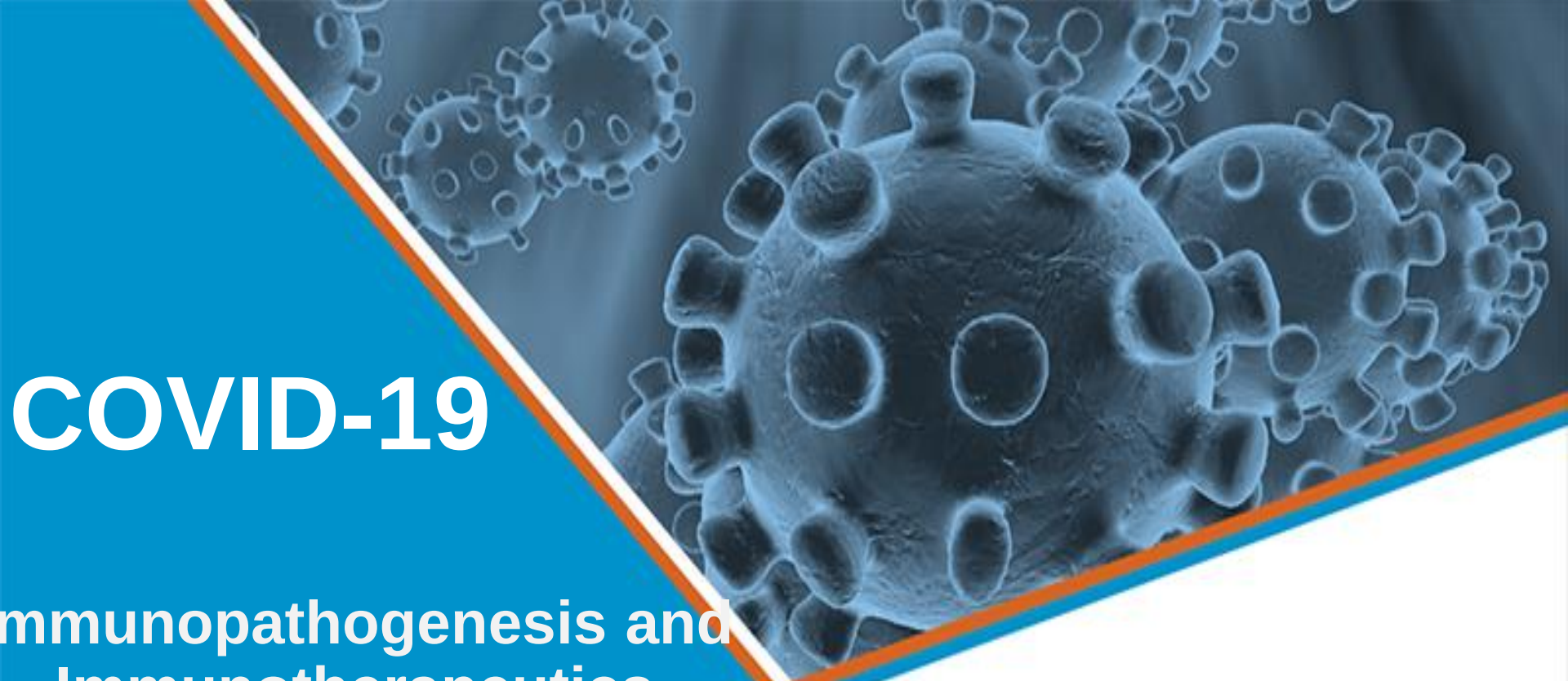


COVID-19

mmunopathogenesis and Immunotherapeutics

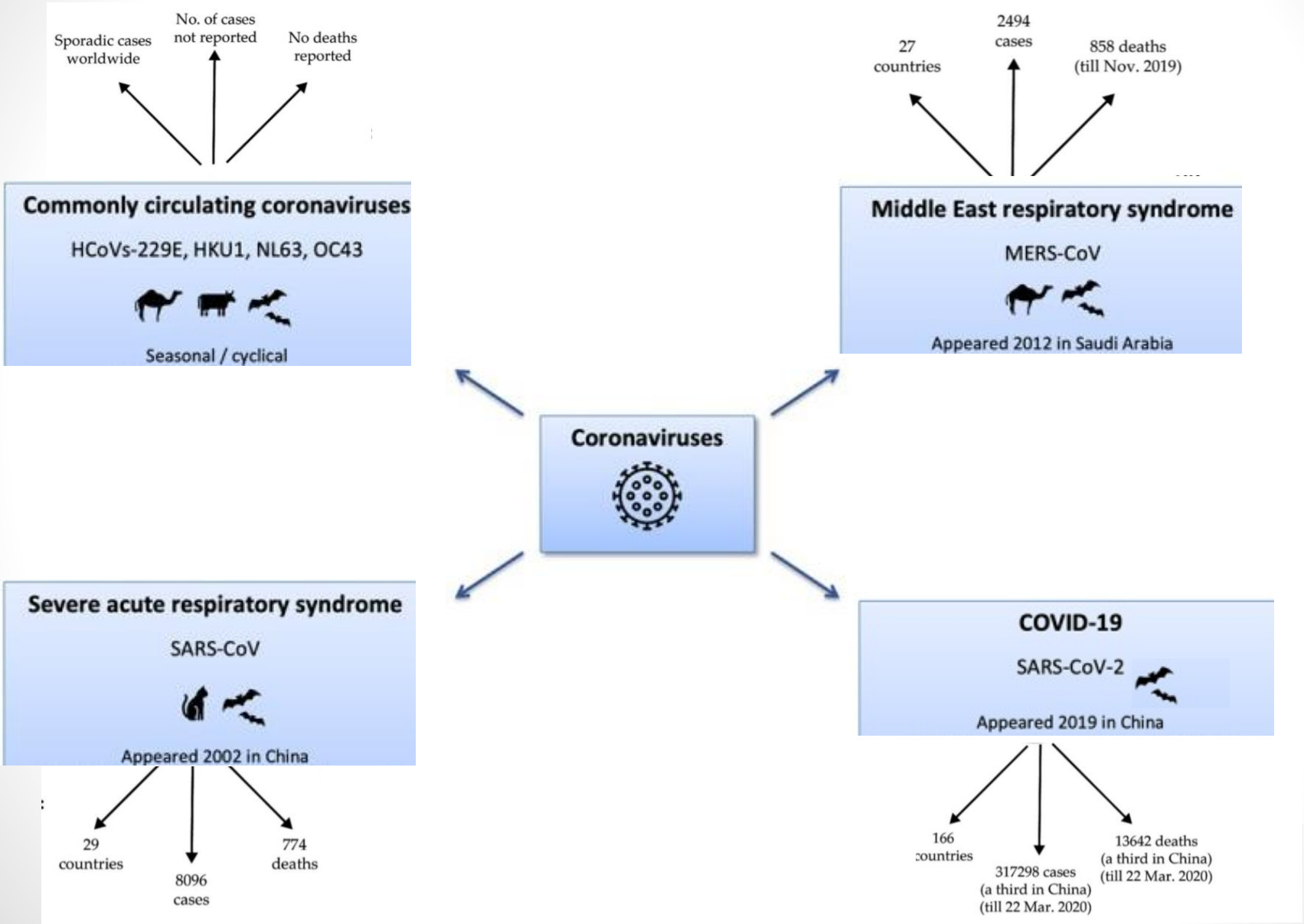
Presented by:

Marzieh Norouzian

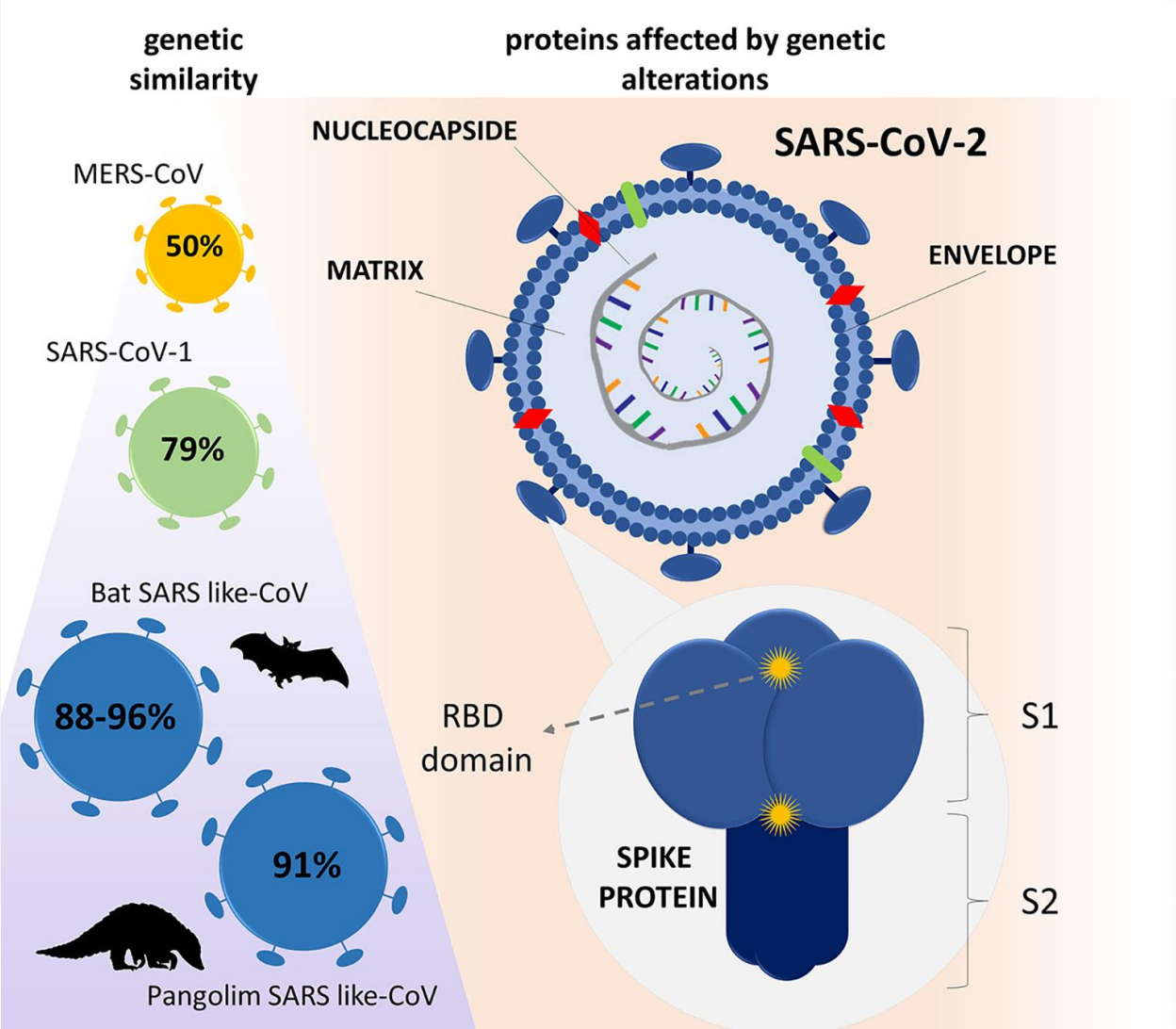
Assistant Professor of Medical Immunology Department of Laboratory Sciences, School of Allied Medical Sciences, Hormozgan University of Medical Sciences

Feb 2021

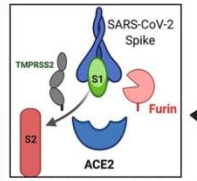
Summary of coronavirus diseases



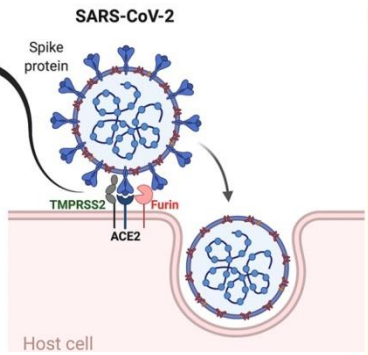
Structure of COVID-19

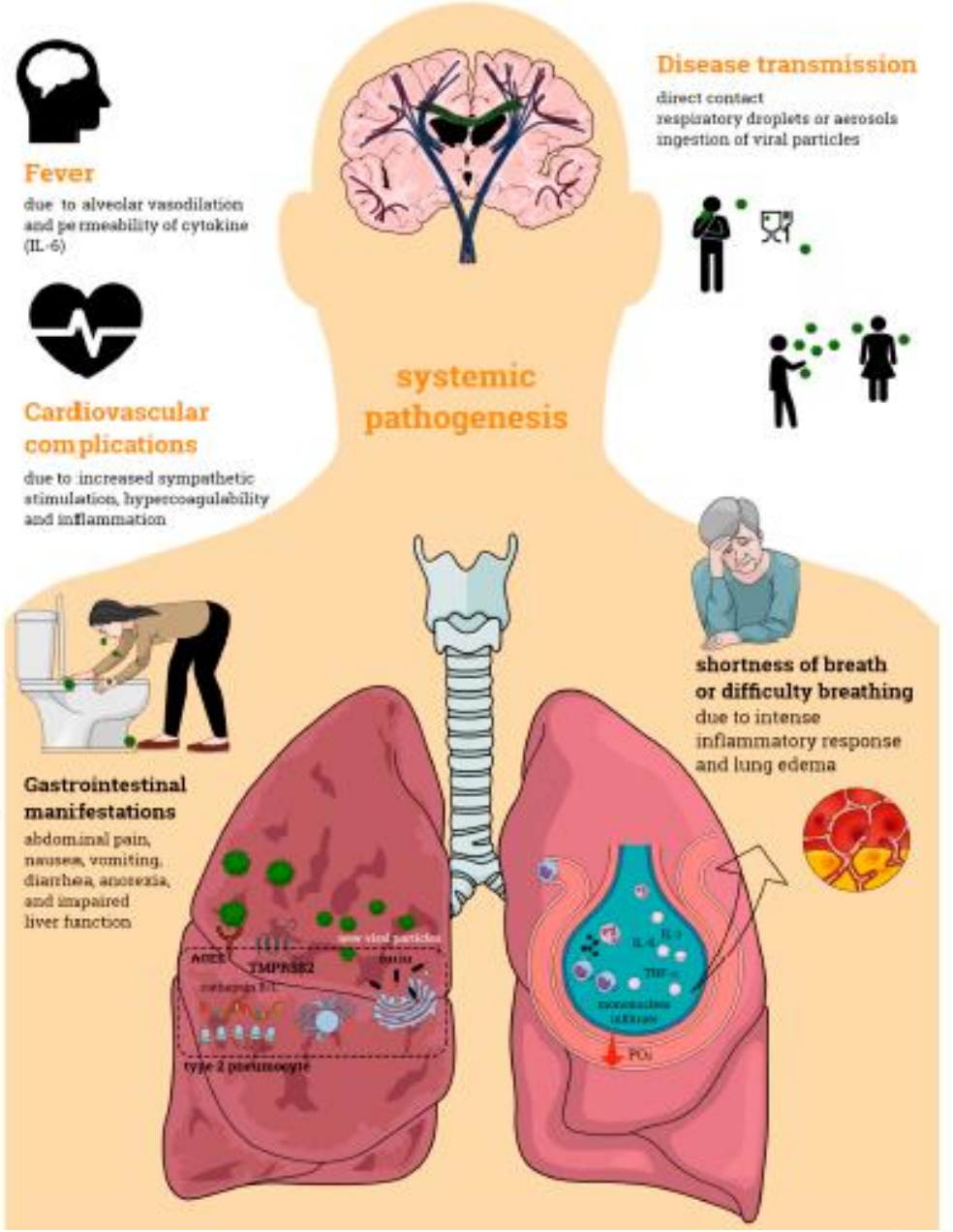


COVID-19

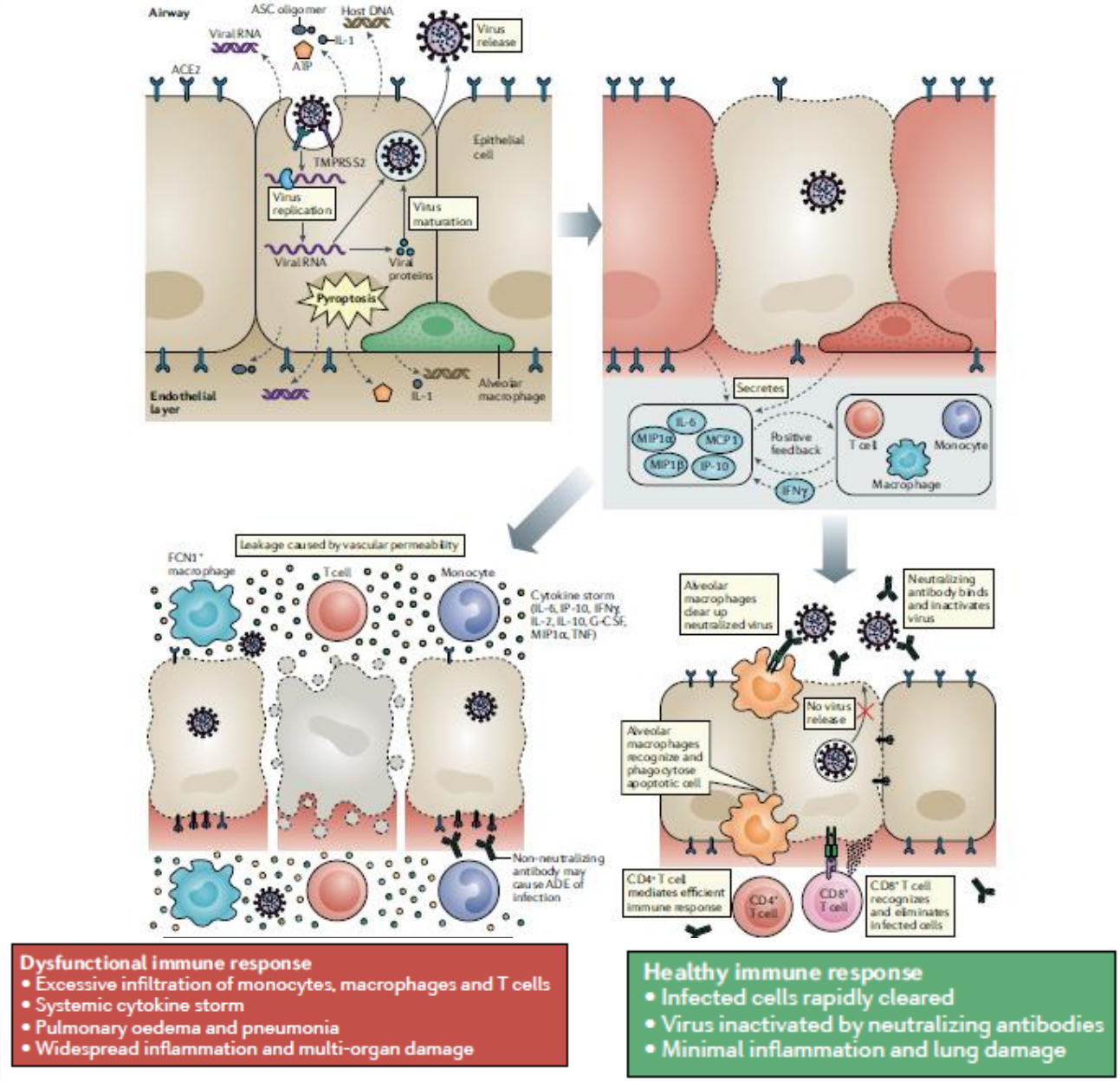


S1/S2 subunits cleavage by furin and SARS-CoV-2 genomes penetrate into the host cell





Immunopathogenesis of COVID-19



Dysfunctional immune response
- Excessive infiltration of monocytes, macrophages and T cells
- Systemic cytokine storm
- Pulmonary oedema and pneumonia
- Widespread inflammation and multi-organ damage

Healthy immune response
- Infected cells rapidly cleared
- Virus inactivated by neutralizing antibodies
- Minimal inflammation and lung damage

- In the majority of SARS-CoV2 infections symptoms remain mild to moderate. Approximately 15% of cases were severe to fatal.

- At this time there are no interventions proven to be effective for patients infected with SARS-CoV2.

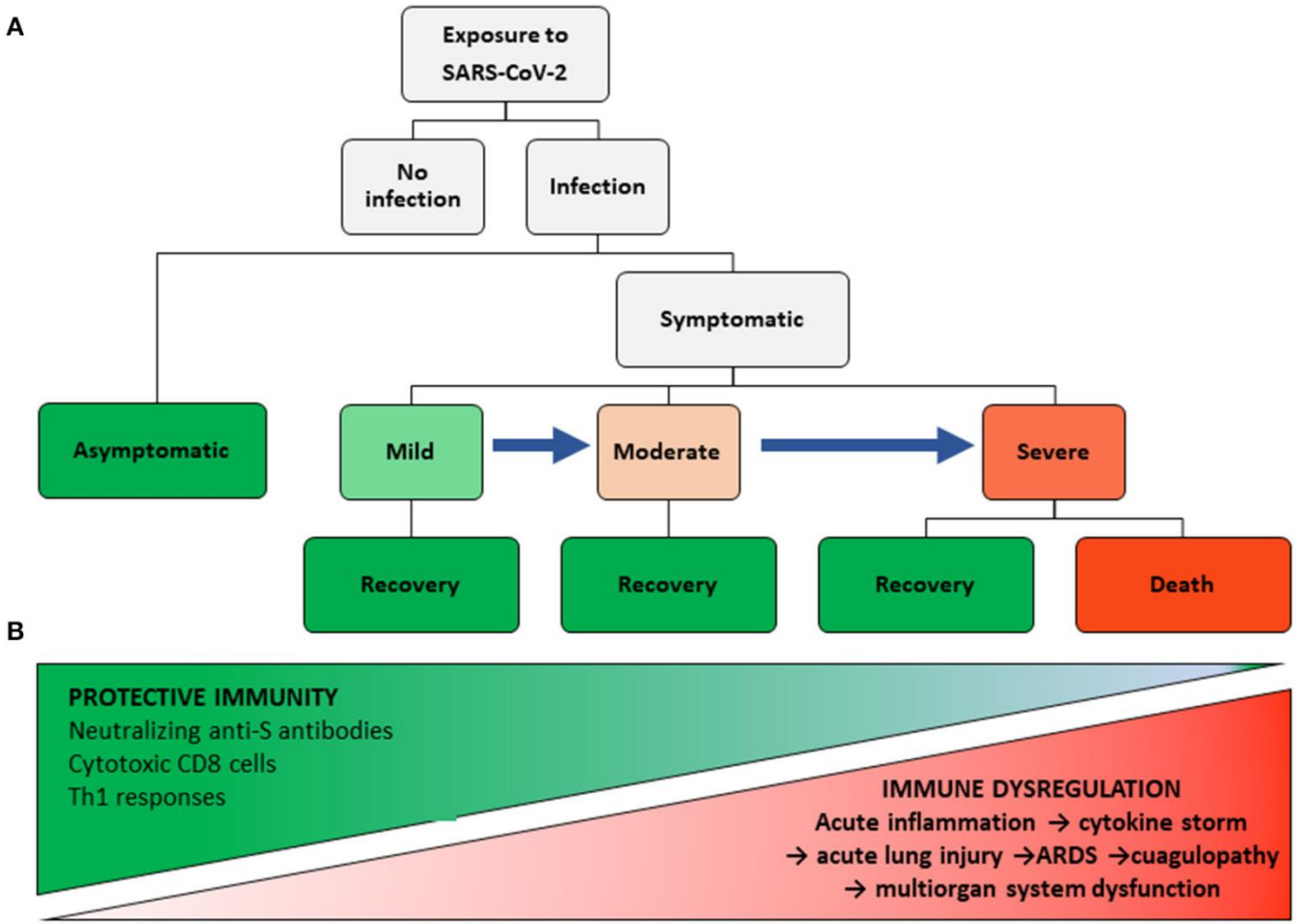
- Understanding the immunological basis of how the severe cases differed from the asymptomatic cases may form the basis for effective treatment.

Immune response to Sever COVID-19 infection

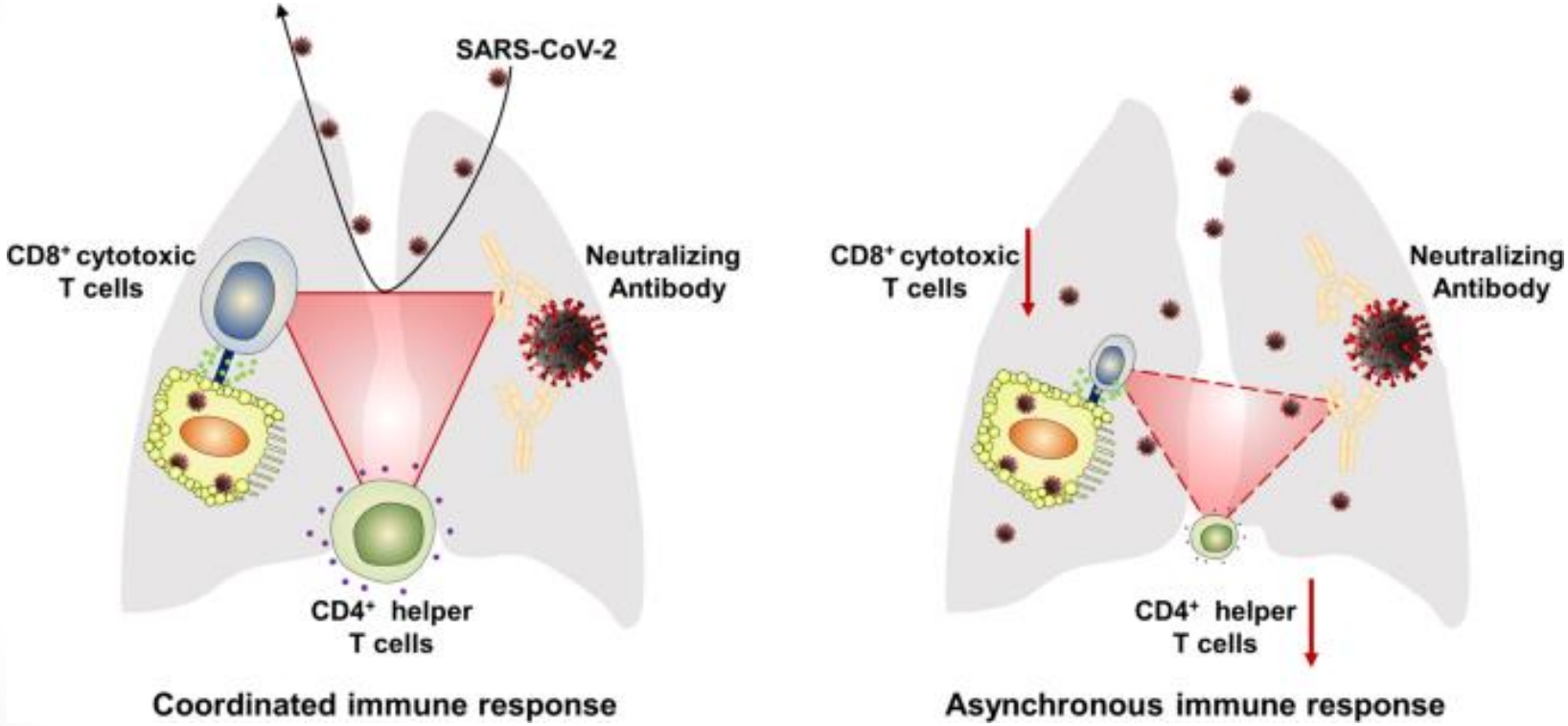
- **Stage 1 – Immunosuppression:**
  - ✓ This is characterized by lymphopenia combined with T cell exhaustion and inadequate adaptive immune response.
  - ✓ The objective is to evade the immune system allowing for unchecked viremia.

- **Stage 2 – Hyperinflammation:**
  - ✓ This is characterized by a cytokine storm with neutrophil, monocyte/ macrophage infiltration and activation.
  - ✓ This is manifested clinically by ARDS, multi organ failure and coagulopathy

COVID-19 Clinical and immunological spectra

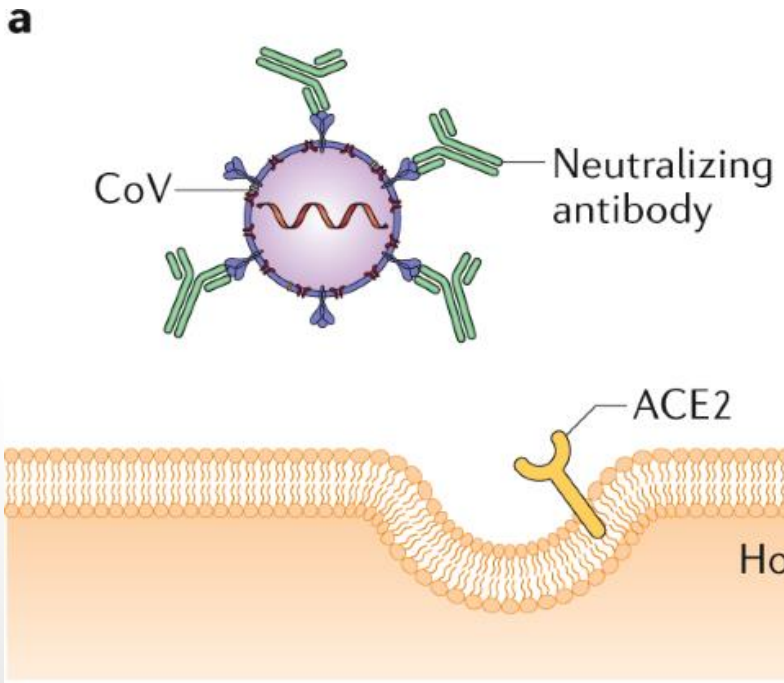


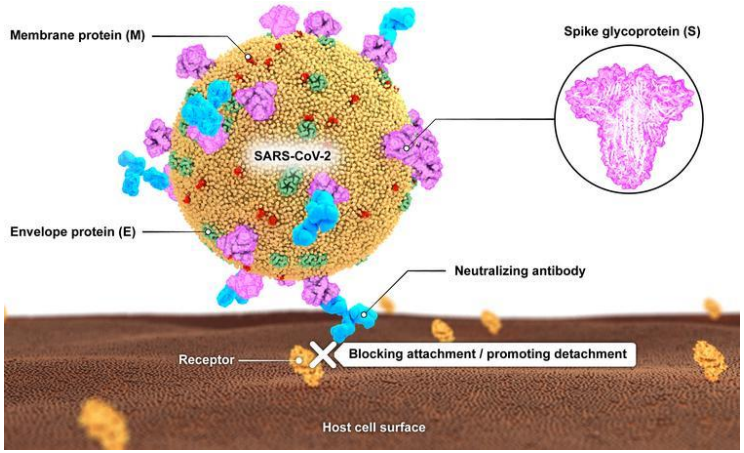
COVID-19 Clinical and immunological spectra



Neutralizing Antibodies

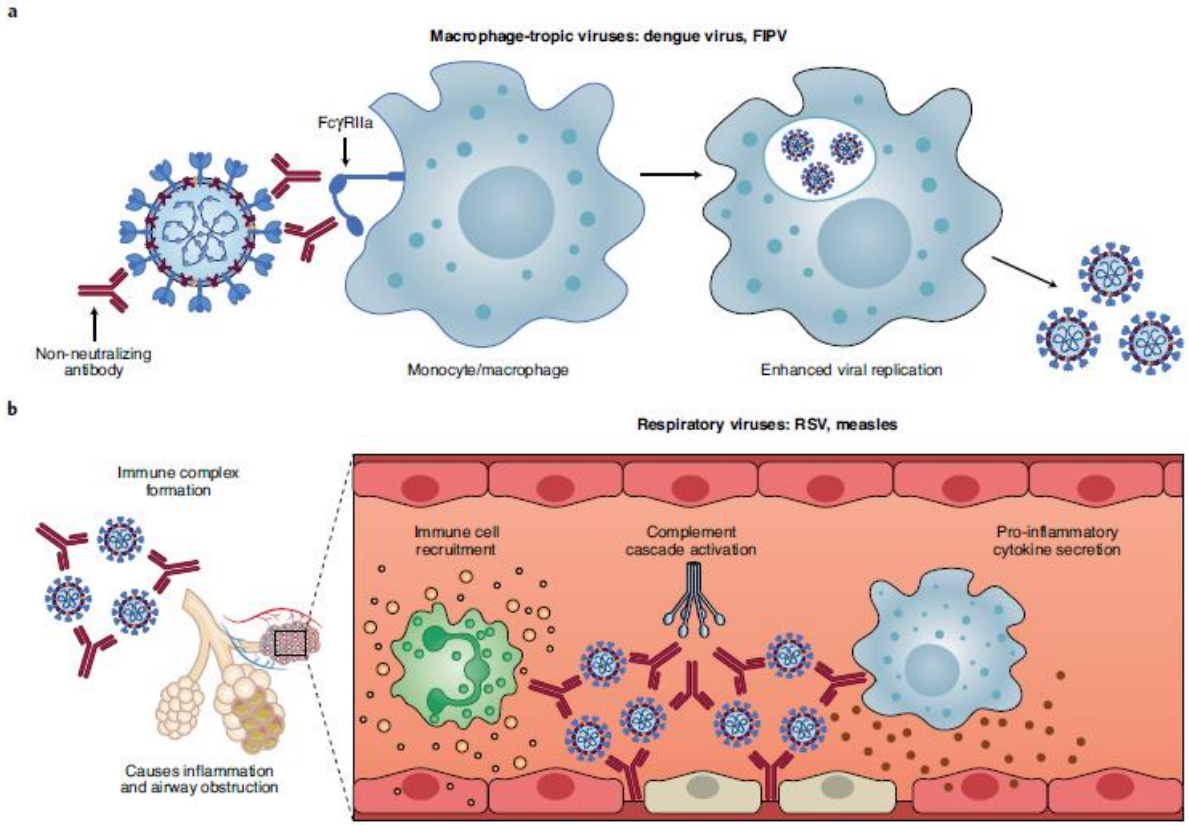
- Neutralizing antibodies play critical roles in blocking viral infections





Antibody-Dependent Enhancement (ADE)

- **Two main ADE mechanisms in viral disease:**
  - *ADE via enhanced infection*
  - *ADE via enhanced immune activation*




Veklury
(Remdesivir)
Coronavirus
Treatment
#StrongerTogether
#UnitedAgainstCoronavirus
European
Commission

Coronavirus Drug and Treatment Tracker

By Katherine J. Wu, Carl Zimmer and Jonathan Corum Updated Jan. 8, 2021

We are following **22 coronavirus treatments** for effectiveness and safety:

Remdesivir

Ventilators

Prone positioning

Dexamethasone& Other Corticosteroids

Favipiravir

Convalescent plasma

Monoclonal antibodies

Interferons

Cytokine Inhibitors

Lopinavir

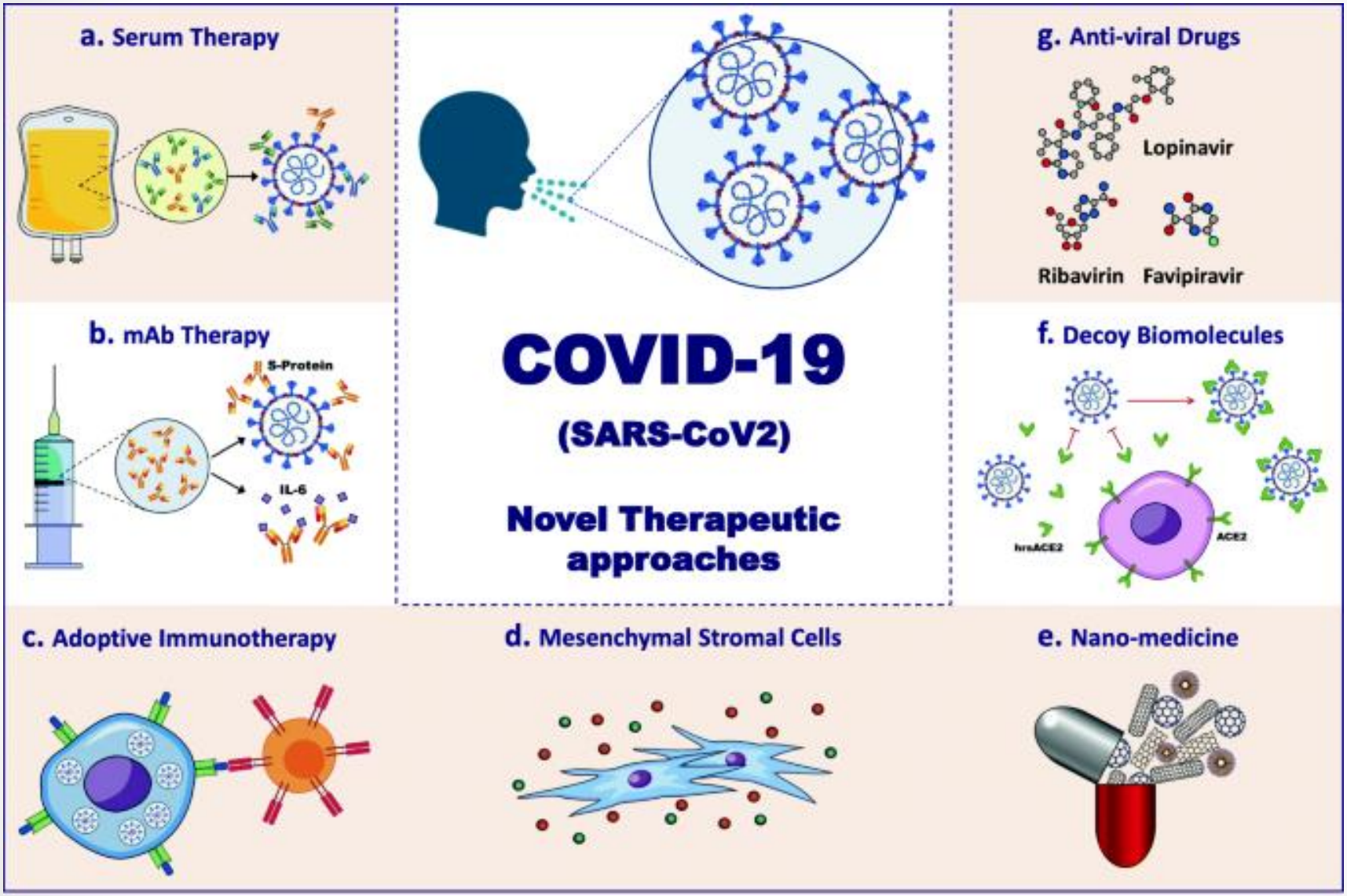
Hydroxychloroquine

chloroquine

Drinking disinfectants

UV light

Silver


a. Serum Therapy
b. mAb Therapy
S-Protein
IL-6
c. Adoptive Immunotherapy
COVID-19
(SARS-CoV2)
Novel Therapeutic approaches
d. Mesenchymal Stromal Cells
g. Anti-viral Drugs
Lopinavir
Ribavirin
Favipiravir
f. Decoy Biomolecules
hrsACE2
ACE2
e. Nano-medicine

Convalescent Plasma - COVID-19 Treatment

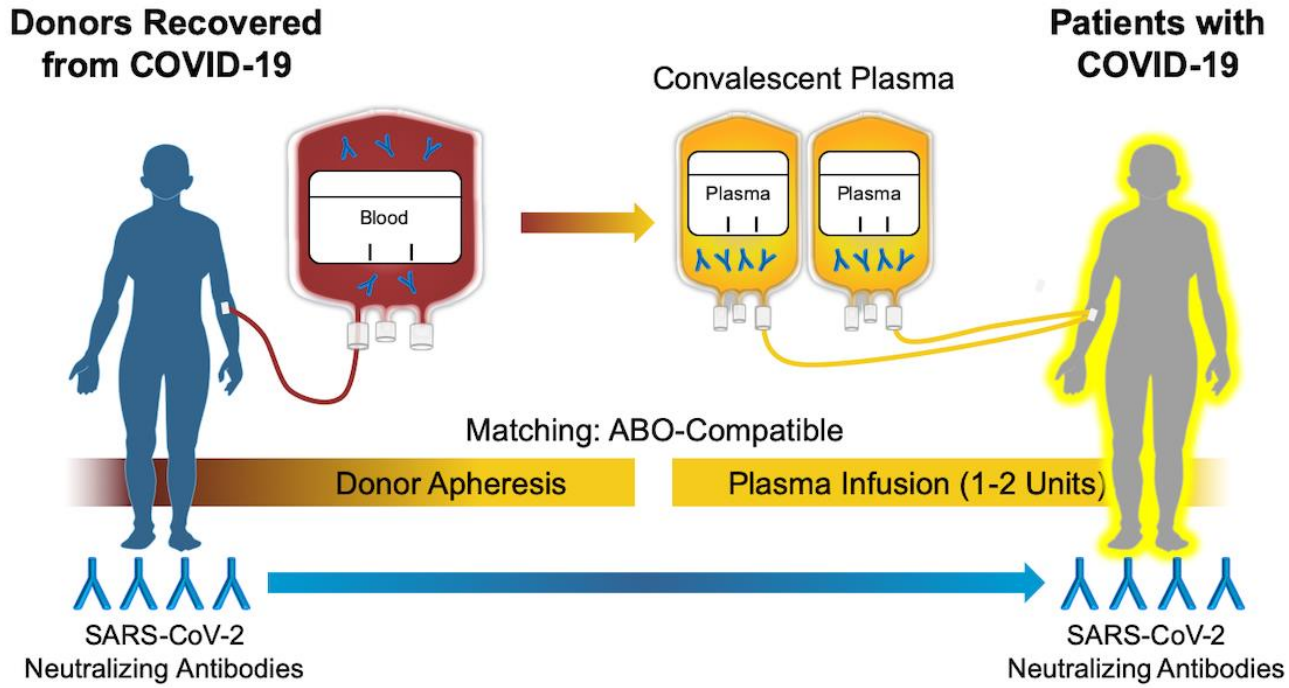
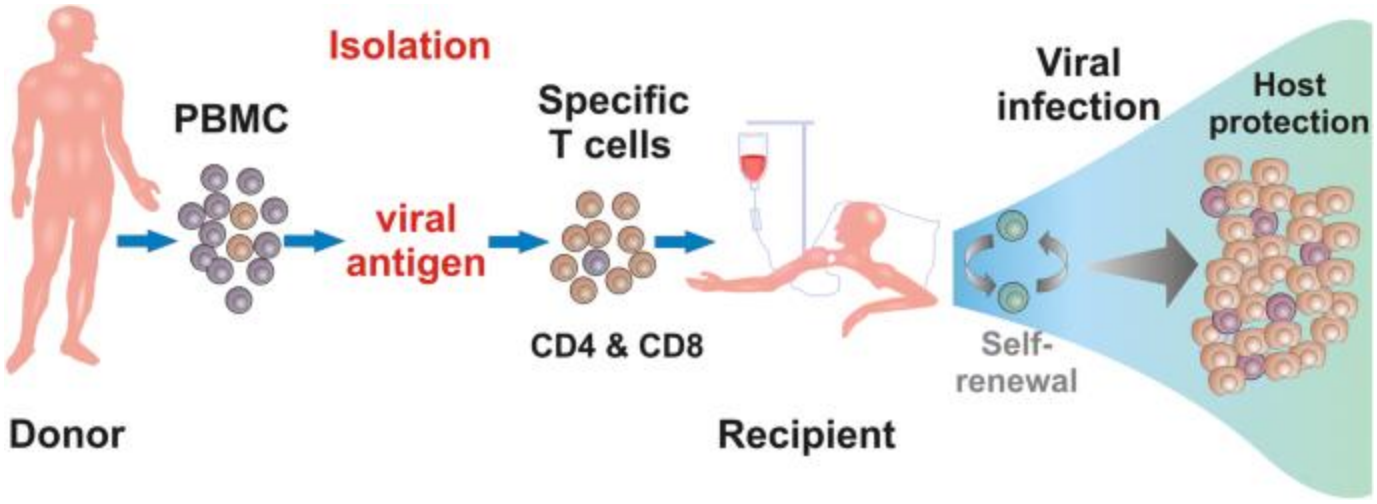


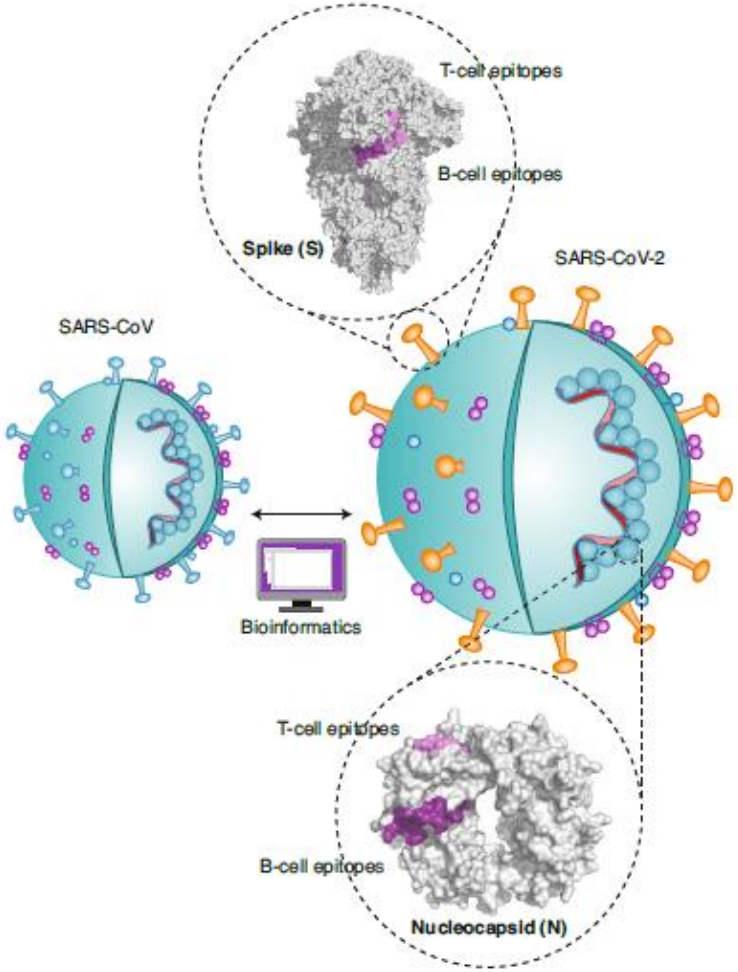
Illustration: David H. Spach, MD

Adoptive immunotherapy

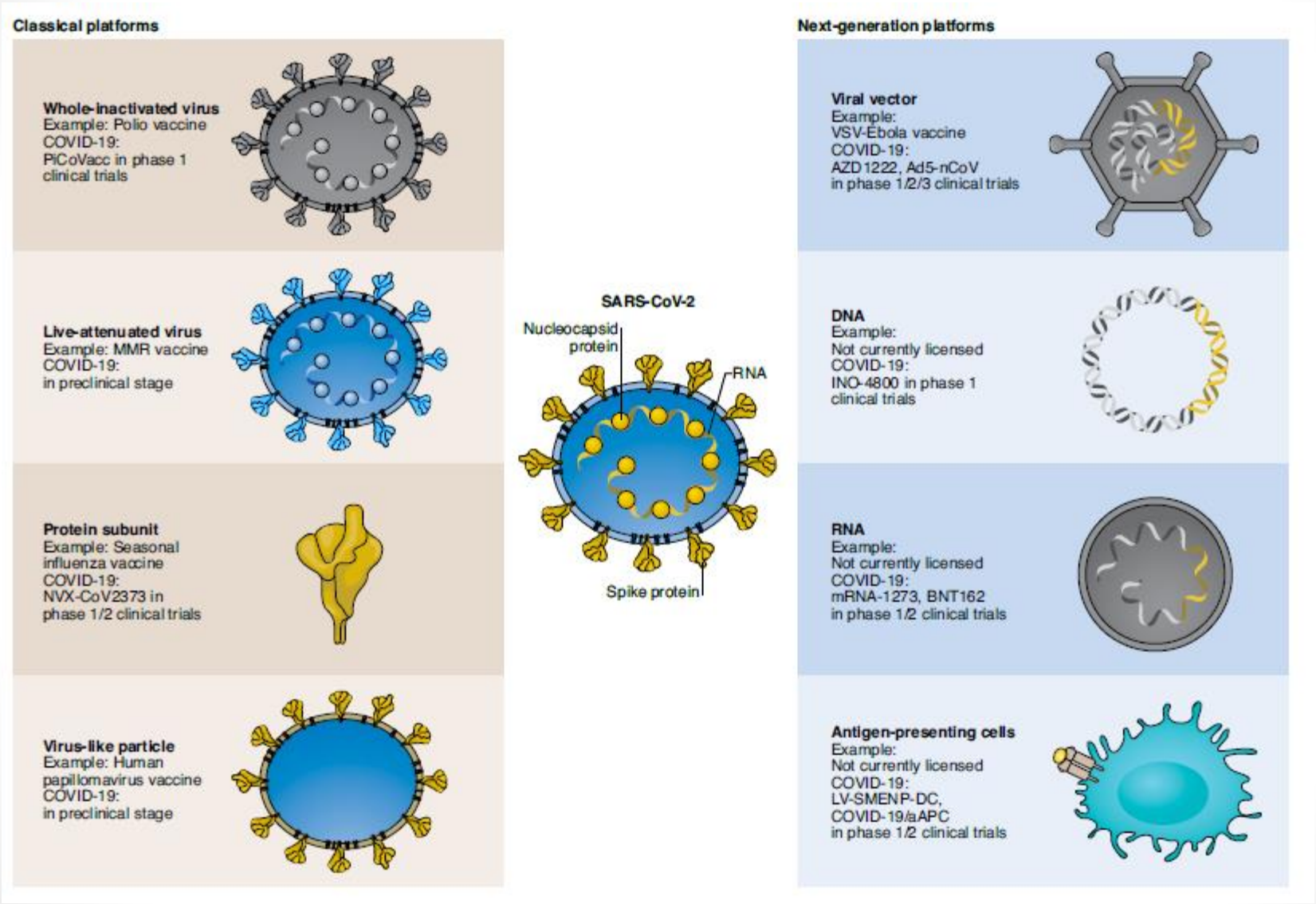


COVID-19 Vaccine

Potential targets for vaccine development to COVID-19



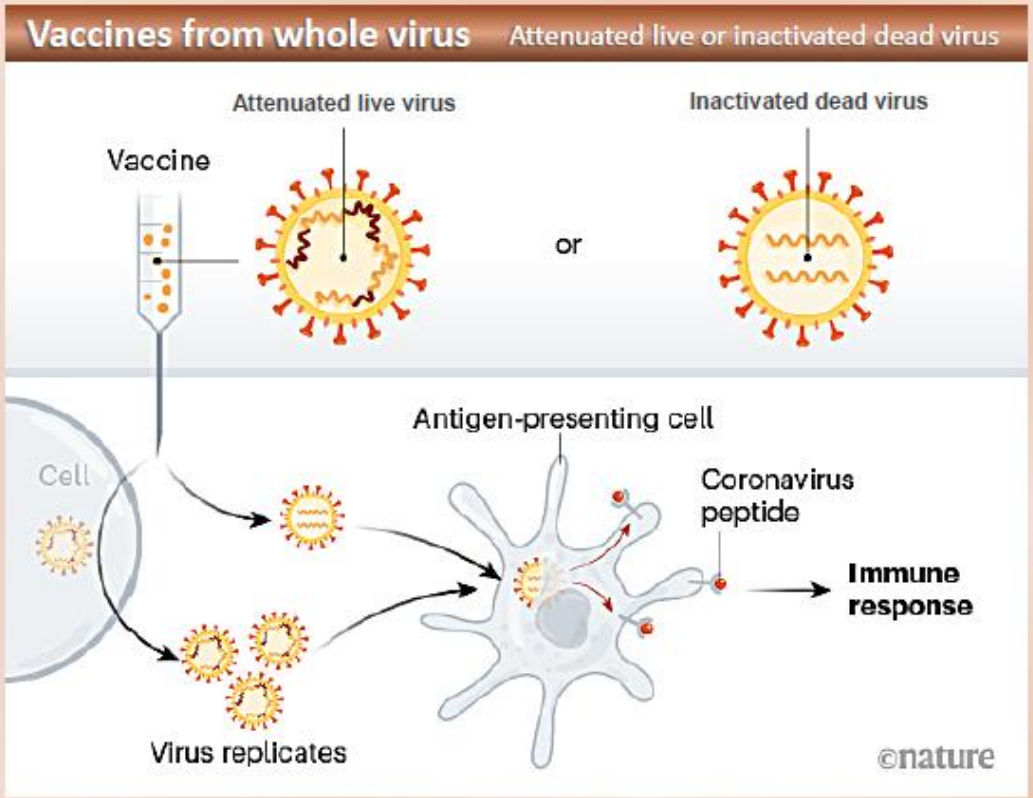
An overview of the different vaccine platforms in development against COVID-19



Virus vaccines

- **Virus is selected, modified (weakened) or completely inactivated** so that it will not cause disease

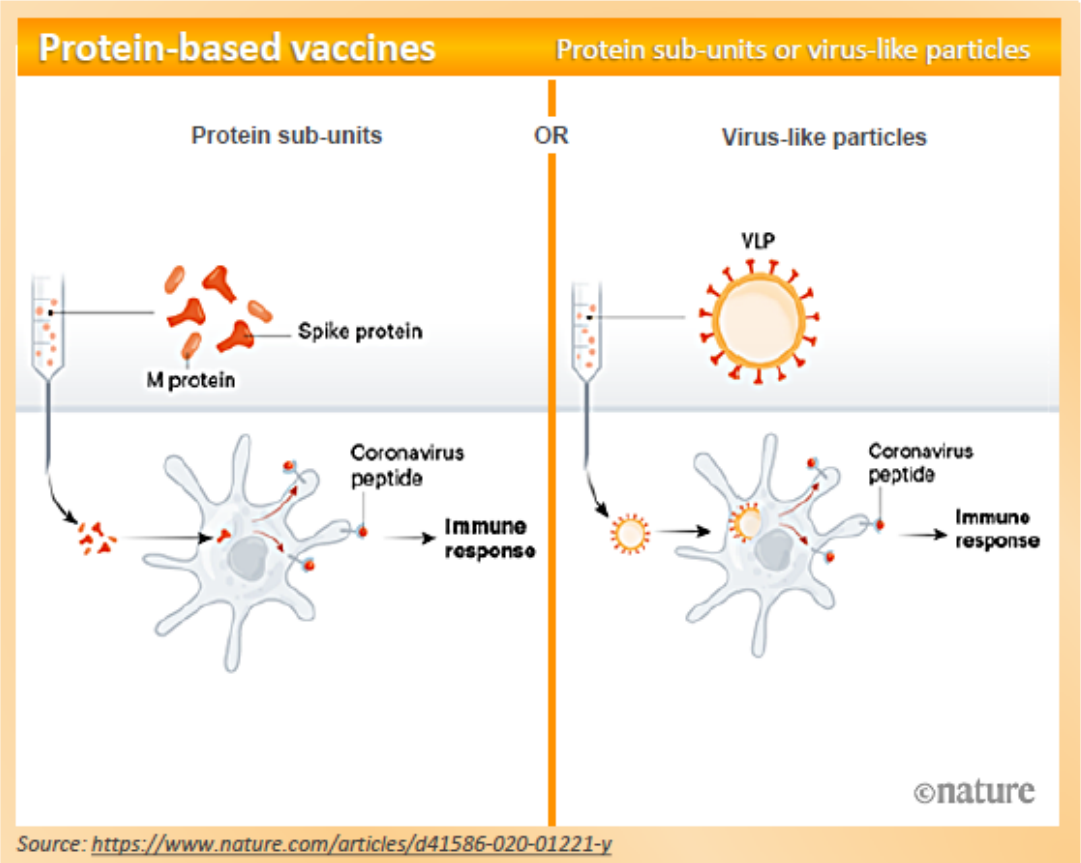
Note:
This illustration shows injectable vaccines. Some vaccines in this category are administered orally



Source: https://www.nature.com/articles/d41586-020-01221-y

Protein-based vaccines

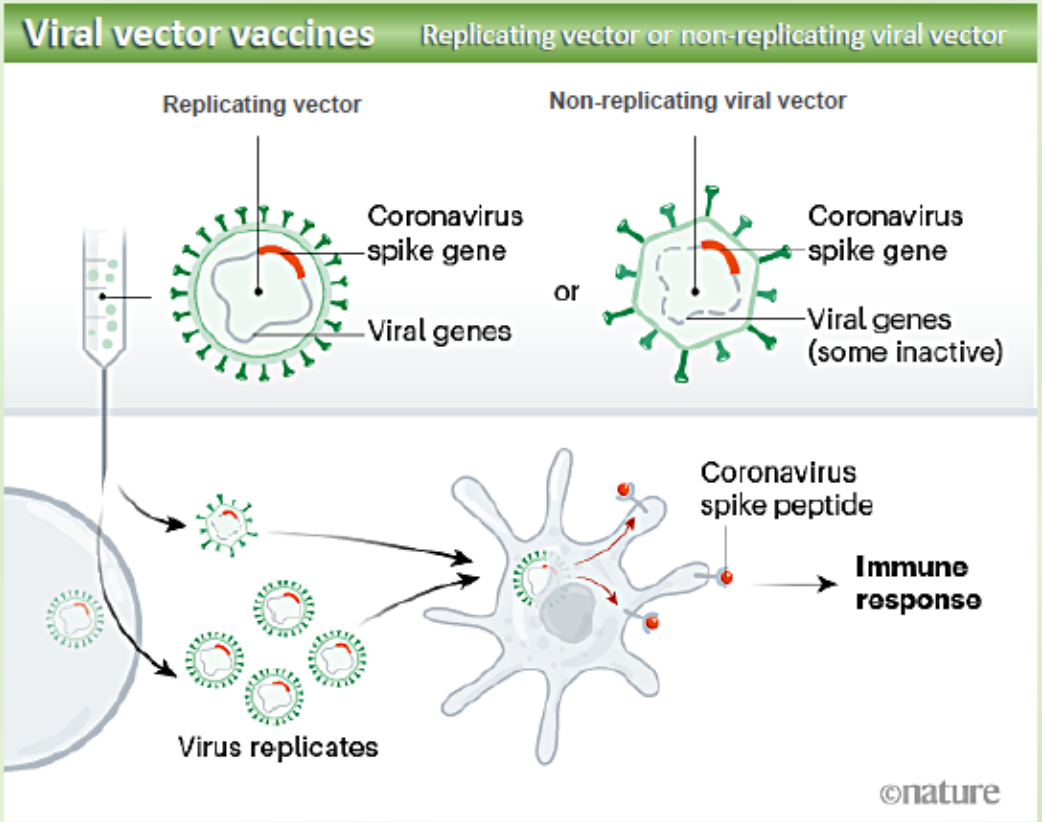
- **A protein is extracted from the virus** (alive or inactivated), purified, and injected as a vaccine
- For coronavirus, this is most commonly the spike protein
- Virus-like particles work in the same way



Source: https://www.nature.com/articles/d41586-020-01221-y

Viral vector vaccines

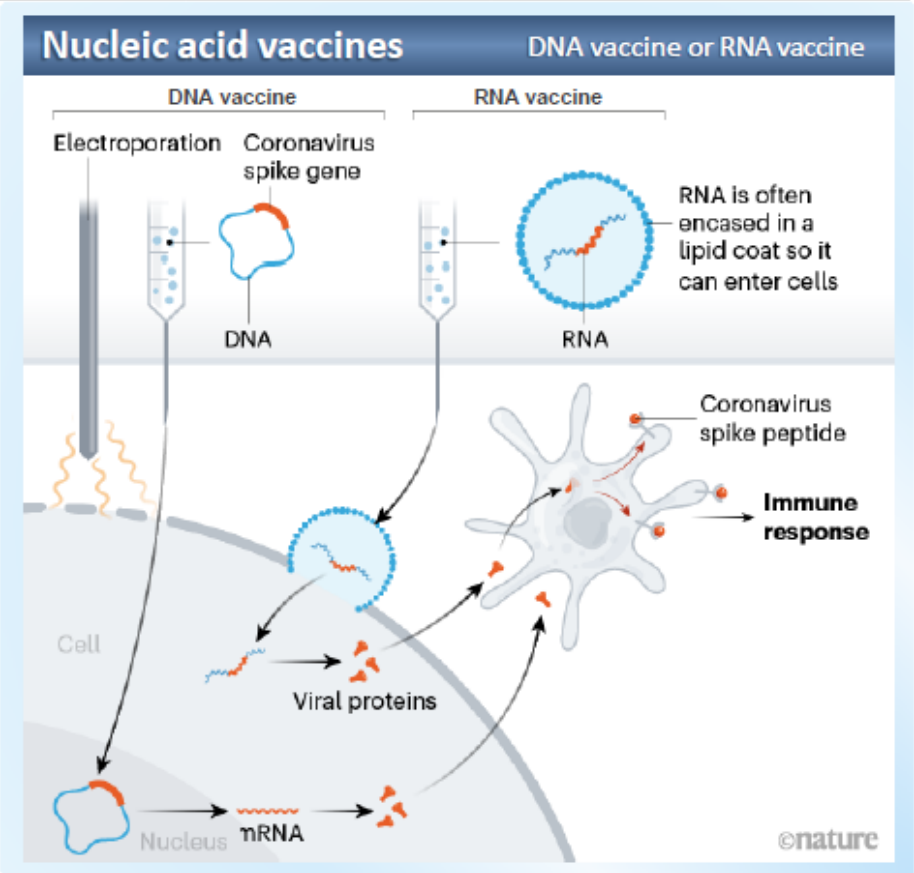
- **The gene for a pathogen protein is inserted into a different virus** that can infect someone without causing disease
- The safe virus serves as a 'platform' or 'vector' to deliver the protein that triggers an immune response
- The safe virus is then injected as a vaccine
- Some replicate (reproduce) in the body and some do not



Source: https://www.nature.com/articles/d41586-020-01221-y

Nucleic acid vaccines

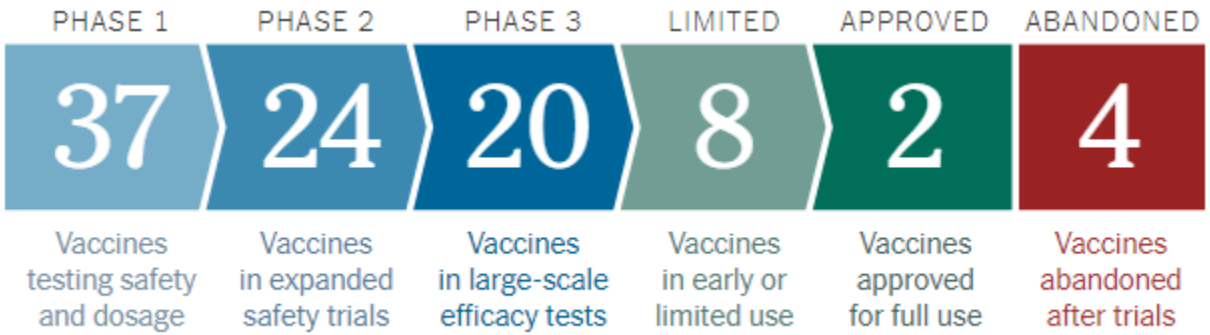
- Instead of a virus, a protein antigen, or a virus expressing the protein, **nucleic acid coding for the antigen is injected**
- DNA plasmid: enters nucleus, translated to mRNA for expression of protein
- Or mRNA can be injected. More direct (no translation required) but less stable than DNA
- This is new technology – no other vaccines for human use have used this



Source: https://www.nature.com/articles/d41586-020-01221-y

Coronavirus Vaccine Tracker

By Carl Zimmer, Jonathan Corum and Sui-Lee Wee Updated Jan. 31, 2021

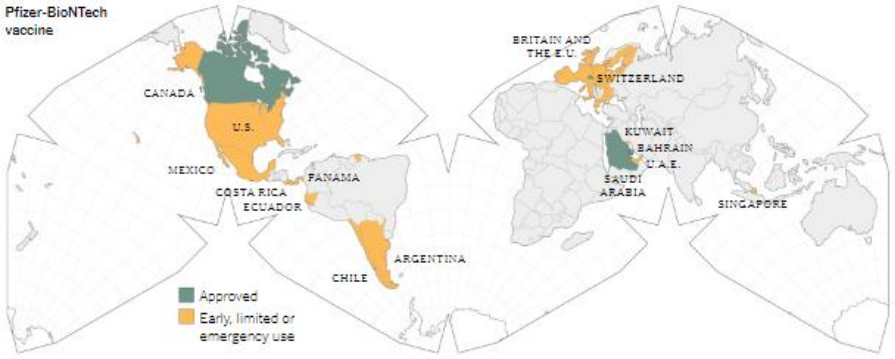


PHASE 2 | PHASE 3 | COMBINED PHASES

APPROVED IN SEVERAL COUNTRIES | EMERGENCY USE IN U.S., ELSEWHERE

Pfizer BIONTECH

VACCINE NAME: Comirnaty (also known as tozinameran or BNT162b2)
EFFICACY: 95%
DOSE: 2 doses, 3 weeks apart
TYPE: Muscle injection
STORAGE: Freezer storage only at -94°F (-70°C)

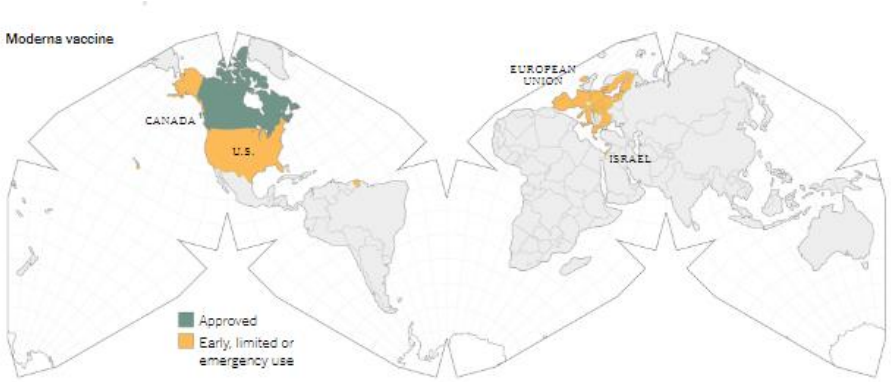


PHASE 3

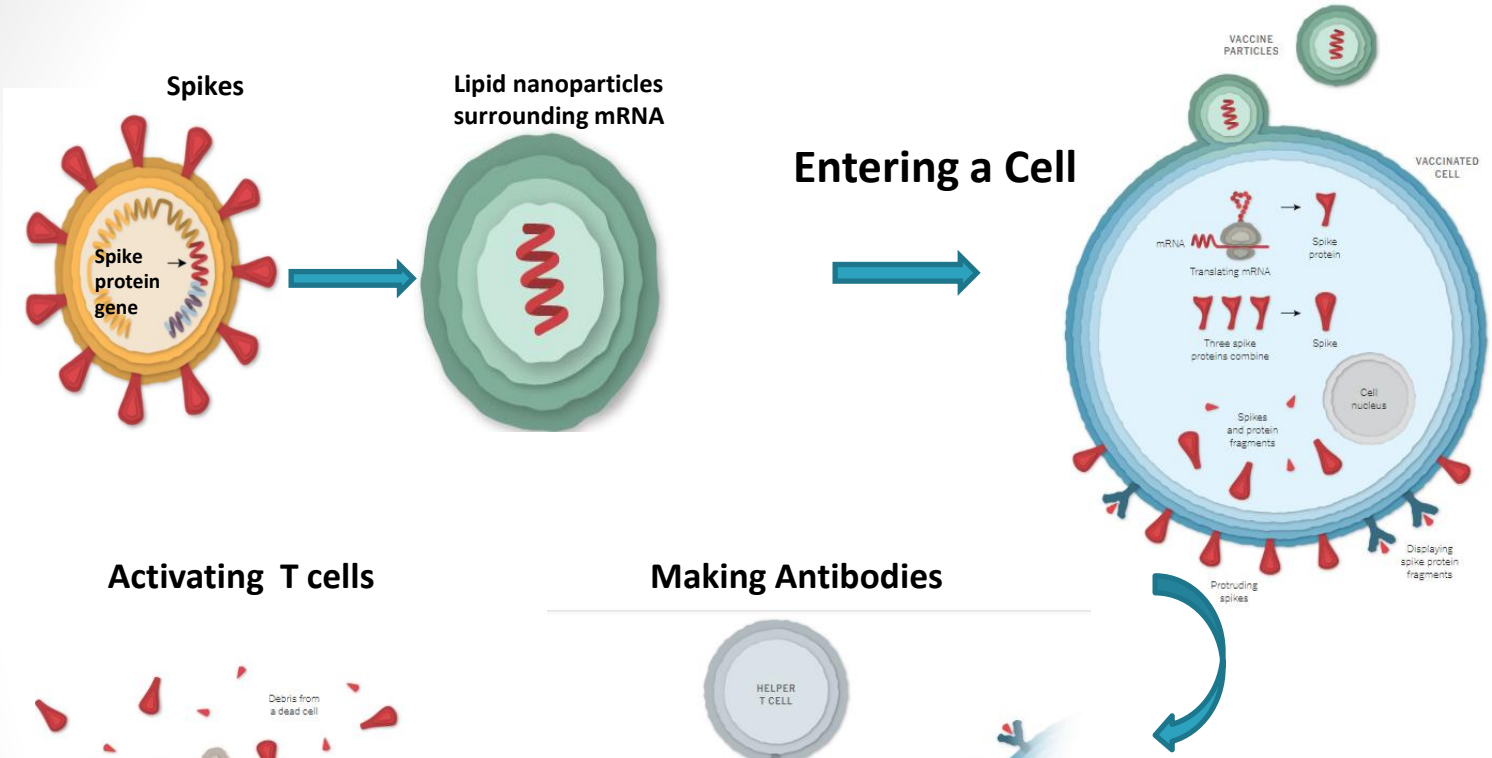
APPROVED IN CANADA | EMERGENCY USE IN U.S., E.U., ISRAEL

moderna NIH National Institutes of Health
Turning Discovery Into Health

VACCINE NAME: mRNA-1273
EFFICACY: 94.5%
DOSE: 2 doses, 4 weeks apart
TYPE: Muscle injection
STORAGE: 30 days with refrigeration, 6 months at -4°F (-20°C)



How the Pfizer-BioNTech Vaccine Works



How some of COVID-19 vaccines compare

	Pfizer/BioNTech	Moderna	AstraZeneca/Oxford
Technology	mRNA	mRNA	Adenoviral vector
Efficacy	95%	95%	62% to 90%
Storage temperature	-94° F	-4° F	36° to 46° F
Shelf-life	5 days	1 month	6 months
Price per dose	$19.50	$32 to $37	$3 to $4
For profit?	Yes	Yes	After pandemic ends
Doses by end of 2020	50 million	20 million	200 million

Sources: American Council on Science and Health (ACSH.org), multiple news outlets

Challenges Associated With Vaccine Production for COVID-19

- ✓ Accelerating vaccine development by combining phases involves trials being done on smaller groups.
- ✓ In the past, platforms based on nucleic acids such as DNA and RNA have not resulted in a successful vaccine for human diseases.
- ✓ Pre-existing immunity to adenoviruses is a concern, particularly for those vaccine candidates utilizing human adenoviruses.
- ✓ Rapid large-scale manufacturing of vaccines still remains a challenge.
- ✓ Vaccine hesitance, identified as a major threat to global health by the WHO.
- ✓ There is a concern that some countries will want to secure the vaccine supply for their citizens.
- ✓ Mutations of the virus can result in vaccines having limited effectiveness against it.

Thanks For Your Attention

پروژه‌های فعال واکسن کرونای ایرانی

ردیف	مؤسسه یا شرکت	نوع واکسن مبتنی بر	فاز	مشابه واکسن کرونای خارجی
۱	ستاد اجرایی فرمان امام خمینی (ره)؛ مؤسسه برکت	ویروس کشته شده یا غیرفعال «Inactivated »	مرحله اول کارآزمایی بالینی	واکسن آکسفورد / استروزنیکا سینوواک اسپوتنیک
			در حال اخذ مجوز بالینی	-
		«DNA »	-	-
		«Subunit »	-	-
		mRNA	اتمام فاز حیوانی	واکسن فایزر / مدرنا
		سلول بنیادی	اتمام فاز حیوانی	-
۲	موسسه واکسن سازی رازی	پروتئین نوترکیب	در حال اخذ مجوز بالینی	واکسن نواوکس
۳	شرکت دانش بنیان	mRNA	در حال اخذ مجوز بالینی	فایزر / مدرنا
۴	انستیتو پاستور ایران	پروتئین نوترکیب	فاز ۳ کارآزمایی بالینی مشترک با کوبا از بهمن ماه	واکسن نواوکس
۵	شرکت دانش بنیان	«آدنو ویروس» ناقل ویروسی غیر تکثیر شونده	فاز حیوانی	از نظر نوع ویروس چین و روسیه؛ از لحاظ تکنولوژی شبیه این دو و آسترازنکا و جانسون
۶	شرکت دانش بنیان- وزارت دفاع	ویروس غیرفعال	بررسی برای اخذ مجوز بالینی	واکسن آکسفورد / استروزنیکا سینوواک اسپوتنیک
۷	شرکت دانش بنیان	ویروس غیرفعال	فاز حیوانی	واکسن آکسفورد / استروزنیکا سینوواک اسپوتنیک
۸	دانشگاه علوم پزشکی بقیه الله (عج)	پروتئین نوترکیب	فاز حیوانی	واکسن نواوکس

Leading vaccines

Developer	How It Works	Phase	Status
Pfizer-BioNTech	mRNA	2 3	Approved in Saudi Arabia, Bahrain, Switzerland. Emergency use in U.S., E.U., other countries.
Moderna	mRNA	3	Emergency use in U.S., U.K., E.U., other countries.
Gamaleya	Ad26, Ad5	3	Early use in Russia. Emergency use in other countries.
Oxford-AstraZeneca	ChAdOx1	2 3	Emergency use in Britain, India, other countries.
CanSino	Ad5	3	Limited use in China.
Johnson & Johnson	Ad26	3	
Vector Institute	Protein	3	Early use in Russia.
Novavax	Protein	3	
Sinopharm	Inactivated	3	Approved in China, U.A.E., Bahrain. Emergency use in Egypt, Jordan.
Sinovac	Inactivated	3	Emergency use in China, Brazil, other countries.
Sinopharm-Wuhan	Inactivated	3	Limited use in China, U.A.E.
Bharat Biotech	Inactivated	3	Emergency use in India.

Coronavirus Vaccine Tracker

New additions and recent updates	
Dec. 31	The W.H.O. gives emergency validation to the Pfizer-BioNTech vaccine.
Dec. 30	China approves the Sinopharm vaccine.
Dec. 30	Britain authorizes the Oxford-AstraZeneca vaccine for emergency use.
Dec. 30	Sinopharm announces an efficacy rate of 79 percent.
Dec. 28	Novavax begins a Phase 3 trial in the United States.
Dec. 27	Kazakhstan moves to Phase 3.
Dec. 24	Iran enters Phase 1.
Dec. 23	Canada approves the Moderna vaccine.
Dec. 22	Maryland-based Altimmune enters Phase 1.
Dec. 21	The European Union authorizes the Pfizer-BioNTech vaccine.
Dec. 19	Kazakhstan moves to Phase 2.
Dec. 18	The F.D.A. authorizes Moderna's vaccine for emergency use.
Dec. 18	Cuba's Soberana 2 vaccine moves to Phase 2.
Dec. 17	Japan's Shionogi launches a Phase 1/2 trial.
Dec. 17	South Korea's GeneOne enters Phase 1/2.

New additions and recent updates	
Jan. 6	Brazil estimates the efficacy of Sinovac's vaccine.
Jan. 6	The European Union authorizes Moderna's vaccine.
Jan. 4	Israel authorizes Moderna's vaccine.
Jan. 4	Taiwan's Medigen moves to Phase 2.
Jan. 3	India authorizes a vaccine from Bharat Biotech.
Jan. 4	Mexico authorizes the Oxford-AstraZeneca vaccine.
Jan. 3	India and Argentina authorize the Oxford-AstraZeneca vaccine.
Jan. 3	India's Zydus Cadila moves to Phase 3.
Dec. 31	The W.H.O. gives emergency validation to the Pfizer-BioNTech vaccine.
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Detection Antibodies and Serological Tests for SARS-CoV-2