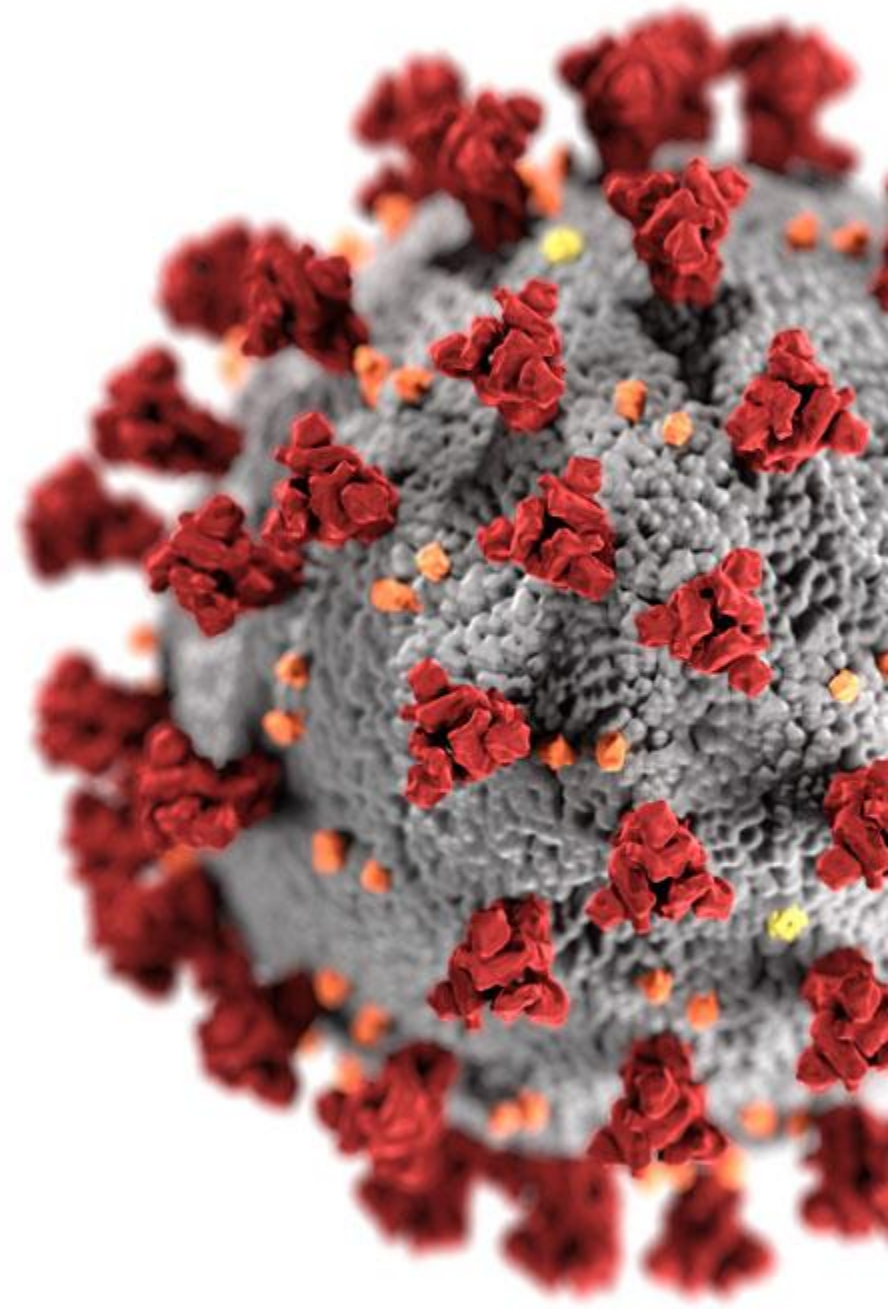


# Coronavirus SARS-CoV-2

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Medicinski fakultet Univerziteta u Beogradu

Mart 2020.



**COVID-19**, engl. Corona virus disease 2019

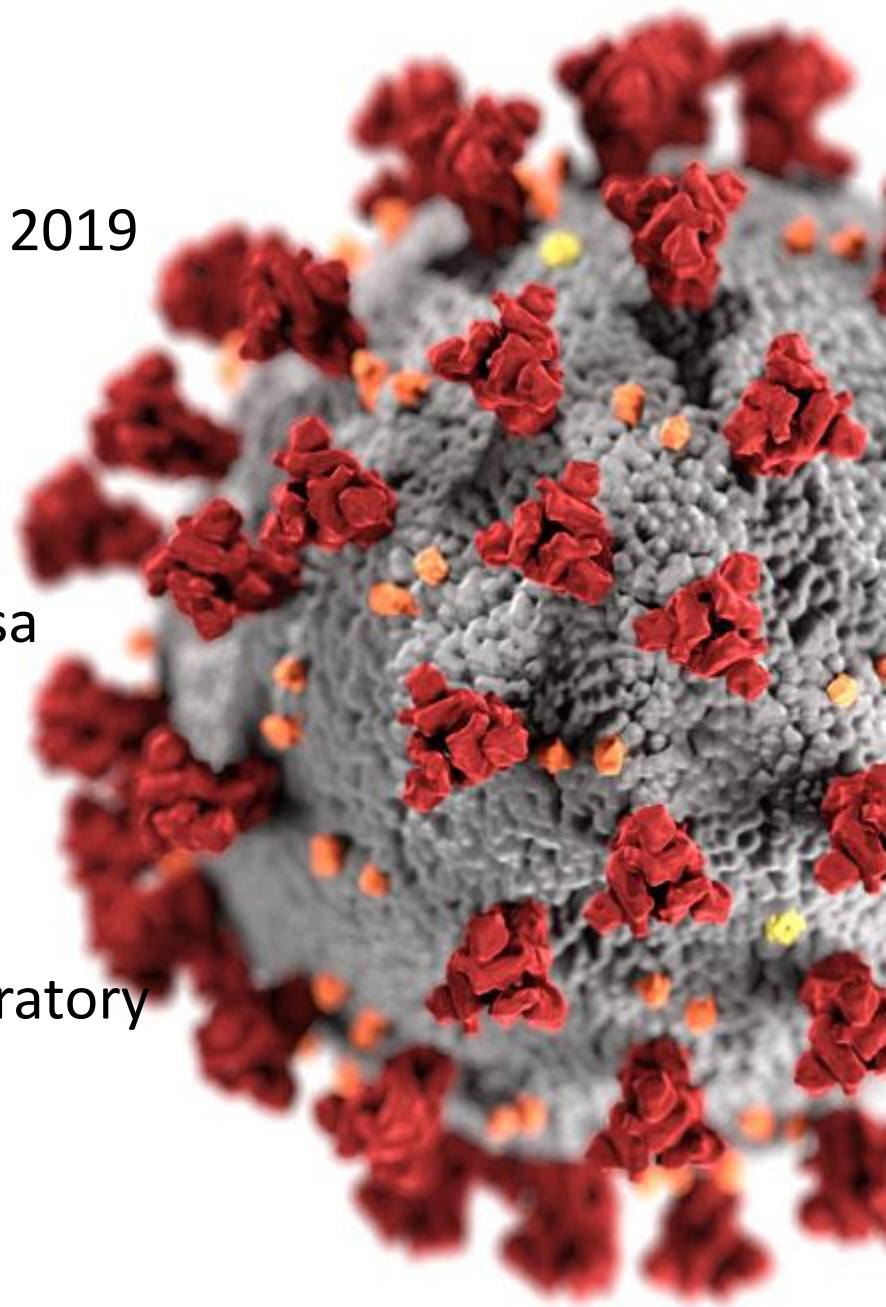
koju izaziva SARS-CoV-2

**CoV**, Koronavirusi, Porodica RNK virusa

koja inficira životinje i ljude

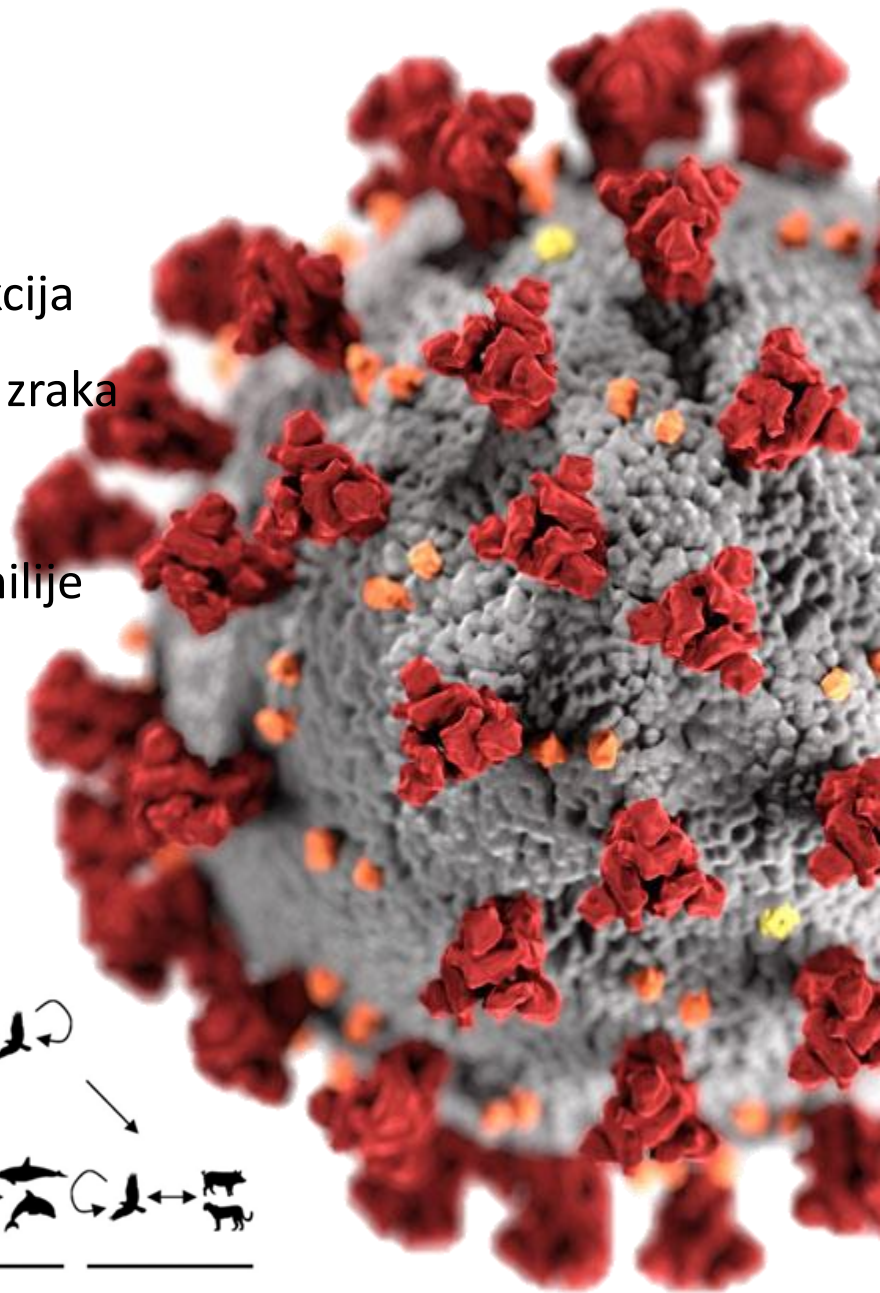
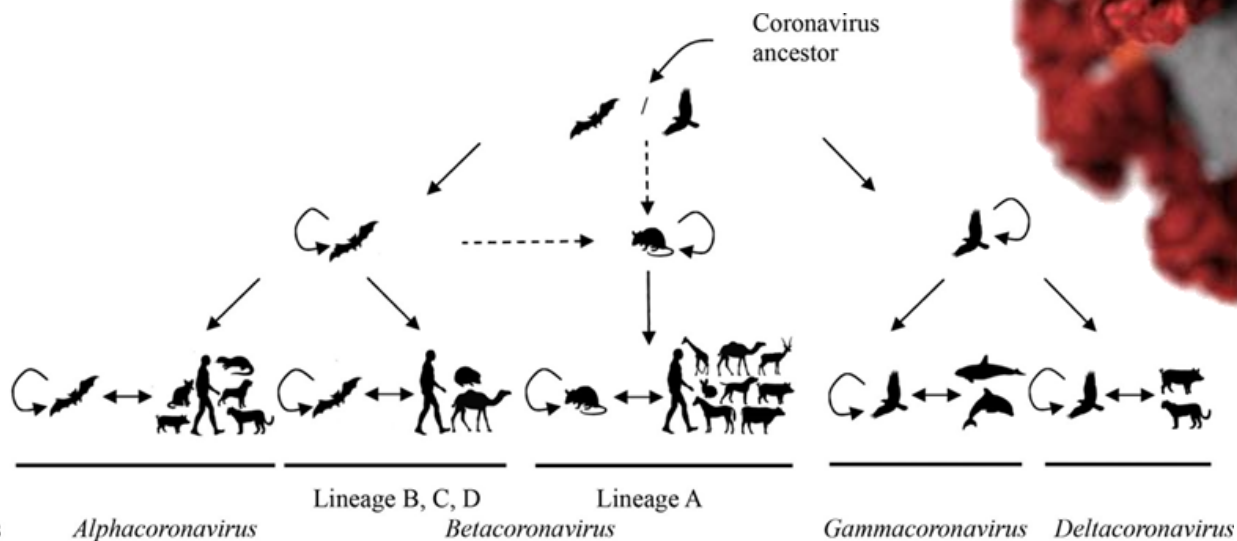
**SARS-CoV-2**, engl. Severe acute respiratory

syndrome coronavirus 2



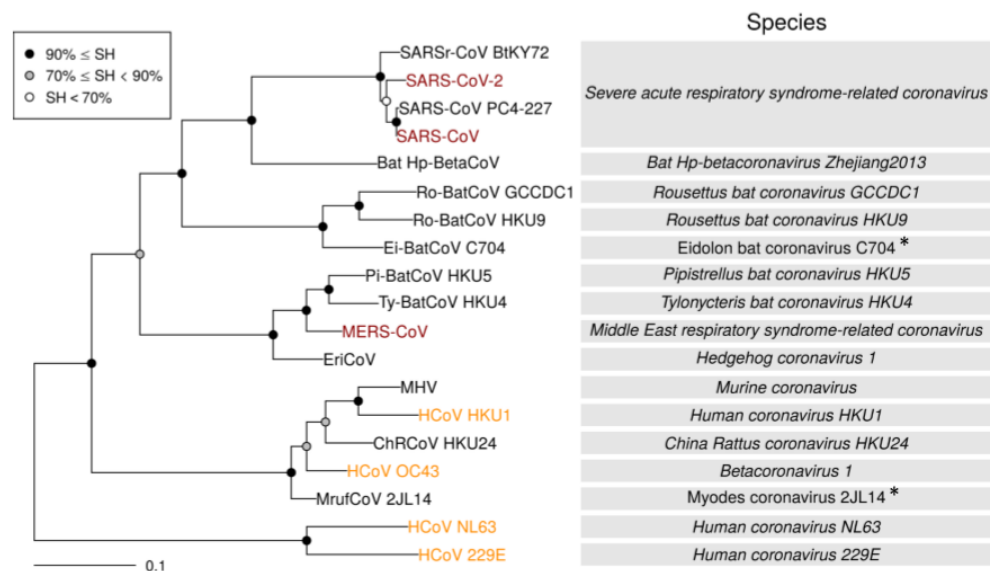
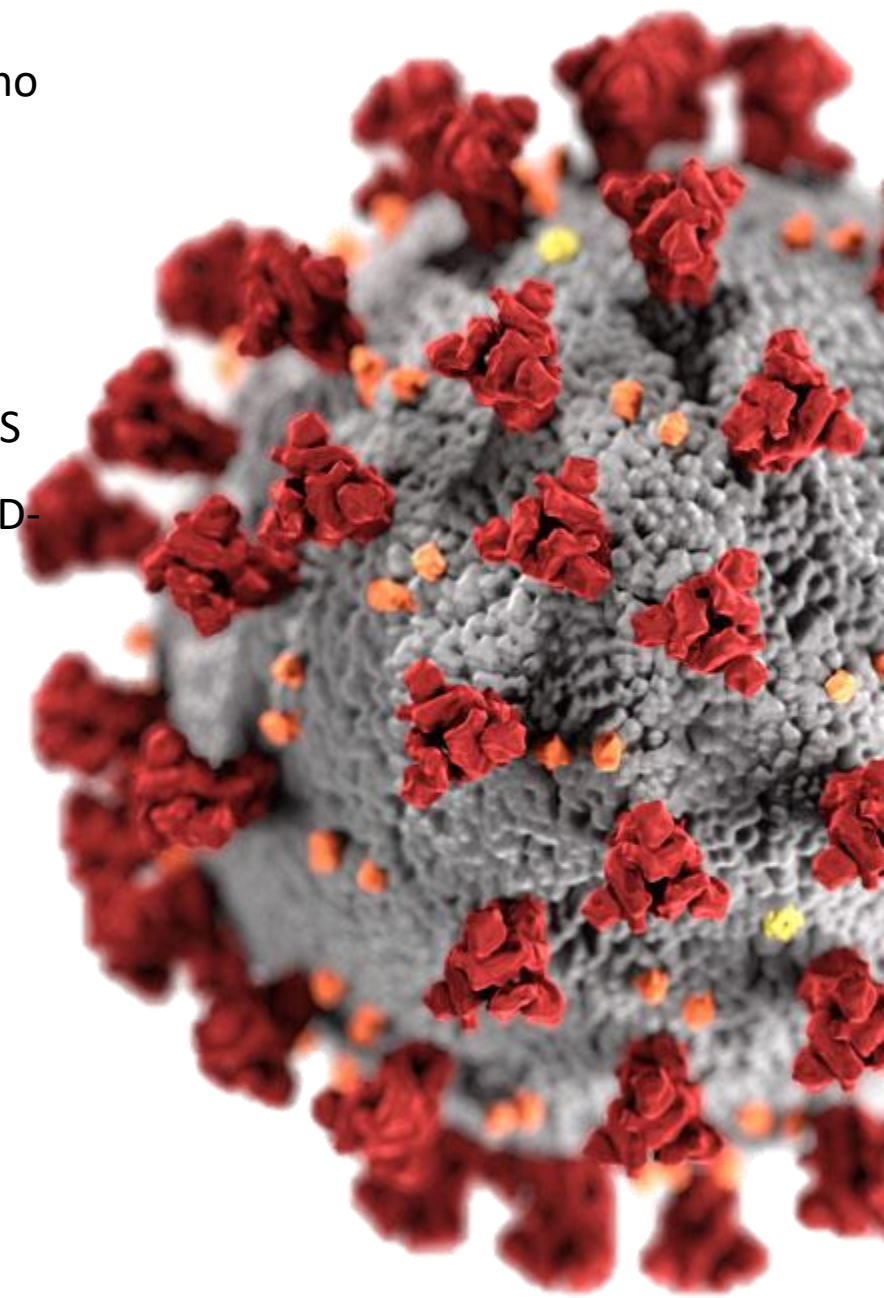
# Koronavirusi

- ✓ Lat. „corona“, karakteristični venac projekcija na površini, nalik vencu (koroni) sunčevih zraka
- ✓ Uglavnom izazivači zoonoza
- ✓ Familija *Coronaviridae* obuhvata 2 potfamilije od kojih se *Coronavirinae* dalje klasifikuju na 4 roda.





- ✓ **Sedam** virusa, uključujući i SARS-CoV-2, povezano je sa humanim infekcijama.
- ✓ **Četiri** su izazivači sezonskog sindroma **prehlade**.
- ✓ **Tri** su izazivači **pretećih virusnih oboljenja**: SARS (engl. severe acute respiratory syndrome), MERS (engl. Middle East respiratory syndrome) i COVID-19 (engl. Corona virus disease-19).



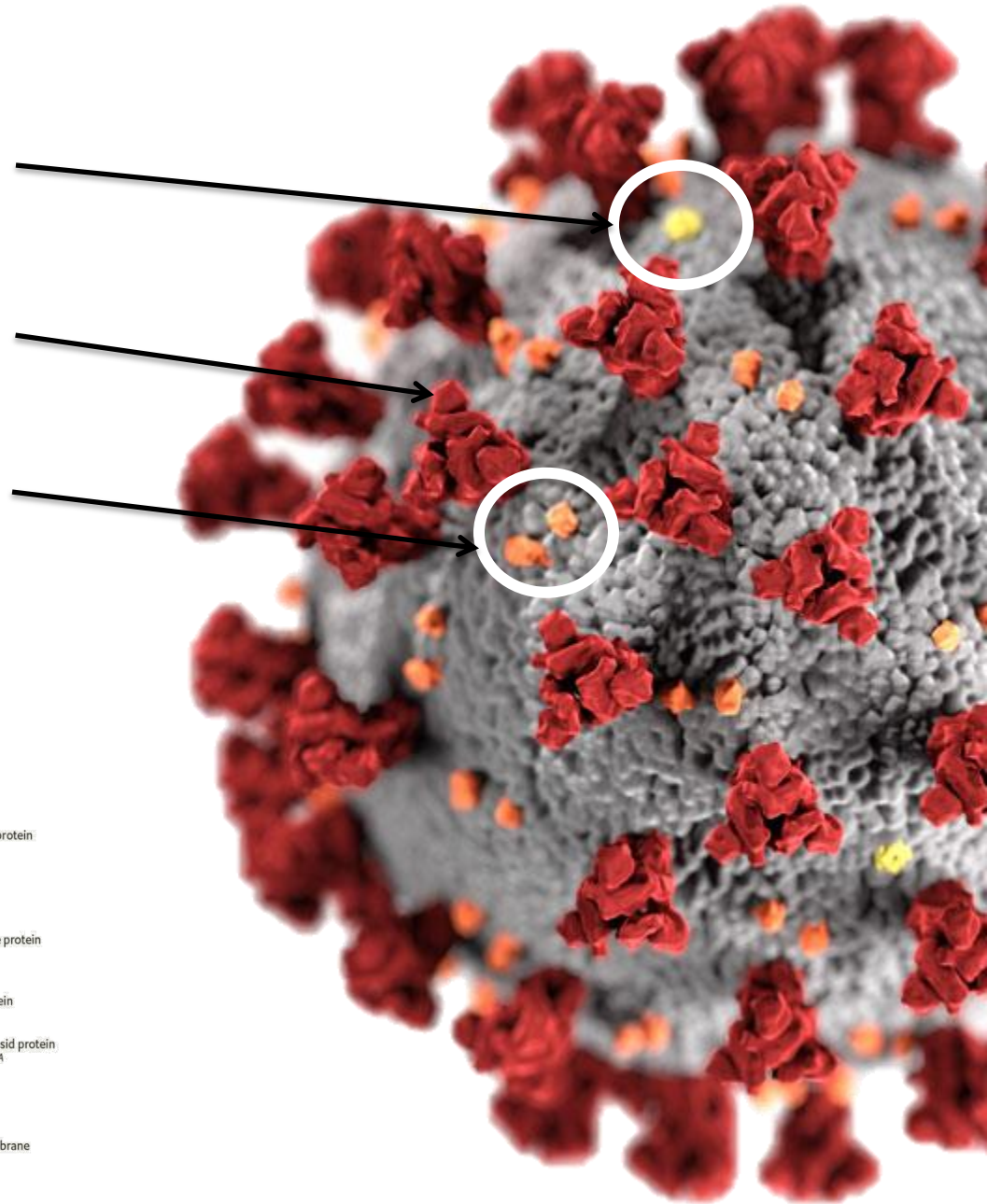
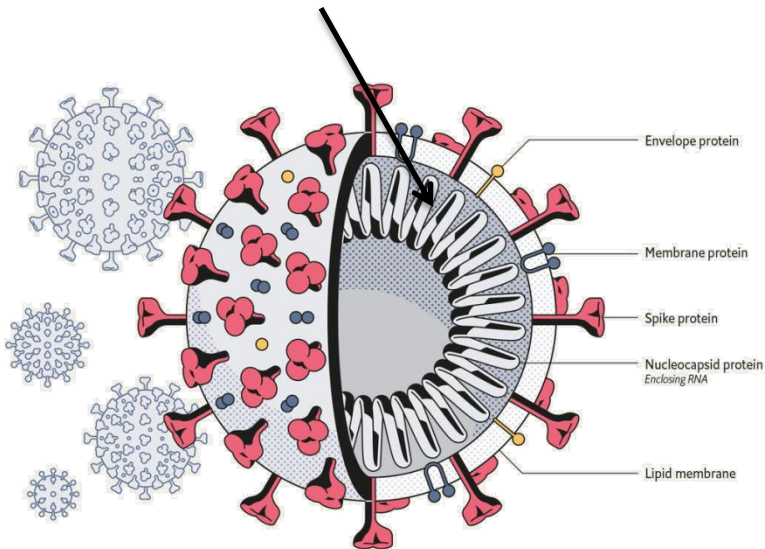
# Koronavirusi, struktura

E (engl. envelope) protein

S (engl. spike) protein

M (engl. membrane) protein

Jednolančana pozitivna RNK





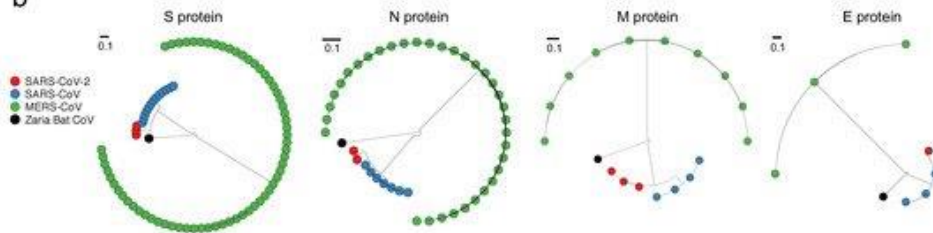
# Istraživanja koja su poredila SARS-CoV-2 sa virusima SARS i MERS

a

Percentage sequence identity with SARS-CoV-2

	S protein	N protein	M protein	E protein
SARS-CoV	76.0%	90.6%	90.1%	94.7%
MERS-CoV	29.4%	45.9%	39.2%	34.1%

b



Ahmed, S.F.; Quadeer, A.A.; McKay, M.R. Preliminary Identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies. *Viruses* 2020, 12, 254.

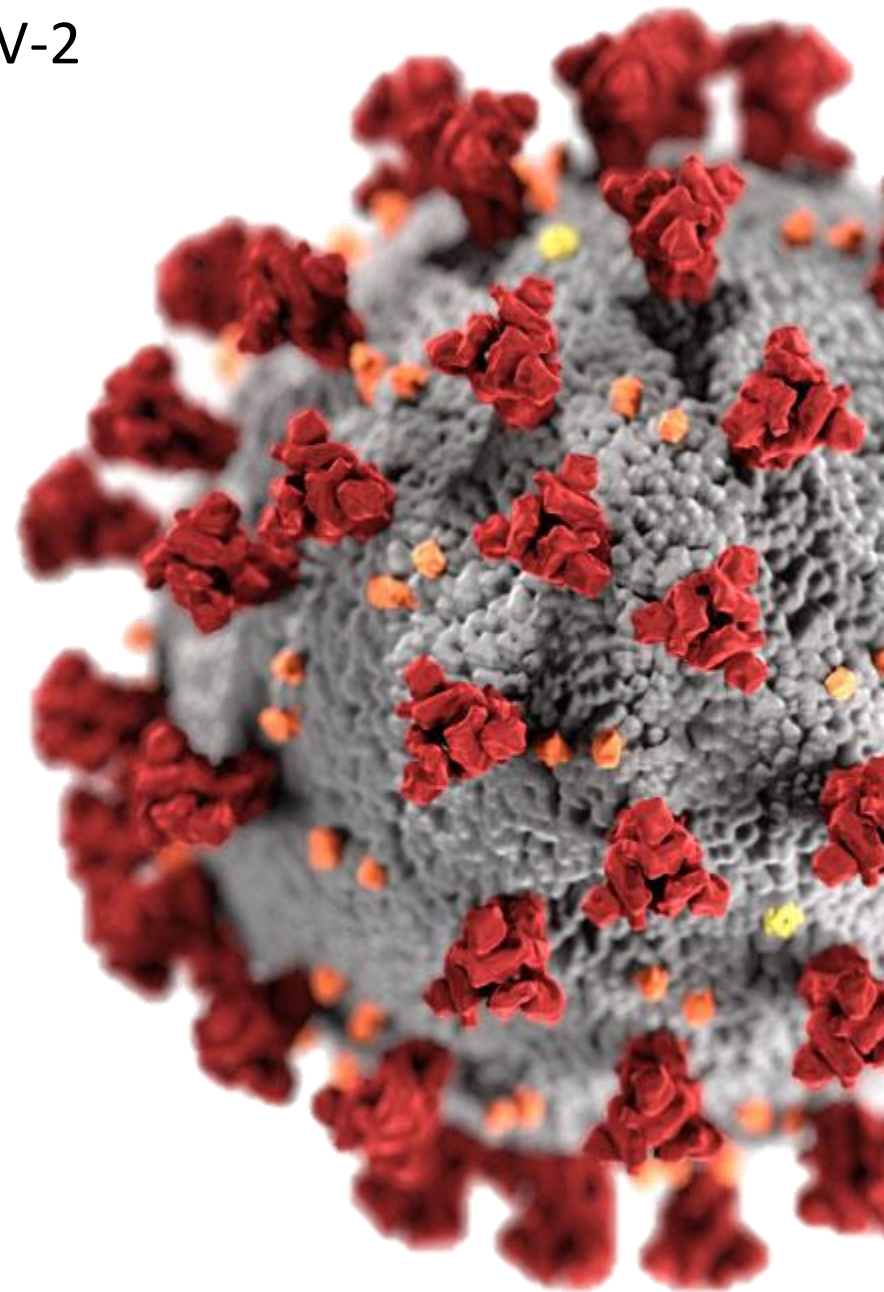
Za inficiranje prvih 1000 ljudi  
 MERS-u su bila potrebna 903 dana, tj. 2.5 godine



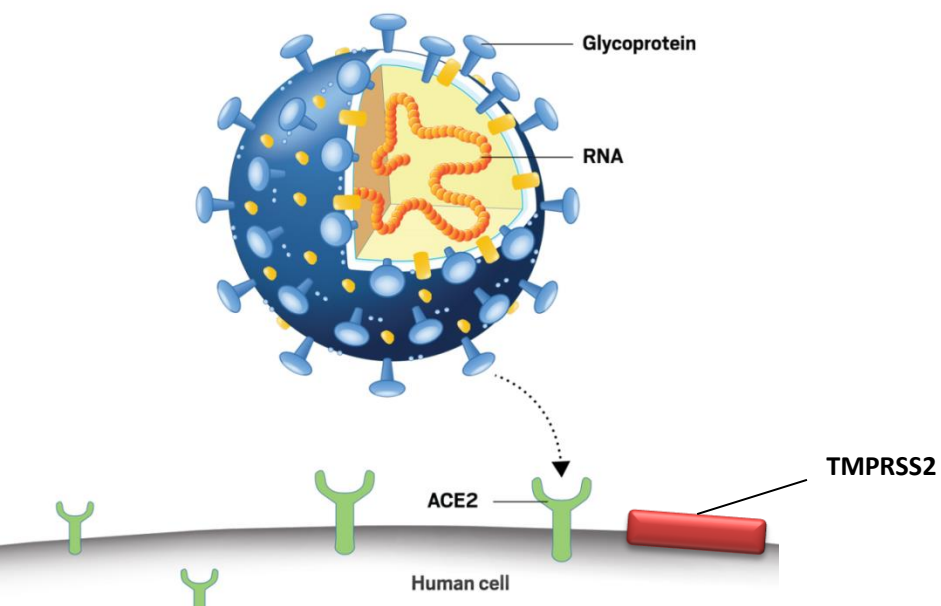
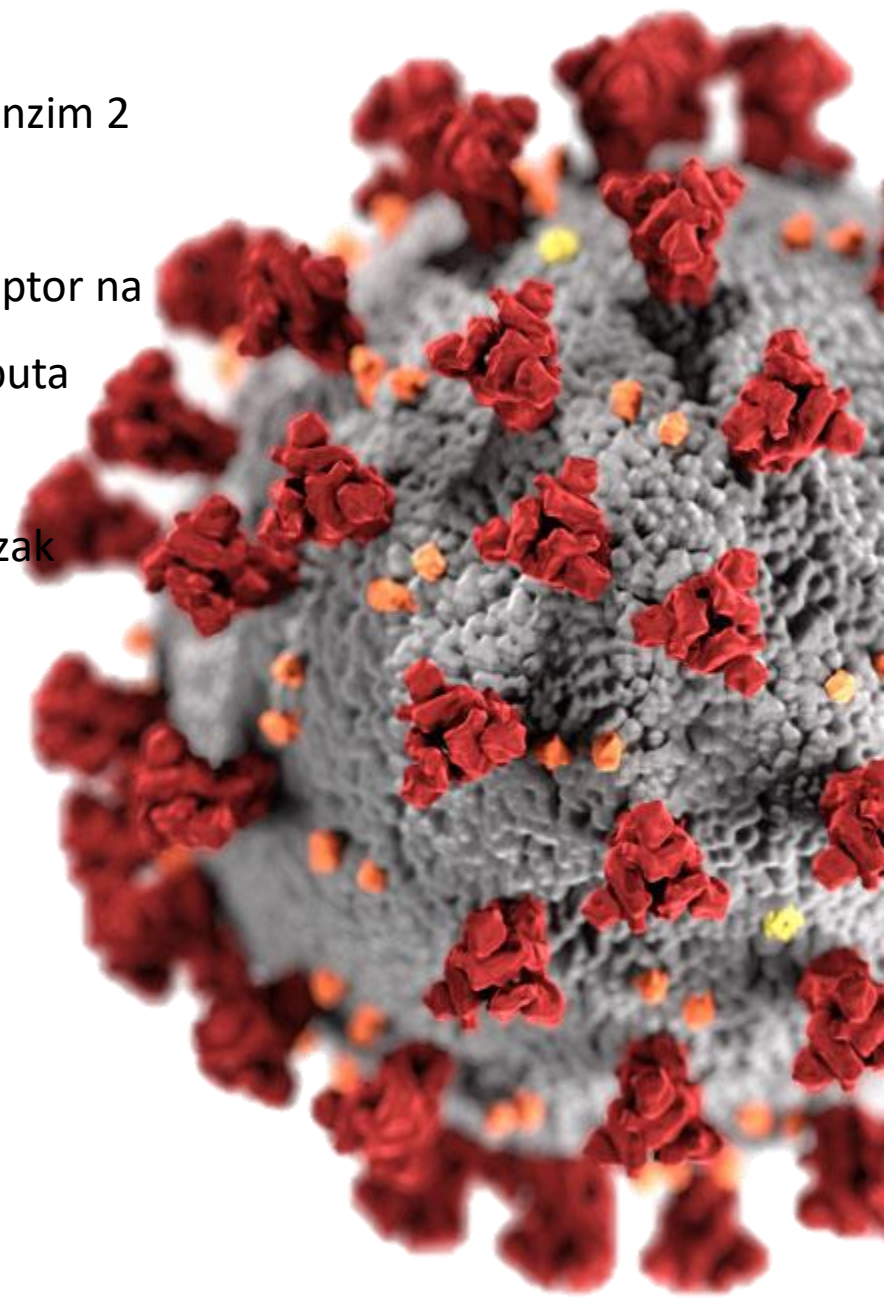
SARS-u je bilo potrebno 130 dana



SARS-CoV-2 je bilo potrebno 48 dana

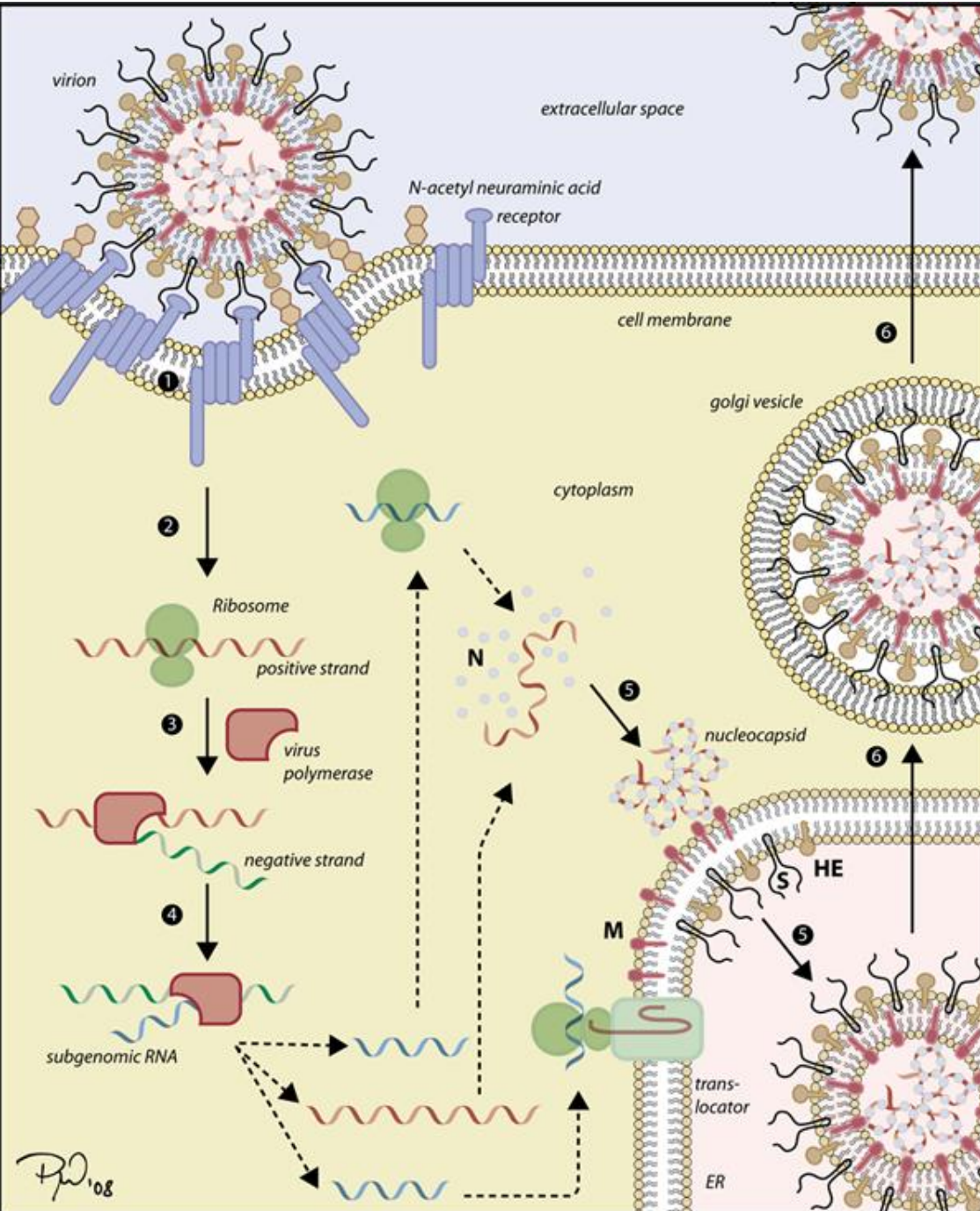


- ✓ Humani receptor: Angiotenzin-konvertujući enzim 2 (**ACE2**),
- ✓ S protein SARS-CoV-2 virusa vezuje se za receptor na isti način kao i SARS, ali potencijalno i do 10 puta jače nego S protein SARS-a,
- ✓ Enzim **TMPRSS2**, serin proteaza, pomaže ulazak viriona u ćeliju domaćina.





## REPLIKACIJA



**1** With their S-protein, coronaviruses bind on cell surface molecules such as the metalloprotease »amino-peptidase N«. Viruses, which accessorily have the HE-protein, can also bind on N-acetyl neuraminic acid that serves as a co-receptor.

**2** So far, it is not clear whether the virus get into the host cell by fusion of viral and cell membrane or by receptor mediated endocytosis in that the virus is in-corporated via an endosome, which is subsequently acidified by proton pumps. In that case, the virus have to escape destruction and transport to the lysosome.

**3** Since coronaviruses have a single positive stranded RNA genome, they can directly produce their proteins and new genomes in the cytoplasm. At first, the virus synthesize its RNA polymerase that only recognizes and produces viral RNAs. This enzyme synthesize the minus strand using the positive strand as template.

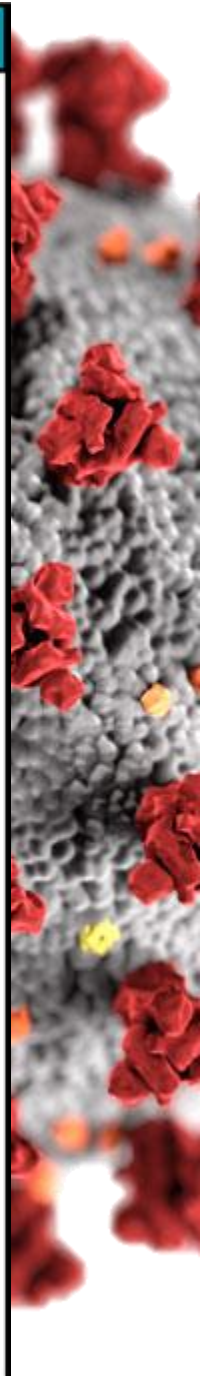
**4** Subsequently, this negative strand serves as template to transcribe smaller subgenomic positive RNAs which are used to synthesize all other proteins. Furthermore, this negative strand serves for replication of new positive stranded RNA genomes.

**5** The protein N binds genomic RNA and the protein M is integrated into the membrane of the endoplasmic reticulum (ER) like the envelope proteins S and HE. After binding, assembled nucleocapsids with helical twisted RNA budd into the ER lumen and are encased with its membrane.

**6** These viral progeny are finally transported by golgi vesicles to the cell membrane and are exocytosed into the extracellular space.

*Not drawn to scale! Not all cellular compartments and enzymes are shown. Colors: positive strand RNA (red), negative strand RNA (green), subgenomic RNAs (blue).*

*Based on: Lai MM, Cavanagh D (1997). The molecular biology of coronavirus. Adv. Virus Res (48) 1-100.*





„Sve što se desi dva puta, sigurno će se desiti i treći put “,

Paulo Koeljo.

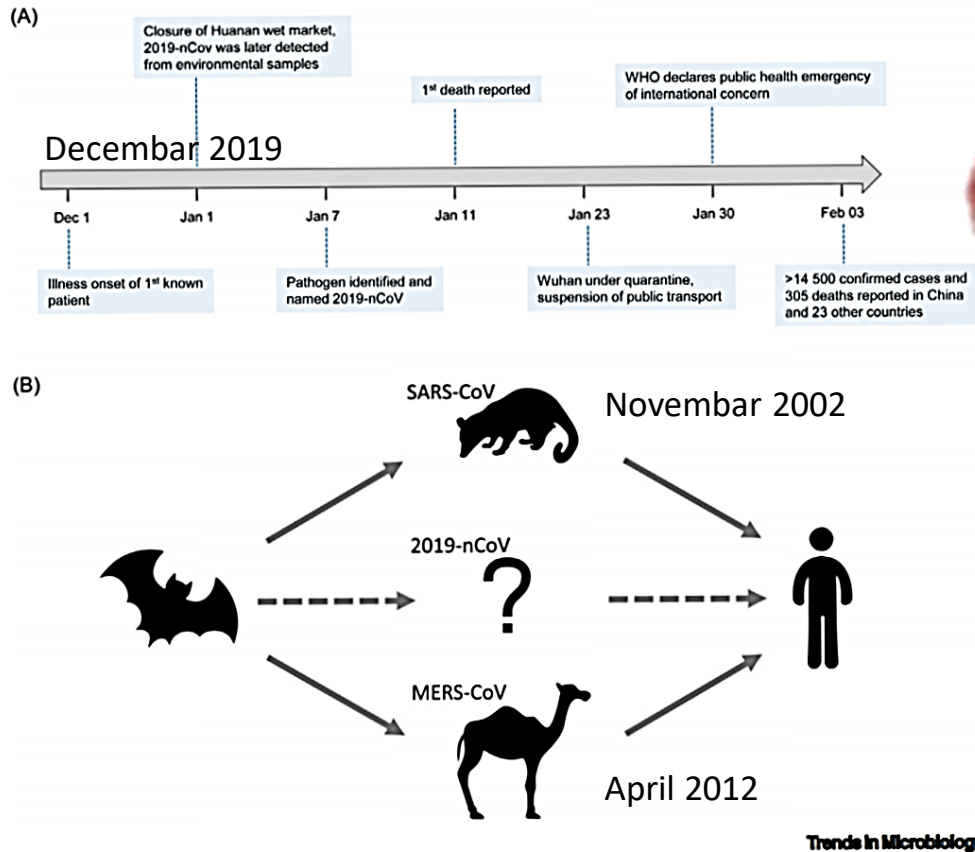
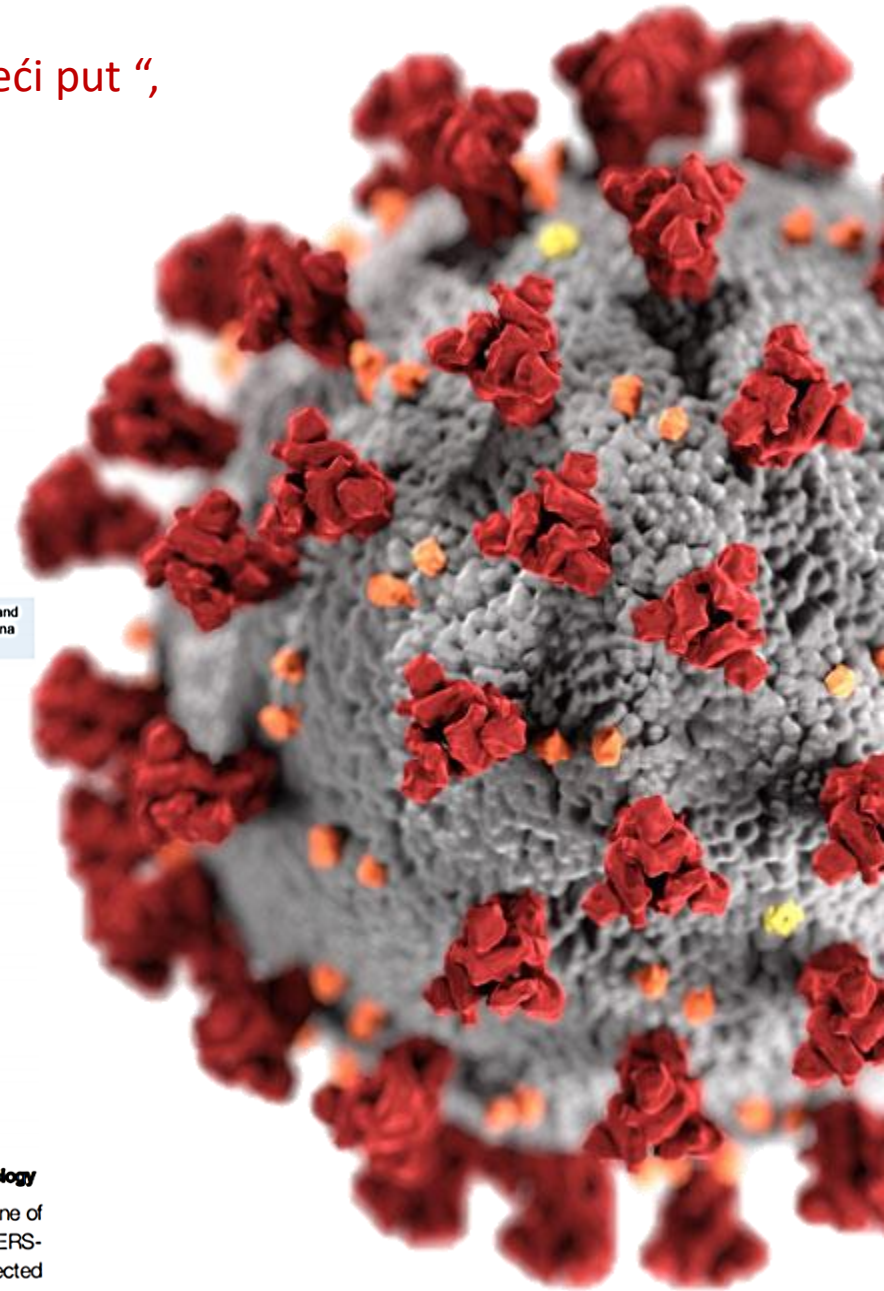


Figure 1. The Possible Interspecies Transmission Route and Timeline of 2019-nCoV. (A) Timeline of major events in the 2019-nCoV outbreak. (B) Potential interspecies transmission routes of SARS-CoV, MERS-CoV, and 2019-nCoV. The question mark and broken line denote unknown intermediate host and suspected transmission.



# Koronavirusi: od životinja do ljudi

Researchers aren't sure how the novel coronavirus first infected people in China, but the viruses that cause SARS and MERS, which originated in bats, provide clues.

1

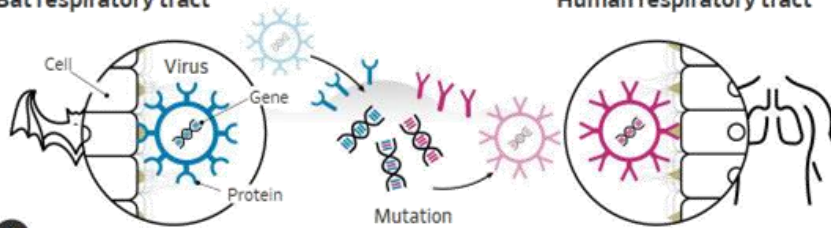
Proteins on the outer shell of the virus allow it to latch onto cells in the host's respiratory tract. The proteins' shapes are determined by the virus's genes.

2

To infect new hosts, the virus's genes undergo mutations that alter its surface proteins, allowing them to latch onto the cells of new species.

## Bat respiratory tract

## Human respiratory tract



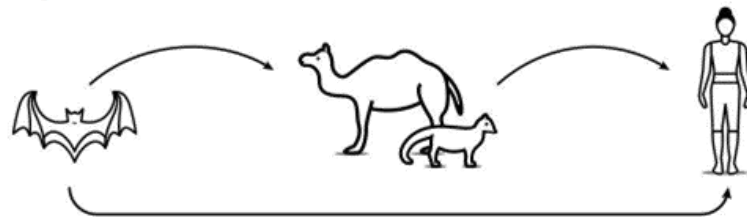
3

In the case of SARS, the virus jumped from bats to civet cats before gaining the ability to infect humans. In the case of MERS, camels served as the intermediate host.

## Original host

## Intermediate host

## Human

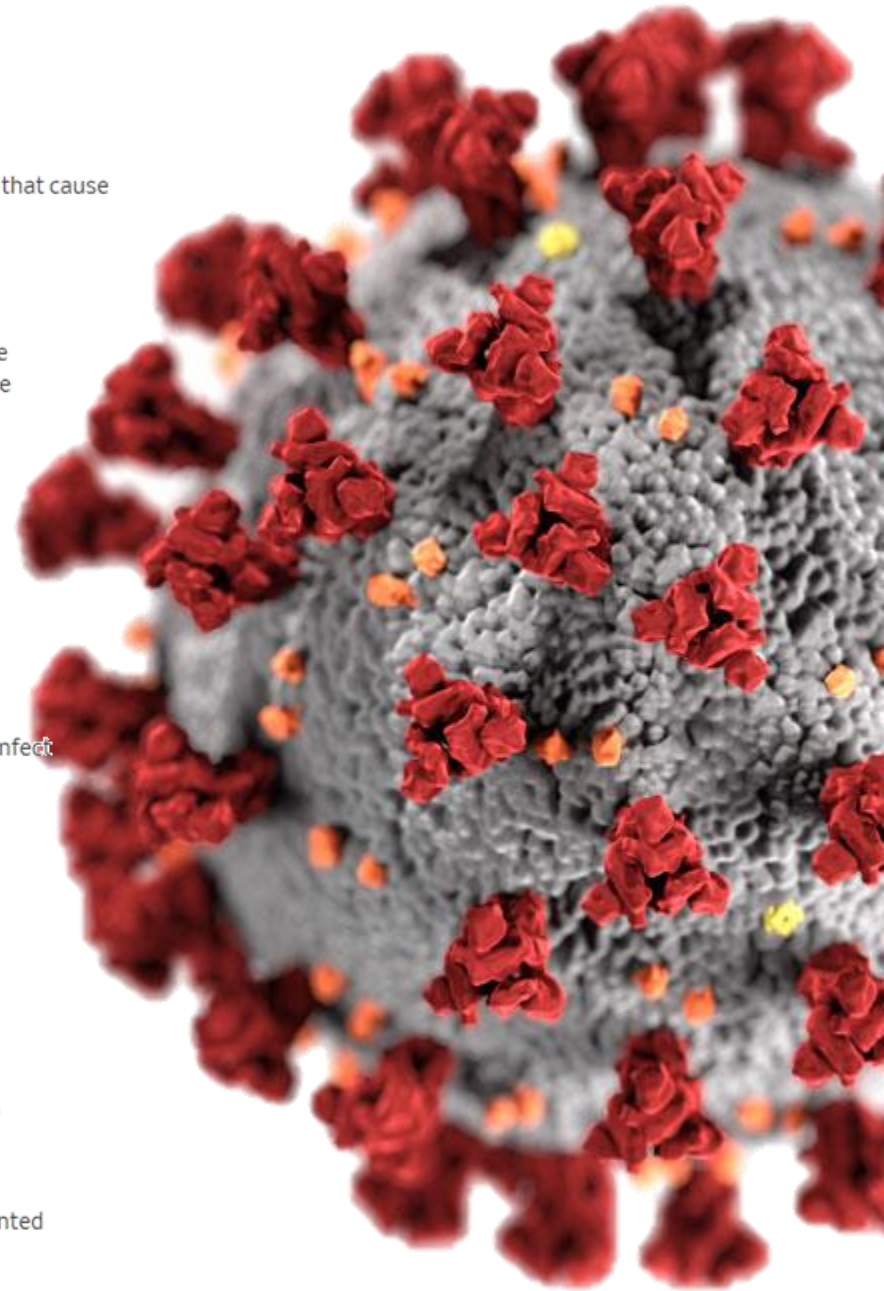


4

Coronaviruses can also jump directly to humans, without mutating or passing through an intermediate species.

5

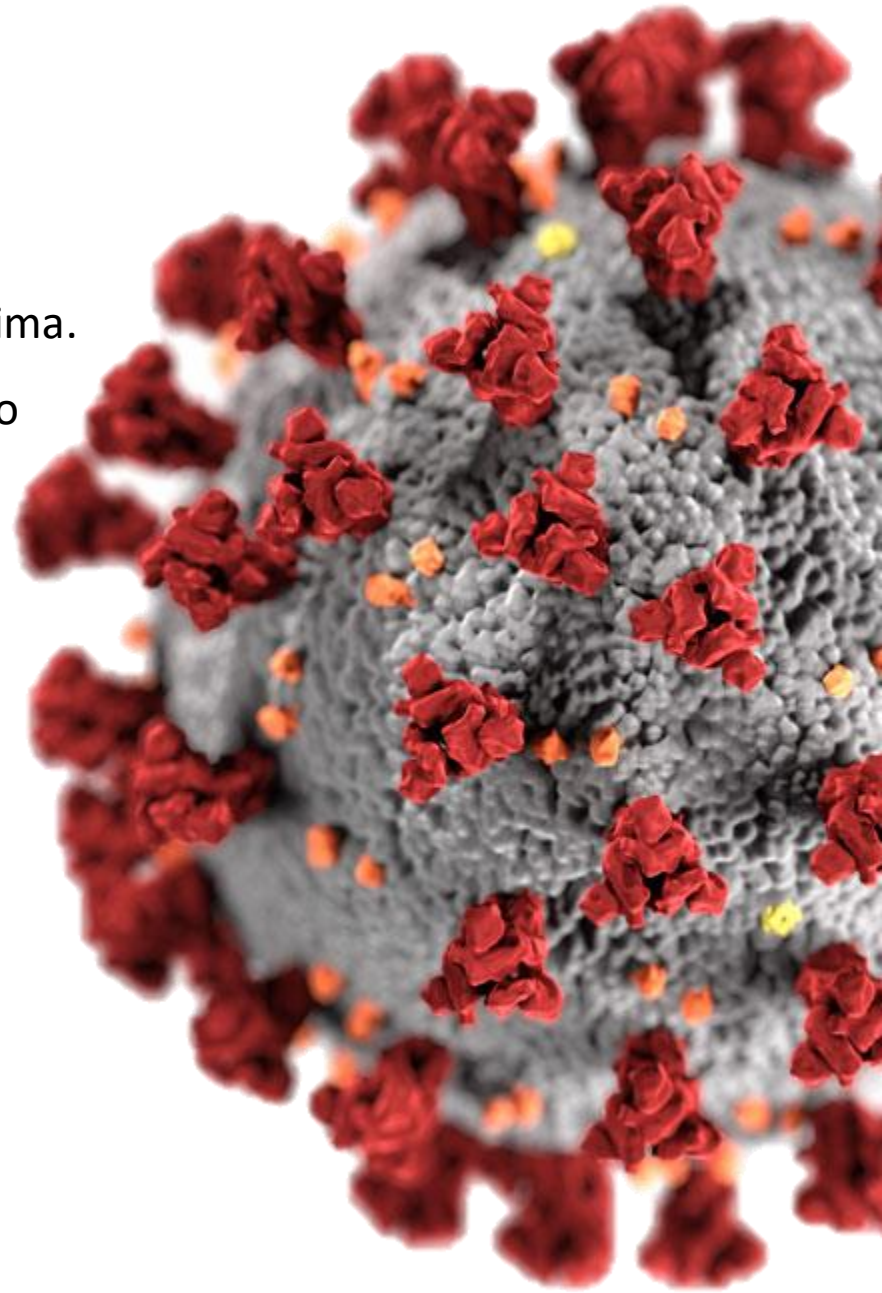
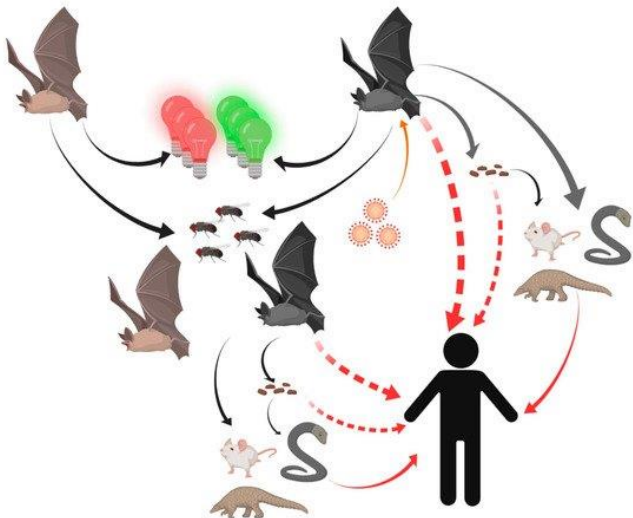
Researchers have found the novel coronavirus likely originated in bats, but haven't pinpointed the source of transmission to humans.





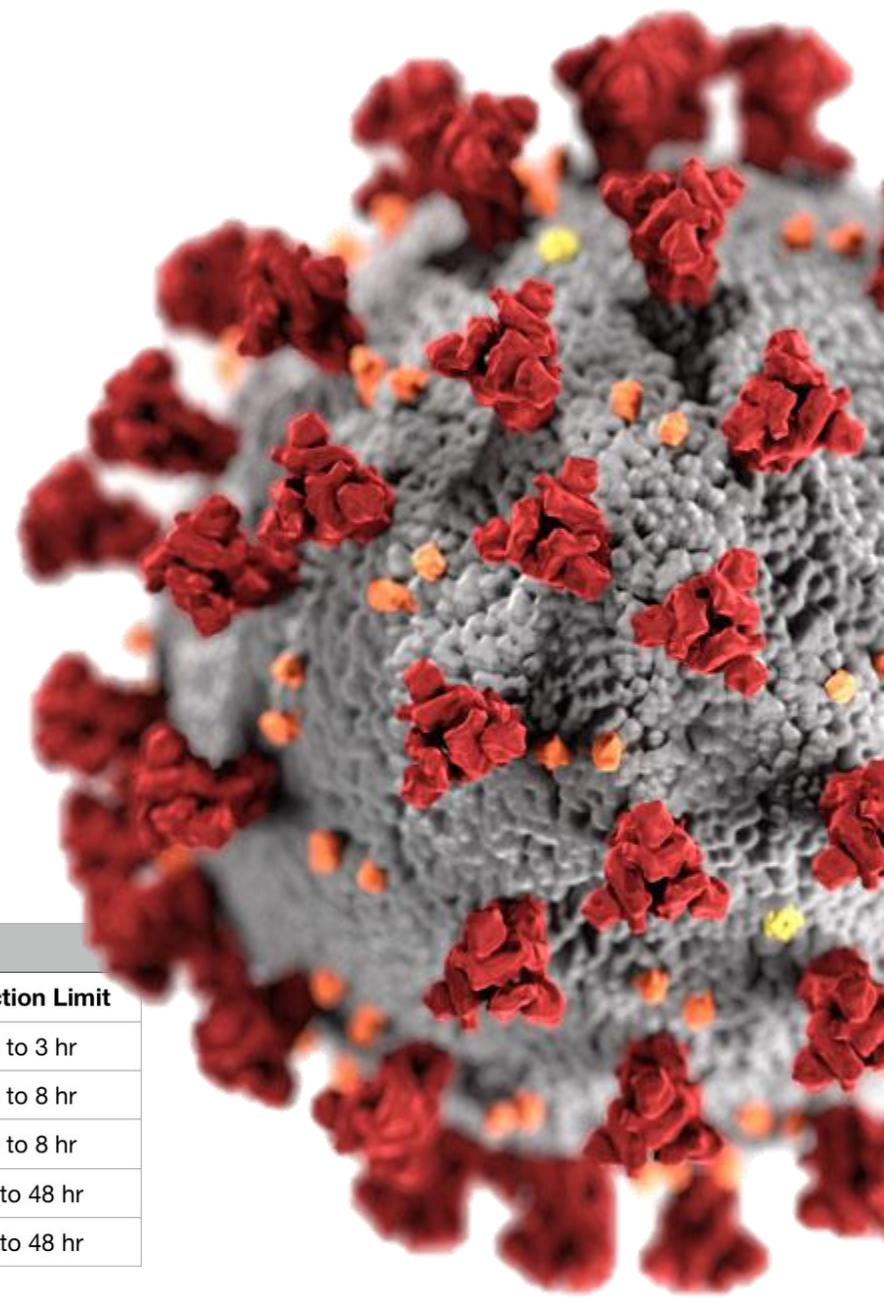
# SARS-CoV-2: od životinja do ljudi

- ✓ Slepí miševi, rezervoari SARS-CoV-2 privučeni zelenim/crvenim svetlom u regije bogate insektima.
- ✓ Prenos na humanog domaćina: direktno ili preko intermedijernih domaćina (pacova, zmija i ljuskavaca), tj. njihovih sekreta i ekskreta.
- ✓ Huanan pijaca, Vuhan, Kina



# Otpornost SARS-CoV-2

- ✓ Aerosol do 3 sata.
- ✓ Bakar do 4 sata.
- ✓ Karton do 24 sata.
- ✓ Plastika i nerđajući čelik do 2-3 dana.

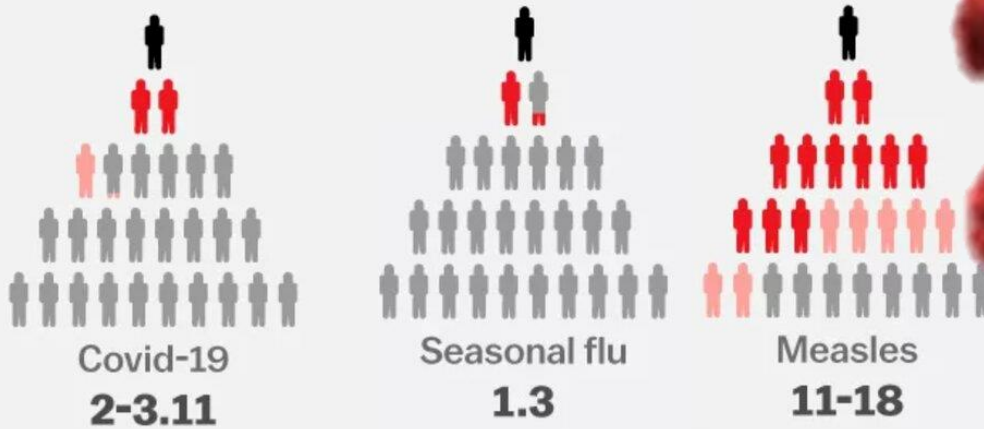


Stability of Infectious Virus

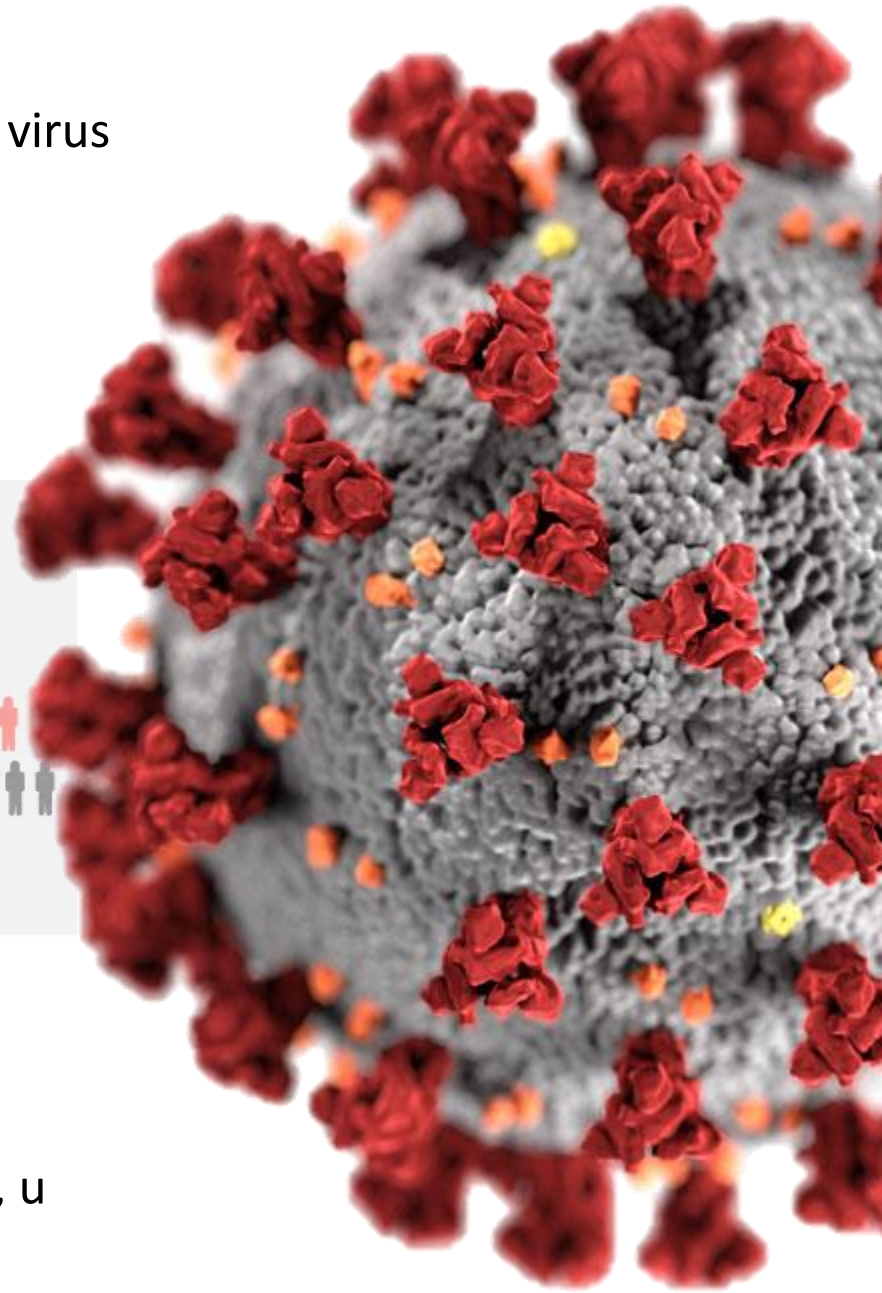
	SARS-CoV-2		SARS-CoV-1	
	Half Life, Hours	Detection Limit	Half Life, Hours	Detection Limit
Aerosol	2.74	Up to 3 hr	2.74	Up to 3 hr
Copper	3.4	Up to 4 hr	3.76	Up to 8 hr
Cardboard	8.45	Up to 24 hr	1.74	Up to 8 hr
Steel	13.1	Up to 48 hr	9.77	Up to 48 hr
Plastic	15.9	Up to 72 hr	17.7	Up to 48 hr



- ✓ Svaka inficirana osoba može da prenese virus na prosečno 2.6 novih osoba (1.5-3.5).



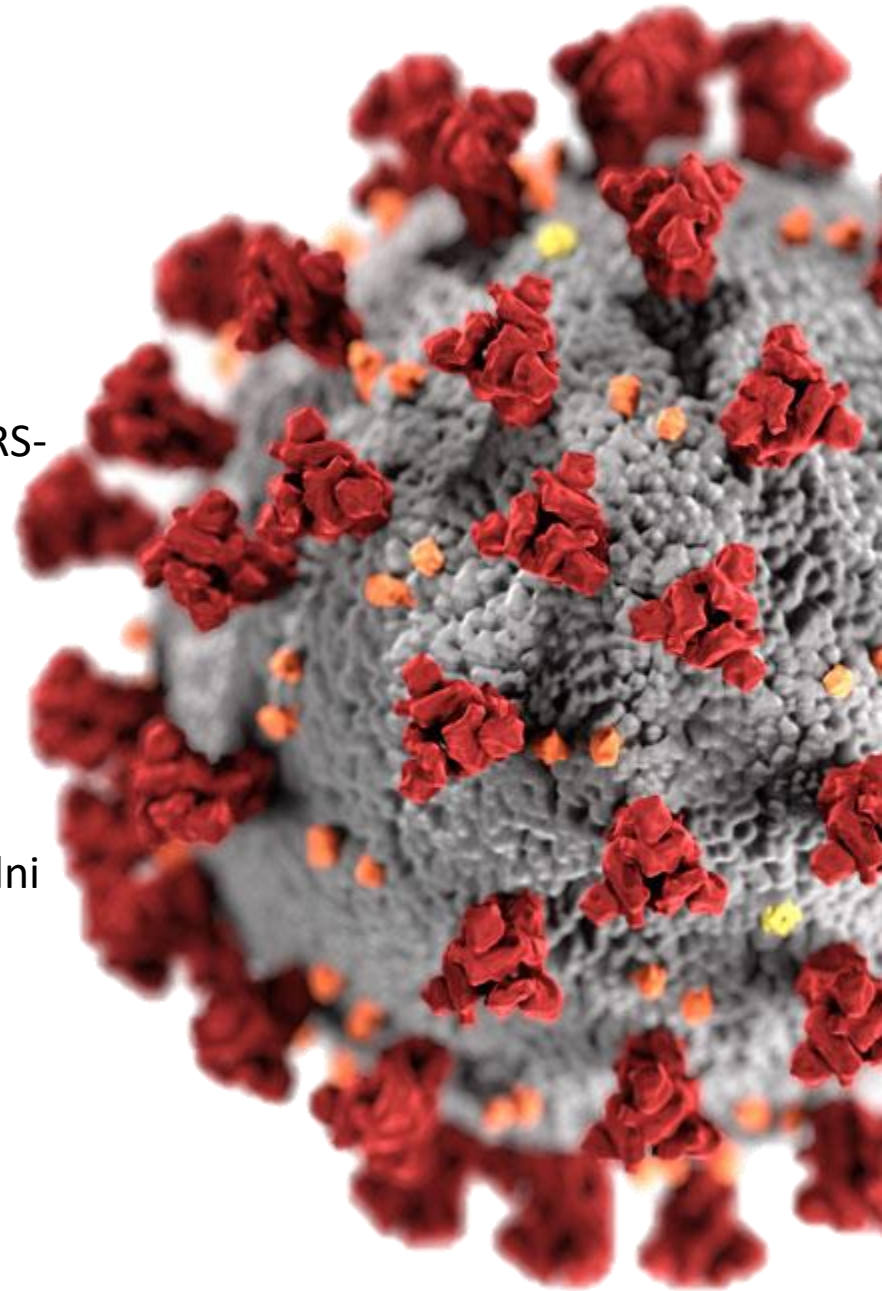
SOURCES: Travel Medicine, PLOS One, JAMA Pediatrics, MDPI, NCBI, New England Journal of Medicine, "The Spread and Control of Norovirus Outbreaks Among Hospitals in a Region"



- ✓ Inkubacioni period je između 1-14 dana, u proseku 5.2.

# Dijagnostički testovi

- ✓ PCR testovi sa reverznom transkriptazom.
- ✓ Specifično dizajnirani prajmeri i probe za SARS-CoV-2.
- ✓ Molekularno testiranje zahteva BSL-2 nivo zaštite.
- ✓ Testiranje iz različitih uzoraka, prema WHO najmanje iz: gornjih partija RT (nazofaringealni i orofaringealni bris) i/ili iz donjih partija RT (sputum i/ili endotrahealni aspirat ili bronhoalveolarni lavat).
- ✓ Virus se može dokazati i u stolici i u krvi.
- ✓ Serološki testovi su u razvoju.







Na dan 15.03.2020. godine,

SARS-CoV-2 je na globalnom nivou potvrđen  
kod **153 517** ljudi.

**5735** ljudi je umrlo od COVID-19.

Zahvaćene su **143** zemlje sveta, od kojih su  
najviše pogođene Kina, Italija, Španija, Iran i  
Južna Koreja.

