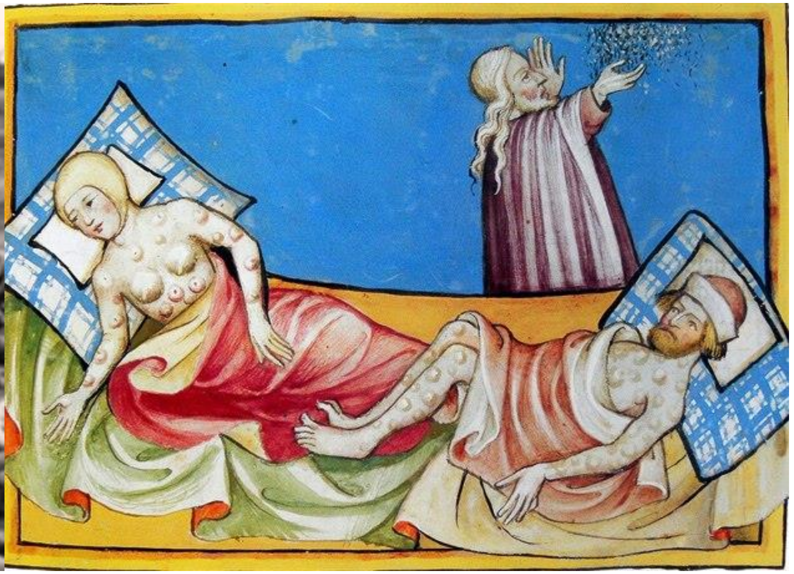
Vakcíny proti covid-19: farmakologické a biotechnologické aspekty, analýza vakcín a výsledky

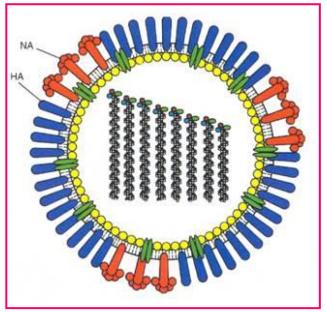
Jaroslav Turánek

Infekční choroby a vliv na společnost v historii lidstva

Flue, Typhus, Smallpox, Plague, Polio, Zika, Ebola, AIDS



Influenza Epidemic in Twentieth Century



high concentration of young people and migration in global scale

reservoir of pathogen – pig, horse, poultry, human (at present busines with exotic animals)

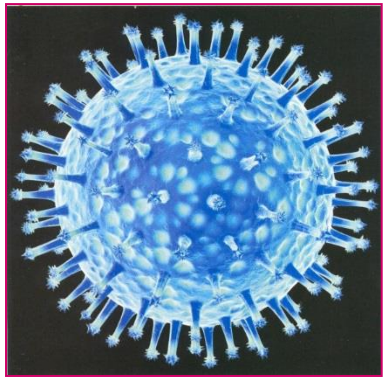
Fig. 1. The huge military camp and hospital base at Etaples.

Northern France (Fig. 1), during the winter of 1916. The base consisted, principally, of a huge reinforcement camp, through which British and other infantry passed to and from the front; plus a dozen or so base hospitals, placed close together along the Northern fringes of the camp. The copious records kept by the Etaples medical and administrative staff permit an hour-by-hour examination of events throughout the war. Those records depict an immense traffic of young soldiers (more than one million of them by September 1917) moving up towards the front; in the hospitals, sick and wounded men

stress factors – war, military and prisoner camps,

injured people in field lazarettes (immunosupressed patients)

Conditions for Influenza pandemy 1918-1919



Smallpox – great succes of immunotherapy

African swine fewer – problem of global market

Opičí neštovice – zavlečeny do amerických zverimexů z Afriky při importů afrických hlodavců

Zoonózy -Smrtící kontakty Jeden svět-Jedno zdraví

„ Nemůžeme se zabývat pouze zdravím volně žijících zvířat nebo lidským zdravím nebo zdravím zemědělských zvířat. Zdraví je jenom jedno – zdraví a vyváženost ekosystémů na celé planetě“

William Karesh, Wildlife Conservation Society

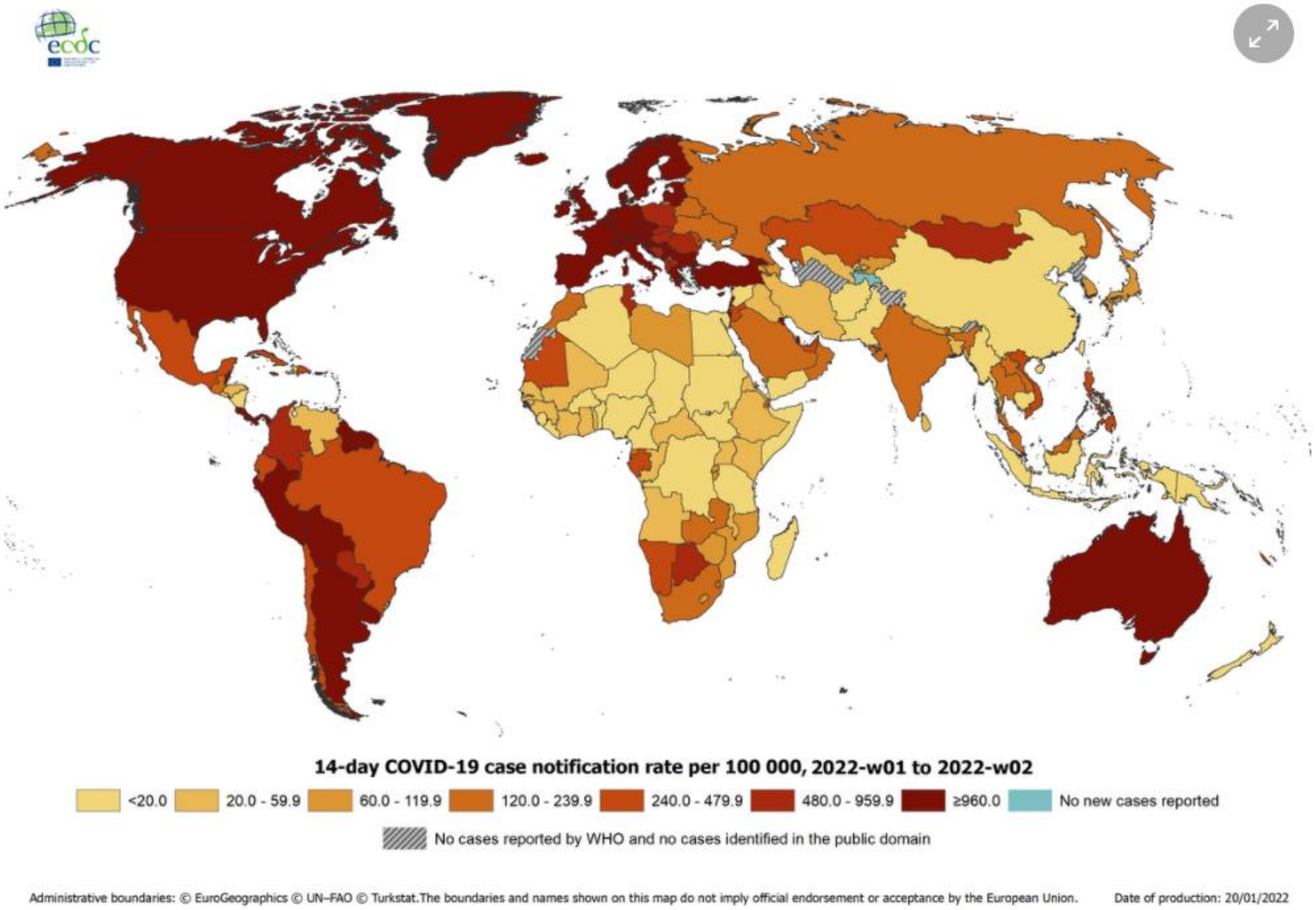
Odkud pocházím a kam kráčím

Tržnice ve Wuhanu


WUHAN INSTITUTE OF VIROLOGY
1956
WUHAN INSTITUTE OF VIROLOGY,CAS

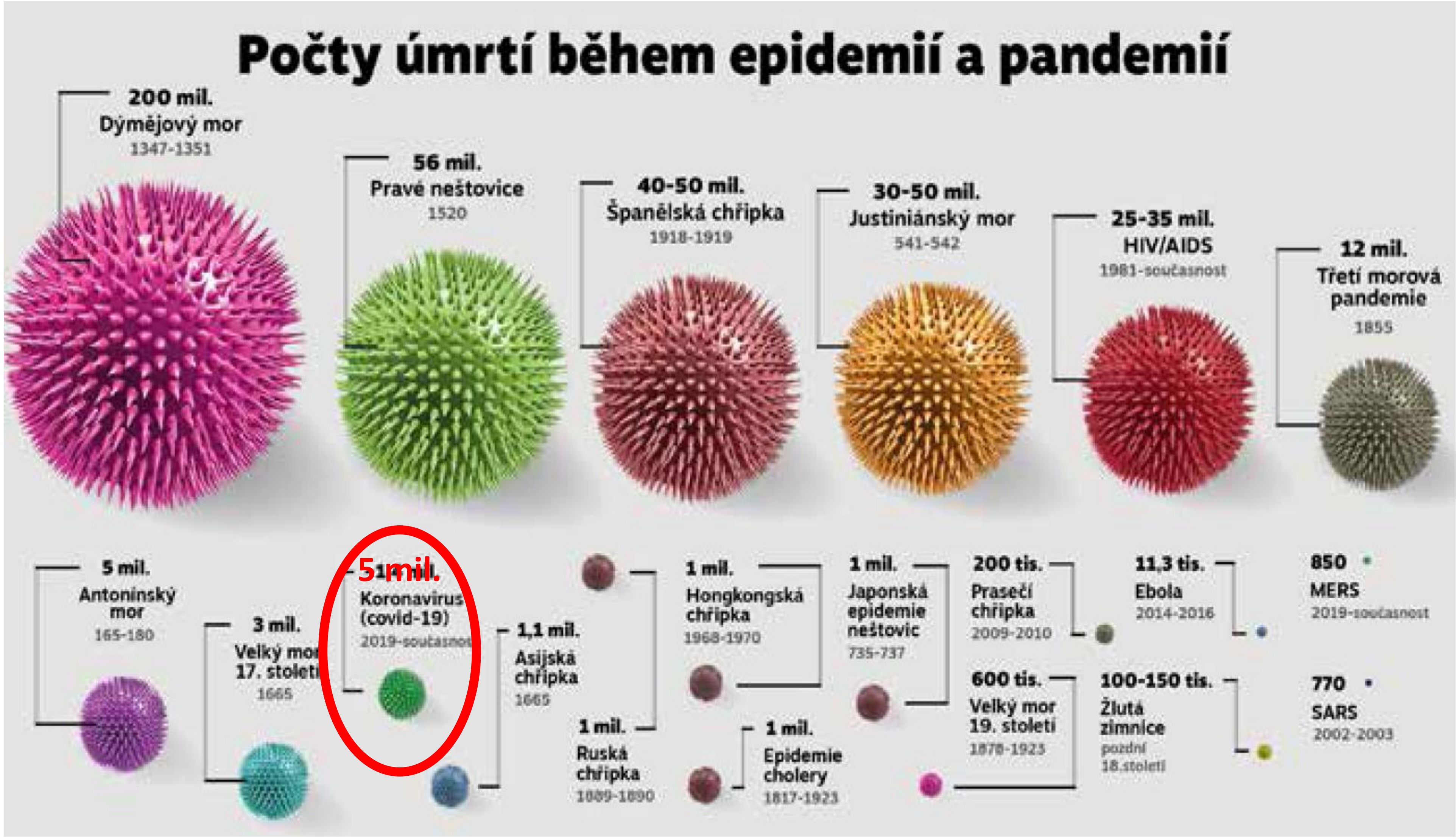
Geographic distribution of COVID-19

14-day COVID-19 case notification rate per 100 000, weeks 1-2

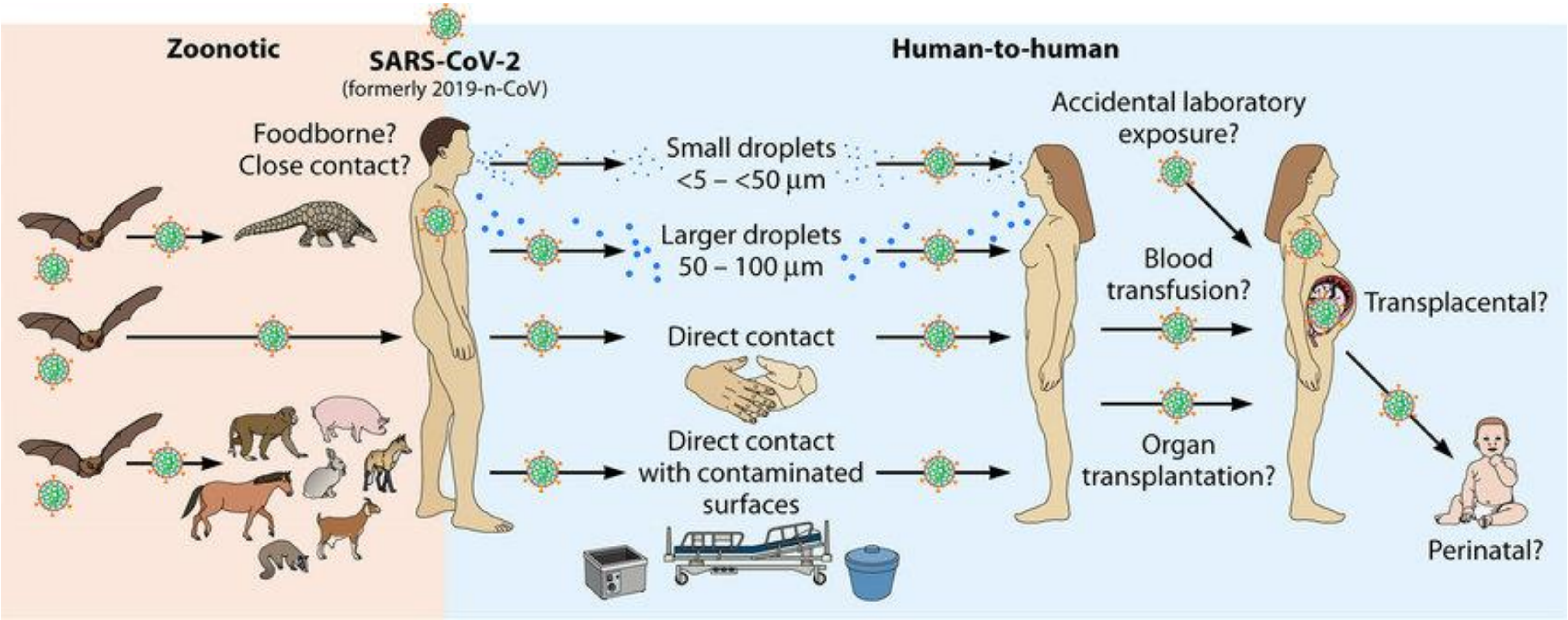


14-day COVID-19 case notification rate per 100 000

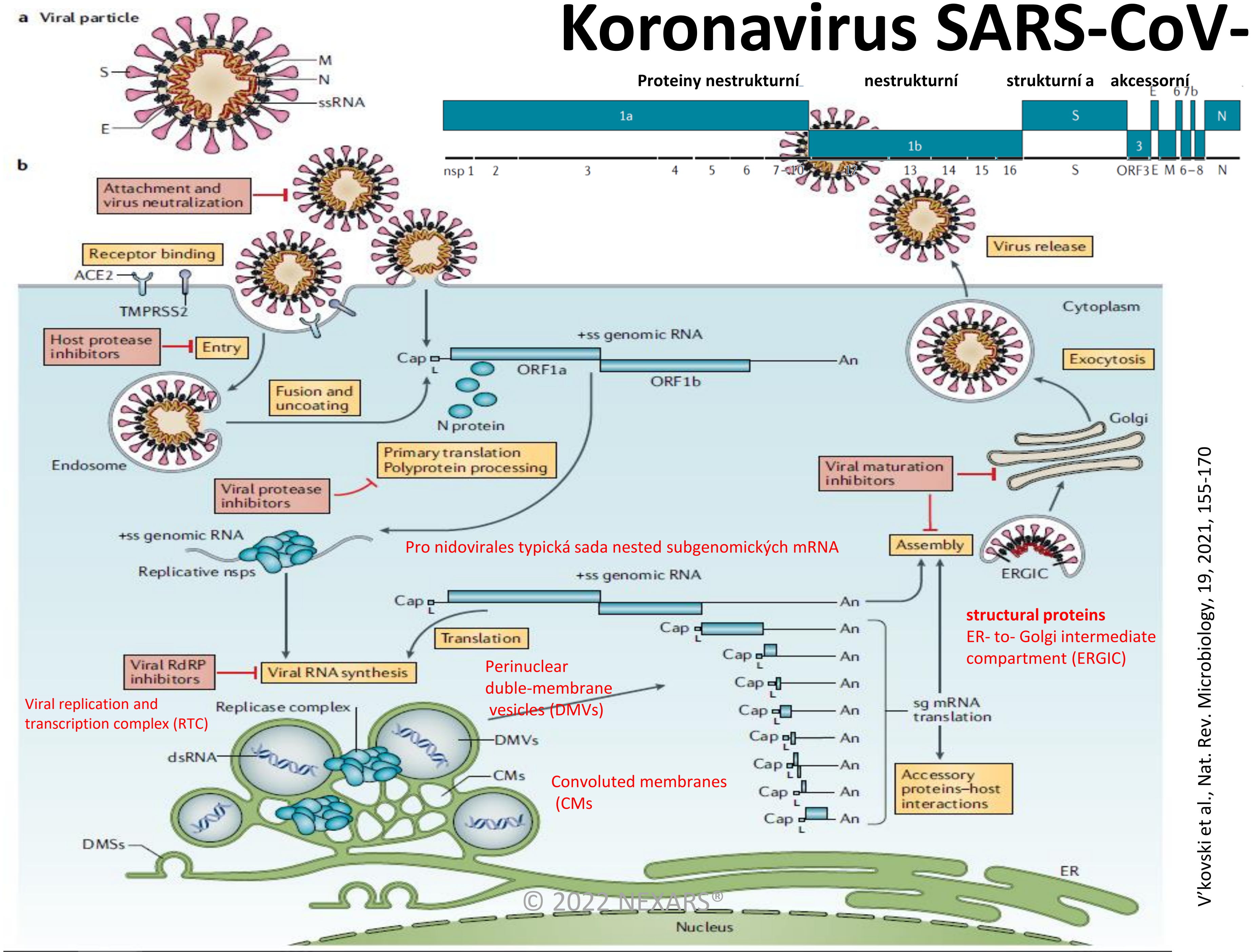
COVID-19


Počty úmrtí během epidemií a pandemií
200 mil.
Dýmějový mor
1347-1351
56 mil.
Pravé neštovice
1520
40-50 mil.
Španělská chřipka
1918-1919
30-50 mil.
Justiniánský mor
541-542
25-35 mil.
HIV/AIDS
1981-současnost
12 mil.
Třetí morová pandemie
1855
5 mil.
Antoninský mor
165-180
3 mil.
Velký mor 17. století
1665
5 mil.
Koronavirus (covid-19)
1,1 mil.
Asijská chřipka
1665
1 mil.
Ruská chřipka
1889-1890
1 mil.
Hongkongská chřipka
1968-1970
1 mil.
Epidemie cholery
1817-1923
1 mil.
Japonská epidemie neštovic
735-737
200 tis.
Prasečí chřipka
2009-2010
600 tis.
Velký mor 19. století
1878-1923
11,3 tis.
Ebola
2014-2016
100-150 tis.
Žlutá zimnice
pozdní 18. století
850
MERS
2019-současnost
770
SARS
2002-2003

SARS-Cov -2

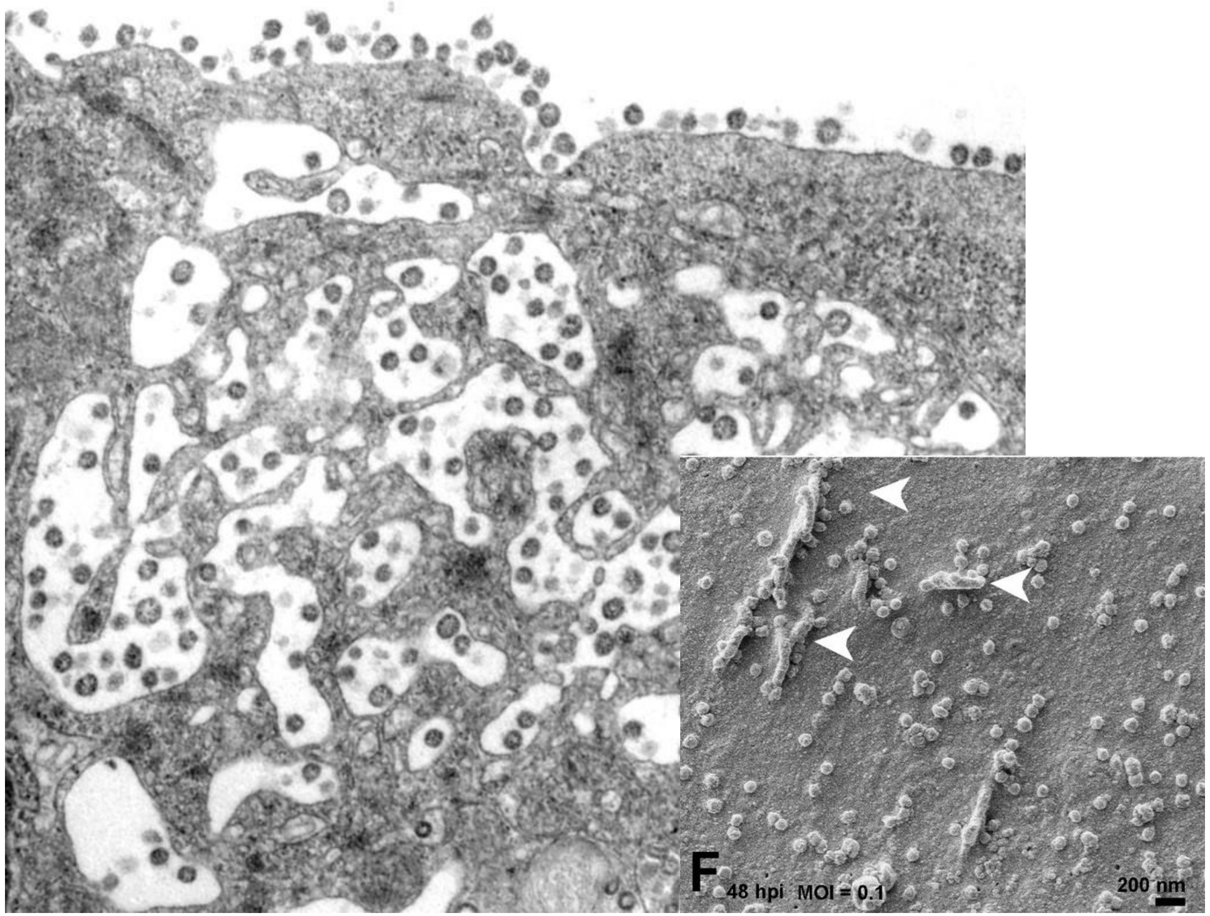

Zoonotic
SARS-CoV-2
(formerly 2019-n-CoV)
Human-to-human
Foodborne?
Close contact?
Small droplets
<5 – <50 µm
Larger droplets
50 – 100 µm
Direct contact
Direct contact
with contaminated
surfaces
Accidental laboratory
exposure?
Blood
transfusion?
Organ
transplantation?
Transplacental?
Perinatal?

Koronavirus SARS-CoV-2

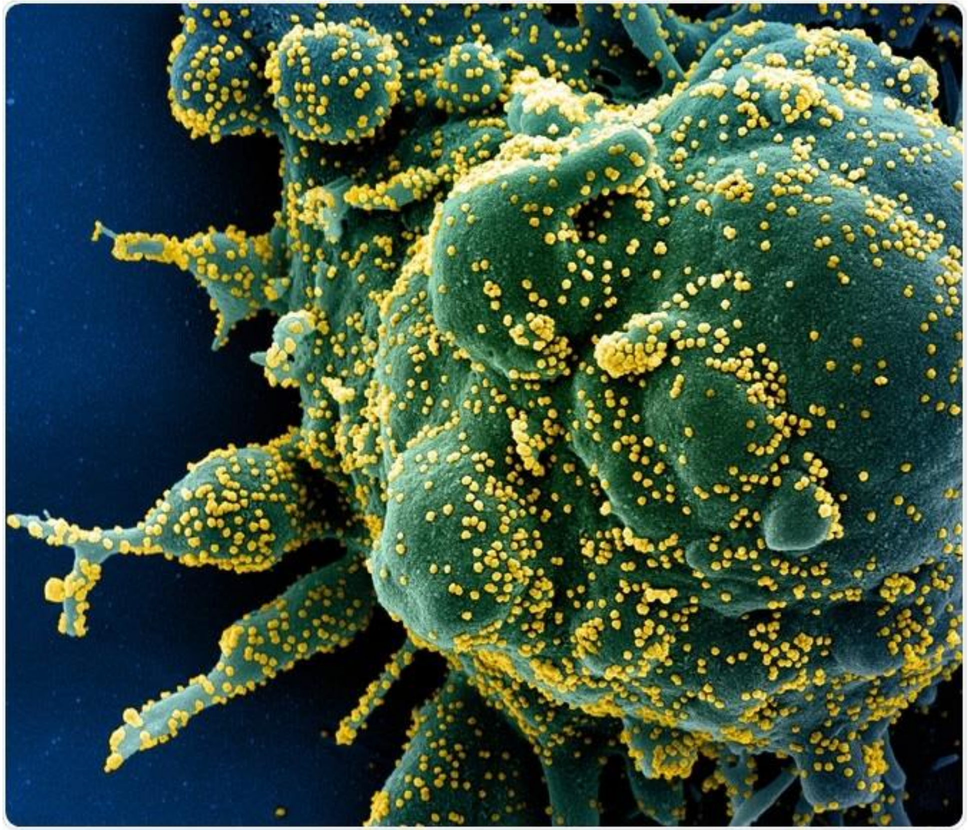


V'kovski et al., Nat. Rev. Microbiology, 19, 2021, 155-170

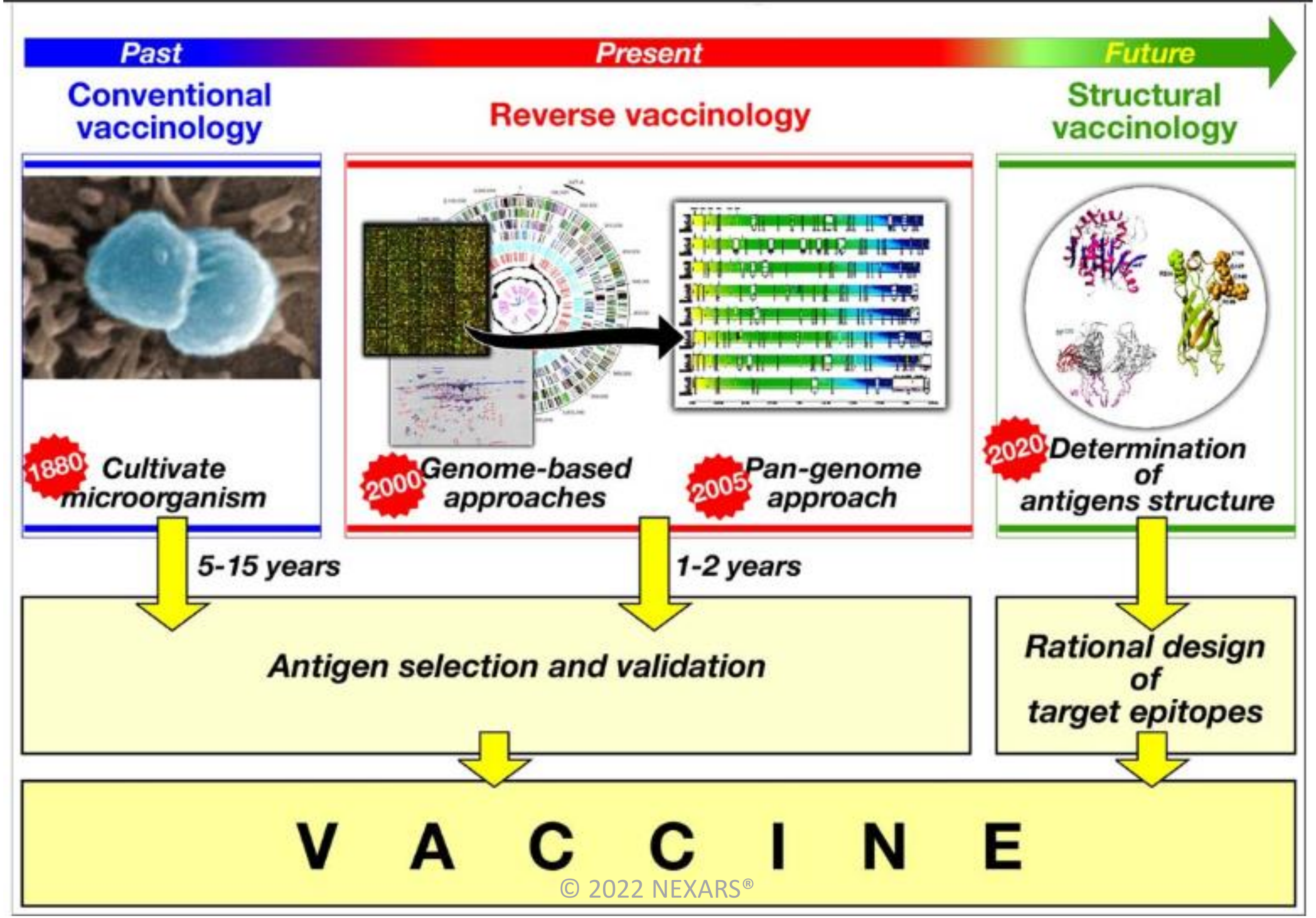
Replication of the virus in the cell



A SARS-CoV-infected cell with virus particles in vesicles, which appear to migrate toward the cell surface and fuse with the plasma membrane, releasing the viral particles. Many of the particles adhere to the plasma membrane, creating a characteristic knob-like appearance on the surface of the cell.
Image source: C.S. Goldsmith, CDC



Novel Coronavirus SARS-CoV-2 Colorized scanning electron micrograph of an apoptotic cell (green) heavily infected with SARS-COV-2 virus particles (yellow), isolated from a patient sample. Image captured at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: NIAID


Past
Present
Future
Conventional vaccinology
Reverse vaccinology
Structural vaccinology
1880 Cultivate microorganism
2000 Genome-based approaches
2005 Pan-genome approach
2020 Determination of antigens structure
5-15 years
1-2 years
Antigen selection and validation
Rational design of target epitopes
V A C C I N E

Classification of modern vaccines

Classic vaccines

Inactivated whole cell vaccines

Attenuated whole cell vaccines - adapted and genetically engineered

Bacterial ghosts

Conjugated vaccines

Splitted vaccines

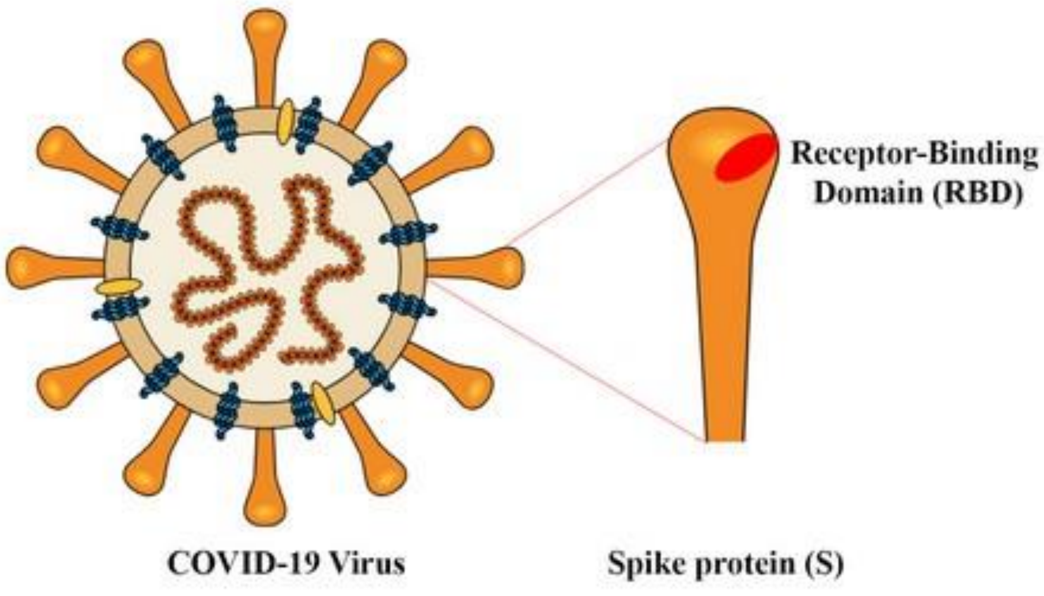
Subunit Vaccines

Reverse Vaccinology

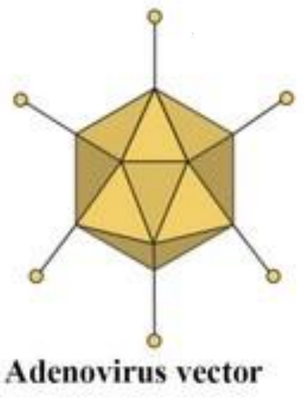
Recombinant vaccines - recombinant protein antigen, VLP and multimeric protein complexes, antigen mimicking binders

Genetic Vaccines – pDNA, mRNA

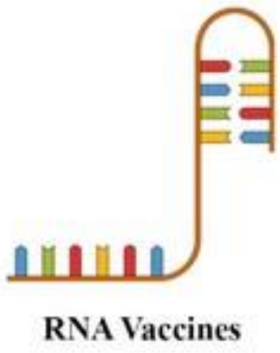
Typy vakcín proti Covid-19 a naše cesta



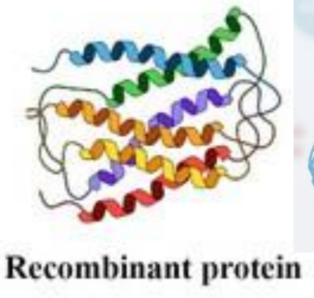
Astra Zeneca,
Jansen
Sputnik



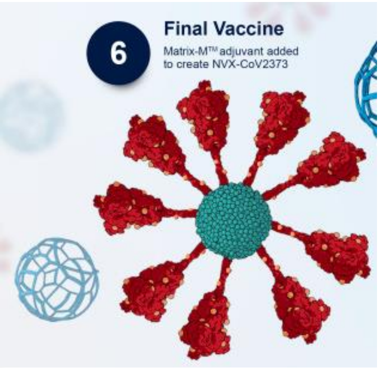
Moderna, Pfizer

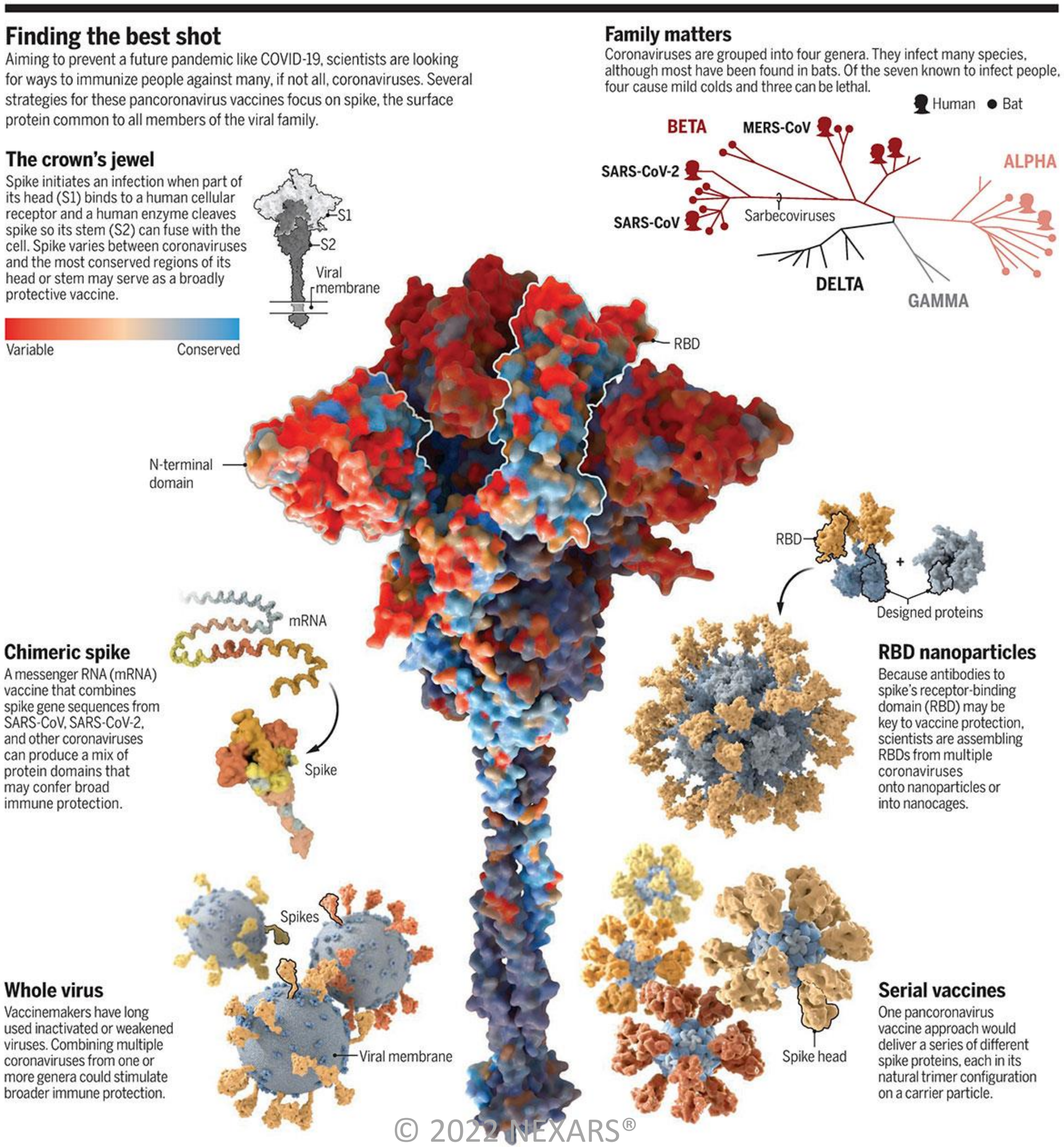


Čína, Indie, Valneva

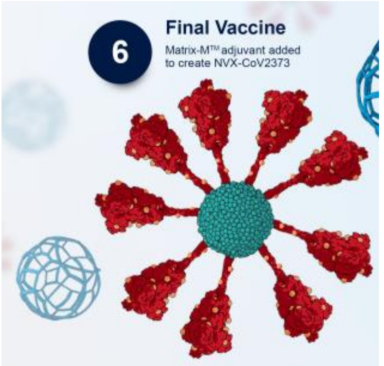


Novavax



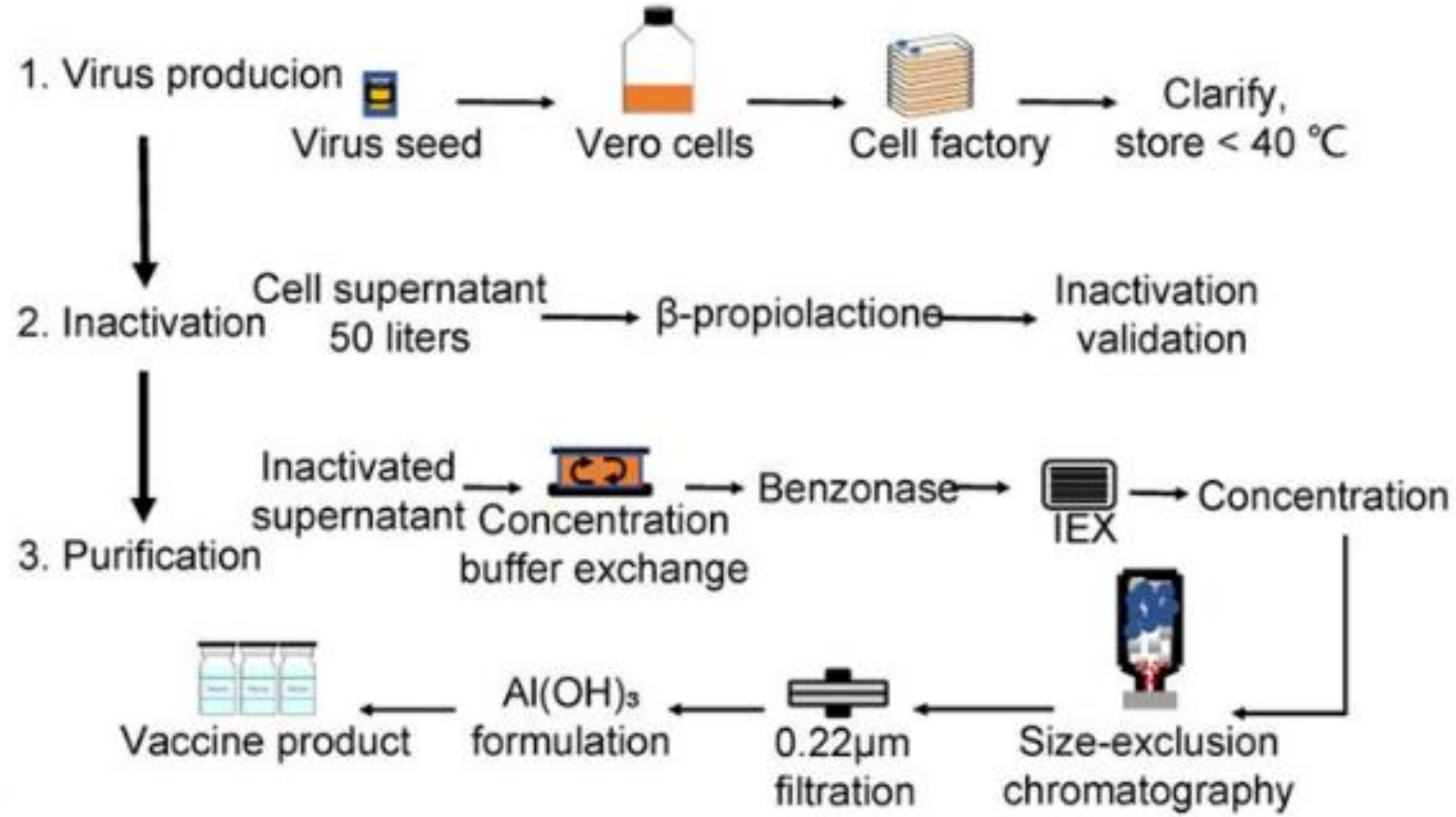


Finding the best shot
Aiming to prevent a future pandemic like COVID-19, scientists are looking for ways to immunize people against many, if not all, coronaviruses. Several strategies for these pancoronavirus vaccines focus on spike, the surface protein common to all members of the viral family.
The crown's jewel
Spike initiates an infection when part of its head (S1) binds to a human cellular receptor and a human enzyme cleaves spike so its stem (S2) can fuse with the cell. Spike varies between coronaviruses and the most conserved regions of its head or stem may serve as a broadly protective vaccine.
S1
S2
Viral membrane
Variable
Conserved
Family matters
Coronaviruses are grouped into four genera. They infect many species, although most have been found in bats. Of the seven known to infect people, four cause mild colds and three can be lethal.
Human
Bat
BETA
MERS-CoV
SARS-CoV-2
SARS-CoV
Sarbecoviruses
ALPHA
DELTA
GAMMA
RBD
N-terminal domain
RBD
Designed proteins
mRNA
Chimeric spike
A messenger RNA (mRNA) vaccine that combines spike gene sequences from SARS-CoV, SARS-CoV-2, and other coronaviruses can produce a mix of protein domains that may confer broad immune protection.
Spike
RBD nanoparticles
Because antibodies to spike's receptor-binding domain (RBD) may be key to vaccine protection, scientists are assembling RBDs from multiple coronaviruses onto nanoparticles or into nanocages.
Spikes
Whole virus
Vaccinemakers have long used inactivated or weakened viruses. Combining multiple coronaviruses from one or more genera could stimulate broader immune protection.
Viral membrane
Spike head
Serial vaccines
One pancoronavirus vaccine approach would deliver a series of different spike proteins, each in its natural trimer configuration on a carrier particle.



6
Final Vaccine
Matrix-M™ adjuvant added to create NVX-CoV2373

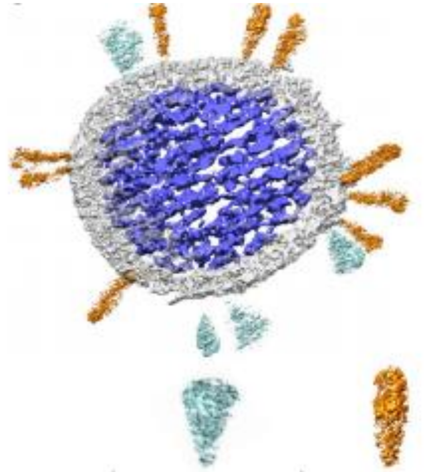
Production of inactivated vaccine



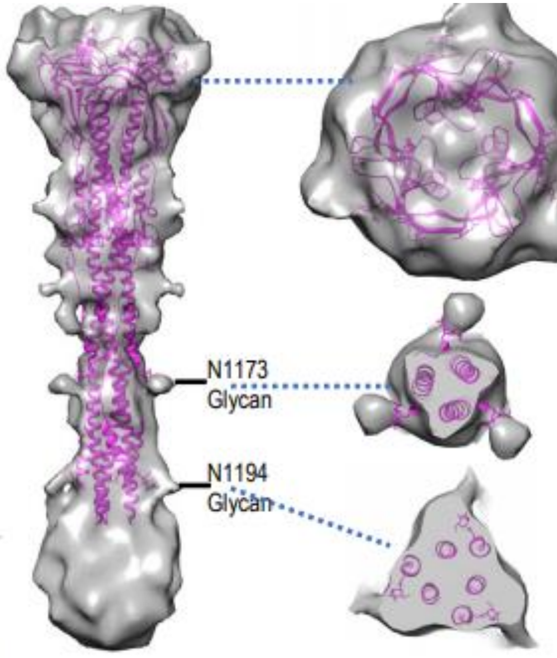
Inactivated vaccines

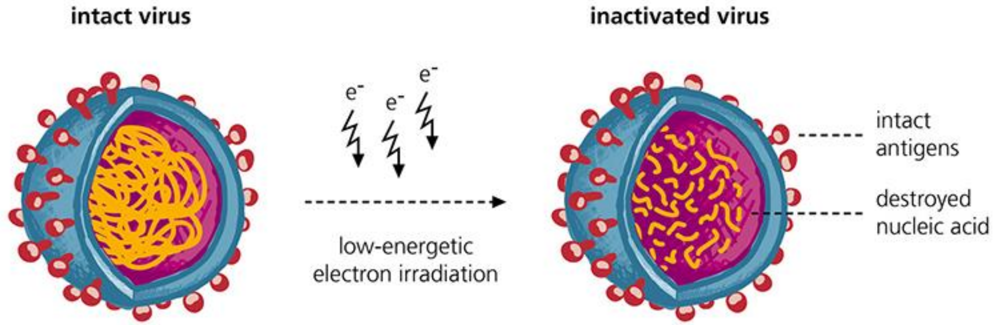
Inactivation processes: thermal, irradiation, chemical (formaldehyde, β-propiolacton)

The use of chemically inactivated pathogens is one of the most common vaccine strategies. It has a good track record of generating long-lasting immunity for many different viral diseases, such as **flu, polio, and yellow fever**. Nonetheless, this strategy is **not universally suited to all viruses** and can even have disastrous consequenceif a molecular and structural understanding of the antigen is lacking. One such unfortunate example is the **formalin-inactivated respiratory syncytial virus** (FI-RSV) vaccine trial of the 1960s, which led to **enhancement of disease symptoms in vaccinated children after natural exposure to RSV, with two fatal cases.**



	Prefusion	Postfusion
Proportion	25.6% (32/125)	74.4% (93/125)
95% CI	18.7% - 33.9%	66% - 81.3%





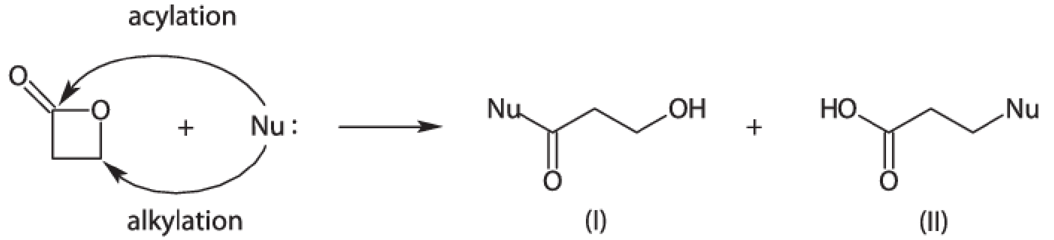


FIGURE 1. **Two possible reaction paths of a nucleophile (*Nu*) with β-propiolactone leading to (*I*) acylated and (*II*) alkylated products.**

1218 Structure 28, 1218–1224, November 3, 2020 ª 2020 The Author(s). Published by Elsevier Ltd

Cryoelectron microscopy of inactivated virus SARS-CoV-2

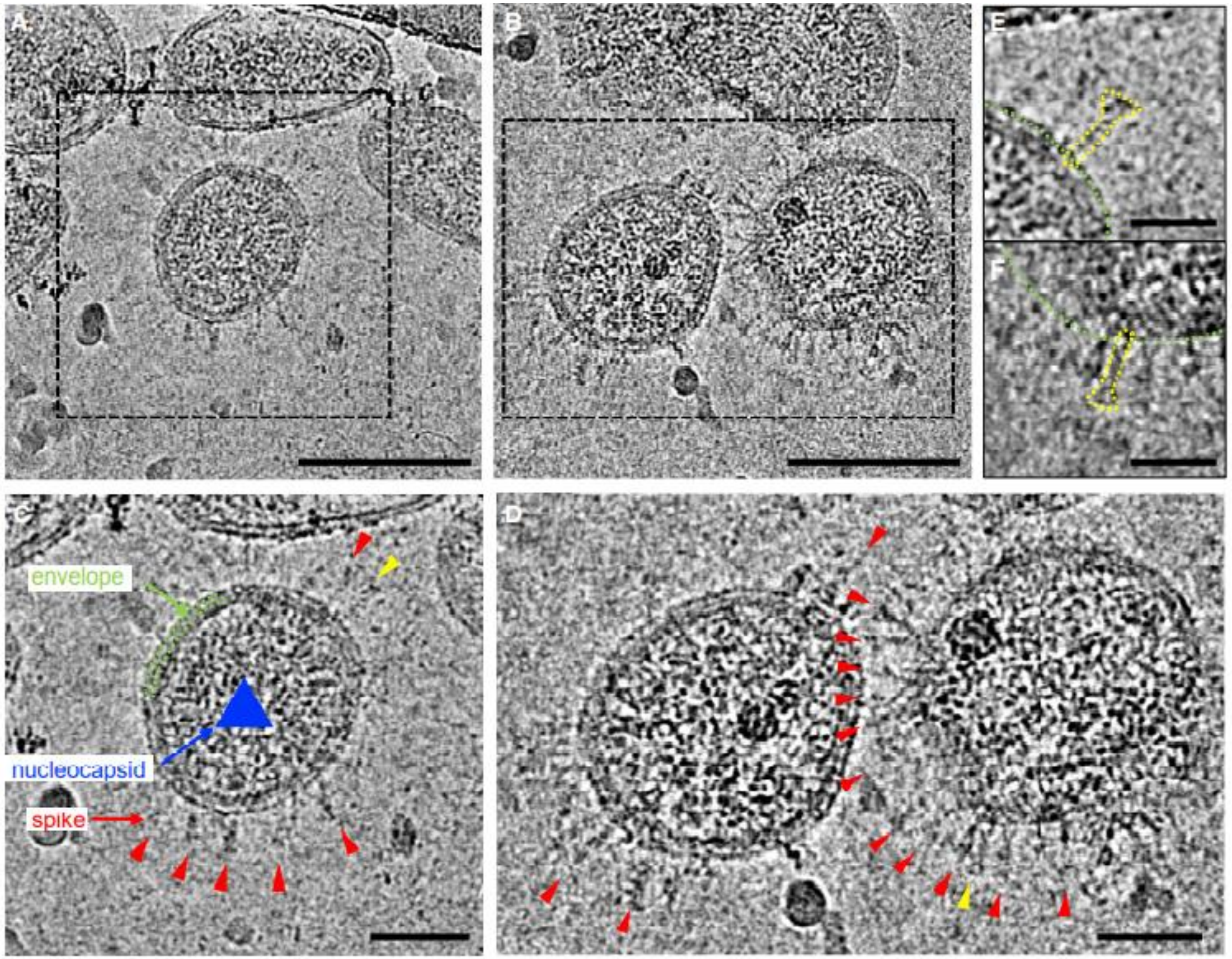


Figure 2. Cryo-EM Analysis of SARS-CoV-2 (A and B) Representative cryo-EM images of purified inactivated SARS-CoV-2 virus particles. (C and D). Zoom-in views of the boxed virions in (A and B). Envelope and nucleocapsids are indicated by green dashed lines and a blue triangle, respectively. Viral spikes are indicated by red arrowheads. (E and F). Enlarged views of the spikes indicated by yellow arrowheads in (C and D), respectively. The shape of the spike is depicted by yellow dotted lines. Green dotted lines indicate the viral envelope. Scale bars, 100 nm in (A and B), 50 nm in (C and D), 25 nm in (E and F).

Vaccines

Advantages of inactivated vaccines

- Gives sufficient humoral immunity if boosters given
- No mutation or reversion
- Can be used with immuno-deficient patients
- Sometimes better in tropics

Disadvantages of inactivated vaccines

- Many vaccinees do not raise immunity
- Boosters needed
- No local immunity (important)
- Higher cost
- Shortage of monkeys (polio)
- Failure in inactivation and immunization with virulent virus

Production of inactivated virus-based vaccines

CoronaVac Sinovac, China

Covaxin
Bharat, India

BBIBP-CorV, Sinopharm, China

VLA 2001 a VLA 2101
Valneva, France

[EMA posuzuje „vakcínu odmítačů" od firmy Valneva.](#)

Vakcinace v Indonésii

Proměna názorů odborníků

Before the Omicron variant emerged, Iwasaki had been advocating single mRNA boosters for recipients of inactivated vaccines. “We were really celebrating how wonderful this strategy is,” she says, “and then — boom! — Omicron hit.” Now, she thinks these people probably need two extra jabs.

“The bar keeps being raised by the variants,” Iwasaki says. “We’re playing catch up all the time.”

***Nature* 601**, 311 (2022)

Než se objevila varianta Omicron, Iwasaki obhajoval jednotlivé mRNA boostery pro příjemce inaktivovaných vakcín.

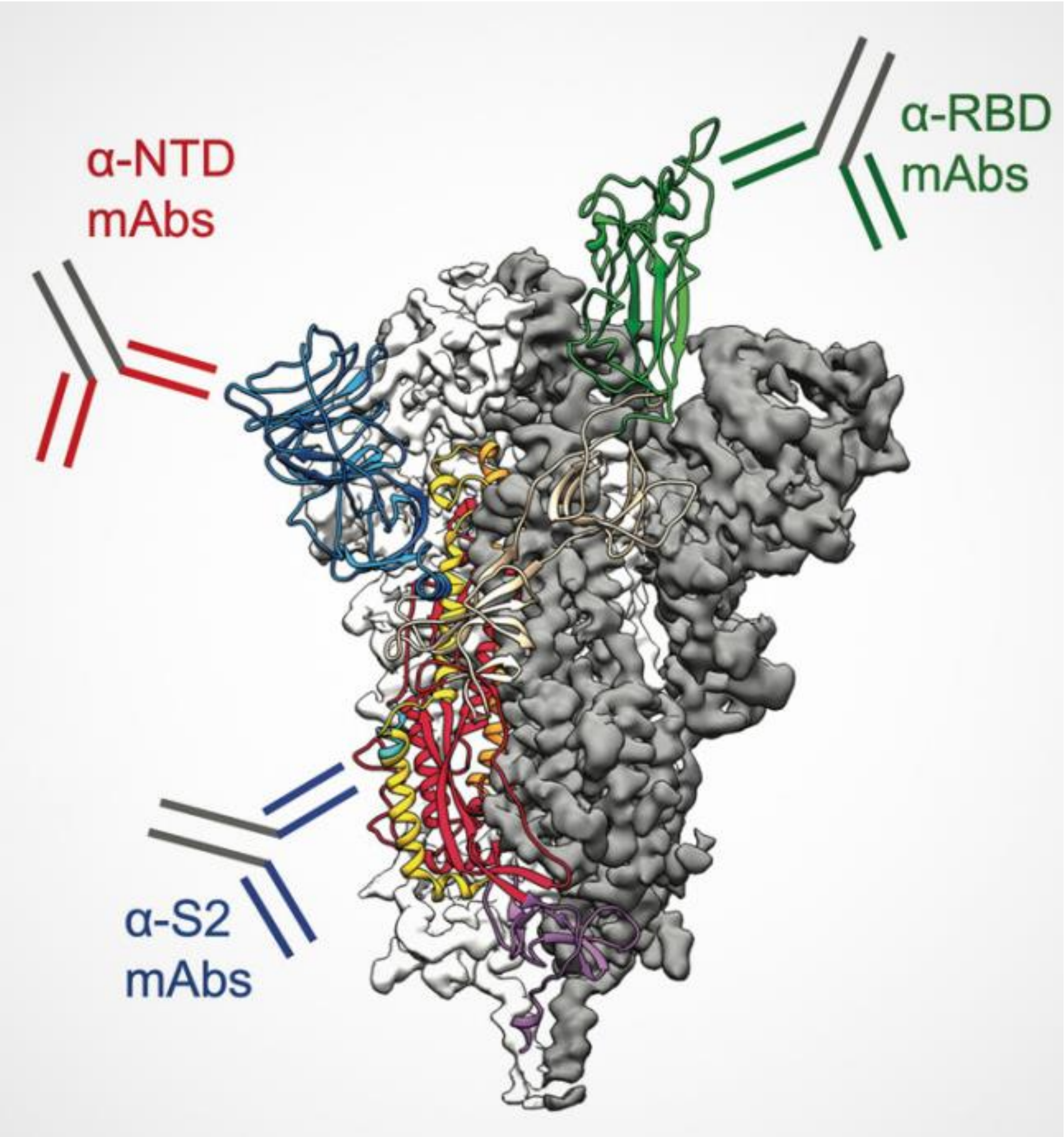
„Opravdu jsme slavili, jak úžasná je tato strategie,“ říká, „a pak – bumbác! — práskl do toho Omikron.“

Teď si myslí, že tito lidé pravděpodobně potřebují dvě dávky navíc.

„Počet variant se stále zvyšuje,“ říká Iwasaki. "Neustále si hrajeme na dohánění."

Nature 601, 311 (2022)

Spike protein – the main antigen for vaccine



An analysis of blood plasma samples from people who recovered from SARS-CoV-2 infections shows that most of the antibodies circulating in the blood -- on average, about 84% -- target areas of the viral spike protein outside the receptor binding domain (RBD, green), including the N-terminal Domain (NTD, blue) and the S2 subunit (red, yellow). Illustration credit: University of Texas at Austin.

S-protein is suspected of pathological effects:

Inflammagen

Penetration BBB

Prion

Fusion of cell membranes and forming syncitium

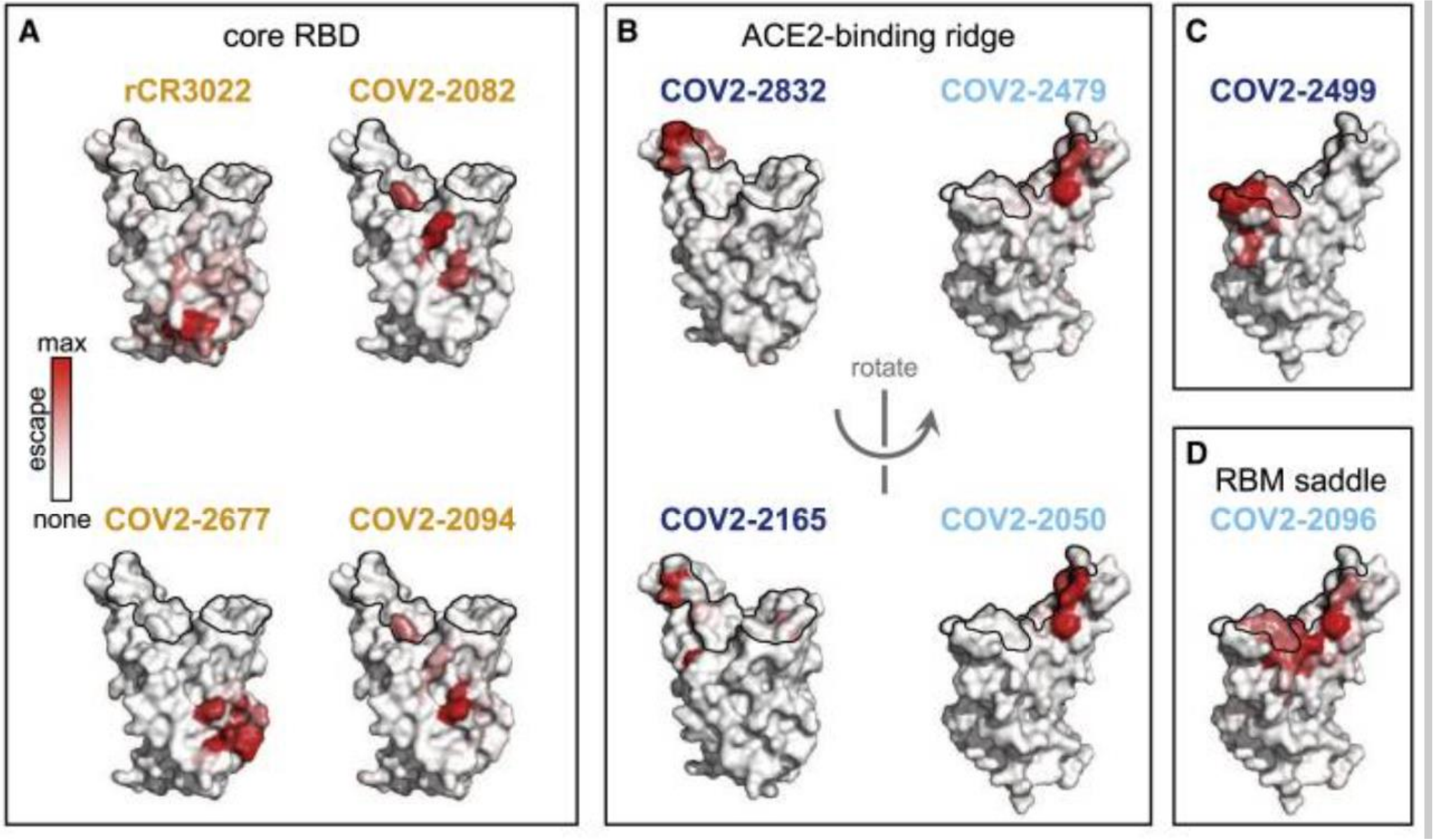
Induction of structural changes to β and γ fibrin(ogen), complement 3, and prothrombin -stabilisation against proteolytic degradation

Endothelial activation and dysfunction

Disbalance ACE2/ACE

Penetration into nucleus and interferention with DNA repair

Structural Mapping of Antibody Binding and Escape

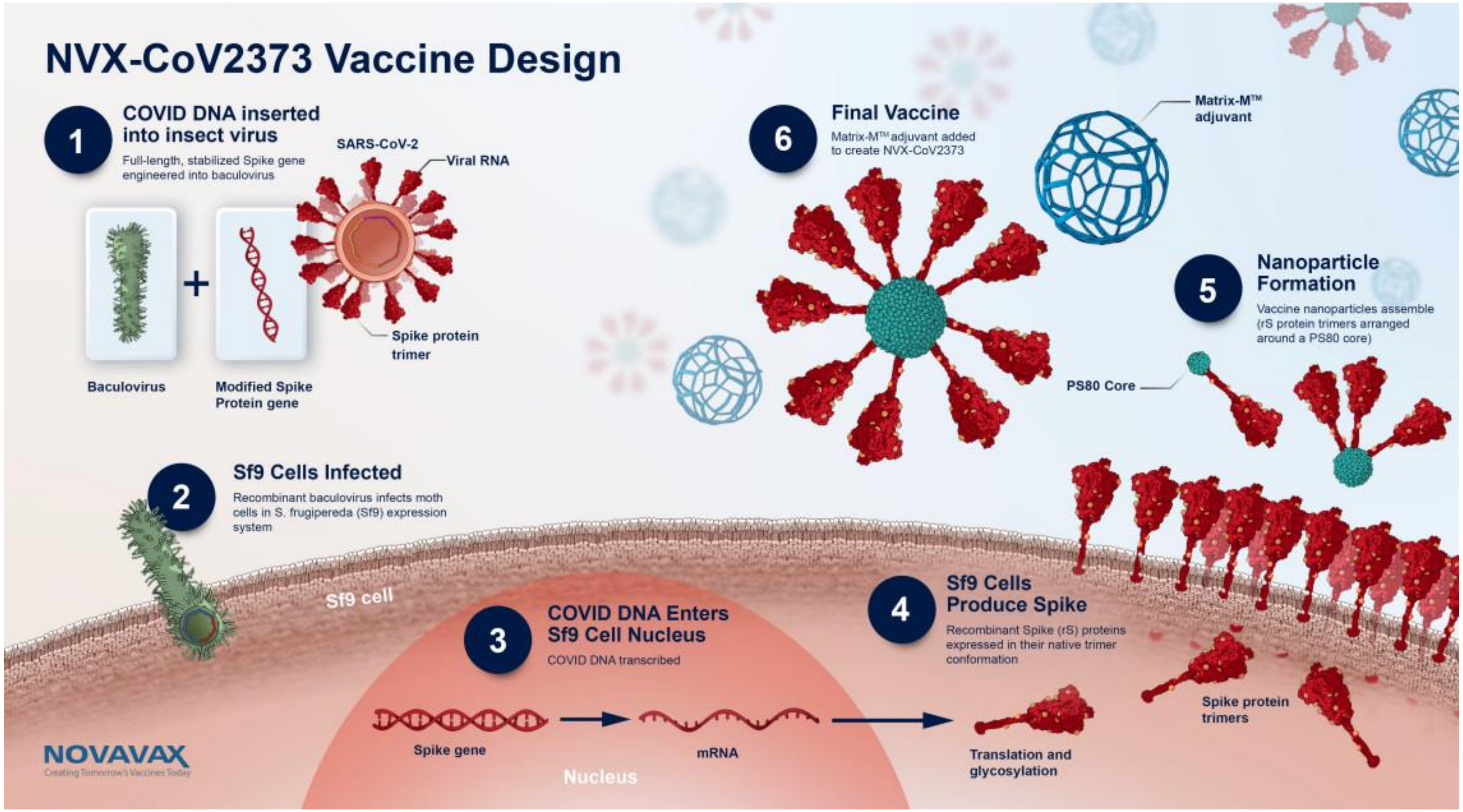


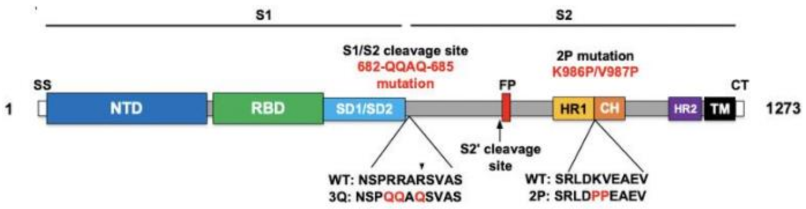
Cell Host Microbe. 2021 Jan 13; 29(1): 44–57.e9.

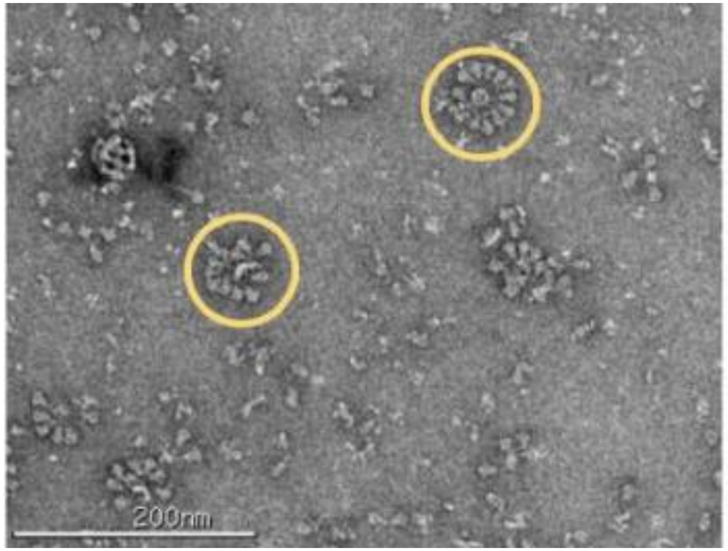
Novavax recombinant protein vaccine

Nuvaxovid dispersion for injection COVID-19 Vaccine (recombinant, adjuvanted) Nuvaxovid (5 ug/0.5mL)

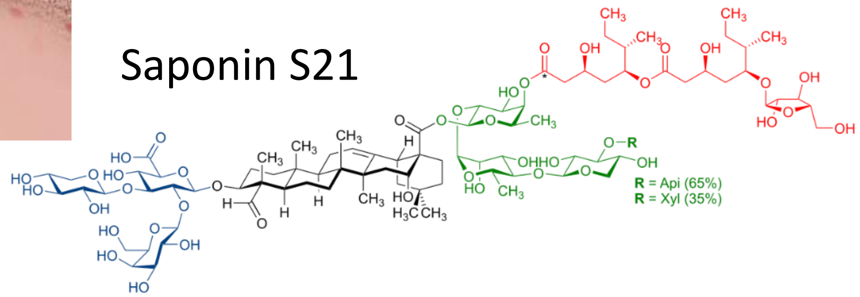
Matrix-M adjuvant is a saponin-based adjuvant, patented by Novavax, that stimulates humoral and cellular immune responses to vaccines. It is composed of nanoparticles from saponins extracted from *Quillaja saponaria* (soapbark) trees, cholesterol, and phospholipids







Saponin S21



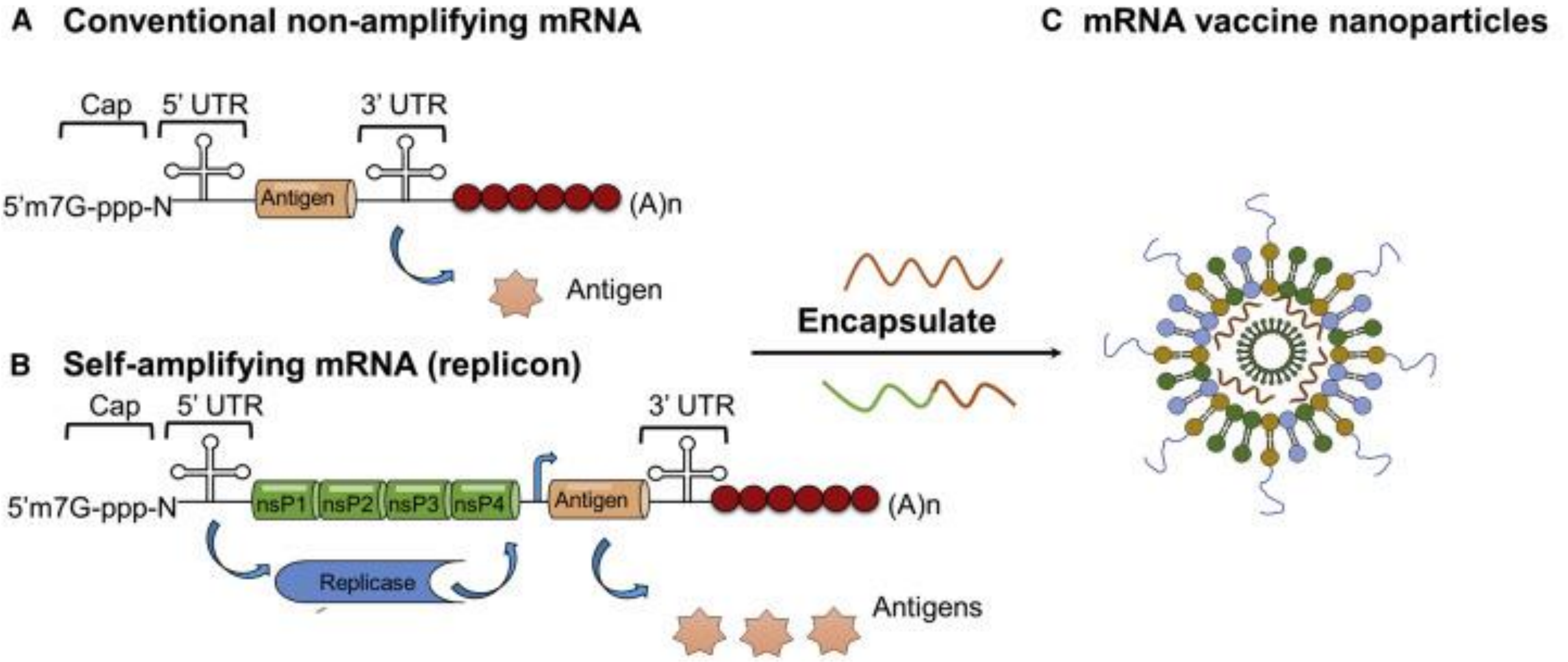
Overall, there was a higher incidence of **adverse reactions in younger age groups**: the incidence of injection site tenderness, injection site pain, fatigue, myalgia, headache, malaise, arthralgia, and nausea or vomiting was higher in adults aged 18 to less than 65 years than in those aged 65 years and above. Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

Genetic mRNA vaccines

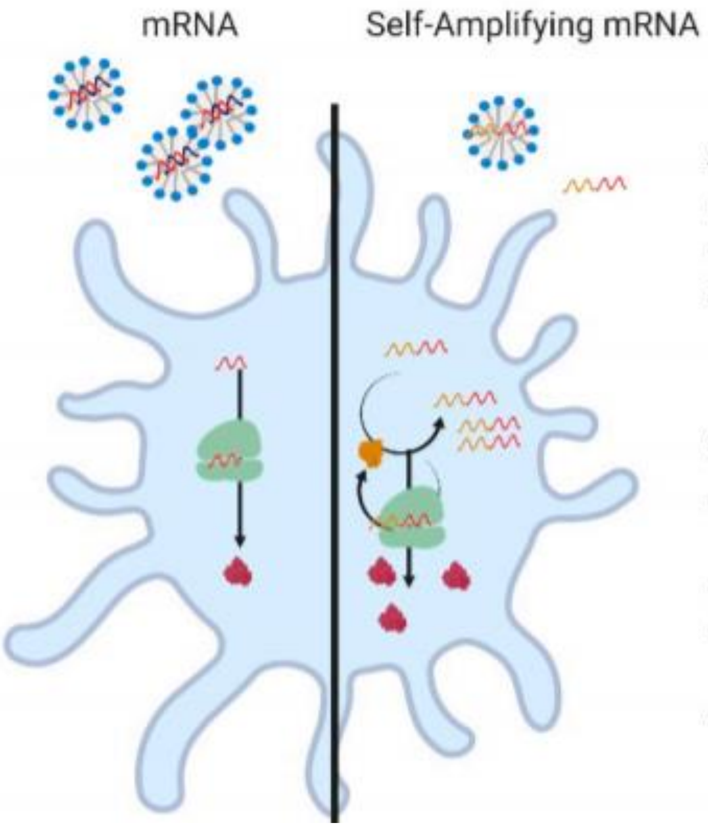
Types of mRNA vaccine

- 1. **Non-replicating mRNA -** The simplest type of RNA vaccine, an mRNA strand is packaged and delivered to the body, where it is taken up by the body's cells to make the antigen.
- 2. **In vivo self-replicating mRNA -** The pathogen-mRNA strand is packaged with additional RNA strands that ensure it will be copied once the vaccine is inside a cell. This means that greater quantities of the antigen are made from a smaller amount of vaccine, helping to ensure a more robust immune response.
- 3. **Cell therapy - In vitro dendritic cell non-replicating mRNA vaccine -** Dendritic cells are immune cells that can present antigens on their cell surface to other types of immune cells to help stimulate an immune response. These cells are extracted from the patient's blood, transfected with the RNA vaccine, then given back to the patient to stimulate an immune reaction.

Non-amplifying and self-amplifying mRNA constructs



Self-amplifying mRNA constructs



Advantages:

- High yield of target antigen
- Prolonged translation
- No need for transfection agents or delivery systems

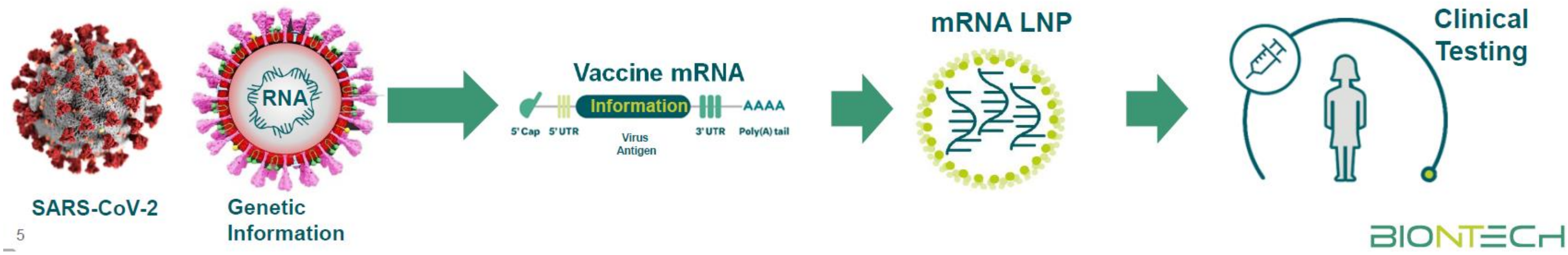
Challenges:

- Longer mRNA sequences are more challenging to produce (possible errors, lower mRNA production yields)
- Strong inflammatory response may limit antigen production
- Prolonged replication of mRNA may decrease the viability of the host cell
- Potential risk for anti-vector immunity

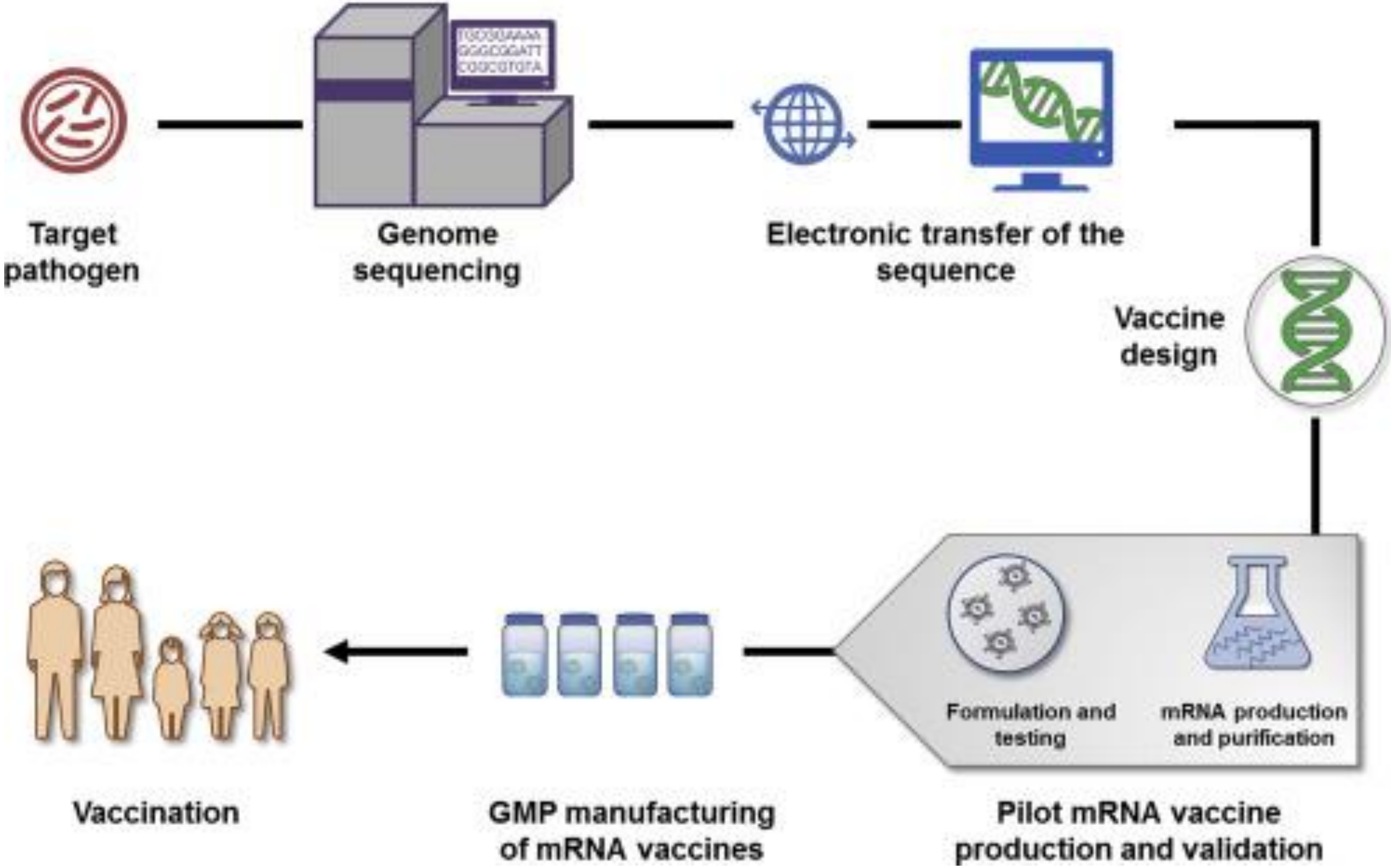
Theoretical benefits of mRNA vaccines over conventional approaches

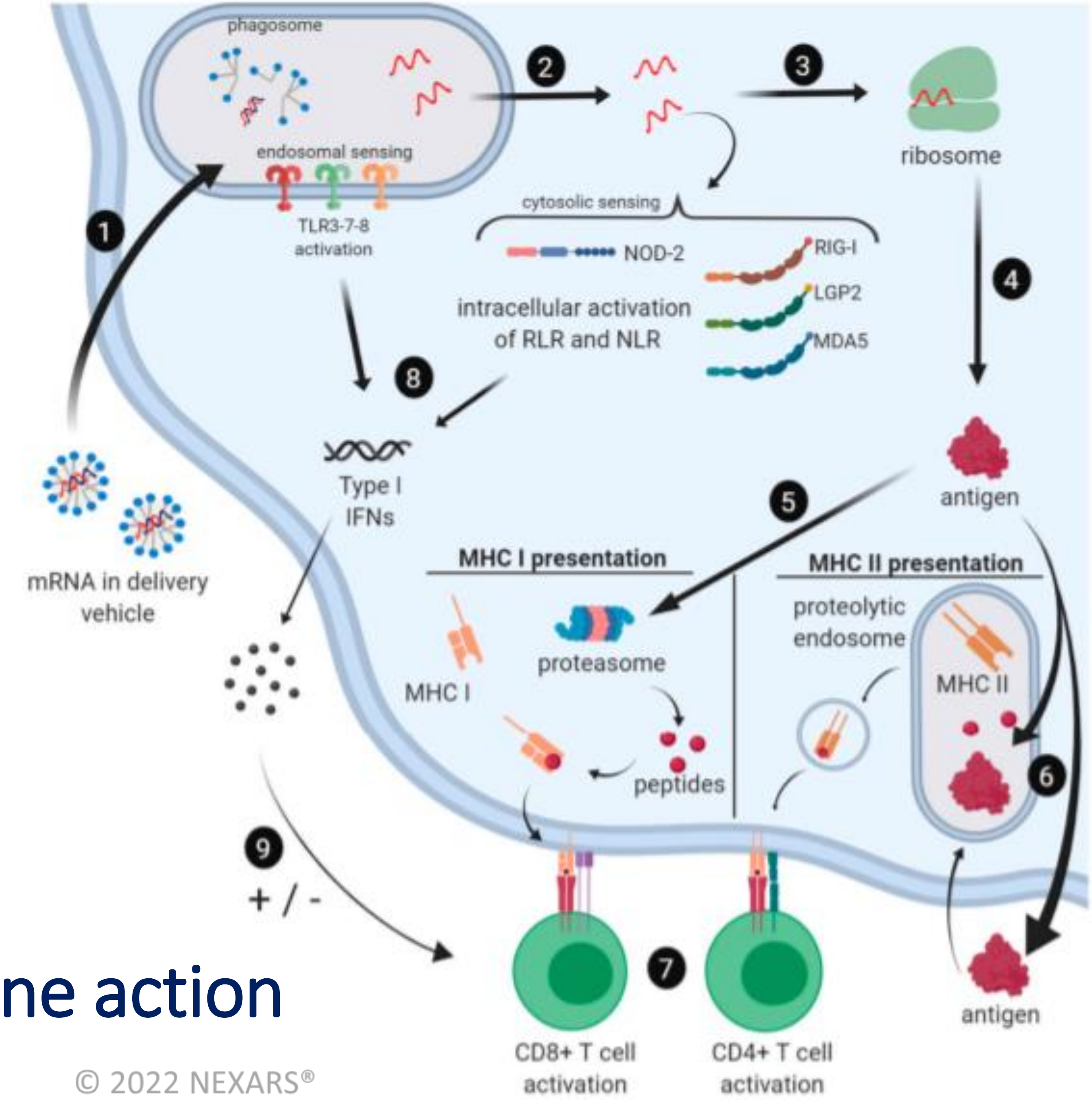
- **Safety:** RNA vaccines are not made with pathogen particles or inactivated pathogen, so are non-infectious. RNA does not integrate itself into the host genome (!?) and the RNA strand in the vaccine is degraded once the protein is made.
- **Efficacy**: early clinical trial results indicate that these vaccines generate a reliable immune response and are well-tolerated by healthy individuals, with few side effects. The cellular immune response can be regulated both by nucleoside modifications and delivery methods.
- **Production:** vaccines can be produced more rapidly in the laboratory in a process that can be standardized, which improves responsiveness to emerging outbreaks.

Genetické vakcíny - mRNA

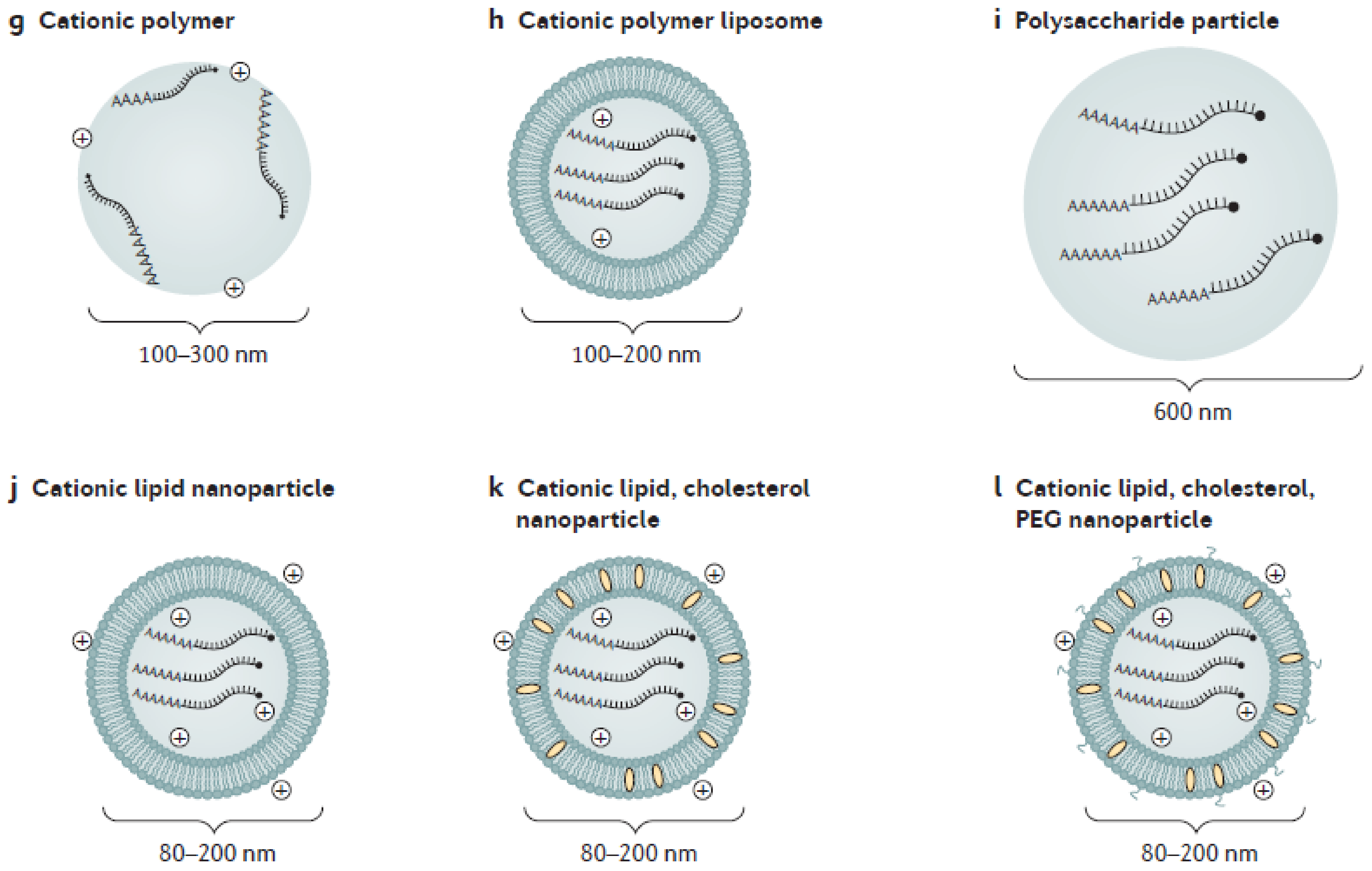


Future of the mRNA vaccine technology and production

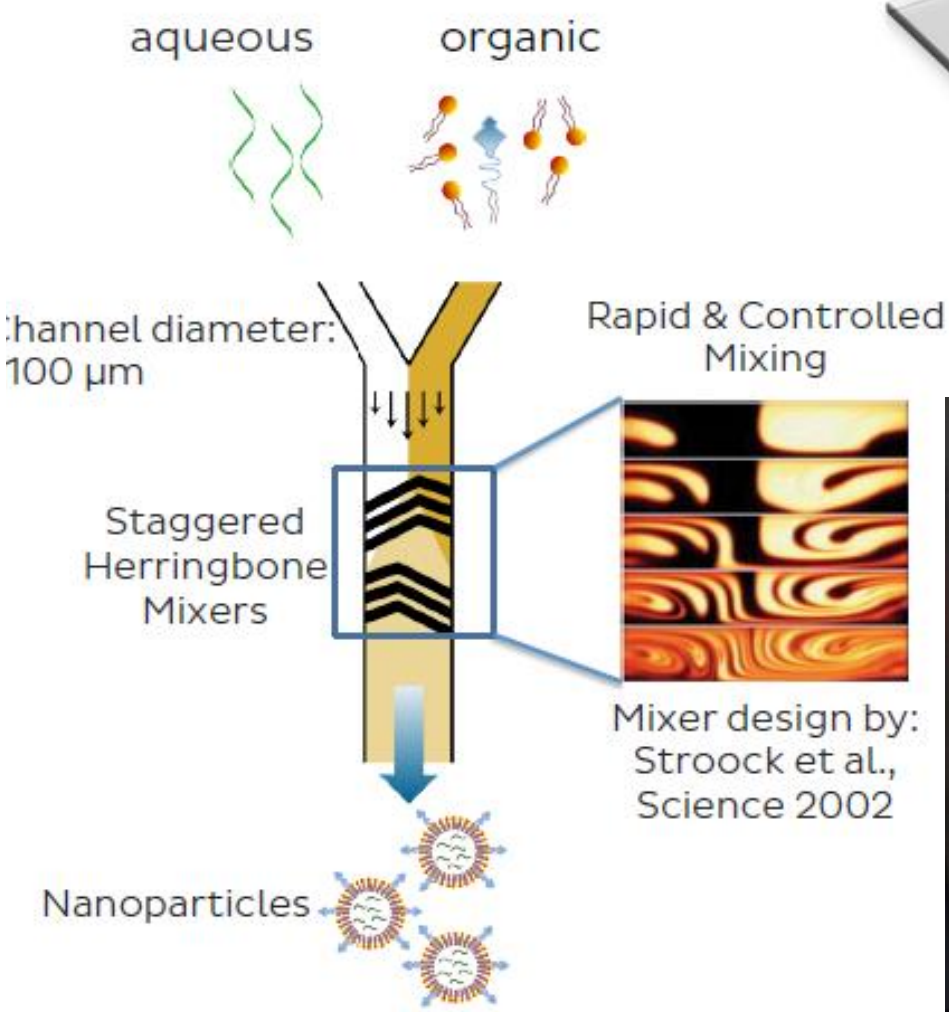


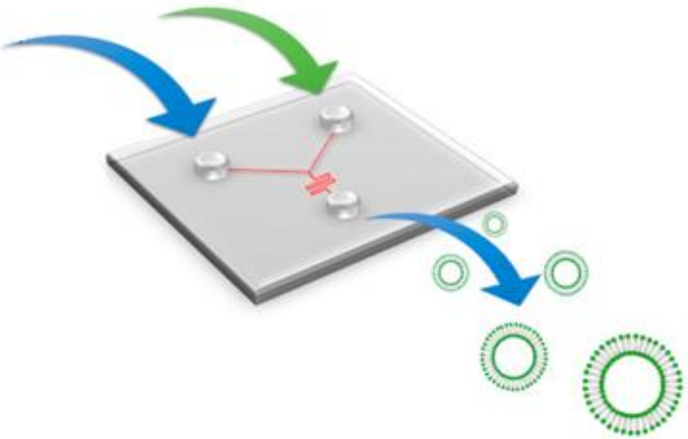


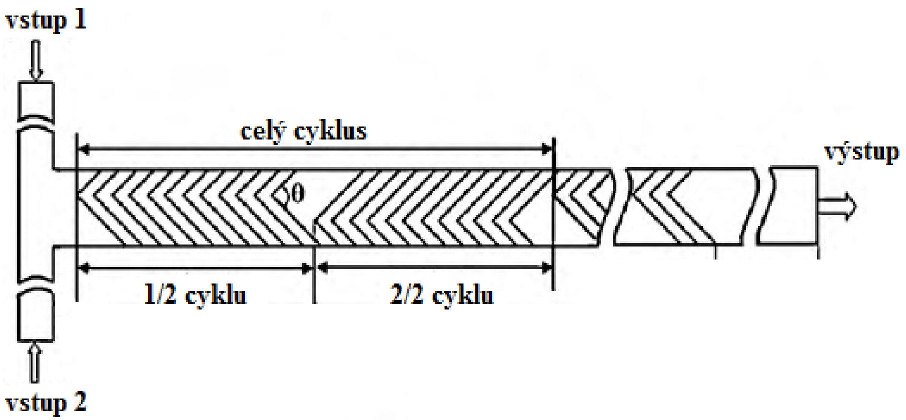
Mechanis(s) of mRNA vaccine action

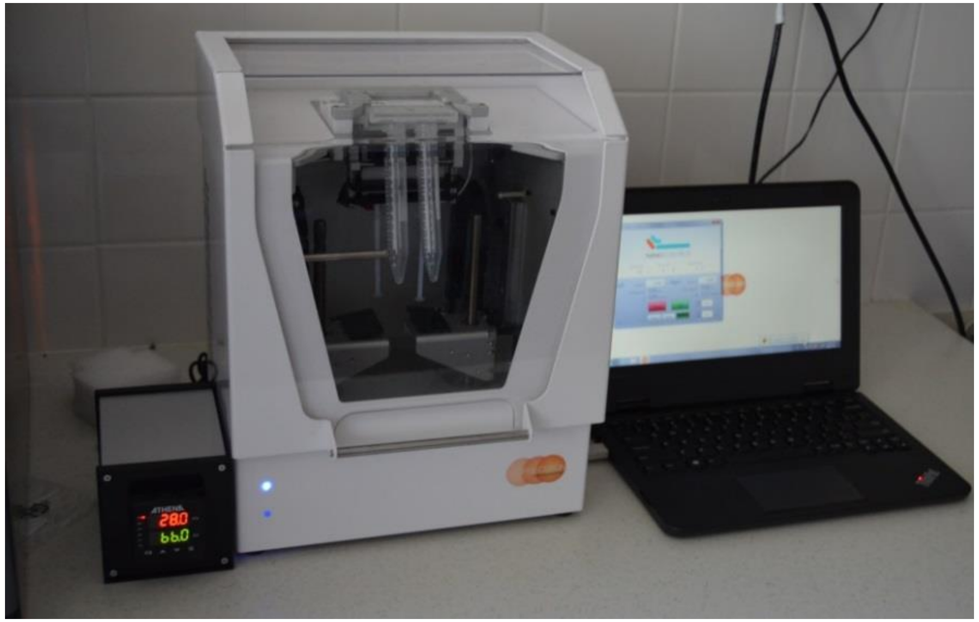

g Cationic polymer
100–300 nm
h Cationic polymer liposome
100–200 nm
i Polysaccharide particle
600 nm
j Cationic lipid nanoparticle
80–200 nm
k Cationic lipid, cholesterol nanoparticle
80–200 nm
l Cationic lipid, cholesterol, PEG nanoparticle
80–200 nm

Precision Nanosystems NanoassemblrTM

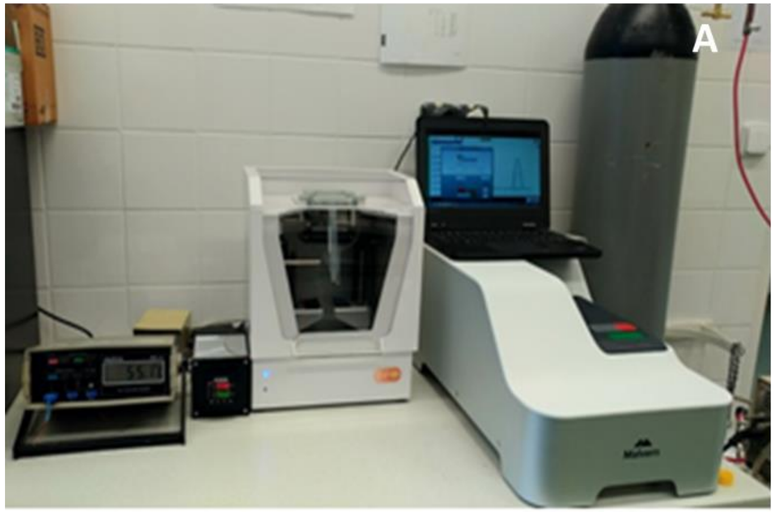


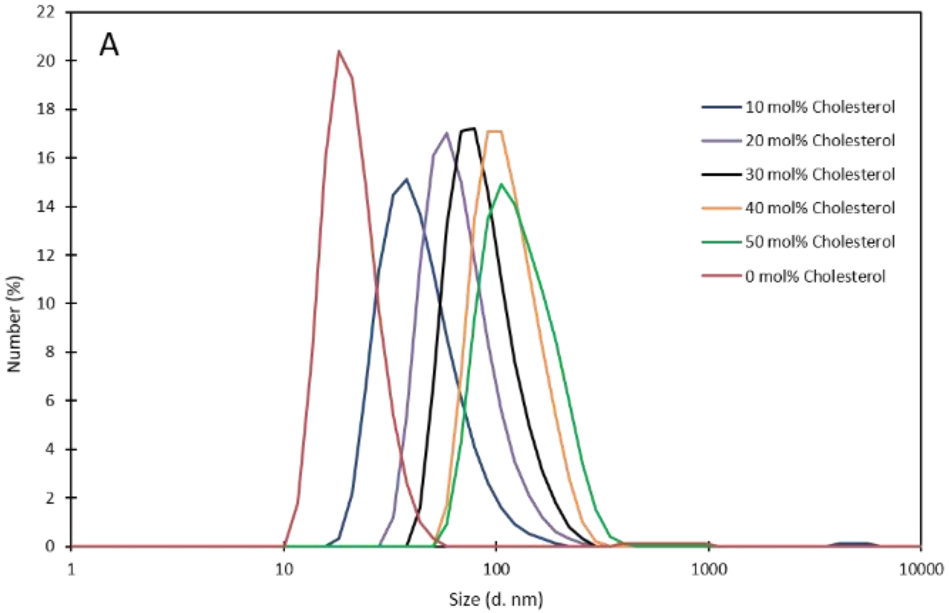


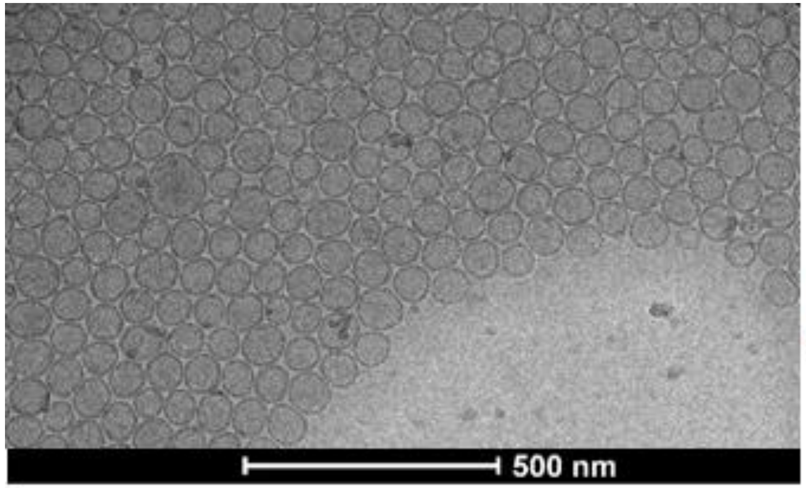


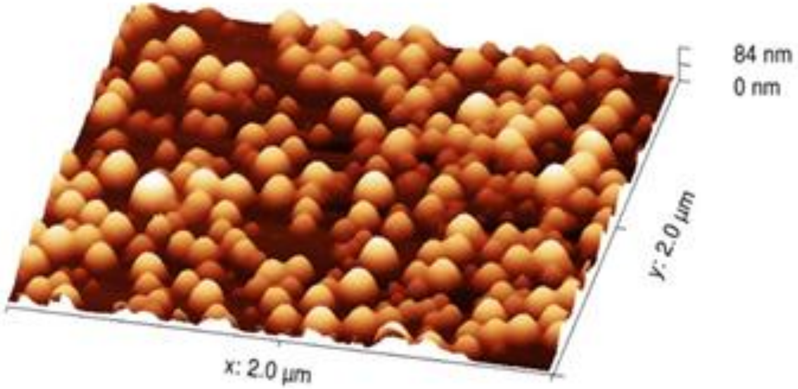


Nanoassemblr Instrument setting



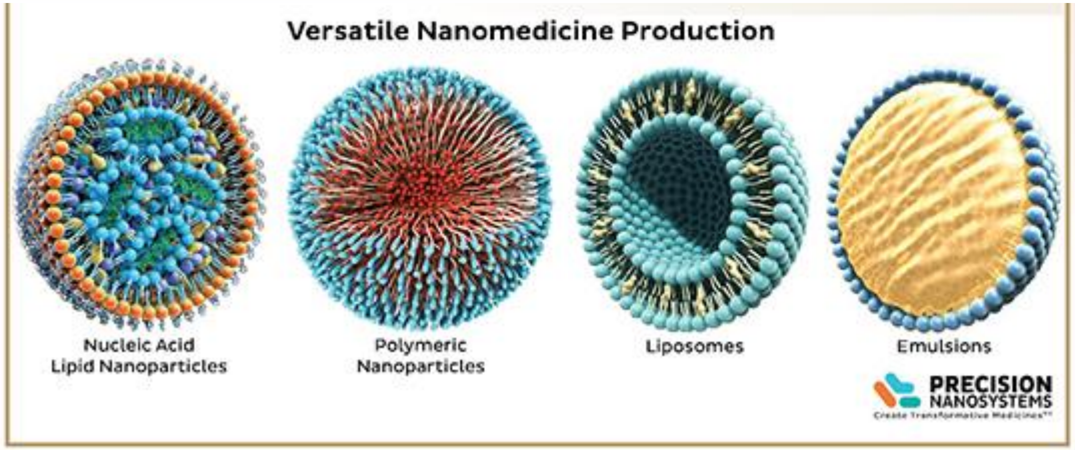






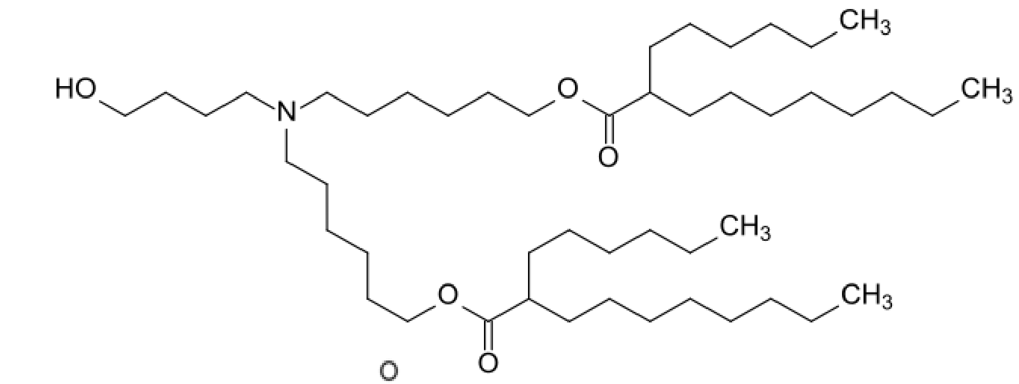

NanoAssemblr™ Systems
PRECISION NANOSYSTEMS
Spark™
Benchtop
Blaze™
8x Scale-Up
25-250 µL
1 - 15 mL
10 - 1000 mL
24L in 4.5h


Microfluidic Nanoparticle Production
Single NanoAssemblr™ Microfluidic Mixer
Multiple Parallel Microfludic Mixers for Seamless Scale-Up
PRECISION NANOSYSTEMS

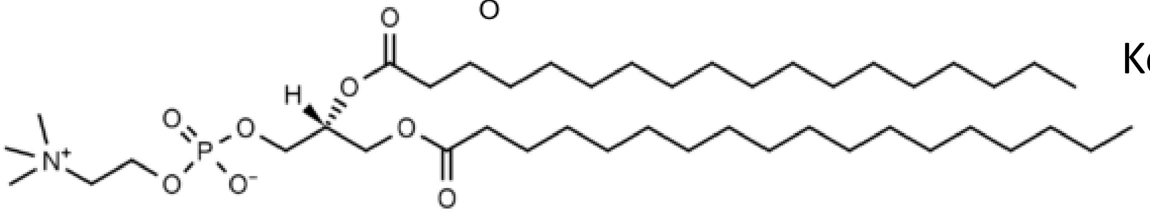

Versatile Nanomedicine Production
Nucleic Acid Lipid Nanoparticles
Polymeric Nanoparticles
Liposomes
Emulsions
PRECISION NANOSYSTEMS

Složení mRNA vakcíny Pfizer/BioNTech

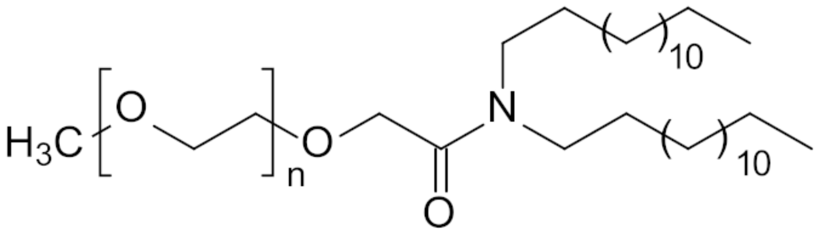
Složení mRNA vakcíny firmy Pfizer
Seznam pomocných látek
ALC-0315
ALC-0159
Kolfosceryl-stearát -DSPC
Cholesterol
Chlorid draselný
Dihydrogenfosforečnan draselný
Chlorid sodný
Dihydrát hydrogenfosforečnanu sodného
Sacharosa
Voda pro injekci



ALC-0315

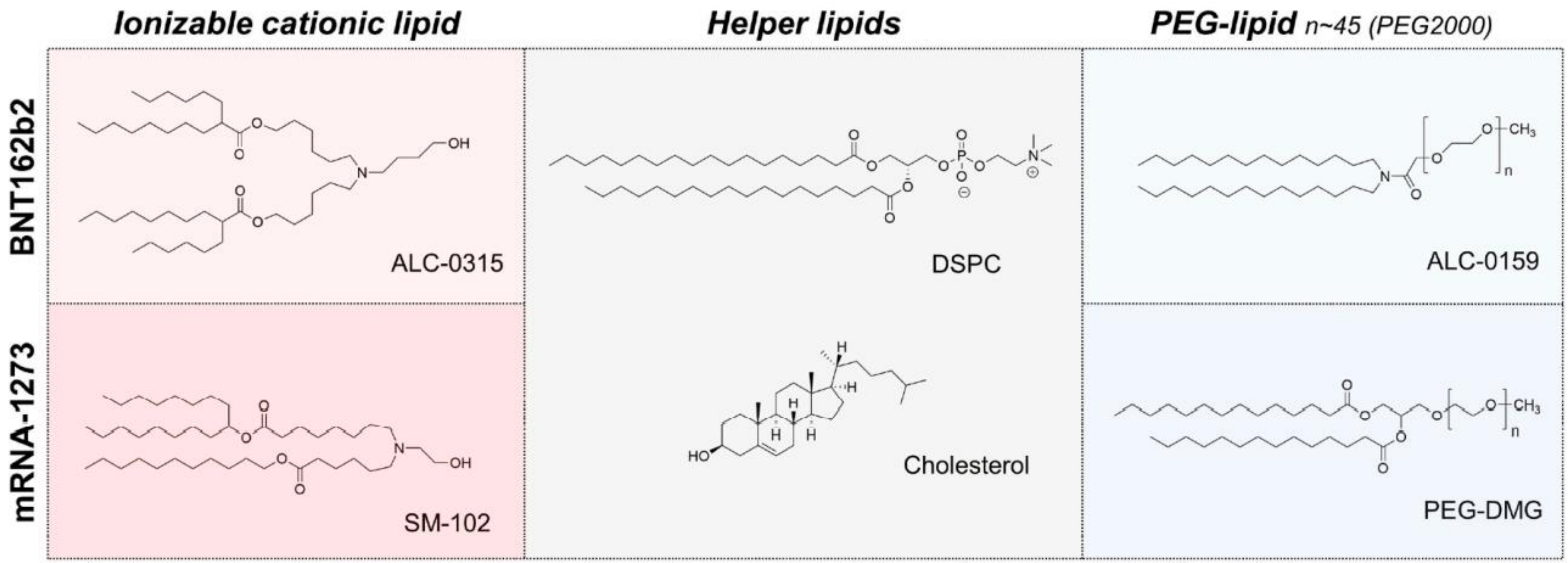


Kolfosceryl-stearát -**DSPC**

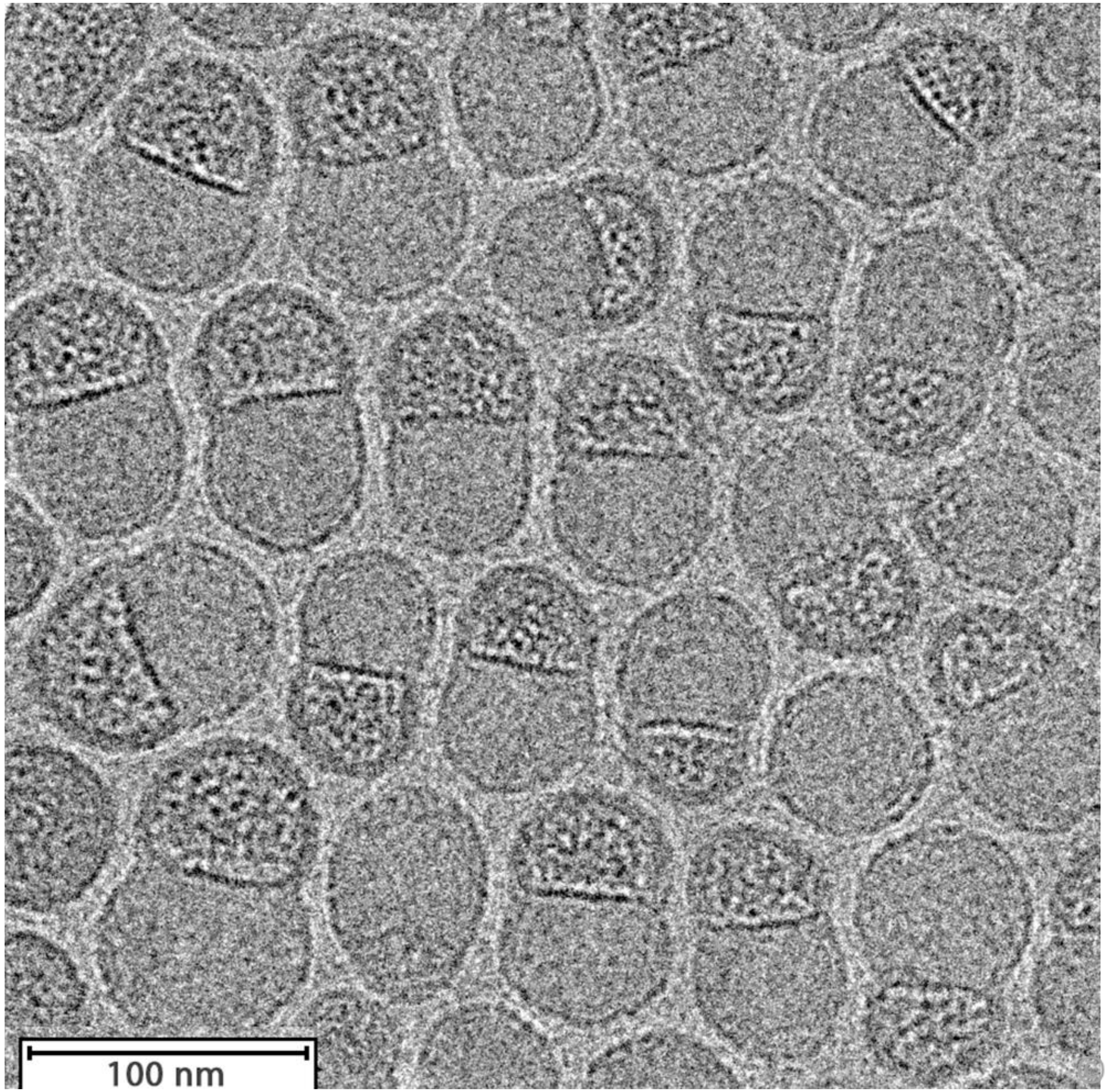


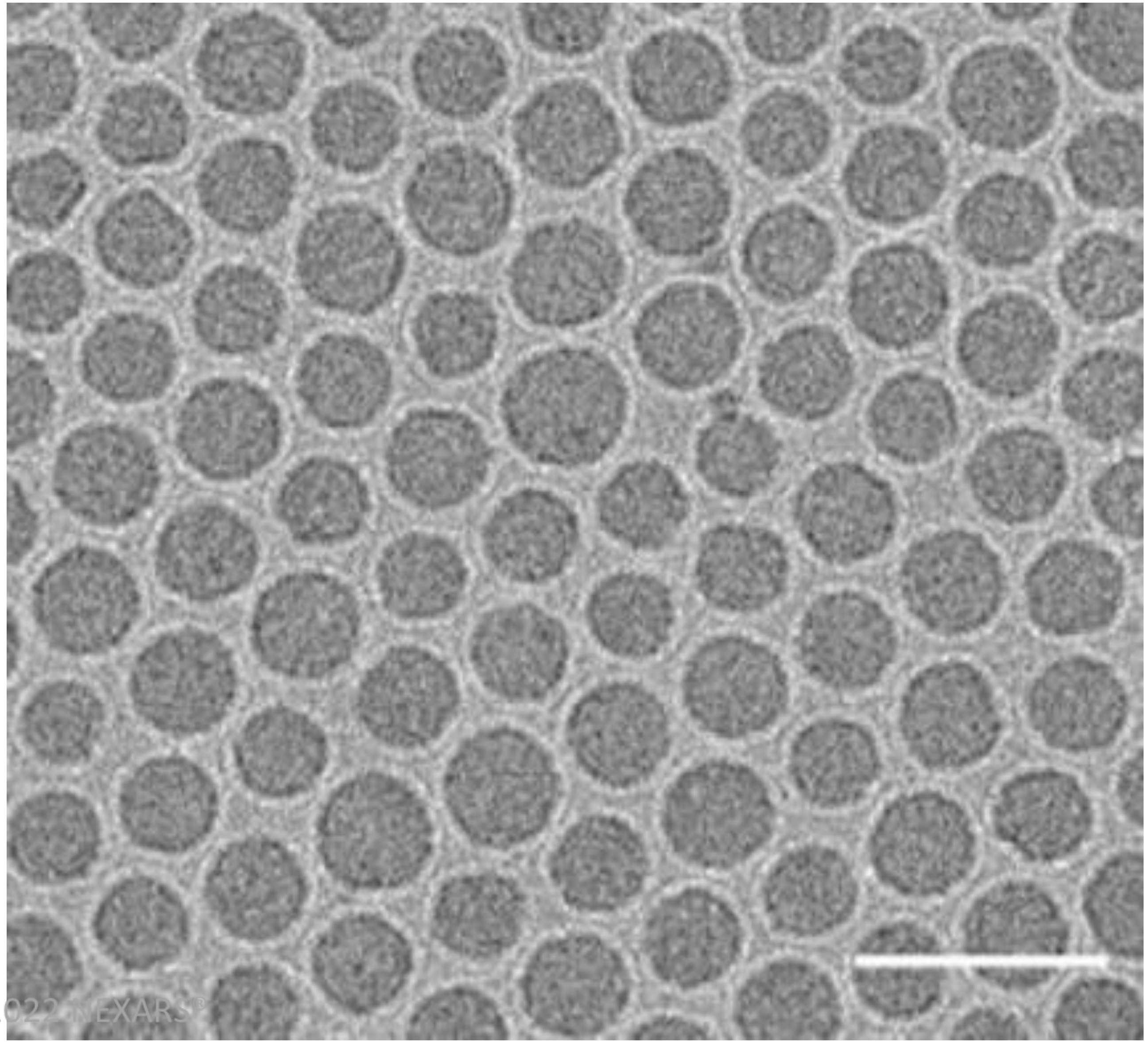
ALC-0159

Lipid used in the mRNA-LNP

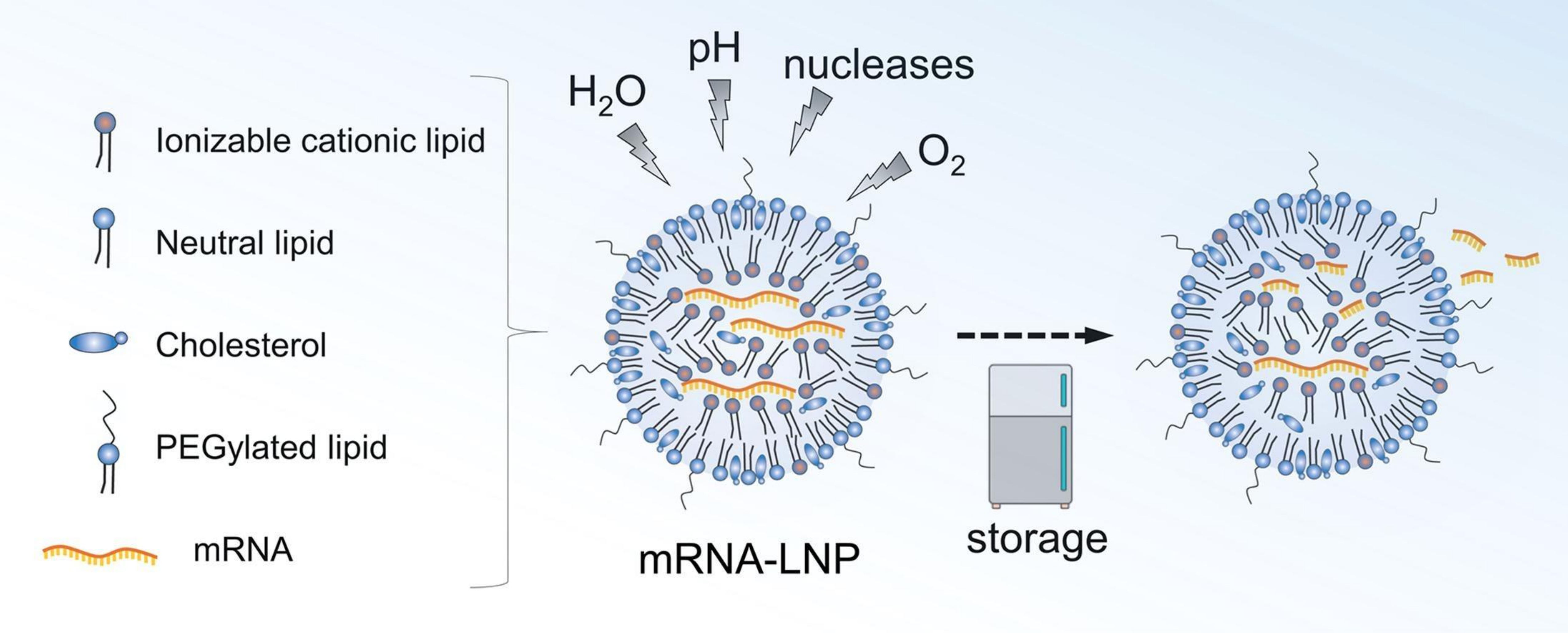


Cryo-electron microscopy of mRNA-LNP



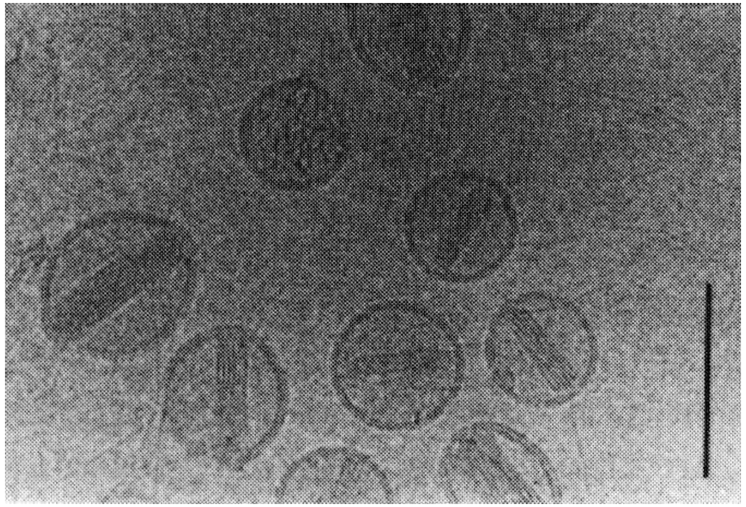


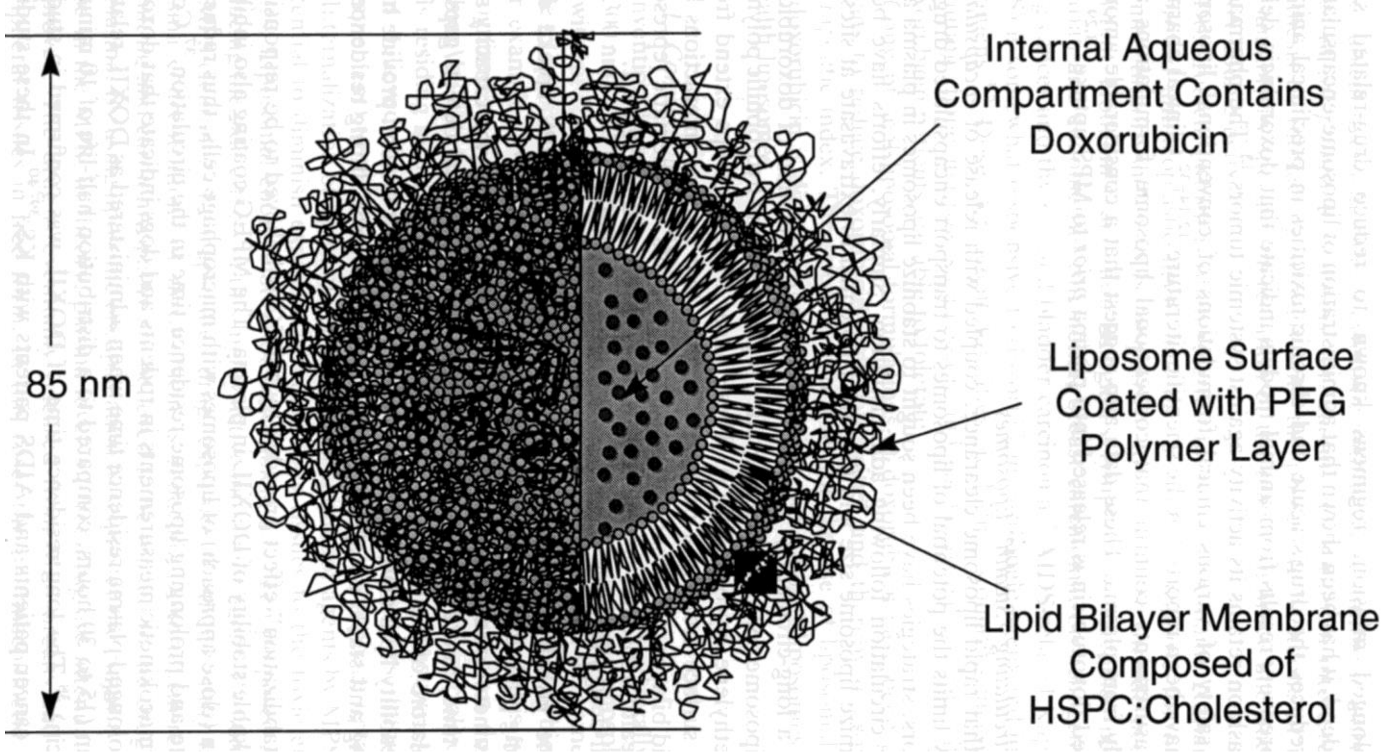
Stability of mRNA vaccines



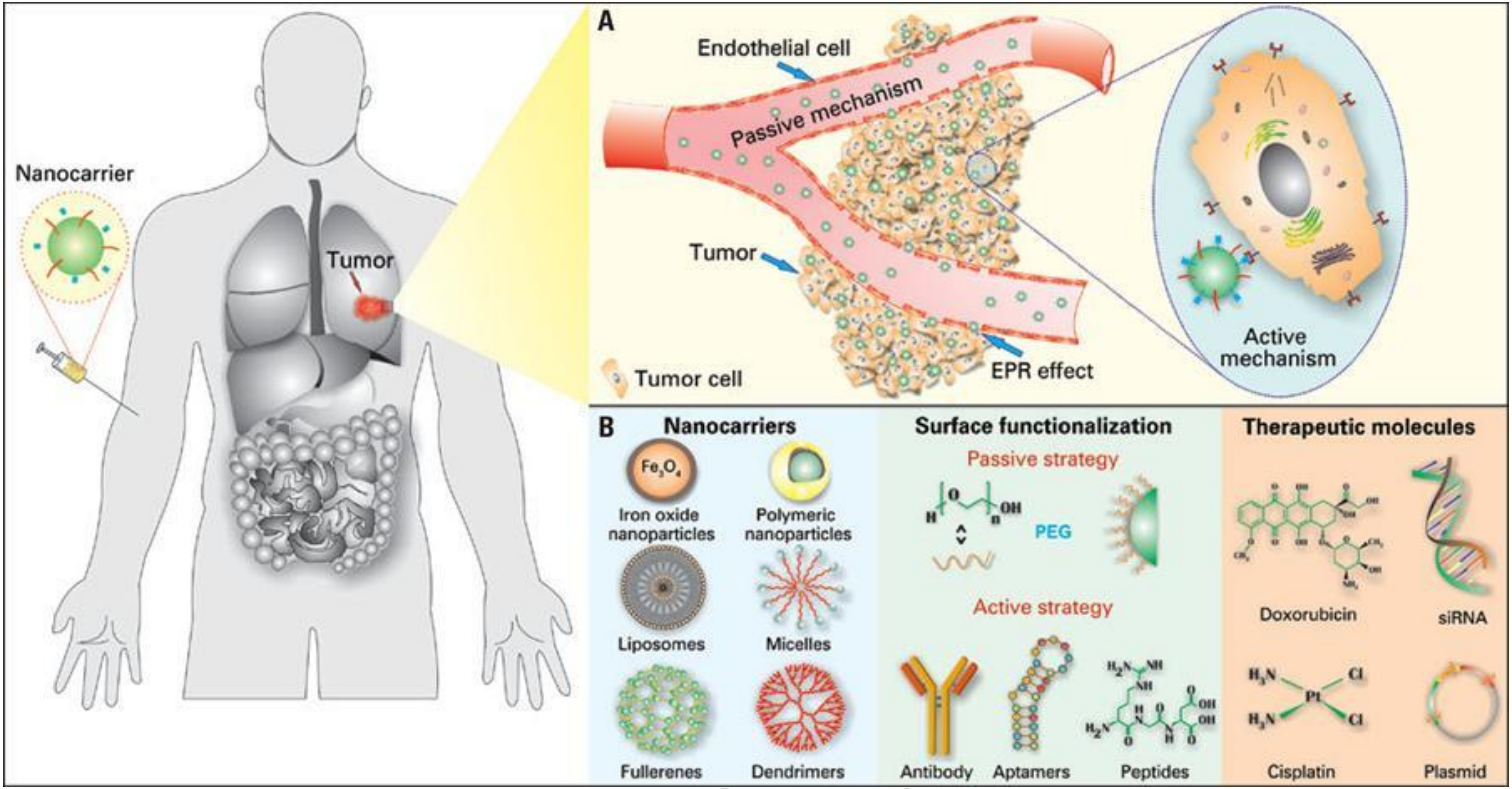
Stealth liposomes

Doxorubicin



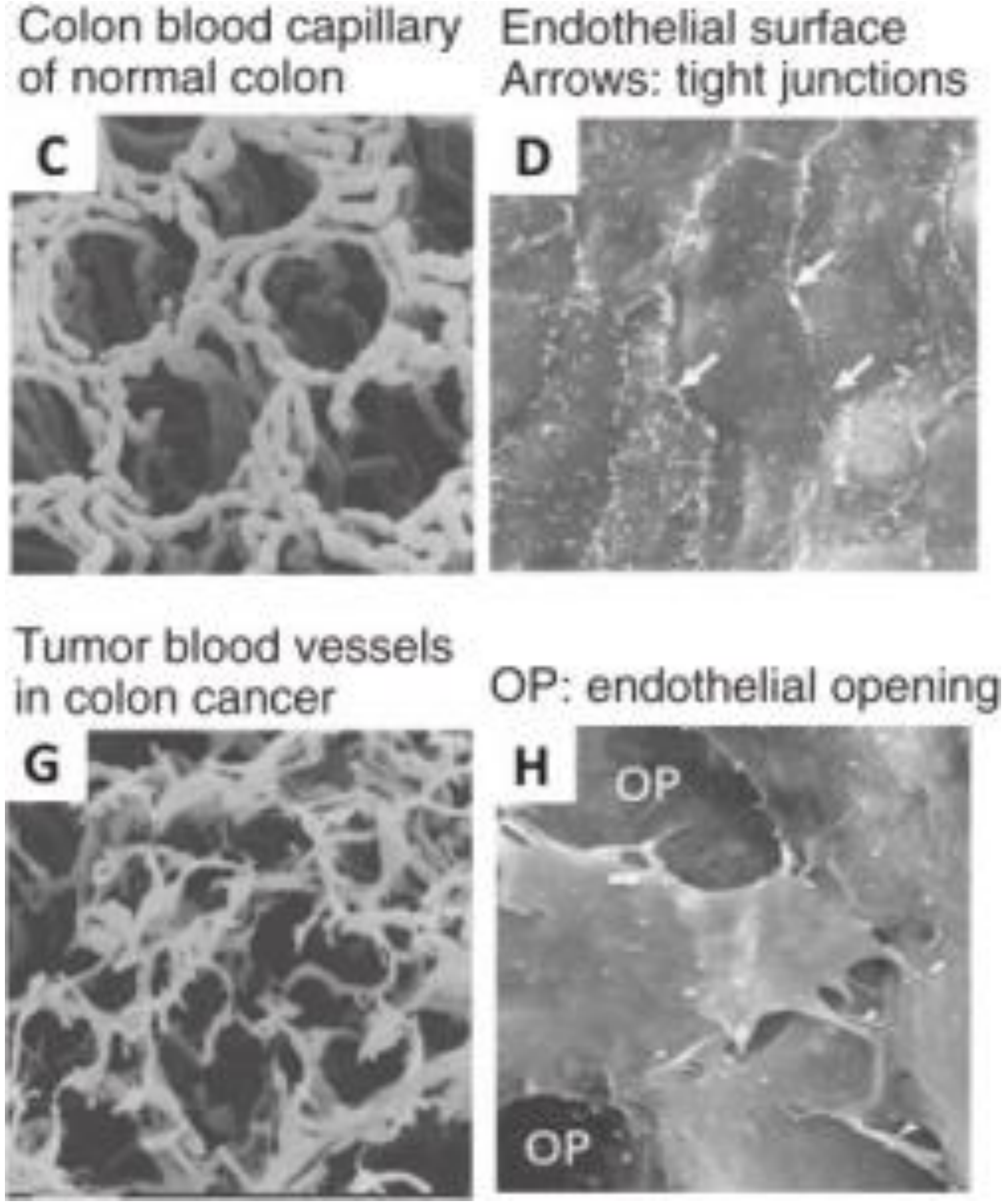


Nanoparticles as carriers of API



Fenestrations

Fig. 5. a. TEM cross sectional view showing fenestrated area of endothelial cell attenuation. ×14,300 **b.** Wide luminal view of sinusoidal endothelium showing the relationship between its fenestrated and non-fenestrated areas. The non-fenestrated areas of the endothelial cell radiate from the nuclear swelling (*N*) and separate fenestrated areas. In the latter areas,



Innate Immune Suppression by SARS-CoV-2 mRNA Vaccinations: The role of Gquadruplexes, exosomes and microRNAs

Preprint · January 2022
DOI: 10.22541/au.164276411.10570847/v1
Stephanie Seneff1, Greg Nigh2, Anthony M. Kyriakopoulos3, and Peter A McCullough4

Gunter Kampf poskytl údaje, které ukazují, že u očkovaných je nyní stejně pravděpodobné, že budou šířit nemoc jako u neočkovaných. Dospěl k závěru: Při rozhodování o opatřeních pro kontrolu veřejného zdraví se zdá být hrubě nedbalé ignorovat očkovanou populaci jako možný a relevantní zdroj přenosu.

Gunter Kampf provided data showing that the vaccinated are now as likely as the unvaccinated to spread disease. He concluded: It appears to be grossly negligent to ignore the vaccinated population as a possible and relevant source of transmission when deciding about public health control measures."

Je nezbytně nutné, aby celosvětová aplikace mRNA vakcin byla okamžitě zastavena dokud nejsou prováděny další studie, které urči rozsah v tomto článku nastíněných potenciálních patologických důsledků. Není možné, aby tato očkování byla považována za součást kampaně veřejného zdraví bez podrobné analýzy potenciálního dopadu vedlejších škodlivých účinků na lidské zdraví. Je také nezbytné aby VAERS a další monitorovací systémy byly optimalizovány pro detekci signálů souvisejících se zdravotními následky mRNA vakcinace, které jsme nastínili.

It is imperative that worldwide administration of the mRNA vaccinations be stopped immediately until further studies are conducted to determine the extent of the potential pathological consequences outlined in this paper. It is not possible for these vaccinations to be considered part of a public health campaign without a detailed analysis of the human impact of the potential collateral damage. It is also imperative that VAERS and other monitoring system be optimized to detect signals related to the health consequences of mRNA vaccination we have outlined.

Možné dopady mRNA vakcinace na imunitní systém

1. Rozsáhle zdokumentovaná **subverze vrozené imunity**, primárně prostřednictvím suprese IFN-α a jeho přidružené signalizační kaskády. Toto potlačení může vést k širokému spektru důsledků, mezi které patří reaktivace latentních virových infekcí a snížená schopnost účinného boje s budoucí infekcí.

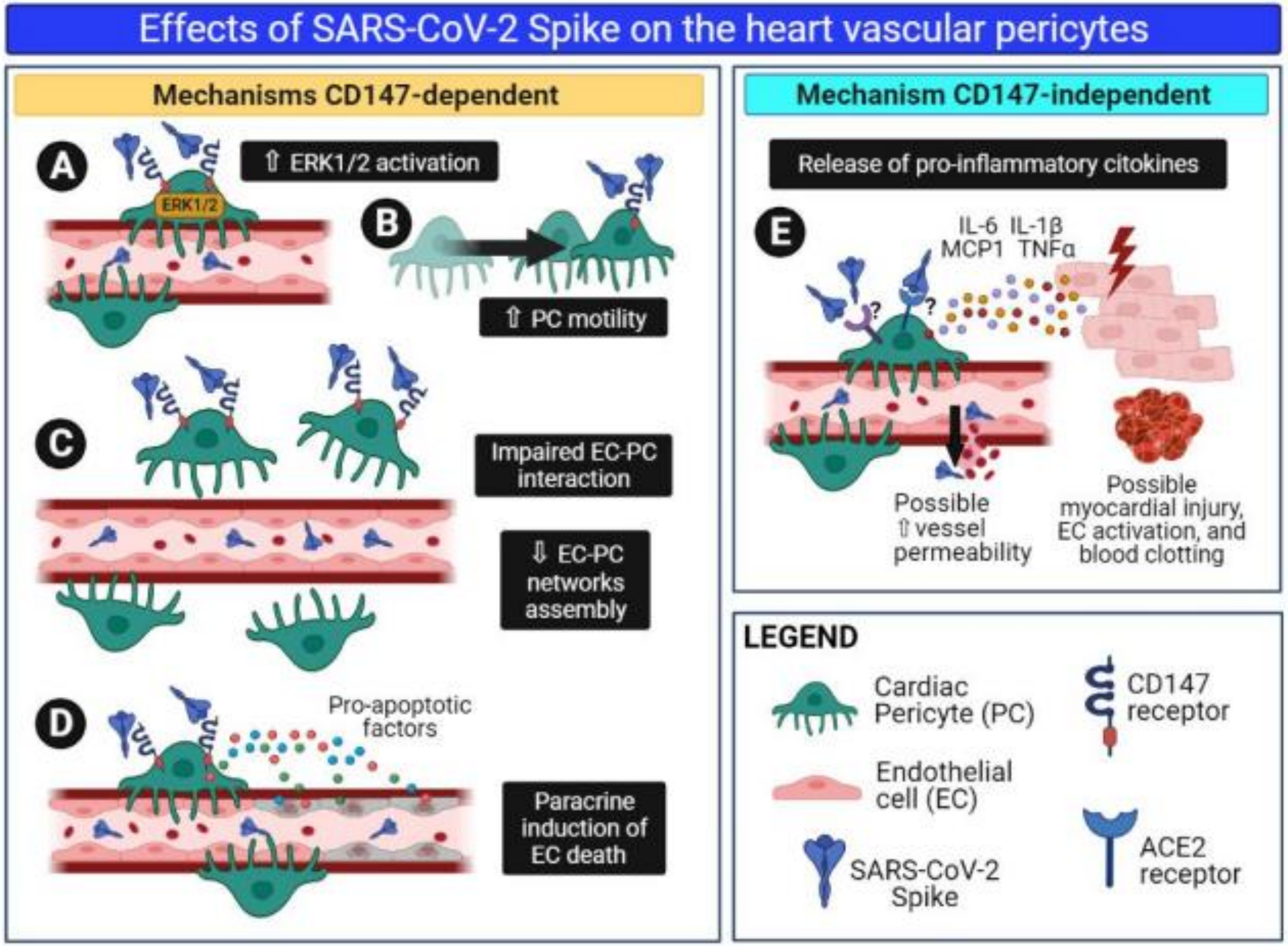
2. **Dysregulace systému** jak pro prevenci, tak pro detekci geneticky řízené maligní transformace v buňkách a následná potenciace těchto změn vakcinací.

3. Vakcinace mRNA potenciálně **narušuje intracelulární komunikaci** zajišťovanou exosomy a přiměje buňky k přijímání spikové mRNA, což vede k produkci vysoké hladiny exosomů nesoucích spike. To může vést k vážným důsledkům skrze zánětlivé stavy. Pokud by se některá z těchto potenciálích hrozeb plně realizovala, dopad na miliardy lidí po celém světě by mohla být obrovský a mohl by přispět jak ke krátkodobý, tak dlouhodobým onemocněním, které budou zatěžovat náš zdravotní systém.

Myokarditida

There has been considerable media attention devoted to the fact that COVID-19 vaccines cause myokarditis and pericarditis, with an increased risk in particular for men below the age of 30. Myocarditis is associated with platelet activation, so this could be one factor at play in the response to the vaccines. However, another factor could be related to **exosomes released by macrophages infected with the mRNA vaccines**, and the specific microRNAs found in those exosomes

Záněty srdce



The SARS-CoV-2 S protein alters cardiac pericyte function. Schematic summary of the research. We hypothesize that in patients with acute COVID-19, S protein molecules are cleaved from the virus particle and released from the respiratory system into the bloodstream. Through the circulation, isolated S protein fragments reach all organs of the body, including the heart. Here, the interaction of the S protein with the CD147 receptor on cardiac PCs triggers the ERK1/2 signalling (A) and provokes PC dysfunction, including increased cell motility (B) and decreased angiogenic activity in cooperation with coronary ECs (C). In addition, the S protein-CD147 interaction prompts cardiac PCs to release pro-apoptotic factors, which cause EC death (D). Finally, through a mechanism CD147-independent, the S protein induces PCs to release pro-inflammatory cytokines, which include MCP-1, IL-6, IL-1β, and TNF-α (E). These cytokines can damage neighbouring cardiomyocytes and activate ECs, potentially promoting blood to clot and increasing vascular permeability.

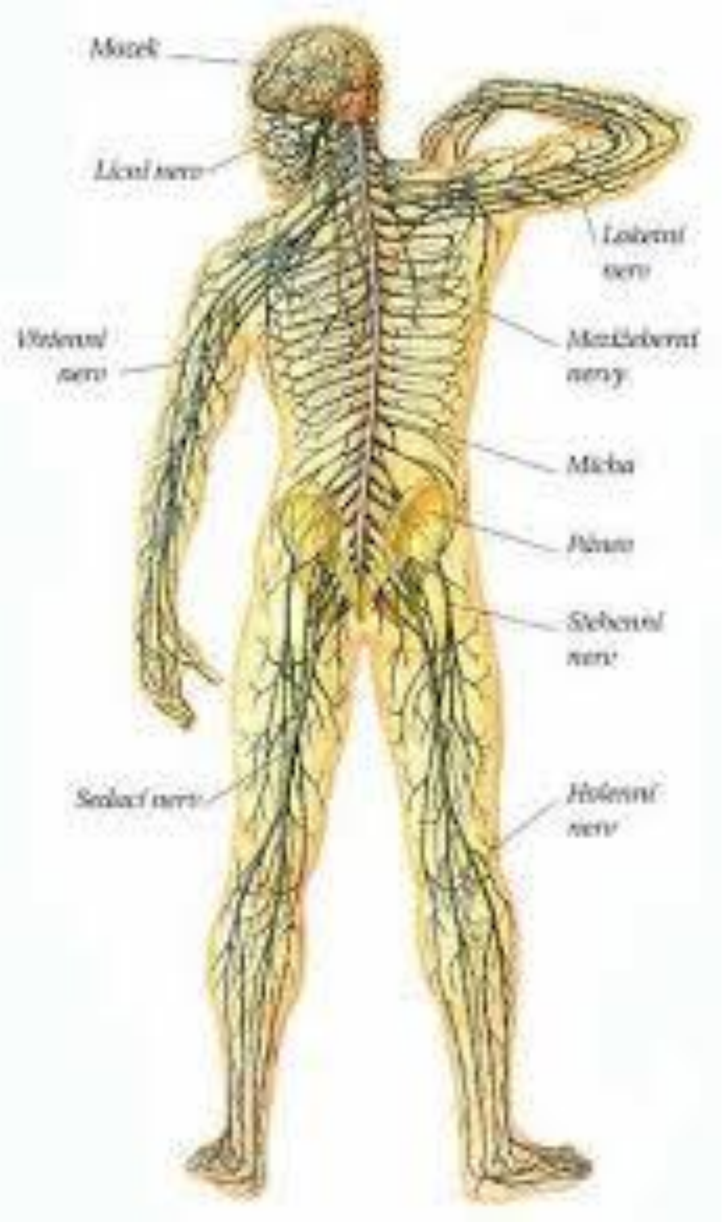
The SARS-CoV-2 Spike protein disrupts human cardiac pericytes function through CD147-receptor-mediated signalling: a potential non-infective mechanism of COVID-19 microvascular disease Elisa Avolio, et al.
Clinical Science doi: 10.1042/CS20210735

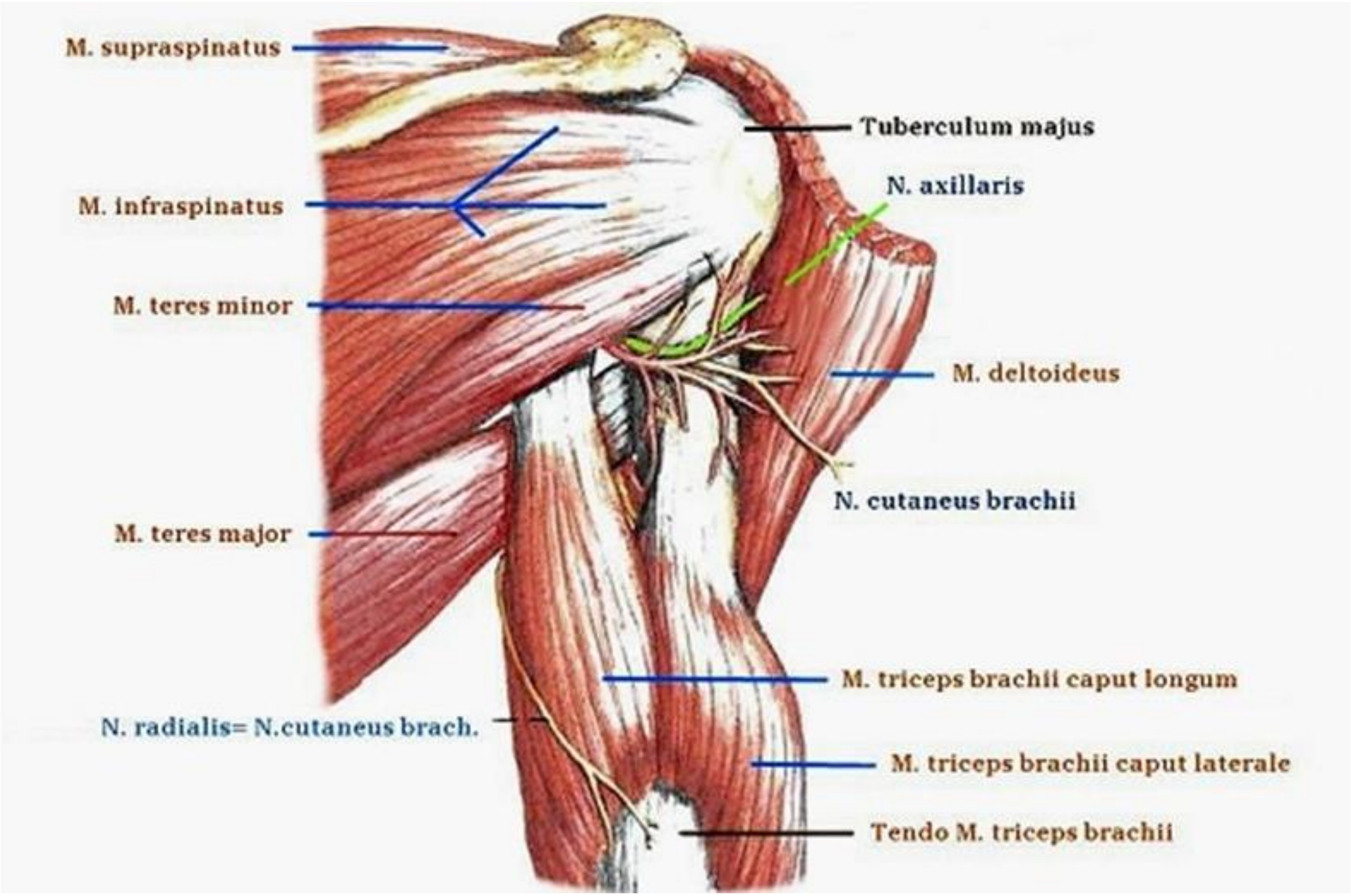
CD147-spike protein is a novel route for SARS-CoV-2 infection to host cells Signal Transduction and Targeted Therapy (2020) 5:283

Table 1. Number of events in the VAERS database from 1990 to December 12, 2021, where several terms indicating cancer occurred in association with COVID-19 vaccines or with all other vaccines, along with the ratio between the two counts. Counts were restricted to data from the United States. Note that counts for all the other vaccines are totals for 31 years, whereas the COVID-19 counts are for a single class of vaccines over less than one year.

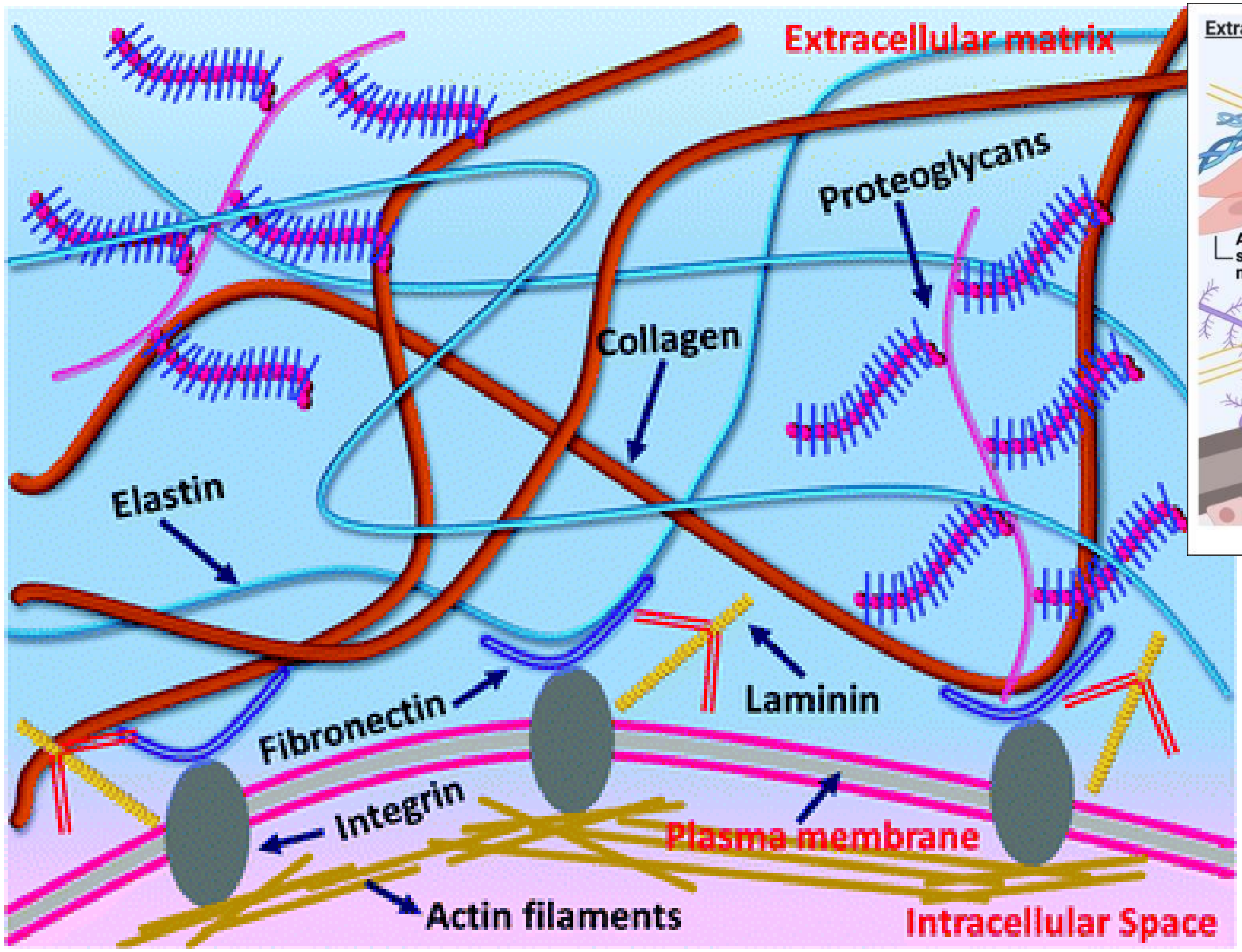
Cancer Reports to VAERS	Counts COVID-19 vaccines	Counts All other vaccines	Ratio: COVID-19 vaccines/ All other vaccines
Breast	147	49	3.00
Prostate	32	13	2.46
Lung	82	46	1.78
Colorectal/Colon	30	7	5.00
Ovarian	24	7	3.43
Uterine	11	5	2.20
Uterine leiomyoma	80	12	6.67
Lymphoma (subtype not identified)	52	47	1.11
B-cell lymphoma	19	3	6.33
Follicular lymphoma	13	1	13.00
Metastasis	13	7	1.86
Glioblastoma	16	3	5.33
Brain neoplasm	22	34	0.65
Neoplasm (unspecified)	71	82	0.87
Hepatic	40	8	5.00
Pancreatic	27	6	4.50
Prostate	23	13	1.77
Squamous cell carcinoma (not otherwise characterized)	33	25	1.32
Total	**735**	**368**	**2.00**

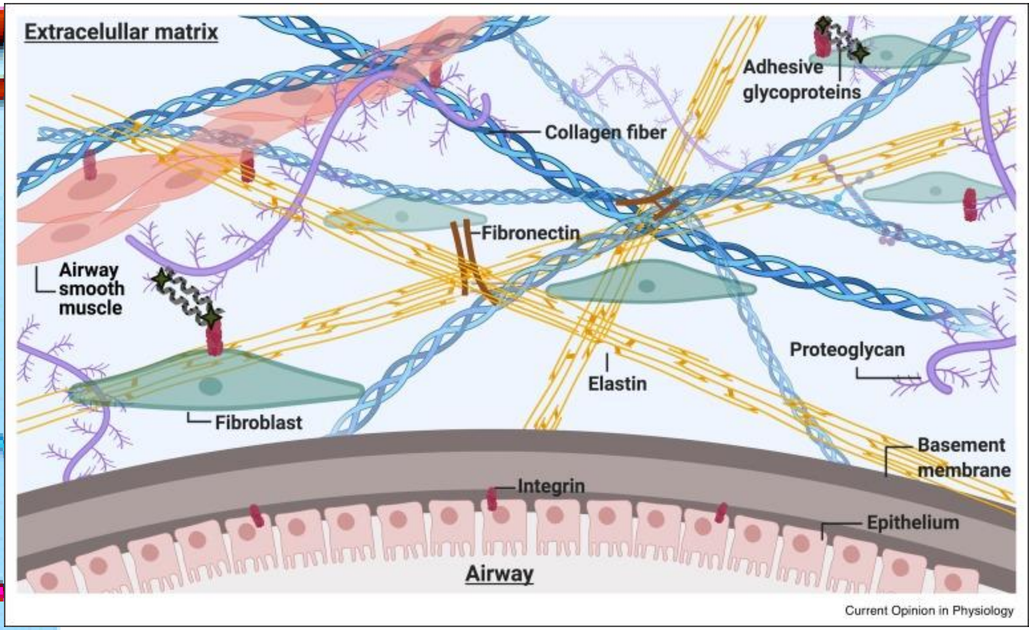
15.2 VAERS Signal for Cancer


Mozek
Lícní nerv
Loketní nerv
Vřetenní nerv
Mezižeberní nervy
Mícha
Pánev
Stehenní nerv
Sedací nerv
Holenní nerv


M. supraspinatus
Tuberculum majus
N. axillaris
M. infraspinatus
M. teres minor
M. deltoideus
N. cutaneus brachii
M. teres major
M. triceps brachii caput longum
N. radialis= N.cutaneus brach.
M. triceps brachii caput laterale
Tendo M. triceps brachii

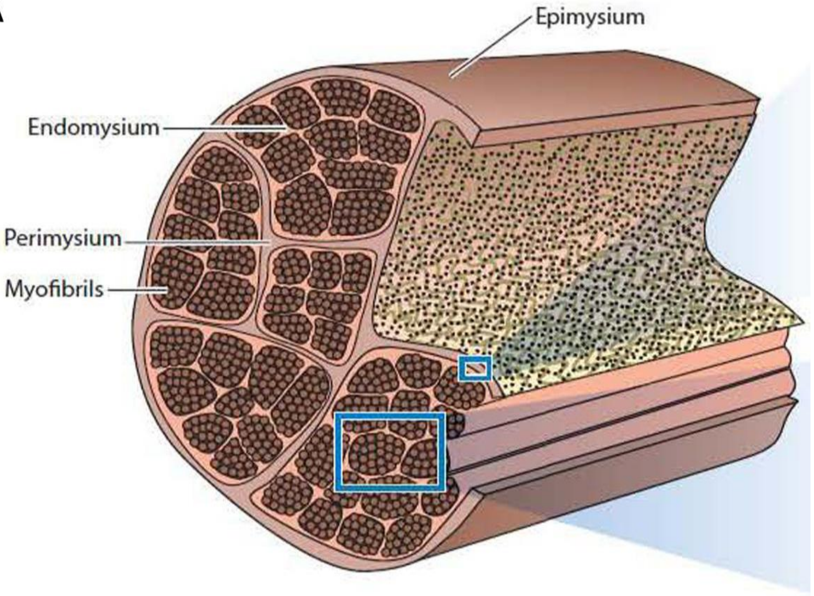
Schematic representation of various components in the extracellular matrix (ECM)



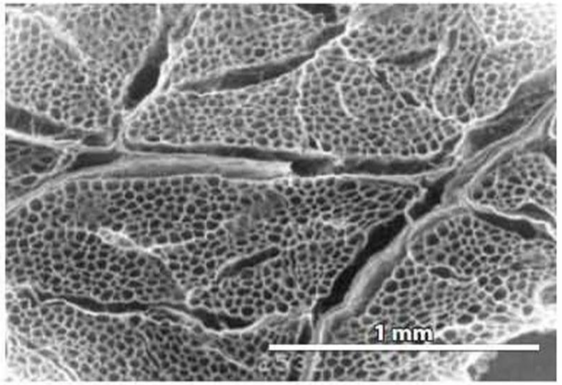


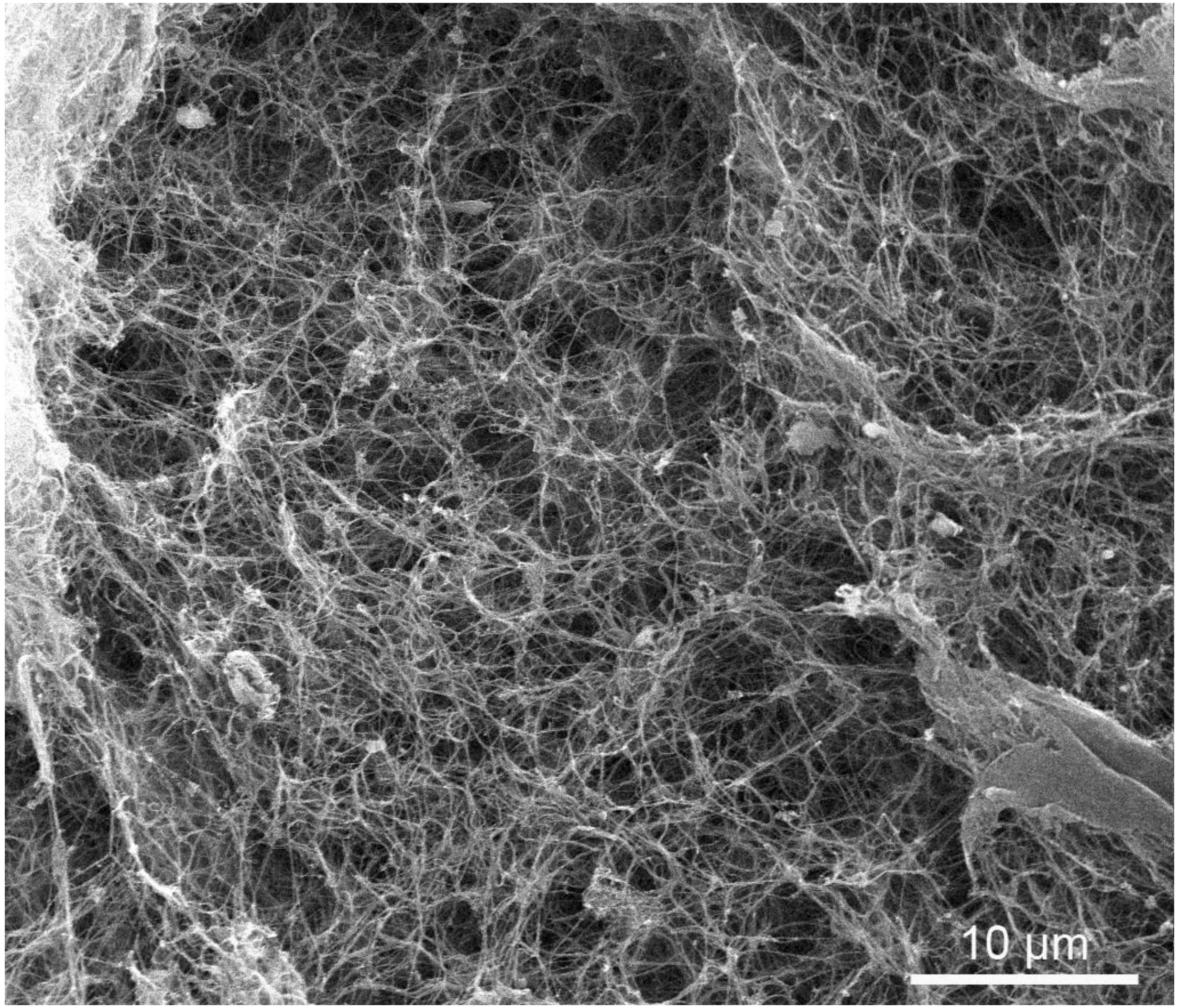
Extracellular matrix

A



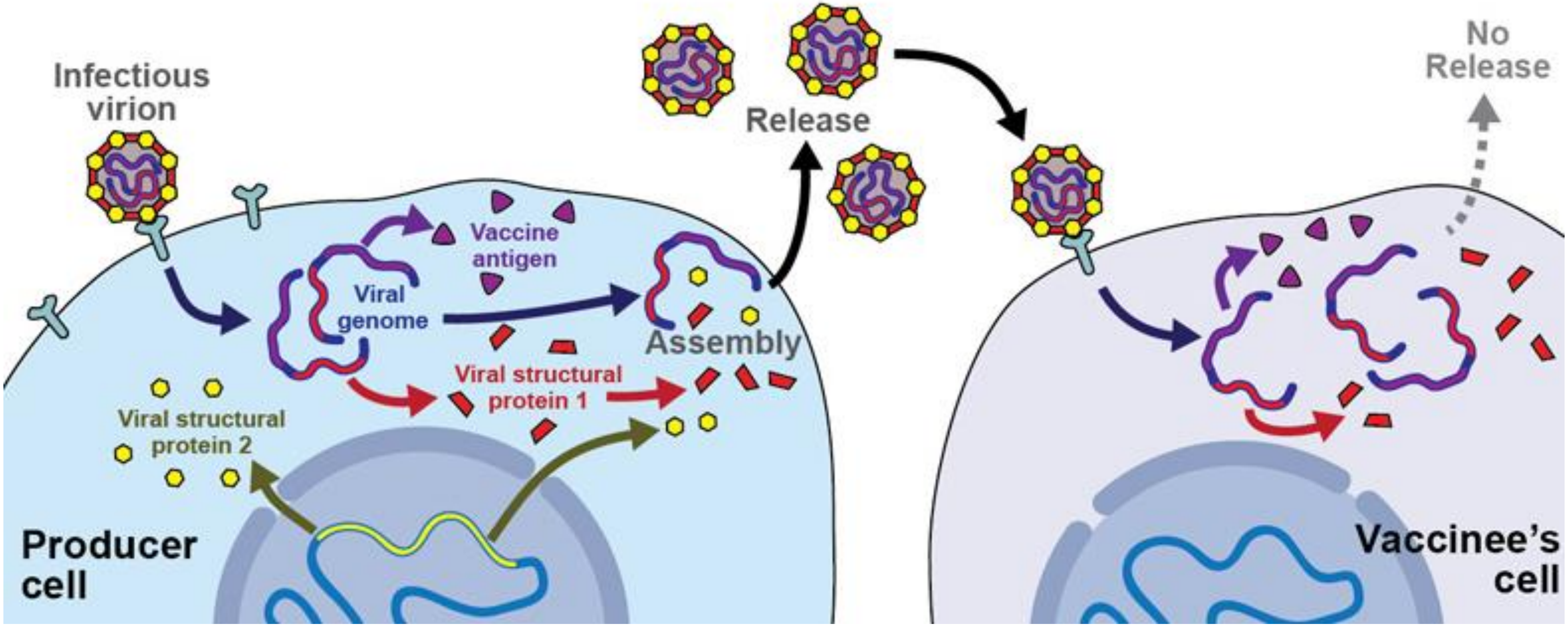
D





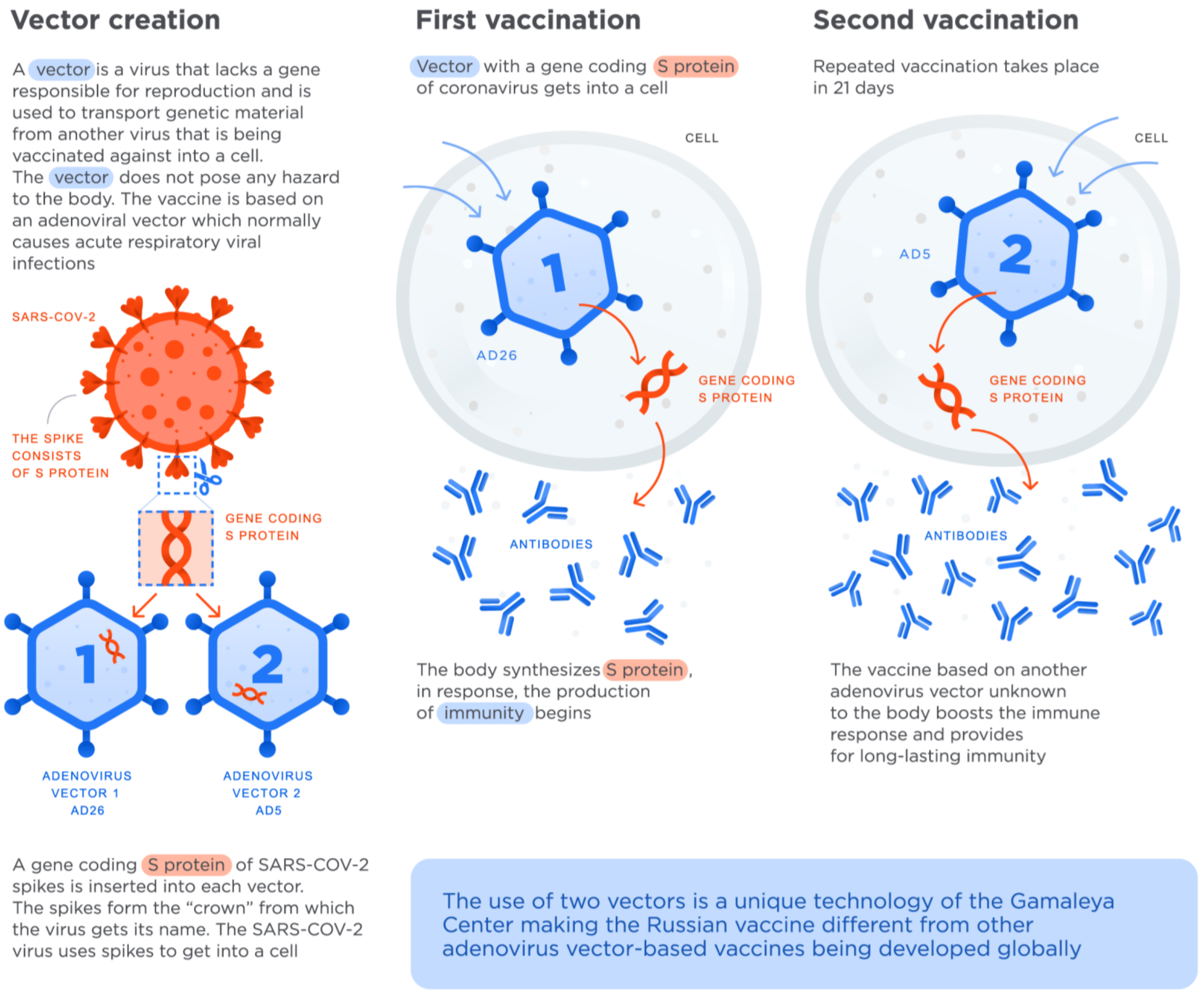
Replikačně defektní adenovirové vakcíny Astra Zeneca, Jansen, Sputnik V

Produkce vakcíny **Imunizace**



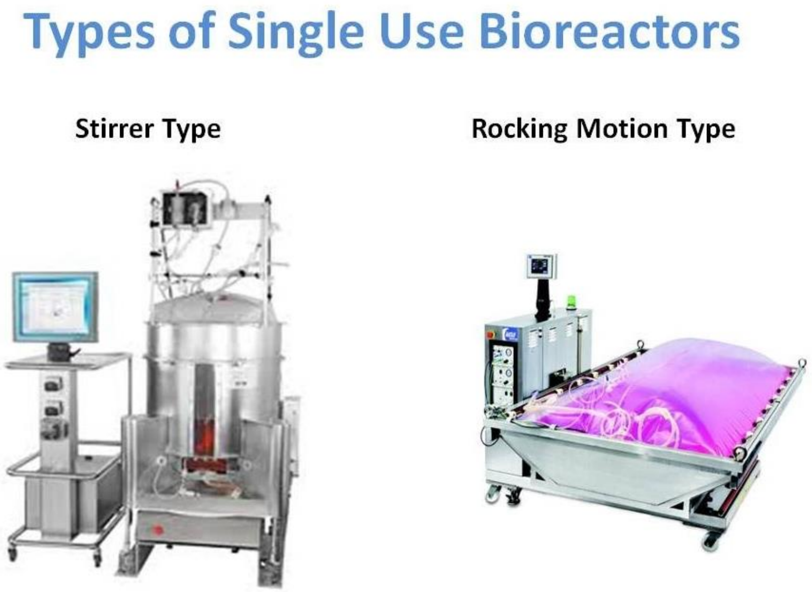
Swiss Med Wkly. 2017;147:w14465

Vakcína Sputnik V – dvouvektorová vakcína



Source: Gamaleya Center, RDIF, 2020

Jednorázové bioreaktory



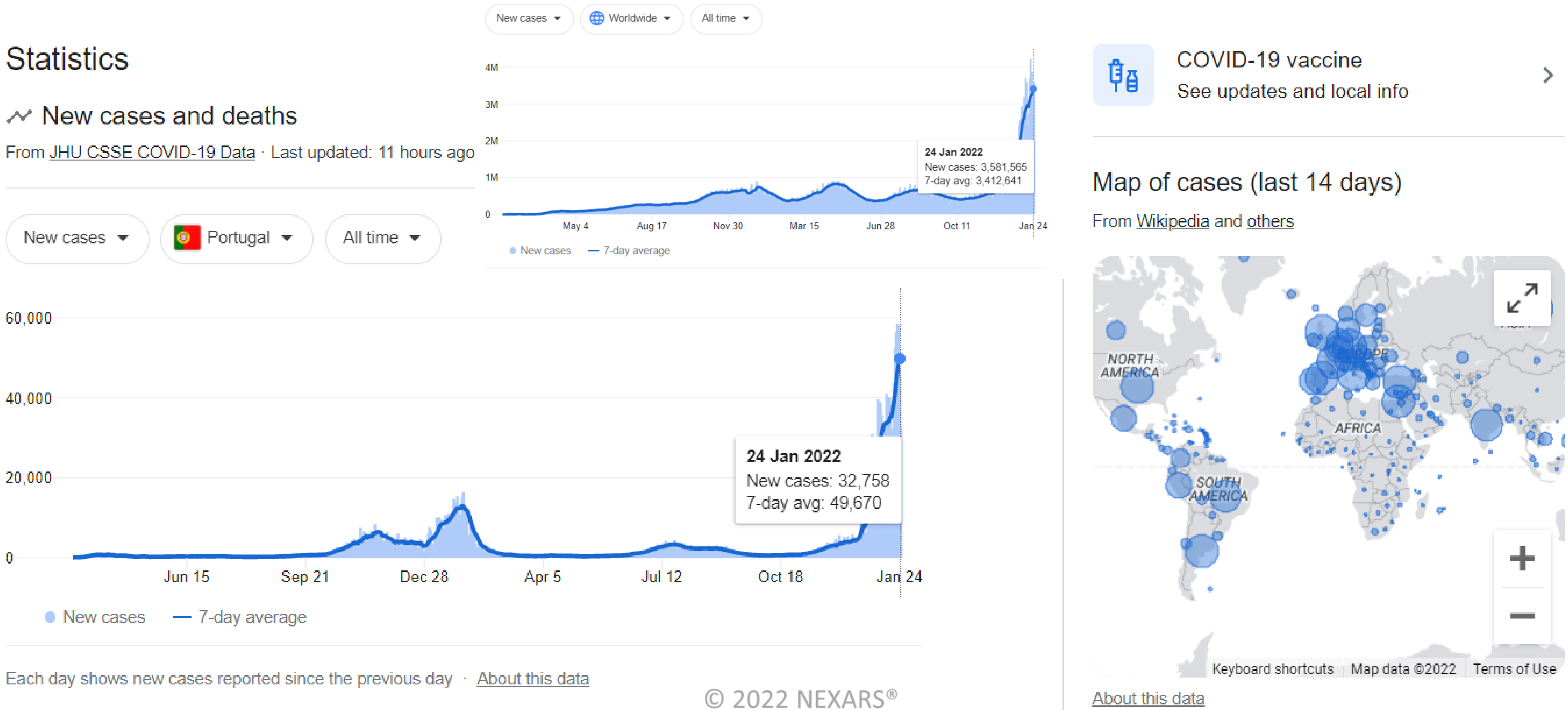
Tři aspekty současné vakcinační kampaně

1. Vakcinace v epidemii – tlak na vznik nových mutací, vznik ADE efektu

2. Vakcinace toxinem – vedlejší reakce

3. Fakticky se u mRNA vakcín jedná o intravenózní vakcinaci – neexistuje kontrola nad distribucí v organismu a mírou exprese ve tkáních

Stav počtu pozitivně diagnostikovaných ve světě a v Portugalsku



Která autorita v České republice kontroluje kvalitu šarží dovážených vakcín proti Covid-19 používaných k vakcinaci obyvatel ?

Návrh souborů testů pro analýzu genetických (mRNA a DNA) a proteinových vakcín

1. Získání ověřených šarží vakcín s historií skladování, notářské potvrzení pravosti
2. Vizuální posouzení stavu vakcín
3. Změření transmitance na přístroji Spekord 600
4. Změření distribuce velikosti, počtu částic a ζ-potenciálu na přístroji ZetaSizer Ultra+
5. Analýza částic pomocí diferenciální gradientové ultracentrifugace a analýza jednotlivých frakcí pomocí DLS a elektronové mikroskopie
6. Změření distribuce velikosti a počtu částic na přístroji nanoAnalyzer
7. Analýza částic ve vakcíně pomocí TEM, SEM a cryoTEM, posouzení strukturní integrity nanočástic
8. Analýza mRNA (mRNA vakcíny) pDNA (vektorové virové vakcíny) ve vakcínách; intaktnost mRNA respektive pDNA, kvantifikace a množství nukleové kyseliny pomocí horizontální elektroforézy; konfirmace sekvence; exaktní kvantifikace metodou QRT-PCR
9. Funkčnost – transfekce a exprese S-proteinu in vitro a kvantifikace proteinu metodou ELISA, průkaz exprese proteinu v buňkách metodou konfokální mikroskopie a imunochemické vizualizace
10. Analýza pomocí elektroforetických metod a případně MS

V případe zjištění dalších částic, které nejsou ve složení vakcín deklarovány, budou tyto částice podrobeny další analýze pomocí Ramanovy spektroskopie a mikroskopie, elektronové mikroskopie s analýzou prvků (EDX detektor)

NEXARS

VE ZDRAVÍ JE BUDOUCNOST

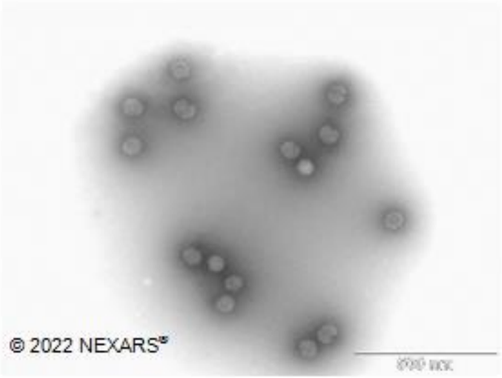
Česká výzkumná organizace

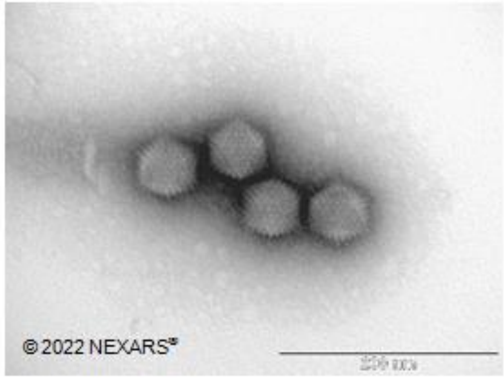
Unikátní biotechnologická výzkumní a výrobní facilita

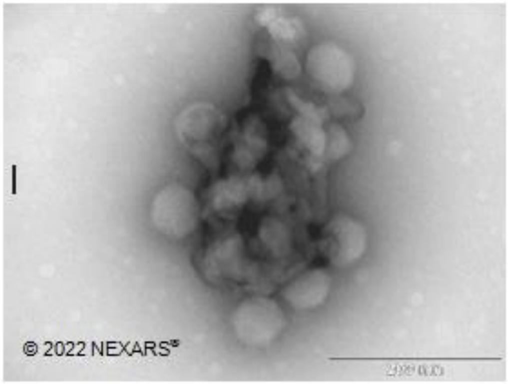
The Campus Science Park, Brno

Zvládnutí analytických metod

Ukázka některých výsledků analýzy vakcíny Jansen

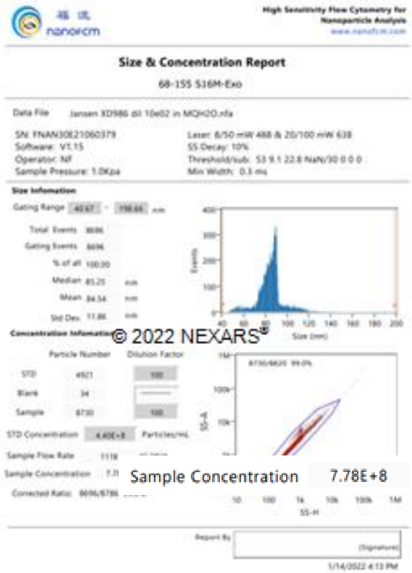


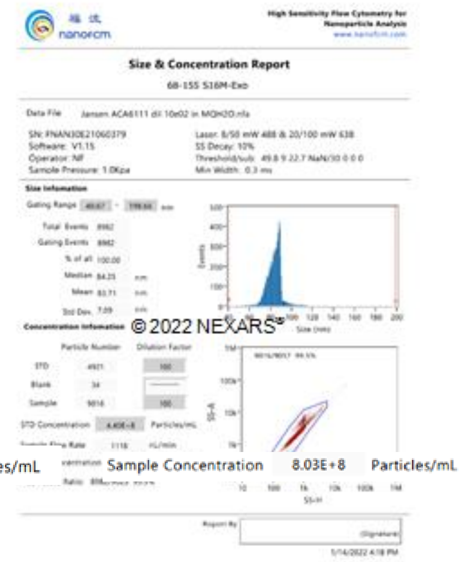




Transmisní elektronová mikroskopie
Vlevo nahoře – přehledový snímek ukazující některé již narušené virové vektory
Vpravo nahoře - detail neporušených virových vektorů
Vlevo dole - detail agregátu virových vektorů se zbytky rozpadlých virových vektorů

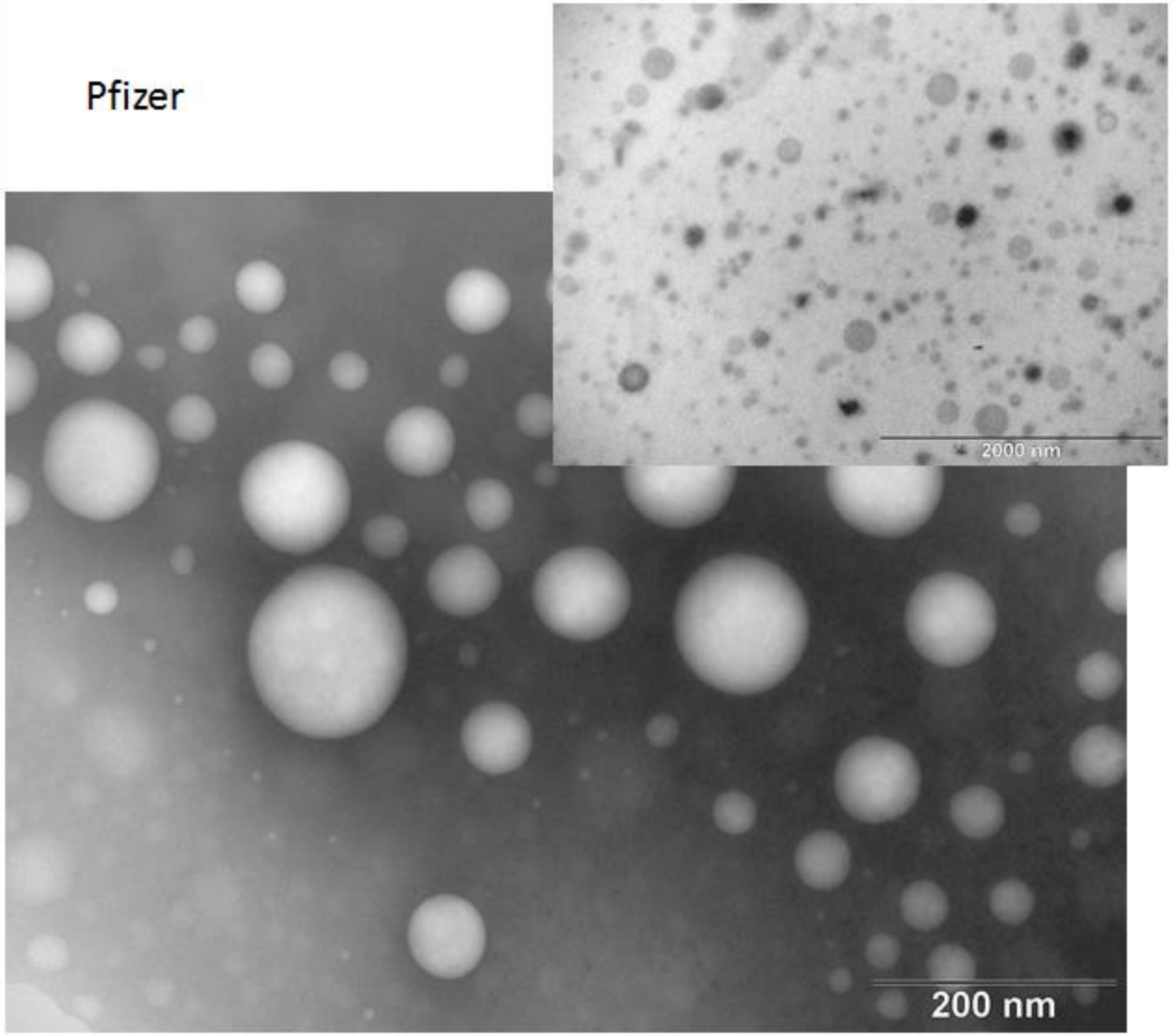
Analýza vakcín na unikátním přístroji Nanoflow Analyzer (NanoFlow) v laboratoři NEXARS.



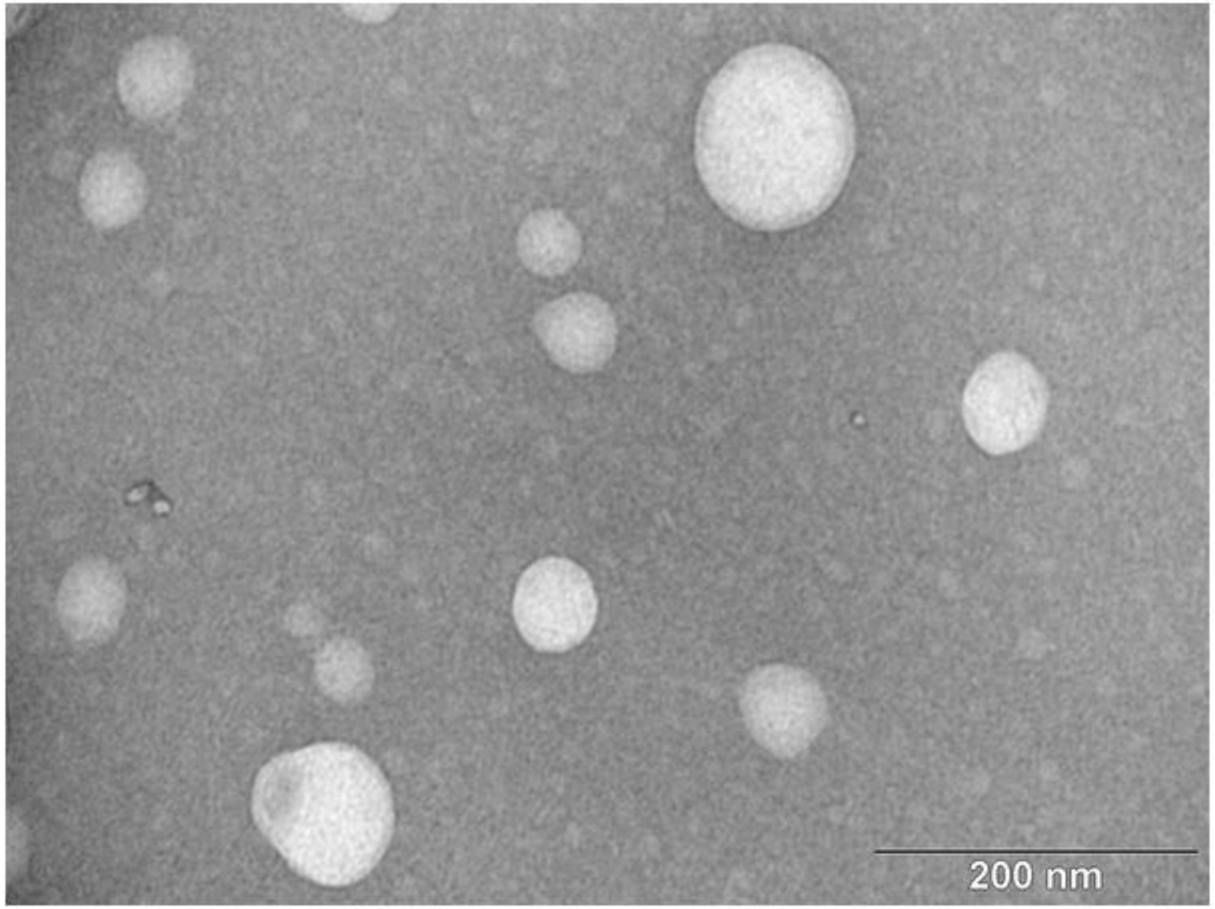


Cryo-electron microscopy of mRNA-LNP

Pfizer

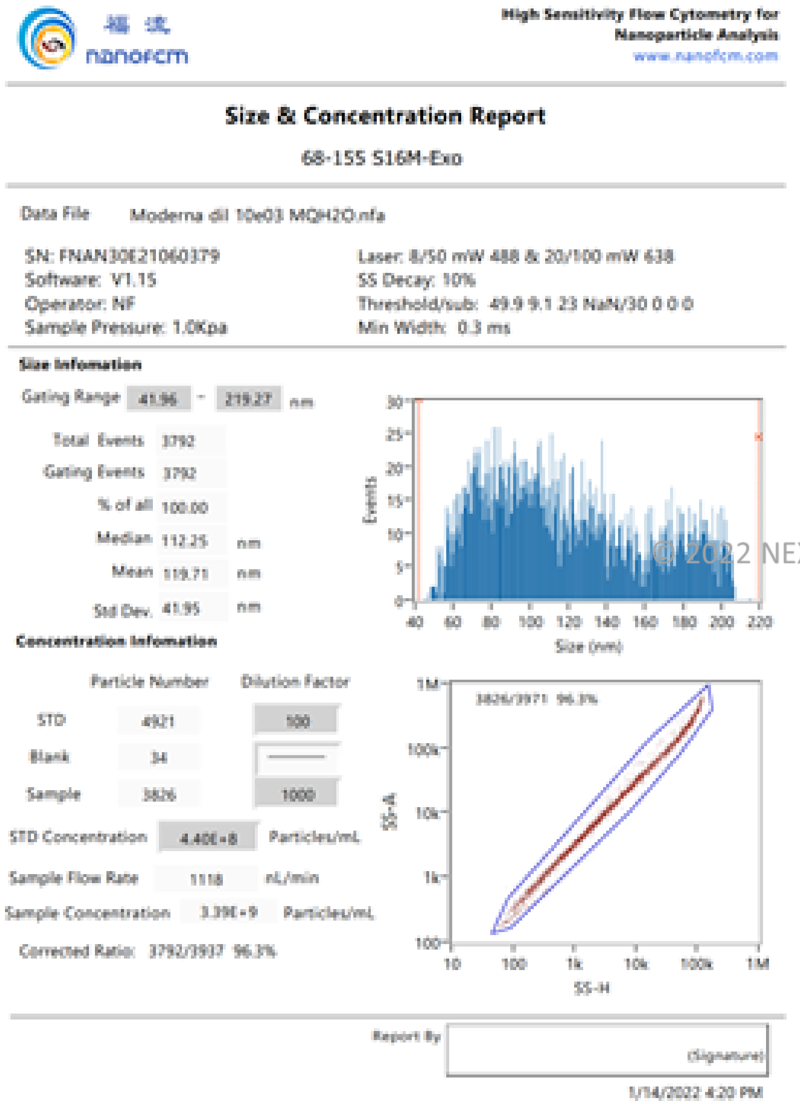


Moderna



Analýza metodou průtokové nanocytometrie

Ukázka některých výsledků analýzy vakcíny Moderna



福 流 nanoFCM

High Sensitivity Flow Cytometry for Nanoparticle Analysis
www.nanofcm.com

Size & Concentration Report

68-155 S16M-Exo

Data File Moderna dil 10e03 MQH2O.nfa

SN: FNAN30E21060379
Software: V1.15
Operator: NF
Sample Pressure: 1.0Kpa

Laser: 8/50 mW 488 & 20/100 mW 638
SS Decay: 10%
Threshold/sub: 49.9 9.1 23 NaN/30 0 0 0
Min Width: 0.3 ms

Size Infomation

Gating Range 41.96 - 219.27 nm

Total Events	3792	
Gating Events	3792	
% of all	100.00	
Median	112.25	nm
Mean	119.71	nm
Std Dev.	41.95	nm

Concentration Infomation

	Particle Number	Dilution Factor
STD	4921	100
Blank	34	
Sample	3826	1000

STD Concentration 4.40E+8 Particles/mL

Sample Flow Rate 1118 nL/min

Sample Concentration 3.39E+9 Particles/mL

Corrected Ratio: 3792/3937 96.3%

Report By (Signature)

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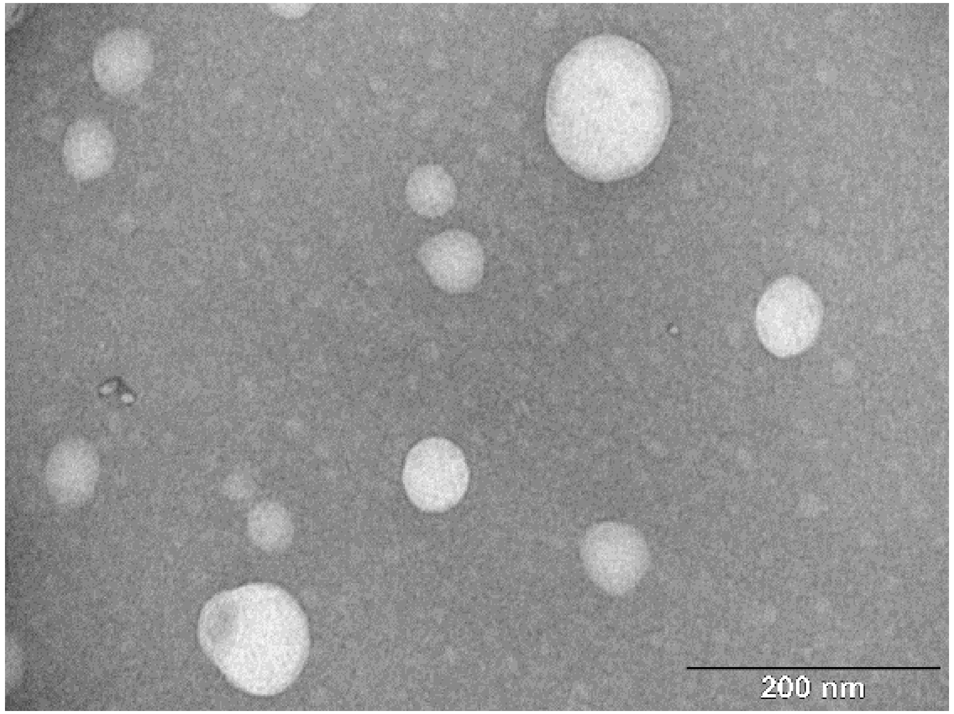
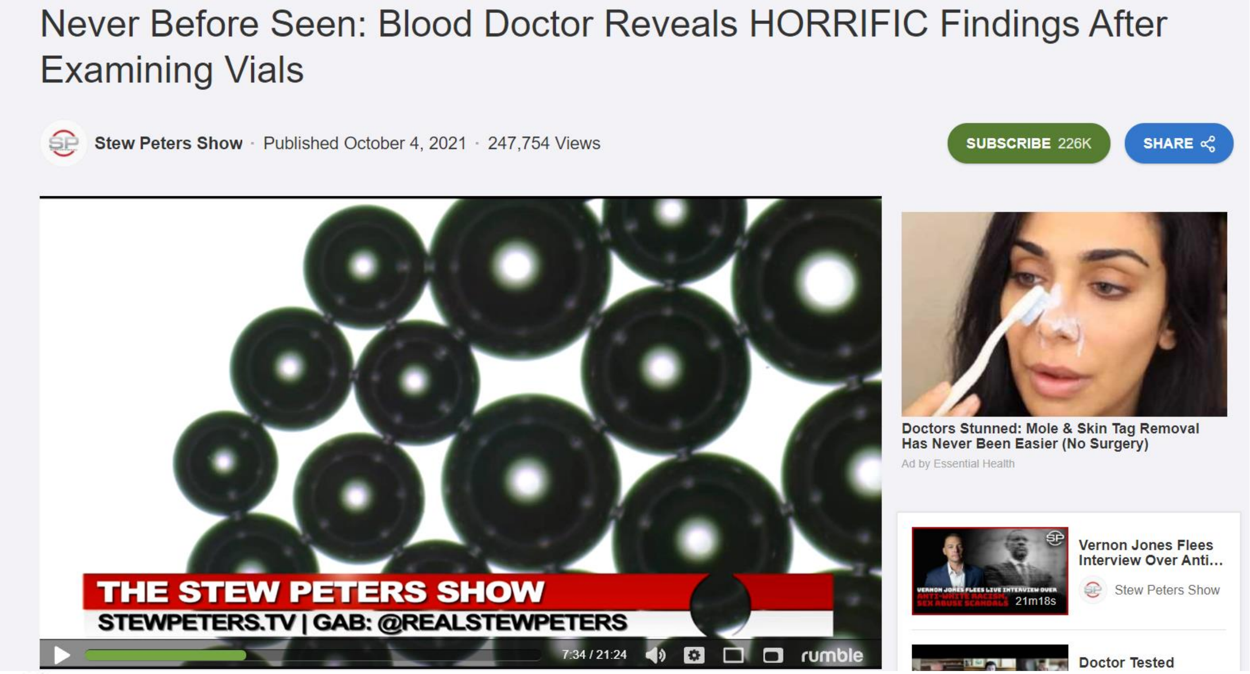


Sample Concentration 3.39E+9 Particles/mL

Omyly a fake news



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Review Article — **Open Access**

A Conceptual Review on Micro Bubbles

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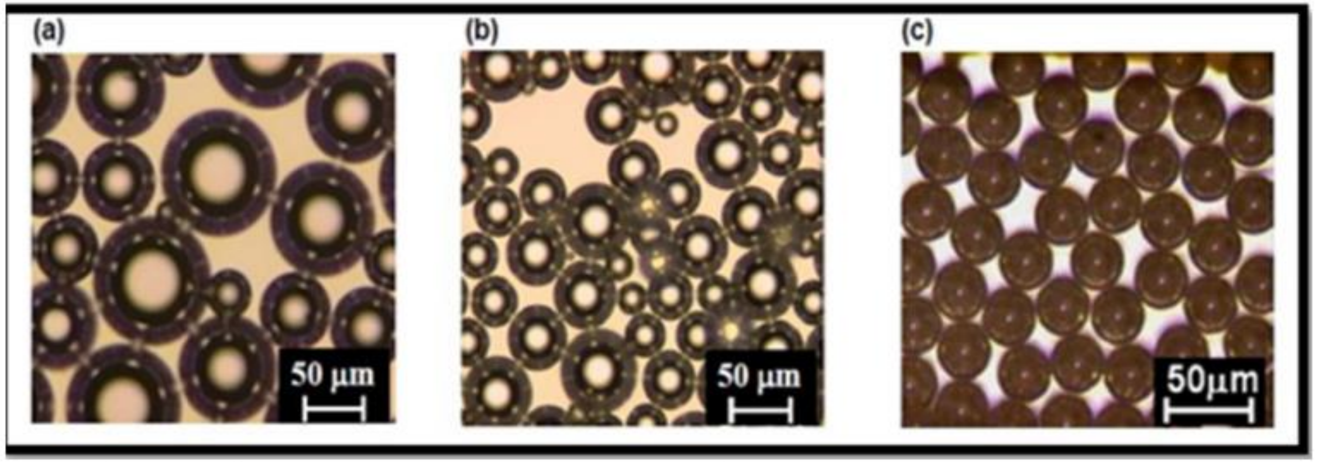


Figure 2: Difference of bubble size and shape when Microbubbles are prepared using (a) Mechanical agitation; (b) Sonication; (c) Microchannel emulsification.

Proč je takový odpor proti dobrovolné vakcinaci proti Covid-19 ?

„Pokud vás někdo musí přesvědčovat, napomínat, tlačit, lhát, lákat na pobídky, nutit, zastrašovat, odhalovat, obviňovat, vyhrožovat, trestat a kriminalizovat… Pokud je toto všechno považováno za nezbytné k získání vašeho souhlasu –

***<u>můžete si být naprosto jisti, že to, co se propaguje, není pro vaše dobro</u>**.“*

Britský autor sci-fi literatury Ian Watson

Nepokoje v Bruselu 500 tis demonstrantů dle organizátorů dle policie 50 tisíc.

https://echo24.cz/a/SrJg2/budovy-eu-v-oblezeni-strety-v-bruselu-az-pul-milionu-lidi-protestovalo-proti-koronavirovym-omezenim

Obrazy z historie české vakcinologie a imunologie

Ústav sér a očkovacích látek ÚSOL

Oběť privatizační hamižnosti a politické krátkozrakosti

1925 - 1997

O otevření Státního zdravotního ústavu přinesl obsáhlý článek Pražský Večerník pod titulkem Státní zdravotní ústav republiky Československé: „Dne 5. listopadu 1925 byl slavnostně otevřen ministrem veřejného zdravotnictví a tělesné výchovy Msgrem Dr. Janem Šrámkem státní zdravotní ústav republiky Československé.
Veliký čin, největší, který mohou zaznamenati dějiny v péči o zdraví národa.

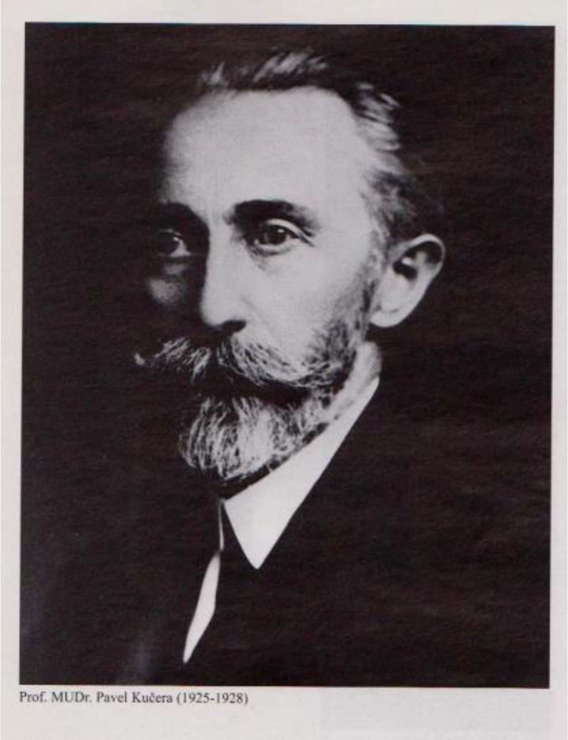
„Státní zdravotní ústav crescat, vivat, floreat!“ K tomuto přání přidružuje se celý národ, k jehož prospěchu dílo bylo vybudováno.“ (Pražský Večerník, 6. 11. 1925

Ministr Šrámek za četné účasti interesovaných kruhů zahájil slavnost a přednesl řeč, kterou ocenil význam ústavu, jeho důležitost a celou jeho historii, od doby iniciativního návrhu až po včerejší den, kdy blok budov a jejich zařízení překvapil sebevětší nadějí. 11 Nejprve pan ministr poděkoval Rockefellerově nadaci, která umožnila a urychlila zbudování tohoto ústavu. Za nadaci byl přítomen pan prof. Gunn, který účastnil se i činně přípravných prací. Rockefellerova nadace přičiněním Dr. Alice Masarykové a Dr. Šrobára podala nezištnou nabídku, která stala se prvním realisováním smělého snu pro boj s epidemiemi, které doprovází války „jako příšerný jezdec Apokalypsy“, o tom, **že republika ušetří miliony vlastní výrobou očkovacích látek a „zdravotnictví, které dosud bylo balastem na lékařské fakultě, dostane vědecký základ“.**

Klíčové osobnosti pro vznik SZÚ

MUDr. Ladislav Prokop Procházka

PhDr. Alice Masaryková



Profesor Selskar Michael Gunn

Prof. MUDr. Pavel Ludvík Kučera

Prof. MUDr. Milan Hašek, DrSc.

MUDr. Dimitrij Slonim, CSc.

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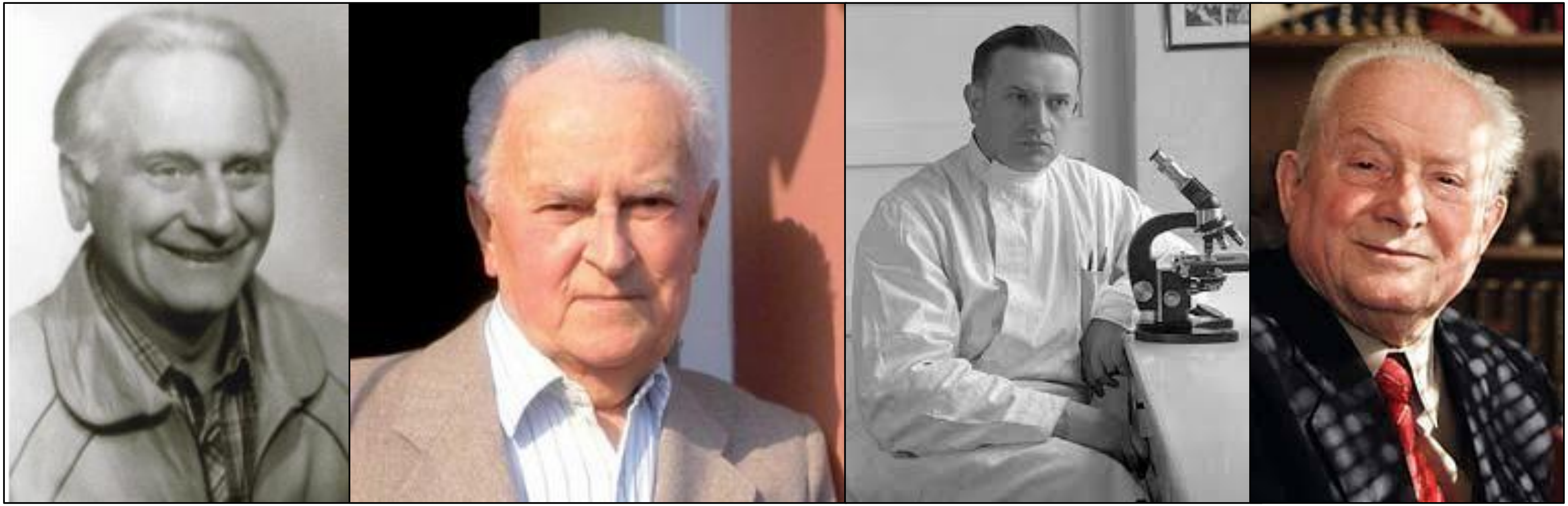
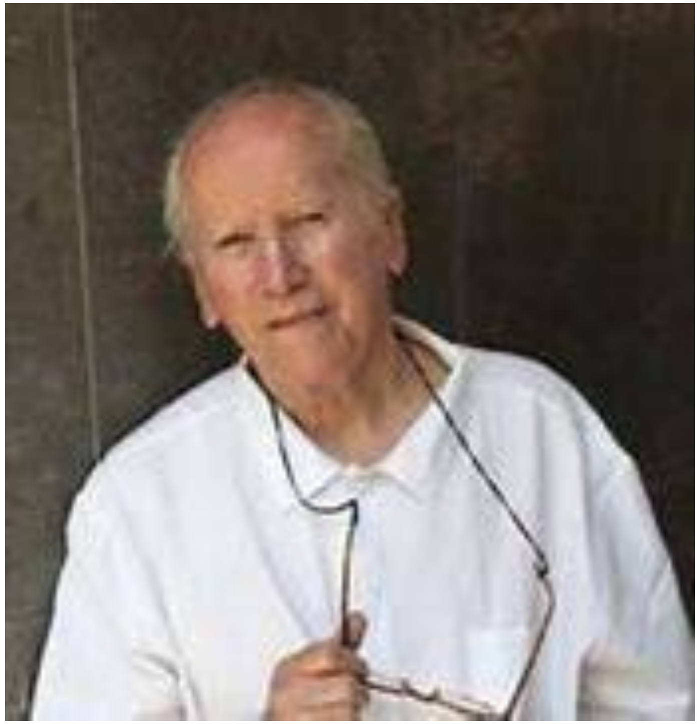
doc. MUDr. Zdeněk Ježek, DrSc.



Virologové a imunologové

Prof. MUDr. Vladimír Vonka, Dr.Sc.



Prof. MUDr. Karel Mestecký, Dr.Sc.

Prof. MUDr. Jaroslav Šterzl, Dr.Sc.

Pár moudrostí na závěr pro politiky

„Věda je národům nezbytná. Stát, který ji nerozvíjí, se nevyhnutelně mění v kolonii.“ – Frédéric Joliot-Curie (Je třeba také rozvíjet odpovídající průmyslovou základnu)

„Lidé, kteří dnes ovládají vědu, skutečně ani sami nepředvídají všechny důsledky toho, co se děje.“ – Norbert Wiener (Jsou schopni je předvídat a nést zodpovědnost za důsledky?)

„Dnešní vědecký výzkum v mnoha oborech už dávno nemá ctižádost ani svobodu naplňovat touhu lidského ducha po poznání pravdy, nýbrž poslušně plní zadání diktovaná ekonomickými, případně politickými zájmy svých mecenášů. Zisk se stal pravdou vědy.“ Tomáš Halík (Amen)

„Žijeme ve společnosti, naprosto závislé na vědě a technologii, a přesto skoro nikdo vědě a technologii nerozumí. To je jasný recept na katastrofu.“ – Carl Sagan (Proto je tak snadné pro politiky poroučet větru, dešti a přírodním zákonům)

„Jakožto humanista miluji vědu. Nesnáším pověry – jejich přičiněním bychom dodneška neměli atomovou bombu.“ Kurt Vonnegut


Thank you for your attention


Život je jen sen a jedinou skutečností v něm je LÁSKA
František Bílek