WARWICK

THE COVID-19 PANDEMIC: WARP SPEED SCIENCE TO FIND A CURE

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2nd July 2020 Webinar.

World Health Organization

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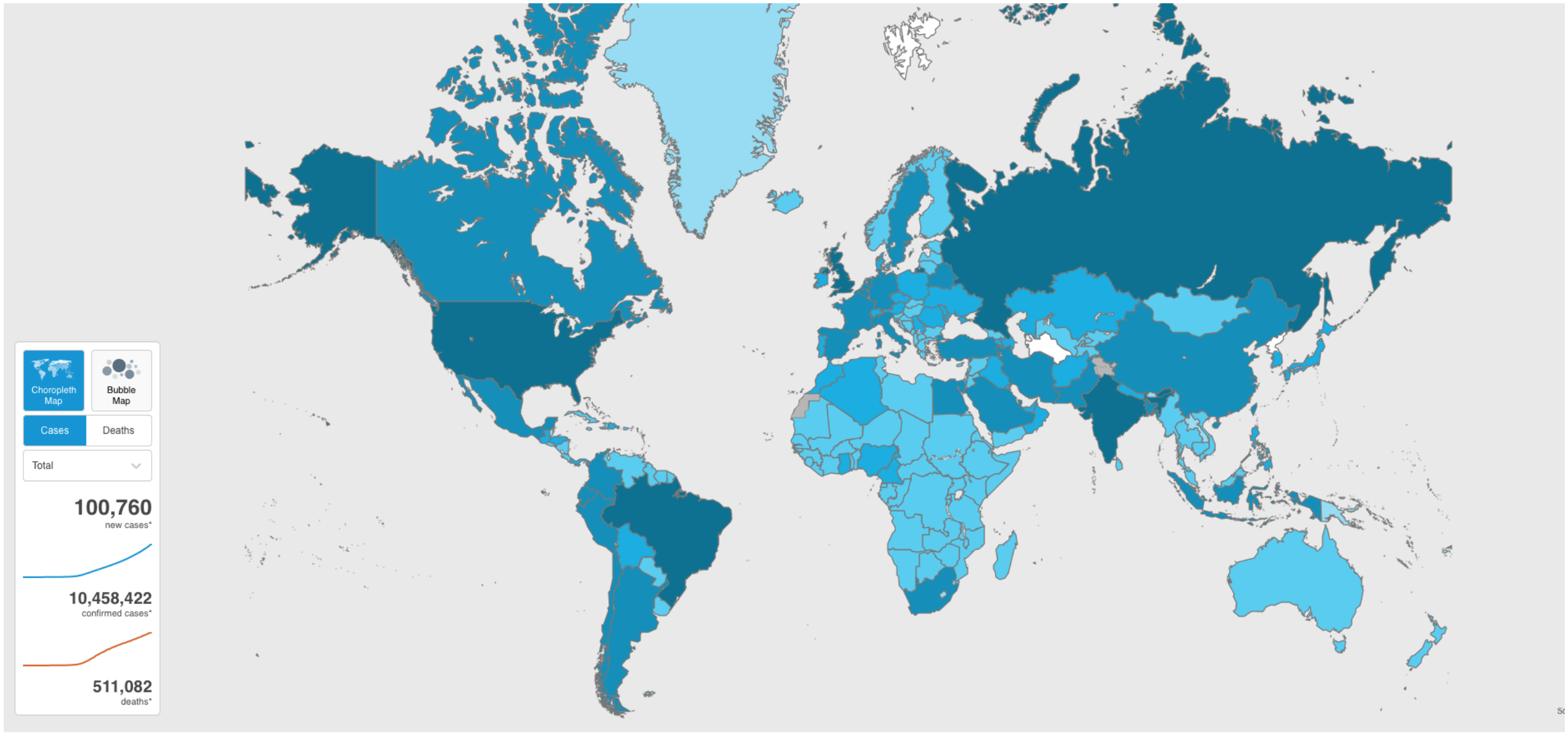
WHO Coronavirus Disease (COVID-19) Dashboard

Data last updated: 2020/7/2, 8:05am CEST

Overview Explorer

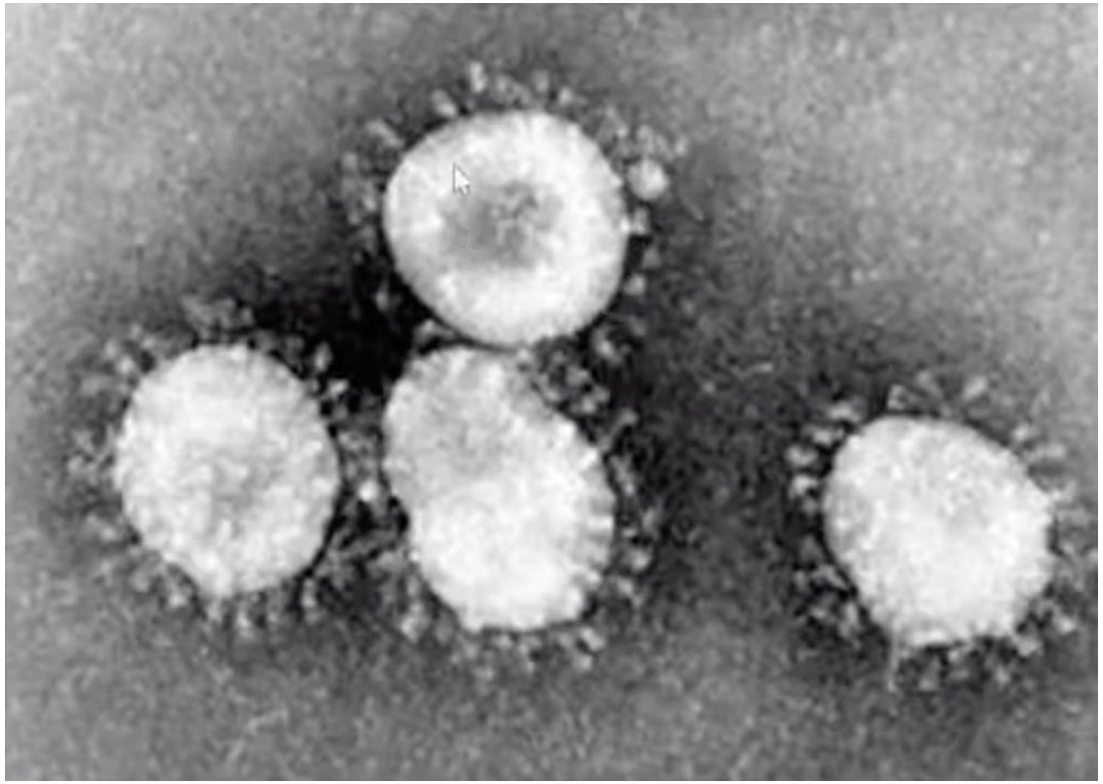


Globally, as of **8:05am CEST, 2 July 2020**, there have been **10,458,422 confirmed cases** of COVID-19, including **511,082 deaths,** reported to WHO.

COVID-19 Topics to Cover

- SARS-CoV-2 infection, replication, evolution and variation.
- Pathogenesis of COVID-19, immune responses and the cytokine storm.
- Repurposed drugs for COVID-19 therapy.
- Towards effective vaccines: what might work and why?

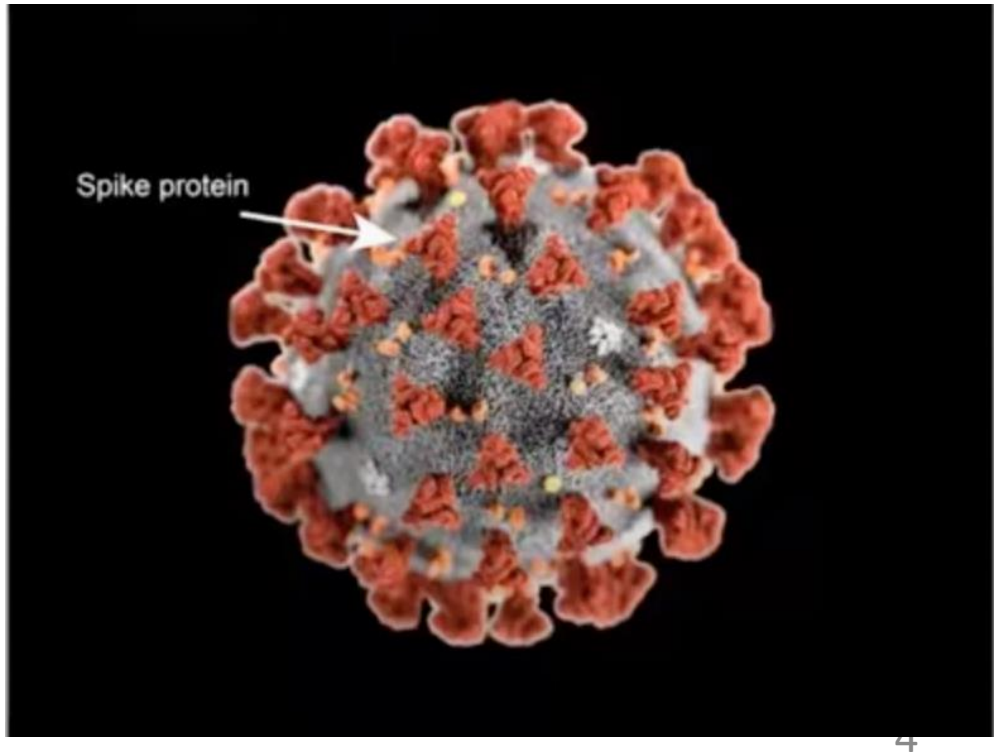
Coronaviridae



Coronaviruses (subfamily orthocoronavirinae)

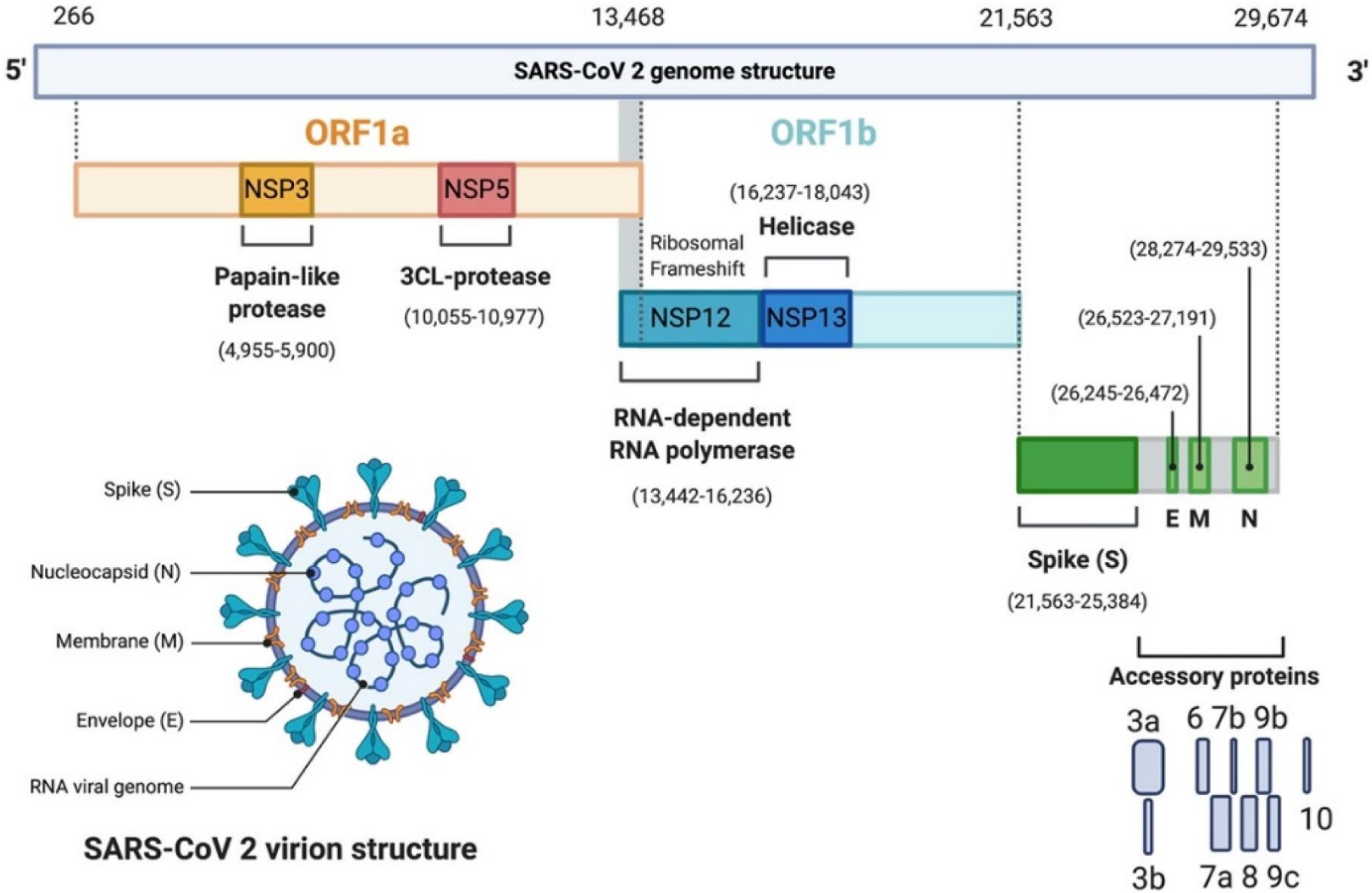
Positive single-stranded RNA virus

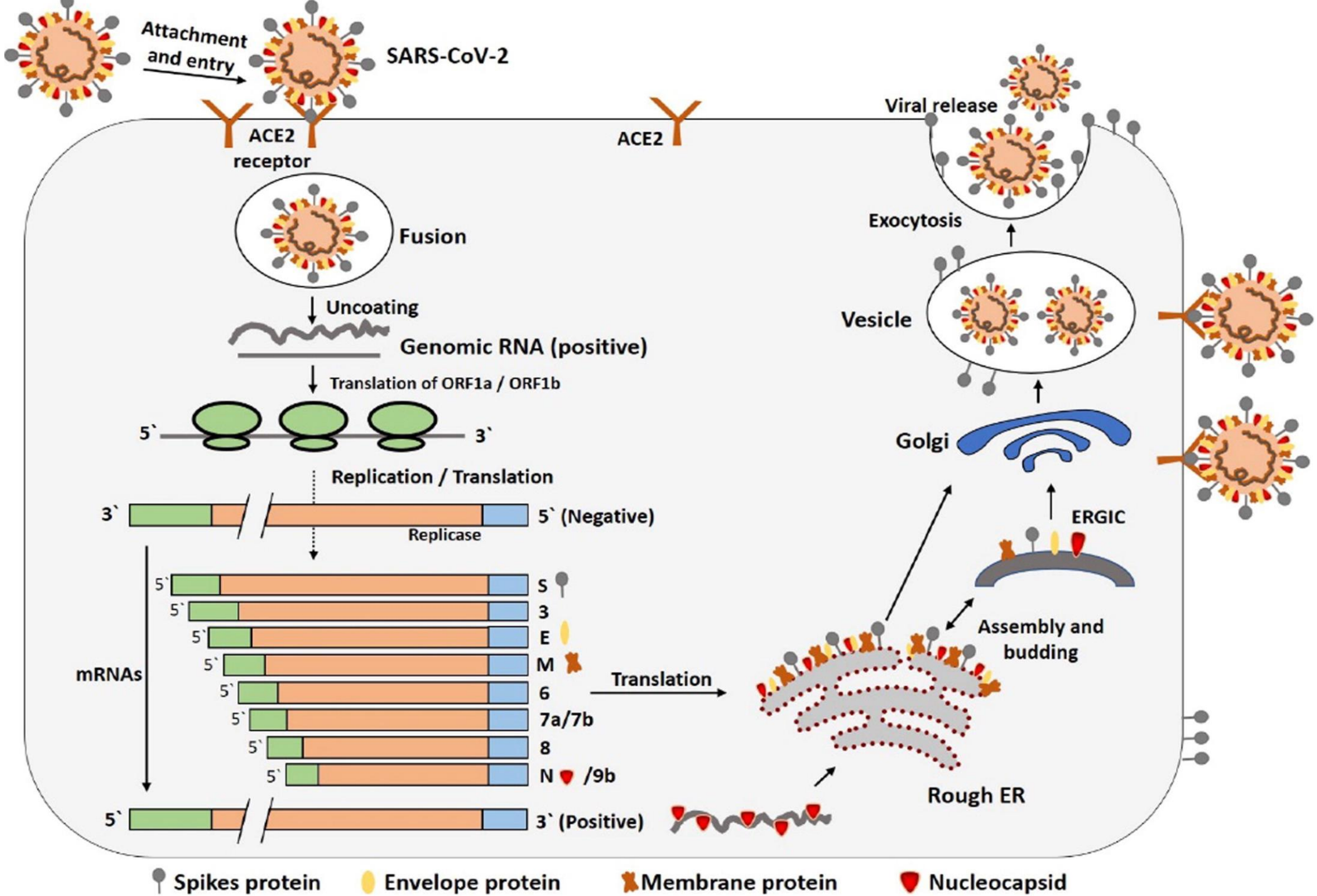
Described in 1968 by June Alemeida and David Tyrell

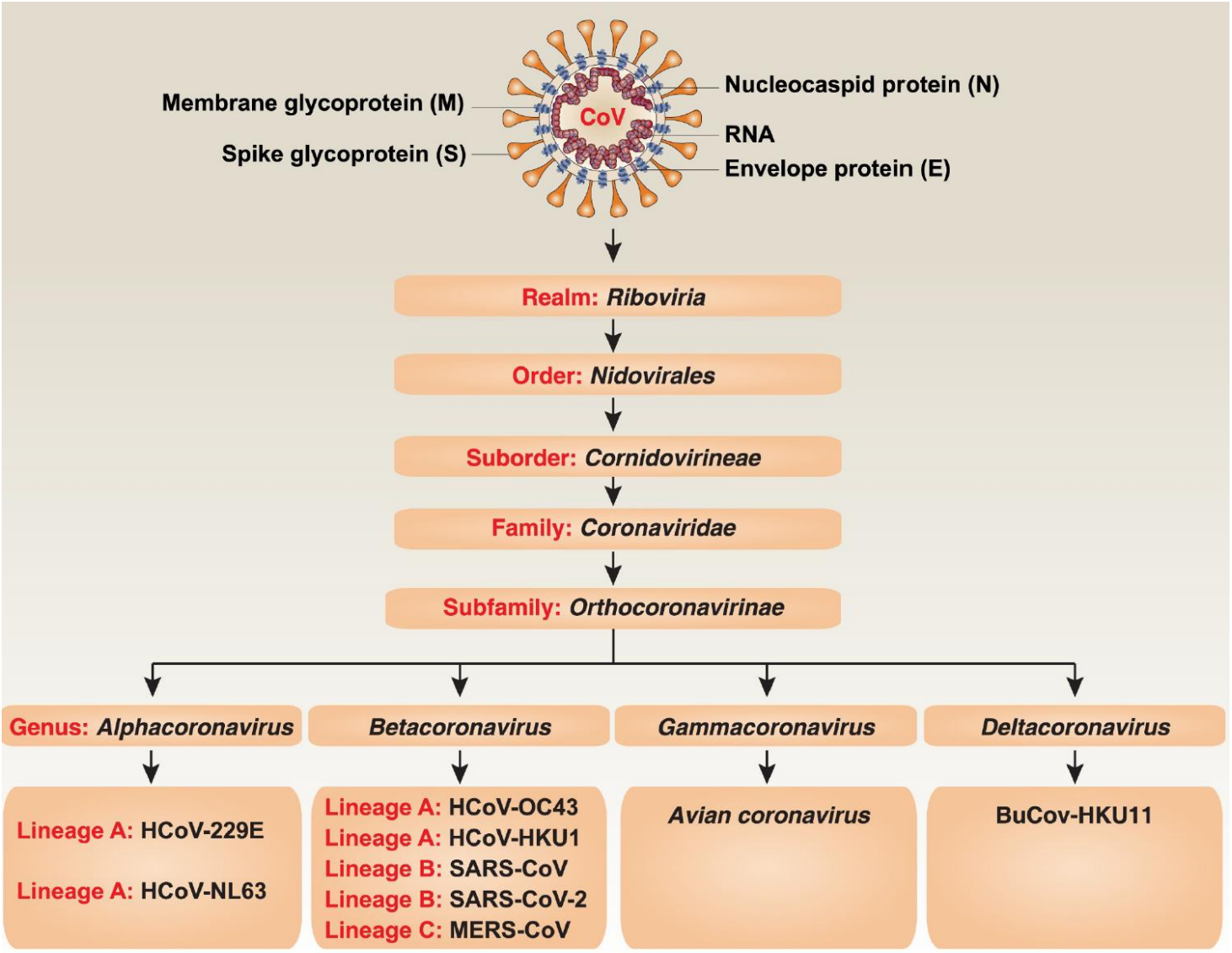


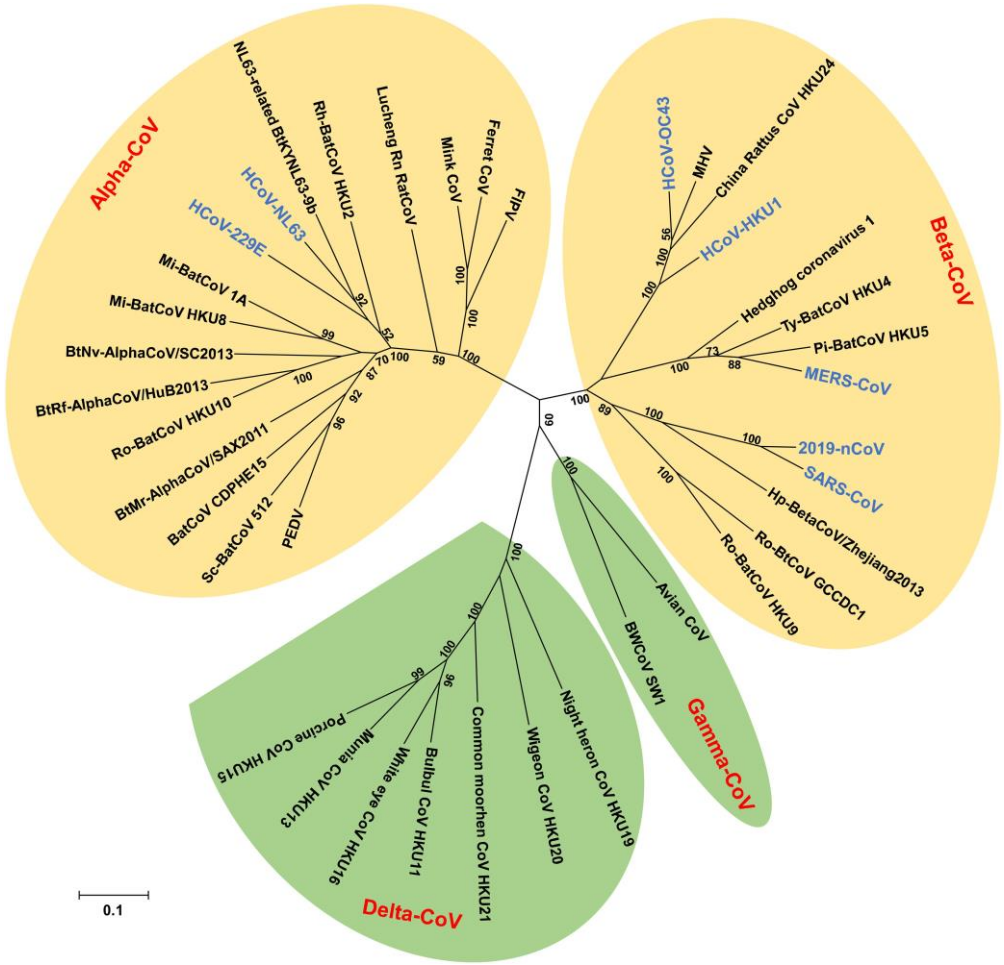
Timelines of the SARS-CoV-2 outbreak

Dec 8th	First case of mysterious pneumonia associated with Wuhan wet market
Jan 1st	Wet market closed
Jan 8th	First official announcement by Chinese state
Jan 11th	First death announced in China. Genome sequence
Jan 20th	China reports cases outside Hubei province – Beijing, Shanghai, Shenzhen.
Jan 23rd	Sequence said to be identical to that of bat coronavirus and similar to pangolin
Jan 27th	Evidence that 2019-nCoronavirus was present in samples from Wuhan wet market
Jan 30th	WHO declare a global emergency
Jan 31st	First two cases in UK.
Feb 9th	Death toll in China is 811 with 37,198 infections
Feb 11th	WHO calls disease COVID-19 and virus SARS-CoV-2
Feb 23rd	Italy confirms 3 deaths from COVID-19
Feb 26th	Cases confirmed across Europe, Brazil, Middle East, Pakistan.
Feb 29th	23 cases in UK and US reports first death.
March 8th	US reports more than 500 cases and state of emergency in 8 states.
March 11th	WHO declares the coronavirus outbreak a pandemic
March 23rd	UK PM announces lockdown, around 422 deaths in UK.

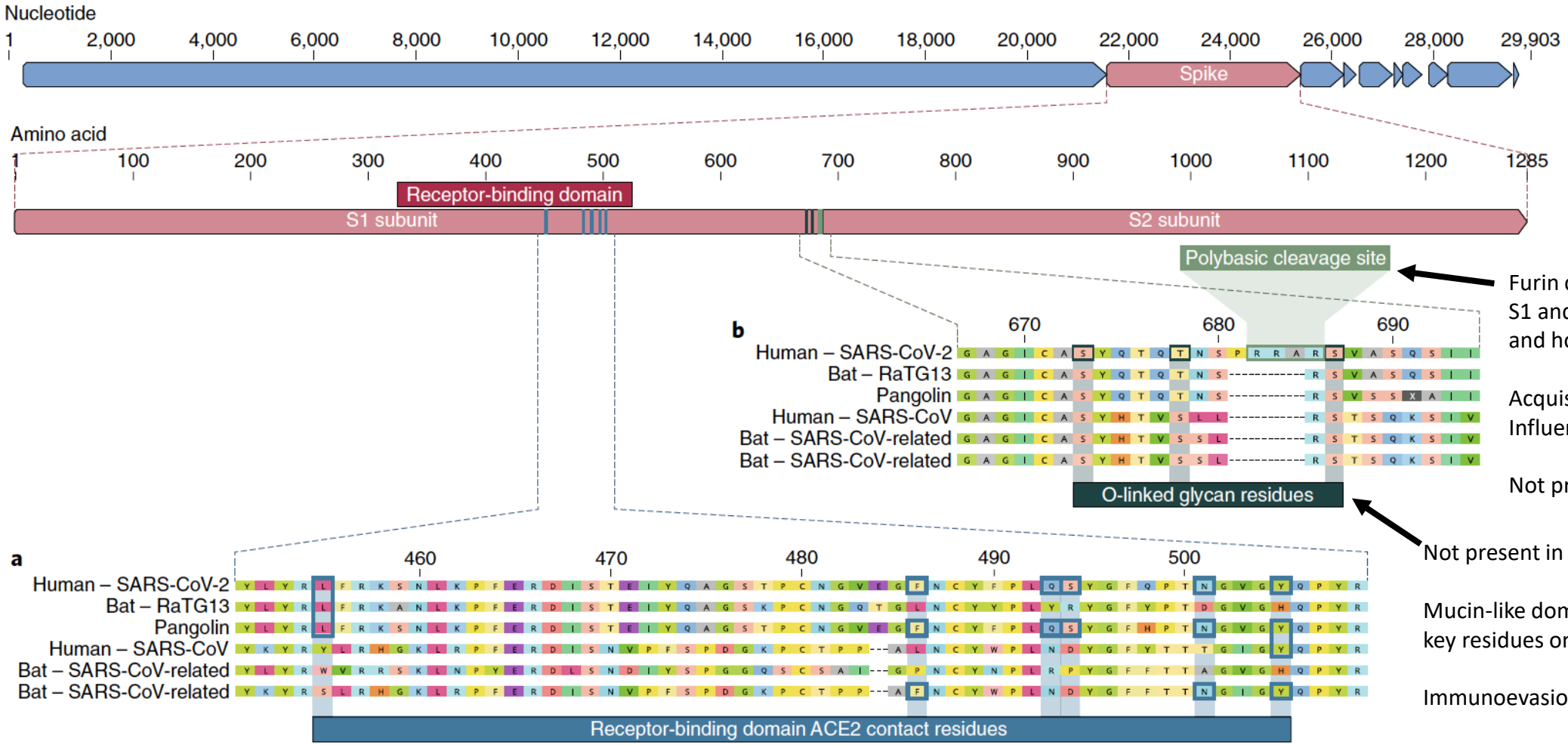

266
13,468
21,563
29,674
5'
SARS-CoV 2 genome structure
3'
ORF1a
ORF1b
NSP3
NSP5
(16,237-18,043)
Helicase
Ribosomal
Frameshift
(28,274-29,533)
Papain-like
protease
(4,955-5,900)
3CL-protease
(10,055-10,977)
NSP12
NSP13
(26,523-27,191)
(26,245-26,472)
RNA-dependent
RNA polymerase
(13,442-16,236)
E M N
Spike (S)
(21,563-25,384)
Accessory proteins
3a 6 7b 9b
10
3b 7a 8 9c
Spike (S)
Nucleocapsid (N)
Membrane (M)
Envelope (E)
RNA viral genome
SARS-CoV 2 virion structure


Attachment and entry
SARS-CoV-2
ACE2 receptor
ACE2
Viral release
Exocytosis
Fusion
Uncoating
Genomic RNA (positive)
Translation of ORF1a / ORF1b
5`
3`
Vesicle
Golgi
ERGIC
Replication / Translation
3`
5` (Negative)
Replicase
mRNAs
S
3
E
M
6
7a/7b
8
N /9b
Translation
Assembly and budding
Rough ER
5` (Positive)
Spikes protein
Envelope protein
Membrane protein
Nucleocapsid


Membrane glycoprotein (M)
Spike glycoprotein (S)
CoV
Nucleocaspid protein (N)
RNA
Envelope protein (E)
Realm: Riboviria
Order: Nidovirales
Suborder: Cornidovirineae
Family: Coronaviridae
Subfamily: Orthocoronavirinae
Genus: Alphacoronavirus
Betacoronavirus
Gammacoronavirus
Deltacoronavirus
Lineage A: HCoV-229E
Lineage A: HCoV-NL63
Lineage A: HCoV-OC43
Lineage A: HCoV-HKU1
Lineage B: SARS-CoV
Lineage B: SARS-CoV-2
Lineage C: MERS-CoV
Avian coronavirus
BuCov-HKU11


Alpha-CoV
Beta-CoV
Gamma-CoV
Delta-CoV
NL63-related BtKYNL63-9b
Rh-BatCoV HKU2
Lucheng Rn RatCoV
Mink CoV
Ferret CoV
FIPV
HCoV-NL63
HCoV-229E
Mi-BatCoV 1A
Mi-BatCoV HKU8
BtNv-AlphaCoV/SC2013
BtRf-AlphaCoV/HuB2013
Ro-BatCoV HKU10
BtMr-AlphaCoV/SAX2011
BatCoV CDPHE15
Sc-BatCoV 512
PEDV
HCoV-OC43
MHV
China Rattus CoV HKU24
HCoV-HKU1
Hedghog coronavirus 1
Ty-BatCoV HKU4
Pi-BatCoV HKU5
MERS-CoV
2019-nCoV
SARS-CoV
Hp-BetaCoV/Zhejiang2013
Ro-BtCoV GCCDC1
Ro-BatCoV HKU9
Avian CoV
BWCoV SW1
Night heron CoV HKU19
Wigeon CoV HKU20
Common moorhen CoV HKU21
Bulbul CoV HKU11
White eye CoV HKU16
Munia CoV HKU13
Porcine CoV HKU15
0.1

Evolution of SARS-CoV-2



Furin cleavage site between S1 and S2 – role in virus infectivity and host range

Acquisition in HA of avian Influenza increases pathogenicity

Not present in betacoronaviruses

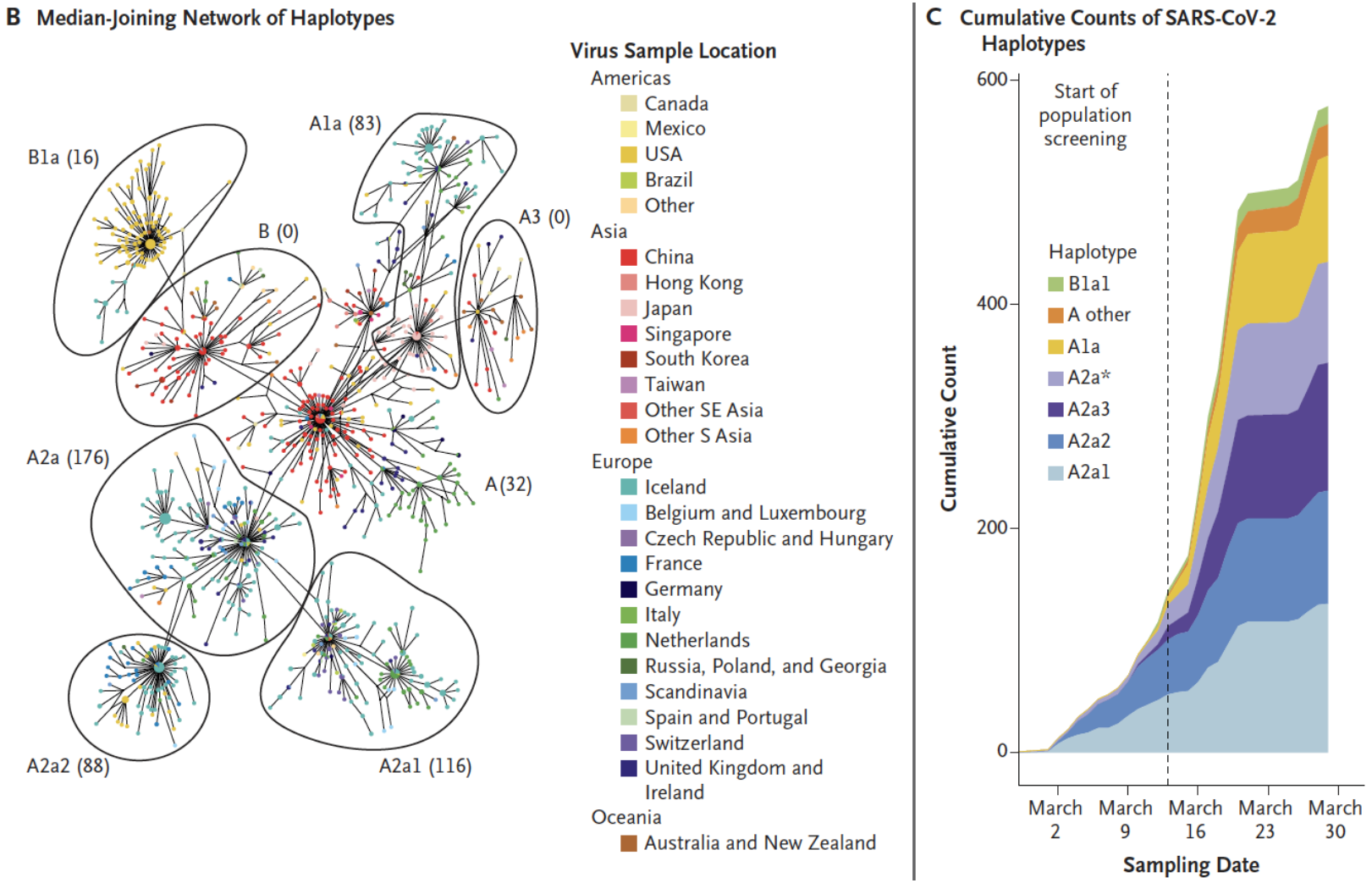
Not present in betacoronaviruses

Mucin-like domain that shields epitopes or key residues on the spike protein.

Immunoevasion

Natural selection in: (i) an animal host before zoonotic transfer or (ii) in humans following zoonotic transfer

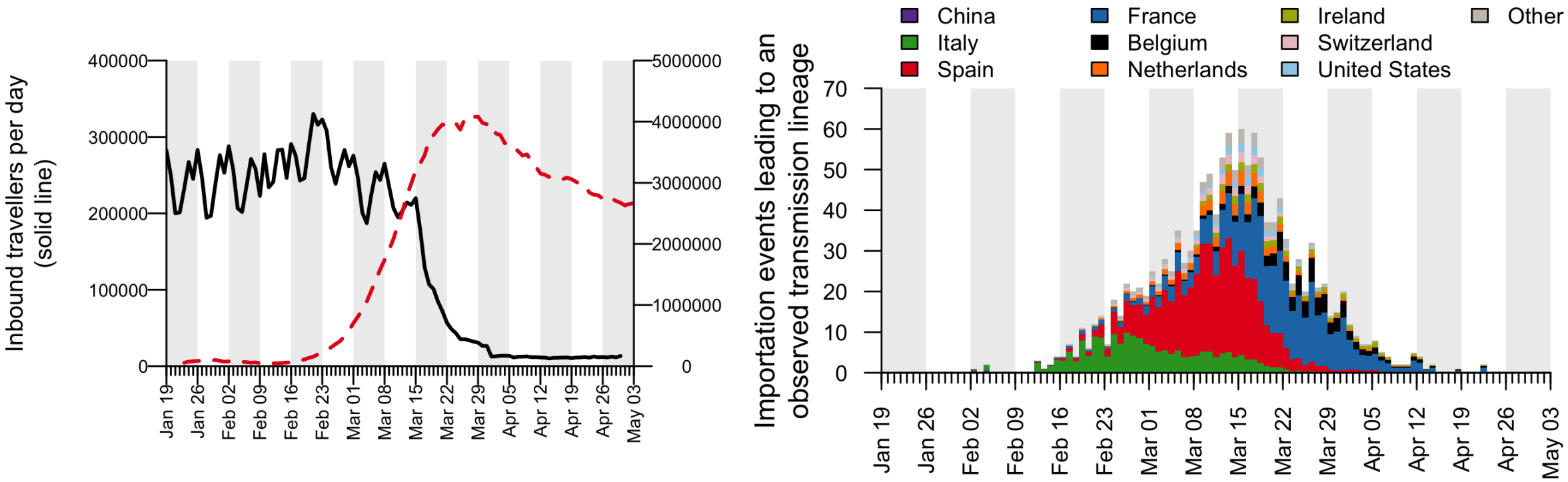
Virus genome sequencing identifies geographically segregated haplotypes



$1x10^{-3}$/site/year = 1 mutation every 1-10 transmissions

Gudbjartsson et al. 2020

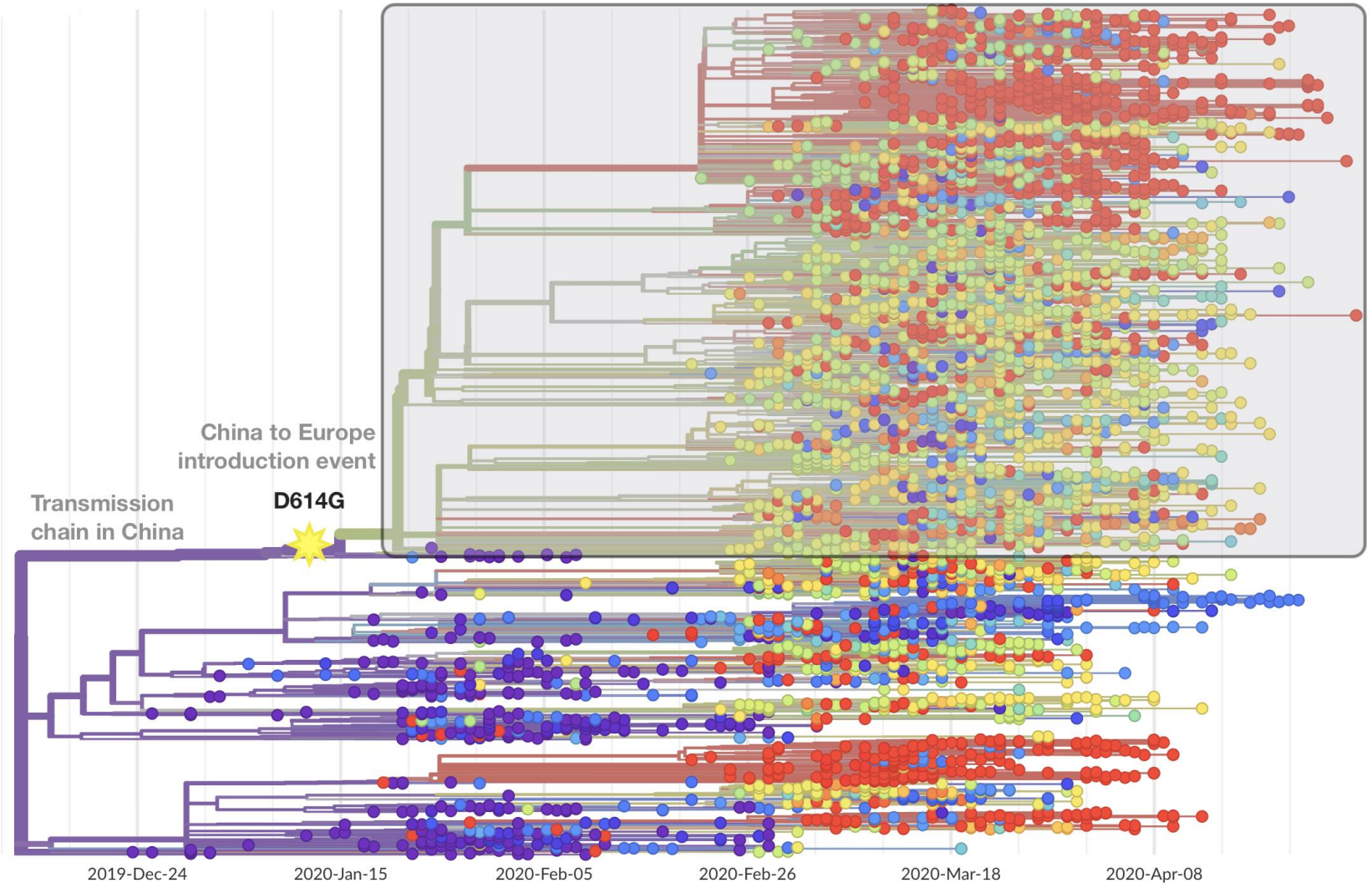
SARS-CoV-2 importation and establishment of UK transmission lineages



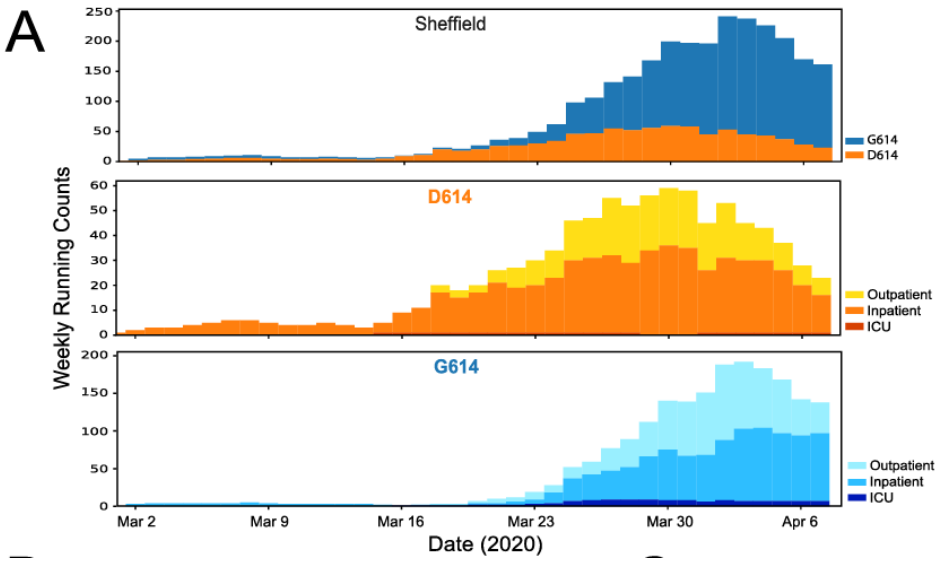
Over 1000 separate introductions into the UK from Europe

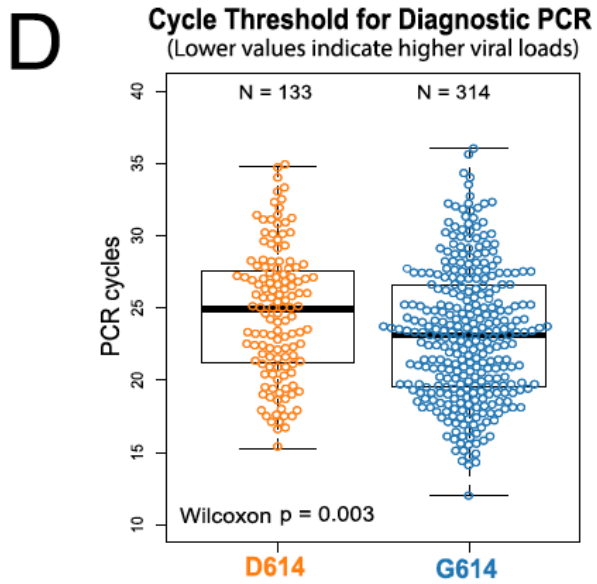
Pybus et al, 2020

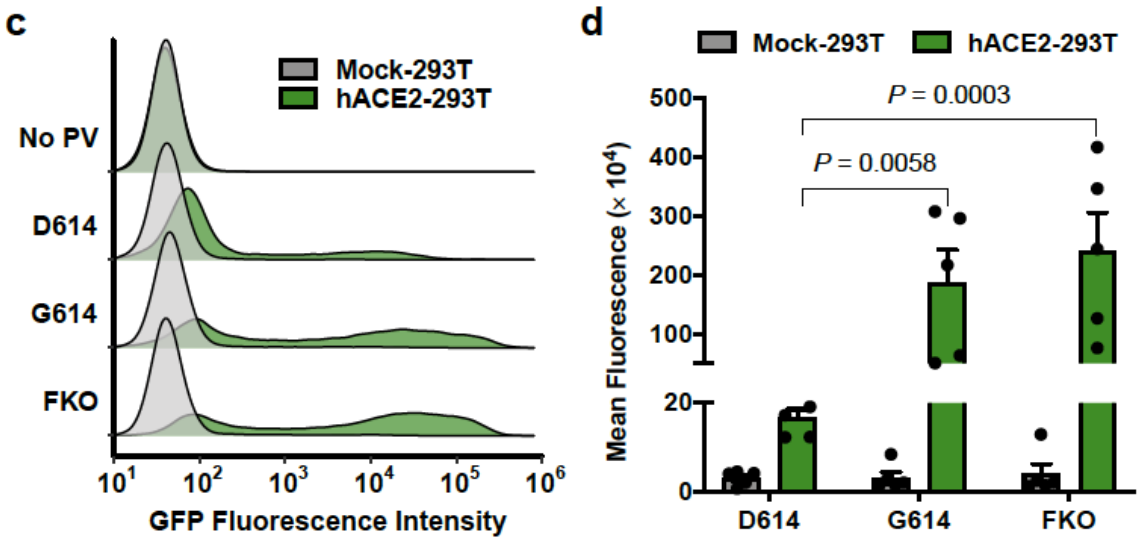
G614 is a founder mutation for European viruses



D614 and G614 spike strains have the same pathogenicity but G614 has higher transmissibility



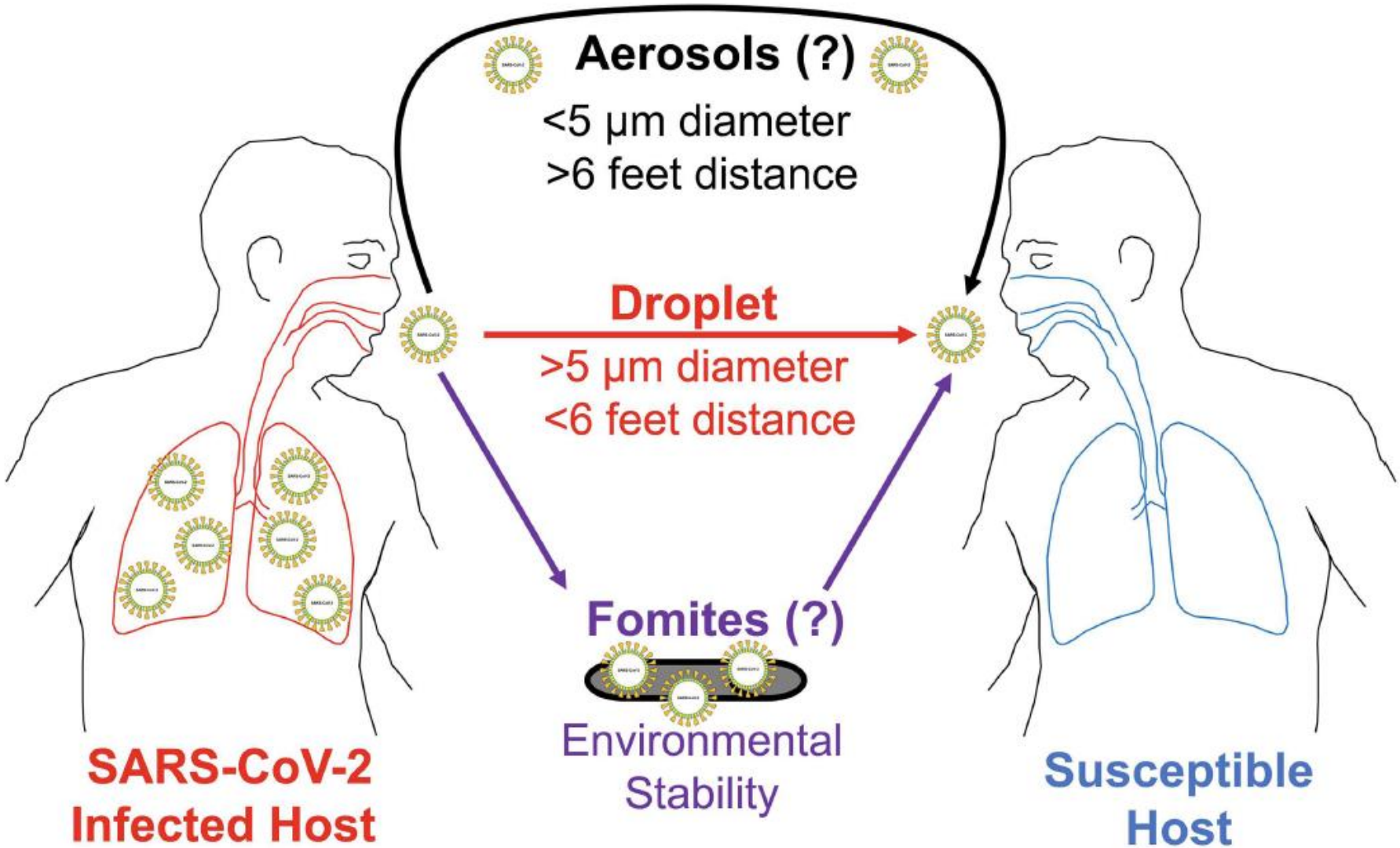




G614 is more stable than D614 – consistent with epidemiological data suggesting that viruses with G614 transmit more efficiently.

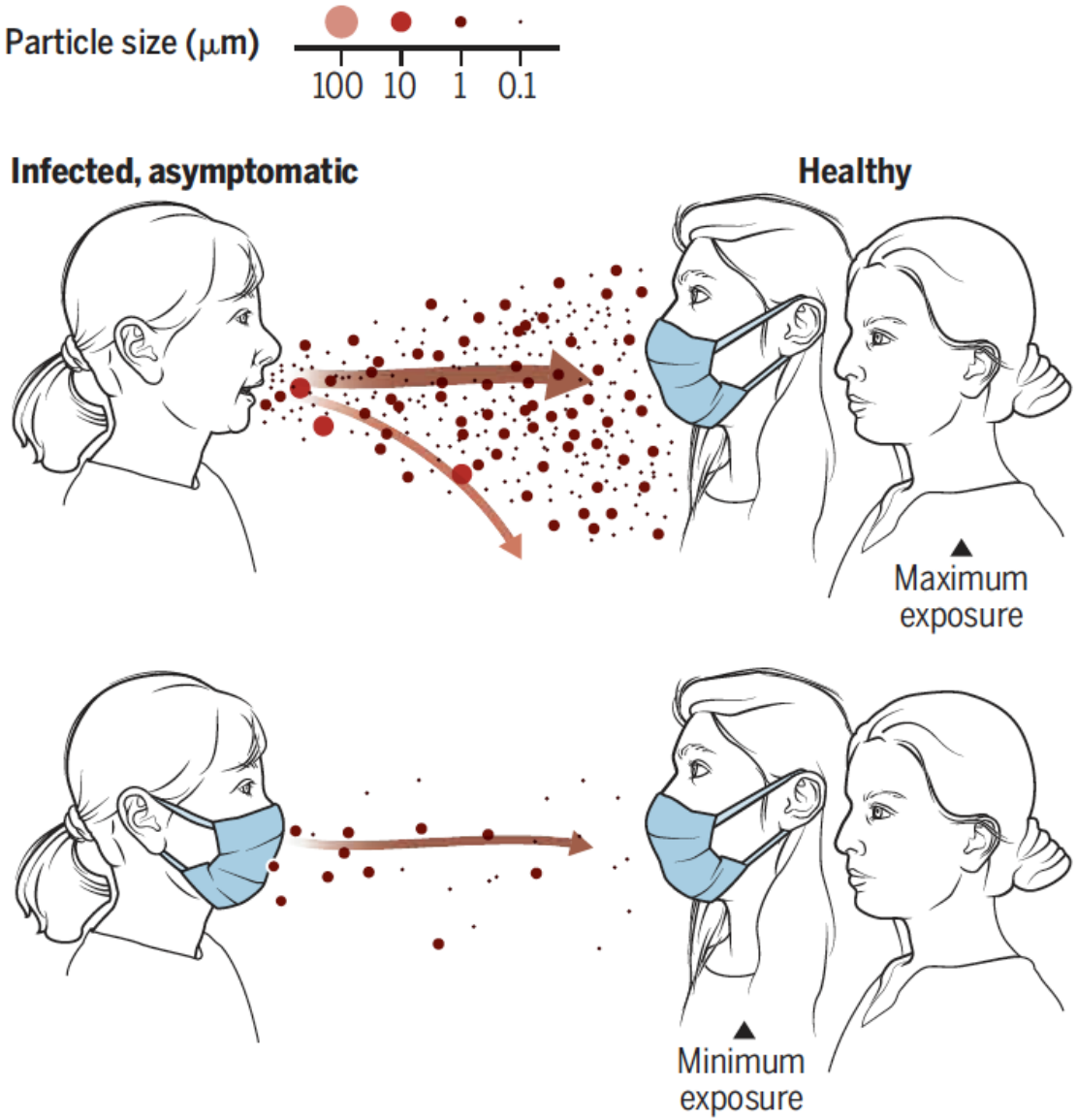
Zhang et al., 2020. Preprint

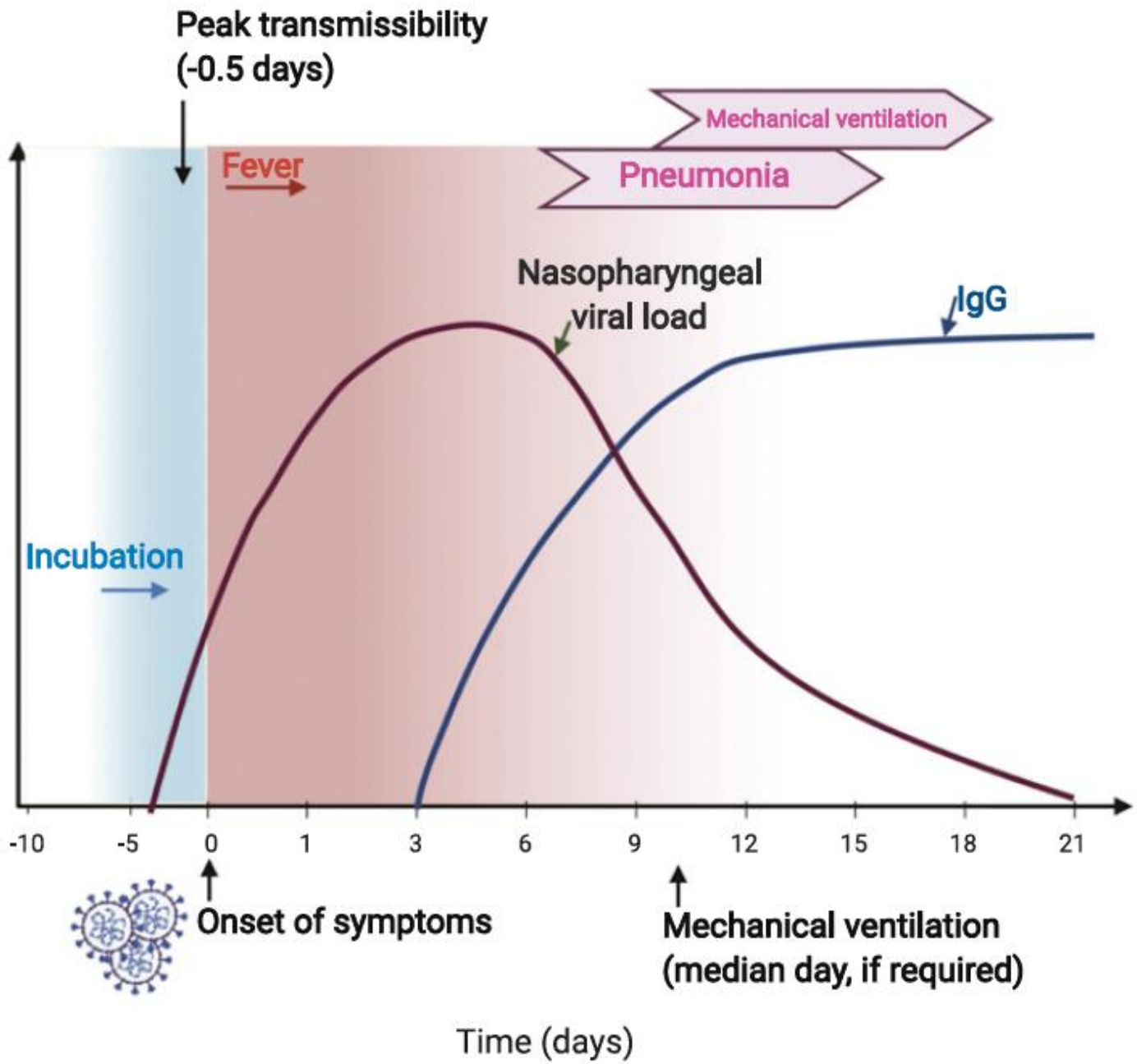
Korber et al (2020) https://www.biorxiv.org/content/10.1101/2020.04.29.069054v2


Aerosols (?)
<5 µm diameter
>6 feet distance
Droplet
>5 µm diameter
<6 feet distance
Fomites (?)
Environmental
Stability
SARS-CoV-2
Infected Host
Susceptible
Host

Masks reduce airborne transmission

Infectious aerosol particles can be released during breathing and speaking by asymptomatic infected individuals. No masking maximizes exposure, whereas universal masking results in the least exposure.




Peak transmissibility
(-0.5 days)
Mechanical ventilation
Fever
Pneumonia
Nasopharyngeal
viral load
IgG
Incubation
-10
-5
0
1
3
6
9
12
15
18
21
Onset of symptoms
Mechanical ventilation
(median day, if required)
Time (days)

Virus Virulence: Capacity to Cause Disease

Virulence depends on a combination of viral and host factors:

- Virus factors
  - dose
  - route of infection
  - isolates - genetically determined
- Host factors
  - age, sex, nutritional status
  - co-morbidities
  - immune status
  - genetics

COVID-19 characteristics

- Onset with high fever and sore throat, developing dry cough
  - 4 – 10 days post-infection
- Other symptoms including GI, loss of taste/smell
- Recovery after a few days (? with longer term issues remaining)
- Can progress to lower respiratory tract disease and viral pneumonia
- Low blood and tissue O_2, increased coagulation, as causes of multiple organ failure, also stroke risk
- Reduction in circulating lymphocytes associated with severe disease

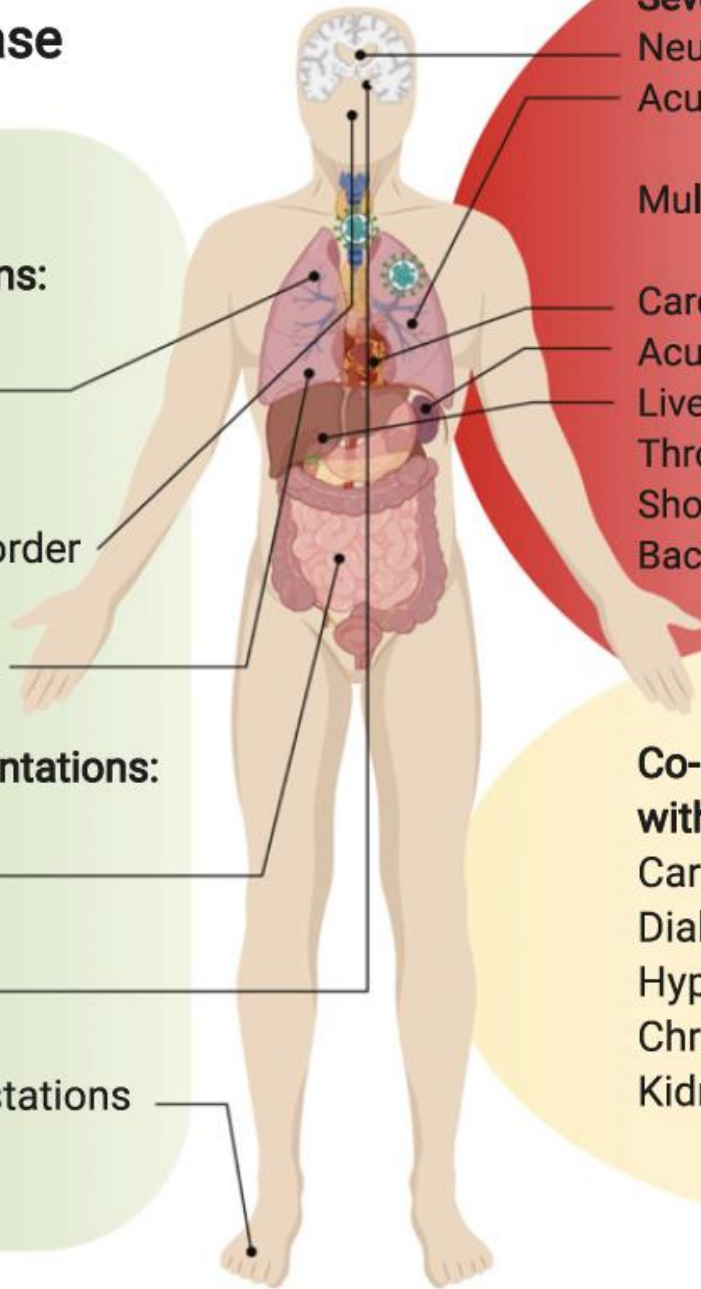
- Can be asymptomatic

A

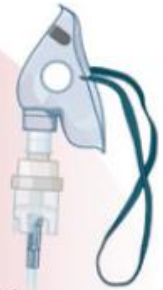
COVID-19 disease

Typical presentations:
- Fever
- Dry cough
- Exhaustion
- Anorexia
- Smell and taste disorder
- Myalgia
- Shortness of breath

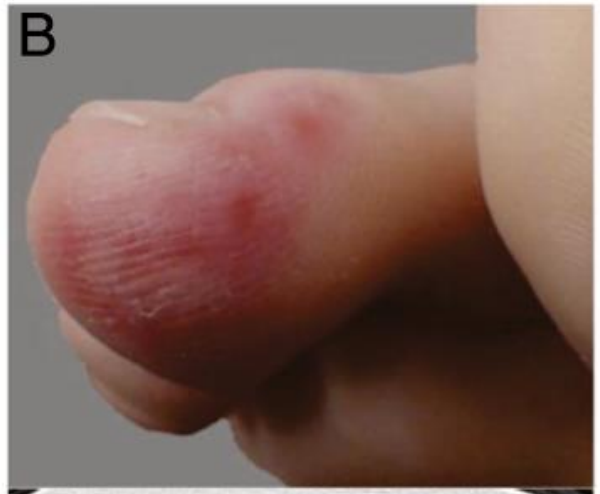
Less frequent presentations:
- Nausea
- Diarrhea
- Sore throat
- Rhinorrhea
- Headache
- Cutaneous manefestations

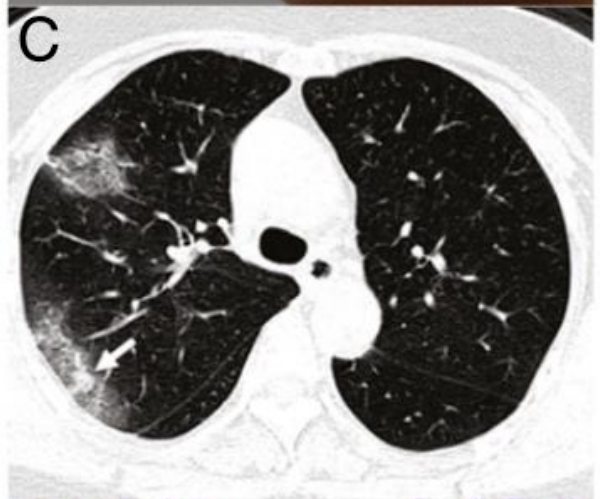


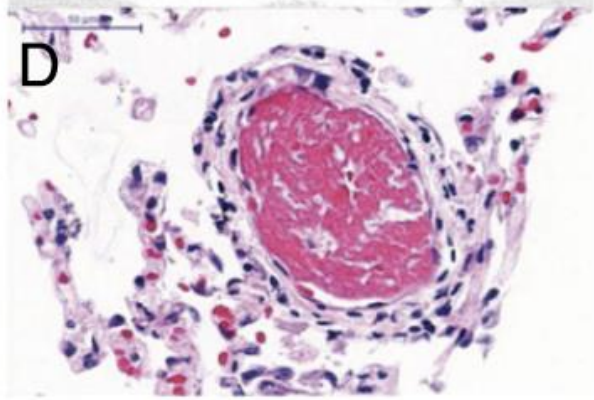
Severe presentations:
- Neurological complications
- Acute respiratory distress syndrome (ARDS)
- Multisystem inflammatory disease in children (MIS-C)
- Cardiac injury
- Acute kidney injury
- Liver dysfunction
- Thrombotic complications
- Shock and multi-organ failure
- Bacterial co-infection

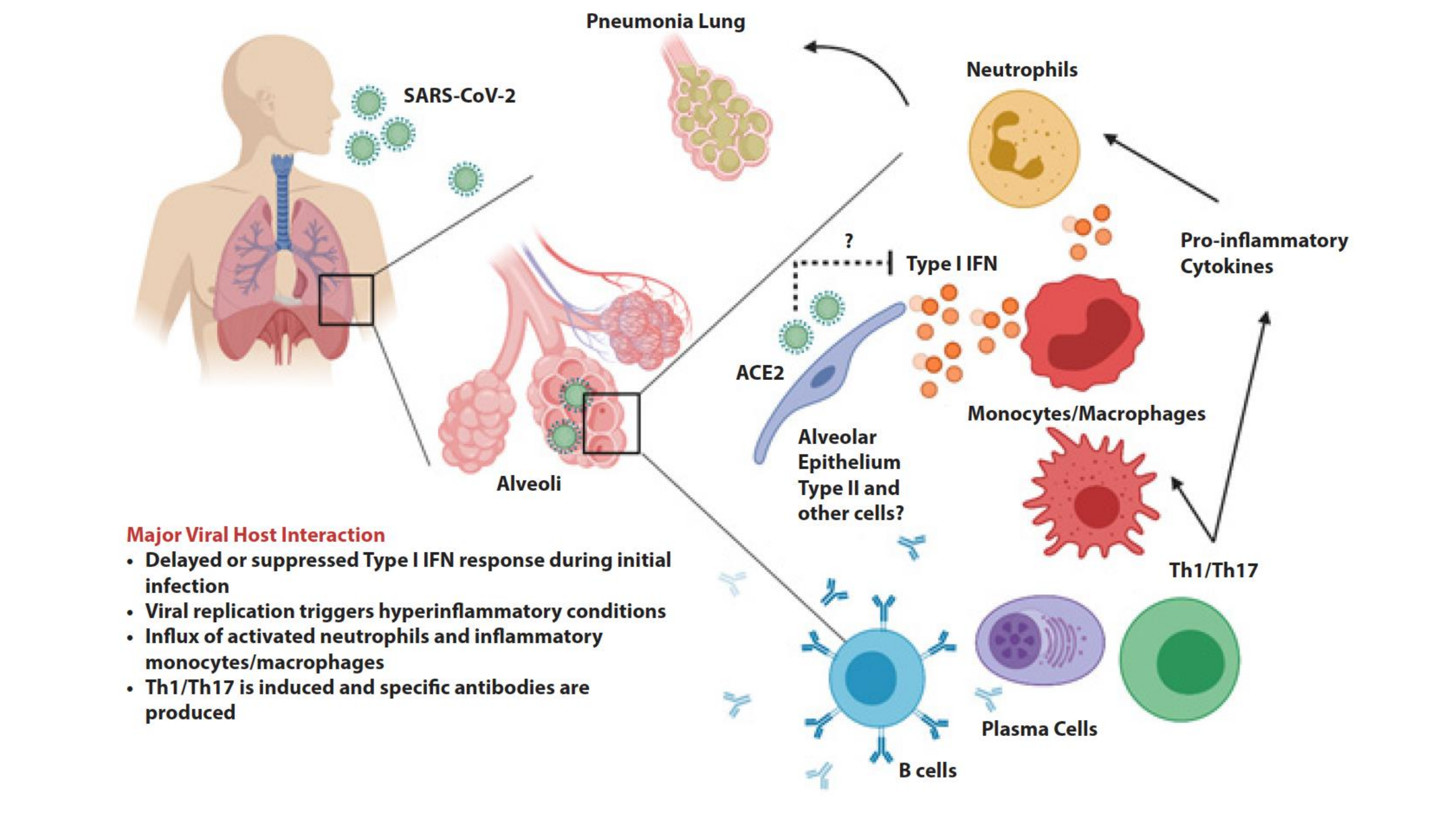


Co-morbidities associated with severe presentations:
- Cardiovascular diseases
- Diabetes
- Hypertension
- Chronic lung illness
- Kidney disease



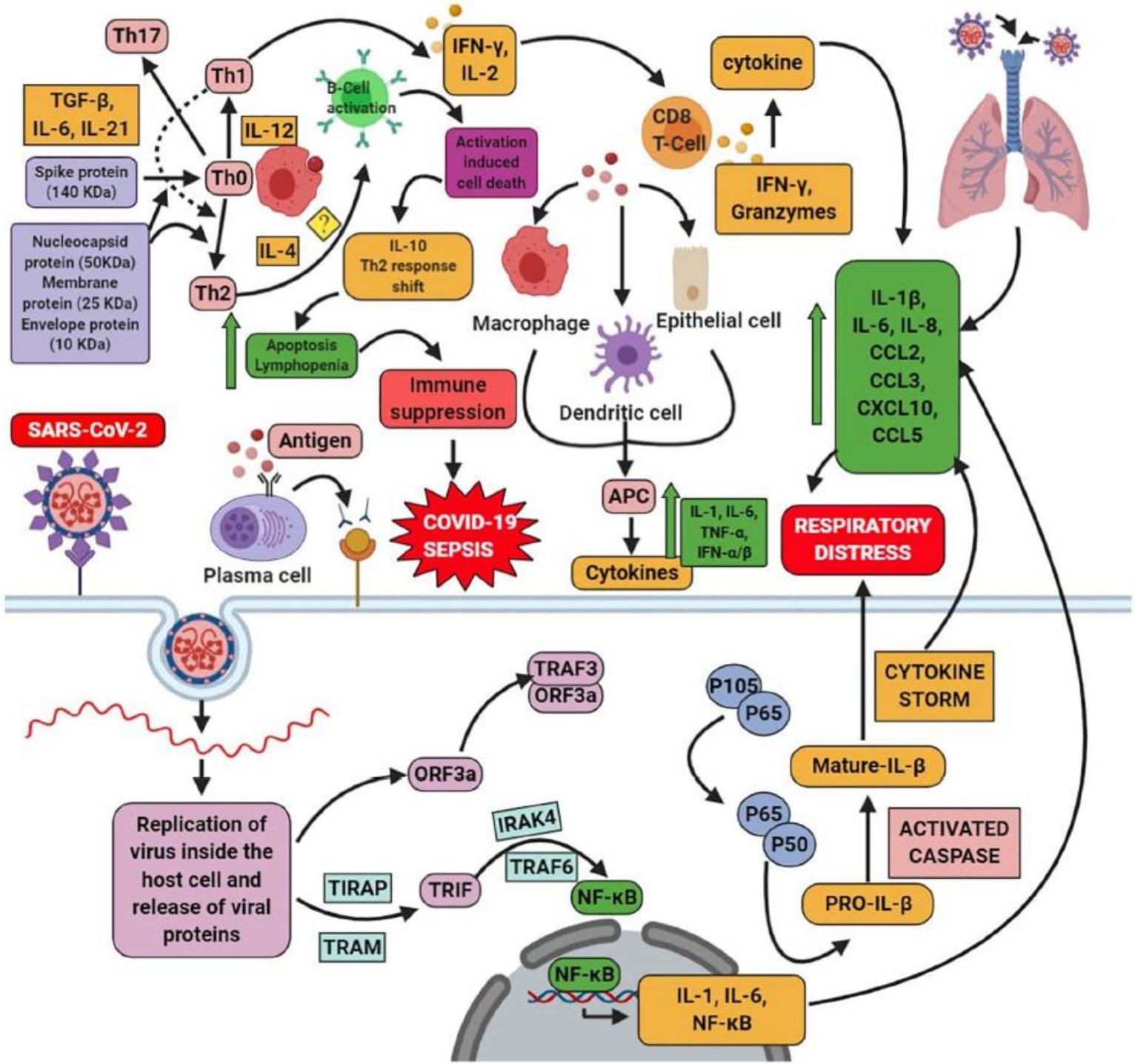






Major Viral Host Interaction

- Delayed or suppressed Type I IFN response during initial infection
- Viral replication triggers hyperinflammatory conditions
- Influx of activated neutrophils and inflammatory monocytes/macrophages
- Th1/Th17 is induced and specific antibodies are produced


Th17
Th1
IFN-γ, IL-2
cytokine
TGF-β, IL-6, IL-21
B-Cell activation
CD8 T-Cell
IL-12
Activation induced cell death
Spike protein (140 KDa)
Th0
IFN-γ, Granzymes
Nucleocapsid protein (50KDa) Membrane protein (25 KDa) Envelope protein (10 KDa)
IL-4
IL-10 Th2 response shift
Th2
Macrophage
Epithelial cell
IL-1β, IL-6, IL-8, CCL2, CCL3, CXCL10, CCL5
Apoptosis Lymphopenia
Immune suppression
Dendritic cell
SARS-CoV-2
Antigen
Plasma cell
COVID-19 SEPSIS
APC
IL-1, IL-6, TNF-α, IFN-α/β
Cytokines
RESPIRATORY DISTRESS
TRAF3
ORF3a
P105
P65
CYTOKINE STORM
ORF3a
Mature-IL-β
Replication of virus inside the host cell and release of viral proteins
IRAK4
TRAF6
P65
P50
ACTIVATED CASPASE
TIRAP
TRIF
NF-κB
PRO-IL-β
TRAM
NF-κB
IL-1, IL-6, NF-κB

Possible explanations for severe/fatal outcome in certain groups

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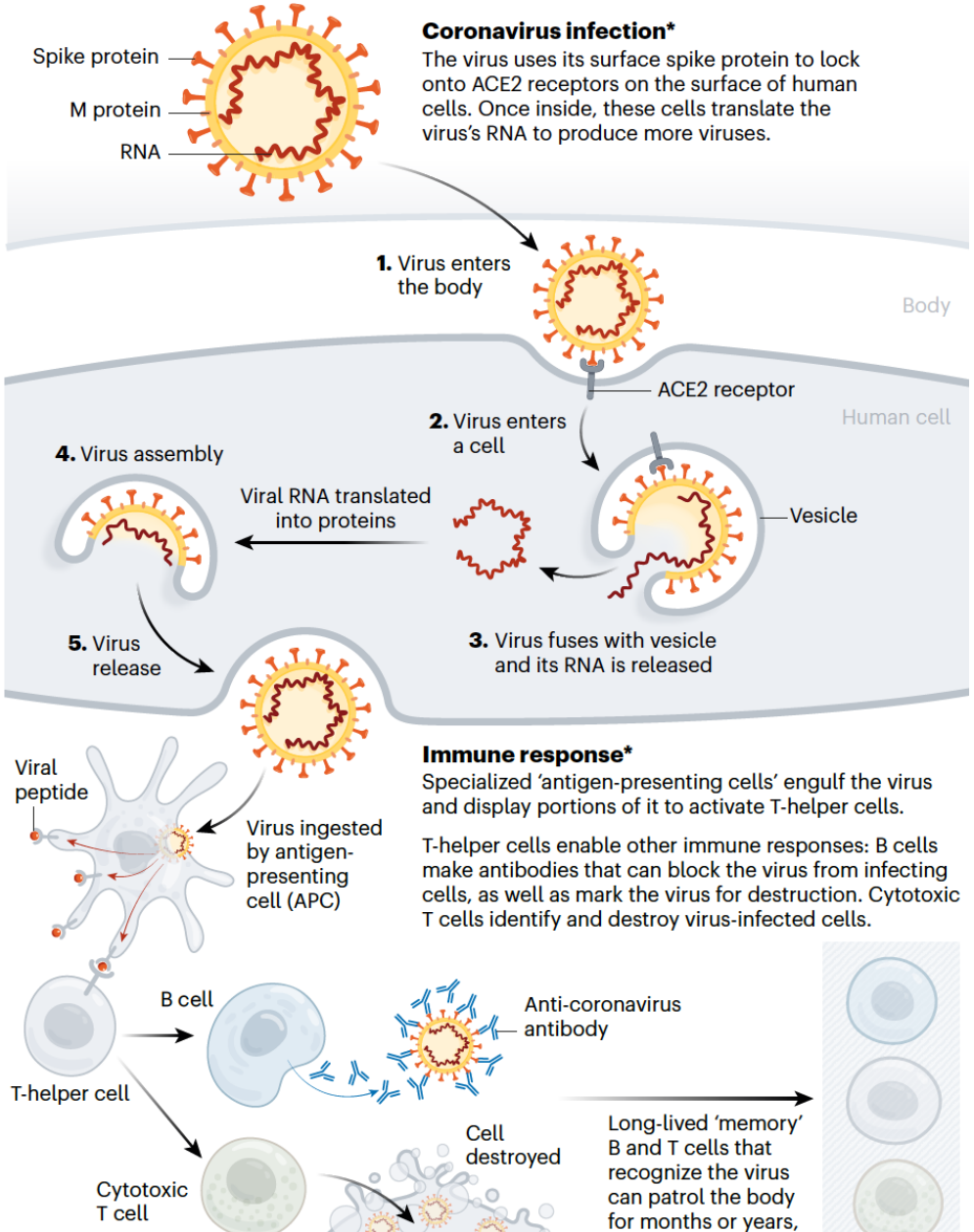
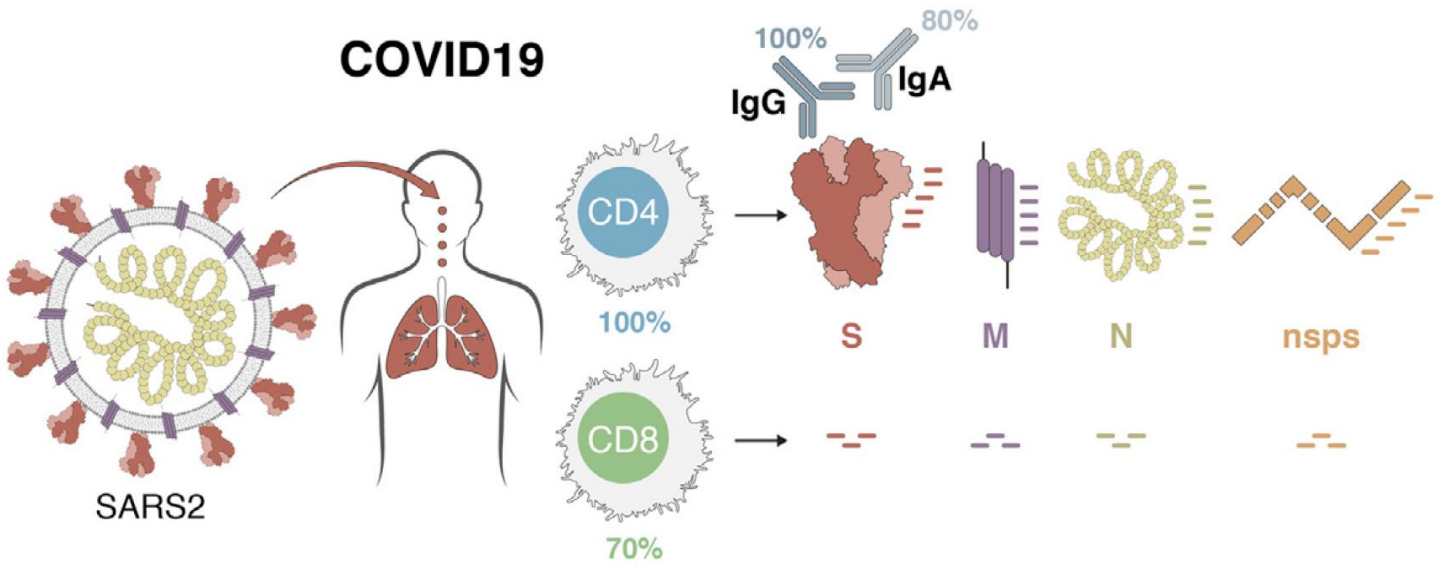
- Excess risk in some BAME groups after allowing for other risk factors (age, sex, socioeconomic etc)
    - ONS report 7 May into COVID-19 mortality and ethnicity
- Rare severe disease in young people with no known risk factors
- Genomics England mass sequencing study announced 13 May
    - Compare 20,000 infected in/were in ICU with 15,000 mild/mod symptom individuals
- Role of the immune response – innate and adaptive?

VACCINE BASICS: HOW WE DEVELOP IMMUNITY

The body's adaptive immune system can learn to recognize new, invading pathogens, such as the coronavirus SARS-CoV-2.





COVID-19
Various treatment options

1. Preventive strategies

Maintaining social distance,,wearing masks and using hand sanitizers

Vaccines: mRNA-1273, BCG, ChAdOx1 nCoV-19 etc.

Immune boosters: Vitamin C, Ocimum, Curcumin etc.

Viral entry inhibitors: Chloroquine, Teicoplanin etc.

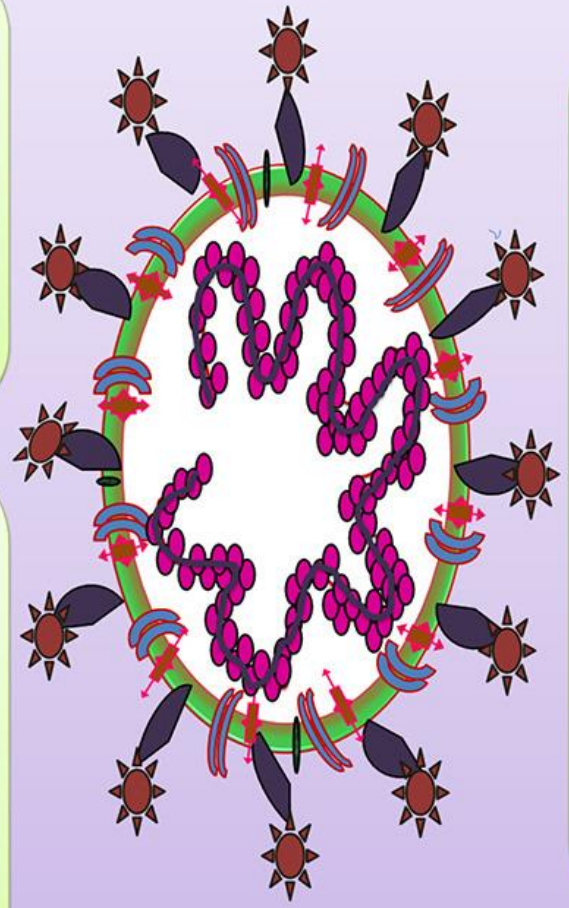
3. Management of ARDS and Cytokine storm

Monoclonal antibodies: Siltuximab, Tocilizumab, Sarilumab etc.

Chloroquine/hydroxychloroquine as immunomodulators

Supportive therapies such as antibacterials, corticosteroids, and NSAIDs: Azithromycin, Dexamethasone, Acetiminophen

Natural products: Curcumin, Resveratrol, Withaferin A, Quercetin etc.



2. Therapeutic options

Repurposing antiviral drugs: Remdesivir, Lopinavir/Ritonavir, Oseltamivir etc.

Novel antiviral drugs: ASC09F

Repurposing antimalarial, anthelmintic and antiparasitic drugs: Chloroquine, niclosamide, Ivermectin etc.

Convalescent plasma

Interferons: Interferon alfacon-1, INF-α and IFN-β

Natural killer cells and cytotoxic T cells

Vaccines: LV-SMENP-DC and Recombinant Novel CoV Vaccine

Mesenchymal stem cells: Wharton's Jelly, Umbilical Cord-Derived, Dental pulp MSCs

ACE inhibitors: Lisinopril and Losartan

Figure. Simplified Representation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Viral Lifecycle and Potential Drug Targets

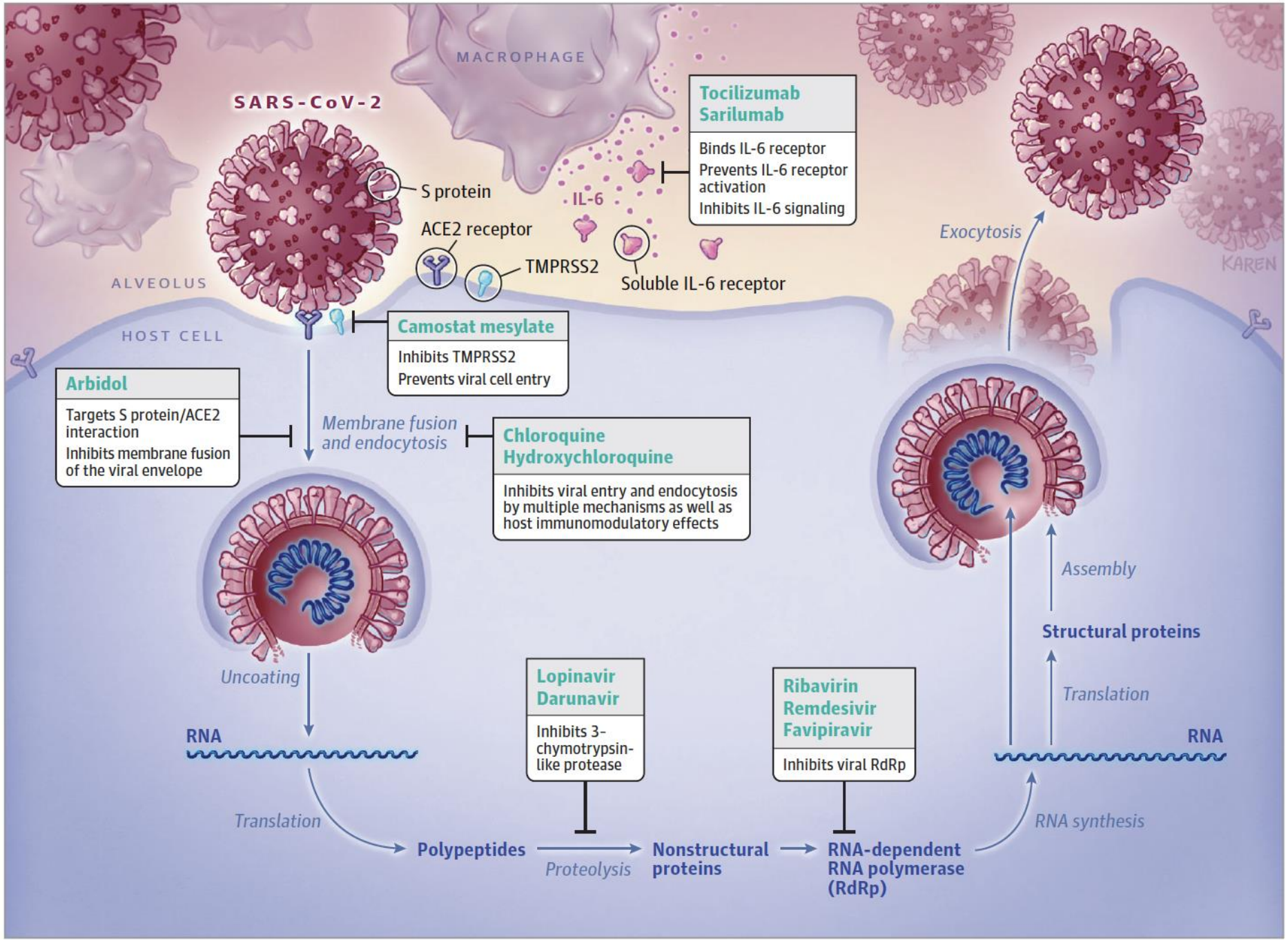


Table 1. Common and potent antiviral drugs.

Drugs	Therapy Strategy Categories	Mechanisms of Therapy	Status
Chloroquine phosphate/ hydroxychloroquine	Anti-malaria anti-viral anti-inflammatory	Increasing endosomal pH, interfering with the glycosylation of cellular receptors of SARS-CoV-2, immunomodulator	FDA approved to be used in an emergency situation, implemented in many treatment protocols
Remdesivir	Antiviral drug (Nucleoside analogue)	Interfering with the viral replication	Investigational antiviral, clinical trials are in progress
Baricitinib	Rheumatoid arthritis (RA) drug, AP2-associated protein kinase 1 (AAK1) inhibitor	Interfering with viral entry by inhibiting one of the endocytosis regulators	FDA approved
lopinavir/ritonavir	HIV protease inhibitor	Could act by inhibiting SARS-CoV-2 protease for proteins cleavage, interfering with virus replication	FDA approved
Darunavir	HIV protease inhibitor	Could act by inhibiting SARS-CoV-2 protease for proteins cleavage, interfering with virus replication	FDA approved
Camostat Mesylate	Transmembrane protease, serine 2 (TMPRSS2) inhibitor	Interfering with viral entry	Japan approved
Favipiravir	Nucleoside analog	Binds to the viral RdRp and reduce its reproduction	Investigational
Cepharanthie, Selamectin, and mefloquine hydrochloride	Anti-viral Anti-inflammatory activities	Significantly reduced cytopathic effects of SARS-CoV-2, and decrease the viral load	Investigational
Ivermectin	Anti-parasite	Inhibits SARS-CoV-2 replication in vitro	FDA approved

Remdesivir for the Treatment of Covid-19 — Preliminary Report

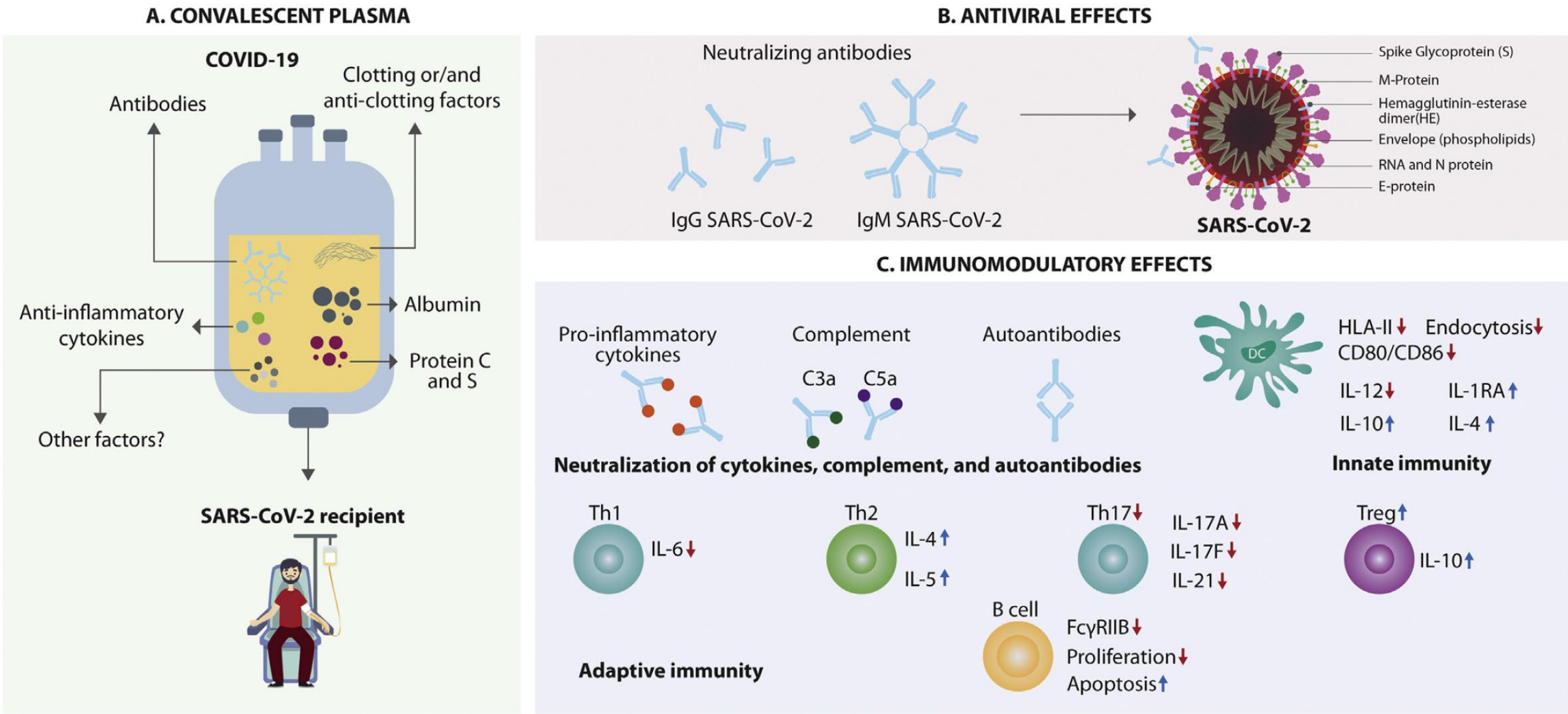
RESULTS

A total of 1063 patients underwent randomization. The data and safety monitoring board recommended early unblinding of the results on the basis of findings from an analysis that showed shortened time to recovery in the remdesivir group. Preliminary results from the 1059 patients (538 assigned to remdesivir and 521 to placebo) with data available after randomization indicated that those who received remdesivir had a median recovery time of 11 days (95% confidence interval [CI], 9 to 12), as compared with 15 days (95% CI, 13 to 19) in those who received placebo (rate ratio for recovery, 1.32; 95% CI, 1.12 to 1.55; P<0.001). The Kaplan-Meier estimates of mortality by 14 days were 7.1% with remdesivir and 11.9% with placebo (hazard ratio for death, 0.70; 95% CI, 0.47 to 1.04). Serious adverse events were reported for 114 of the 541 patients in the remdesivir group who underwent randomization (21.1%) and 141 of the 522 patients in the placebo group who underwent randomization (27.0%).

CONCLUSIONS

Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with Covid-19 and evidence of lower respiratory tract infection. (Funded by the National Institute of Allergy and Infectious Diseases and others; ACCT-1 ClinicalTrials.gov number, NCT04280705.)

Beigel et al., NEJM DOI: 10.1056/NEJMoa2007764


A. CONVALESCENT PLASMA
COVID-19
Antibodies
Clotting or/and anti-clotting factors
Anti-inflammatory cytokines
Albumin
Protein C and S
Other factors?
SARS-CoV-2 recipient
B. ANTIVIRAL EFFECTS
Neutralizing antibodies
IgG SARS-CoV-2
IgM SARS-CoV-2
Spike Glycoprotein (S)
M-Protein
Hemagglutinin-esterase dimer(HE)
Envelope (phospholipids)
RNA and N protein
E-protein
SARS-CoV-2
C. IMMUNOMODULATORY EFFECTS
Pro-inflammatory cytokines
Complement
C3a
C5a
Autoantibodies
DC
HLA-II
Endocytosis
CD80/CD86
IL-12
IL-1RA
IL-10
IL-4
Neutralization of cytokines, complement, and autoantibodies
Innate immunity
Th1
IL-6
Th2
IL-4
IL-5
Th17
IL-17A
IL-17F
IL-21
Treg
IL-10
B cell
FcγRIIB
Proliferation
Apoptosis
Adaptive immunity

Vir Biotechnology

Platform: Patient-derived mAb tech from Humabs BioMed

Target: SARS-CoV-2 spike protein

Program 1: mAbs from patients recovered from SARS, other coronaviruses

Program 2 (Pending): mAbs from recovered COVID-19 patients

Abcellera Biologics/ DARPA/NIH

Platform: single cell mAb discovery tech (Pandemic Prevention Platform) deployed on patient samples

Target: SARS-CoV-2 spike protein

Program 1: mAbs from recovered SARS patients

Program 2 (Pending): mAbs from recovered COVID-19 patients

Regeneron Pharmaceuticals/BARDA

Platform: Mice engineered to generate human antibody repertoires (VelocImmune)

Target: SARS-CoV-2 spike protein

Program 1: mAbs generated against SARS-CoV-2 spike on pseudovirus

Program 2: mAbs generated against MERS

Flanders Institute for Biotechnology (VIB)/ Ghent University

Platform: Llama-derived single domain antibodies (VHHs)

Target: SARS-CoV-2 spike protein

Program 1: VHH generated against spike protein domain conserved across SARS-CoV and SARS-CoV-2

Program 2 (Pending): VHH generated against SARS-CoV-2

Ligand Pharmaceuticals

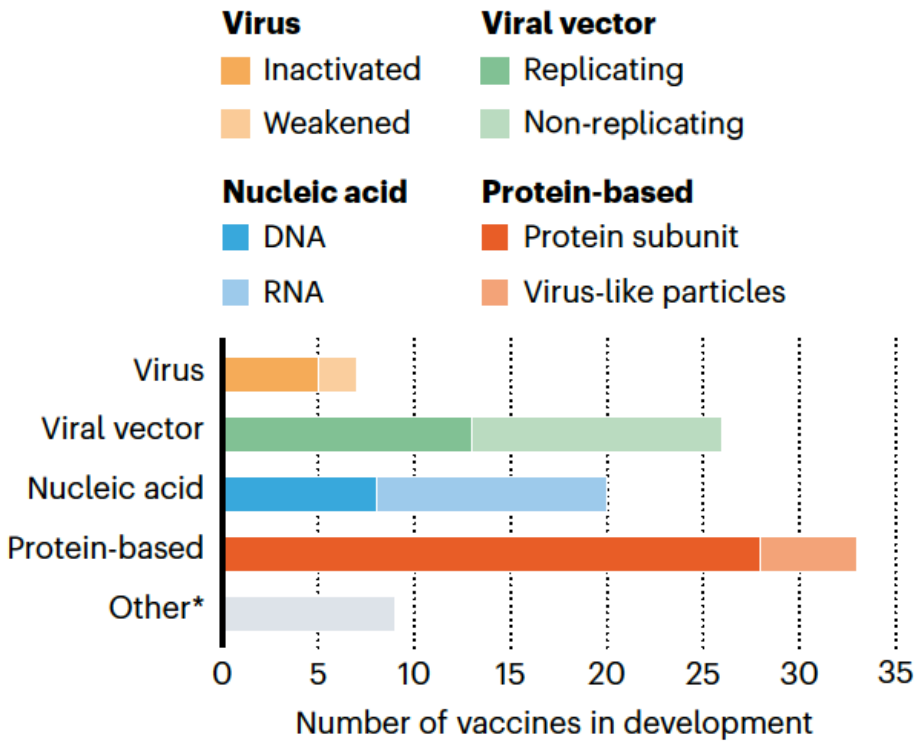
Platform: Chickens engineered to generate human antibody repertoires (OmniChicken)

Target: Not disclosed

Programs: Not disclosed

AN ARRAY OF VACCINES

All vaccines aim to expose the body to an antigen that won't cause disease, but will provoke an immune response that can block or kill the virus if a person becomes infected. There are at least eight types being tried against the coronavirus, and they rely on different viruses or viral parts.



* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

VIRUS VACCINES

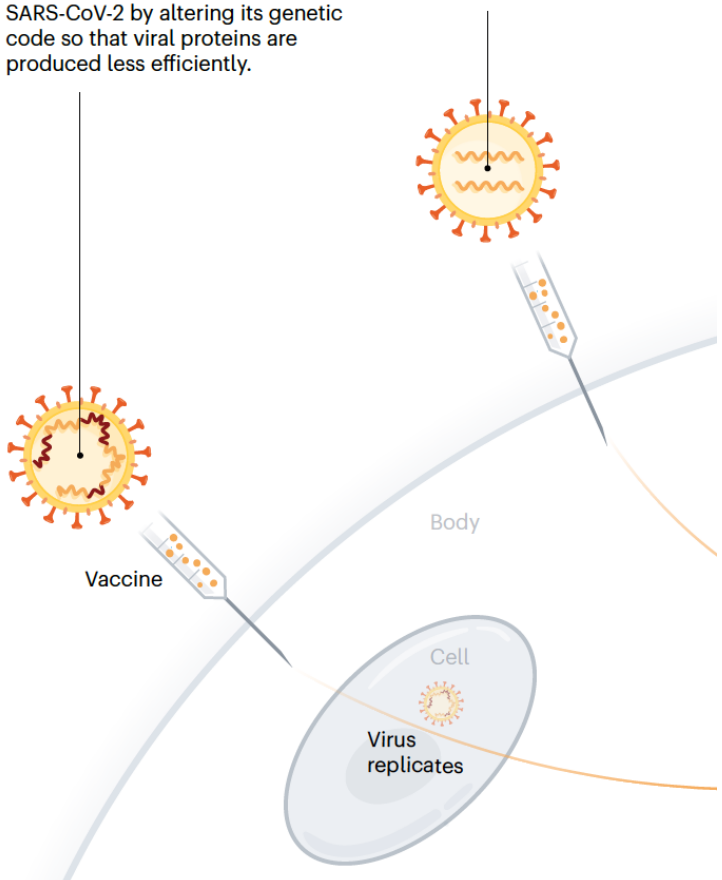
At least seven teams are developing vaccines using the virus itself, in a weakened or inactivated form. Many existing vaccines are made in this way, such as those against measles and polio, but they require extensive safety testing. Sinovac Biotech in Beijing has started to test an inactivated version of SARS-CoV-2 in humans.

Weakened virus

A virus is conventionally weakened for a vaccine by being passed through animal or human cells until it picks up mutations that make it less able to cause disease. Codagenix in Farmingdale, New York, is working with the Serum Institute of India, a vaccine manufacturer in Pune, to weaken SARS-CoV-2 by altering its genetic code so that viral proteins are produced less efficiently.

Inactivated virus

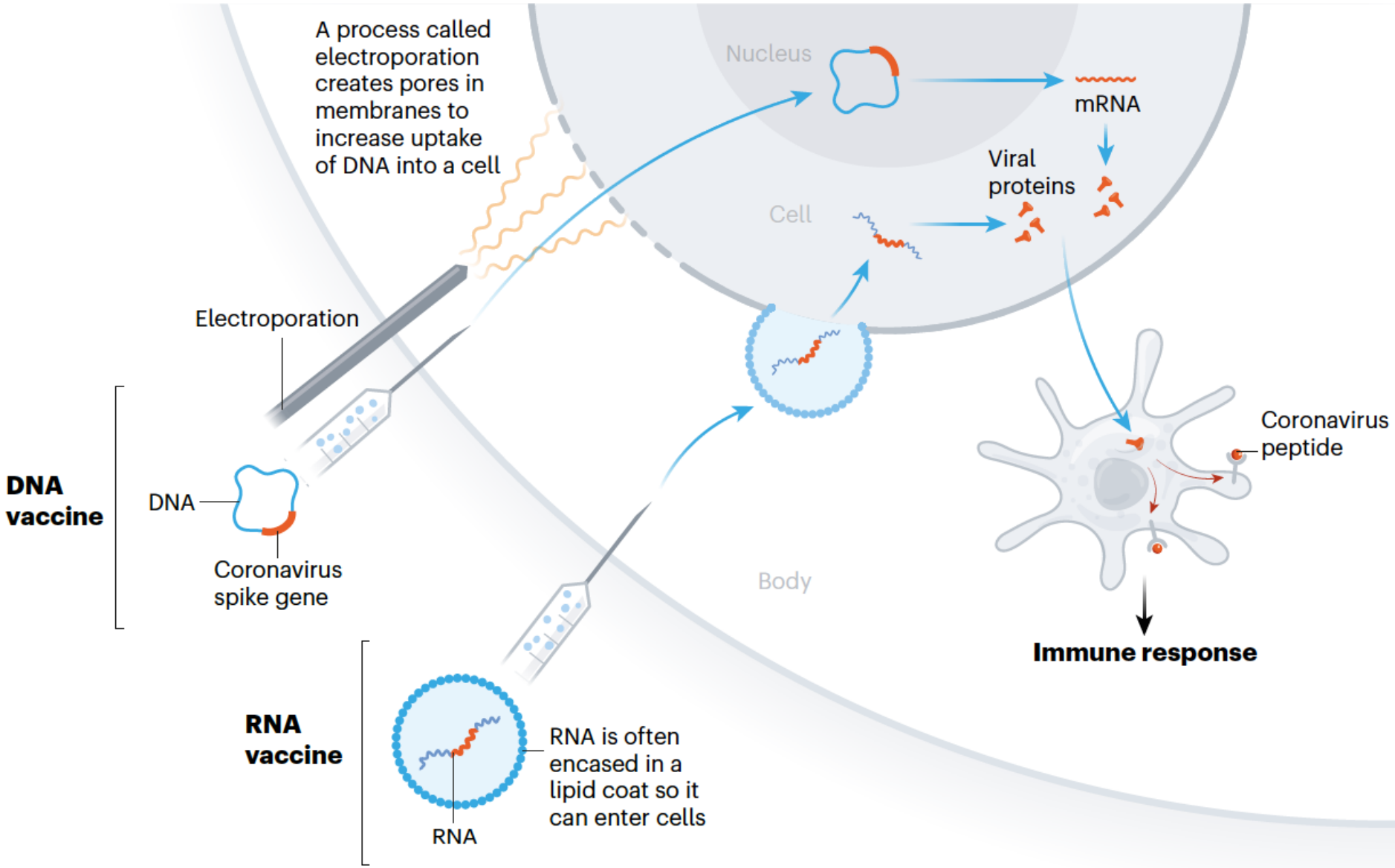
In these vaccines, the virus is rendered uninfectious using chemicals, such as formaldehyde, or heat. Making them, however, requires starting with large quantities of infectious virus.



NUCLEIC-ACID VACCINES

At least 20 teams are aiming to use genetic instructions (in the form of DNA or RNA) for a coronavirus protein that prompts an immune response. The nucleic acid is inserted into human cells, which then churn out copies of the virus protein; most of these vaccines encode the virus's spike protein.

RNA- and DNA-based vaccines are safe and easy to develop: to produce them involves making genetic material only, not the virus. But they are unproven: no licensed vaccines use this technology.



VIRAL-VECTOR VACCINES

Around 25 groups say they are working on viral-vector vaccines. A virus such as measles or adenovirus is genetically engineered so that it can produce coronavirus proteins in the body. These viruses are weakened so they cannot cause disease. There are two types: those that can still replicate within cells and those that cannot because key genes have been disabled.

Replicating viral vector (such as weakened measles)

The newly approved Ebola vaccine is an example of a viral-vector vaccine that replicates within cells. Such vaccines tend to be safe and provoke a strong immune response. Existing immunity to the vector could blunt the vaccine's effectiveness, however.

Non-replicating viral vector (such as adenovirus)

No licensed vaccines use this method, but they have a long history in gene therapy. Booster shots can be needed to induce long-lasting immunity. US-based drug giant Johnson & Johnson is working on this approach.

PROTEIN-BASED VACCINES

Many researchers want to inject coronavirus proteins directly into the body. Fragments of proteins or protein shells that mimic the coronavirus's outer coat can also be used.

Protein subunits

Twenty-eight teams are working on vaccines with viral protein subunits — most of them are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven't been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.

Virus-like particles

Empty virus shells mimic the coronavirus structure, but aren't infectious because they lack genetic material. Five teams are working on 'virus-like particle' (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.

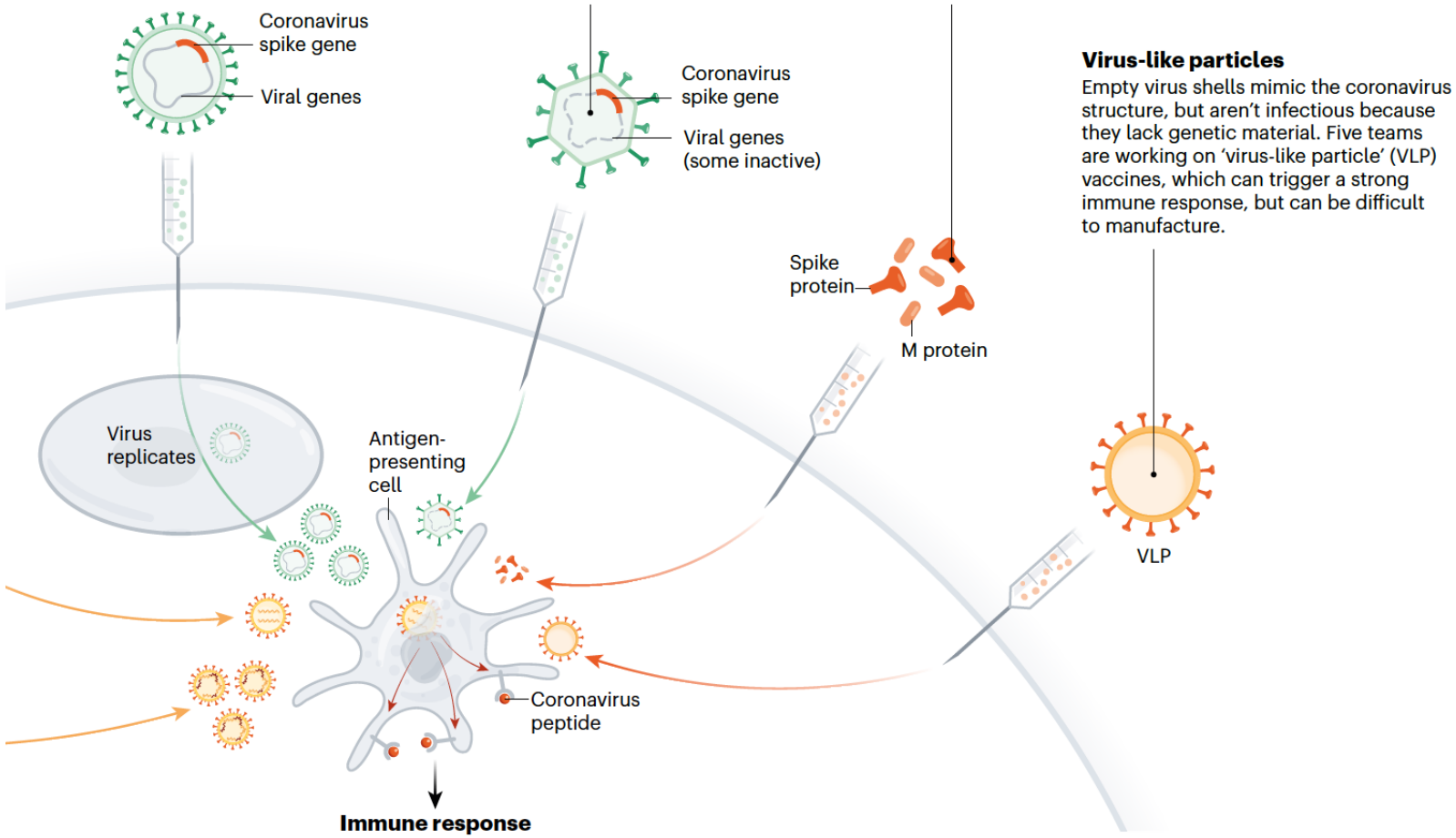
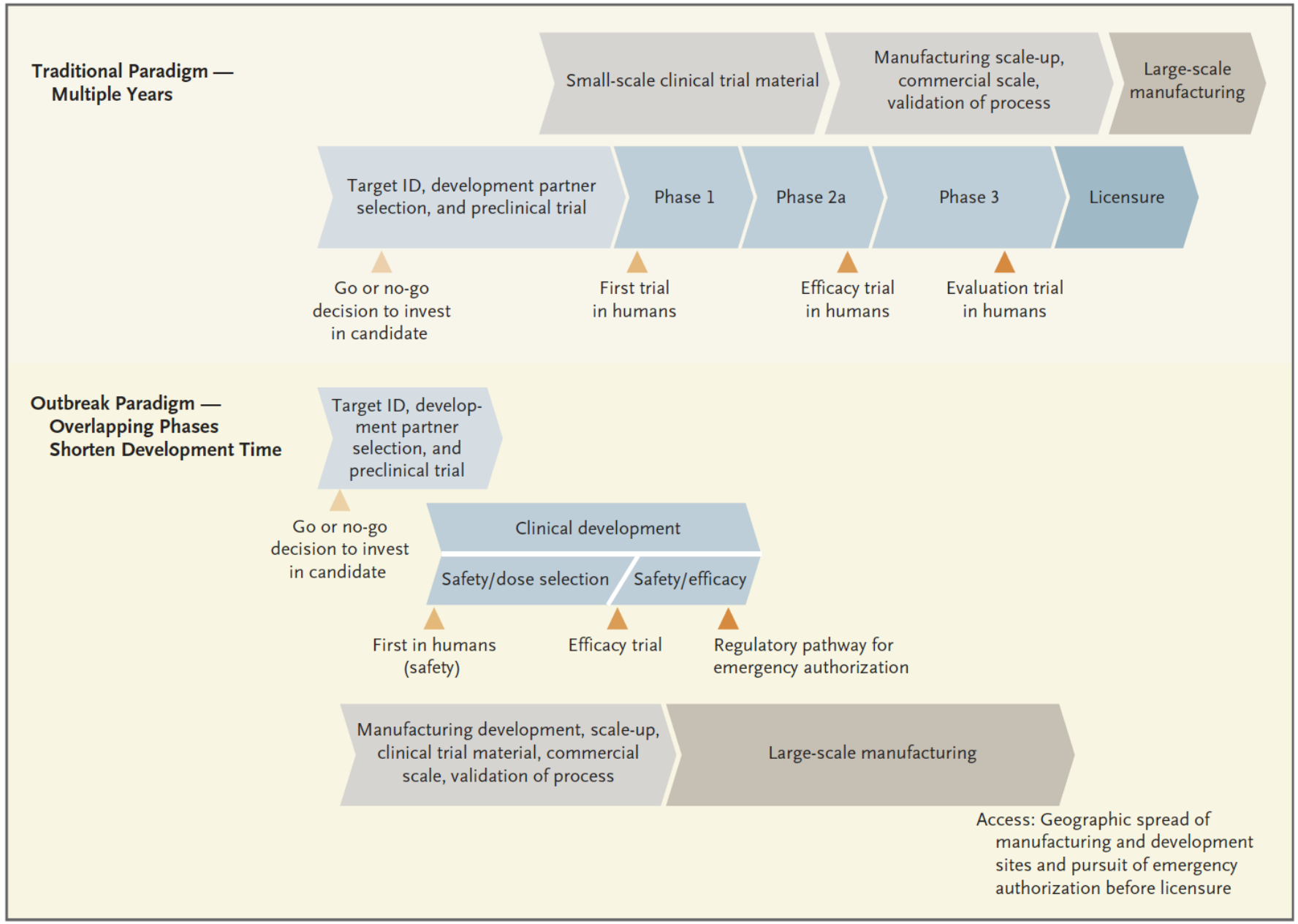


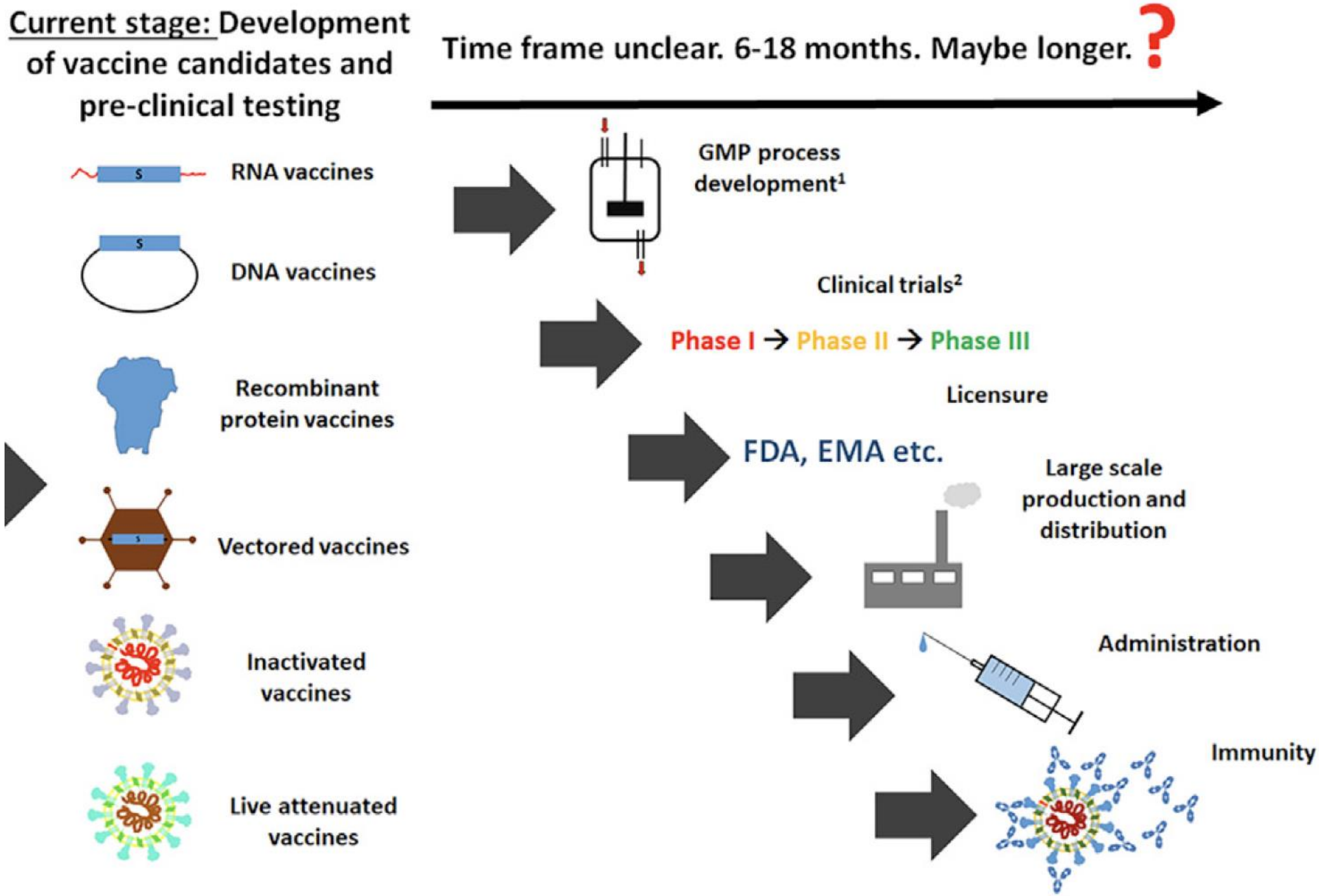
Table 1. Overview of Vaccine Production Platforms and Technologies for SARS-CoV-2

Platform	Target	Existing, Licensed Human Vaccines Using the Same Platform	Advantages	Disadvantages
RNA vaccines	S protein	No	No infectious virus needs to be handled, vaccines are typically immunogenic, rapid production possible.	Safety issues with reactogenicity have been reported.
DNA vaccines	S protein	No	No infectious virus needs to be handled, easy scale up, low production costs, high heat stability, tested in humans for SARS-CoV-1, rapid production possible.	Vaccine needs specific delivery devices to reach good immunogenicity.
Recombinant protein vaccines	S protein	Yes for baculovirus (influenza, HPV) and yeast expression (HBV, HPV)	No infectious virus needs to be handled, adjuvants can be used to increase immunogenicity.	Global production capacity might be limited. Antigen and/or epitope integrity needs to be confirmed. Yields need to be high enough.
Viral vector-based vaccines	S protein	Yes for VSV (Ervebo), but not for other viral vectored vaccines	No infectious virus needs to be handled, excellent preclinical and clinical data for many emerging viruses, including MERS-CoV.	Vector immunity might negatively affect vaccine effectiveness (depending on the vector chosen).
Live attenuated vaccines	Whole virion	Yes	Straightforward process used for several licensed human vaccines, existing infrastructure can be used.	Creating infectious clones for attenuated coronavirus vaccine seeds takes time because of large genome size. Safety testing will need to be extensive.
Inactivated vaccines	Whole virion	Yes	Straightforward process used for several licensed human vaccines, existing infrastructure can be used, has been tested in humans for SARS-CoV-1, adjuvants can be used to increase immunogenicity.	Large amounts of infectious virus need to be handled (could be mitigated by using an attenuated seed virus). Antigen and/or epitope integrity needs to be confirmed.



Difference between Traditional Vaccine Development and Development Using a Pandemic Paradigm.

The pandemic paradigm requires multiple activities to be conducted at financial risk to developers and manufacturers and without knowing whether the vaccine candidate will be safe and effective, including very early manufacturing scale-up to commercial scale before establishment of clinical proof of concept. ID denotes identification.


Current stage: Development of vaccine candidates and pre-clinical testing
Time frame unclear. 6-18 months. Maybe longer.
?
RNA vaccines
DNA vaccines
Recombinant protein vaccines
Vectored vaccines
Inactivated vaccines
Live attenuated vaccines
GMP process development[1]
Clinical trials[2]
Phase I → Phase II → Phase III
Licensure
FDA, EMA etc.
Large scale production and distribution
Administration
Immunity

Summary

WARWICK

- Unprecedented pace of science – 6 months!
- SARS-CoV-2 is highly transmissible – UK epidemic from imported European strains
- A viral genotype that emerged in late Jan 2020 now dominates the pandemic
  - It may have better transmission than earlier genotypes
  - Its disease profile appears to be unchanged
- Human genotypic variation may play a part in disease severity but still to be demonstrated
- Host immune response being defined - what does a protective immune response look like?
- Repurposing old anti-viral drugs – what about new ones?
- 136 vaccines in development – 10 candidates in clinical evaluation, many using unproven technology platforms.

VIROLOGY – lack of investment in research over 20 years, no large pharma working on antivirals in UK