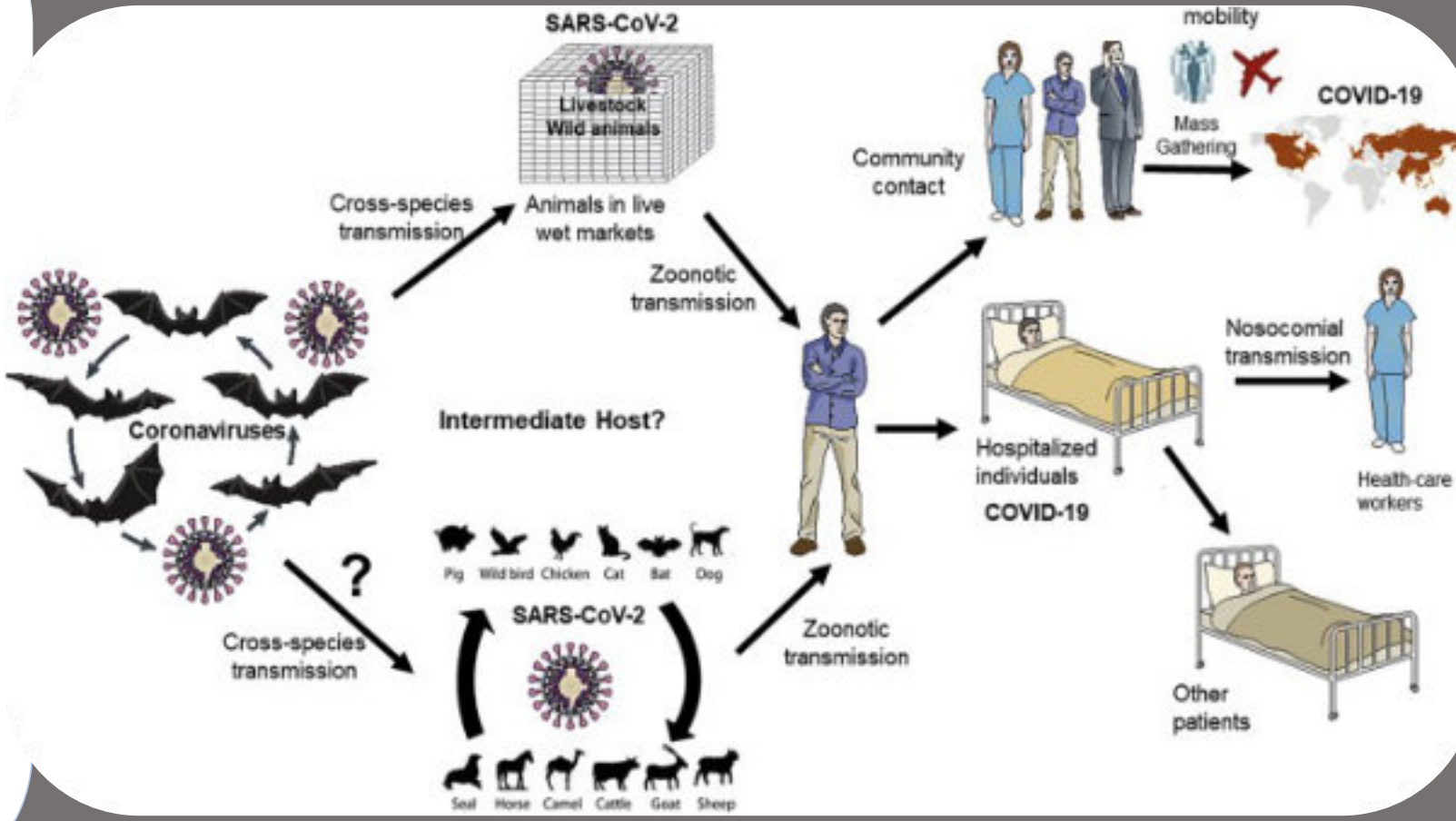
Vaccini e varianti

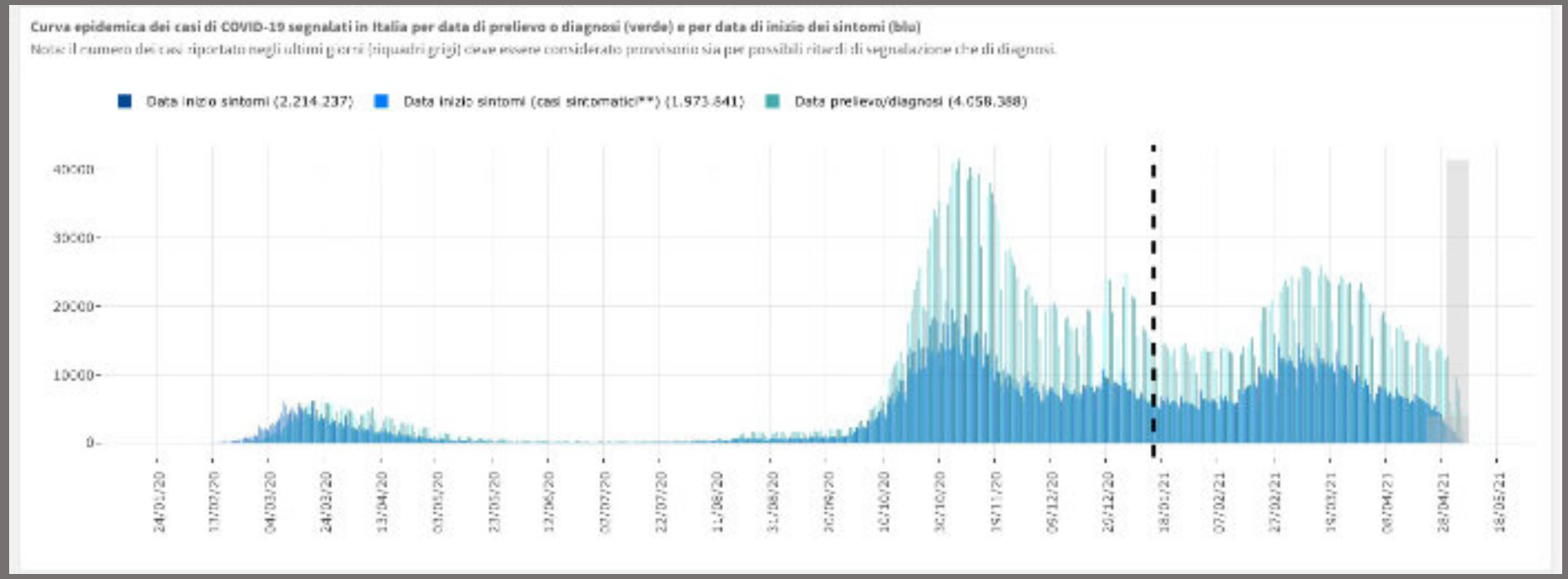
Massimo Ciccozzi,
Director of Unit of medical statistic and molecular epidemiology
Campus Biomedico University
Rome

LA TRASMISSIONE DEL COVID-19

COVID-19(acronimo dell'inglese *CoronaVirus Disease* 1 9) o malattia respiratoria acuta da SARS-CoV-2 e più semplicemente malattia da Coronavirus 2019,è la malattia infettiva respiratoria causata dal virus SARS-CoV-2.
Una persona infetta può presentare sintomi dopo un **periodo di incubazione** che varia tra **2 e 1 4 giorni circa** (raramente ci sono stati casi di 2 9 giorni), durante i quali può comunque essere contagiosa.



Epidemiologia



4.061.431	133.327	47 anni	48,8% | 51,2%	120.718 (3%)	3.266.249
Casi***	Casi tra gli operatori sanitari*	Età mediana dei casi	Maschi (%) | Femmine (%)	Deceduti (CFR)	Guariti

TABELLA 4 - DISTRIBUZIONE DEI CASI (N= 3.966.050) E DEI DECESSI (N= 118.592) PER COVID-19 DIAGNOSTICATI IN ITALIA PER FASCIA DI ETÀ E SESSO

Classe di età (anni)	Soggetti di sesso maschile					Soggetti di sesso femminile					Casi totali				
	N. casi	% casi totali	N. deceduti	% del totale deceduti	Letalità %	N. casi	% casi totali	N. deceduti	% del totale deceduti	Letalità %	N. casi	% casi per classe di età	N. deceduti	% deceduti per classe di età	Letalità %
0-9	106.302	51.8	4	40	0	98.905	48.2	6	60	0	205.207	5.2	10	0	0
10-19	193.596	52	8	57.1	0	178.360	48	6	42.9	0	371.956	9.4	14	0	0
20-29	237.720	50.7	37	62.7	0	231.453	49.3	22	37.3	0	469.177	11.8	59	0	0
30-39	240.191	48.8	135	63.4	0.1	251.561	51.2	78	36.6	0	491.756	12.4	213	0.2	0
40-49	302.049	47.6	711	70	0.2	333.000	52.4	305	30	0.1	635.050	16	1.016	0.9	0.2
50-59	339.894	49	2.900	72.2	0.9	354.206	51	1.119	27.8	0.3	694.102	17.5	4.019	3.4	0.6
60-69	229.667	52	8.555	72.9	3.7	211.724	48	3.173	27.1	1.5	441.392	11.1	11.728	9.9	2.7
70-79	164.949	50.9	20.000	67.8	12.1	159.369	49.1	9.488	32.2	6	324.318	8.2	29.488	24.9	9.1
80-89	101.328	41	26.449	54.4	26.1	146.009	59	22.175	45.6	15.2	247.344	6.2	48.624	41	19.7
≥90	20.697	24.2	8.060	34.4	38.9	64.943	75.8	15.358	65.6	23.6	85.640	2.2	23.418	19.7	27.3
Età non nota	51	47.2	3	100	5.9	57	52.8	-	0	0	108	0	3	0	2.8
Totale	**1.936.444**	**48,8**	**66.862**	**56,4**	**3.5**	**2.029.587**	**51,2**	**51.730**	**43,6**	**2,5**	**3.966.050**	**-**	**118.592**	**-**	**3**

NOTA: LA TABELLA NON INCLUDE I CASI PER CUI NON È NOTO IL SESSO

Nuovi decessi giornalieri
Italia - dati al 17 maggio
Totale 124.296
1000
900
800
700
600
500
400
300
200
100
0
140
19 APR
21 APR
23 APR
25 APR
27 APR
29 APR
01 MAG
03 MAG
05 MAG
07 MAG
09 MAG
11 MAG
13 MAG
15 MAG
17 MAG
Fonte: Ministero della Salute

Nuovi tamponi positivi giornalieri
Italia - dati al 17 maggio
Totale 4.162.576
45.000
40.000
35.000
30.000
25.000
20.000
15.000
10.000
5.000
0
3.45
19 APR
21 APR
23 APR
25 APR
27 APR
29 APR
01 MAG
03 MAG
05 MAG
07 MAG
09 MAG
11 MAG
13 MAG
15 MAG
Fonte: Ministero della Salute

Rai 1 HD
TOP DIECI
QUESTA SERA ORE 21:25
COVID-19: MONITORAGGIO
SETTIMANA 5-11 MAGGIO
DECESSI 1.544 (-15,4%)
TERAPIA INTENSIVA - 367 (-15,1%)
RICOVERATI CON SINTOMI - 3.239 (-17,8%)
ISOLAMENTO DOMICILIARE -46.424 (-11,8%)
NUOVI CASI 63.409 (-19%)
CASI ATTUALMENTE POSITIVI -50.030 (-12,1%)
ELABORAZIONE GIMBE SU DATI MINISTERO DELLA SALUTE
1 mattina
6:43

Ricoverati in terapia intensiva
Italia - dati al 17 maggio
Dato giornaliero -25
3 APRILE
4.068
2021
1.754
5.000
4.000
3.000
2.000
1.000
0
24 FEB
28 APR
01 LUG
03 SET
05 NOV
09 GEN
14 FEB
17 MAG
Fonte: Ministero della Salute

Received: 25 January 2020 | Accepted: 27 January 2020

DOI: 10.1002/jmv.25688

RESEARCH ARTICLE

JOURNAL OF MEDICAL VIROLOGY WILEY

The 2019-new coronavirus epidemic: Evidence for virus evolution

Domenico Benvenuto[1] | Marta Giovanetti[2] | Alessandra Ciccozzi[1] | Silvia Spoto[3] | Silvia Angeletti[4] | Massimo Ciccozzi[2]

PATHOGENS AND GLOBAL HEALTH
2020, VOL. 114, NO. 2, 64–67
https://doi.org/10.1080/20477724.2020.1725339

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The global spread of 2019-nCoV: a molecular evolutionary analysis

Domenico Benvenuto[a*], Marta Giovanetti[b*], Marco Salemi[c,d], Mattia Prosperi[c,d], Cecilia De Flora[a], Luiz Carlos Junior Alcantara[b], Silvia Angeletti[e*] and Massimo Ciccozzi[b*]

[a]Unit of Medical Statistics and Molecular Epidemiology, University Campus Bio-Medico of Rome, Italy; [b]Laboratório de Flavivírus, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil; [c]Department of Epidemiology, University of Florida, Gainesville, FL, USA; [d]Emerging Pathogens Institute, University of Florida, Gainesville, FL, USA; [e]Unit of Clinical Laboratory Science, University Campus Bio-Medico of Rome, Italy

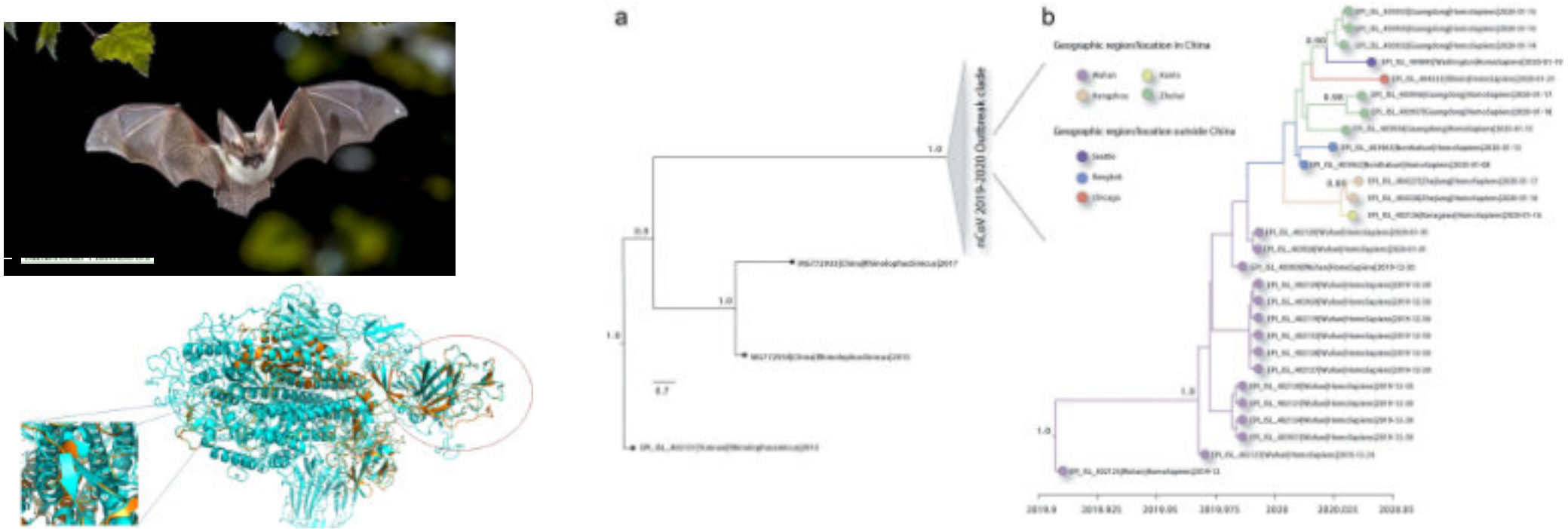


FIGURE 3 Cartoon model of the structural superposition between the homology model of the 2019-nCoV in blue and the spike glycoprotein of SARS coronavirus (PDB code 6acc.1) in orange. The red circle highlights the presence of a variable region on the 2019-nCoV at the beginning of the protein, whereas the blue square highlights the presence of two beta-sheets on the 2019-nCoV (401:KYR and 440:LND) that are not present on the SARS-CoV structure; SARS, severe acute respiratory syndrome

Received: 11 March 2020 | Accepted: 16 March 2020
DOI: 10.1002/jmv.25773

SHORT COMMUNICATION

JOURNAL OF MEDICAL VIROLOGY WILEY

A doubt of multiple introduction of SARS-CoV-2inItaly: A preliminary overview

Marta Giovanetti[1,2] | Silvia Angeletti[3] | Domenico Benvenuto[4] | Massimo Ciccozzi[4]

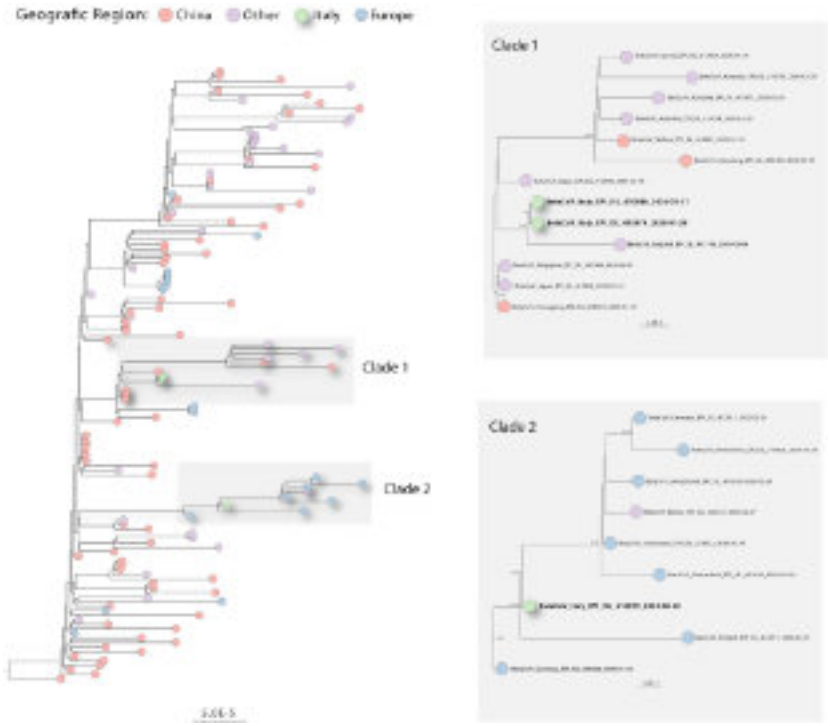
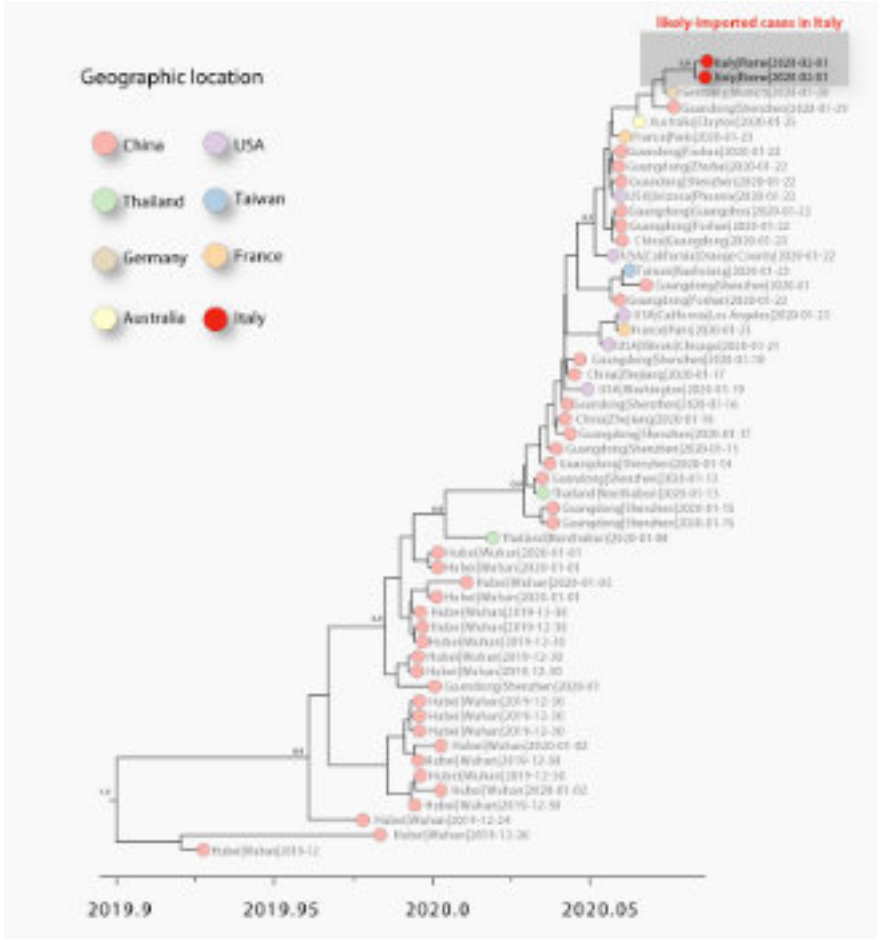


FIGURE 1 Maximum likelihood phylogeny, estimated from complete and near-complete coronavirus (CoV) genomes using genome data available in GISAID. Colors represent different locations (panels A and B represent expansions of the clades containing the Italian CoV isolates [green]) in clade 1 closely related with sequence from England, in clade B closely related with sequences from Germany



Received: 2 February 2020 | Accepted: 3 February 2020
DOI: 10.1002/jmv.25699

SHORT COMMUNICATION

JOURNAL OF MEDICAL VIROLOGY WILEY

The first two casesof 2019-nCoV in Italy: Where they come from?

Marta Giovanetti[1] | Domenico Benvenuto[2] | Silvia Angeletti[3] | Massimo Ciccozzi[2]

Received: 13 February 2020 | Accepted: 19 February 2020

DOI: 10.1002/jmv.25719

RESEARCH ARTICLE

JOURNAL OF MEDICAL VIROLOGY WILEY

COVID-2019:Theroleof thensp2andnsp3initspathogenesis

Silvia Angeletti[1] | Domenico Benvenuto[2] | Martina Bianchi[3] | Marta Giovanetti[4] | Stefano Pascarella[3] | Massimo Ciccozzi[2]

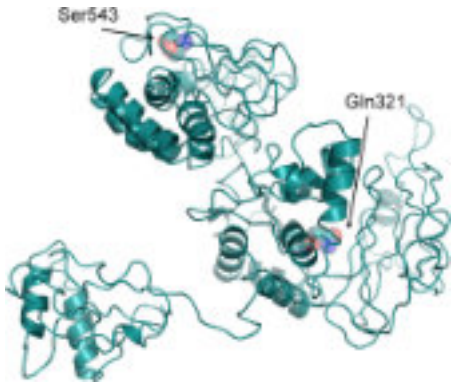
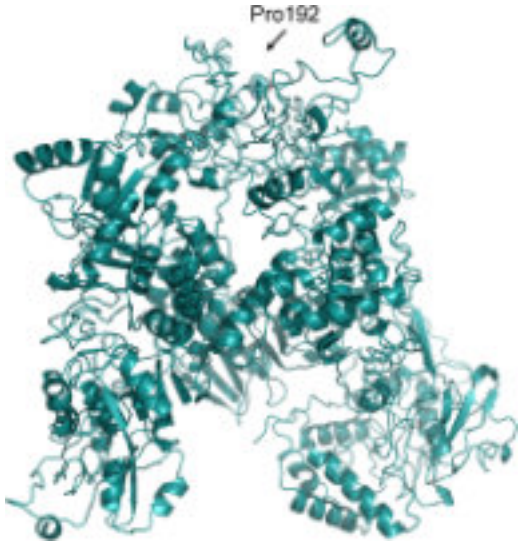


FIGURE 2 I-Tasser model of the COVID-2019 nsp2. Residues under positive selective pressure with a P< .05 are shown as sticks and transparent spheres and are marked by the corresponding labels. COVID-2019, novel Coronavirus; nsp2, non structural protein-2



FI GURE 3 I-Tasser model of the COVID-2019 nsp3. The residue under positive selective pressure with a P< .05 is shown as sticks and transparent spheres and is marked by the corresponding label. COVID-2019, novel Coronavirus; nsp, non structural protein

Pachetti et al. J Transl Med (2020) 18:179
https://doi.org/10.1186/s12967-020-02344-6

Journal of Translational Medicine

RESEARCH Open Access

Emerging SARS-CoV-2mutation hot spots include a novel RNA-dependent-RNA polymerase variant

Maria Pachetti[1,2†], Bruna Marini[4†], Francesca Benedetti[5], Fabiola Giudici[3], Elisabetta Mauro[4], Paola Storici[1], Claudio Masciovecchio[1], Silvia Angeletti[6], Massimo Ciccozzi[6], Robert C. Gallo[7,8], Davide Zella[5,9*] and Rudy Ippodrino[4*]

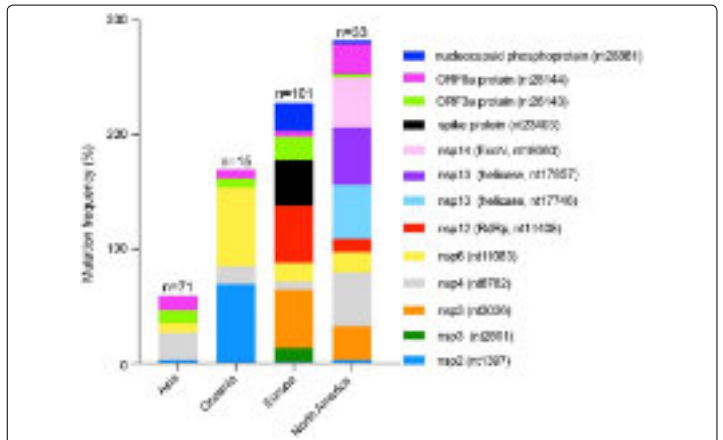


Fig. 1 SARS-CoV-2mutationfrequencyindifferentgeographicareas.Eightnovelrecurrenthotspotsmutations(namely1397,2891,14408,17746, 17857,18060,23403and28881)and5hotspotsalreadyreportedinliterature(namely3036,8782,11083,28144and26143)weresubdividedinto 4geographicareas:Asia(n=71),Oceania(n=15),Europe(n=101),NorthAmerica(n=33).Themutationfrequencywasestimatedforeachof them,bynormalizingthenumberofgenomescarryingagivenmutationinageographicarea,bytheoverallnumberofretrievedgenomesper geographicarea;thegraphshowsthecumulativemutationfrequencyofallgivenmutationspresentineachgeographicarea.Mutationlocations inviralgenesarereportedinthelegendaswellastheproteins(i.e.non-structuralprotein,nsp)presentingthesemutations.Thefigureshowsthat genomesfromEuropeanandNorthAmericanpatientspresentanincreaseinmutationfrequencycomparedtoAsia.Itisalsopossibletoobserve thatEuropeandNorthAmericashowadifferentialpatternofmutations:mutation14408(red),23403(black),28881(electricblue)and26143(light green)arepresentmostlyinEurope,whereas18060(pink),17857(purple)and17746(lightblue)arepresentmostlyinNorthAmerica

Journal of Infection 81 (2020) e24–e27

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Journal of Infection

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

Evolutionary analysis of SARS-CoV-2:how mutation of Non-Structural Protein 6 (NSP6) could affect viral autophagy

Domenico Benvenuto[a,*], Silvia Angeletti[b], Marta Giovanetti[c], Martina Bianchi[d], Stefano Pascarella[d], Roberto Cauda[e,f], Massimo Ciccozzi[a], Antonio Cassone[g]

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[e] UOC Malattie Infettive – Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Largo Agostino Gemelli, 8, Rome 00168, Italy
[f] Department of Healthcare Surveillance and Bioethics, Catholic University of Sacred Heart, Largo Francesco Vito, 1, Rome 00168, Italy
[g] Center of genomics, genetics and biology, University of Siena, Petriccio e Belriguardo, 35, Siena 53100, Italy

Thus, its role would be to limit autophagosome expansion, directly or indirectly by starvation or chemical inhibition

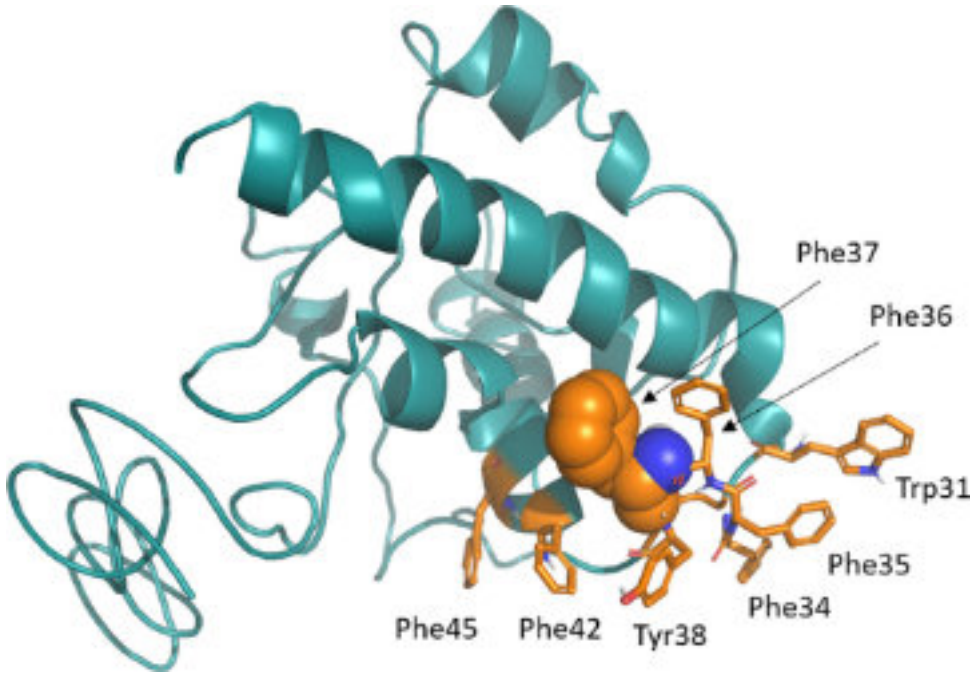


Fig. 1. I-TASSERmodel of NSP6. Residue under positive selective pressure with a $p < 0.05$ is shown as a sphere. Residuesfound in the structure proximity are shown in sticks. All residues are marked by the corresponding labels.

Benedetti et al. J Transl Med (2020) 18:329
https://doi.org/10.1186/s12967-020-02507-5

Journal of
Translational Medicine

RESEARCH Open Access

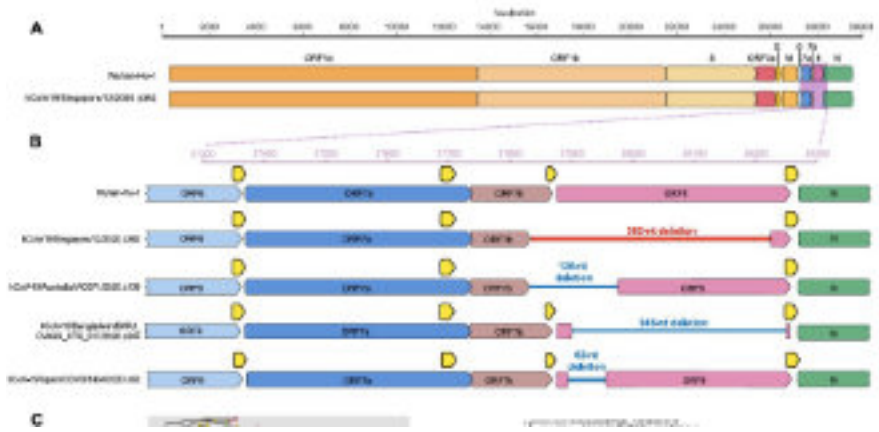
Emerging of a SARS-CoV-2 viral strain with a deletion in nsp1

Francesca Benedetti[1,2†], Greg A. Snyder[1,3†], Marta Giovanetti[4], Silvia Angeletti[5], Robert C. Gallo[1,6,7], Massimo Ciccozzi[5*] and Davide Zella[1,2,7*]

Methods: A total of 17,928 genome sequences were obtained from the GISAID database (December 2019 to July 2020) from patients infected by SARS-CoV-2 from different areas around the world. Genomes alignment was performed using MAFFT (REFF) and the nsp1 genomic regions were identified using BioEdit and verified using BLAST. Nsp1 protein of SARS-CoV-2 with and without deletion have been subsequently modelled using I-TASSER.

Results: We identified SARS-CoV-2 genome sequences, from several Countries, carrying a previously unknown deletion of 9 nucleotides in position 686-694, corresponding to the AA position 241-243 (KSF). This deletion was found in different geographical areas. Structural prediction modelling suggests an effect on the C-terminal tail structure.

Conclusions: Modelling analysis of a newly identified deletion of 3 amino acids (KSF) of SARS-CoV-2 nsp1 suggests that this deletion could affect the structure of the C-terminal region of the protein, important for regulation of viral replication and negative effect on host's gene expression. In addition, substitution of the two amino acids (KS) from nsp1 of SARS-CoV was previously reported to revert loss of interferon-alpha expression. The deletion that we describe indicates that SARS-CoV-2 is undergoing profound genomic changes. It is important to: (i) confirm the spreading of this particular viral strain, and potentially of strains with other deletions in the nsp1 protein, both in the population of asymptomatic and pauci-symptomatic subjects, and (ii) correlate these changes in nsp1 with potential decreased viral pathogenicity.



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RESEARCH ARTICLE
Ecological and Evolutionary Science

Discovery and Genomic Characterization of a 382-Nucleotide Deletion in ORF7b and ORF8 during the Early Evolution of SARS-CoV-2

Yvonne C. F. Su,[a] Danielle E. Anderson,[a] Barnaby E. Young,[b,c,d] Martin Linster,[a] Feng Zhu,[a] Jayanthi Jayakumar,[a] Yan Zhuang,[a] Shirin Kalimuddin,[a,e] Jenny G. H. Low,[a,e] Chee Wah Tan,[a] Wan Ni Chia,[a] Tze Minn Mak,[b] Sophie Octavia,[b] Jean-Marc Chavatte,[b] Raphael T. C. Lee,[f] Surinder Pada,[g] Seow Yen Tan,[h] Louisa Sun,[i] Gabriel Z. Yan,[j] Sebastian Maurer-Stroh,[f,k] Ian H. Mendenhall,[a,m] Yee-Sin Leo,[b,c,d,l,n] David Chien Lye,[b,c,d,n] Lin-Fa Wang,[a,m,o] Gavin J. D. Smith[a,m,o]

J Med Virol. 2020 Jun 3 : 10.1002/jmv.26104.
doi: 10.1002/jmv.26104 [Epub ahead of print]
PMCID: PMC7300971
PMID: 32492183

Evidence for mutations in SARS-CoV-2 Italian isolates potentially affecting virus transmission

Domenico Benvenuto, [1] Ayse Banu Demir, [2] Marta Giovanetti, [3] Martina Bianchi, [4] Silvia Angeletti, [5] Stefano Pascarella, [4] Roberto Cauda, [6], [7] Massimo Ciccozzi, [1] and Antonio Cassone [8]

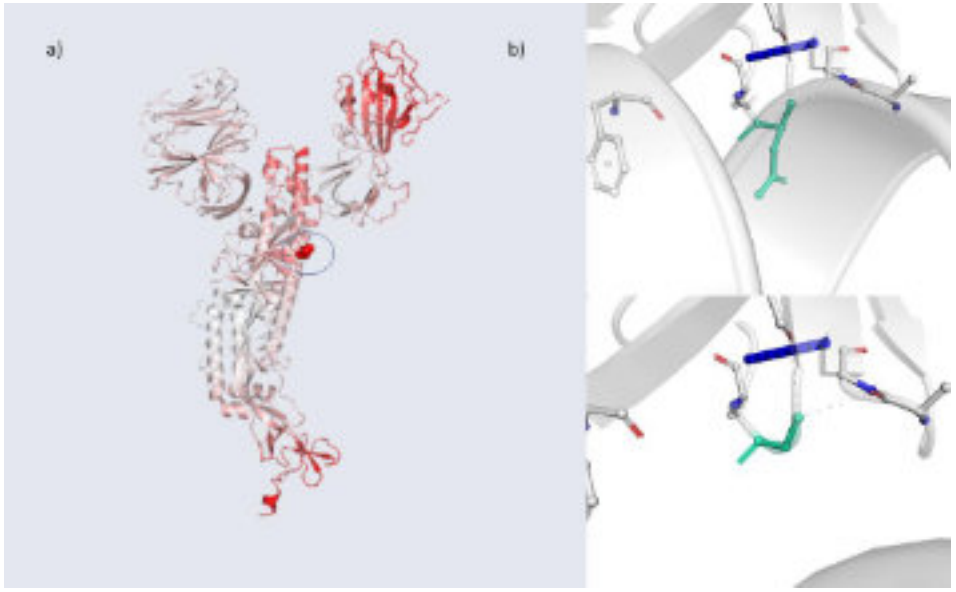


Figure 1, a) A model of spike glycoprotein monomer displaying the amino acids coloured according to the vibrational entropy change upon mutation, Red regions are those gaining in flexibility, The amino acidic mutation is blue circled; b) the top image shows the molecular interaction between the side chain of the wild-type amino acid and the side chains of the surrounding amino acid; the bottom image shows the molecular interaction between the side chain of the mutated amino acid and the side chains of the surrounding amino acid

Many questions are open and need an answer..

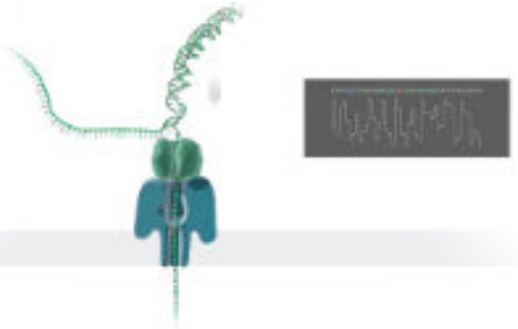
THERAPY?

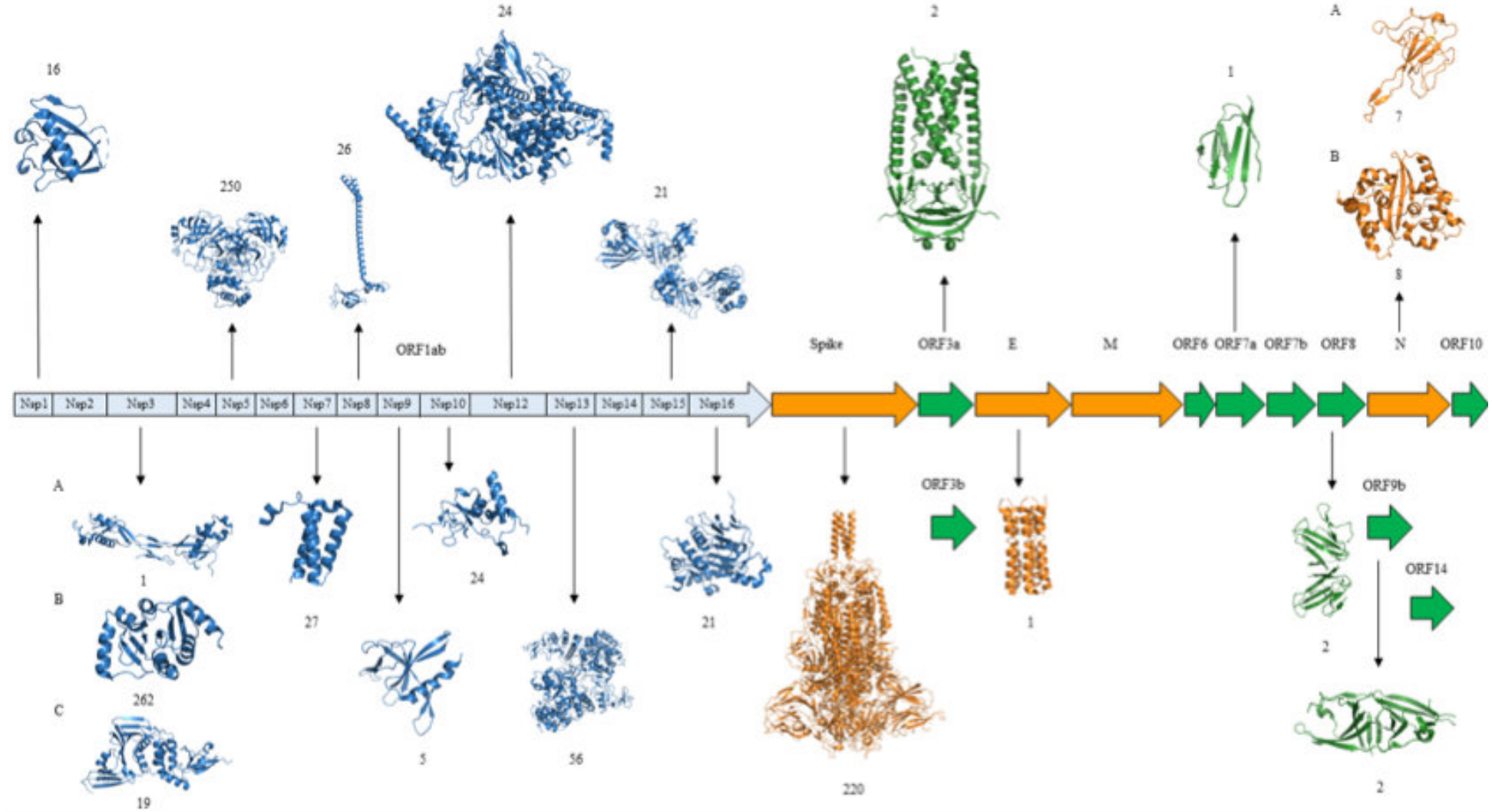
VACCINE?

Pathogenesis

Differential clinical outcomes

Nanopore sequencing: The genomic revolution




16
250
26
24
21
2
1
A
7
B
8
ORF1ab
Nsp1
Nsp2
Nsp3
Nsp4
Nsp5
Nsp6
Nsp7
Nsp8
Nsp9
Nsp10
Nsp12
Nsp13
Nsp14
Nsp15
Nsp16
Spike
ORF3a
E
M
ORF6
ORF7a
ORF7b
ORF8
N
ORF10
A
1
B
262
C
19
27
5
24
56
21
ORF3b
1
220
ORF9b
2
ORF14
2

Evidence for mutations in SARS-CoV-2 Italian isolates potentially affecting virus transmission

Domenico Benvenuto1 , Ayse Banu Demir2 , Marta Giovanetti3 , Martina Bianchi4 , Silvia Angeletti5
Stefano Pascarella4 , Roberto Cauda6,7, Massimo Ciccozzi1 , Antonio Cassone8

Regarding the Spike glycoprotein, the transition from an Adenosine to Guanine occurring on the 1901st nucleotide has led to non-synonymous mutation from an Aspartate to a Glycine residue in the 614 aminoacidic position

First detection of SARS-CoV-2 spike protein N501 mutation in Italy in August, 2020

Bioinformatic analyses showed that the MB61-Aug SARS-CoV-2 isolate had accumulated ten amino acid changes compared with early Italian isolates, and three more had emerged along its evolution by the end of November

A

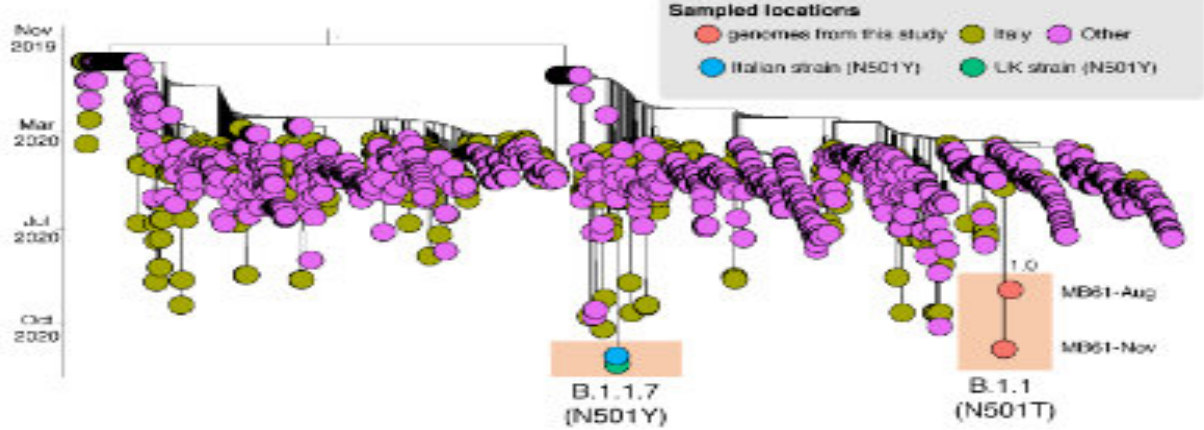
Mutational patten MB61-Aug

Gene	Nucleotide	Amino acid
ORF1a	C5180	D1639N
	C14408T	P4715L
	C21005T	A8914V
Spike	A22108C	K182N
	22285-22288 del CTT	L242 del
	C23039A	Q493K
	A23064C	**N501T**
	A23403G	D614G
N	G28881A e G28882A	R203K
	G28883C	G204R

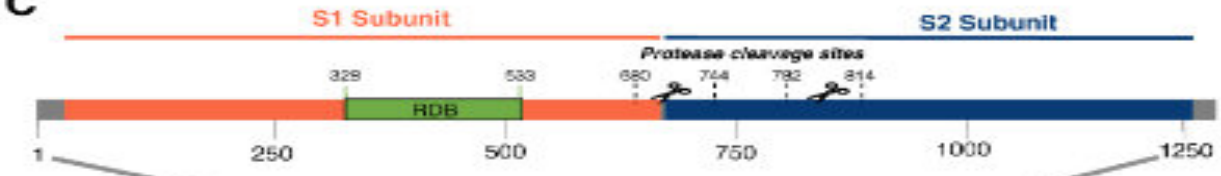
Mutational patten MB61-Nov

Gene	Nucleotide	Amino acid
ORF1a	G5180	D1639N
	C14408T	P4715L
	C17245T	R5561C
	G19883A	V6207I
	C21005T	A8914V
Spike	A22108C	K182N
	22285-22288 del CTT	L242 del
	C23039A	Q493K
	A23064C	**N501T**
	A23403G	D614G
ORF3a	G25714T	L168F
N	G28881A e G28882A	R203K
	G28883C	G204R

B



C



Position	Reference yp_009724390	MB61	EPI_ISL_728343 EPI_ISL_717978
69-70	HV	HV	del
144	Y	Y	del
182	K	N	K
241	L	del	L
493	Q	K	Q
501	N	T	Y
571	A	A	D
614	D	G	G
681	P	P	H
706	T	T	I
982	S	S	A
1118	D	D	H

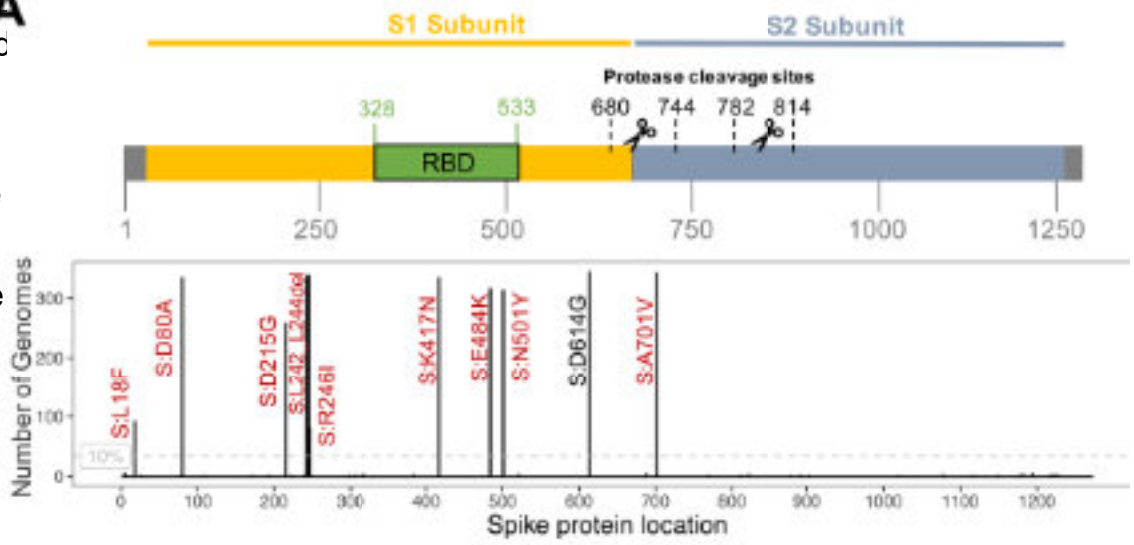
nature

https://doi.org/10.1038/s41586-021-03402-9

Accelerated Article Preview

Emergence of a SARS-CoV-2 variant of concern with mutations in spike glycoprotein

Continued uncontrolled transmission of the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) in many parts of the world is creating the conditions for significant virus evolution[1,2]. Here, we describe a new SARS-CoV-2 lineage (501Y.V2) characterised by eight lineage-defining mutations in the spike protein, including three at important residues in the receptor-binding domain (K417N, E484K and N501Y) that may have functional significance[3–5]. This lineage was identified in South Africa after the first epidemic wave in a severely affected metropolitan area, Nelson Mandela Bay, located on the coast of the Eastern Cape Province. This lineage spread rapidly, becoming dominant in the Eastern Cape, Western Cape and KwaZulu-Natal Provinces within weeks. Whilst the full significance of the mutations is yet to be determined, the genomic data, showing the rapid expansion and displacement of other lineages in multiple regions, suggest that this lineage is associated with a selection advantage, most plausibly as a result of increased transmissibility or immune escape[6–8].



ARTICLE PREVIEW

SARS-CoV-2 shifting transmission dynamics and hidden reservoirs potentially limit efficacy of public health interventions in Italy

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We investigated SARS-CoV-2 transmission dynamics in Italy, one of the countries hit hardest by the pandemic, using phylodynamic analysis of viral genetic and epidemiological data.
We observed the co-circulation of multiple SARS-CoV-2 lineages over time, which were linked to multiple importations and characterized by large transmission clusters concomitant with a high number of infections.

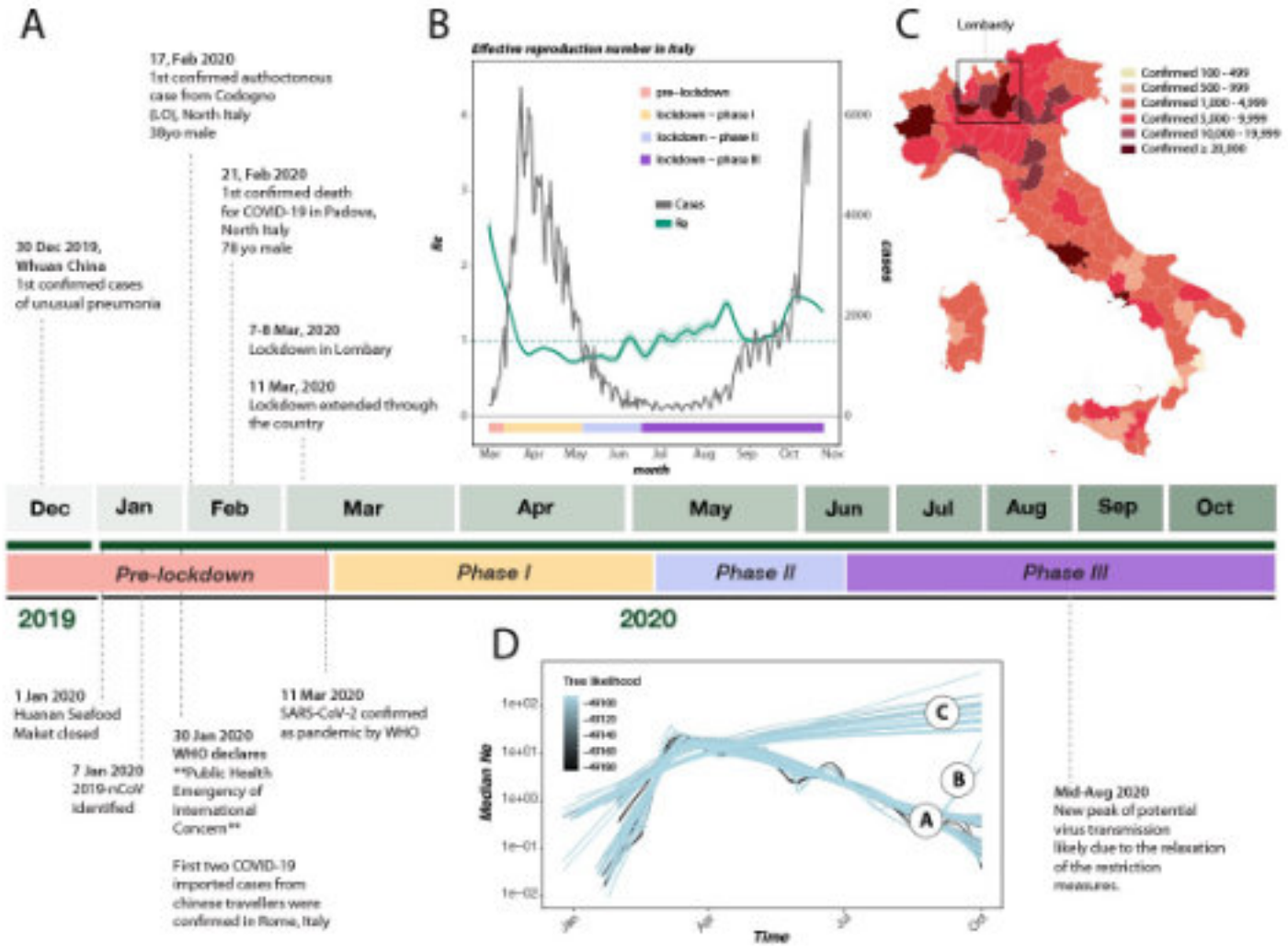


Figure 1. History of SARS-CoV-2 epidemic in Italy. A) Timeline of key events following the first confirmed cases of SARS-CoV-2 infection in Italy. **B**) Epidemiological curve showing the progression of daily viral infection numbers in Italy from the beginning of the epidemic in March (black) and changes in *Re* estimations in the same period (green), with lockdown phases indicated along the bottom. **C**) Map of SARS-CoV-2 cases per 100,000 inhabitants in Italy up to Oct 2020; **D)** Estimates of the viral effective population size (*Ne*) using a sample of 100 phylogenetic trees with the highest log-likelihood values.

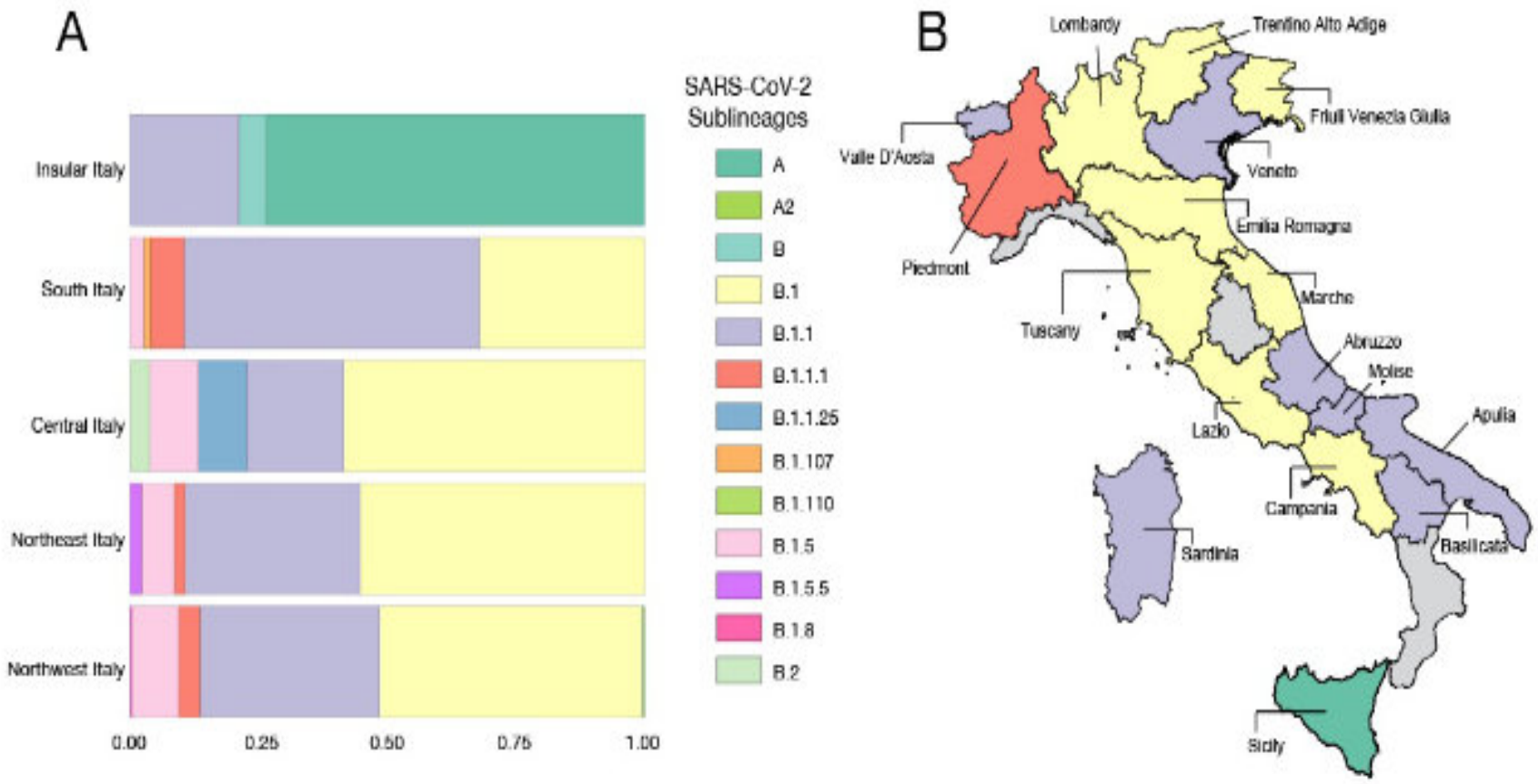


Figure 2. Frequency and distribution of SARS-CoV-2 lineages in Italy. **A**) Frequency of the lineages and sub lineages of SARS-CoV-2 identified into the Italian macro regions. **B**) Distribution of the most prevalent lineage and sub lineage across the country.

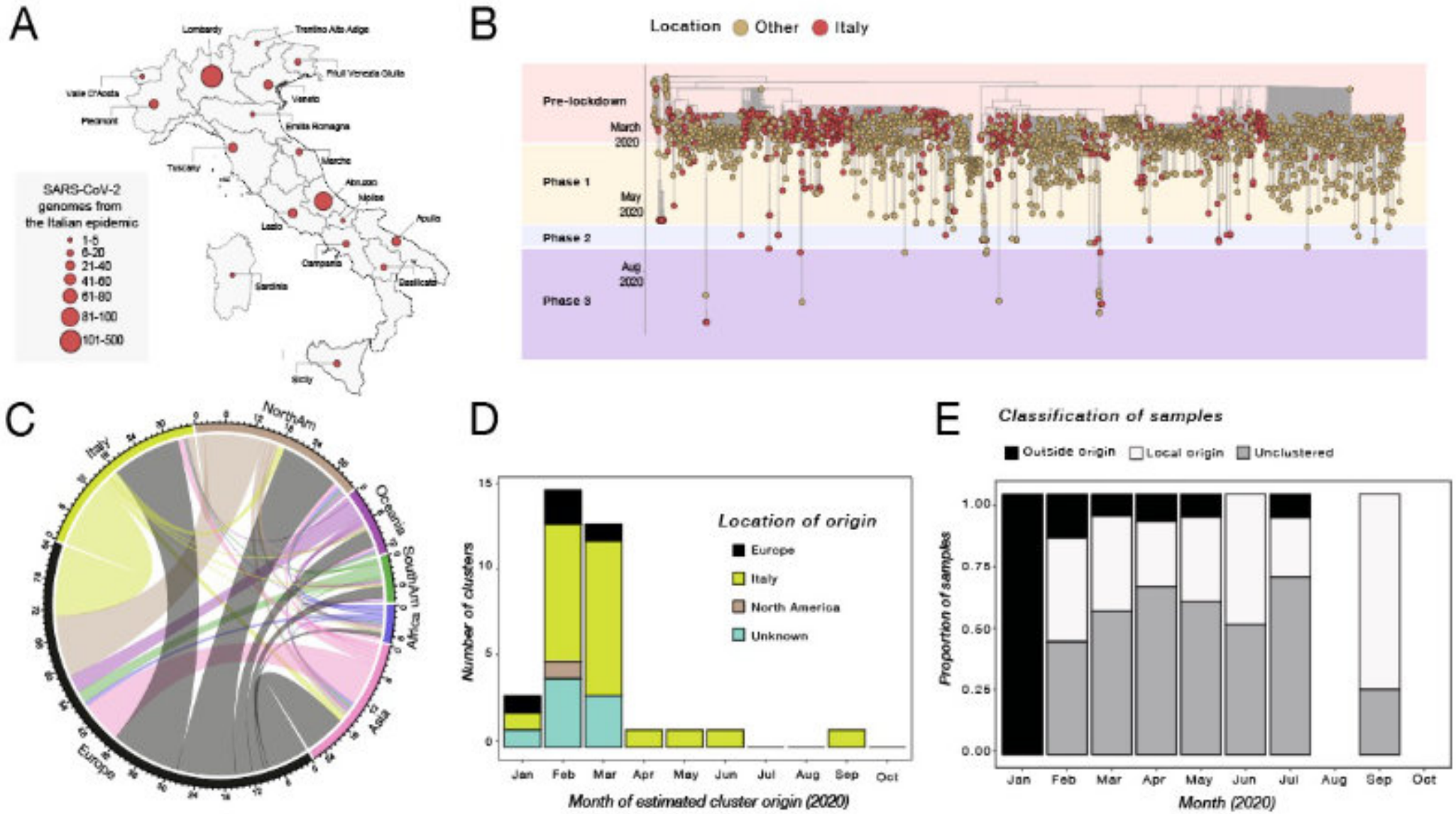
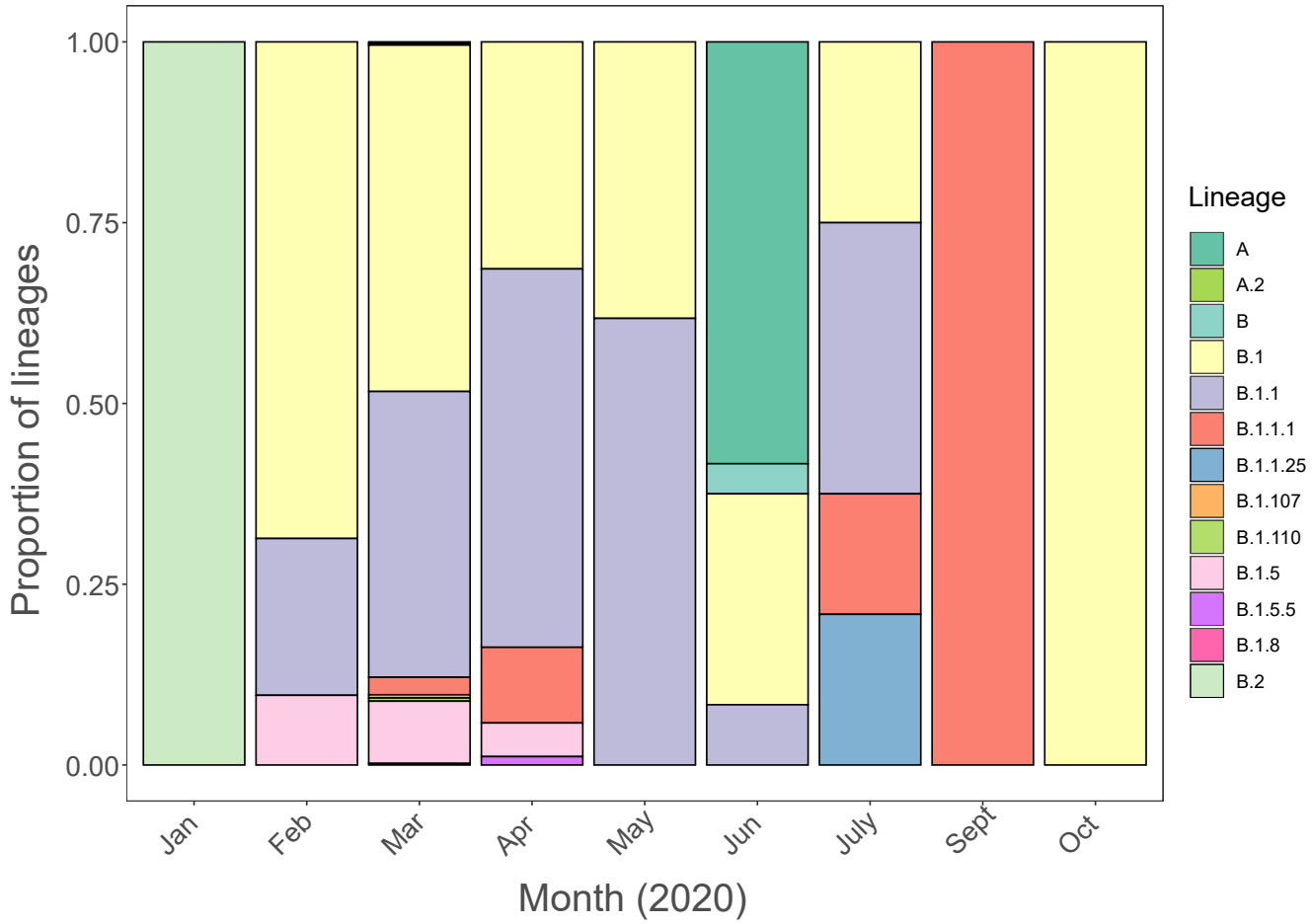
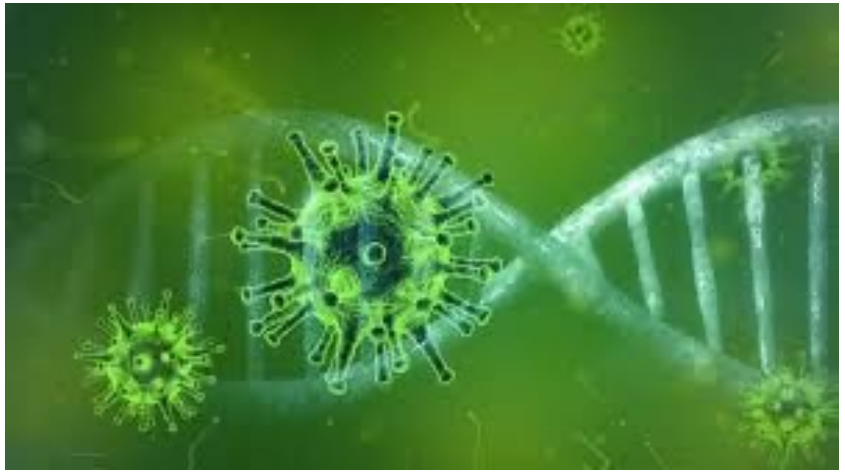


Figure 3. Phylogenetic characterization of Italian SARS-CoV-2 sequences. A) Map of Italy showing the number of SARS-CoV-2 genome sequences by region. The size of the circles indicates the number of new genomes available since the beginning of the epidemic in Italy; B) Time-resolved maximum likelihood tree of 1421 SARS-CoV-2 sequences including 714 from Italy (red circles). C) Chord diagram of estimated numbers of migration flows between the geographic areas. **D)** Frequency of estimated geographical origins for identified transmission clusters involving Italy and originating in the months of January through October of 2020. **E)** Frequency of Italian sequences (sampled from January through October) classified as unclustered (grey) or belonging to clusters with Italian (white) or non-Italian origins (black).



Supplementary Figure 2. Frequency and distribution of SARS-CoV-2 lineages in Italy over time.

variants



mutations in SARS-CoV-2will be launched with Research and Innovation
We have to study how mutations in the virus affect key outcomes such as:

•how transmissible it is
•the severity of COVID-19it causes
•the effectiveness of vaccines and treatments.

We are trying to built a surveillance system bringing together leading virologists from research institutions**. They have to work alongside the COVID-19Genomics

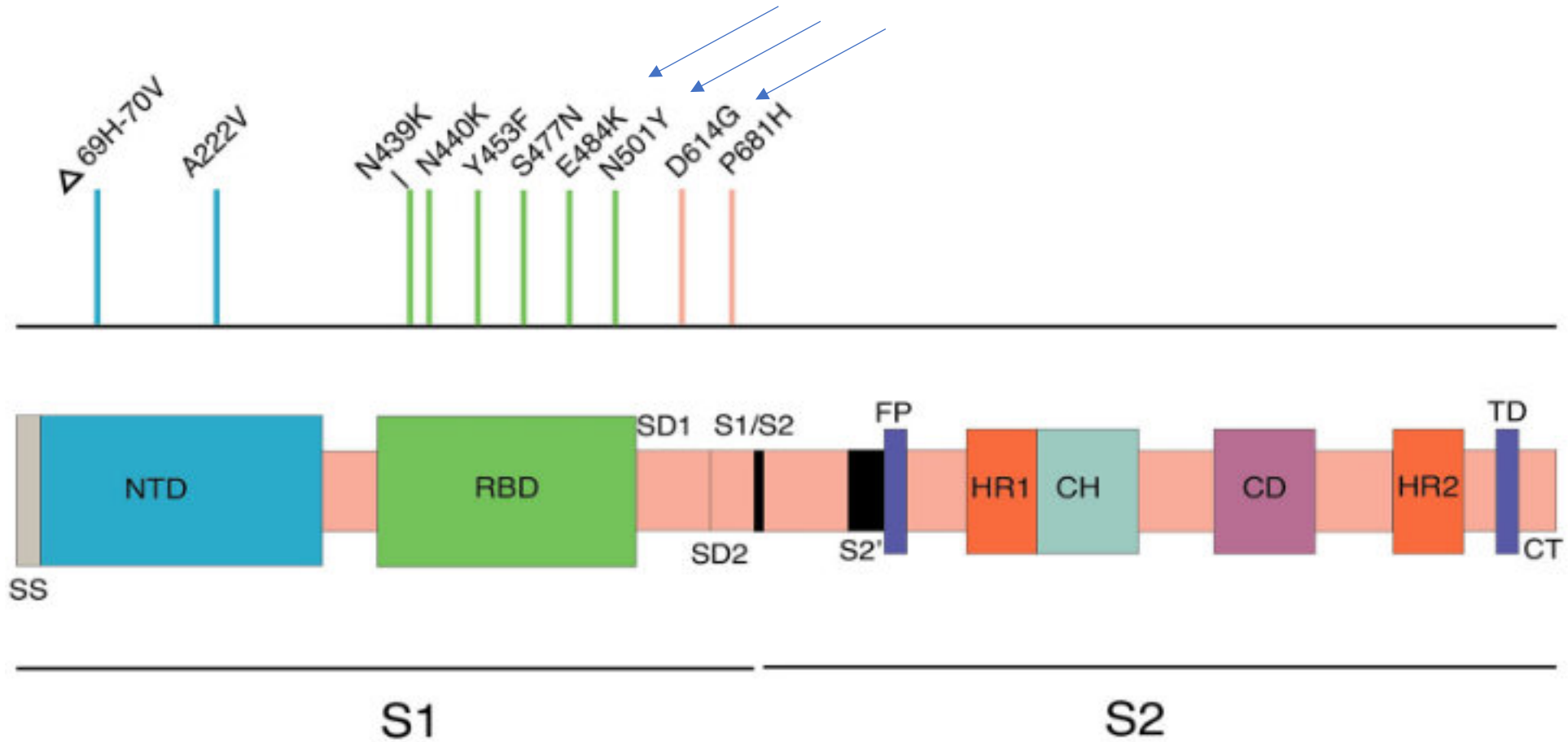
The surveillance system have to play a world-leading role in virus genome sequencing, and Public Health capacity to study newly identified virus variants and rapidly inform government policy.

Although the terms *mutation*, *variant*, and *strain* are often used interchangeably in describing the epidemiology of SARS-CoV-2, the distinctions are important. *Mutation* refers to the actual change in sequence:

D614G is an aspartic acid-to-glycine substitution at position 614 of the spike glycoprotein.
Genomes that differ in sequence are often called *variants*.

This term is somewhat less precise because 2 variants can differ by 1 mutation or many.

Strictly speaking, a variant is a *strain* when it has a demonstrably different phenotype



NTD - N-terminal domain RBD - Receptor-binding domain SD - Subdomain S1/S2 - S1-S2 boundary FP - Fusion peptide
HR - Heptad repeat CH - Central helix CD - Connector domain TD - Transmembrane domain CT - Cytoplasmic tail

Did the variant achieve prominence through natural selection or chance events?

If the evidence suggests natural selection, which mutation(s) are being selected?

What is the adaptive benefit of these mutations?

What effect do these mutations have on transmissibility and spread, antigenicity, or virulence?

We have to work in sequencing viral genomes and identifying new variants –

1) to better understand which mutations affect the virus in a way that might affect our control strategies.

2) to determine the effects of the recent virus variants identified in the UK and South Africa and Brazil the meaning for the transmission of SARS-CoV-2 and vaccine effectiveness.

Now the virus has circulated in humans for more than one year and is prevalent all around the world,

we're in a phase where the virus is constantly throwing up new variants and we need to known and to assess the risk they pose, and to understand the mechanisms by which they act.

Mutations in the virus's genome occur naturally and some of these will be inconsequential, while others will change how it functions.

As new virus variants arise, the surveillance system will flag the riskiest variants, such as those associated with fast spreading virus.

We can create standardised versions of the virus with and without each mutation, so we can study the effects of each change individually.

We can study how these new variants alter the virus proteins, particularly the key spike protein on the surface.

This is important because changes to the spike protein can affect transmissibility and could potentially alter the effectiveness of vaccines and antibodies that target the protein.

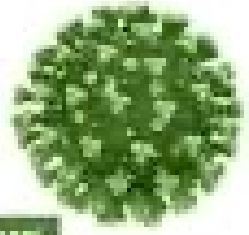
Le varianti principali

D

Il ceppo virale portatore della mutazione D614G è diventato dominante con l'epidemia a Wuhan, in Cina a fine 2019 e la sua diffusione in Europa dal febbraio 2020. È la variante responsabile della prima ondata del virus

Eu

È la variante europea del virus. La mutazione 20A.EU1 è stata individuata la prima volta in Spagna a giugno e si è diffusa in Europa (seconda ondata)



Visoni

Il mese scorso individuata in Danimarca una variante trasmessa all'uomo dai visoni, mutazione Y453F, con un migliaio di infezioni confermate. La chiusura degli allevamenti e l'isolamento immediato dei positivi ha permesso di contenere la minaccia

VUI

La variante VUI-202012/01 (variant under investigation), identificata per la prima volta a metà settembre a Londra e nel Kent, si diventata predominante in poco più di due mesi. Presenta diverse mutazioni, tra cui la principale (N501Y) a livello della proteina spike

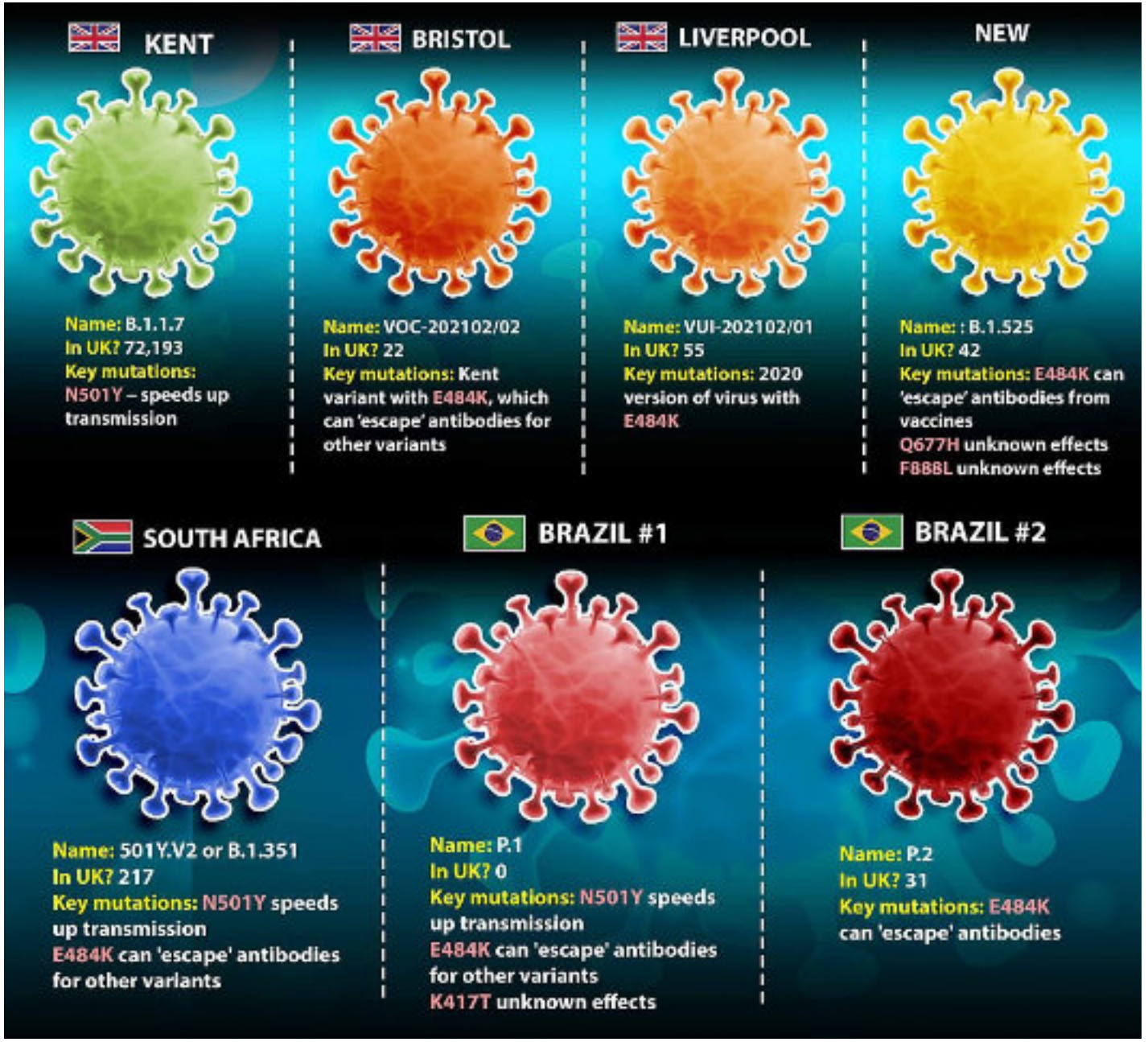


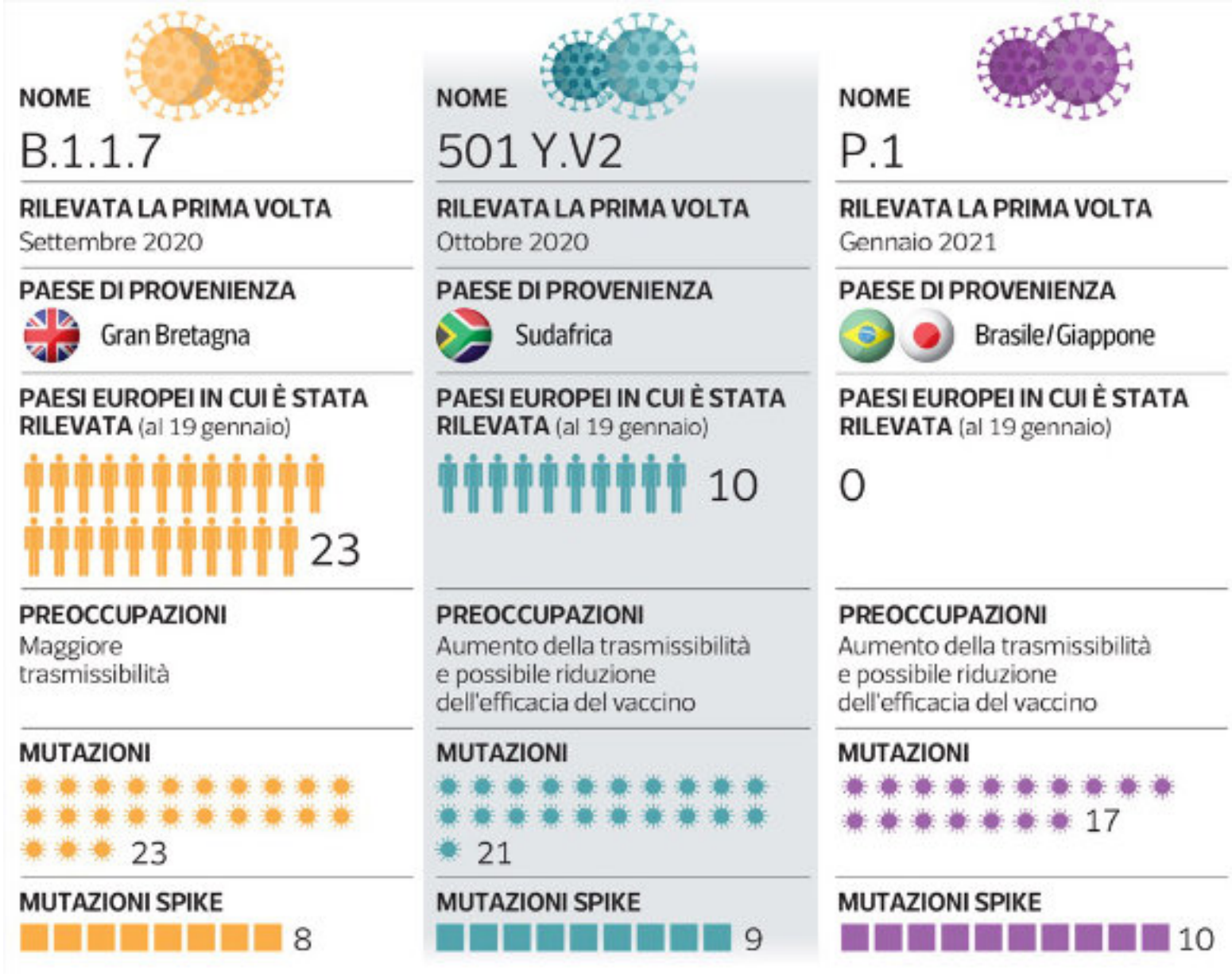
Table 2. Selected SARS-CoV-2 variants

Variant	Definition (amino acid changes)	Potential public health impact of variant	Geographical spread	References
VOC 202012/01	S: **del 69-70**, del 144, **N501Y**, A570D, P681H, T716I, S982A, D1118H	Report of increased transmissibility from the UK.	Prevalent in parts of the UK, cases increasingly detected in other countries.	[56]
501.V2	S: D80A, D215G, E484K, **N501Y** and A701V.	Report of increased transmissibility from South Africa.	Dominant in South Africa, two cases recently detected in the UK.	[50,51,57]
Danish mink variant	S: **del 69-70**, Y453F	Transmission from mink to humans and community spread confirmed, no changes in transmissibility reported.	Prevalent in Denmark. Not detected elsewhere.	[58]
Danish mink cluster 5	S: **del 69-70**, Y453F, I692V, M1229I	Preliminary report of moderate reduction of neutralisation by convalescent sera.	Denmark, not observed since September 2020.	[58]
Various variants with spike amino acid change N439K	S: N439K, often with **del 69-70**	Reports of minor reduction of neutralisation by convalescent sera.	Common in Czechia, Denmark, Ireland, found in lower proportions in many countries.	[59-62]
Nextstrain cluster 20A.EU1	S: A222V	Rapid increase in Spain and then the rest of the EU/EEA at the start of the second wave, probably due to random events and travel patterns.	First observed in Spain, the most common variant in the EU/EEA.	[60]
Nextstrain cluster 20A.EU2	S: S477N N: A376T	Rapid increase in France at the start of the second wave, probably due to founder effects.	First observed in France, prevalent also in Belgium, Czechia, Denmark, Hungary, the Netherlands, Switzerland.	[60]
D614G	S: D614G	Rapid increase during the early stages of the pandemic in the EU/EEA and then worldwide, probably due to a mix of founder effects and increased transmissibility.	Worldwide. All other variants described here are descendant from this one.	[63-66]

Table 3. S gene mutations of concern that require monitoring via genome sequencing

Mutation	Cause for concern
469H-70V	Immune escape, diagnostic failure in assays targeting S gene, identified as part of lineage of UK Variant of Concern (VOC) 202012/01 (B.1.1.7 or 501Y.V1), part of Cluster 5 mink set
A222V	Fast growing lineage in Europe
N439K	Enhanced binding affinity to hACE2 receptor and can likely evade neutralizing antibodies
N440K	High frequency in Andhra Pradesh
Y453F	Enhanced binding affinity to hACE2 receptor and can likely evade neutralizing antibodies, part of Cluster 5 mink set
N501Y	Enhanced binding affinity to hACE2 receptor, possible role in increased transmission, identified as part of lineage of UK Variant of Concern (VOC) 202012/01, identified as part of lineage of South African 501Y.V2 (B.1.351), and as part of lineage 501Y.V2 (B.1.351) in South Africa, and 501Y.V3 (P.1) in Brazil
D614G	Enhanced binding affinity to hACE2 receptor, increased transmission, current predominantly prevalent strain
P681H	Immediately adjacent to the furin cleavage site, identified as part of lineage of UK Variant of Concern (VOC) 202012/01, identified as part of lineage in Nigeria (B.1.1.207)
E484K	Reduced susceptibility to neutralization by antibodies, identified as part of lineage of South African 501Y.V2 (B.1.351), identified as part of lineage in Brazil (B.1.1.28), and as part of the B.1.1.28 lineage in Brazil (501Y.V3 or P.1)

Indian and global mutations identified in the S-gene that cause an alteration in the spike protein and may be detrimental to the human population in terms of viral transmission, infectivity and immune escape.



LE VARIANTI DEL CORONAVIRUS

Le mutazioni sono frequenti in ogni tipo di virus. Sono state scoperte parecchie varianti del SARS-CoV-2. Cinque sono di grande interesse

INGLESE

Riportata all'OMS

14 dicembre

Tracciata nel Kent a settembre

Responsabile di oltre il 50% dei casi nel sudest del Regno Unito nell'ultimo trimestre 2020. Scoperta ora in dozzine di Paesi in tutto il mondo

SUDAFRICANA

Riportata all'OMS

18 dicembre

Apparsa in Sud Africa a ottobre

Partendo dall'Eastern Cape, si è poi diffusa in tutto il Paese a fine 2020. Trovata ora in diverse altre zone del mondo

GIAPPONESE

Riportata all'OMS

10 gennaio

Comparsa in Giappone il 2 gennaio 2021

Riscontrata in due adulti e in due ragazzi rientrati dal Brasile

BRASILIANA

Descritta in un articolo

12 gennaio

Sembra identica a quella comparsa in Giappone

Partita da Manaus (Amazzonia) si è diffusa esponenzialmente e ora mette in crisi il sistema sanitario

FRANCESE

Autorità sanitarie indicano cluster di variante 501Y.V2 in parecchie regioni della Francia

Casi iniziali erano in un gruppo di viaggiatori rientrati a dicembre da un raduno religioso in Mozambico

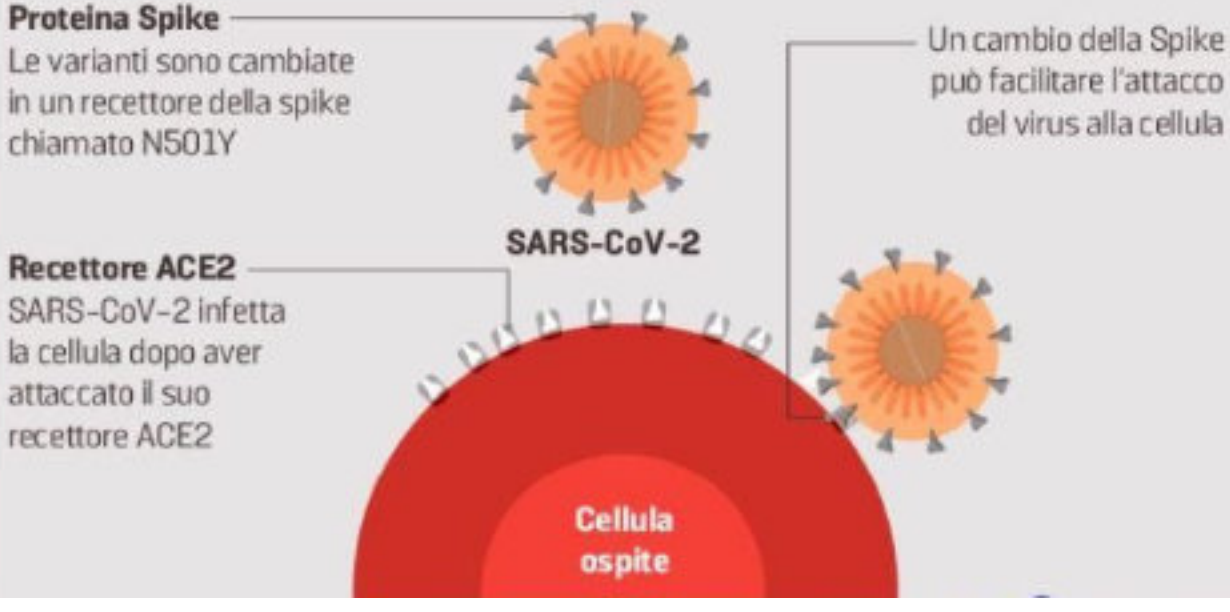
PROBLEMI APERTI

- Il tema della trasmissibilità è al momento preoccupante
- Le varianti inglese e sudafricana sembrano significativamente più infettive

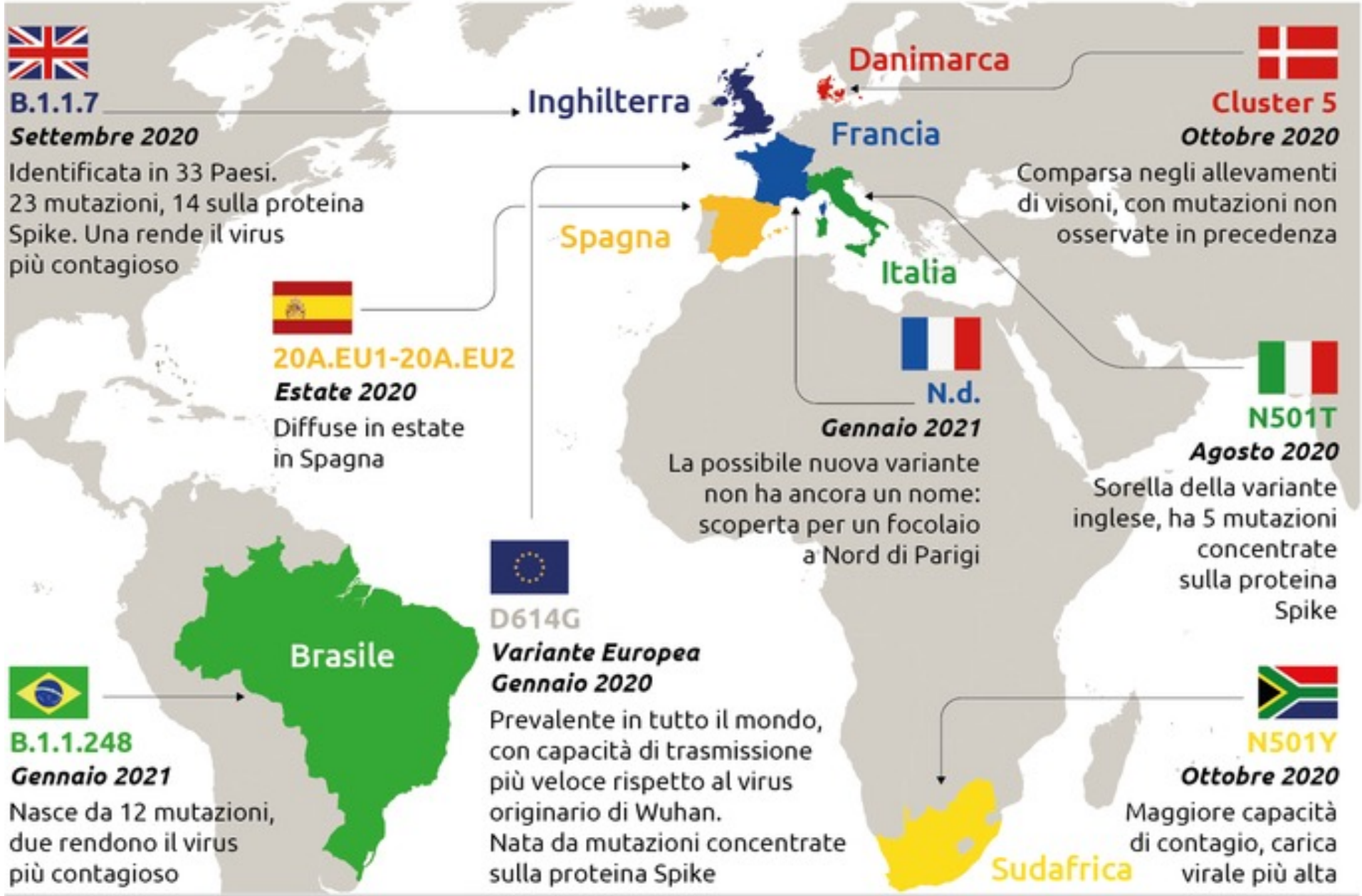
Altri interrogativi

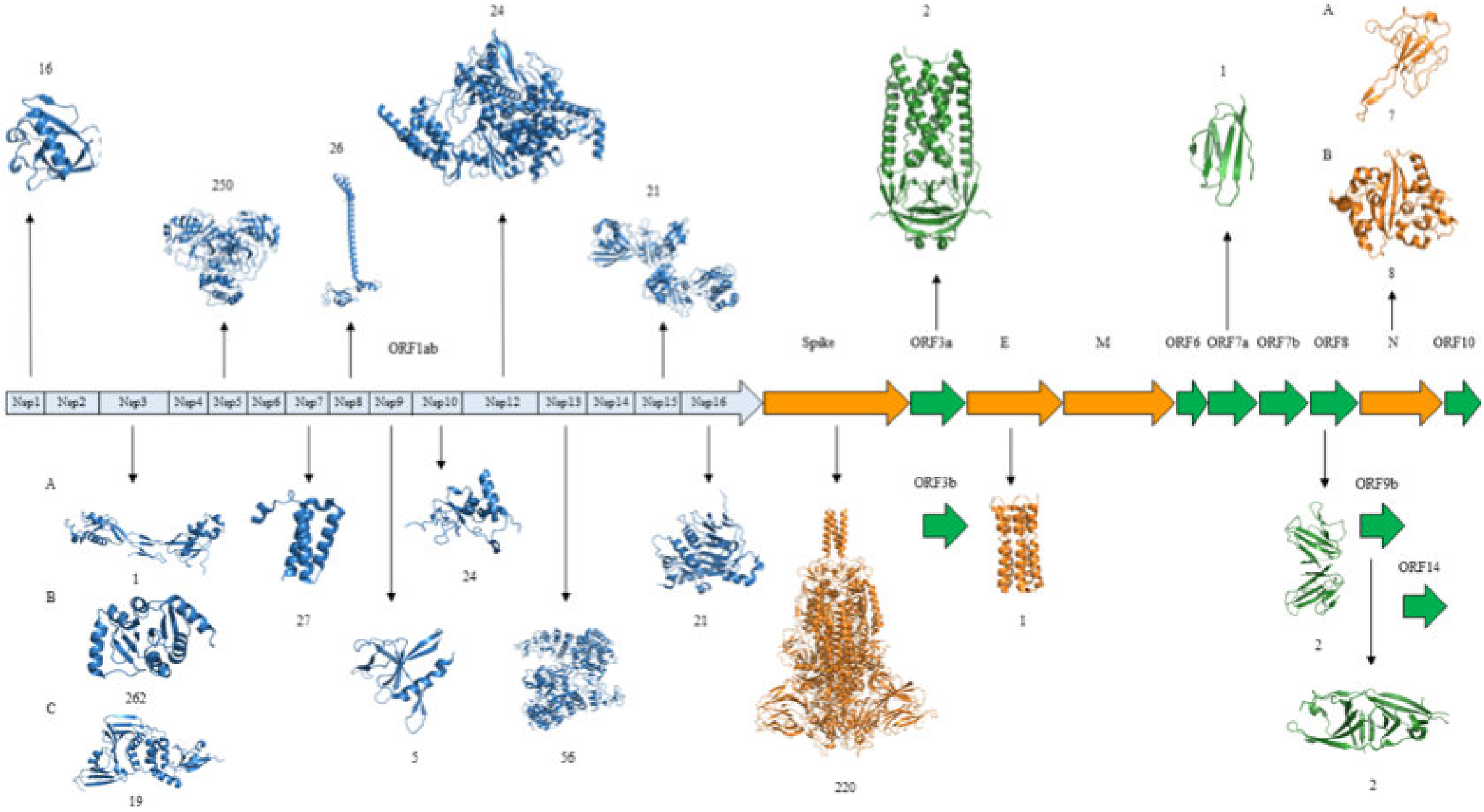
- Può ogni tipo di variante portare malattie più gravi?
- I vaccini anti Covid-19 combattono anche le varianti?

Al momento non ci sono abbastanza evidenze per rispondere



Le varianti pericolose del Covid

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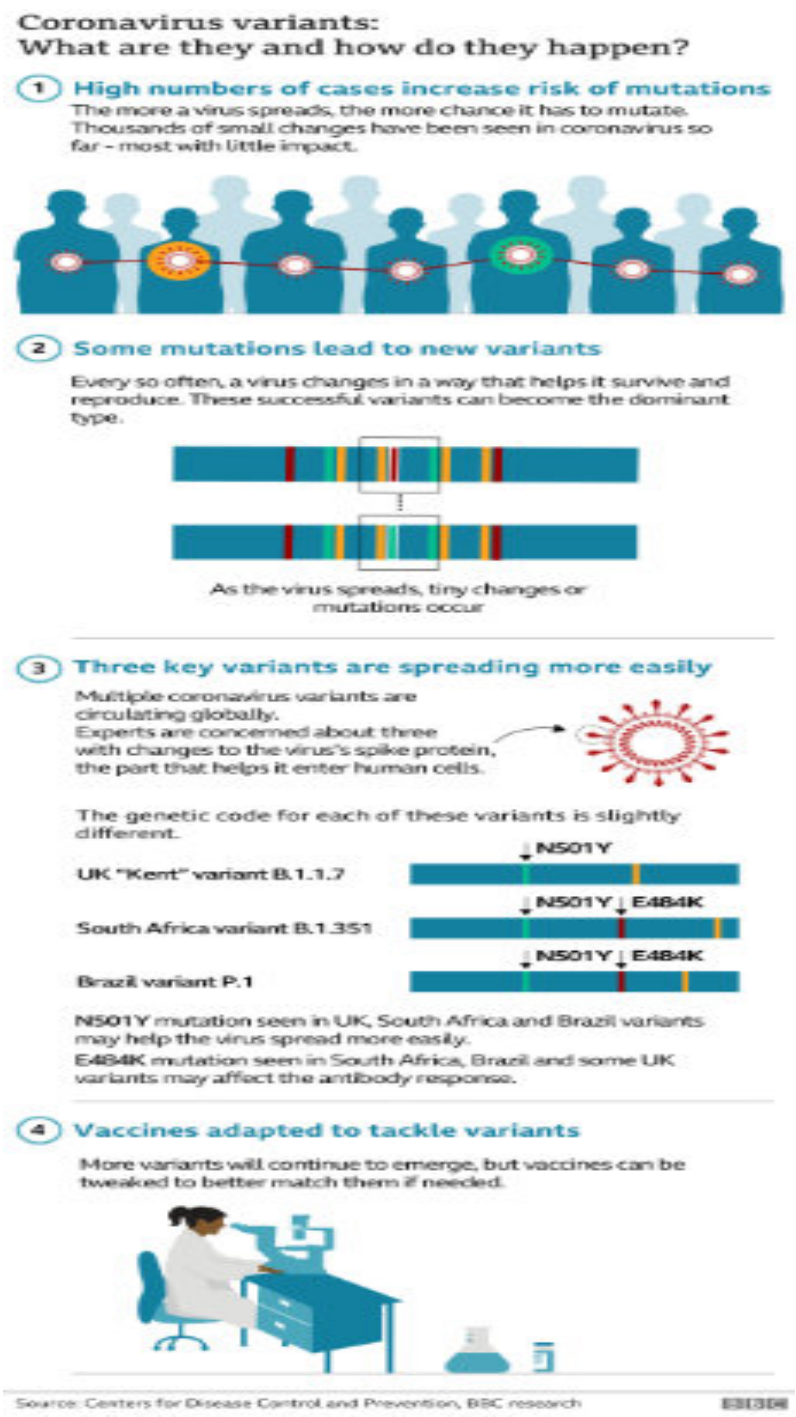
In Italia al 18 marzo scorso la prevalenza della cosiddetta '**variante inglese**' del virus Sars-CoV-2 era del **86,7%**, con valori oscillanti tra le singole regioni tra il 63,3% e il 100%.

Per quella '**brasiliana**' la prevalenza era del **4,0%** (0%-32,0%), mentre le altre monitorate sono sotto lo 0,5%.

Le stime di prevalenza a livello nazionale sono le seguenti: a) per la variante lineage B.1.1.7 86.7% (range: 63,6%-100%)
b) per la variante lineage P.1 4.0% (range: 0%-32%)
c) per la variante lineage B.1.351 0.1% (range: 0%-4,8%)
d) per la variante linegae P.2 0%
e) per la variante lineage B.1.525 0.6% (range: 0%-13,3%)

‘variante indiana’, classificata con la sigla **B.1.671** e divenuta predominante in **India.** Nel **Regno Unito** finora è stata riscontrata in 77 casi. Per **Danny Altmann**, professore di immunologia dell’Imperial College, la nuova variante potrebbe “fare naufragare” il cammino verso la libertà della Gran Bretagna, anche se per i **medici britannici** si tratta al momento di “una **variante d’interesse**“, e non di un’allerta vera e propria tenuto conto dell’impatto ancora **limitato** e **circoscritto**.

doppia mutazione", individuata per la prima volta in India.
Questa variante è nota per la caratteristica doppia alterazione, che interessa L452R, la stessa osservata in una variante californiana, e E484Q,



Current vaccines were designed around earlier versions of coronavirus, but scientists believe they should still work against the new ones, although perhaps not quite as well.

Early results suggest the Pfizer vaccine protects **against the new variants**, but is slightly less effective.

Two new coronavirus vaccines **Novavax** and another from **Janssen** - appear to offer some protection too.

Data from the Oxford-AstraZeneca vaccine team suggests it protects just as well against the new UK variant. It offers less protection against the South Africa variant - although it should **still protect against severe illness**.

Early results **from Moderna suggest its vaccine is effective against the South Africa variant**, although the immune response may not be as strong or long-lasting.

Variants could emerge in the future that are more different again.

Even in the worst case scenario, vaccines could be redesigned and tweaked to be a better match - in a matter or weeks or months, if necessary,

As with flu, where a new shot is given each year to account for any changes in circulating flu viruses, something similar could happen for coronavirus.

Un vaccino a RNA contiene una piccola porzione del codice genetico necessario per produrre uno o più tipi di proteine nel virus. Nel caso del vaccino contro il coronavirus, l'RNA messaggero contiene solo le informazioni necessarie per produrre le proteine a forma di chiodo che circondano il coronavirus (spicole). Pertanto, il vaccino non può causare il COVID-19. Gli RNA messaggeri sono racchiusi in minuscole gocce di grasso da iniettare nel corpo. Il vaccino non contiene un coadiuvante

Una volta iniettate nel corpo umano, le gocce di grasso vengono "inghiottite" dalle cellule circostanti. Queste cellule leggono il codice dell'RNA messaggero e per circa 2 giorni producono delle proteine “spike” che vengono individuate dal sistema immunitario. In risposta, il nostro sistema immunitario produce anticorpi tanto come cellule speciali, che possono riconoscere ed eliminare rapidamente il coronavirus in caso di infezione.

vaccini ad adenovirus come vettore

utilizzano come ‘vettore’ un virus, modificato in laboratorio e totalmente inattivato, capace di portare alle cellule immunitarie l’informazione della proteina Spike, utilizzata dal Sars-Cov-2 per infettare le nostre cellule.
Entrando in contatto con la Spike, i linfociti T del nostro organismo si attivano contro di essa:

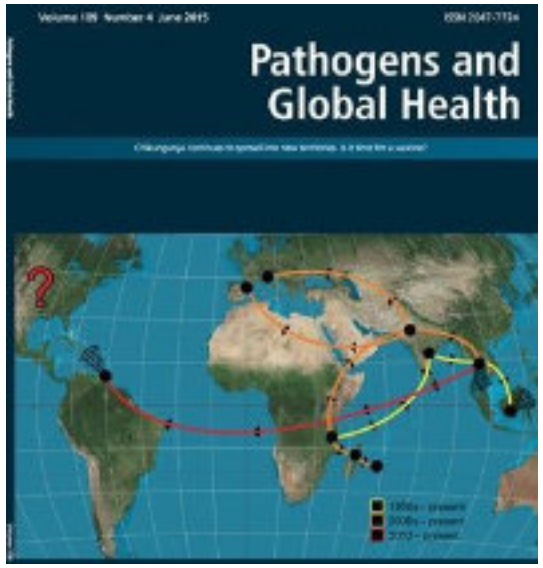
- producendo anticorpi specifici;
- trasmettendo ai linfociti B l’indicazione di sintetizzare quelli definitivi;
- mantenendo l’informazione per il futuro”.

- **Astrazeneca utilizza un adenovirus tipico degli scimpanzé;**
- **Janssen (di Johnson&Johnson) un adenovirus umano (Ad26).**

Sputnik V, il vaccino russo a vettore virale sviluppato per Covid-19, sarebbe efficace nel prevenire lo sviluppo della malattia nel 91% dei casi. Ad annunciarlo è una pubblicazione sulla rivista "The Lancet". Un risultato importante raggiunto nella sperimentazione di fase III su oltre 20 mila individui.

un virus reso innocuo (la scatola) contenente una piccola porzione di Dna che serve a far produrre la proteina spike.

Il vaccino Sputnik, a differenza degli altri a vettore virale, sfrutta due "scatole" differenti. Nella prima iniezione viene utilizzato il virus Ad26 per la prima dose e Ad25 per la seconda, a 21 giorni dalla prima. Una scelta, quella di utilizzare due vettori differenti



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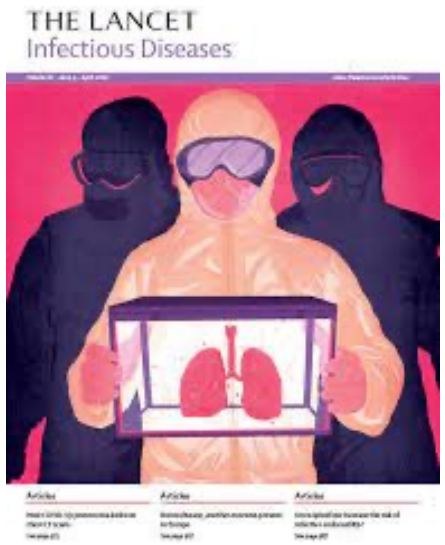
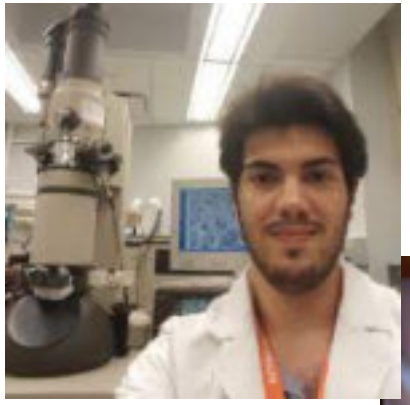
March 2021

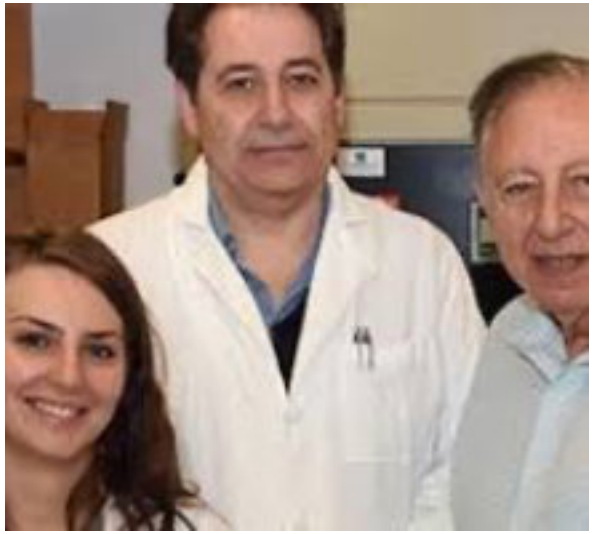


PRONTI A FERMARLO?
Insieme ce la faremo.

PROF TULIO DE OLIVEIRA

SILVIA ANGELETTI Campus bioMedico





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