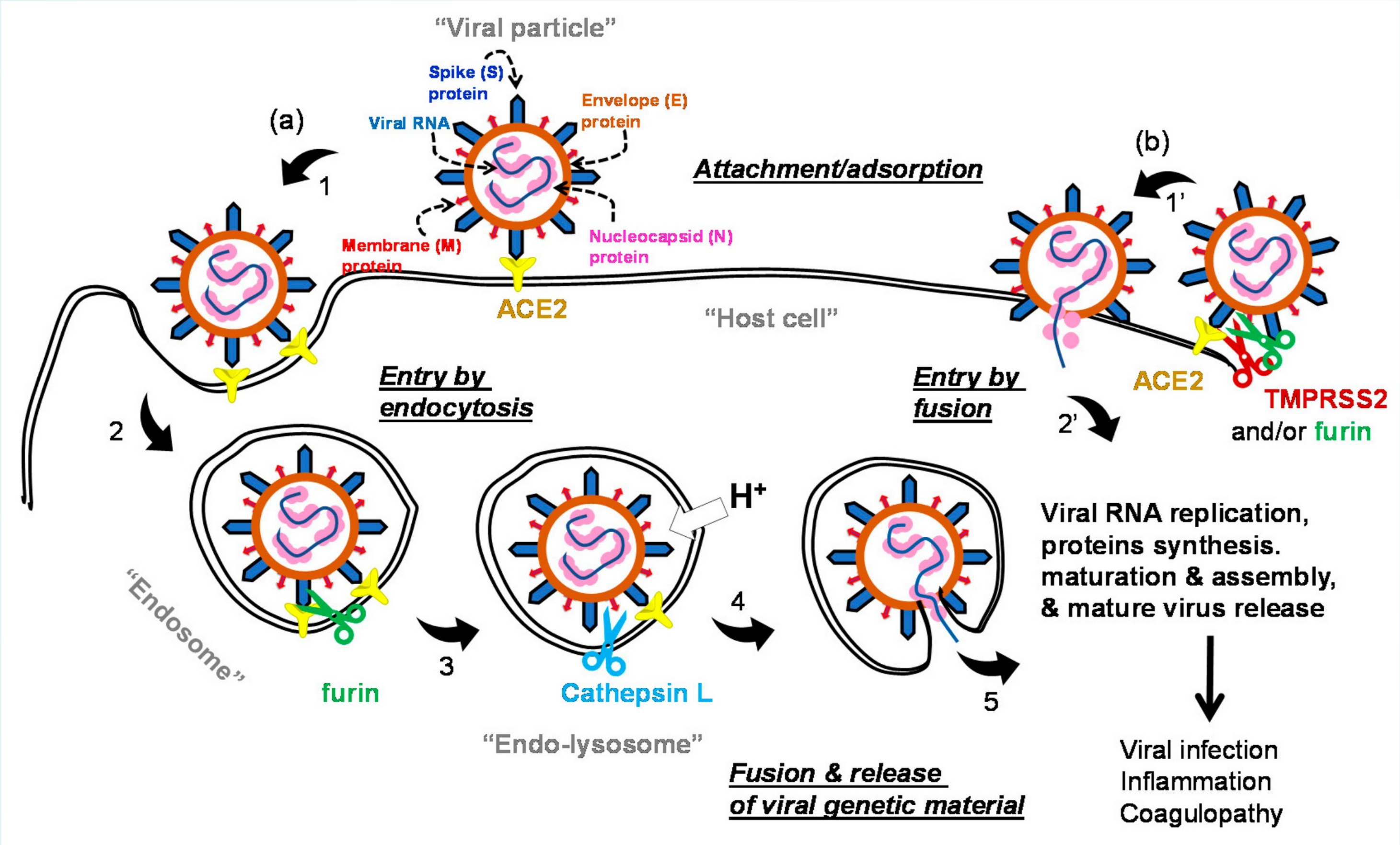


Cell Research

www.nature.com/cr
www.cell-research.com

LETTER TO THE EDITOR OPEN

Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro



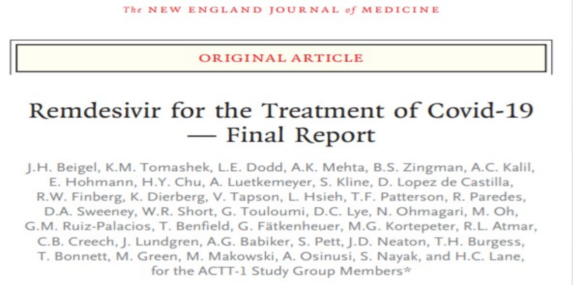
“Viral particle”
Spike (S) protein
Envelope (E) protein
Viral RNA
(a)
1
Attachment/adsorption
(b)
1’
Membrane (M) protein
Nucleocapsid (N) protein
ACE2
“Host cell”
Entry by endocytosis
Entry by fusion
ACE2
TMPRSS2 and/or furin
2
2’
H+
“Endosome”
furin
3
Cathepsin L
4
5
“Endo-lysosome”
Viral RNA replication, proteins synthesis. maturation & assembly, & mature virus release
Fusion & release of viral genetic material
Viral infection
Inflammation
Coagulopathy

La idrossiclorochina blocca la via della endocitosi

I primi studi di replicazione furono condotti in linee cellulari che **non esprimevano la TMPRESS2.** L’ ingresso nella cellula era quindi dipendente dalla endocitosi

Terapi antivirale:
Risultati molto deludenti

Nonostante siano state testate grandi librerie di farmaci potenzialmente capaci di inibire la replicazione virale,
non si è ancora individuato
un farmaco clinicamente efficace.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19
— Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

the
PHARMACEUTICAL JOURNAL

News
Medicines in children
CPD & Learning
Research
Log in
Subscribe
Home / Feature

Clinical research

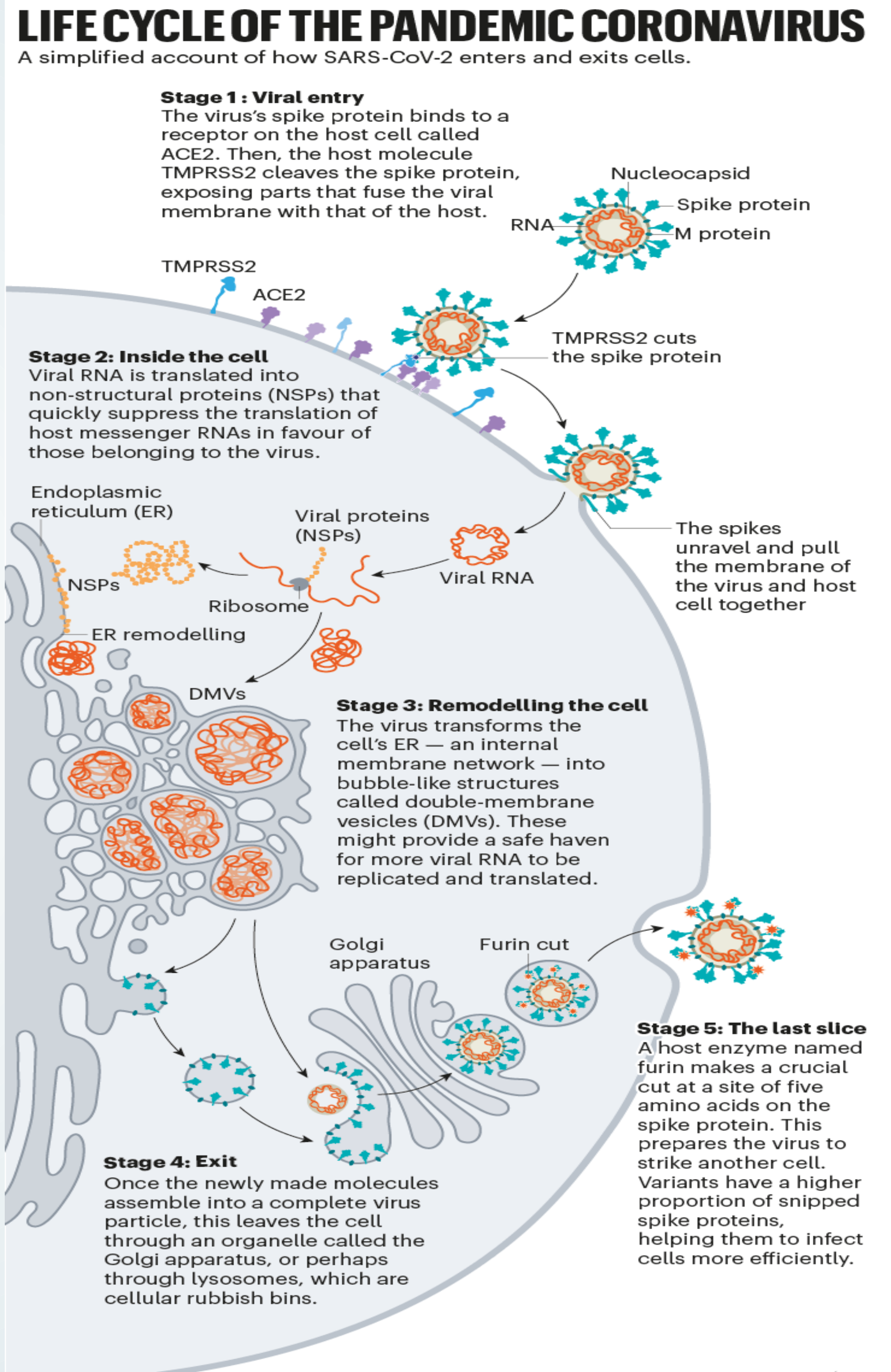
26 August 2021

By Julia Robinson

Everything you need to know about the COVID-19 therapy trials

There are thousands of clinical trials investigating treatments and preventative measures for COVID-19.

ADVERTISEMENT
Copy link to page



LIFE CYCLE OF THE PANDEMIC CORONAVIRUS

A simplified account of how SARS-CoV-2 enters and exits cells.

Stage 1 : Viral entry
The virus's spike protein binds to a receptor on the host cell called ACE2. Then, the host molecule TMPRSS2 cleaves the spike protein, exposing parts that fuse the viral membrane with that of the host.

Stage 2: Inside the cell
Viral RNA is translated into non-structural proteins (NSPs) that quickly suppress the translation of host messenger RNAs in favour of those belonging to the virus.

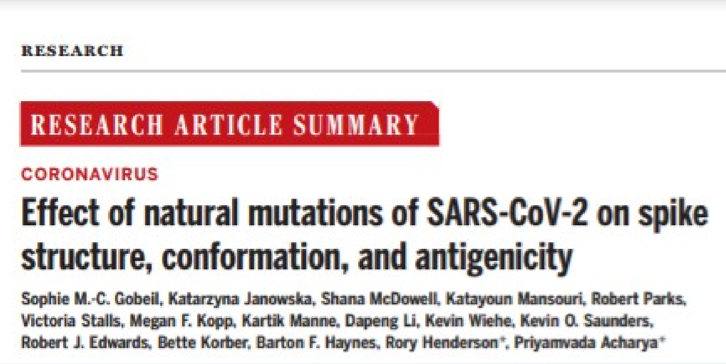
Stage 3: Remodelling the cell
The virus transforms the cell's ER — an internal membrane network — into bubble-like structures called double-membrane vesicles (DMVs). These might provide a safe haven for more viral RNA to be replicated and translated.

Stage 4: Exit
Once the newly made molecules assemble into a complete virus particle, this leaves the cell through an organelle called the Golgi apparatus, or perhaps through lysosomes, which are cellular rubbish bins.

Stage 5: The last slice
A host enzyme named furin makes a crucial cut at a site of five amino acids on the spike protein. This prepares the virus to strike another cell. Variants have a higher proportion of snipped spike proteins, helping them to infect cells more efficiently.

Nucleocapsid
Spike protein
RNA
M protein
TMPRSS2
ACE2
TMPRSS2 cuts the spike protein
The spikes unravel and pull the membrane of the virus and host cell together
Endoplasmic reticulum (ER)
Viral proteins (NSPs)
NSPs
Viral RNA
Ribosome
ER remodelling
DMVs
Golgi apparatus
Furin cut

Le Varianti
del SARS COV 2



RESEARCH

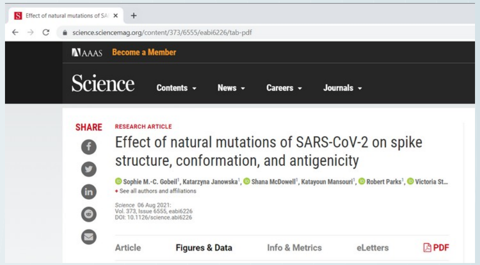
RESEARCH ARTICLE SUMMARY

CORONAVIRUS

Effect of natural mutations of SARS-CoV-2 on spike structure, conformation, and antigenicity

Sophie M.-C. Gobeil, Katarzyna Janowska, Shana McDowell, Katayoun Mansouri, Robert Parks, Victoria Stalls, Megan F. Kopp, Kartik Manne, Dapeng Li, Kevin Wiehe, Kevin O. Saunders, Robert J. Edwards, Bette Korber, Barton F. Haynes, Rory Henderson*, Priyamvada Acharya*

Variante				
	Escape Vaccinale	**Fitness**	**Diffusione**	**Mutazione**
Inglese	+	alta	Media	Maggiore Affinità ACE2 Sito Clivaggio Furina
Sud Africana	++++	bassa	Limitata	Proteina spike
Brasiliana	++++	Poco studiata?	Limitata	Proteina spike
Indiana	++	Altissima	Elevatissima	Sito Clivaggio Furina
Peruviana	+	Media	Limitata	Maggiore Affinità ACE2



Effect of natural mutations of SA
science.sciencemag.org/content/373/6555/eabi6226/tab-pdf
AAAS
Become a Member
Science
Contents
News
Careers
Journals
SHARE
Article
Figures & Data
Info & Metrics
eLetters
PDF

RESEARCH ARTICLE

Effect of natural mutations of SARS-CoV-2 on spike structure, conformation, and antigenicity

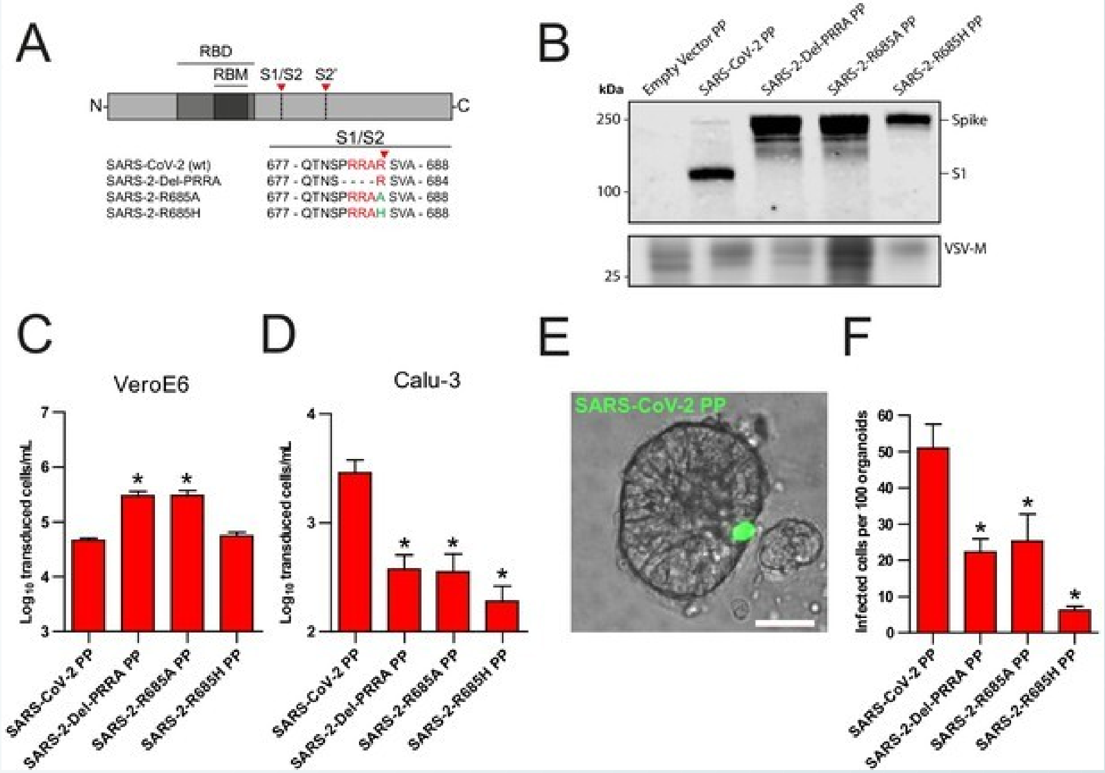
Sophie M.-C. Gobeil[1], Katarzyna Janowska[1], Shana McDowell[1], Katayoun Mansouri[1], Robert Parks[1], Victoria St...

+ See all authors and affiliations

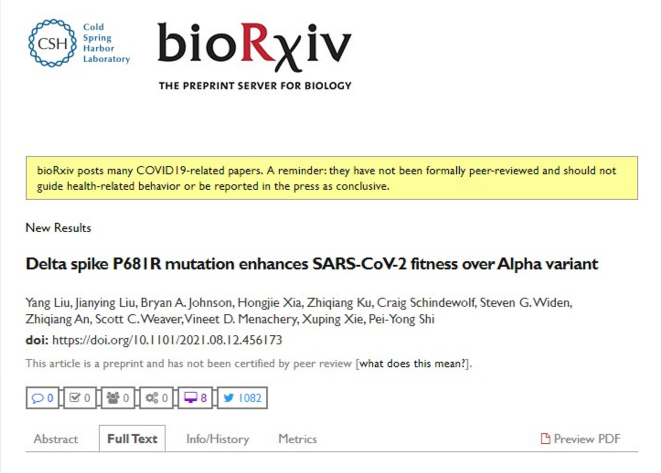
Science 06 Aug 2021:
Vol. 373, Issue 6555, eabi6226
DOI: 10.1126/science.abi6226

Le Varianti del SARS COV 2
Mutazioni del sito di legame la Furina

Variante		
	% dei Recettori idrolizzati dalla Furina	Mutazione Sito proteolitico Furina
Wild	50%	PRRA
Inglese	>50%	HRRA
Indiana	>75%	RRRA



La efficienza replicativa in vitro della Variante Delta è molto elevata


Cold Spring Harbor Laboratory
CSH
bioRχiv
THE PREPRINT SERVER FOR BIOLOGY
0
0
0
0
8
1082
Abstract
Full Text
Info/History
Metrics
Preview PDF

bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

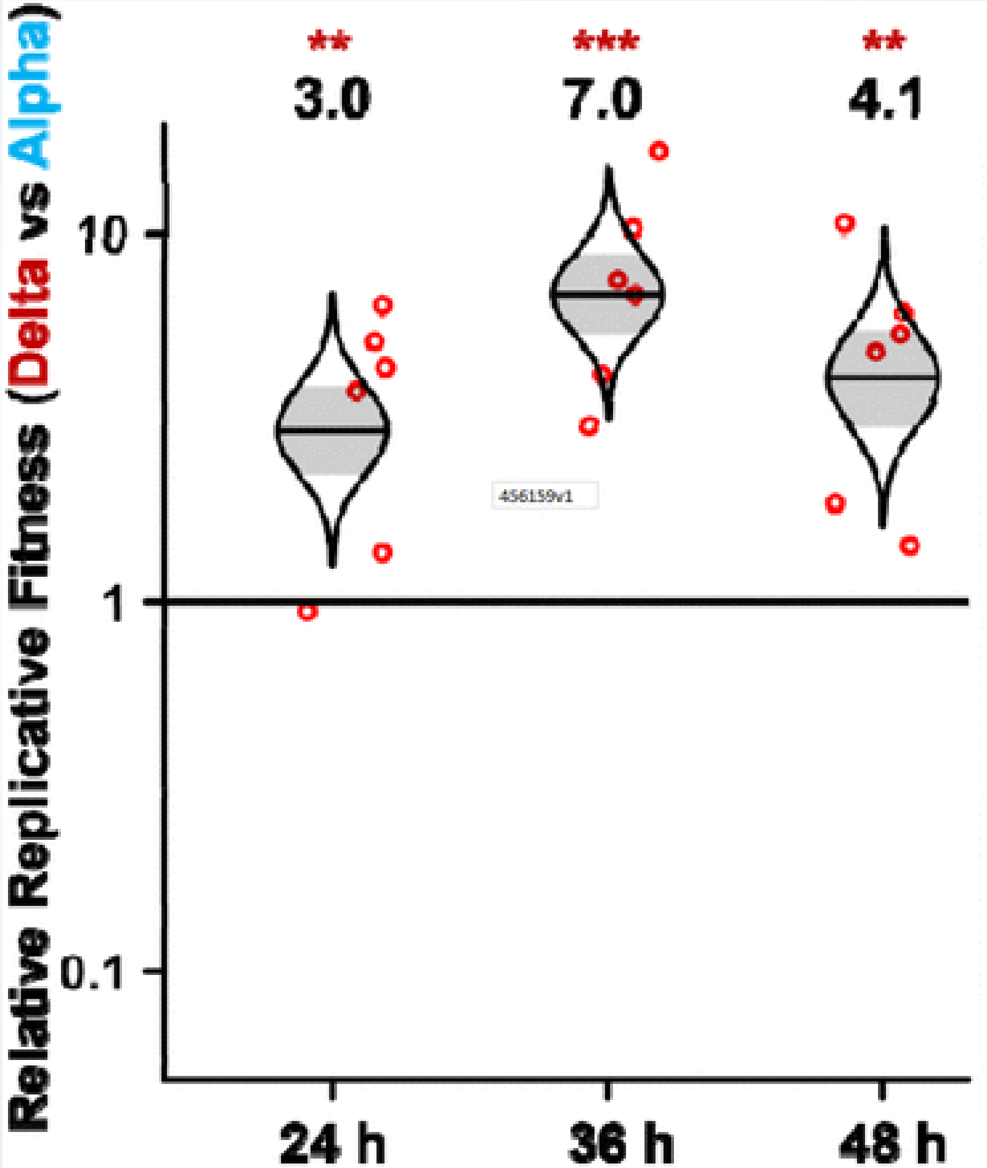
New Results

Delta spike P681R mutation enhances SARS-CoV-2 fitness over Alpha variant

Yang Liu, Jianying Liu, Bryan A. Johnson, Hongjie Xia, Zhiqiang Ku, Craig Schindewolf, Steven G. Widen, Zhiqiang An, Scott C. Weaver, Vineet D. Menachery, Xuping Xie, Pei-Yong Shi

doi: https://doi.org/10.1101/2021.08.12.456173

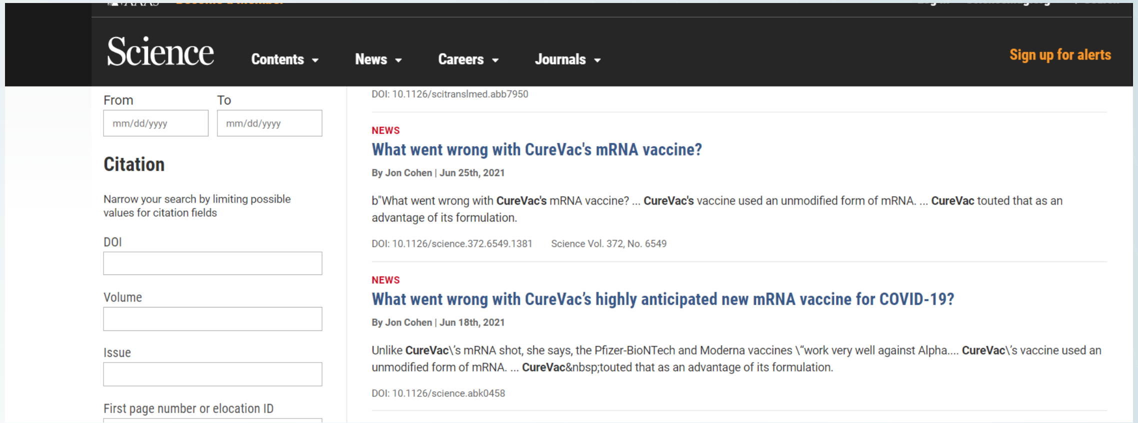
This article is a preprint and has not been certified by peer review [what does this mean?].



I vaccini

Produttore	Tipo di vaccino	Stato di utilizzo
Pfitzer BionTec	m RNA	In uso
Moderna	m RNA	In uso
GSK CureVac	m RNA	In sviluppo?
Astra Zeneca	Vettore virale	In uso
Sputnik	Doppio Vettore virale	In uso
Johnson & Johnson	Vettore virale	In uso
SinoVac	Virus inattivato	In uso
Novovax	Proteico/adiuvante	In sviluppo ?
Sanofi	Proteico/adiuvante	In sviluppo

Il diavolo è nei dettagli!


Science
Contents
News
Careers
Journals
Sign up for alerts
From
To
mm/dd/yyyy
mm/dd/yyyy
Citation
Narrow your search by limiting possible values for citation fields
DOI
Volume
Issue
First page number or elocation ID

DOI: 10.1126/scitranslmed.abb7950

NEWS

What went wrong with CureVac's mRNA vaccine?

By Jon Cohen | Jun 25th, 2021

b"What went wrong with **CureVac's** mRNA vaccine? ... **CureVac's** vaccine used an unmodified form of mRNA. ... **CureVac** touted that as an advantage of its formulation.

DOI: 10.1126/science.372.6549.1381 Science Vol. 372, No. 6549

NEWS

What went wrong with CureVac's highly anticipated new mRNA vaccine for COVID-19?

By Jon Cohen | Jun 18th, 2021

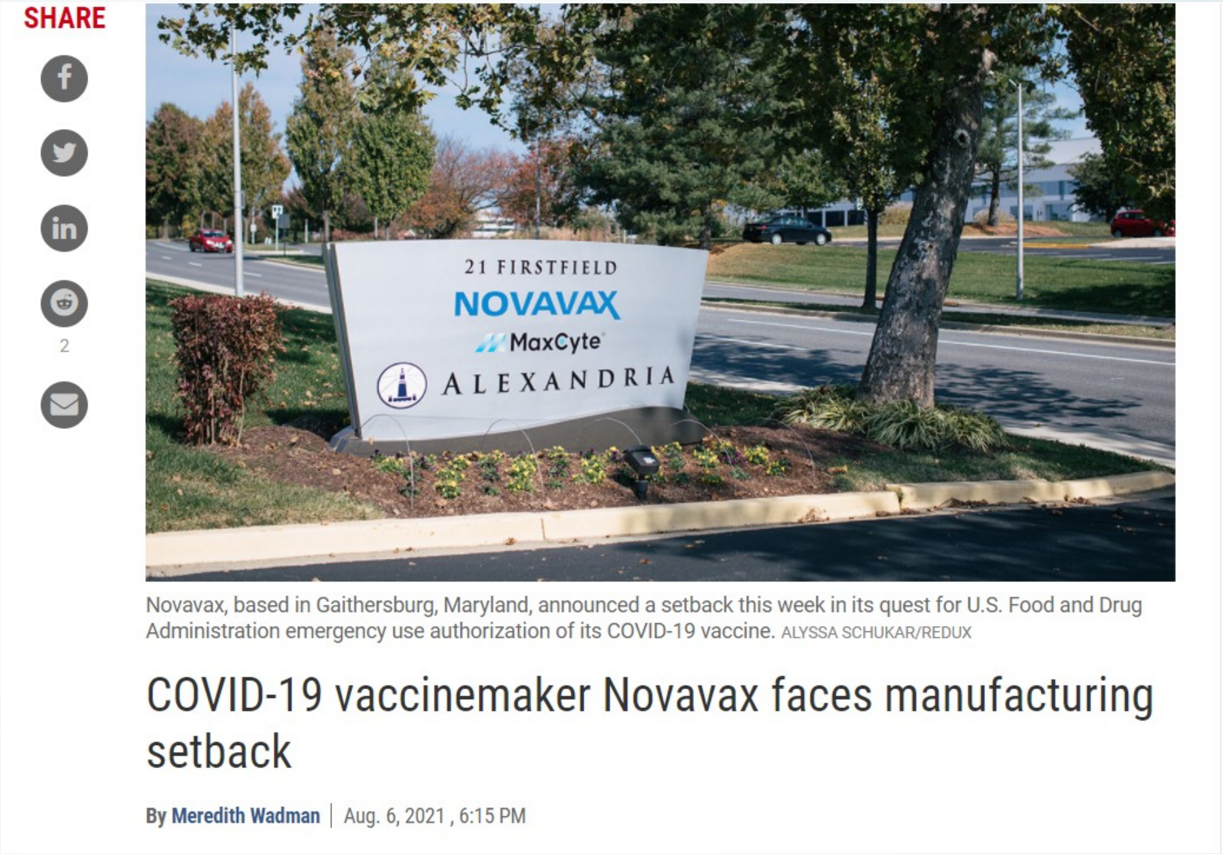
Unlike **CureVac**\'s mRNA shot, she says, the Pfizer-BioNTech and Moderna vaccines \"work very well against Alpha.... **CureVac**\'s vaccine used an unmodified form of mRNA. ... **CureVac** touted that as an advantage of its formulation.

DOI: 10.1126/science.abk0458

Produttore	Tipo di vaccino	Efficacia clinica di utilizzo
Pfitzer BionTec	m RNA pseudouridina	Ottima risposta
Moderna	m RNA pseudouridina	Ottima risposta
GSK Cure Vac	m RNA –naturale-	Effetti collaterali Interferon mediati Riduzione della dose Risposta insufficiente

Vaccino Novavax:
Difficoltà a standardizzare le dosi

Contributo governativo
1,75 miliardi di dollari


SHARE
2
21 FIRSTFIELD
NOVAVAX
MaxCyte
ALEXANDRIA

Novavax, based in Gaithersburg, Maryland, announced a setback this week in its quest for U.S. Food and Drug Administration emergency use authorization of its COVID-19 vaccine. ALYSSA SCHUKAR/REDUX

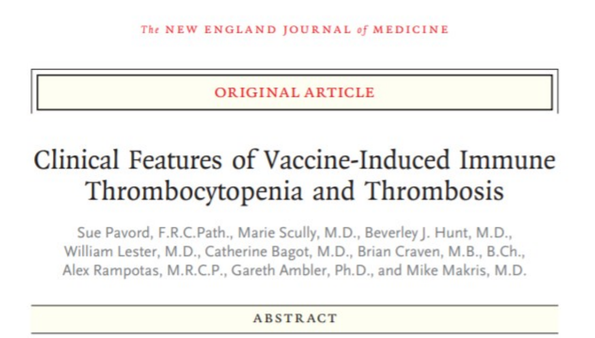
COVID-19 vaccinemaker Novavax faces manufacturing setback

By **Meredith Wadman** | Aug. 6, 2021 , 6:15 PM

Effetti collaterali

Produttore	Tipo di vaccino	Effetti Collaterali/ Problemi
Pfitzer BionTec	m RNA	Miocarditi Porpora Trombocitopenica
Moderna	m RNA	Nessuno
GSK Cure Vac	m RNA	Sindrome influenzale grave Scarsa efficacia
Astra Zeneca	Vettore virale	VITT
Sputnik	Vettore virale	Mancanza dati
Johnson & Johnson	Vettore virale	VITT(1 caso in fase 3) Trombosi Gulliam Barrè
Novovax	Proteico/adiuvante	Non testato
Sanofi	Proteico/adiuvante	Non testato

La VITT


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

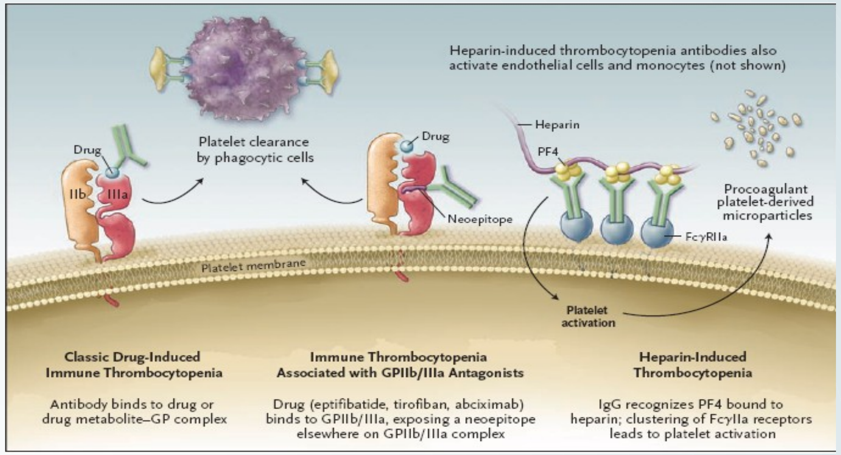
Clinical Features of Vaccine-Induced Immune Thrombocytopenia and Thrombosis

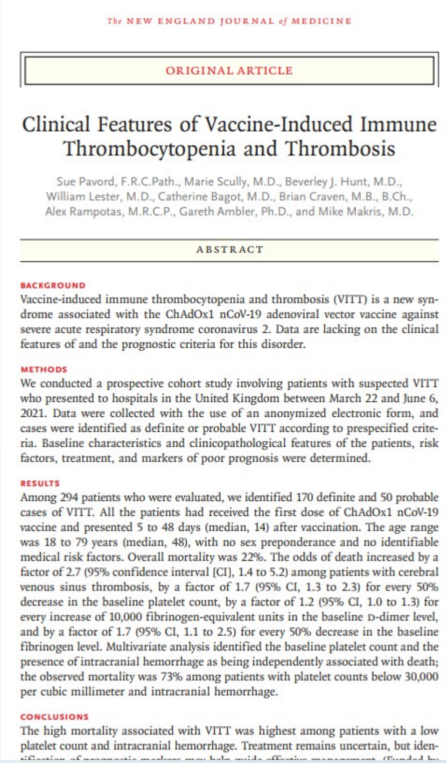
Sue Pavord, F.R.C.Path., Marie Scully, M.D., Beverley J. Hunt, M.D., William Lester, M.D., Catherine Bagot, M.D., Brian Craven, M.B., B.Ch., Alex Rampotas, M.R.C.P., Gareth Ambler, Ph.D., and Mike Makris, M.D.

ABSTRACT

Aprile 2021

Impurità
Frammenti del m RNA spliced
(si con astra zeneca no con J J)
Ceppo dell’ Adeno Virus
(carico negativamente)


Heparin-induced thrombocytopenia antibodies also activate endothelial cells and monocytes (not shown)
Drug
IIb
IIIa
Platelet clearance by phagocytic cells
Drug
Neoepitope
Heparin
PF4
Procoagulant platelet-derived microparticles
FcγRIIa
Platelet membrane
Platelet activation
Classic Drug-Induced Immune Thrombocytopenia
Antibody binds to drug or drug metabolite–GP complex
Immune Thrombocytopenia Associated with GPIIb/IIIa Antagonists
Drug (eptifibatide, tirofiban, abciximab) binds to GPIIb/IIIa, exposing a neoepitope elsewhere on GPIIb/IIIa complex
Heparin-Induced Thrombocytopenia
IgG recognizes PF4 bound to heparin; clustering of FcγIIa receptors leads to platelet activation


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clinical Features of Vaccine-Induced Immune Thrombocytopenia and Thrombosis

Sue Pavord, F.R.C.Path., Marie Scully, M.D., Beverley J. Hunt, M.D., William Lester, M.D., Catherine Bagot, M.D., Brian Craven, M.B., B.Ch., Alex Rampotas, M.R.C.P., Gareth Ambler, Ph.D., and Mike Makris, M.D.

ABSTRACT

BACKGROUND
Vaccine-induced immune thrombocytopenia and thrombosis (VITT) is a new syndrome associated with the ChAdOx1 nCoV-19 adenoviral vector vaccine against severe acute respiratory syndrome coronavirus 2. Data are lacking on the clinical features of and the prognostic criteria for this disorder.

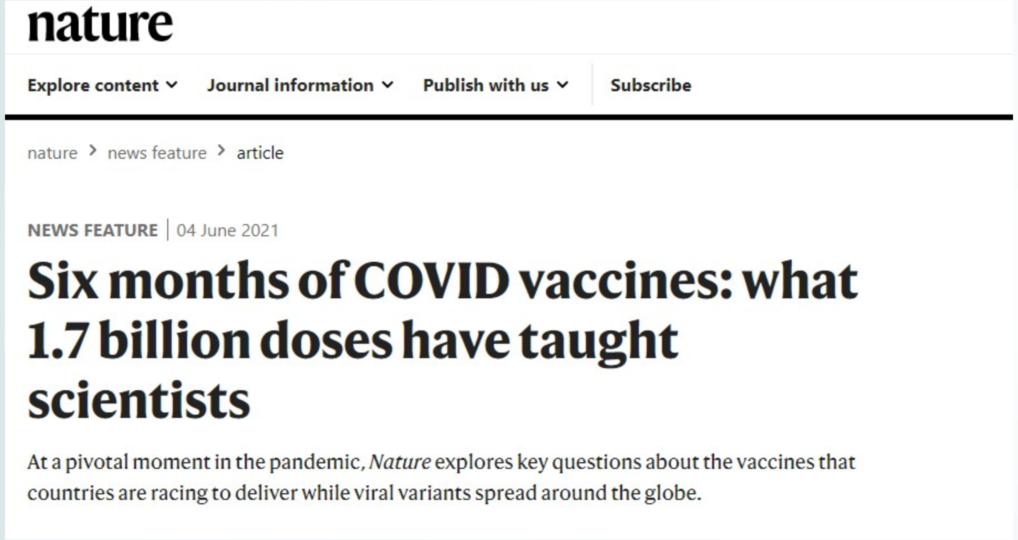
METHODS
We conducted a prospective cohort study involving patients with suspected VITT who presented to hospitals in the United Kingdom between March 22 and June 6, 2021. Data were collected with the use of an anonymized electronic form, and cases were identified as definite or probable VITT according to prespecified criteria. Baseline characteristics and clinicopathological features of the patients, risk factors, treatment, and markers of poor prognosis were determined.

RESULTS
Among 294 patients who were evaluated, we identified 170 definite and 50 probable cases of VITT. All the patients had received the first dose of ChAdOx1 nCoV-19 vaccine and presented 5 to 48 days (median, 14) after vaccination. The age range was 18 to 79 years (median, 48), with no sex preponderance and no identifiable medical risk factors. Overall mortality was 22%. The odds of death increased by a factor of 2.7 (95% confidence interval [CI], 1.4 to 5.2) among patients with cerebral venous sinus thrombosis, by a factor of 1.7 (95% CI, 1.3 to 2.3) for every 50% decrease in the baseline platelet count, by a factor of 1.2 (95% CI, 1.0 to 1.3) for every increase of 10,000 fibrinogen-equivalent units in the baseline D-dimer level, and by a factor of 1.7 (95% CI, 1.1 to 2.5) for every 50% decrease in the baseline fibrinogen level. Multivariate analysis identified the baseline platelet count and the presence of intracranial hemorrhage as being independently associated with death; the observed mortality was 73% among patients with platelet counts below 30,000 per cubic millimeter and intracranial hemorrhage.

CONCLUSIONS
The high mortality associated with VITT was highest among patients with a low platelet count and intracranial hemorrhage. Treatment remains uncertain, but iden-

Settembre 2021

Cosa abbiamo imparato da una vaccinazione con un 1,7 miliardi di dosi?



nature

Explore content
Journal information
Publish with us
Subscribe
nature > news feature > article

NEWS FEATURE | 04 June 2021

Six months of COVID vaccines: what 1.7 billion doses have taught scientists

At a pivotal moment in the pandemic, *Nature* explores key questions about the vaccines that countries are racing to deliver while viral variants spread around the globe.

Effetti collaterali :

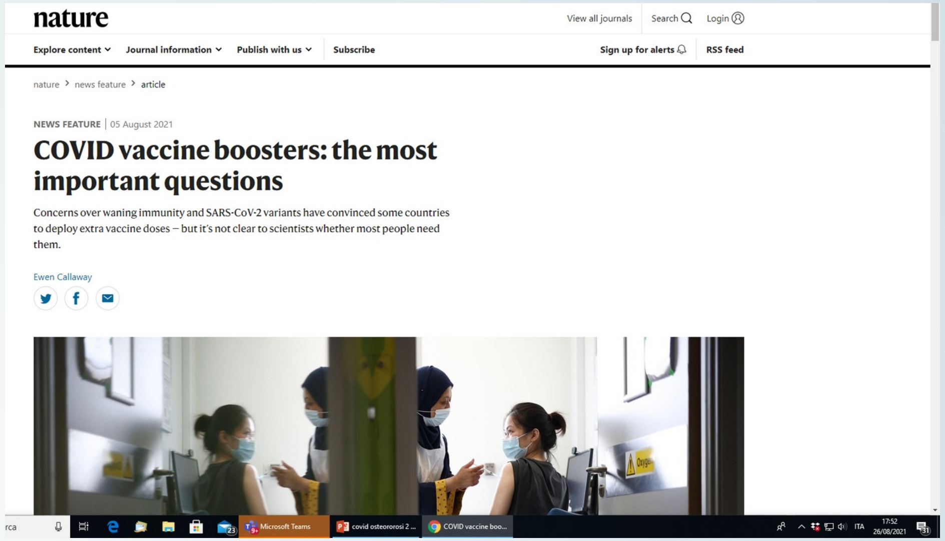
con incidenza < 1:100000 sono difficili da tracciare in studi registrativi,

ma diventano evidenti con milioni di somministrazioni contemporanee

Protocollo vaccinale

vaccino	Intervallo dosi	Proposta	Evidenze a supporto
Pfitzer BionTec	15-45 giorni	Terza dose	Livelli anticorpi neutralizzanti
Moderna	15-45 giorni	Terza dose	Livelli anticorpi neutralizzanti
Astra Zeneca	90 giorni	Seconda dose con vaccino a RNA	nessuna
Johnson **&** Johnson	Mono dose	nessuna	In corso studio con seconda somministrazione

La terza dose:
le perplessità del WHO

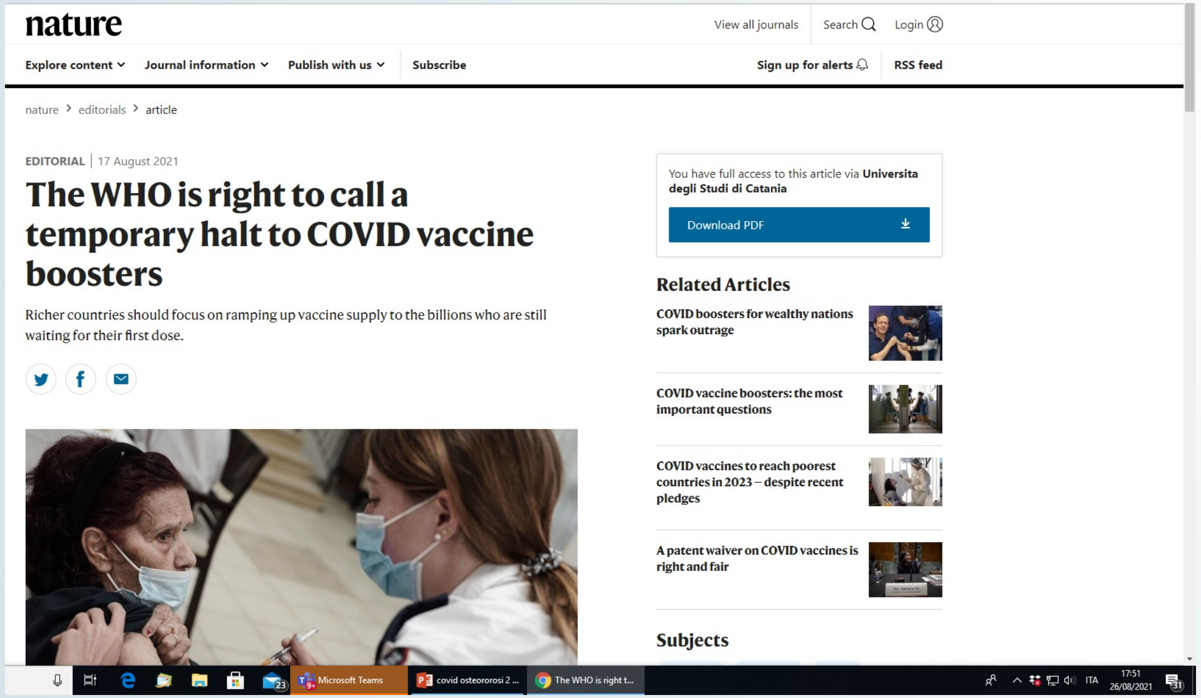

nature
View all journals
Search
Login
Explore content
Journal information
Publish with us
Subscribe
Sign up for alerts
RSS feed
nature › news feature › article

NEWS FEATURE | 05 August 2021

COVID vaccine boosters: the most important questions

Concerns over waning immunity and SARS-CoV-2 variants have convinced some countries to deploy extra vaccine doses – but it's not clear to scientists whether most people need them.

Ewen Callaway


nature
View all journals
Search
Login
Explore content
Journal information
Publish with us
Subscribe
Sign up for alerts
RSS feed
nature › editorials › article
Download PDF

EDITORIAL | 17 August 2021

The WHO is right to call a temporary halt to COVID vaccine boosters

Richer countries should focus on ramping up vaccine supply to the billions who are still waiting for their first dose.

You have full access to this article via **Universita degli Studi di Catania**

Related Articles

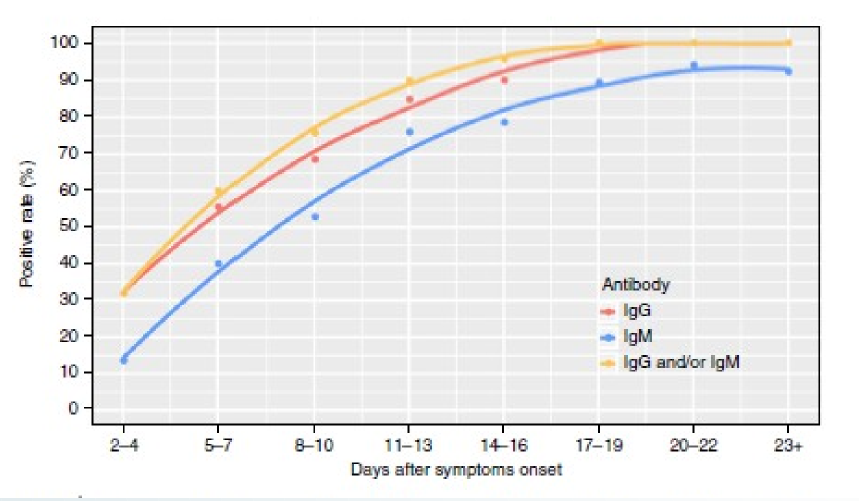
- COVID boosters for wealthy nations spark outrage
- COVID vaccine boosters: the most important questions
- COVID vaccines to reach poorest countries in 2023 – despite recent pledges
- A patent waiver on COVID vaccines is right and fair

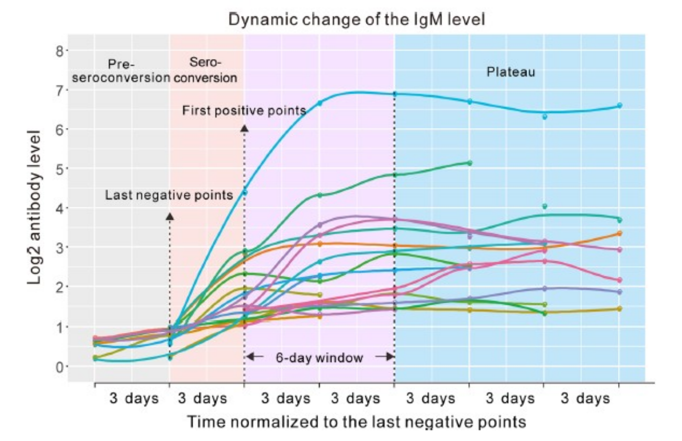
Subjects

La efficacia rimane elevata contro le forme gravi
Da somministrare solo a gruppi ristretti
es Trapiantati
Nazioni «ricche» 60% vaccinati
Nazioni «povere» 2%

USA: già 1,5 mln di terze dosi
In Italia dal 20 settembre

Risposta anticorpale



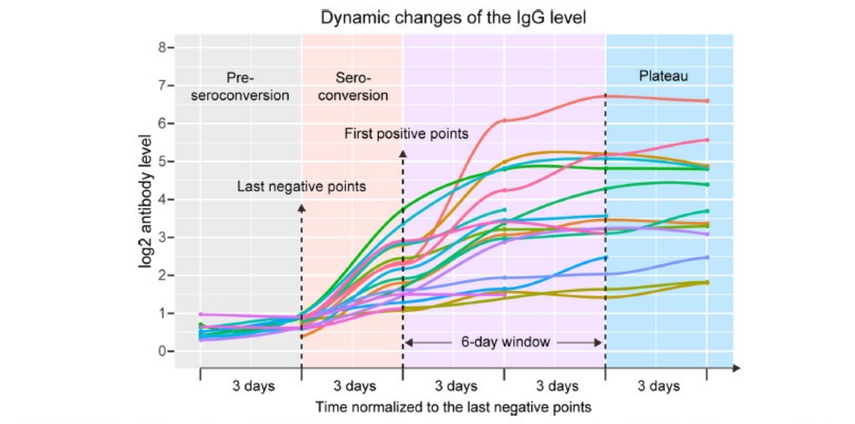


Extended Data Fig. 4 | Dynamic changes of the SARS-CoV-2 specific IgM. Time course of the virus-specific IgM level in 20 patients experienced IgM titer plateau. IgM in each patient reached plateau within 6 days since IgM became positive.

285 pazienti, tutti positivi:

- alle IgG entro **19 giorni** dall’esordio dei sintomi;
- alle IgM entro **20-22 giorni** dall’esordio dei sintomi.

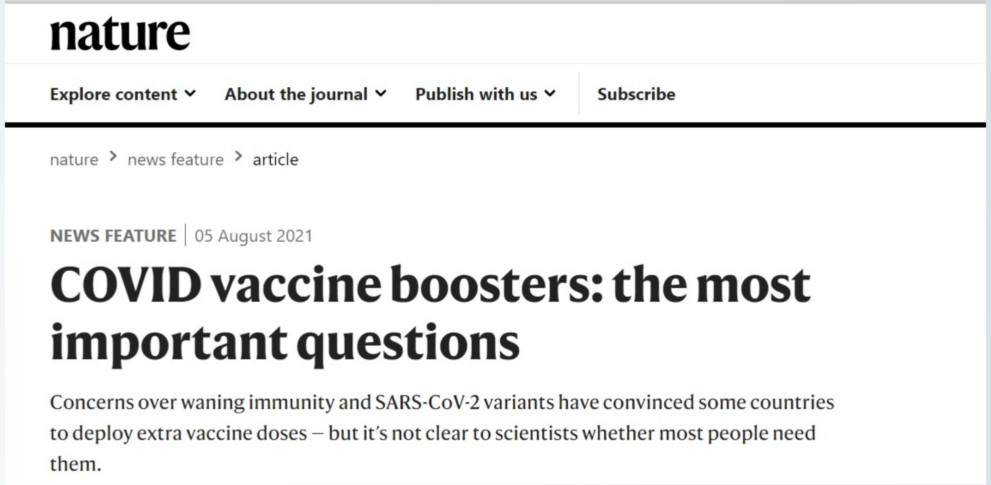
Entrambi i titoli di IgG e IgM raggiungono il **plateau entro 6 giorni** dalla sieroconversione.



Extended Data Fig. 3 | Dynamic changes of the SARS-CoV-2 specific IgG. Time course of the virus-specific IgG level in 19 patients experienced IgG titer plateau. IgG in each patient reached plateau within 6 days since IgG became positive.

Antibody responses to SARS-CoV-2 in patients with COVID-19
Long et Al. Nature 29 Apr 2020

Correlati di Protezione


nature
Explore content
About the journal
Publish with us
Subscribe
nature › news feature › article

NEWS FEATURE | 05 August 2021

COVID vaccine boosters: the most important questions

Concerns over waning immunity and SARS-CoV-2 variants have convinced some countries to deploy extra vaccine doses – but it's not clear to scientists whether most people need them.

Teams around the world are racing to determine what level of neutralizing antibodies or another immune marker is most closely associated with a vaccine's effectiveness. They're seeking what's known as a correlate of protection.
Nature Agosto 2021

https://doi.org/10.1038/d41586-021-02158-6

Non è chiaro quale parametro biologico sia indicativo di una protezione
NEL SINGOLO PAZIENTE

Correlati di protezione:
Vaccino Pfitzer BionTec vs Sino Vac

Vaccino	Struttura del vaccino	Efficacia	Titolo anticorpale
Pfitzer BioNtec	m RNA	80- 90 %	10
SinoVac	Virus Inattivato	50-90 %	1

Titolo del Messagero del 22-7-2021:
Flop del Vaccino cinese:
col Pfitzer 10 volte più anticorpi

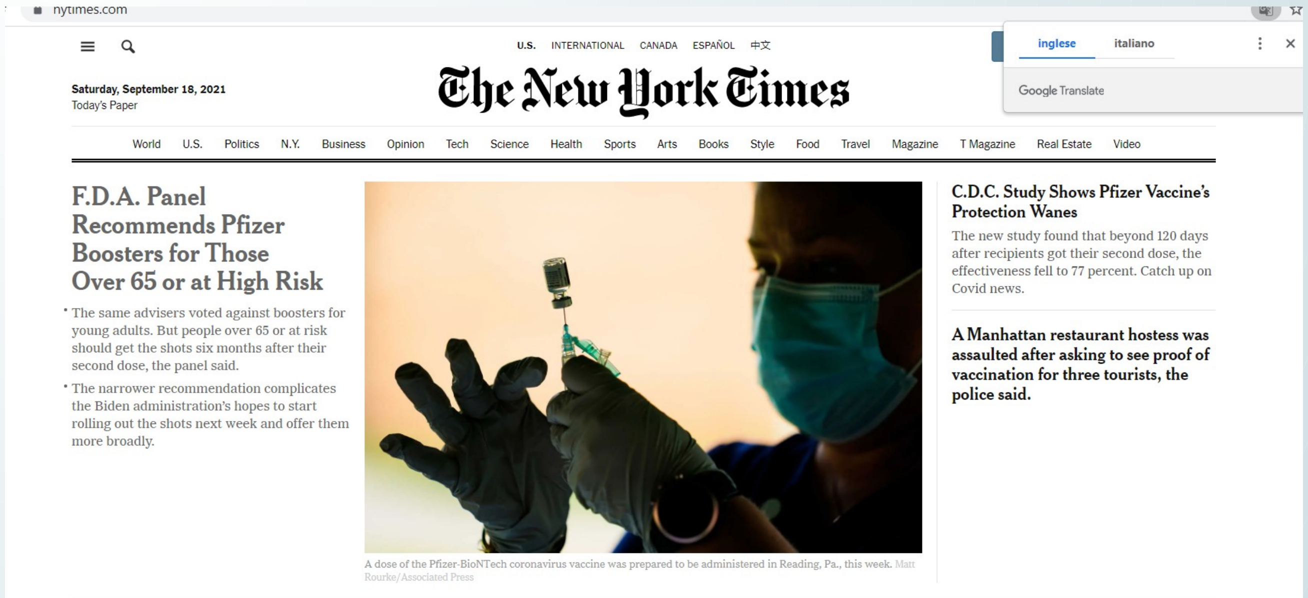
A quali gruppi di popolazione è necessario somministrare una terza dose?

Livelli anticorpali totali?
Anticorpi neutralizzanti?
Dati di popolazione?
Altro??

Dati Pfizer e Moderna:
Riduzione degli anticorpi neutralizzanti

Dati epidemiologici
Trapiantati
Immuno depressi
Pazienti oncologici
Over 65
Sindrome di Down

BMJ settembre 2021


nytimes.com
U.S.
INTERNATIONAL
CANADA
ESPAÑOL
中文
inglese
italiano
Google Translate
The New York Times
World
U.S.
Politics
N.Y.
Business
Opinion
Tech
Science
Health
Sports
Arts
Books
Style
Food
Travel
Magazine
T Magazine
Real Estate
Video

Saturday, September 18, 2021
Today's Paper

F.D.A. Panel Recommends Pfizer Boosters for Those Over 65 or at High Risk

- The same advisers voted against boosters for young adults. But people over 65 or at risk should get the shots six months after their second dose, the panel said.
- The narrower recommendation complicates the Biden administration's hopes to start rolling out the shots next week and offer them more broadly.

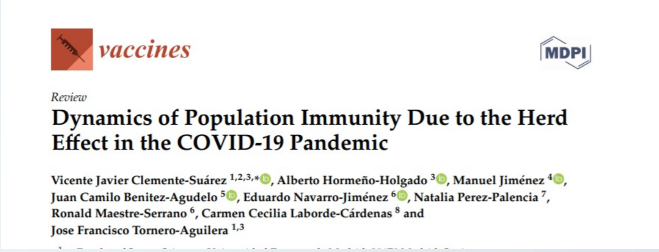
A dose of the Pfizer-BioNTech coronavirus vaccine was prepared to be administered in Reading, Pa., this week. Matt Rourke/Associated Press

C.D.C. Study Shows Pfizer Vaccine's Protection Wanes

The new study found that beyond 120 days after recipients got their second dose, the effectiveness fell to 77 percent. Catch up on Covid news.

A Manhattan restaurant hostess was assaulted after asking to see proof of vaccination for three tourists, the police said.

Immunità di gregge



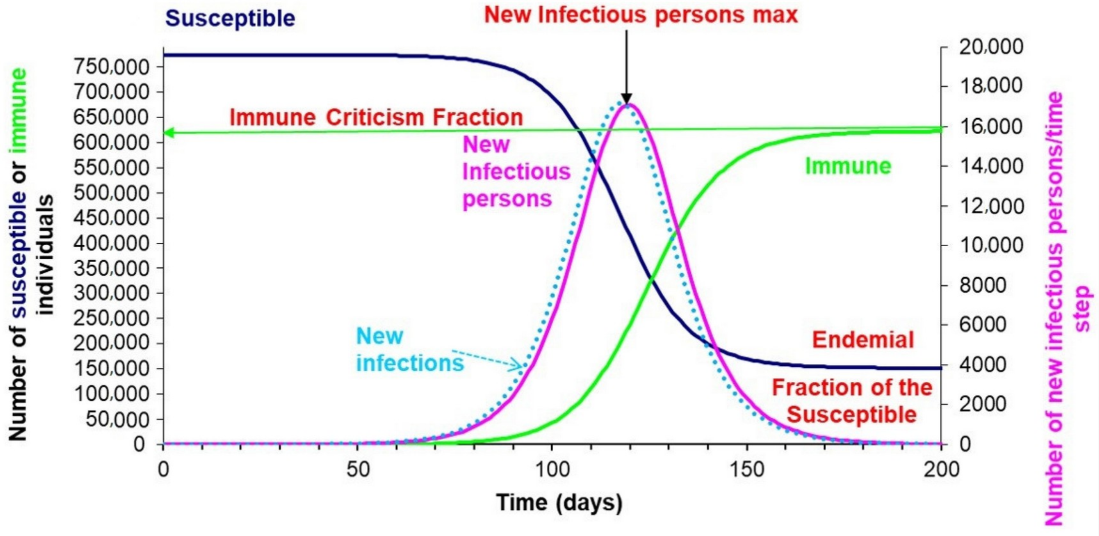
vaccines

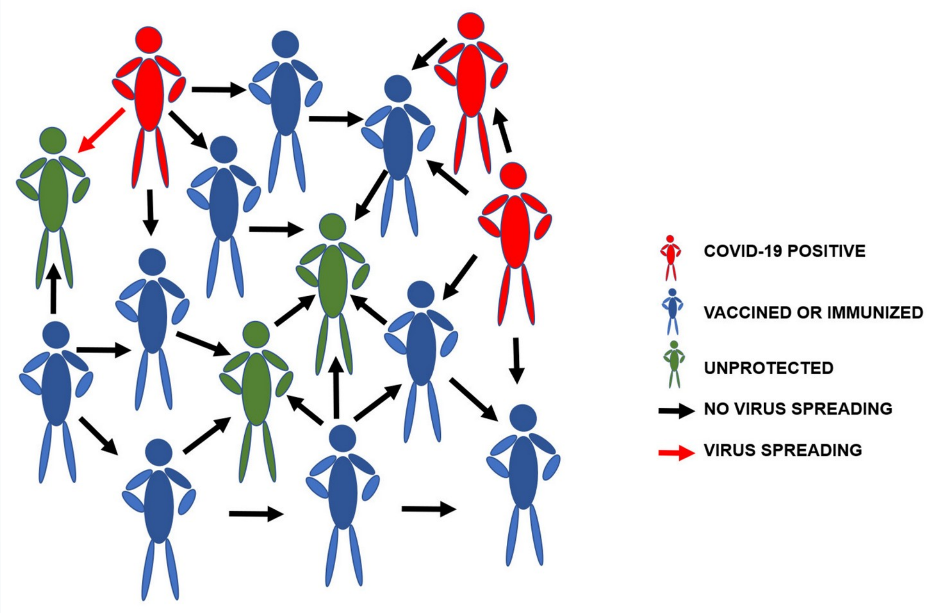
MDPI

Review

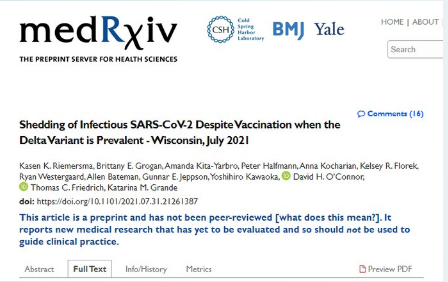
Dynamics of Population Immunity Due to the Herd Effect in the COVID-19 Pandemic

Vicente Javier Clemente-Suárez [1,2,3,*], Alberto Hormeño-Holgado [3], Manuel Jiménez [4], Juan Camilo Benitez-Agudelo [5], Eduardo Navarro-Jiménez [6], Natalia Perez-Palencia [7], Ronald Maestre-Serrano [6], Carmen Cecilia Laborde-Cárdenas [8] and Jose Francisco Tornero-Aguilera [1,3]




COVID-19 POSITIVE
VACCINED OR IMMUNIZED
UNPROTECTED
NO VIRUS SPREADING
VIRUS SPREADING

Immunità di gregge
Carica virale nei soggetti vaccinati



medRχiv
THE PREPRINT SERVER FOR HEALTH SCIENCES
CSH Cold Spring Harbor Laboratory
BMJ
Yale
HOME | ABOUT
Search
Comments (16)

Shedding of Infectious SARS-CoV-2 Despite Vaccination when the Delta Variant is Prevalent - Wisconsin, July 2021

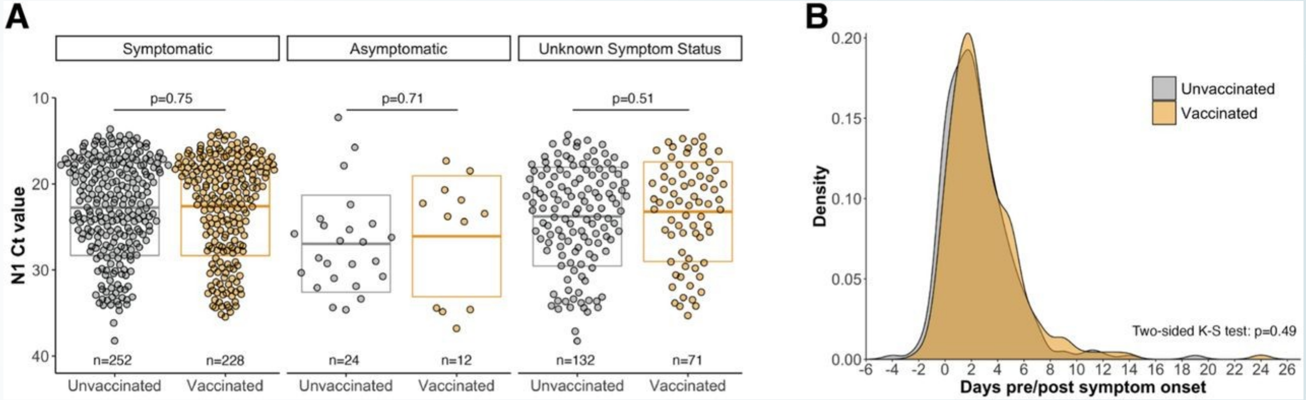
Kasen K. Riemersma, Brittany E. Grogan, Amanda Kita-Yarbro, Peter Halfmann, Anna Kocharian, Kelsey R. Florek, Ryan Westergaard, Allen Bateman, Gunnar E. Jeppson, Yoshihiro Kawaoka, David H. O'Connor, Thomas C. Friedrich, Katarina M. Grande

doi: https://doi.org/10.1101/2021.07.31.21261387

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

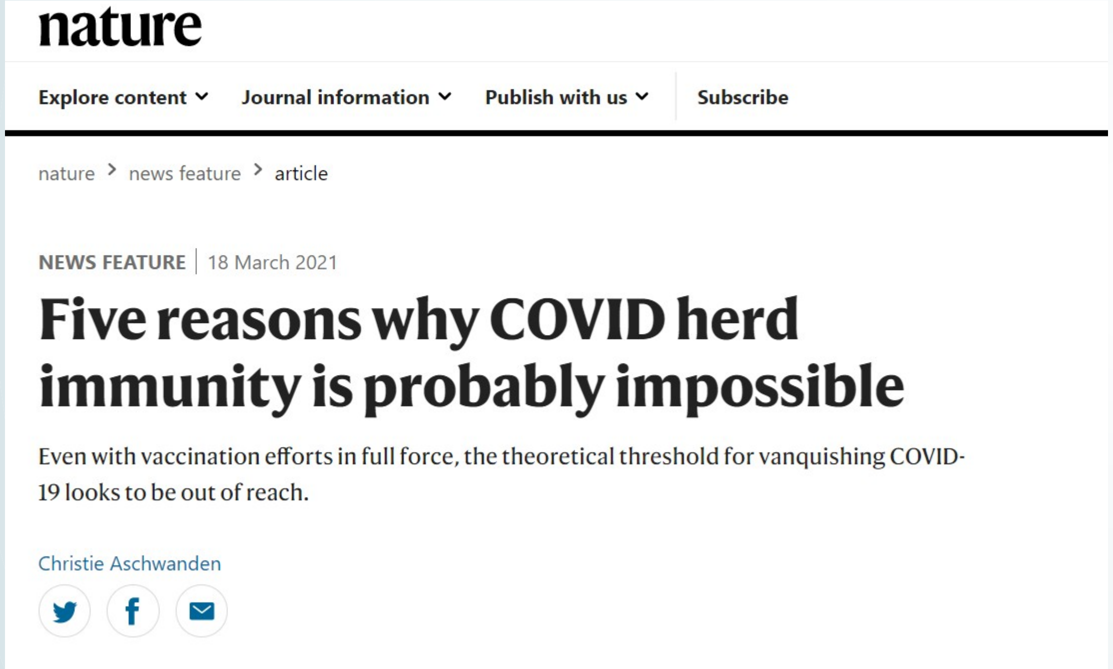
Abstract
Full Text
Info/History
Metrics
Preview PDF

Not Peer reviewed



Risk disinhibition may lead vaccinated people to increase behaviors that expose them to SARS-CoV-2 infection, and individuals who are infected despite vaccination could serve as sources of onward transmission to others.

Immunità di gregge


nature
Explore content
Journal information
Publish with us
Subscribe
nature > news feature > article

NEWS FEATURE | 18 March 2021

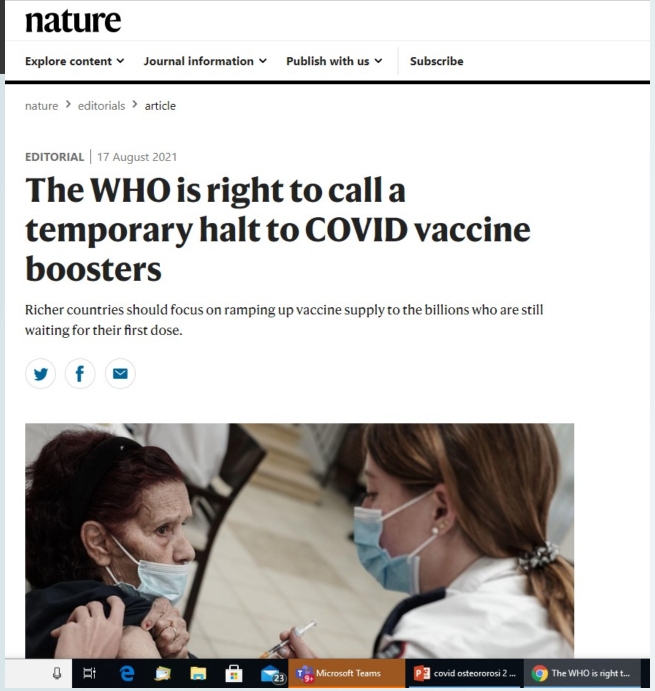
Five reasons why COVID herd immunity is probably impossible

Even with vaccination efforts in full force, the theoretical threshold for vanquishing COVID-19 looks to be out of reach.

Christie Aschwanden

Trasmissione nei vaccinati
Disuguaglianze tra nazioni
Nuove varianti
Immunità non permanente
Comportamento sociale

Nature 18 marzo 2021

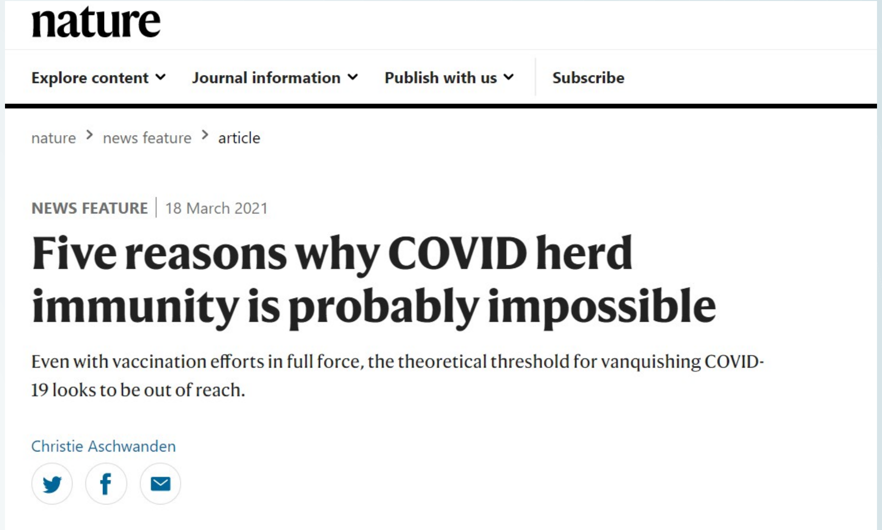

nature
Explore content
Journal information
Publish with us
Subscribe
nature > editorials > article
Microsoft Teams
covid osteororosi 2 ...
The WHO is right t...

EDITORIAL | 17 August 2021

The WHO is right to call a temporary halt to COVID vaccine boosters

Richer countries should focus on ramping up vaccine supply to the billions who are still waiting for their first dose.

Quale scelta?


nature
Explore content
Journal information
Publish with us
Subscribe
nature > news feature > article

NEWS FEATURE | 18 March 2021

Five reasons why COVID herd immunity is probably impossible

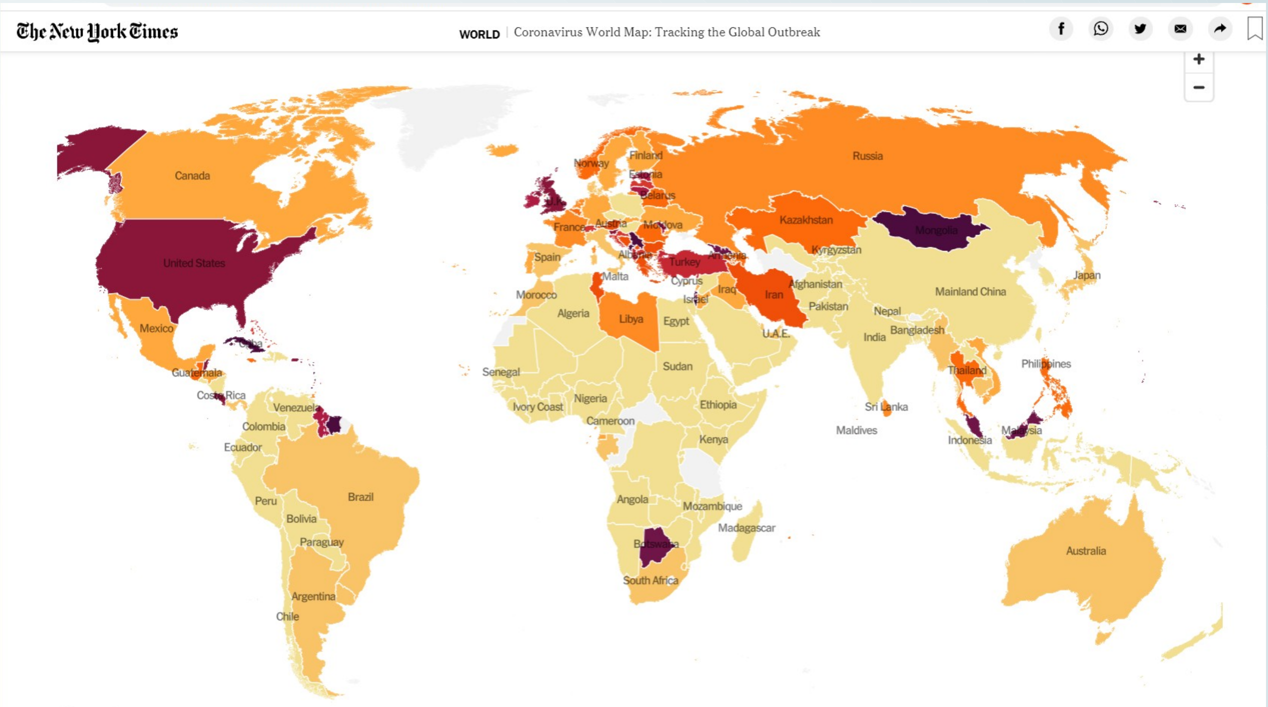
Even with vaccination efforts in full force, the theoretical threshold for vanquishing COVID-19 looks to be out of reach.

Christie Aschwanden

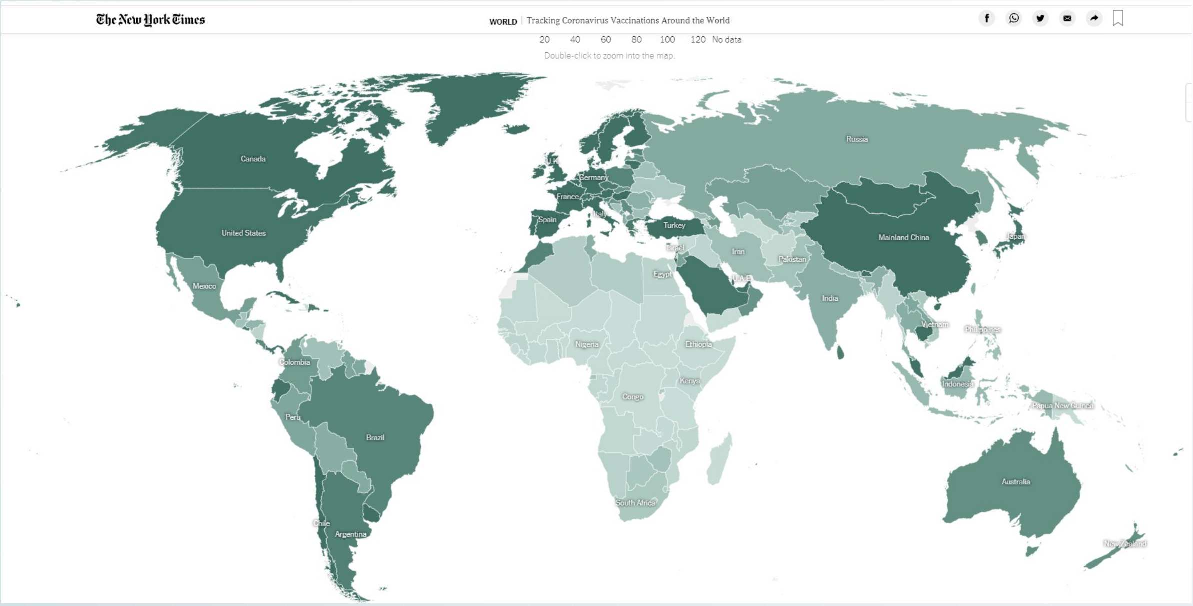
La efficacia rimane elevata contro le forme gravi
Da somministrare solo a gruppi ristretti
es Trapiantati
Nazioni «ricche» 60% vaccinati
Nazioni «povere» 2%

Trasmissione nei vaccinati
Disuguaglianze tra nazioni
Nuove varianti
Immunità non permanente
Comportamento sociale

Gli hot spot

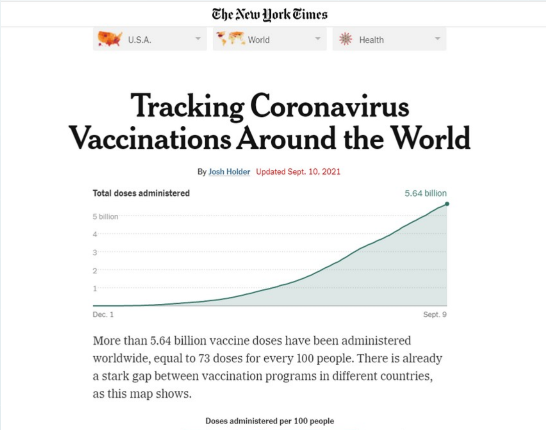

The New York Times WORLD | Coronavirus World Map: Tracking the Global Outbreak

+
−
Canada
United States
Mexico
Guatemala
Costa Rica
Venezuela
Colombia
Ecuador
Peru
Bolivia
Brazil
Paraguay
Argentina
Chile
Norway
Finland
Estonia
Belarus
France
Austria
Moldova
Spain
Albania
Malta
Turkey
Armenia
Cyprus
Israel
Iraq
Iran
Morocco
Algeria
Libya
Egypt
Senegal
Ivory Coast
Nigeria
Cameroon
Sudan
Ethiopia
Kenya
Angola
Mozambique
Madagascar
Botswana
South Africa
Russia
Kazakhstan
Mongolia
Kyrgyzstan
Afghanistan
Pakistan
U.A.E.
Nepal
India
Bangladesh
Mainland China
Japan
Thailand
Philippines
Sri Lanka
Maldives
Malaysia
Indonesia
Australia


The New York Times WORLD | Tracking Coronavirus Vaccinations Around the World

20
40
60
80
100
120
No data
Double-click to zoom into the map.
Canada
United States
Mexico
Colombia
Peru
Brazil
Chile
Argentina
Russia
Germany
France
Spain
Turkey
Iran
Egypt
Pakistan
Mainland China
Japan
India
Vietnam
Philippines
Indonesia
Papua New Guinea
Nigeria
Ethiopia
Kenya
Congo
South Africa
Australia
New Zealand

La Campagna vaccinale


The New York Times

U.S.A.
World
Health

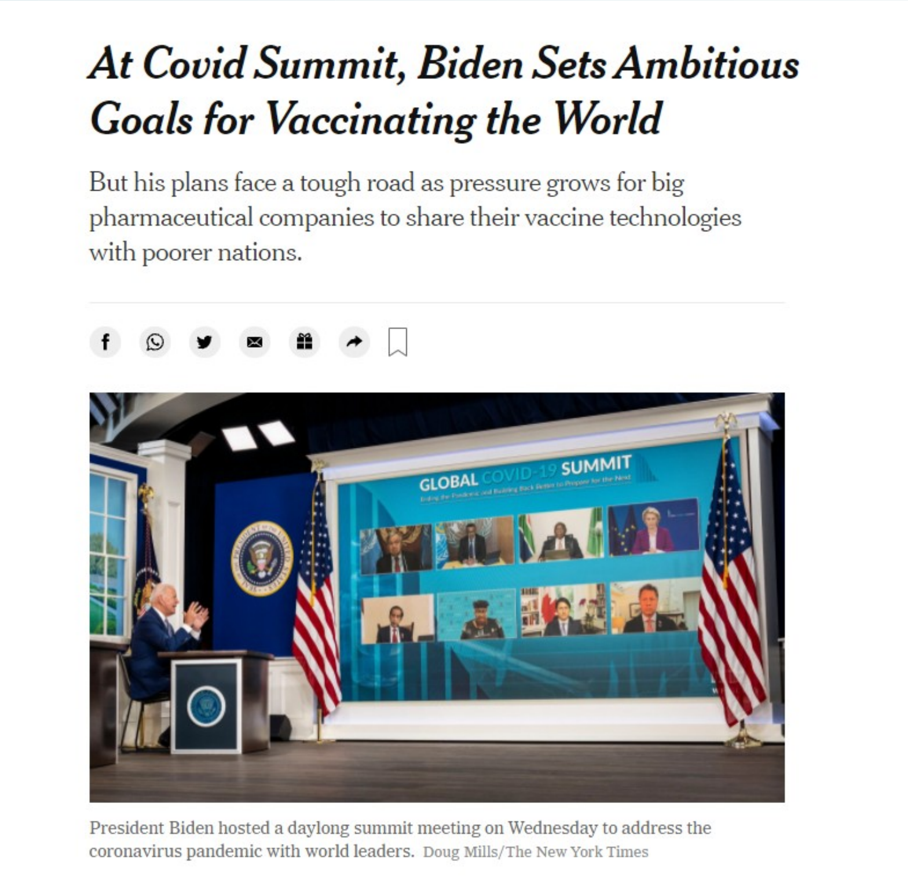
Tracking Coronavirus Vaccinations Around the World

By Josh Holder Updated Sept. 10, 2021

Total doses administered
5.64 billion
5 billion
4
3
2
1
Dec. 1
Sept. 9

More than 5.64 billion vaccine doses have been administered worldwide, equal to 73 doses for every 100 people. There is already a stark gap between vaccination programs in different countries, as this map shows.

Doses administered per 100 people



At Covid Summit, Biden Sets Ambitious Goals for Vaccinating the World

But his plans face a tough road as pressure grows for big pharmaceutical companies to share their vaccine technologies with poorer nations.

GLOBAL COVID-19 SUMMIT

President Biden hosted a daylong summit meeting on Wednesday to address the coronavirus pandemic with world leaders. Doug Mills/The New York Times

COVAX

CEPI

Gavi
The Vaccine Alliance

unicef

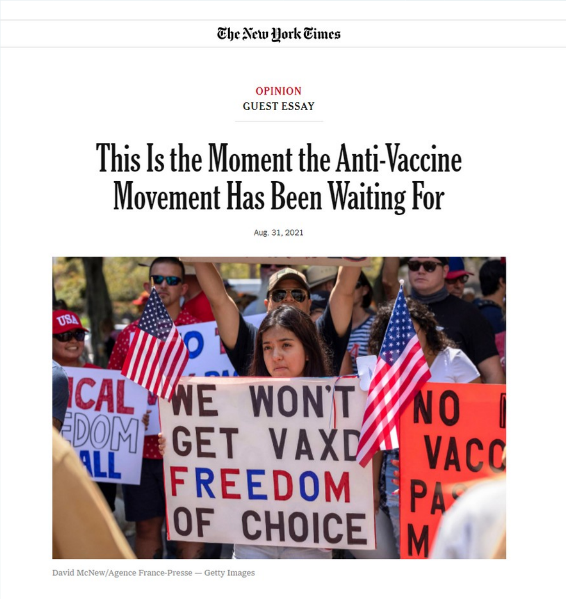
World Health Organization

COVAX
CEPI
Gavi
unicef
Emirates

Stati Uniti 1,1 MLD di dosi
Italia 45 MLN di dosi

The nature of the scientific process during a pandemic, with its unrelenting influx of new data and constantly evolving understanding of it, makes health communication incredibly challenging.

That reality, combined with botched messaging from public health agencies, has emboldened vaccine opponents.



The New York Times

OPINION
GUEST ESSAY

This Is the Moment the Anti-Vaccine Movement Has Been Waiting For

Aug. 31, 2021

David McNew/Agence France-Presse — Getty Images

Con una comunicazione trasparente ed onesta. Distinguendo quello che è scienza da quello che è ricerca: la scienza è un patrimonio di conoscenze grosso modo acquisite che non è più ragionevole mettere in discussione. La ricerca è una parte della scienza ancora oggetto di discussione con margini di incertezza che vanno comunicate con onestà.

La ipersemplificazione porta a messaggi contrastanti per cui le persone non si fidano.

I non vaccinati

Spaventati / confusi

Auto gestiti

Negazionisti

No Vax

- Ministro della salute
- Consulenti del ministro della salute
- Presidente Istituto superiore di Sanità
- Componenti Istituto superiore di Sanità
- Membri del Comitato Medico Scientifico Nazionale
- Governatori regionali
- Assessori regionali
- Membri Comitati Medico Scientifico Regionali
- Infettivologi/Virologi
- Pneumologi
- Pediatri
- Medici di Medicina di Base
- Rianimatori
- Epidemiologi
- Nefrologi riciclati in epidemiologi
- Veterinarie

Perché ci sono persone che scelgono di fidarsi di Facebook e non delle istituzioni? Come si può recuperare questa fiducia?

- Con una comunicazione trasparente ed onesta. Distinguendo quello che è scienza da quello che è ricerca: la scienza è un patrimonio di conoscenze grosso modo acquisite che non è più ragionevole mettere in discussione. La ricerca è una parte della scienza ancora oggetto di discussione con margini di incertezza che vanno comunicate con onestà.
- La ipersemplificazione porta a messaggi contrastanti per cui le persone non si fidano.

COVID 19 : il salto di specie

Animale

↓

Possibile

Uomo

↓

Virus Ebola

Altissima Infettività
Altissima Letalità

Trasmissione cutanea

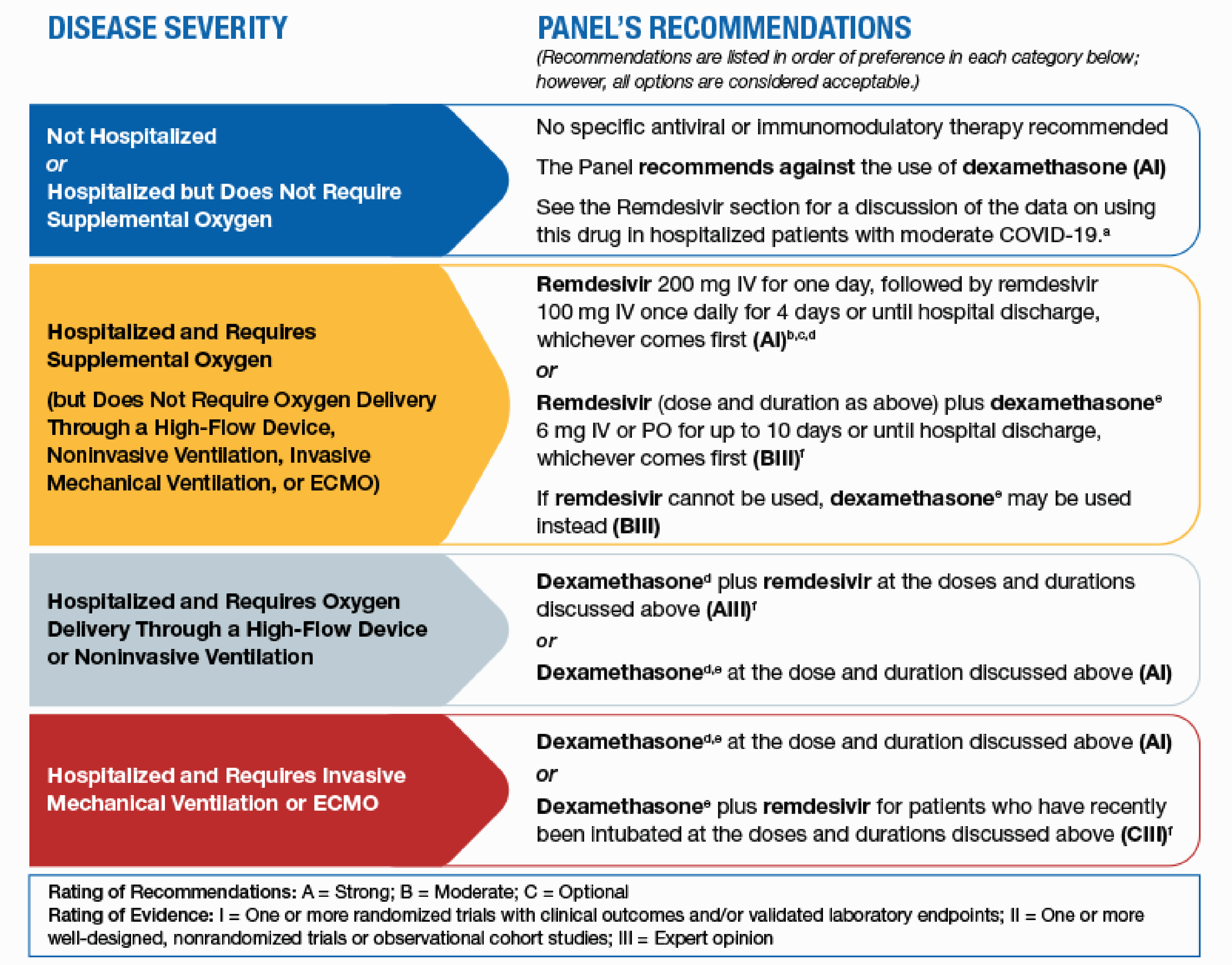
Molto Raro
SARS, MERS, Influenza Suina

Bassa Infettività
Alta Letalità

Trasmissione respiratoria

Uomo

COVID-19 Treatment Guidelines Panel-NIH



DISEASE SEVERITY	PANEL'S RECOMMENDATIONS *(Recommendations are listed in order of preference in each category below; however, all options are considered acceptable.)*
Not Hospitalized *or* **Hospitalized but Does Not Require Supplemental Oxygen**	No specific antiviral or immunomodulatory therapy recommended The Panel **recommends against** the use of **dexamethasone (AI)** See the Remdesivir section for a discussion of the data on using this drug in hospitalized patients with moderate COVID-19.[a]
Hospitalized and Requires Supplemental Oxygen **(but Does Not Require Oxygen Delivery Through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or ECMO)**	**Remdesivir** 200 mg IV for one day, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge, whichever comes first **(AI)**[b,c,d] *or* **Remdesivir** (dose and duration as above) plus **dexamethasone**[e] 6 mg IV or PO for up to 10 days or until hospital discharge, whichever comes first **(BIII)**[f] If **remdesivir** cannot be used, **dexamethasone**[e] may be used instead **(BIII)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	**Dexamethasone**[d] plus **remdesivir** at the doses and durations discussed above **(AIII)**[f] *or* **Dexamethasone**[d,e] at the dose and duration discussed above **(AI)**
Hospitalized and Requires Invasive Mechanical Ventilation or ECMO	**Dexamethasone**[d,e] at the dose and duration discussed above **(AI)** *or* **Dexamethasone**[e] plus **remdesivir** for patients who have recently been intubated at the doses and durations discussed above **(CIII)**[f]

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies; III = Expert opinion

a) The Panel finds the available data insufficient to recommend either for or against routine treatment with remdesivir for all hospitalized patients with moderate COVID-19. However, the Panel recognizes there may be situations in which a clinician judges that remdesivir is an appropriate treatment for a hospitalized patient with moderate disease (e.g., a person who is at a particularly high risk for clinical deterioration).

b) Remdesivir therapy may be extended to up to 10 days if no substantial clinical improvement is seen at Day 5.

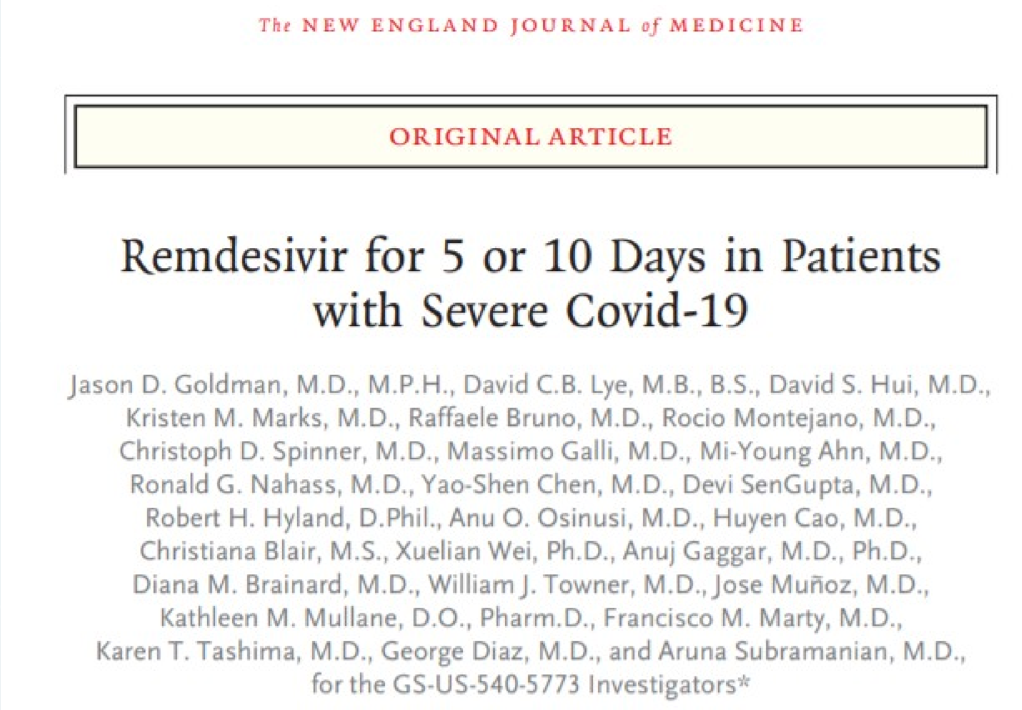
c) The Panel recognizes there are theoretical rationale for adding dexamethasone to remdesivir in patients with rapidly progressing COVID-19.

d) For patients who initially received remdesivir monotherapy and progressed to requiring high-flow oxygen supplementation or noninvasive ventilation, dexamethasone should be initiated and remdesivir should be continued until the treatment course is completed.

e) If dexamethasone is not available, an alternative corticosteroid such as prednisone, methylprednisolone, or hydrocortisone can be used (BIII).

f) The combination of remdesivir and dexamethasone has not been studied in clinical trials; however, there are theoretical reasons for combining these drugs.

Remdesivir



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for 5 or 10 Days in Patients with Severe Covid-19

Jason D. Goldman, M.D., M.P.H., David C.B. Lye, M.B., B.S., David S. Hui, M.D., Kristen M. Marks, M.D., Raffaele Bruno, M.D., Rocio Montejano, M.D., Christoph D. Spinner, M.D., Massimo Galli, M.D., Mi-Young Ahn, M.D., Ronald G. Nahass, M.D., Yao-Shen Chen, M.D., Devi SenGupta, M.D., Robert H. Hyland, D.Phil., Anu O. Osinusi, M.D., Huyen Cao, M.D., Christiana Blair, M.S., Xuelian Wei, Ph.D., Anuj Gaggar, M.D., Ph.D., Diana M. Brainard, M.D., William J. Towner, M.D., Jose Muñoz, M.D., Kathleen M. Mullane, D.O., Pharm.D., Francisco M. Marty, M.D., Karen T. Tashima, M.D., George Diaz, M.D., and Aruna Subramanian, M.D., for the GS-US-540-5773 Investigators*

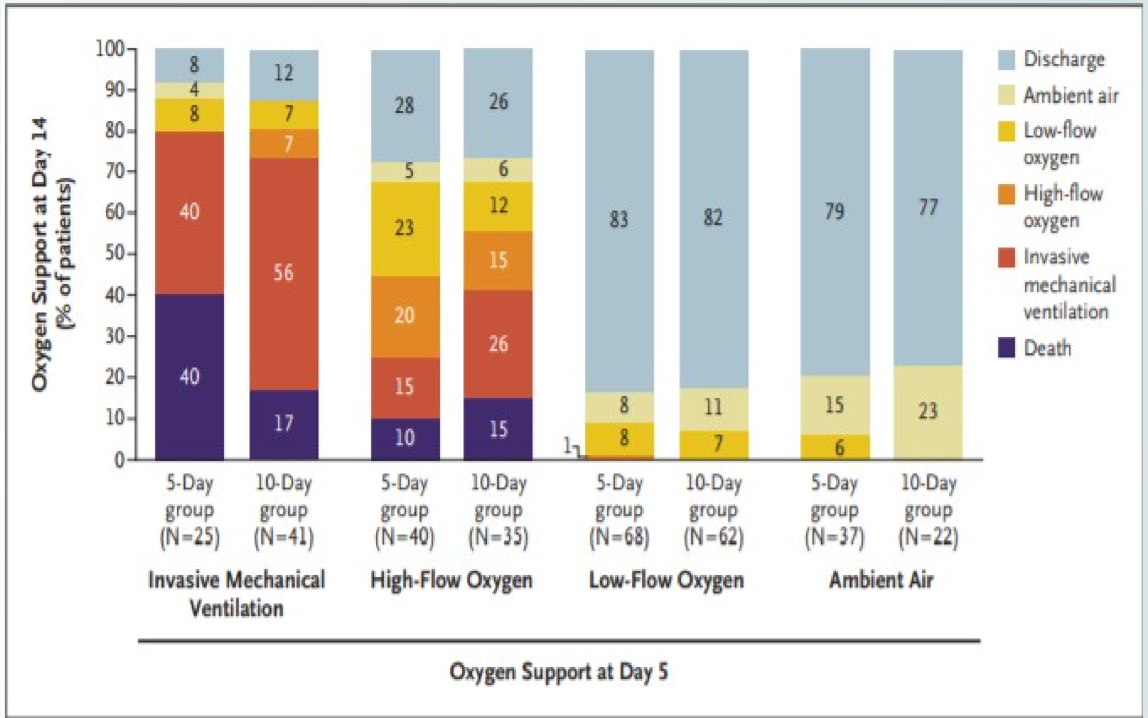
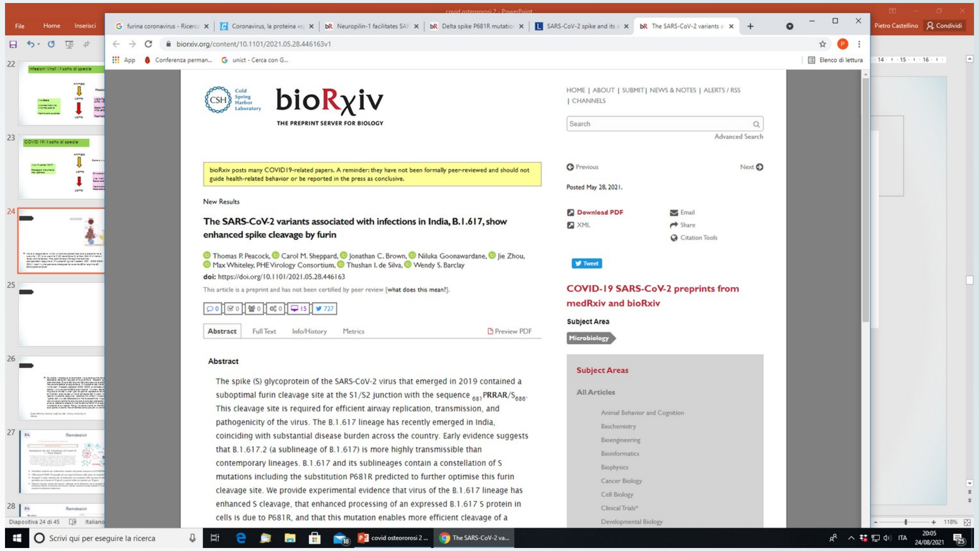


Figure 2. Oxygen Support on Day 14 According to Oxygen Support on Day 5.

Shown is the distribution of oxygen-support status on day 14 for the 5-day and 10-day treatment groups according to oxygen-support status at day 5 of therapy. Percentages are based on patients with both day 5 and day 14 oxygen-support data available and exclude those with missing oxygen-support data for day 14. Oxygen-support status is derived from the clinical status according to the seven-point ordinal scale, as follows: 1, death; 2, receiving invasive mechanical ventilation; 3, receiving high-flow oxygen; 4, receiving low-flow oxygen; 5 or 6, breathing ambient air; and 7, discharge. Data on high-flow oxygen were missing for 1 patient in the 10-day group; data on low-flow oxygen were missing for 3 patients in the 5-day group and 6 patients in the 10-day group, and data on ambient air were missing for 3 patients in the 5-day group.

Confronto con studio clinico randomizzato in cui la somministrazione di remdesivir per 5 giorni mostra più benefici che la somministrazione per 10 giorni.


bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

New Results

The SARS-CoV-2 variants associated with infections in India, B.1.617, show enhanced spike cleavage by furin

Thomas P. Peacock, Carol M. Sheppard, Jonathan C. Brown, Niluka Goonawardane, Jie Zhou, Max Whiteley, PHE Virology Consortium, Thushan I. de Silva, Wendy S. Barclay

doi: https://doi.org/10.1101/2021.05.28.446163

This article is a preprint and has not been certified by peer review [what does this mean?].

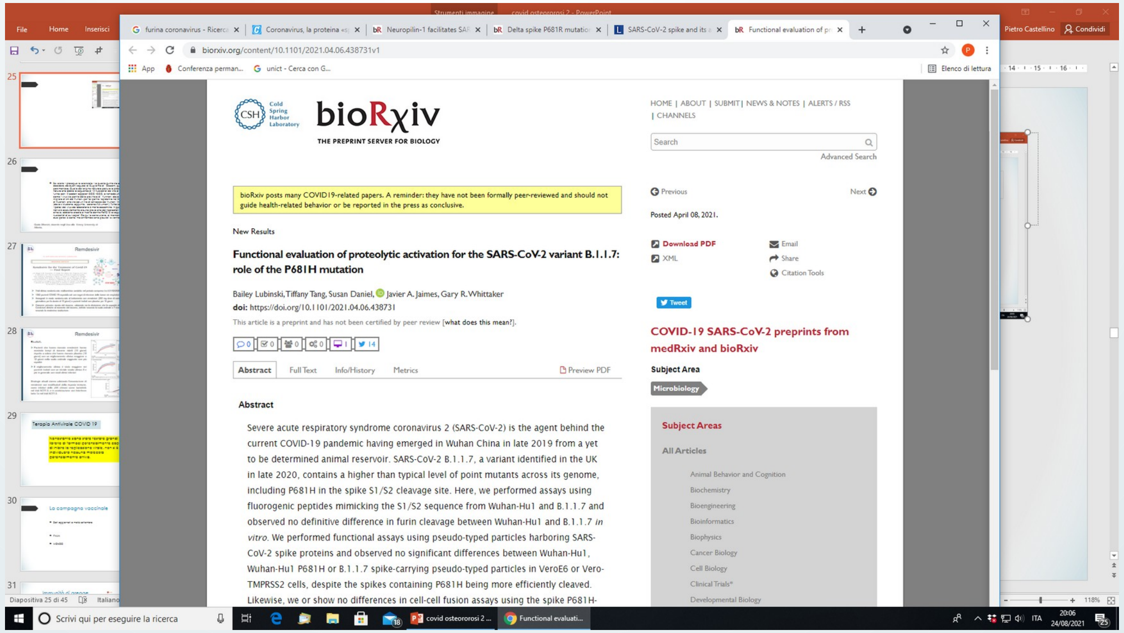
Posted May 28, 2021.

COVID-19 SARS-CoV-2 preprints from medRxiv and bioRxiv

Subject Area: Microbiology

Abstract

The spike (S) glycoprotein of the SARS-CoV-2 virus that emerged in 2019 contained a suboptimal furin cleavage site at the S1/S2 junction with the sequence $_{681}$PRRAR/S$_{686}$. This cleavage site is required for efficient airway replication, transmission, and pathogenicity of the virus. The B.1.617 lineage has recently emerged in India, coinciding with substantial disease burden across the country. Early evidence suggests that B.1.617.2 (a sublineage of B.1.617) is more highly transmissible than contemporary lineages. B.1.617 and its sublineages contain a constellation of S mutations including the substitution P681R predicted to further optimise this furin cleavage site. We provide experimental evidence that virus of the B.1.617 lineage has enhanced S cleavage, that enhanced processing of an expressed B.1.617 S protein in cells is due to P681R, and that this mutation enables more efficient cleavage of a


bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

New Results

Functional evaluation of proteolytic activation for the SARS-CoV-2 variant B.1.1.7: role of the P681H mutation

Bailey Lubinski, Tiffany Tang, Susan Daniel, Javier A. Jaimes, Gary R. Whittaker

doi: https://doi.org/10.1101/2021.04.06.438731

This article is a preprint and has not been certified by peer review [what does this mean?].

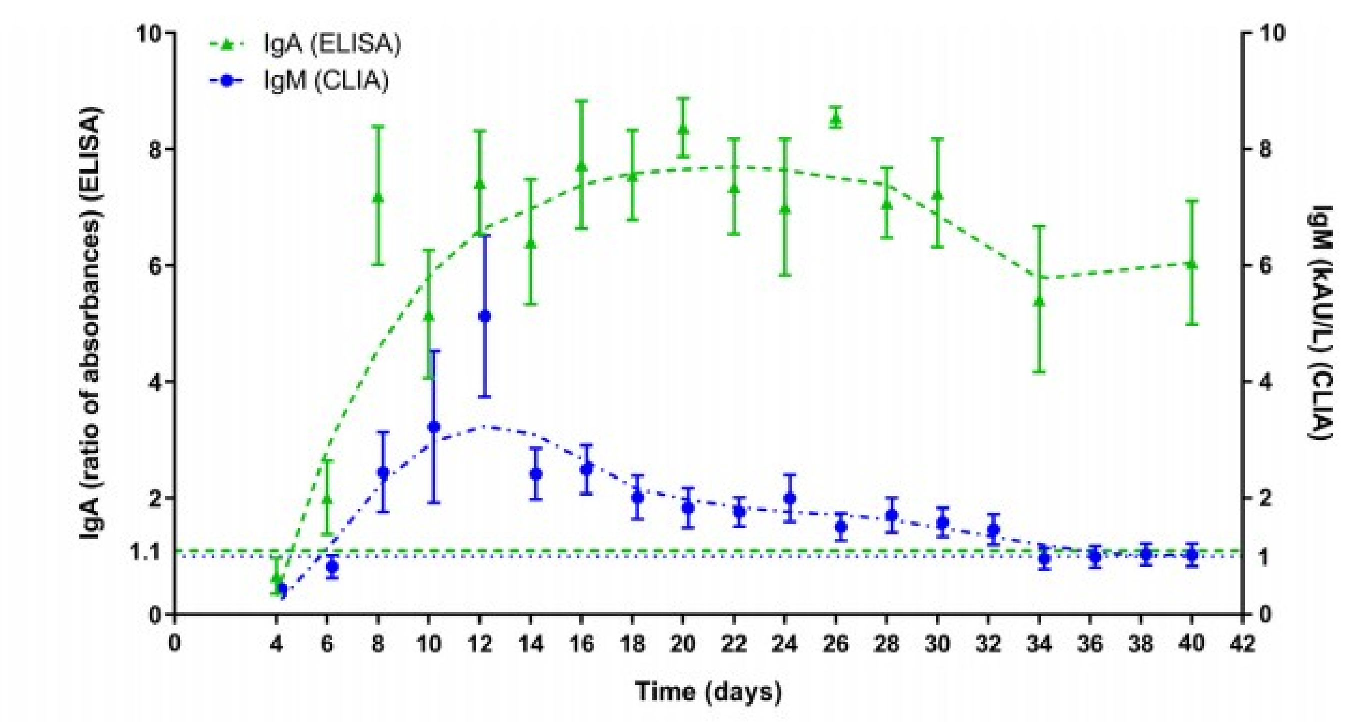
Posted April 08, 2021.

COVID-19 SARS-CoV-2 preprints from medRxiv and bioRxiv

Subject Area: Microbiology

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the agent behind the current COVID-19 pandemic having emerged in Wuhan China in late 2019 from a yet to be determined animal reservoir. SARS-CoV-2 B.1.1.7, a variant identified in the UK in late 2020, contains a higher than typical level of point mutants across its genome, including P681H in the spike S1/S2 cleavage site. Here, we performed assays using fluorogenic peptides mimicking the S1/S2 sequence from Wuhan-Hu1 and B.1.1.7 and observed no definitive difference in furin cleavage between Wuhan-Hu1 and B.1.1.7 *in vitro*. We performed functional assays using pseudo-typed particles harboring SARS-CoV-2 spike proteins and observed no significant differences between Wuhan-Hu1, Wuhan-Hu1 P681H or B.1.1.7 spike-carrying pseudo-typed particles in VeroE6 or Vero-TMPRSS2 cells, despite the spikes containing P681H being more efficiently cleaved. Likewise, we or show no differences in cell-cell fusion assays using the spike P681H-



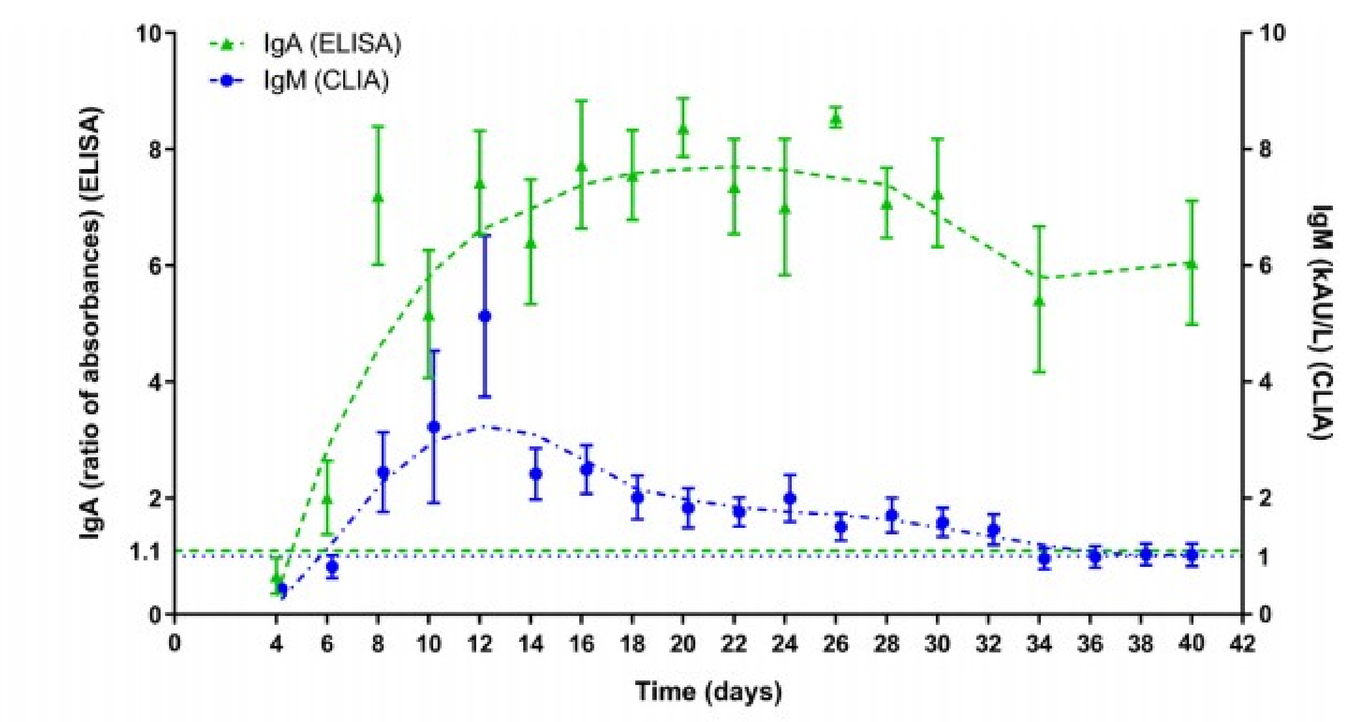
Cinetica anticorpi **IgA ed IgM** anti-SARS-COV-2 in infezione confermata tramite rRT-PCR

Studiata la risposta anticorpale per **6 settimane** dall'insorgenza dei sintomi

Cinetica IgA testata in 19 pazienti, cinetica IgM in 51 pazienti

La risposta delle IgA appare e cresce precocemente, con picco a 20-22 giorni, ed è più forte e più persistente (permanenza per 38 giorni di follow-up) rispetto alla risposta delle IgM (picco 10-12 giorni, riduzione titolo dopo 18 giorni).

IgA-Ab response to spike glycoprotein of SARS-CoV-2 in patients with COVID-19: A longitudinal study
Padoan A, Sciacovelli L, Basso D, et al [published online ahead of print, 2020 Apr 25]. Clin Chim Acta. 2020



Cinetica anticorpi **IgA ed IgM** anti-SARS-COV-2 in infezione confermata tramite rRT-PCR

Studiata la risposta anticorpale per **6 settimane** dall'insorgenza dei sintomi

Cinetica IgA testata in 19 pazienti, cinetica IgM in 51 pazienti

La risposta delle IgA appare e cresce precocemente, con picco a 20-22 giorni, ed è più forte e più persistente (permanenza per 38 giorni di follow-up) rispetto alla risposta delle IgM (picco 10-12 giorni, riduzione titolo dopo 18 giorni).

IgA-Ab response to spike glycoprotein of SARS-CoV-2 in patients with COVID-19: A longitudinal study
Padoan A, Sciacovelli L, Basso D, et al [published online ahead of print, 2020 Apr 25]. Clin Chim Acta. 2020

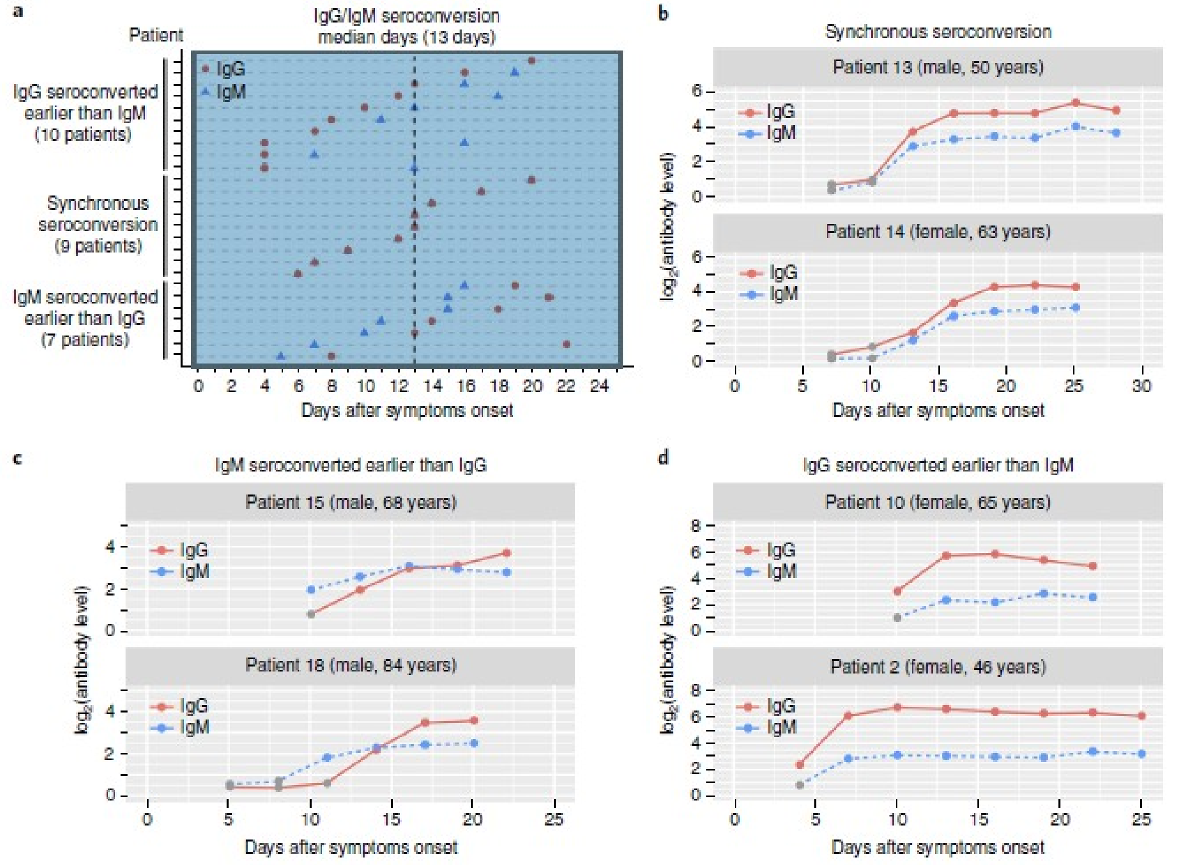


Fig. 2 | Seroconversion time of the antibodies against SARS-CoV-2. a, Seroconversion type of 26 patients who were initially seronegative during the observation period. The days of seroconversion for each patient are plotted. **b–d**, Six representative examples of the three seroconversion type: synchronous seroconversion of IgG and IgM (**b**), IgM seroconversion earlier than that of IgG (**c**) and IgM seroconversion later than that of IgG (**c**).

Antibody responses to SARS-CoV-2 in patients with COVID-19
Long et Al. Nature 29 Apr 2020

Seguita sieroconversione in 26 pazienti.
Mediana sieroconversione sia per IgG che per IgM: **13 giorni** dall'inizio dei sintomi.

3 modelli di sieroconversione

- sieroconversione **sincrona** di IgG e IgM per 9 pazienti su 26;
- sieroconversione **prima delle IgM** e poi delle IgG per 7 pazienti su 26;
- sieroconversione **prima delle IgG** e poi delle IgM per 10 pazienti su 26.

Correlati di Protezione

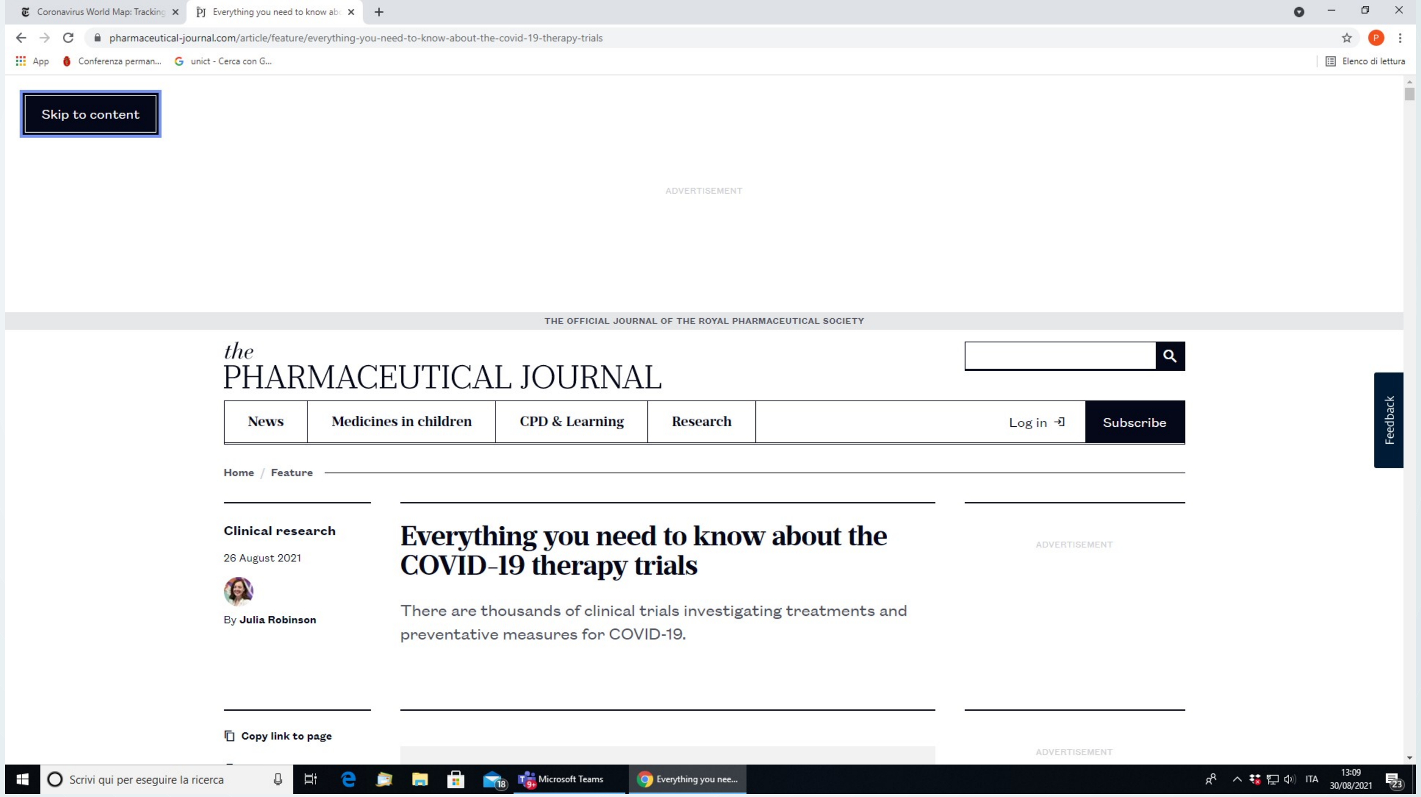
- Epitopi Lineari : Risposta T mediata
- Epitopi Conformazionali : Risposta anticorpale

Non è chiaro quale parametro biologico sia indicativo di una protezione

Teams around the world are racing to determine what level of neutralizing antibodies or another immune marker is most closely associated with a vaccine’s effectiveness. They’re seeking what’s known as a correlate of protection.

Nature , Agosto 2021

https://doi.org/10.1038/d41586-021-02158-6



Coronavirus World Map: Tracking
Everything you need to know ab
pharmaceutical-journal.com/article/feature/everything-you-need-to-know-about-the-covid-19-therapy-trials
App
Conferenza perman...
unict - Cerca con G...
Elenco di lettura
Skip to content
ADVERTISEMENT
THE OFFICIAL JOURNAL OF THE ROYAL PHARMACEUTICAL SOCIETY
the PHARMACEUTICAL JOURNAL
News
Medicines in children
CPD & Learning
Research
Log in
Subscribe
Feedback
Home / Feature
Copy link to page
ADVERTISEMENT
ADVERTISEMENT
Scrivi qui per eseguire la ricerca
Microsoft Teams
Everything you nee...
ITA
13:09
30/08/2021

Clinical research

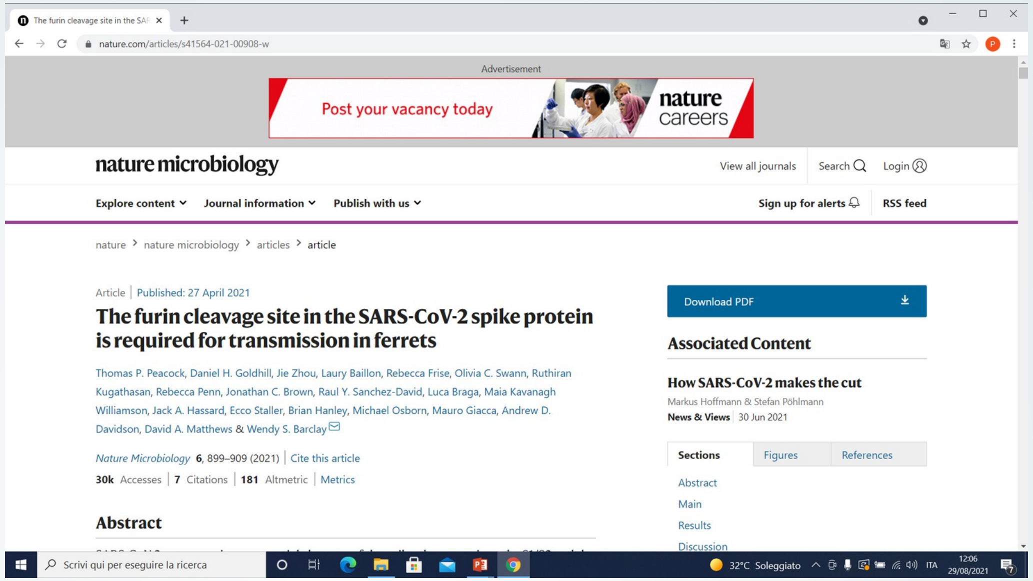
26 August 2021

By **Julia Robinson**

Everything you need to know about the COVID-19 therapy trials

There are thousands of clinical trials investigating treatments and preventative measures for COVID-19.

Variante	Escape Vaccinale	Fitness	Diffusione
Inglese	+	alta	media
Sud Africana	+++	bassa	limitata
Indiana	++	altissima	elevatissima
Peruviana	+	alta	limitata


The furin cleavage site in the SAR
nature.com/articles/s41564-021-00908-w
Advertisement
Post your vacancy today
nature careers
View all journals
Search
Login
Explore content
Journal information
Publish with us
Sign up for alerts
RSS feed
Download PDF
Sections
Figures
References
Abstract
Main
Results
Discussion
Scrivi qui per eseguire la ricerca
32°C Soleggiato
ITA
12:06
29/08/2021

nature microbiology

nature › nature microbiology › articles › article

Article | Published: 27 April 2021

The furin cleavage site in the SARS-CoV-2 spike protein is required for transmission in ferrets

Thomas P. Peacock, Daniel H. Goldhill, Jie Zhou, Laury Baillon, Rebecca Frise, Olivia C. Swann, Ruthiran Kugathasan, Rebecca Penn, Jonathan C. Brown, Raul Y. Sanchez-David, Luca Braga, Maia Kavanagh Williamson, Jack A. Hassard, Ecco Staller, Brian Hanley, Michael Osborn, Mauro Giacca, Andrew D. Davidson, David A. Matthews & Wendy S. Barclay

Nature Microbiology **6**, 899–909 (2021) | Cite this article

30k Accesses | **7** Citations | **181** Altmetric | Metrics

Abstract

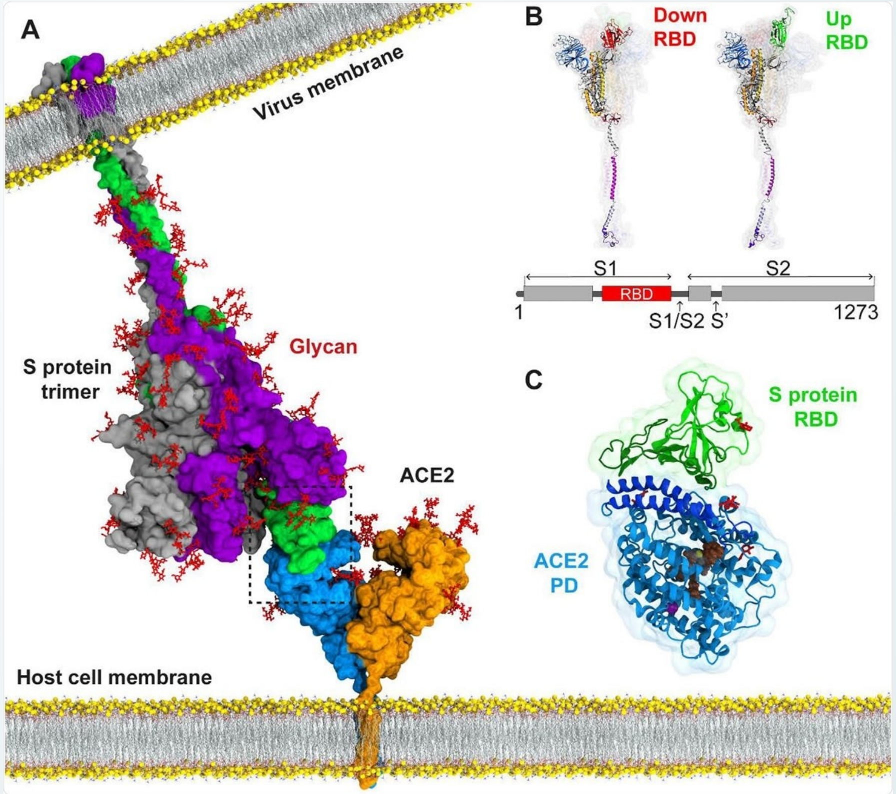
Associated Content

How SARS-CoV-2 makes the cut

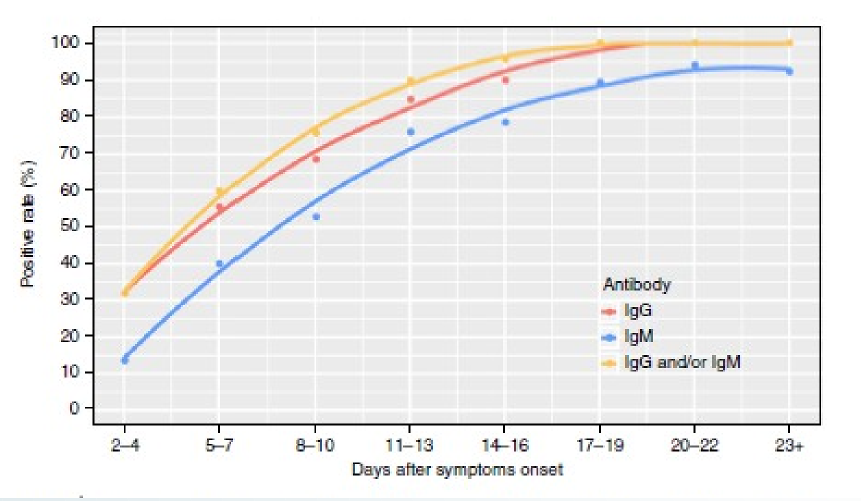
Markus Hoffmann & Stefan Pöhlmann

News & Views | 30 Jun 2021

Il recettore


A
Virus membrane
Glycan
S protein trimer
ACE2
Host cell membrane
B
Down RBD
Up RBD
S1
S2
RBD
1
S1/S2
S'
1273
C
S protein RBD
ACE2 PD

Risposta anticorpale

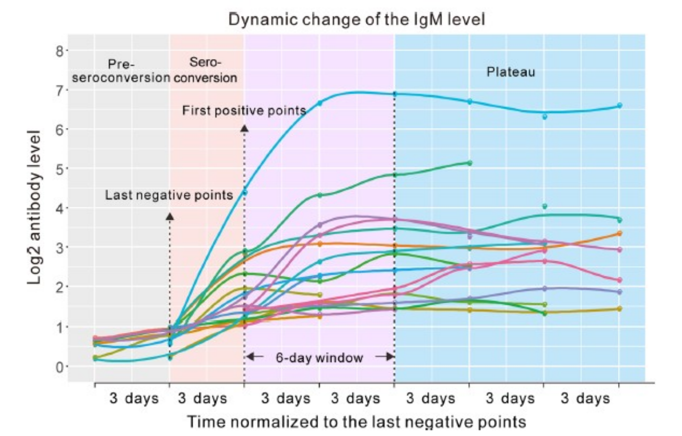


285 pazienti, tutti positivi:

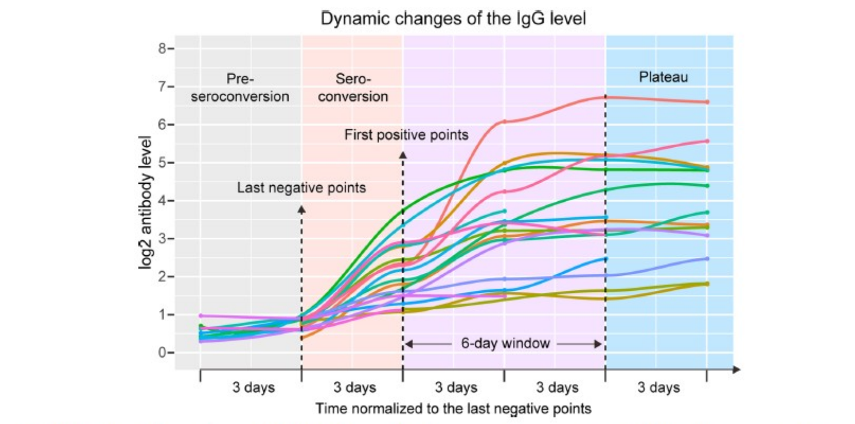
- alle IgG entro **19 giorni** dall'esordio dei sintomi;
- alle IgM entro **20-22 giorni** dall'esordio dei sintomi.

Entrambi i titoli di IgG e IgM raggiungono il **plateau entro 6 giorni** dalla sieroconversione.

Antibody responses to SARS-CoV-2 in patients with COVID-19
Long et Al. Nature 29 Apr 2020



Extended Data Fig. 4 | Dynamic changes of the SARS-CoV-2 specific IgM. Time course of the virus-specific IgM level in 20 patients experienced IgM titer plateau. IgM in each patient reached plateau within 6 days since IgM became positive.



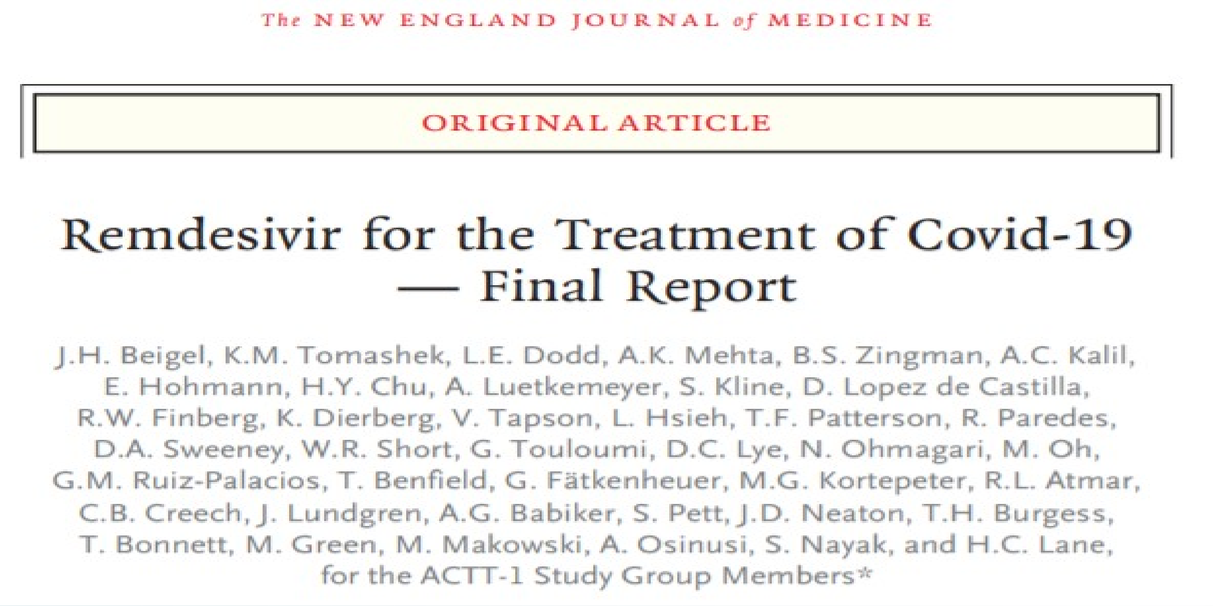
Extended Data Fig. 3 | Dynamic changes of the SARS-CoV-2 specific IgG. Time course of the virus-specific IgG level in 19 patients experienced IgG titer plateau. IgG in each patient reached plateau within 6 days since IgG became positive.

Ingresso per endocitosi

- Se volete - prosegue lo scienziato - a questo punto sta ad ognuno di noi decidere, da buoni seguaci di Guglielmo di Occam, quale ipotesi sia più parsimoniosa. Quella dell'origine naturale postula la presenza di un virus in natura che abbia la sequenza di 12 nucleotidi del sito di clivaggio per la furina con i 2 codoni appaiati CGG-CGG, e richiede una spiegazione di come il virus sia partito dalla provincia di Yunnan, dove stanno i pipistrelli a migliaia di km da Wuhan, per far partire l'epidemia nel mercato del pesce di Huanan, che sta ad un tiro di schioppo dal Wuhan Institute of Virology (dove si studiano, appunto, i coronavirus umani). Tuttavia nemmeno l'ipotesi del virus da laboratorio è molto occamista, in quanto al momento non c'è assolutamente alcuna prova che dei ricercatori, a Wuhan o altrove, abbiano creato e inserito dentro RaTG13 la sequenza di 12 nucleotidi di cui sopra". Da qui la conclusione: al momento nessuna delle due ipotesi è certa, ma entrambe sono plausibili e vanno indagate.

Guido Silvestri, docente negli Usa alla Emory University di Atlanta,

Remdesivir

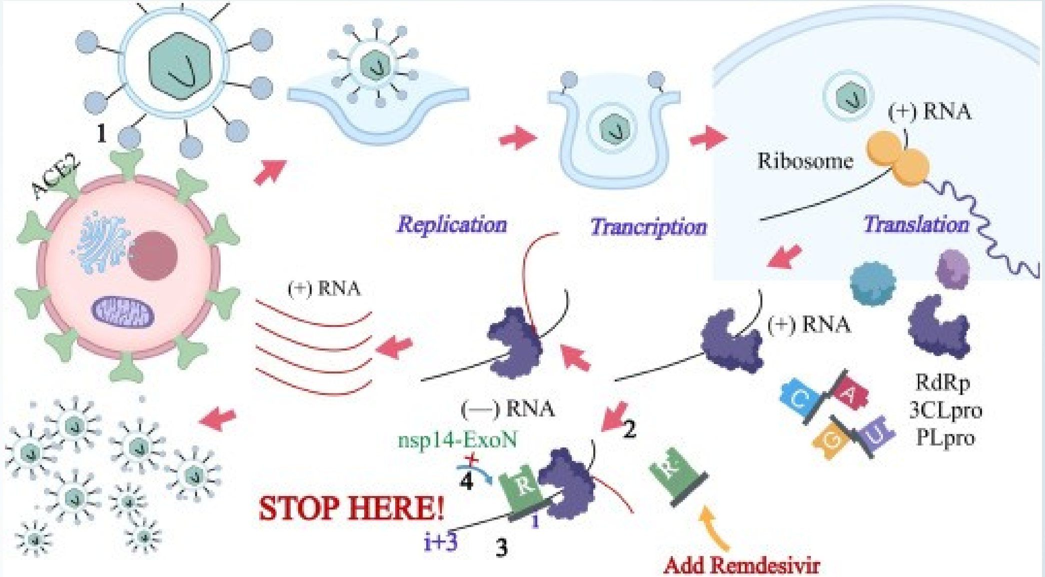


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

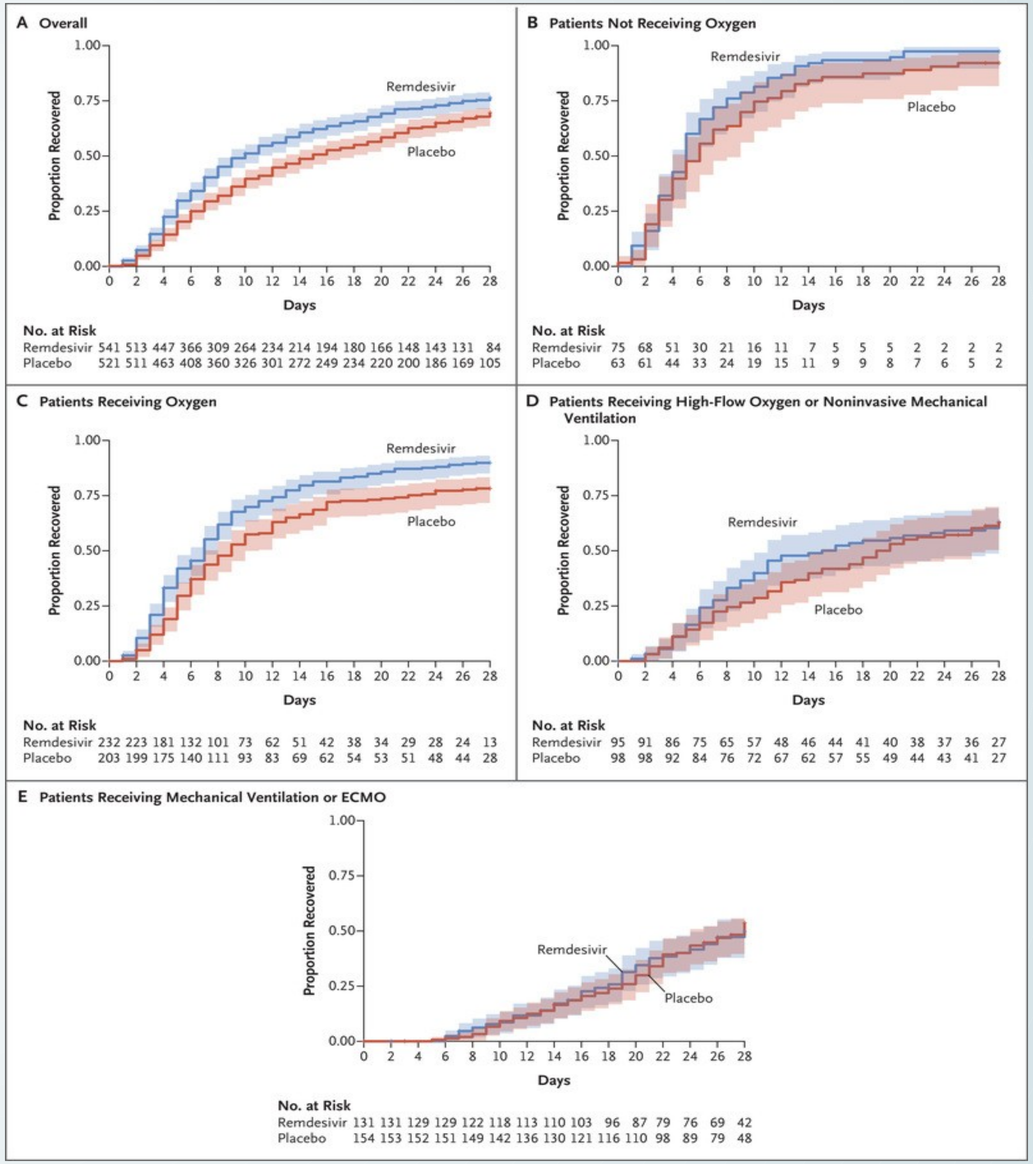

1
ACE2
Replication
Trancription
Translation
(+) RNA
Ribosome
(+) RNA
(+) RNA
RdRp
3CLpro
PLpro
C
A
G
U
(—) RNA
nsp14-ExoN
2
4
R
R
STOP HERE!
i+3
3
1
Add Remdesivir

- Trial clinico randomizzato multicentrico condotto nel periodo compreso tra il 21/02/2020 e il 19/04/2020
- 1062 pazienti COVID-19 ospedalizzati con segni di infezione delle basse vie respiratorie e malattia severa
- Assegnati in modo randomizzato al trattamento con remdesivir (200 mg dose di carico e 100 mg come dose giornaliera per la durata di 10 giorni) e pazienti trattati con placebo per 10 giorni
- Outcome primario: durata del ricovero, valutando sia la dimissione che la capacità di controllo dell’infezione . Condizioni cliniche al momento del ricovero, definite secondo la scala ordinale a 7 stadi, e variabilità a 15 giorni secondo la medesima stadiazione.

Remdesivir

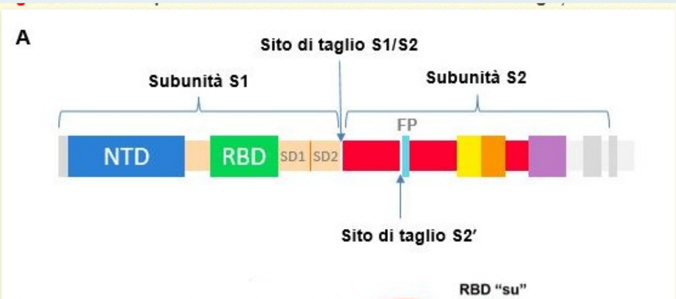
Risultati:

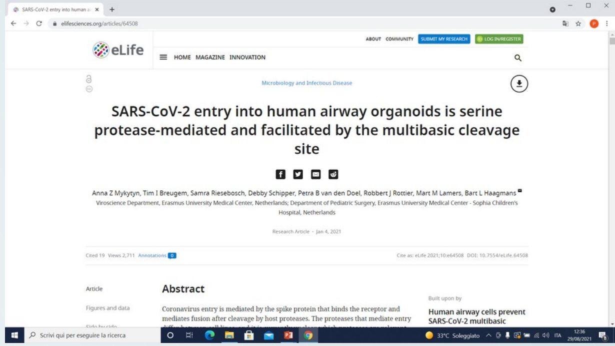
- Pazienti che hanno ricevuto remdesivir hanno mostrato tempi di ricovero ridotti (10 giorni) rispetto a coloro che hanno ricevuto placebo (15 giorni) con un miglioramento clinico maggiore a 15 giorni nella scala ordinale raggiunto con più rapidità
- Il miglioramento clinico è stato maggiore nei pazienti trattati con un iniziale stadio clinico 5 e più in generale con stadi clinici inferiori



Strategie attuali stanno valutando l’associazione di remdesivir con modificatorI della risposta immune, come inibitori delle JAK chinasi come baricitinib nel trial ACTT-2, e in combinazione con Interferon beta-1a nel trial ACTT-3.

La proteina spike presenta un sito di clivaggio per la proteasi FURINA

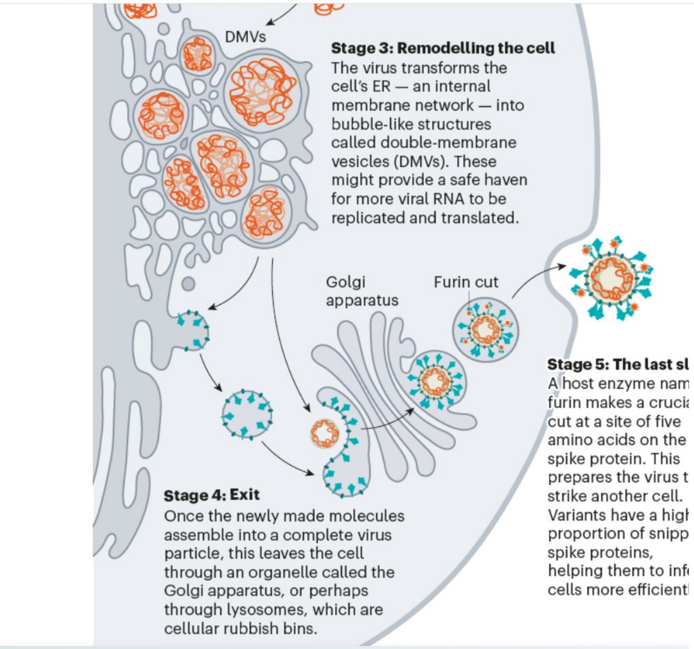

A
Sito di taglio S1/S2
Subunità S1
Subunità S2
FP
NTD
RBD
SD1
SD2
Sito di taglio S2'
RBD "su"


eLife
HOME MAGAZINE INNOVATION
Microbiology and Infectious Disease

SARS-CoV-2 entry into human airway organoids is serine protease-mediated and facilitated by the multibasic cleavage site

Anna Z Mykytyn, Tim I Breugem, Samra Riesebosch, Debby Schipper, Petra B van den Doel, Robbert J Rottier, Mart M Lamers, Bart L Haagmans

Abstract


DMVs
Golgi apparatus
Furin cut

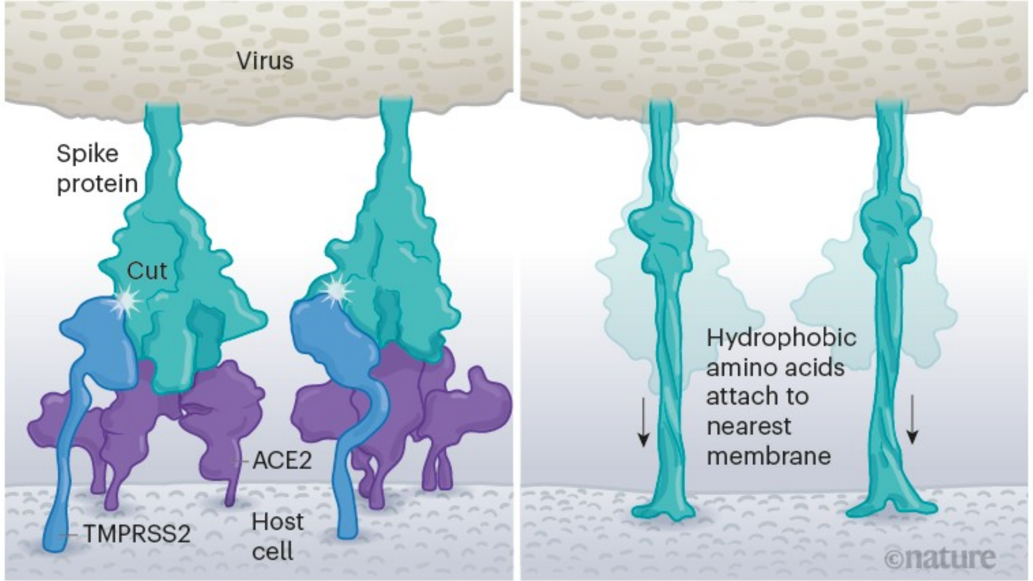
Stage 3: Remodelling the cell
The virus transforms the cell's ER — an internal membrane network — into bubble-like structures called double-membrane vesicles (DMVs). These might provide a safe haven for more viral RNA to be replicated and translated.

Stage 4: Exit
Once the newly made molecules assemble into a complete virus particle, this leaves the cell through an organelle called the Golgi apparatus, or perhaps through lysosomes, which are cellular rubbish bins.

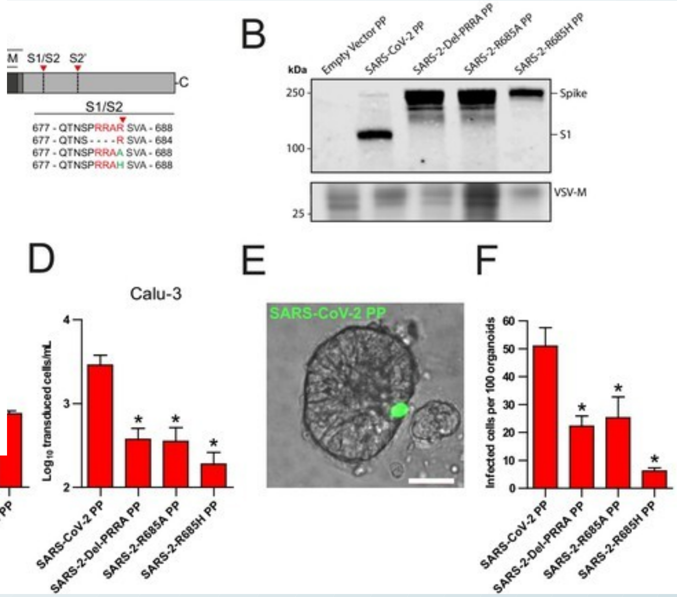
Stage 5: The last st
A host enzyme nam furin makes a crucia cut at a site of five amino acids on the spike protein. This prepares the virus t strike another cell. Variants have a high proportion of snipp spike proteins, helping them to inf cells more efficient

VIRAL ENTRY UP CLOSE

Virus and host-cell membranes fuse after the TMPRSS2 enzyme cuts a SARS-CoV-2 spike protein. This exposes hydrophobic amino acids in the spike that rapidly embed themselves into the nearest membrane — that of the host cell.


Virus
Spike protein
Cut
ACE2
TMPRSS2
Host cell
Hydrophobic amino acids attach to nearest membrane
©nature

Source: Janet Iwasa, Univ. Utah; Graphic: Nik Spencer/*Nature*



Sito di clivaggio della furina (un en subunità 1 (S1) e la subunità 2 (S2) residui amino-acidici, Prra (prolin corrispondenti appunto a 12 nucle CGG-GCA), inseriti in una posizione strategica tra la serina 680 e l'arginina 681 della proteina Spike.

Terapia Antivirale COVID 19

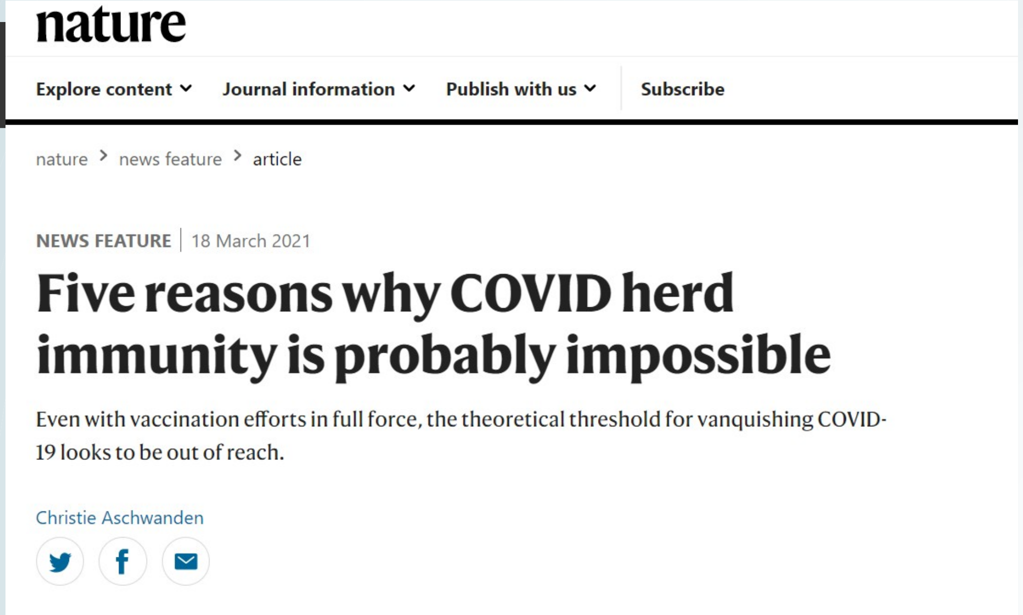
Nonostante siano state testate grandi librerie di farmaci potenzialmente capaci di inibire la replicazione virale, non si è individuato nessuna molecola potenzialmente attiva.

La campagna vaccinale

- Dati aggiornati a metà settembre

- ITALIA

- MONDO


nature
Explore content
Journal information
Publish with us
Subscribe
nature > news feature > article

NEWS FEATURE | 18 March 2021

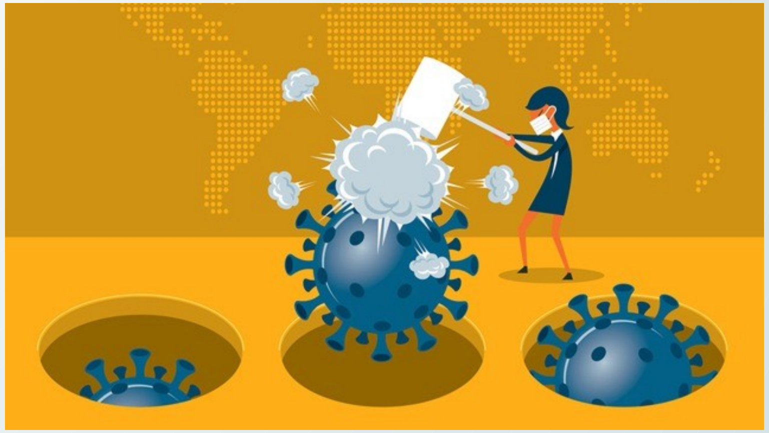
Five reasons why COVID herd immunity is probably impossible

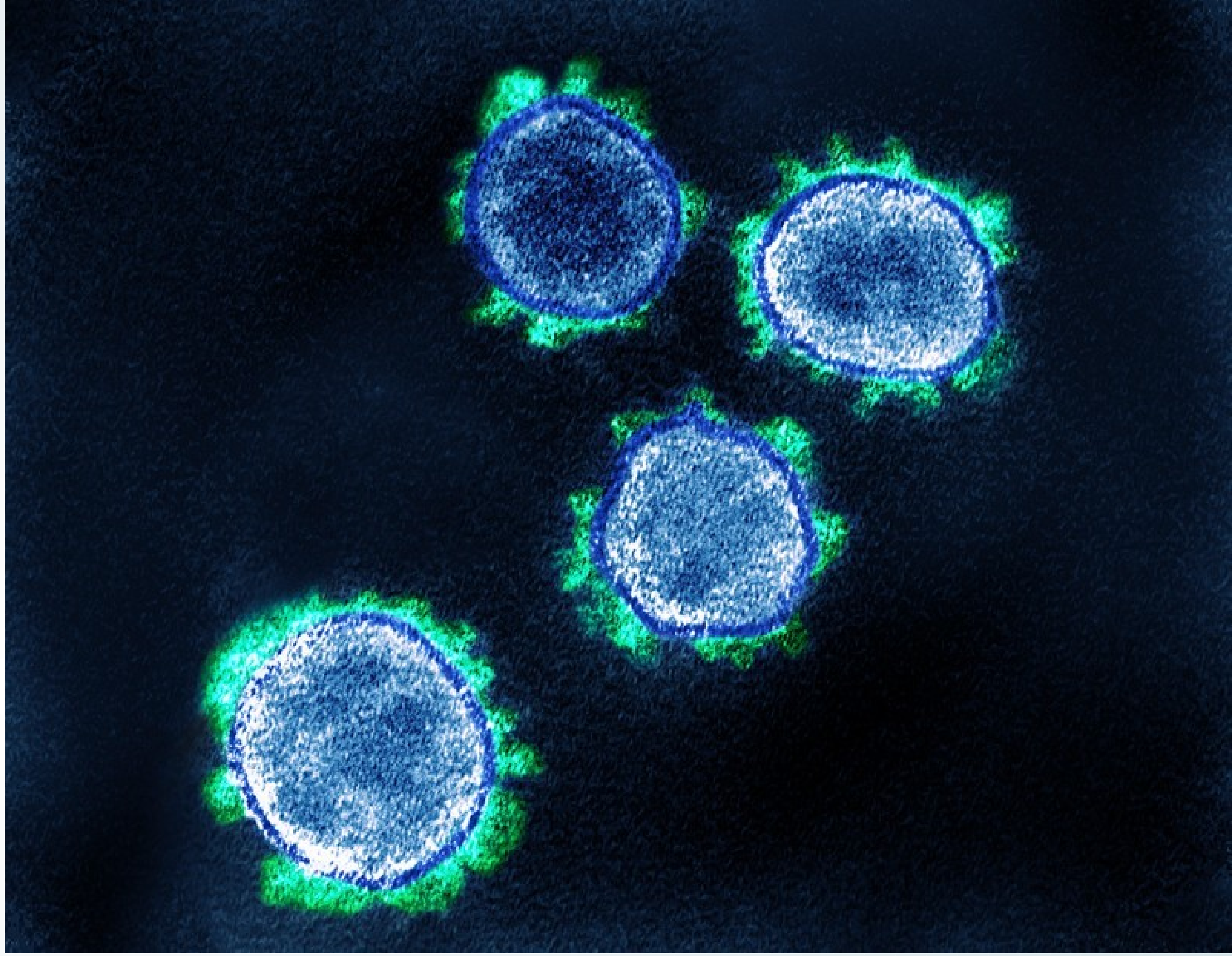
Even with vaccination efforts in full force, the theoretical threshold for vanquishing COVID-19 looks to be out of reach.

Christie Aschwanden

Trasmissione nei vaccinati
Disuguaglianze tra nazioni
Nuove varianti
Immunità non permanente
Comportamento sociale

The whack-a-mole Strategy





Il Virus

Correlati di Protezione: Vaccino Pfitzer BionTec

- A 14 gg dalla prima dose:
- Risposta anticorpale molto bassa o nulla
- Protezione clinicamente rilevante

Come definire nel tempo
la necessità di una terza dose?

Livelli anticorpali totali?
Anticorpi neutralizzanti?
Dati di popolazione?
Altro??