SEVERE COVID-19 the most untuned symphony of the Immune system it ever played M.Taghadosi

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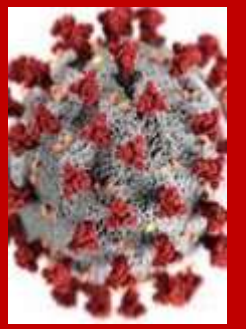
Credit: Simon Bradbrook/Springer Nature Limited



Hyper inflammation

Paediatric inflammatory multisystem syndrome (PIMS)

Severe pneumonia & Acute Respiratory distress syndrome (ARDS)

COVID-19 skin lesion

COVID-19

Metabolic disorders

Coagulopathy and thrombosis

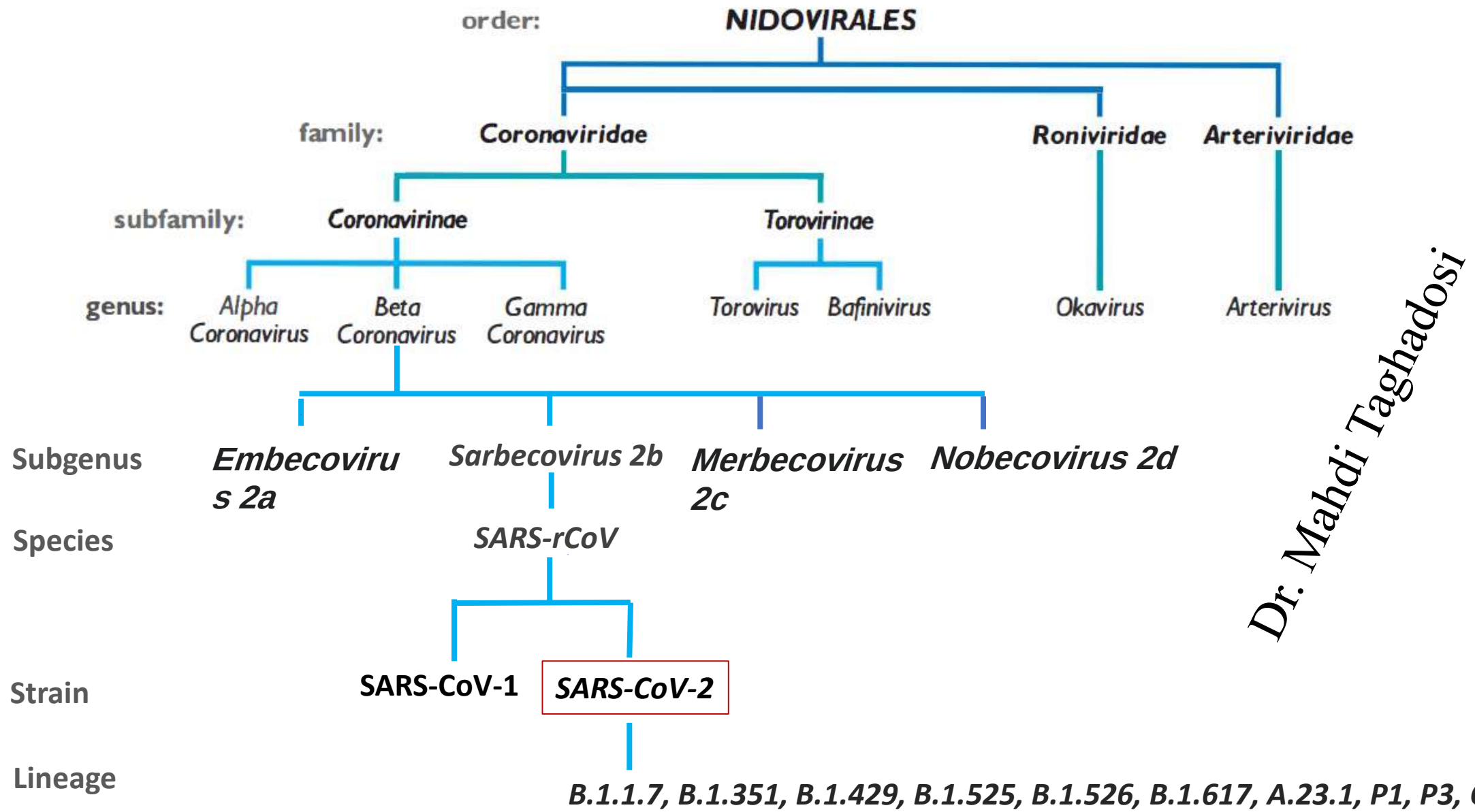
Vasculitis

Neurologic Manifestations

Acute coronary syndrome (ACS)

Dr. Mahdi Taghadosi

SARS-CoV-2 in Taxonomy of the order Nidovirales



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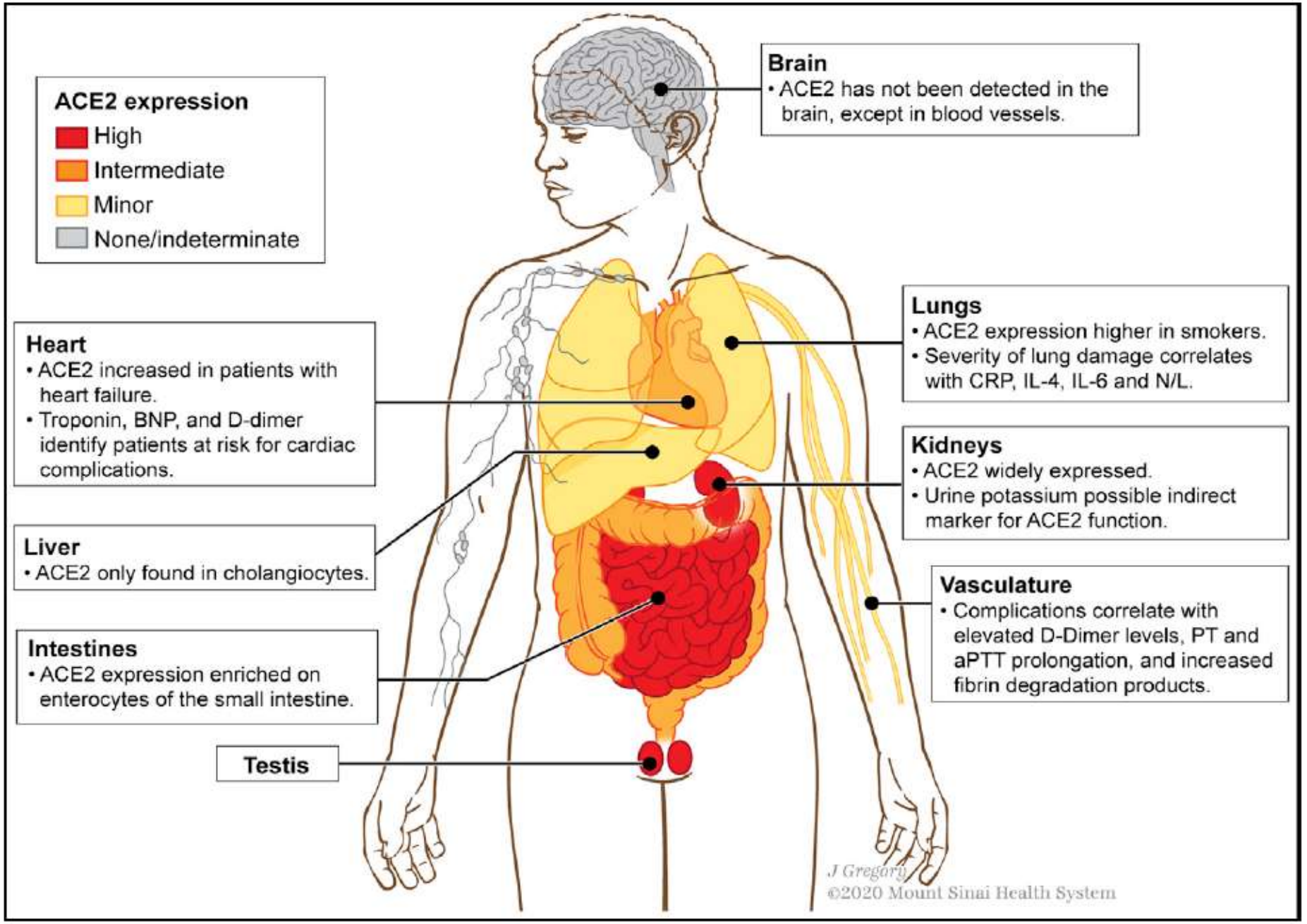
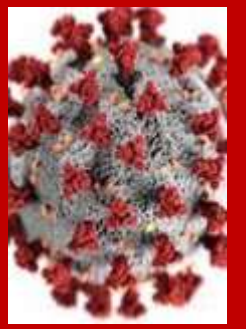
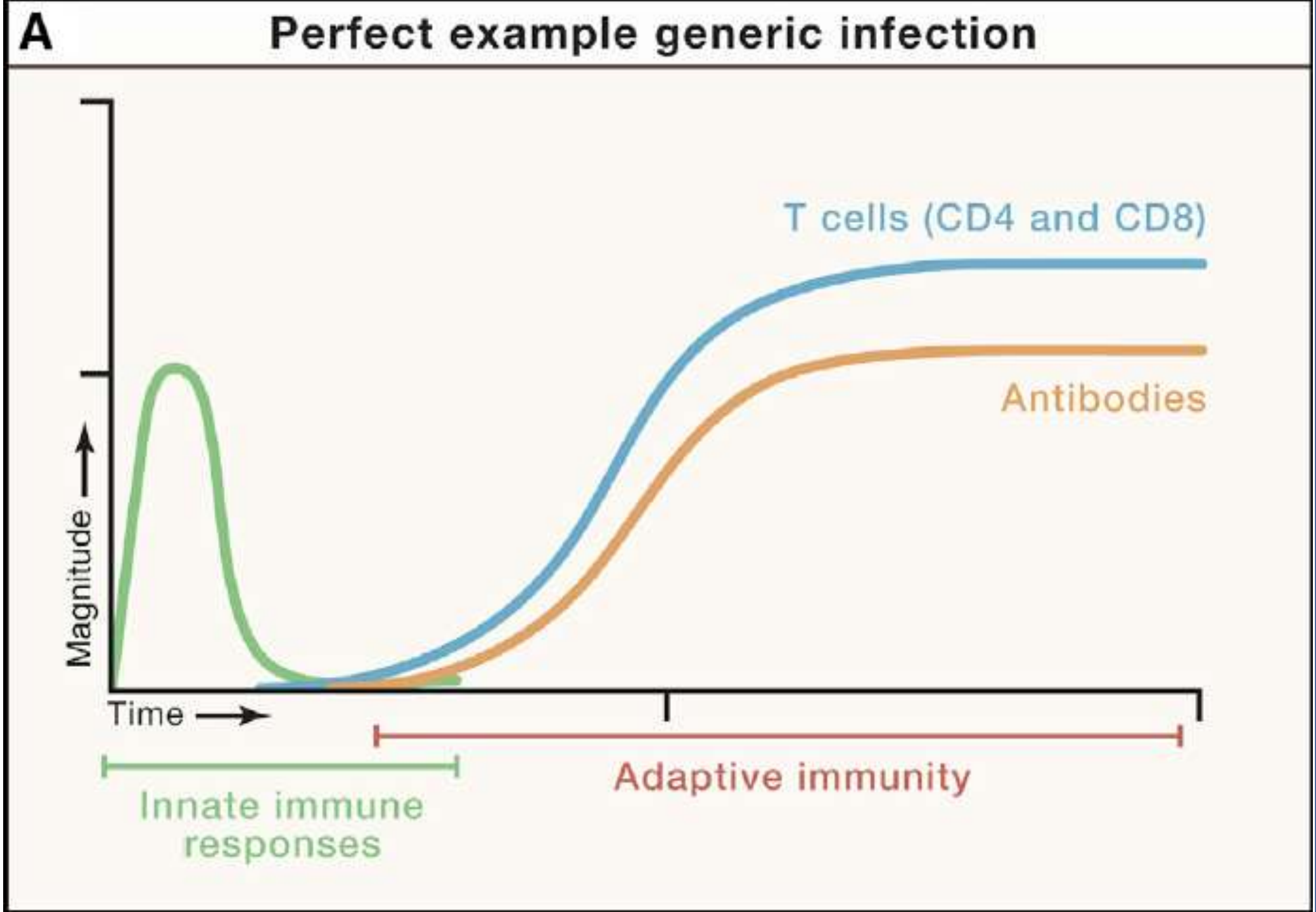
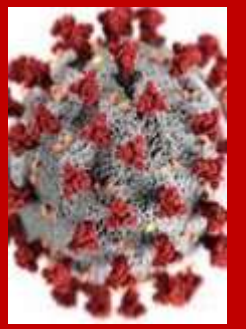
ACE2 Expression in Organs and Systems Most Frequently Implicated inCOVID-19 Complications

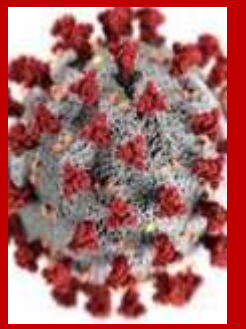


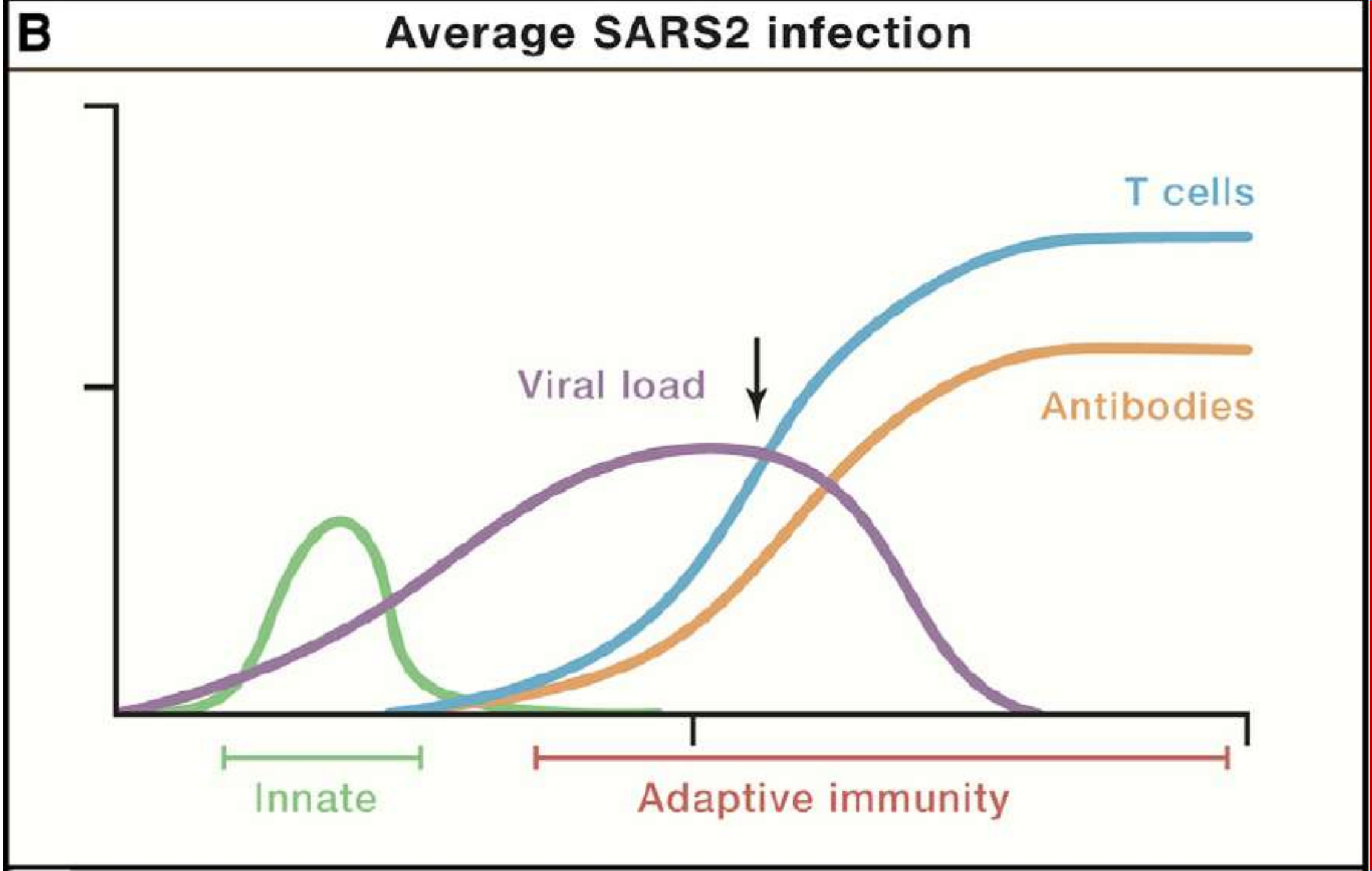
https://doi.org/10.1016/j.immuni.2020.05.002




A
Perfect example generic infection
T cells (CD4 and CD8)
Antibodies
Magnitude
Time
Innate immune responses
Adaptive immunity

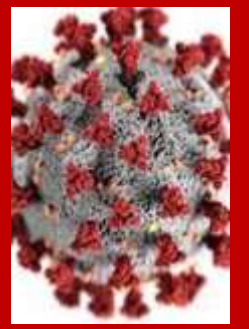


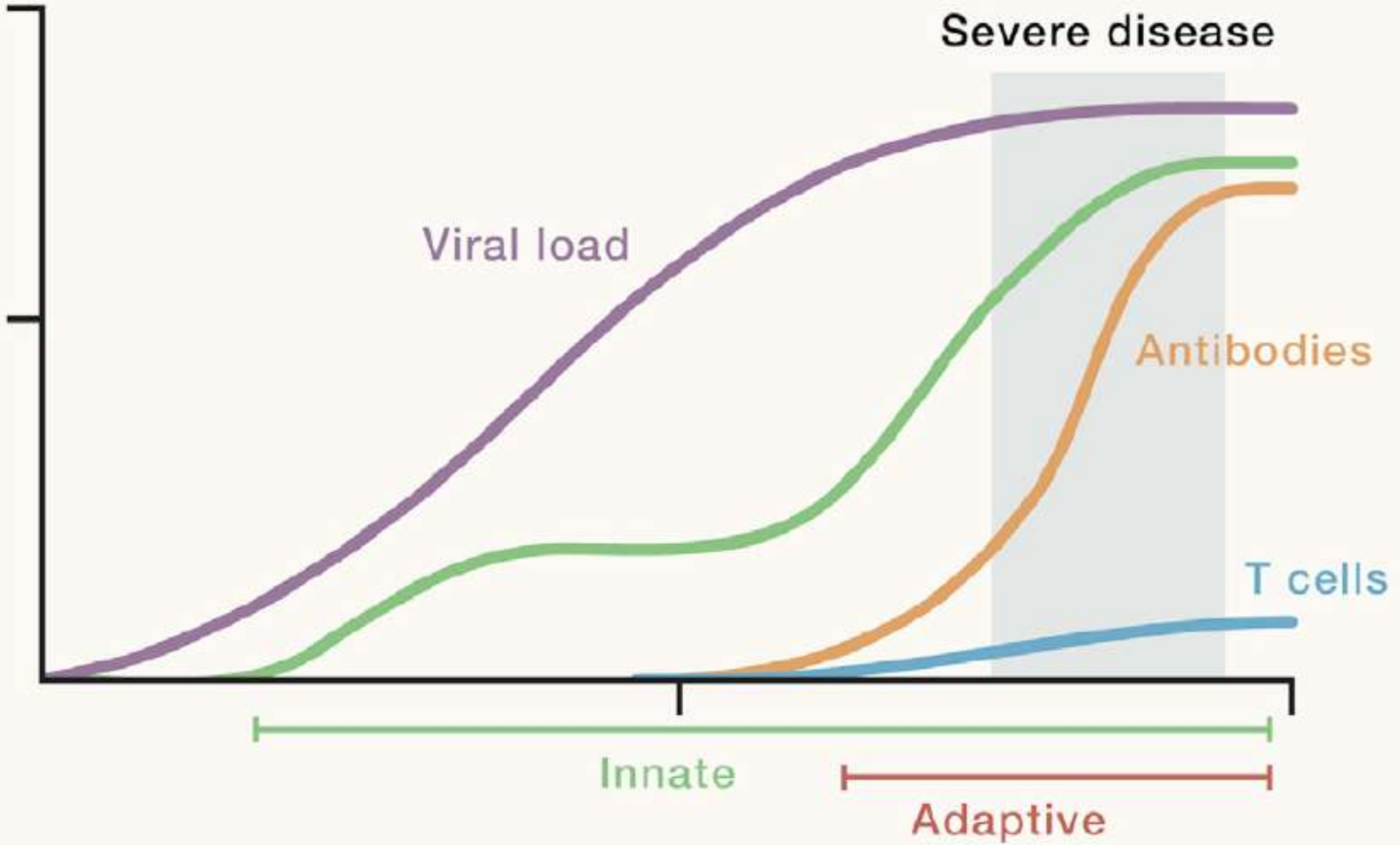



B
Average SARS2 infection
T cells
Viral load
Antibodies
Innate
Adaptive immunity

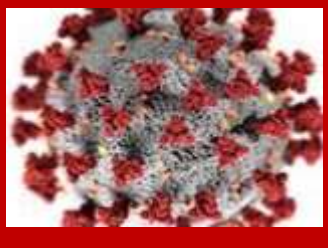
C

Severe SARS2 infection

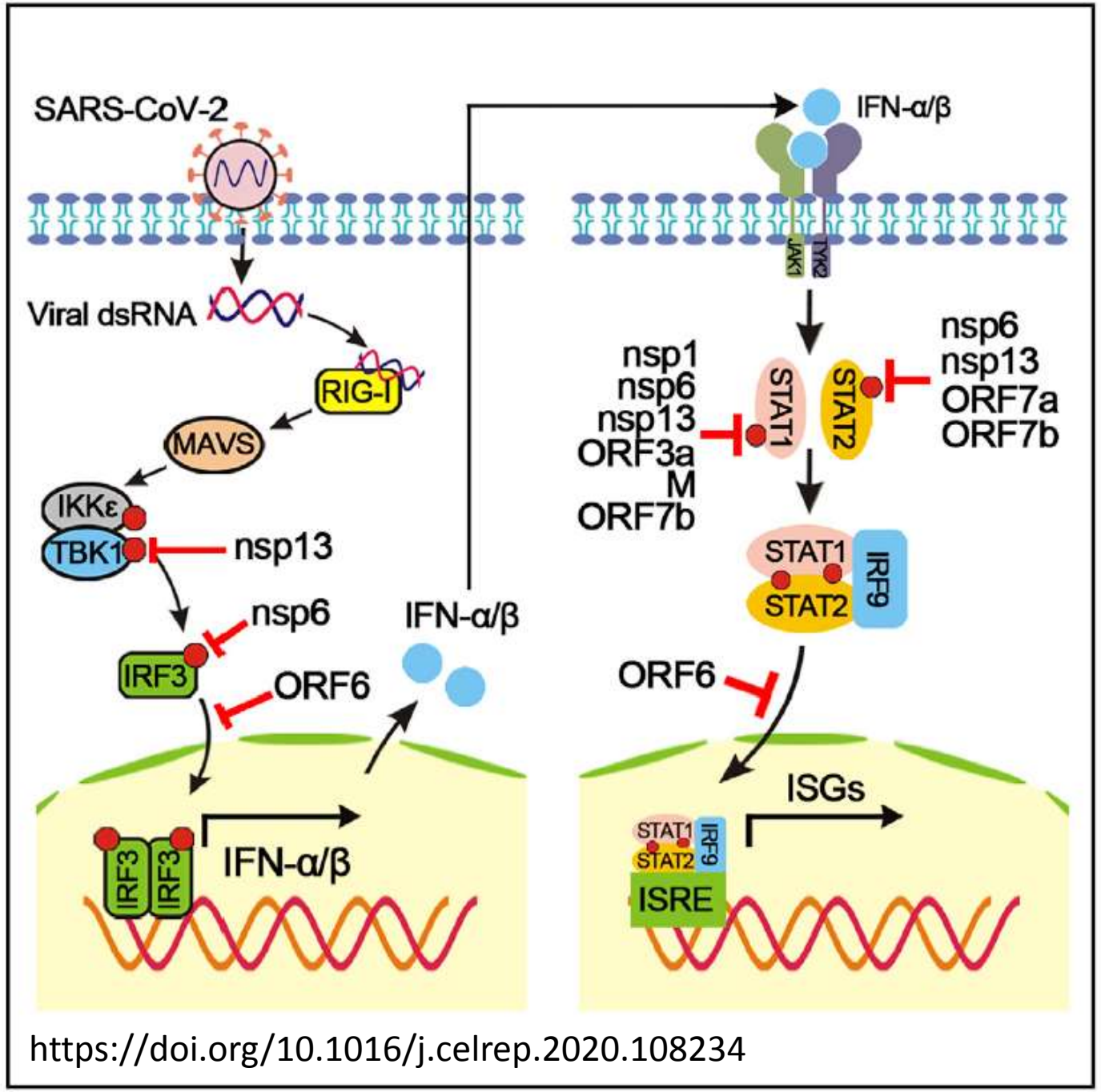




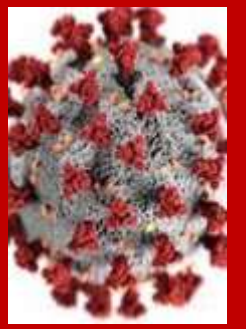
Cytokine storm



Compared with SARS-CoV and MERS-CoV, the IFN-I signaling is
more efficiently suppressed by the SARSCoV-2 nsp1 and nsp6 proteins.

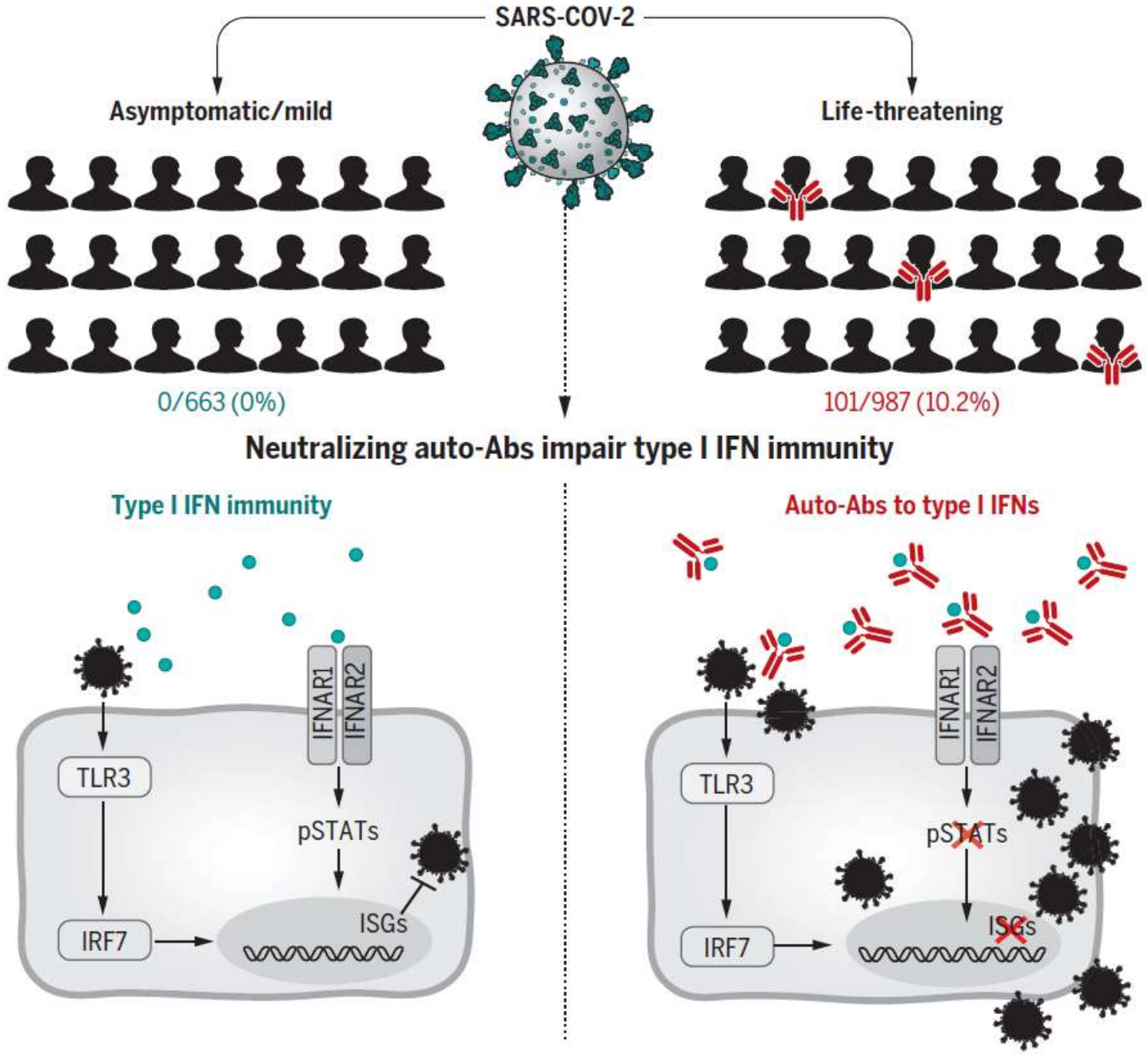


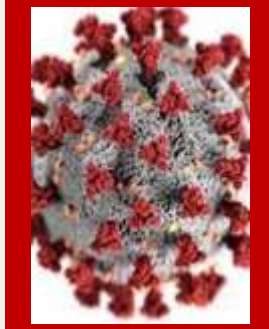
https://doi.org/10.1016/j.celrep.2020.108234



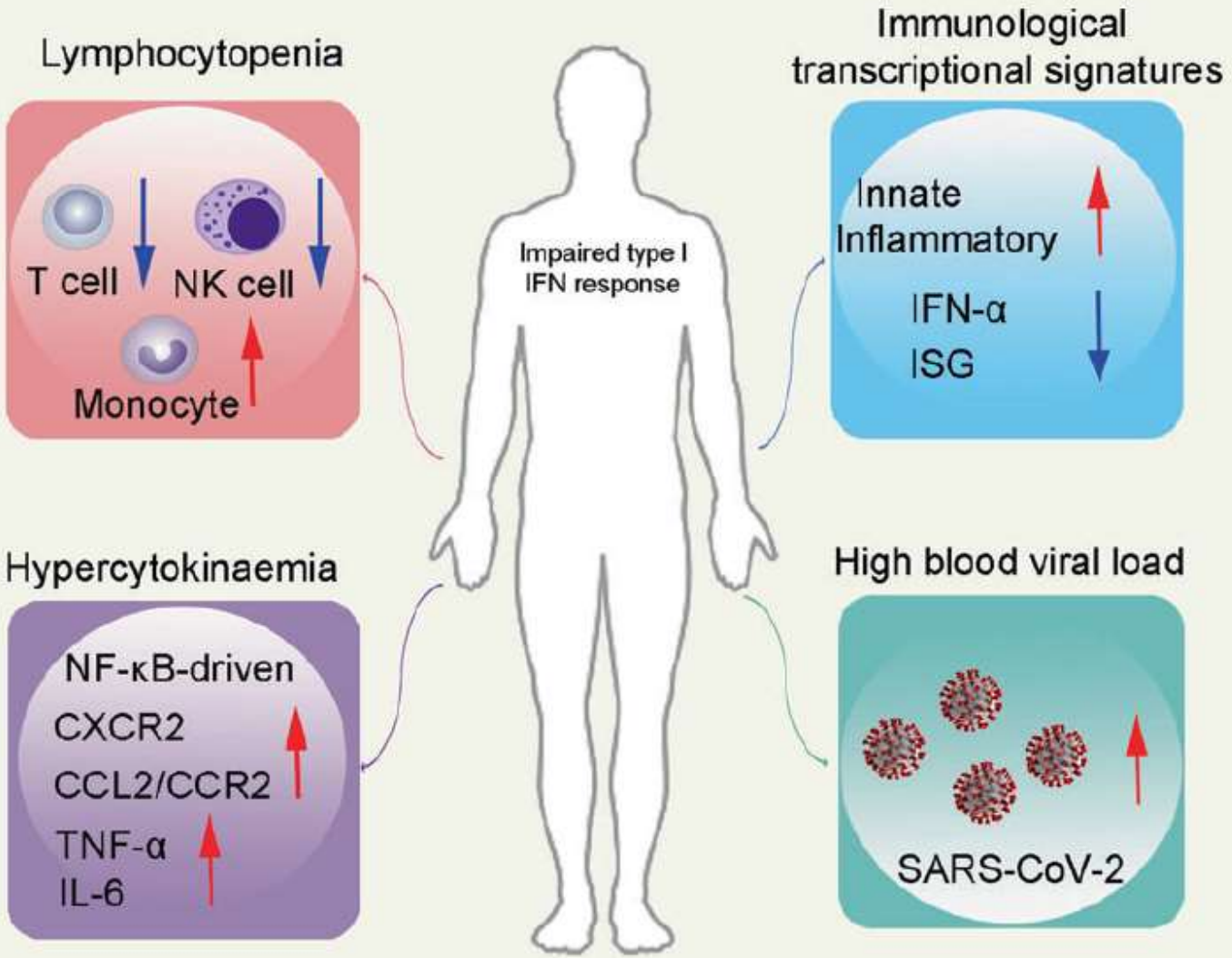
Science Contents

A B cell autoimmune phenocopy of inborn errors of type I IFN immunity accounts for life-threatening COVID-19 pneumonia in at least 2.6% of women and 12.5% of men.



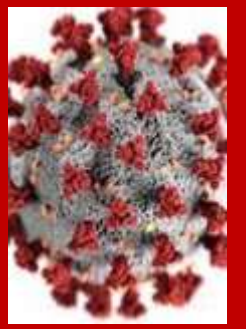


Immunological Characteristics of Severe COVID-19



Severe and Critical COVID-19

https://doi.org/10.1038/s41392-020-00306-4



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RESEARCH ARTICLE

Systems biological assessment of immunity to mild versus severe COVID-19 infection in humans

Prabhu S. Arunachalam[1,*], Florian Wimmers[1,*], Chris Ka Pun Mok[2,*], Ranawaka A. P. M. Perera[3,*], Madeleine...

+ See all authors and affiliations

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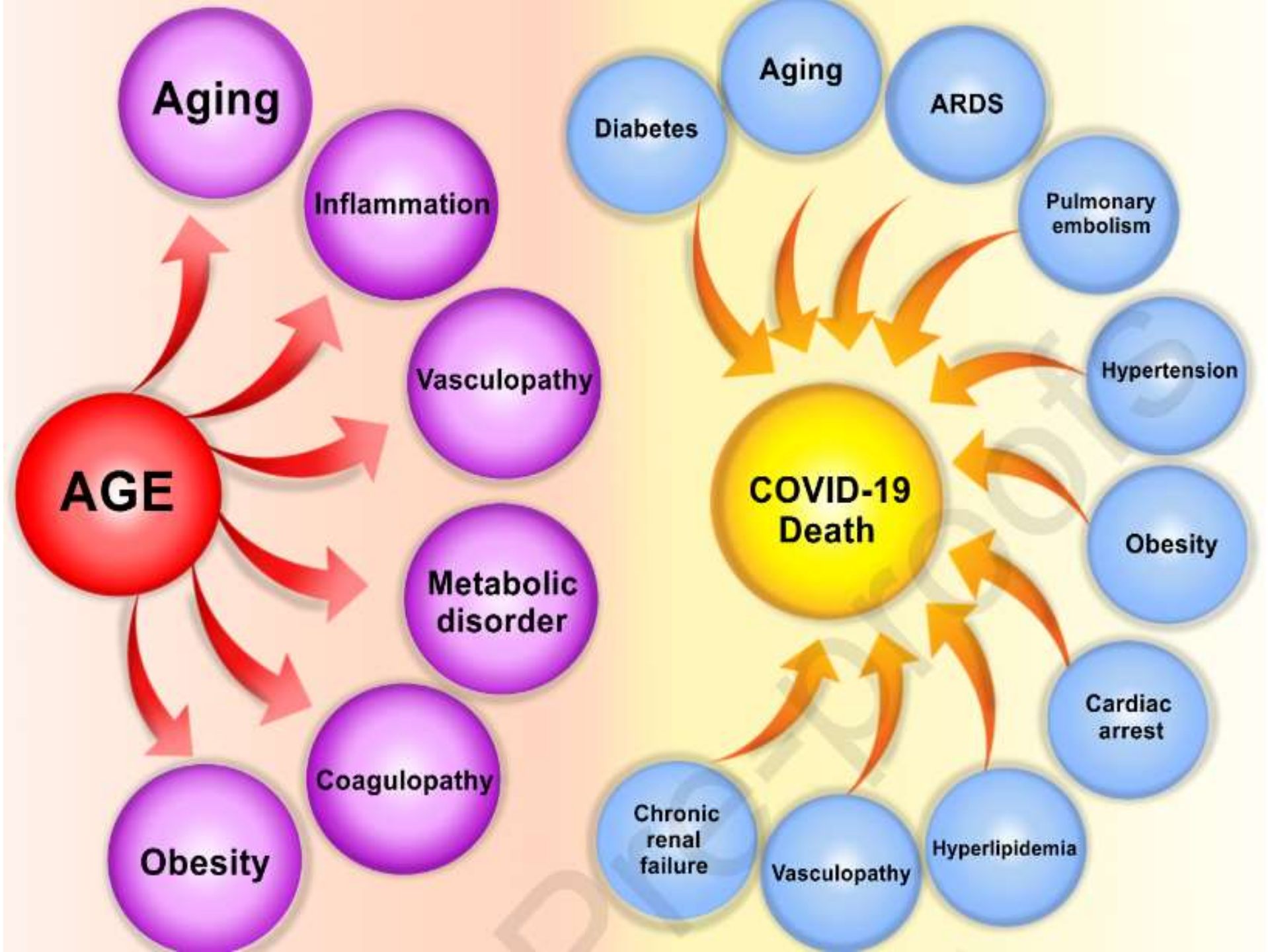
Article Figures & Data Info & Metrics eLetters PDF

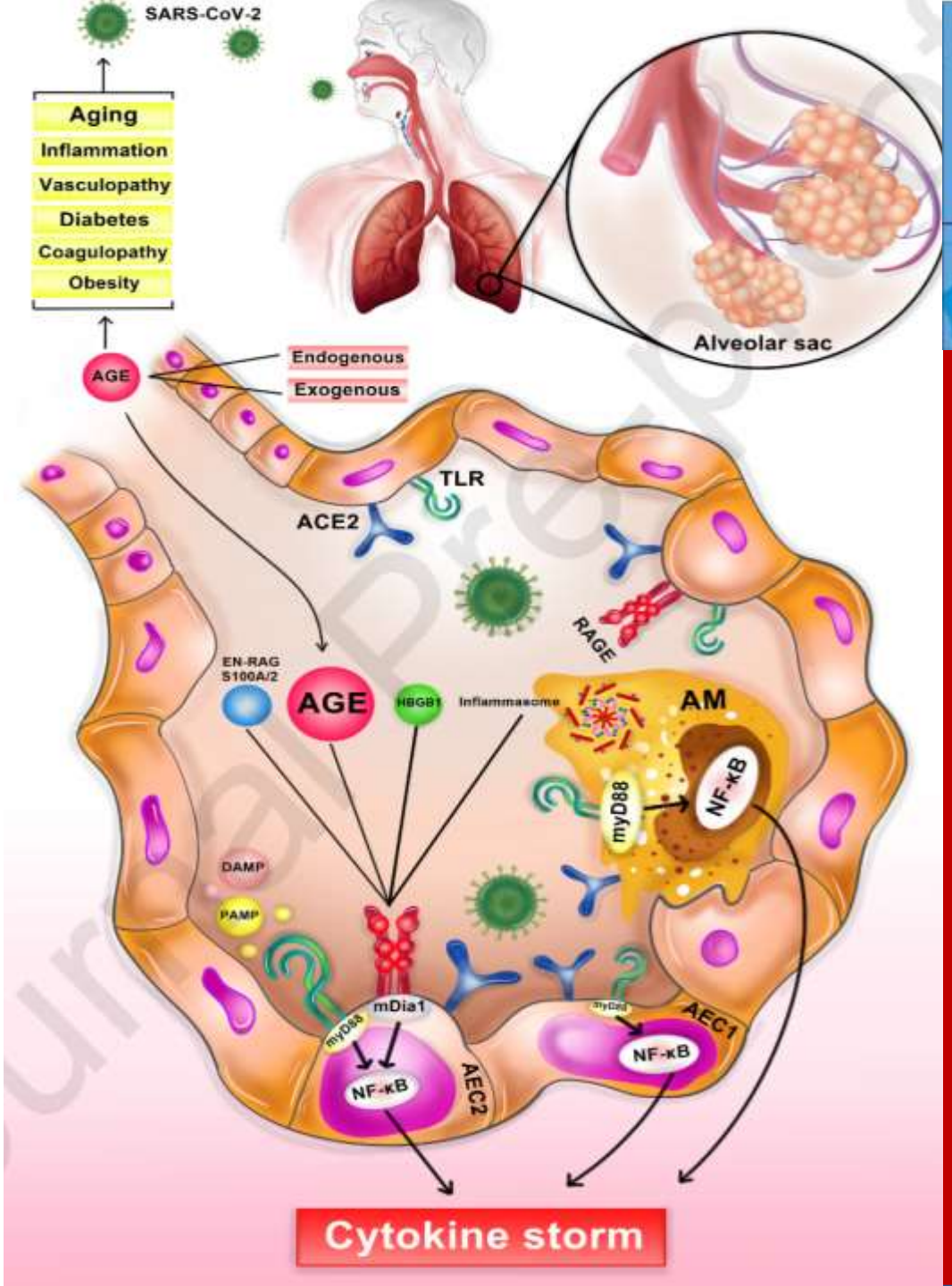
EN-RAGE –RAGE interaction

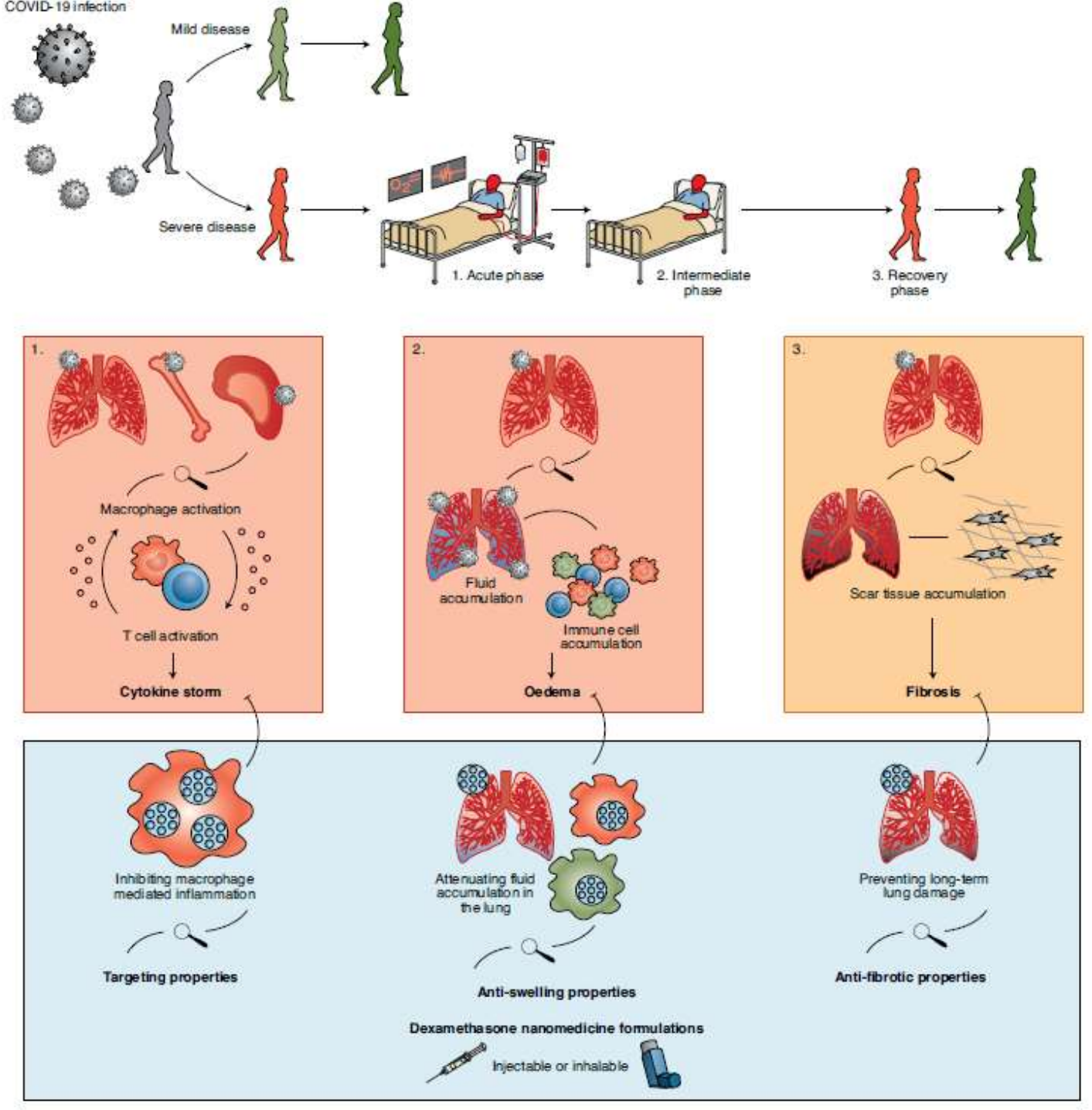
RAGE: Receptor for advance glycation end product

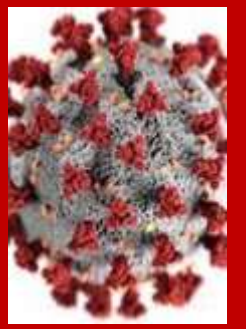


International Immunopharmacology

S. No	Compound/Drug	Mechanism of Action
1	Metformin	Anti-inflammatory
2	Algaebrium chloride	Improves cardiac function, reduce collagen crosslinking
3	Carnisone	Inhibits Methylglyoxal
4	Homocarnisobe	Reduce glycation process
5	Anserine	Reduce glycation process
6	LR90	Inhibits MGO induced cytotoxicity
7	Amino guanidine	Inhibits MGO induced cytotoxicity
8	N-acetyl cystine (NAC)	Inhibits MGO induced cytotoxicity
9	Azeliragon (TTP488)	RAGE innhibitor
10	FPS-ZM1	RAGE innhibitor
11	Pyrazole-5-carboxamides	RAGE inhibitors
12	6-Phenoxy-2-phenylbenzoxazoles	RAGE inhibitors
13	Pyridoxine	RAGE signaling Inhibitor
14	Flavonoids	Enhances the Glyoxalase Pathway
15	DNA RNA aptamers	Reduce AGEs induced stress and removal of AGEs
16	B alanine	Reduce glycation process
17	Histidine	Reduce glycation process
18	3-[2-(4-Bromo-phenyl)-1-methyl-2-oxo-ethyl]-4,5,6,7-tetrahydro-benzothiazol-3-ium bromide (C16)	Reduce AGEs accumulation




COVID-19 infection
Mild disease
Severe disease
1. Acute phase
2. Intermediate phase
3. Recovery phase
1.
Macrophage activation
T cell activation
Cytokine storm
2.
Fluid accumulation
Immune cell accumulation
Oedema
3.
Scar tissue accumulation
Fibrosis
Inhibiting macrophage mediated inflammation
Targeting properties
Attenuating fluid accumulation in the lung
Anti-swelling properties
Preventing long-term lung damage
Anti-fibrotic properties
Dexamethasone nanomedicine formulations
Injectable or inhalable



The RECOVERY Trial:
Dexamethasone for COVID-19?

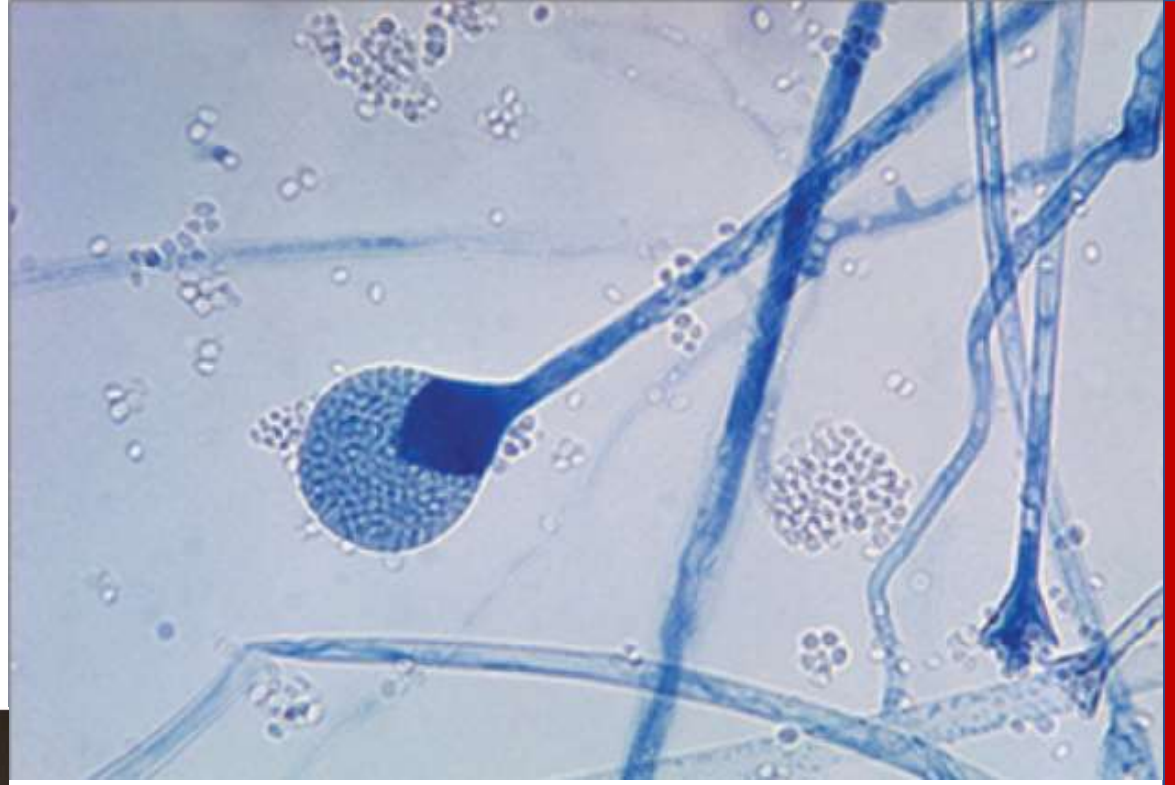
RECOVERY

Randomised Evaluation of COVID-19 Therapy

REBEL COVID-19

Oral or intravenous dexamethasone (at a dose of 6 mg once daily) for up to 10 days

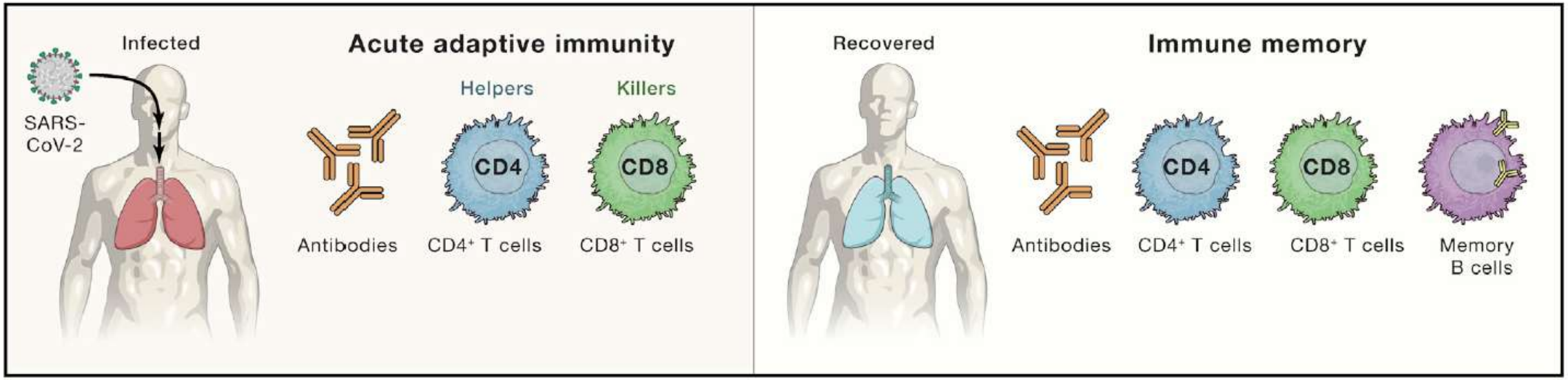
Mucormycosis



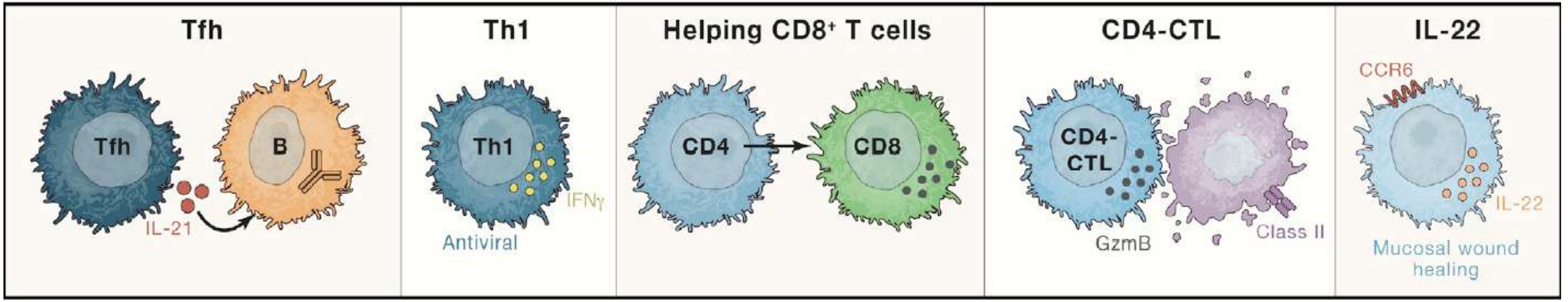
Mature sporangium of a Mucor

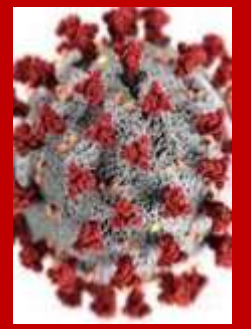
Amphotericin B

The major components of adaptive immunity in viral immune responses

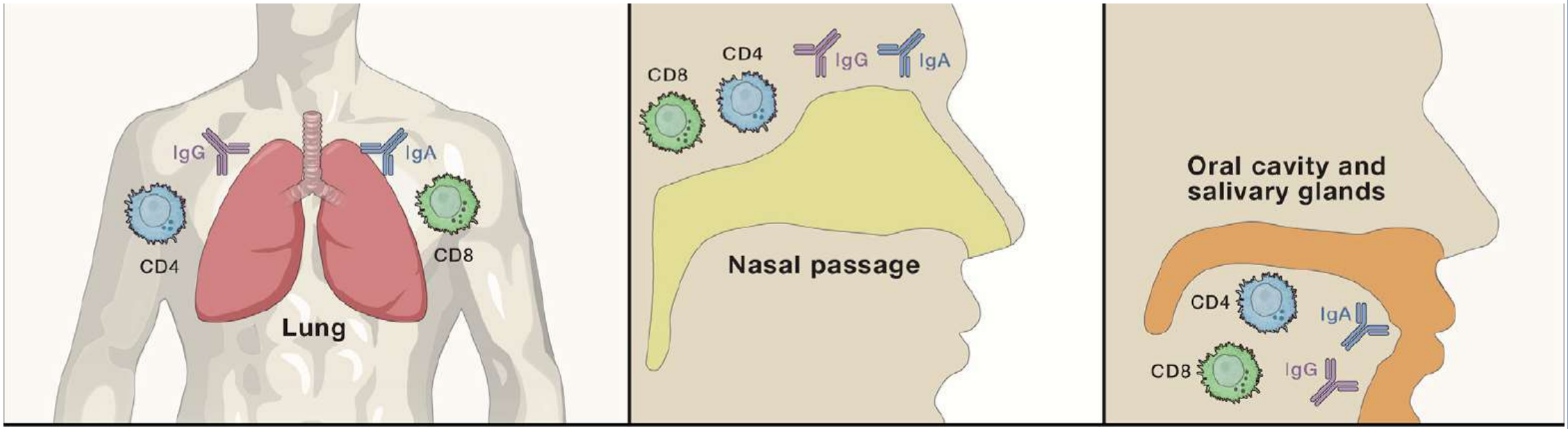


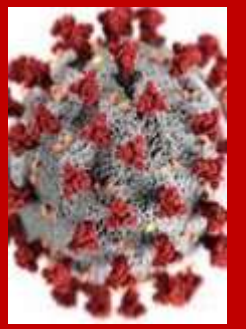
$CD4^+$ T cell functions observed in COVID-19





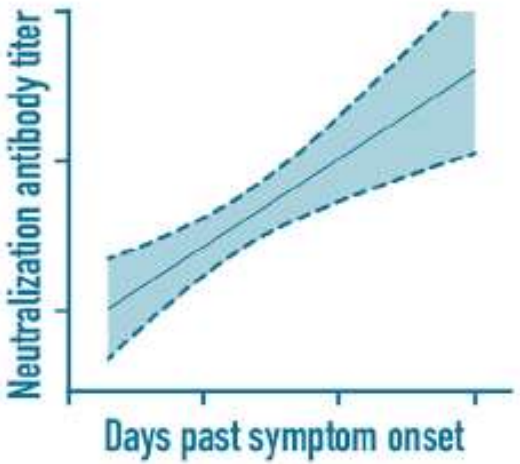
Components of local immunity

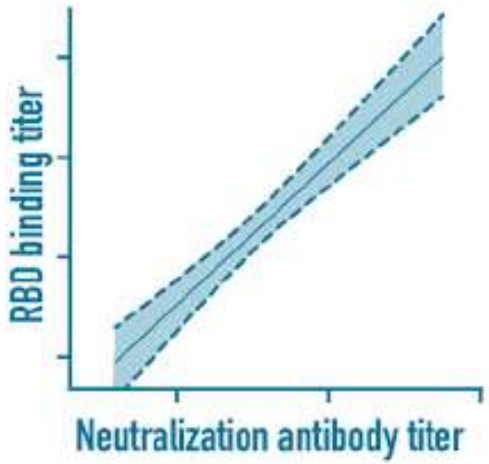


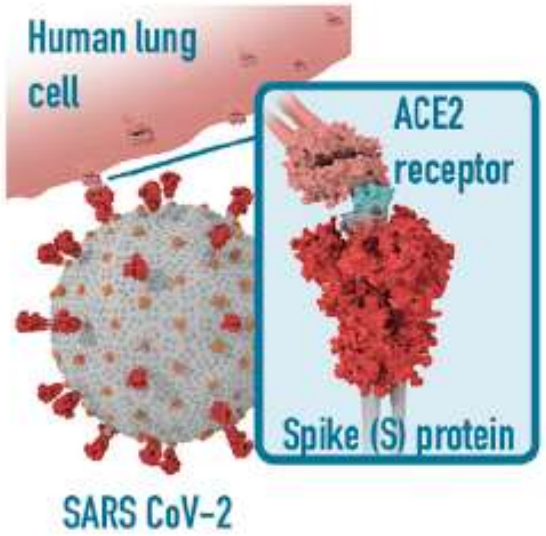


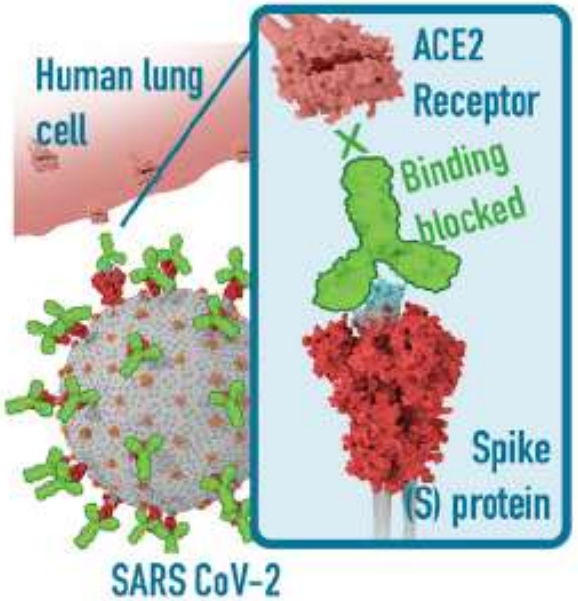
Mehul S. Suthar

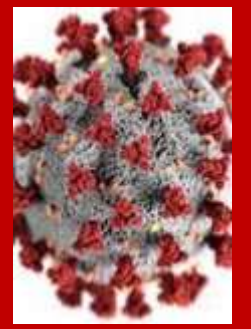
RBD-specific IgG responses detectable in all patients 6 days after PCR confirmation
Neutralizing titers are detectable in all patients 6 days after PCR confirmation
RBD-specific IgG titers correlate with the neutralizing potency







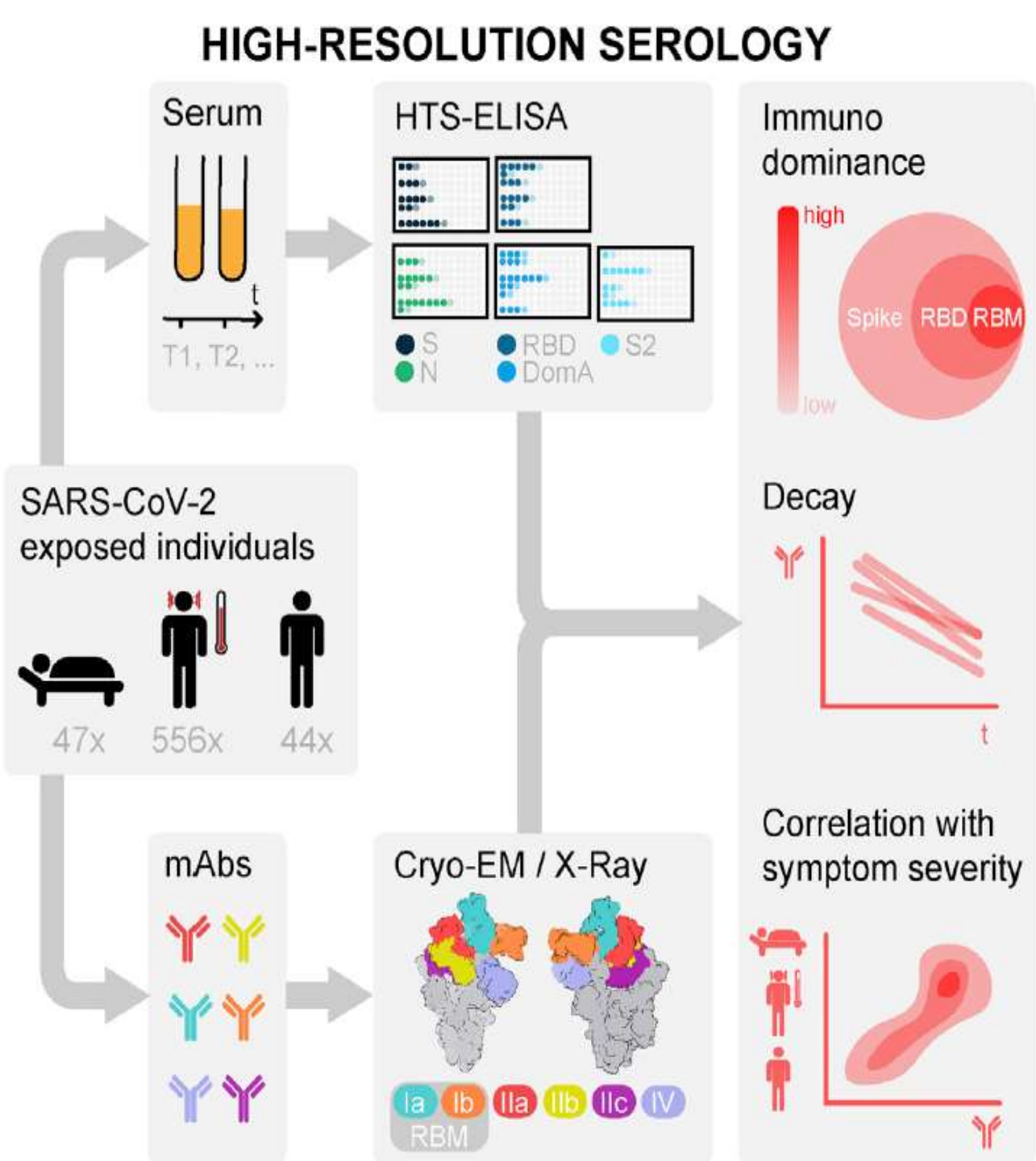


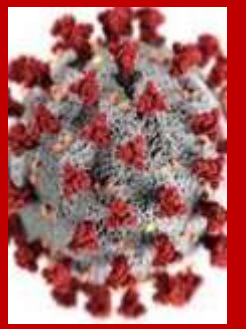


Using a high-resolution serologic epitope-mapping approach: Piccoli et al. revealed the blueprint of antibody responses to the RBD.

Owing to a low level of glycosylation and higher surface accessibility, the RBD is a highly critical immunogenic region of S protein and the target of 90% of the neutralizing activity present in SARS-CoV-2 immune sera

RBM is a highly immunodominant motif in the RBD with two strategic sites, namely Ia and Ib, that contribute to ACE2 and antibody binding, respectively.

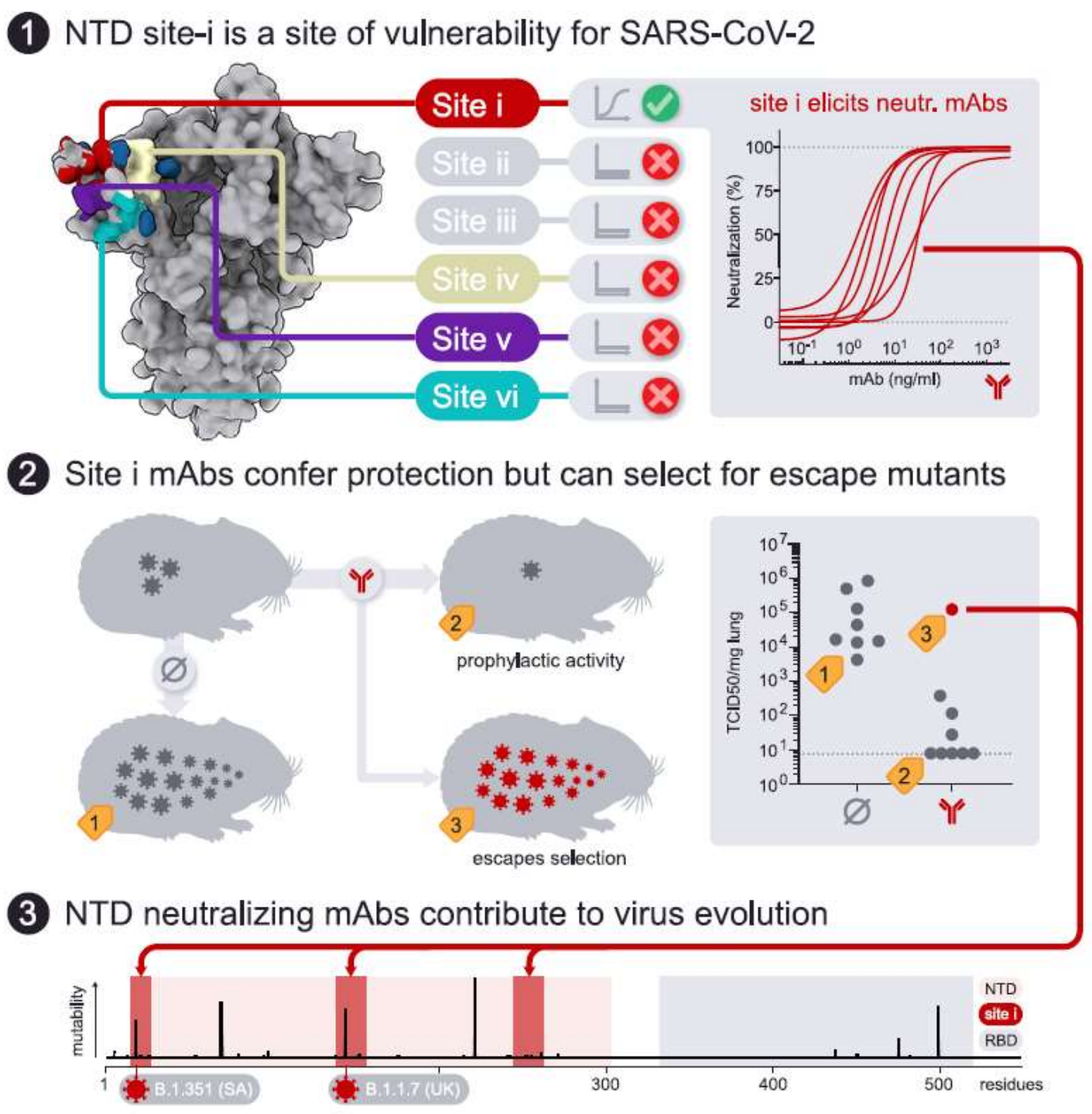


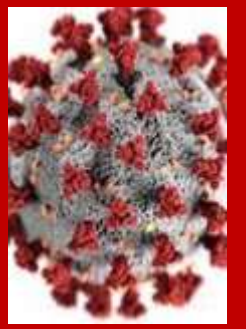


NTD is the other significant spike antigenic site, with limited antigenicity compared with RBD, owing to its widespread N-linked glycan shielding.

A recent groundbreaking study conducted by McCallum revealed the detailed serologic map of NTD. This domain is targeted by (6%-20%) of mAb response, and the second remarkable spike antigenic determinant that contains the super antigenic determinant, which designated site I and considered as vulnerability SARS-CoV-2 site and a target of mAb response.

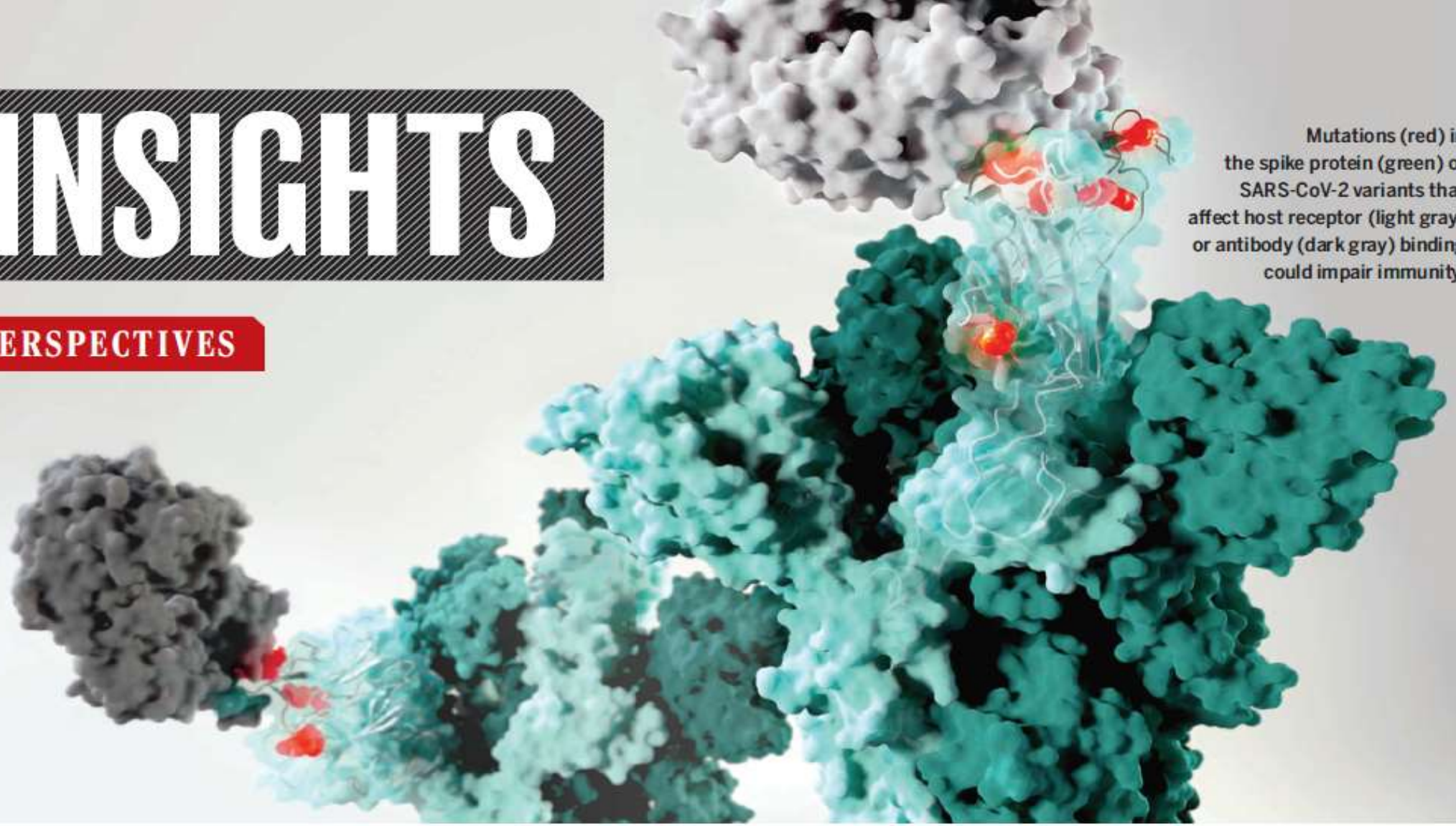
McCallum and colleagues showed that effective NTD mAbs, targeting the antigenic supersite (the site I), enforce a selection pressure, driving viral evolution by mutation and deletion to escape neutralization.



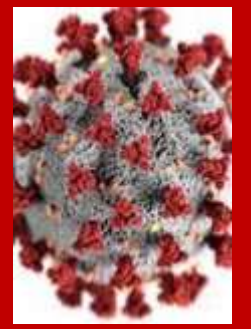


INSIGHTS

PERSPECTIVES



Mutations (red) in the spike protein (green) of SARS-CoV-2 variants that affect host receptor (light gray) or antibody (dark gray) binding could impair immunity.

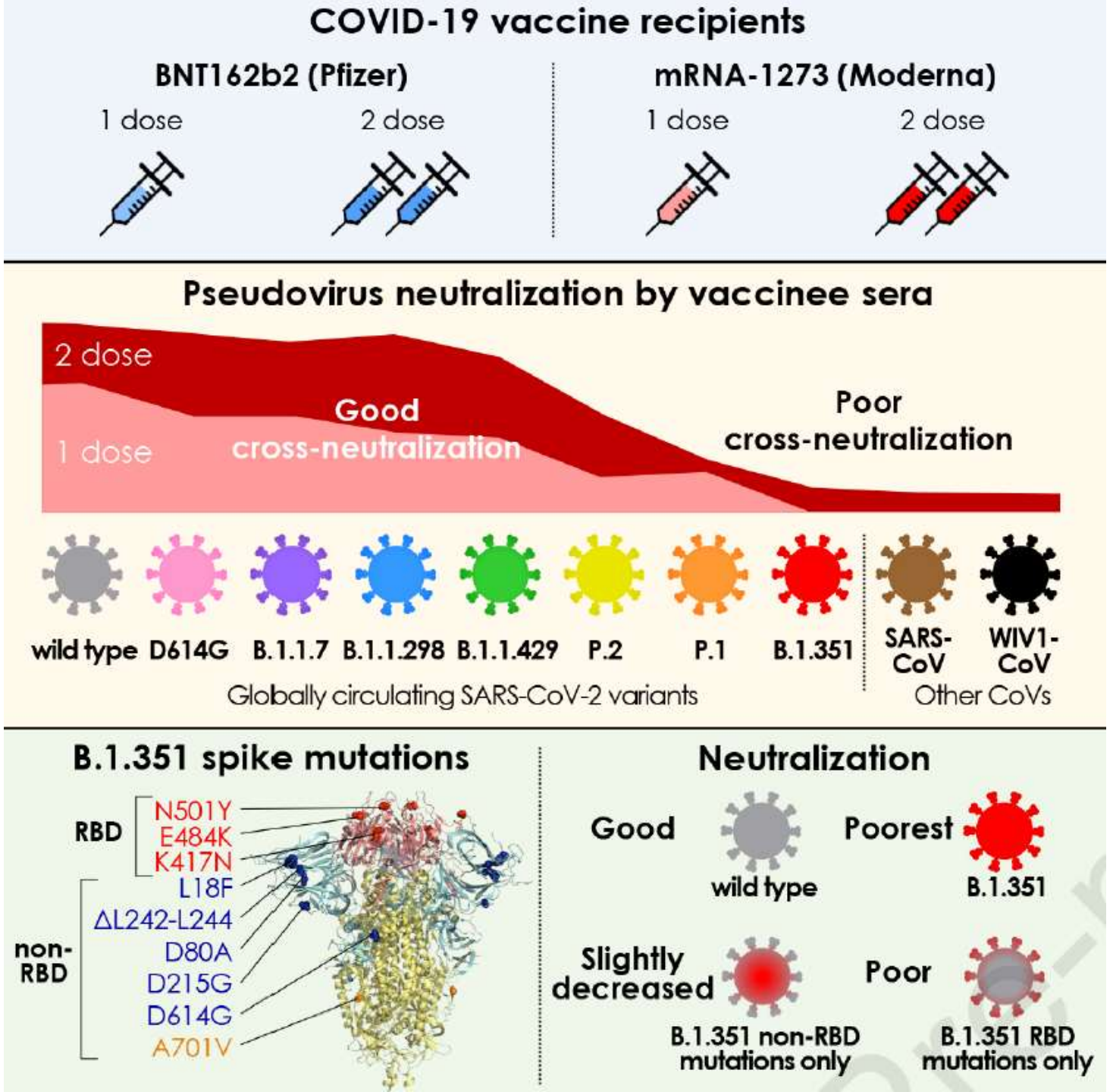


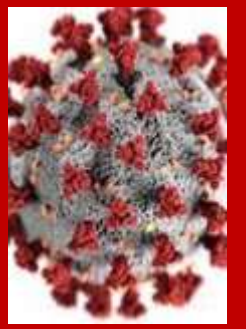
VIEWPOINT: COVID-19

The emerging plasticity of SARS-CoV-2

The evolution of SARS-CoV-2 poses challenges for vaccines and immunotherapies

Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity





B.1.617.2

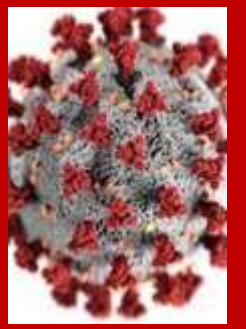
The Mutations

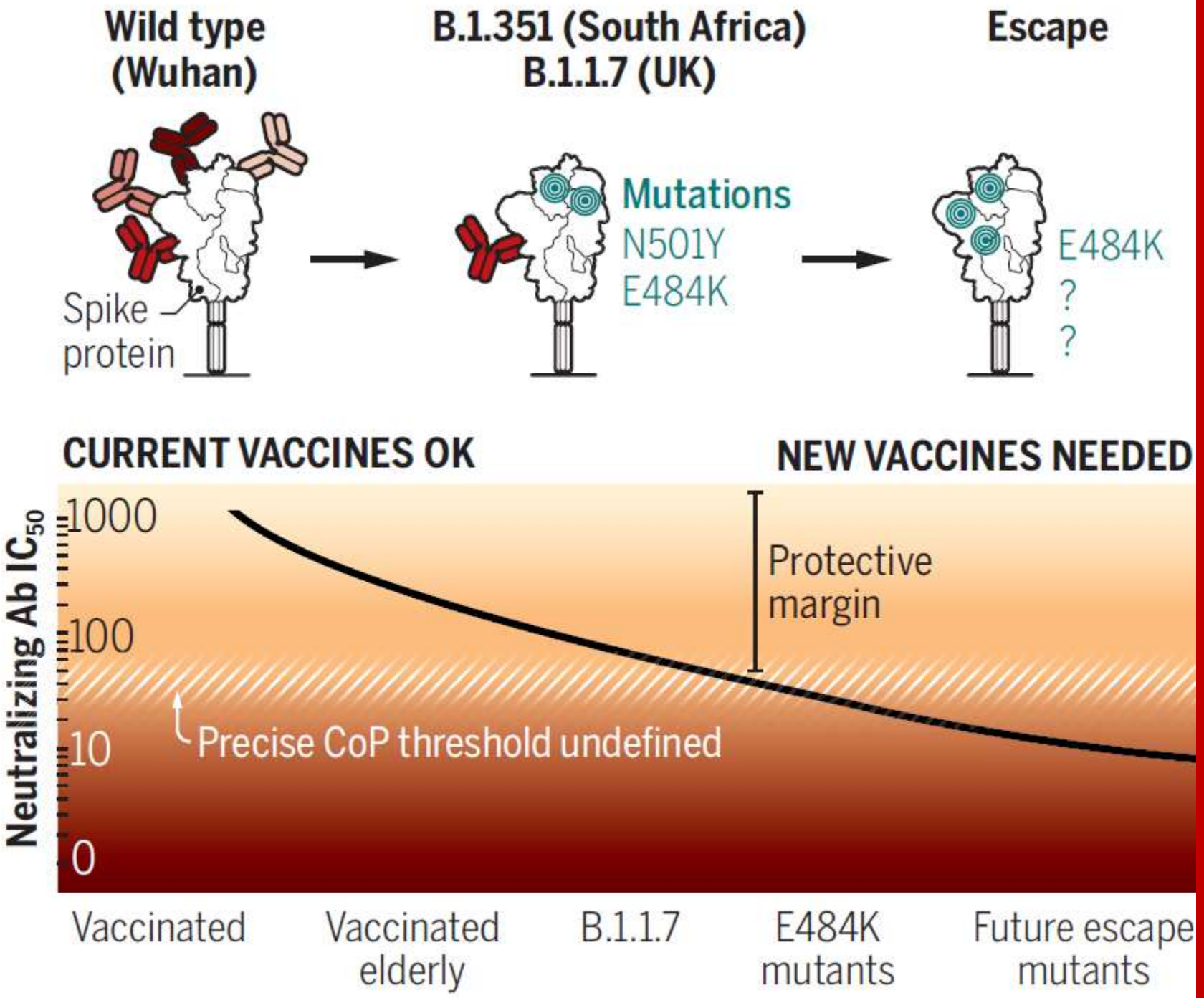
E484Q and L452R mutations

are found in the virus's spike protein.

Daniel M. Altmann[1]

IC50
(half maximal inhibitory concentration) greater than ~1/100 serum dilution would likely
be safe from infection, or at least from symptomatic infection.





Briefly:

- SARS-CoV-2 is continuously evolving.
- Variant number is growing
- The government should keep the variant under close scrutiny
- to maintain tip-top efficacy, the vaccines will need to be updated.

Take Home message:

- The government should keep the variant under close scrutiny