COVID19 AŞILARININ GELECEĞİ

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Eskişehir Osmangazi Üniversitesi Tıp Fakültesi
Çocuk Sağlığı ve Hastalıkları Anabilim Dalı

9 Mart 2022
KLİMİK 2022

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- COVID-19 “**AŞILARININ**” GELECEĞİ

a. Dünyada yaygın olarak kullanılan COVID-19 aşılarına rağmen yeni aşılara ya da yeni aşı teknolojilerine gereksinim var mı?
b. Mevcut yeni varyantlar ve olası yeni endişe verici varyantlar için yeni nesil aşılar mümkün mü (Panbetacoronavirus vaccine?)
c. Solunum yolu virüslerinde kombine aşılama stratejileri mevcut mu?
d. Pandemi aşılaması sonrası: Endemik solunum yolu virüslerinde aşılama?

- COVID-19 “**AŞILAMASININ**” GELECEĞİ

a. COVID-19 aşılarının tüm dünyada yüksek risk gruplarına eşit ve adil dağıtımı
b. COVID-19 pandemisinin rutin aşılama üzerine etkileri
c. Pandemi aşılamasının geleceği

- “**AŞILAMANIN**” GELECEĞİ

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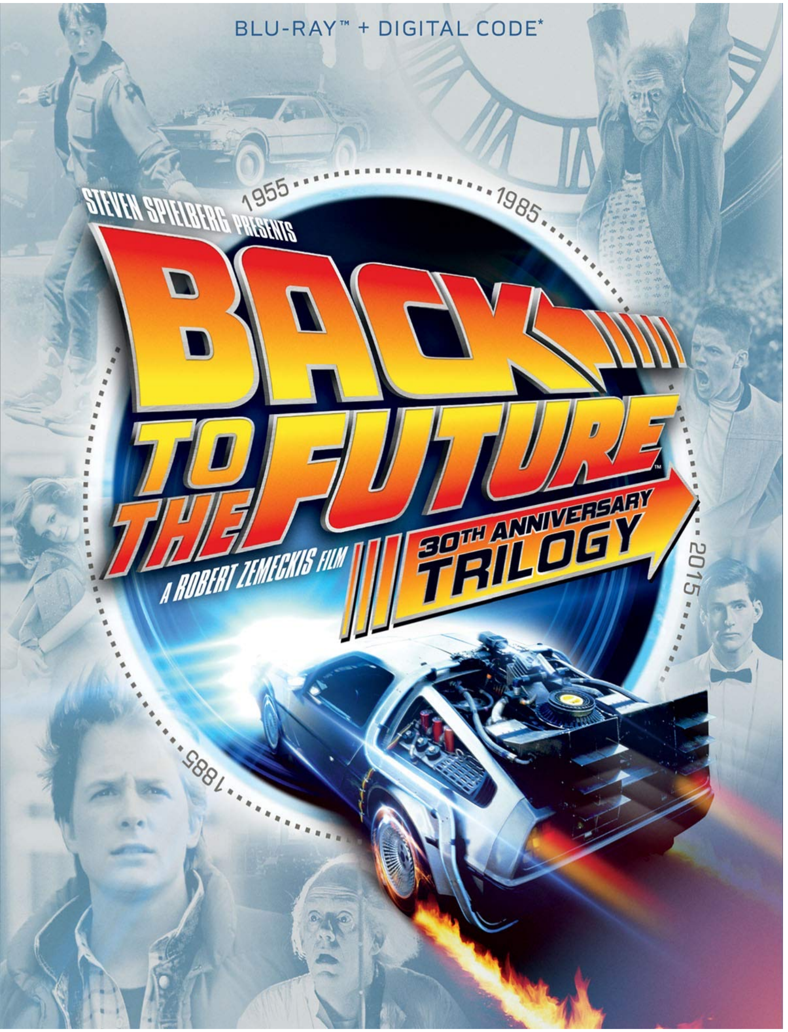
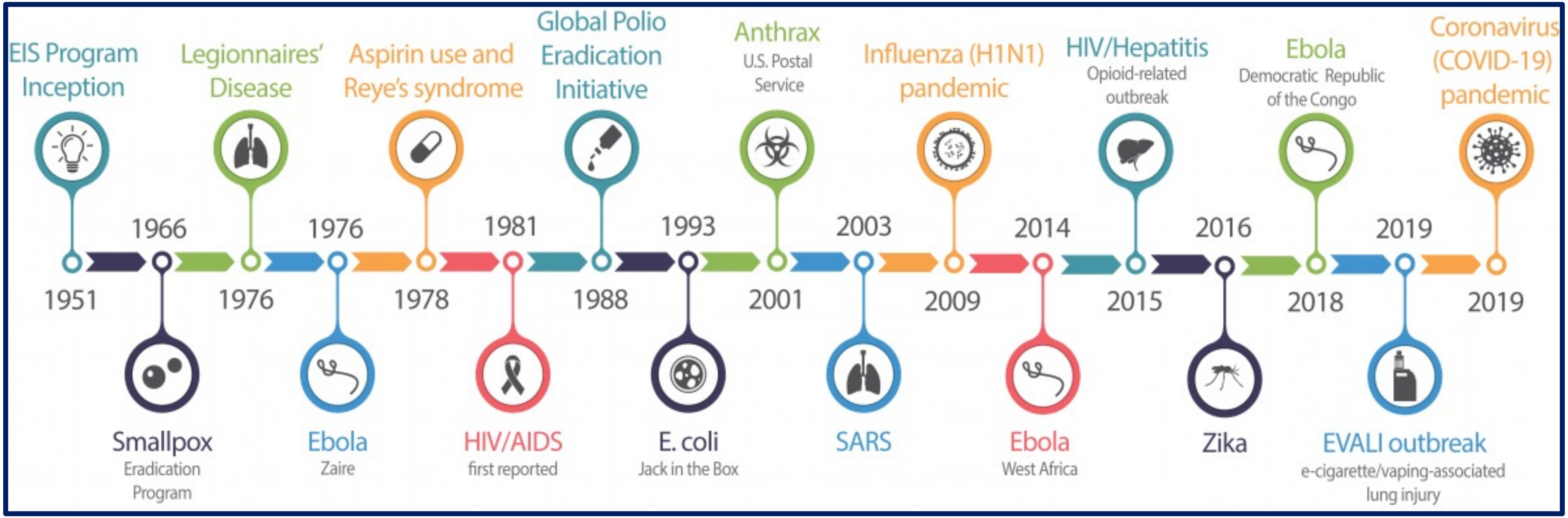
COVID-19 AŞILARI



ENFEKSİYON VE BARIŞ ÖYKÜLERİ



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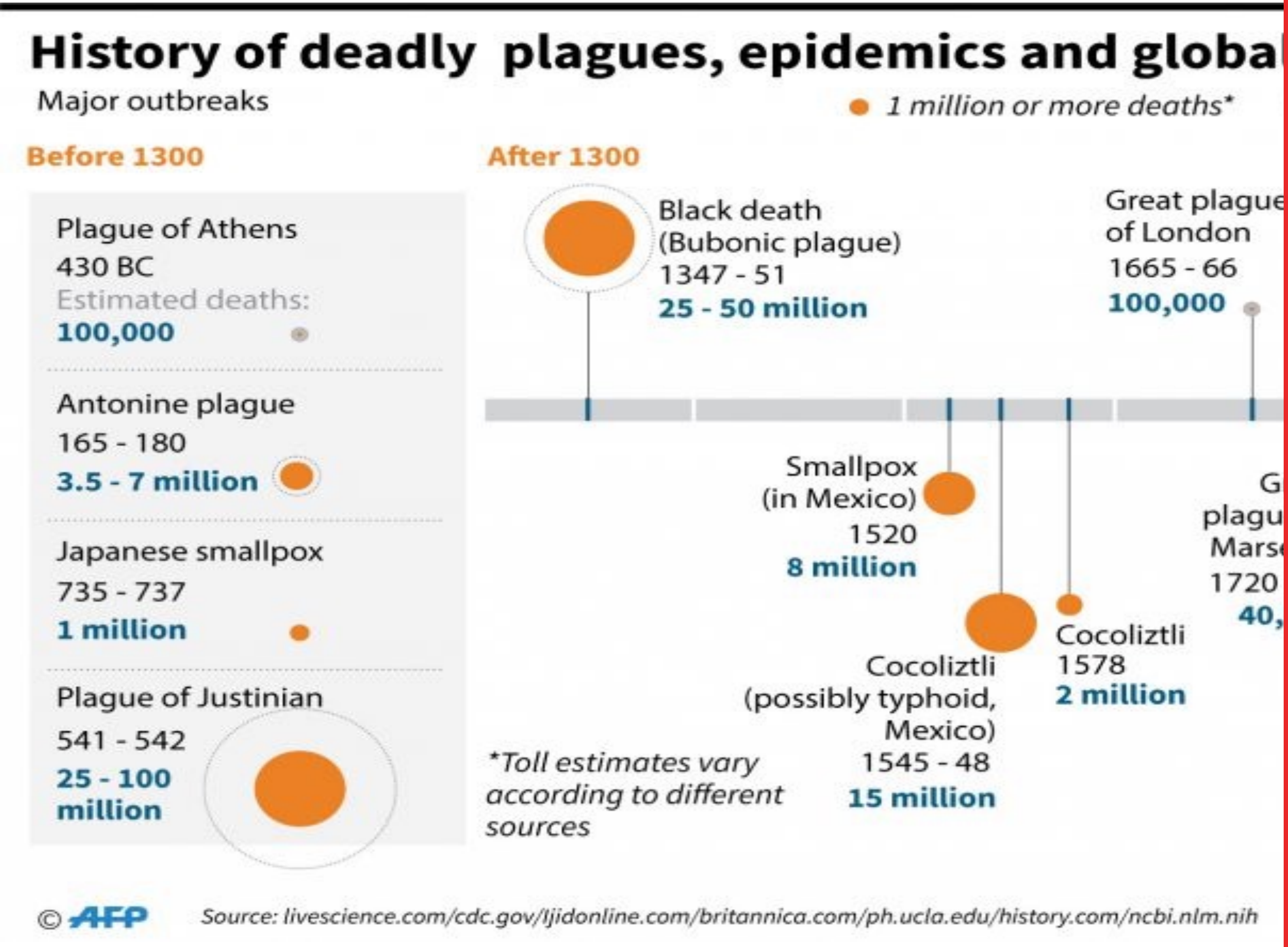
GLOBAL PANDEMİLER…



SALGIN AŞILAMASI

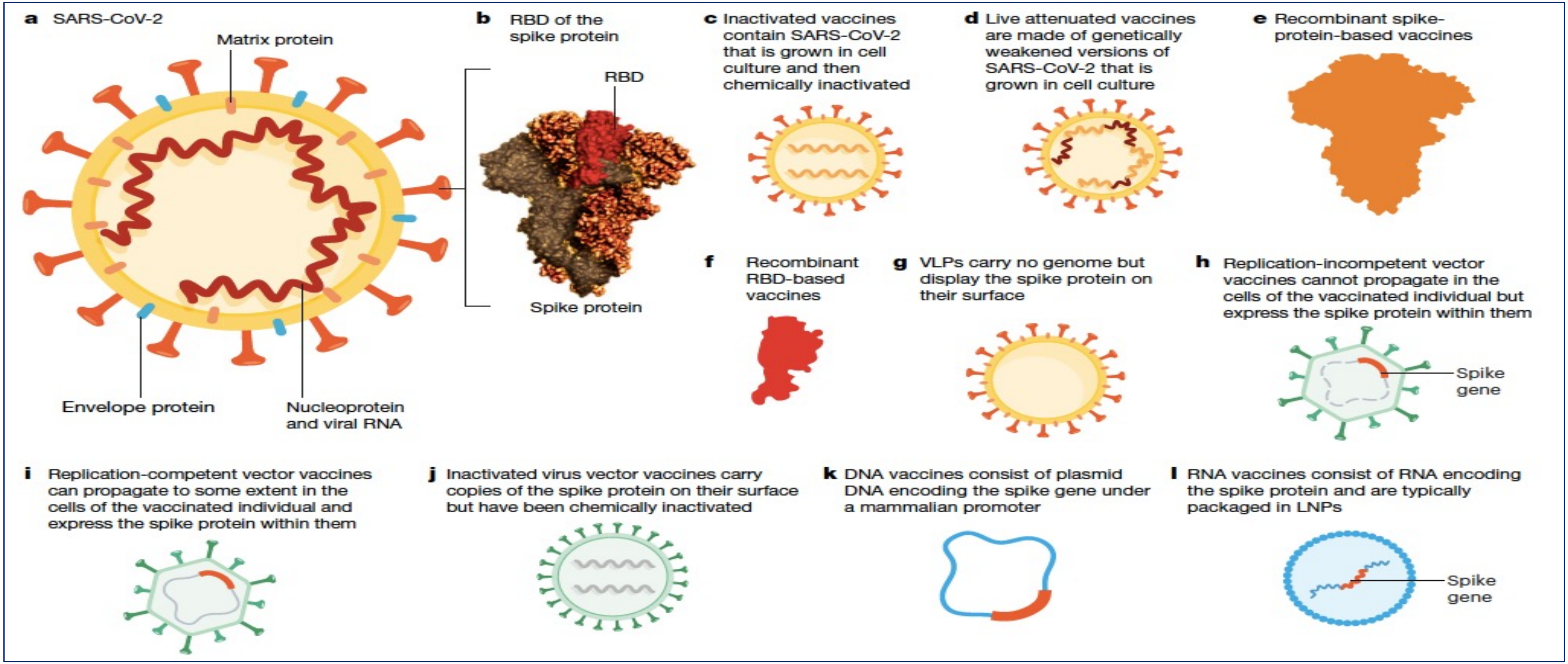
Table 5. Status of chimpanzee adenovirus vector (ChAd) vaccine development for a range of outbreak pathogens at the Jenner Institute, University of Oxford (as May 2017). The genetic background for all vectors is ChAdOx1 (a species E modified chimpanzee adenovirus based on isolate Y25).[23] Antigens are inserted at the E1 locus via Gateway® recombination. For preclinical immunogenicity testing, mice typically receive a single-dose of 10^8 infectious units (intramuscular).

Pathogen	ChAd construct made	Immunogenicity demonstrated in mice	Neutralising antibody activity demonstrated	Animal efficacy demonstrated	GMP production funded	Phase I/II evaluation commenced
Pandemic Influenza virus	✓	✓	✓	✓	✓	✓
Rift Valley Fever virus	✓	✓	✓	✓	✓	
MERS CoV	✓	✓	✓	✓	✓	
Zika virus	✓	✓		✓	✓	
Chikungunya virus	✓	✓	✓		✓	
Crimean Congo Haemorrhagic Fever virus	✓	✓				
Lassa virus	✓	✓				
Zaire ebolavirus	✓	✓				
Sudan ebolavirus	✓	✓				
Zaire + Sudan ebolavirus + Marburg	✓	✓				
Yersinia pestis	✓	✓				
Nipah virus	✓	✓				
SARS CoV	✓	✓				

ceener çağrı dinleyici

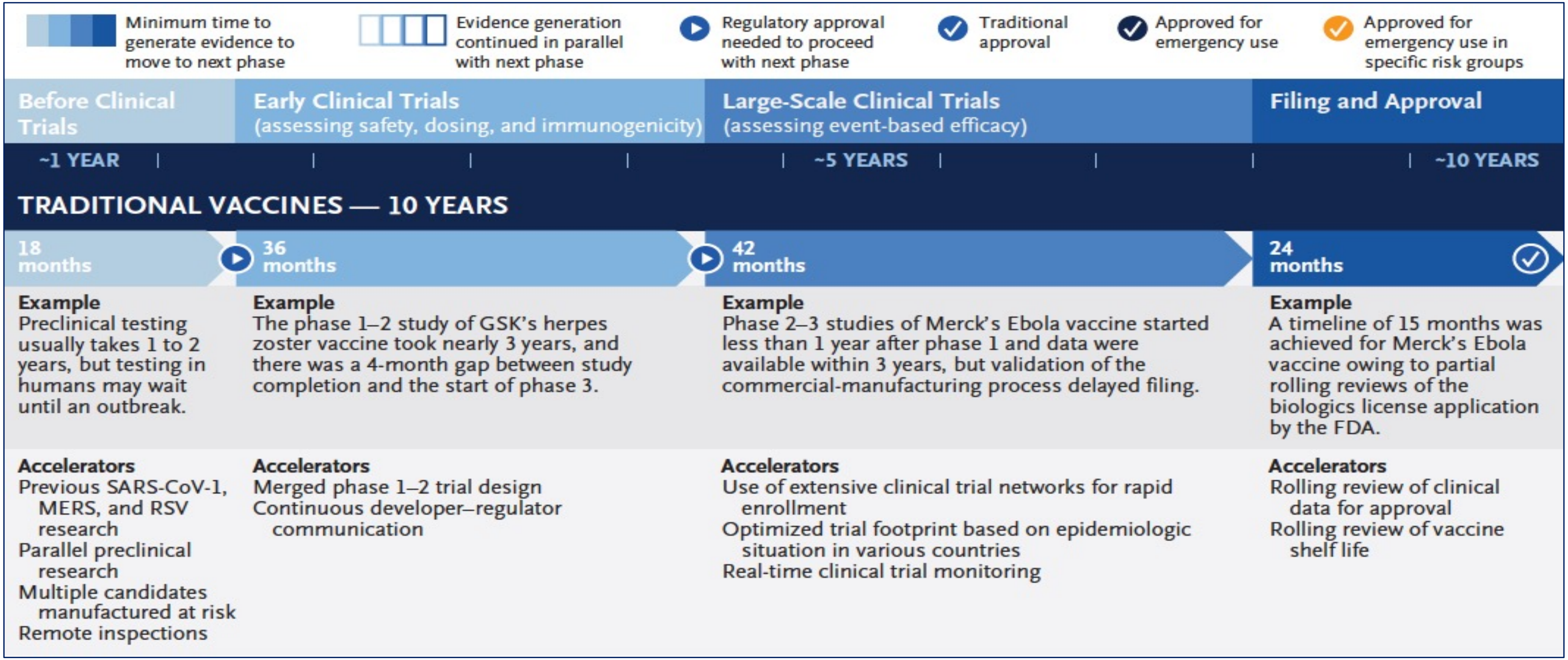
Ewer et al. Human Vaccines Immunotherapeutics 2017

COVID-19 AŞILARI



Florian Kramer. Nature 2020

COVID-19 AŞILARI



Saville et al. NEJM, 2022, 2 March.

COVID-19 AŞILARI

1 YEAR | 5 YEARS | 10 YEARS

COVID-19 VACCINES — 1 YEAR

9–14 weeks	14–19 weeks	15–16 weeks	5 weeks
Example Oxford University's ChAdOx1 platform optimization allowed the first vaccines to be ready within 60 days after sequence availability.	**Example** Moderna tested its vaccine in separate phase 1 and 2 trials, taking a combined 19 weeks until phase 3 start, whereas Pfizer moved within 13 weeks into phase 2–3 testing.	**Example** Pfizer–BioNTech achieved rapid enrollment of patients by leveraging its global-site network and a merged phase 1–3 trial design, with 30,000 patients enrolled by day 54 of the study.	**Example** Pfizer–BioNTechreceived emergency use authorization from the FDA within 3 weeks after filing and within 5 weeks after publishing interim phase 3 results.
Accelerators Previous manufacturing-process development Earlier technology transfer to production sites Rapid quality control and release No gap between batch release and trial start	**Accelerators** Reduced time between interim data and phase 3 start Platform readiness for commercial-scale manufacturing	**Accelerators** Best-in-class enrollment speed through more extensive use of global clinical trial networks and predictive site selection	**Accelerators** Best-practice filing timelines with rolling review process

ener çağrı dinleyici

Saville et al. NEJM, 2022, 2 March.

COVID-19 AŞILARI

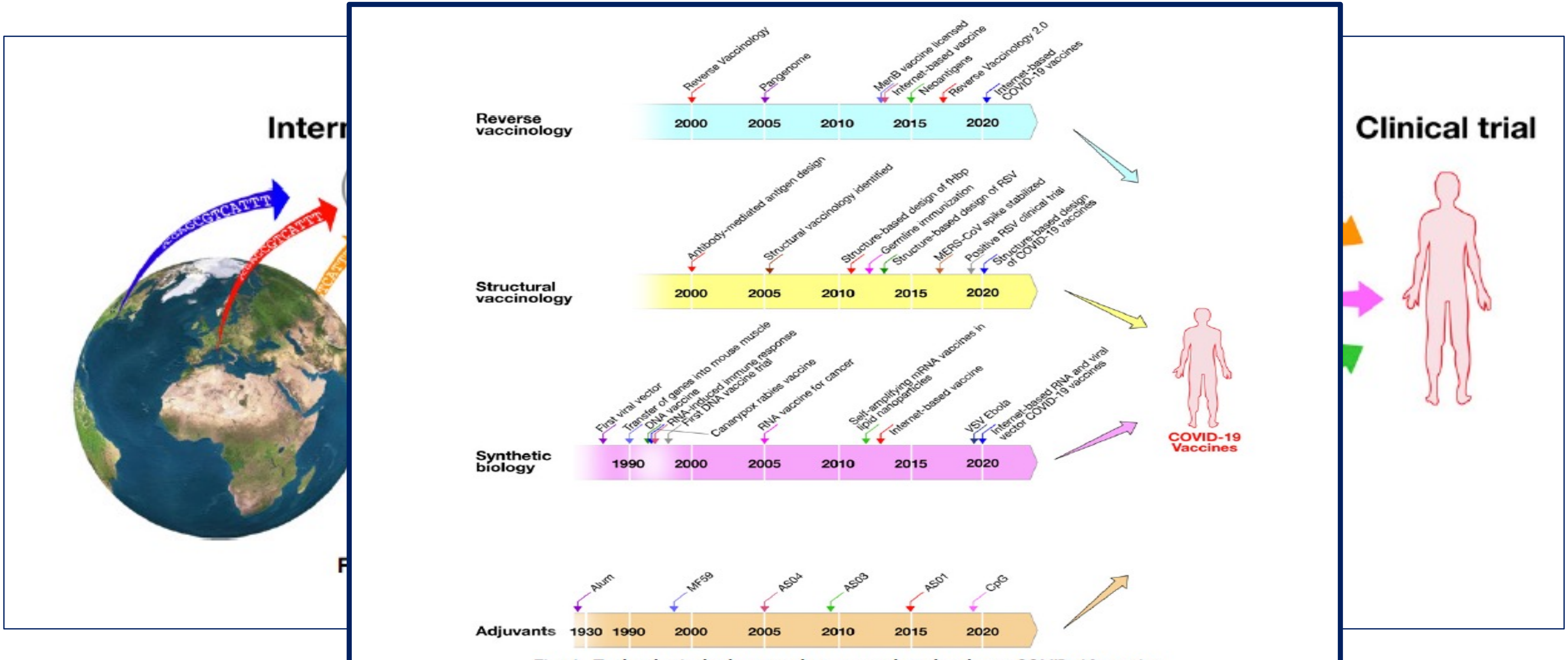


Fig. 1. Technological advances that merged to develop a COVID-19 vaccine.

Rappuoli et al. PNAS 2021

YENİ COVID-19 AŞILARI

Varyantlar, VOI, VOC

Linage	Named	First Identified	WHO Label	Spike Protein Substitutions
B.1.1.7	501.Y.V1	United Kingdom	Alpha (α)	69del, 70del, 144del, (E484K*), (S494P*), N501Y, A570D, D614G, P681H, T716I, S982A, D1118H (K1191N*)
B.1.351	501.V2	South Africa	Beta (β)	D80A, D215G, 241del, 242del, 243del, K417N, E484K, N501Y, D614G, A701V
B.1.617.2	478K	India	Delta (δ)	T19R, (G142D*), 156del, 157del, R158G, L452R, T478K, D614G, P681R, D950N
P.1	501Y.V3	Japan/Brazil (Manaus)	Gamma (γ)	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I
B.1.1.529	21K	South Africa	Omicron ('O)	A67V, del69-70, T95I, del142-144, Y145D, del211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F

YENİ COVID-19 AŞILARI

Varyantlar, VOI, VOC

HOW TO REDESIGN COVID VACCINES SO THEY PROTECT AGAINST VARIANTS

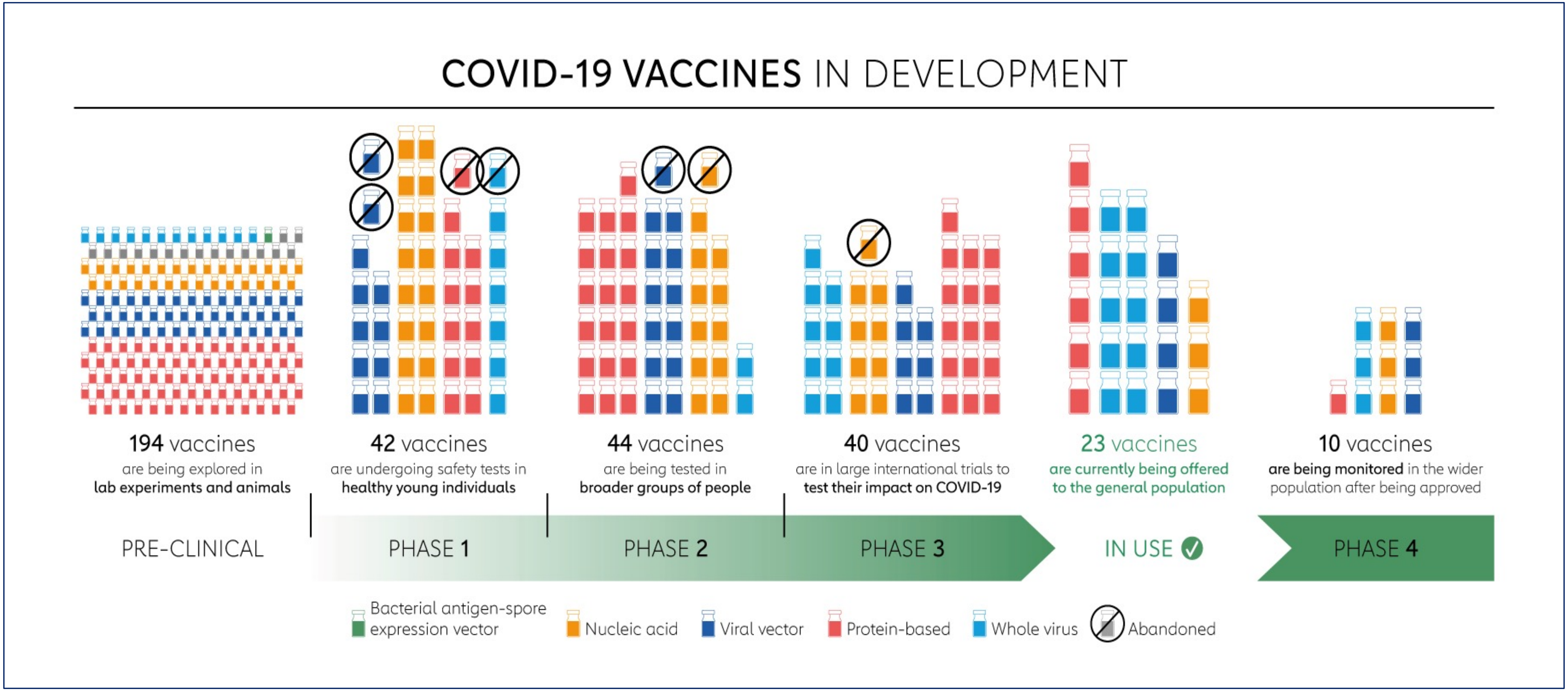
frontiers in Microbiology

REVIEW
published: 06 October 2021
doi: 10.3389/fmicb.2021.750124

Vaccine Development Against Tuberculosis Over the Last 140 Years: Failure as Part of Success

Stefan H. E. Kaufmann[1,2,3*]

YENİ COVID-19 AŞILARI



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YENİ COVID-19 AŞILARI

yeni mRNA AŞILARI

Company	Name of vaccine candidate: immunogen, route of administration	mRNA dose (μg)	Development phase
Pfizer/BioNTech (US FDA approved)	BNT162b2: mod S-2P, IM	30	III (NCT04368728, 5)
	BNT162b1: mod RBD, IM	1–100	II (NCT04368728, 15, 16)
	BNT162a1: unmod RBD, IM	n/a	I (NCT04380701)
	BNT162c2: SAM S-2P, IM	n/a	I (NCT04380701)
Moderna (US FDA EUA)	mRNA-1273: mod S-2P, IM	100	III (NCT04470427, 6, 95)
CureVac	CVnCoV: unmod S-2P, IM	12	IIb/III (NCT04652102, 13)
Academy of Military Medical Science, Walvax Biotechnology, Suzhou Abogen Biosciences	ARCoV: mod RBD, IM	15	III (NCT04847102)
Translate Bio/Sanofi	MRT5500: unmod S-2P/GSAS, IM	15–135	I/II (NCT04798027, 42)
Arcturus	ARCT-021: SAM WT S, IM	5 and 7.5	II (NCT04480957)
Imperial College London	LNP-nCoVsaRNA: SAM S-2P, IM	0.1–10	I/II (ISRCTN17072692)
Daiichi Sankyo Co., Ltd	DS5670a: n/a, IM	10–100	I/II (NCT04821674)
Elixirgen Therapeutics, Inc	EXG-5003: SAM RBD, ID	n/a	I/II (NCT04863131)
GlaxoSmithKline	CoV2 SAM (LNP): SAM S, IM	1	I (NCT04758962)
Providence Therapeutics	PTX-COVID19-B: n/a, IM	16–100	I (NCT04765436) and II
SENAI CIMATEC	HDT-301: SAM S, IM	1–25	I (NCT04844268)
Chulalongkorn University	ChulaCov19: mod WT S, IM	10–50	I (NCT04566276)
MRC/UVRI, LSHTM Uganda Research Unit	LNP-nCOV saRNA-02: SAM S, n/a	5	I (NCT04934111)

ener çağrı dinleyici

Hogan and Pardi. Annu Rev Med 2022

YENİ COVID-19 AŞILARI

yeni LNP

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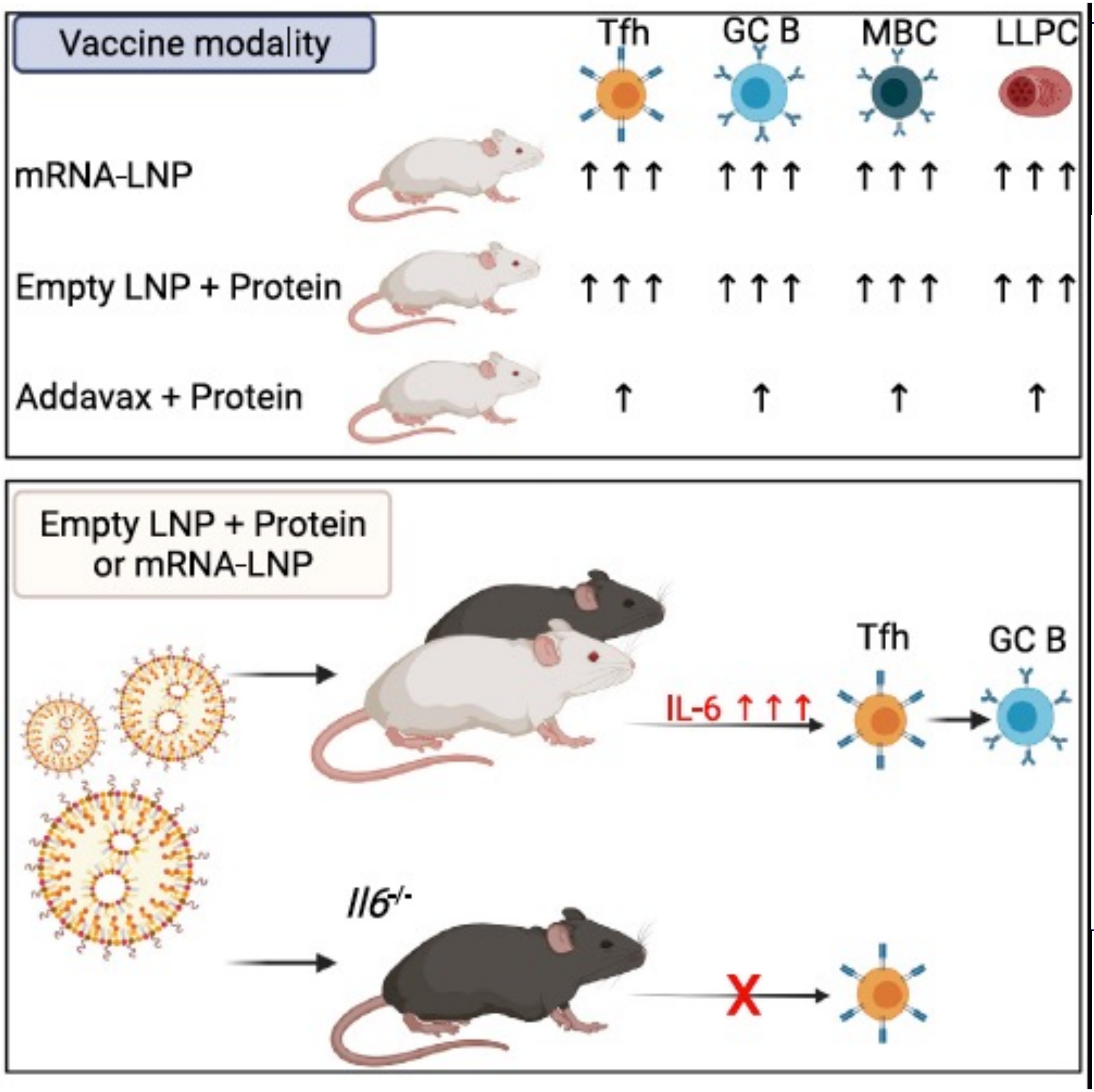

CellPress

Highlights

- LNPs are immunostimulatory and act as an adjuvant component of modified mRNA vaccines
- LNP-adjuvanted protein subunit vaccines foster potent Tfh cell and humoral responses
- LNPs are not sensed by receptors signaling through MyD88 or MAVS
- IL-6 induction and the ionizable lipid are critical for the adjuvant activity of LNPs

Immunity 54, 2877–2892, December 14, 2021

YENİ COVID-19 AŞILARI

<u>yeni</u> mRNA AŞILARI

Recent Advances in the Noninvasive Delivery of mRNA

Published as part of the Accounts of Chemical Research special issue "mRNA Therapeutics".

Ming Qin, Guangsheng Du,* and Xun Sun*

Cite This: *Acc. Chem. Res.* 2021, 54, 4262−4271

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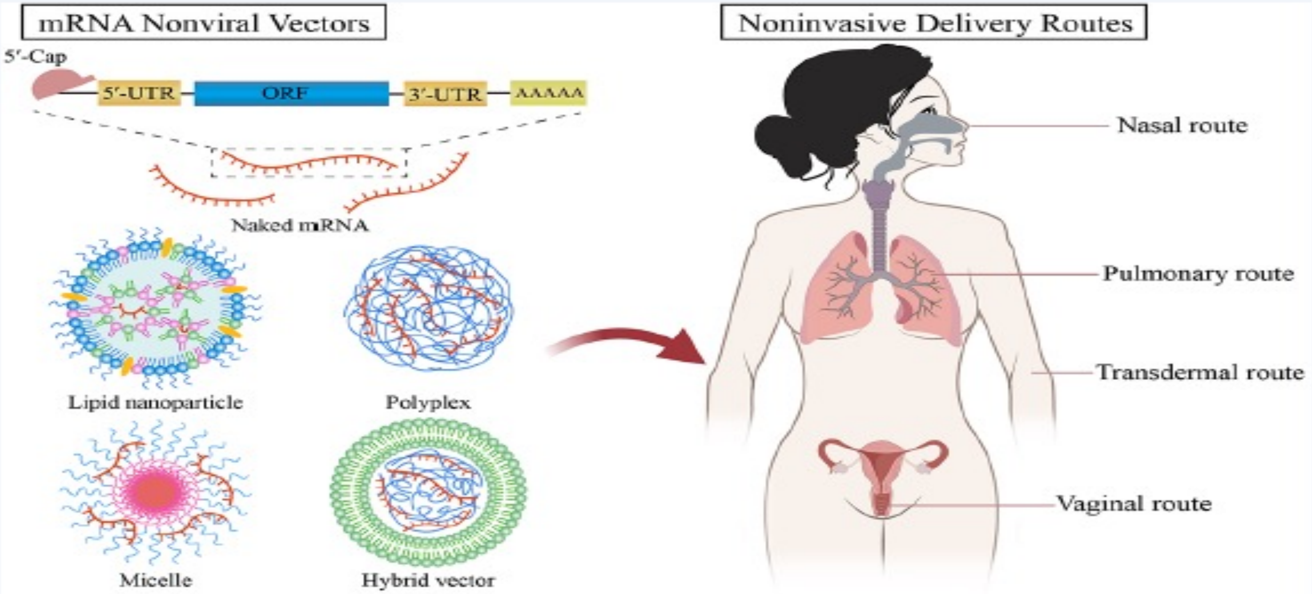


VİRAL VEKTÖR AŞILARI

Seminars in Immunology 50 (2020) 101430

Contents lists available at ScienceDirect

Seminars in Immunology

journal homepage: www.elsevier.com/locate/ysmim

Review

New viral vectors for infectious diseases and cancer

Emanuele Sasso[a,b,1], Anna Morena D'Alise[a,1], Nicola Zambrano[b,c], Elisa Scarselli[a], Antonella Folgori[d], Alfredo Nicosia[b,c,*]

Sasso et al. Seminars in Immunology 2020

VİRAL VEKTÖR AŞILARI

COVID19 AŞILARI

World Health Organization

R&DBlueprint
Powering research to prevent epidemics

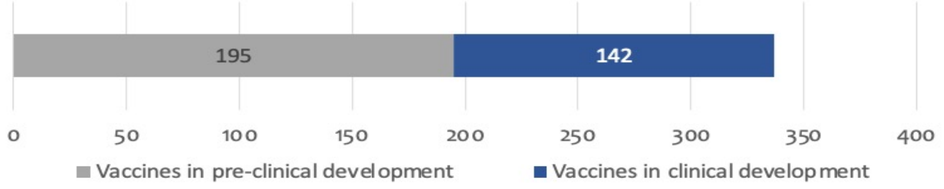
COVID-19 - Landscape of novel coronavirus candidate vaccine development worldwide

11 Şubat 2022 Cuma

Summary Information on Vaccine Products in Clinical Development

1. - Number of vaccines in clinical development 142

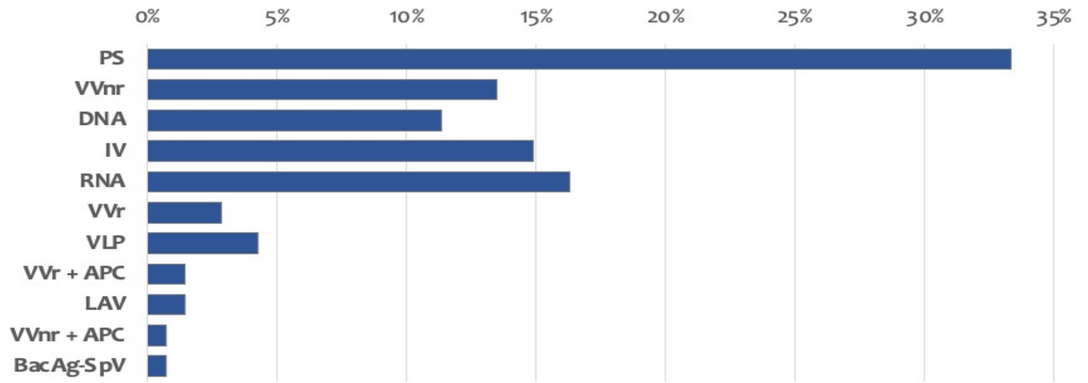
2. - Number of vaccines in pre-clinical development 195



3. - Candidates in clinical phase

Filter: All — Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	47	33%
VVnr	Viral Vector (non-replicating)	19	13%
DNA	DNA	16	11%
IV	Inactivated Virus	21	15%
RNA	RNA	23	16%
VVr	Viral Vector (replicating)	4	3%
VLP	Virus Like Particle	6	4%
VVr + APC	VVr + Antigen Presenting Cell	2	1%
LAV	Live Attenuated Virus	2	1%
VVnr + APC	VVnr + Antigen Presenting Cell	1	1%
BacAg-SpV	Bacterial antigen-spore expression vector	1	1%
		142	



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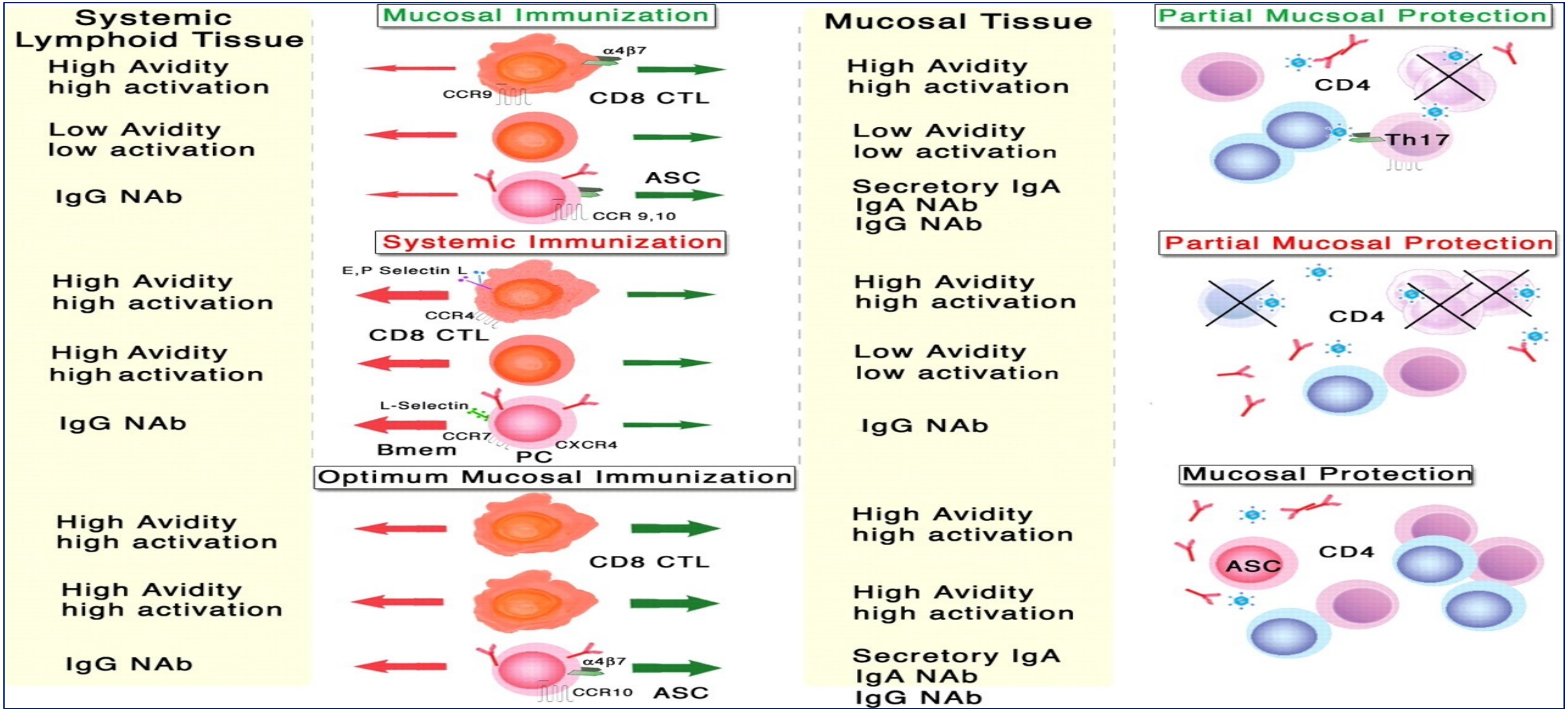
WHO. Landscape of novel coronavirus candidate vaccibe development worldwide. 11 Feeruary 2022

YENİ COVID-19 AŞILARI

MUKOZAL AŞILAMA



Belvakon and Ahlers. Journal of Immunology 2009

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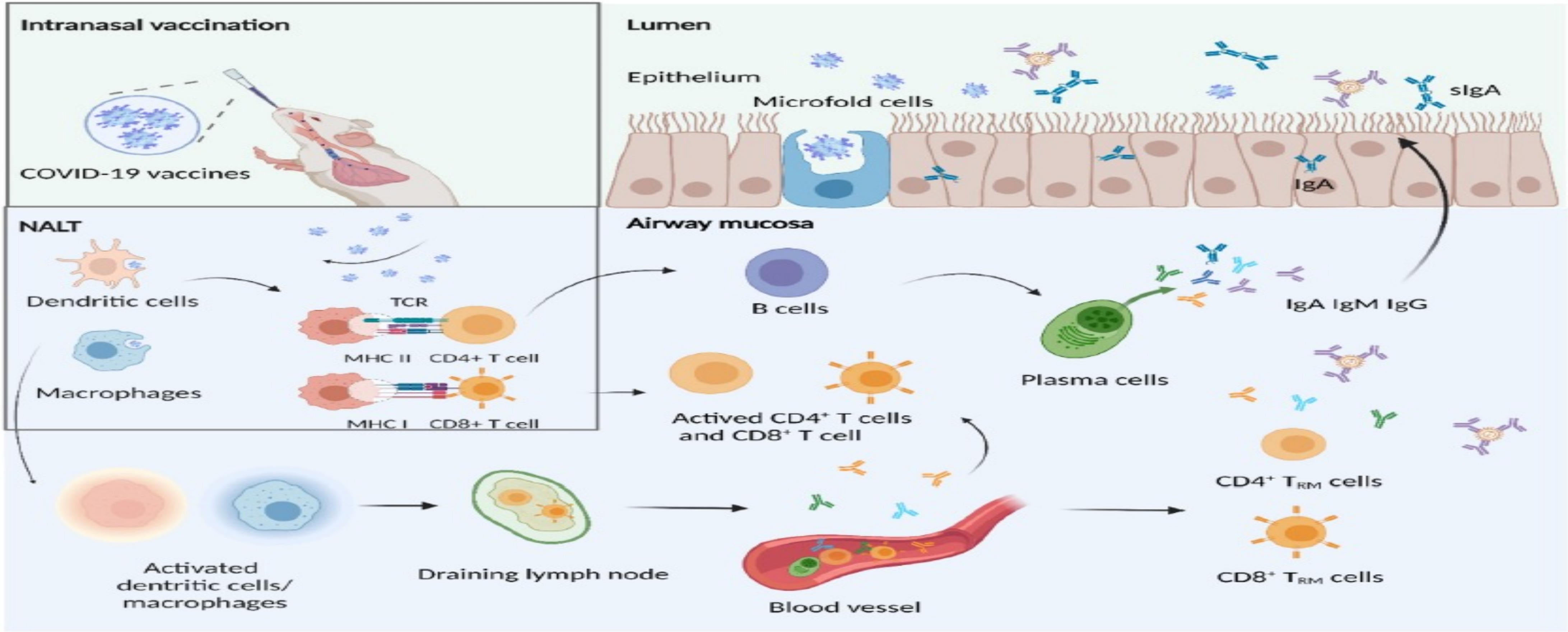
İNTRANAZAL AŞILAR



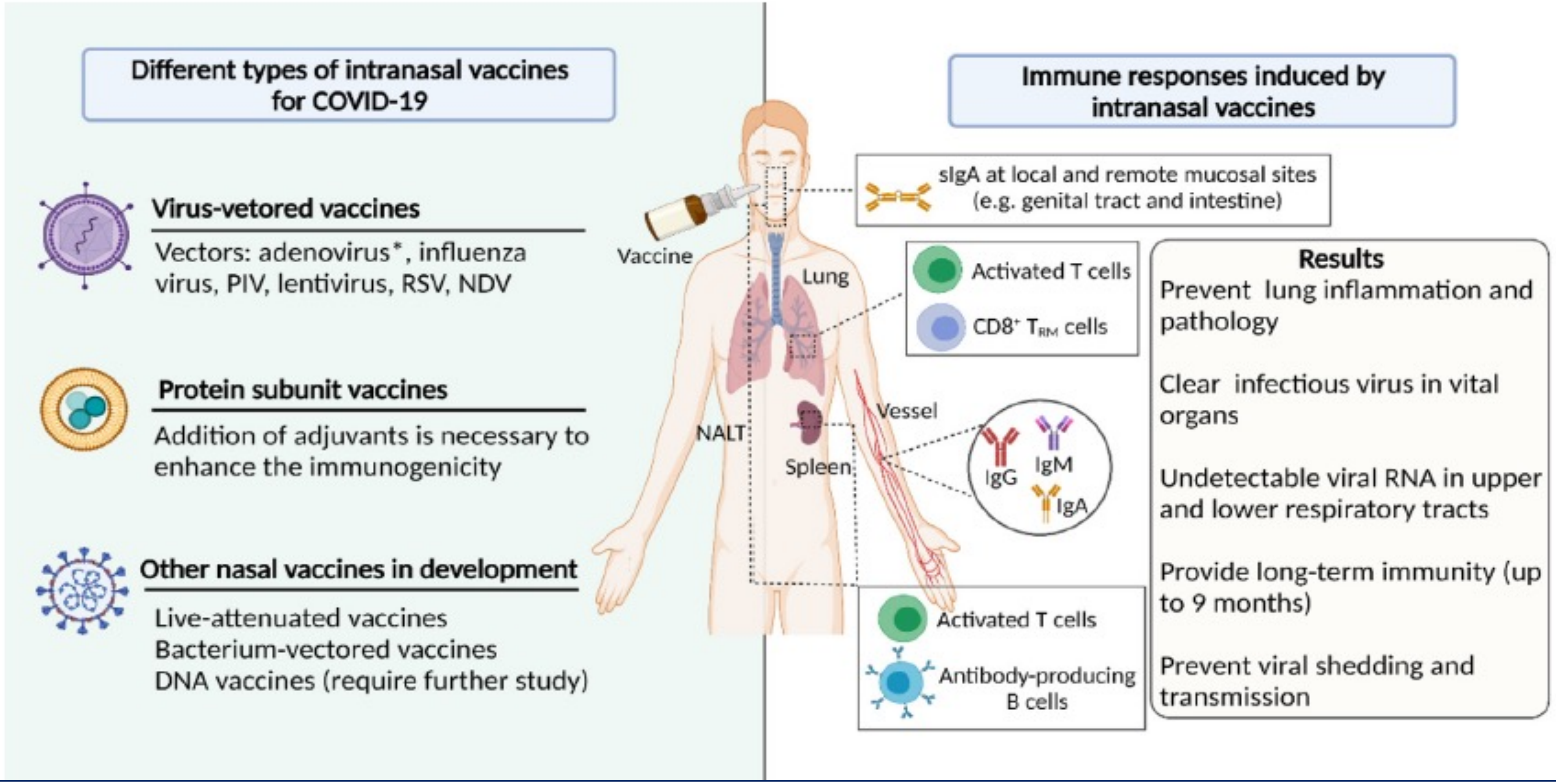
Intranasal COVID-19 vaccines: From bench to bed

Aqu Alu,[1] Li Chen,[1] Hong Lei Yuquan Wei Xiaohe Tian, and Xiawei Wei **

Laboratory of Aging Research and Cancer Drug Target, State Key Laboratory of Biotherapy and Cancer Center, National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, Chengdu 610041, China

YENİ COVID-19 AŞILARI

İNTRANAZAL AŞILAR



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YENİ COVID-19 AŞILARI

İNTRANAZAL AŞILAR

Type	Vaccine	Target	Route (no. of doses)	Animal used
PIV5-vectored vaccine	CVXGA1	S protein	IN (1)	K18-hACE2 mice and ferrets[55]
hPIV2-vectored vaccine	BCPIV/S-2PM	S protein	IN (1or 2)	Mice and golden hamsters[56]
NDV-vectored vaccine	AVX/COVID-12-HEXAPRO	S protein	IN +IN, IM + IM, or IN + IM, (2)	Mice, hamsters[60], and pigs[59]
	NDV-FLS	S protein	IN (1 or 2)	Hamsters[61]
	rNDV-S	S protein	IN (2)	Mice and hamsters[62]
VSV-vectored vaccine	rVSVSARS-CoV-2	S protein	IN or IM, (1)	Normal/hACE2 mice, and macaques[63]
	VSV-SARS2-EBOV	SARS-CoV-2 S protein and/or the EBOV glycoprotein	IM or IN, (1)	Hamsters[64] and rhesus macaques[65]
Virus like particles		RBD protein	IM alone or IM + IN, (3)	Ferrets[72]
Live-attenuated vaccine	SARS-CoV-2/ human/ Korea/ CNUHV03-CA22 ℃ /2020		IN spray (1)	hACE2 transgenic mice[76]
	COVI-VAC		IN (1)	Syrian golden hamsters[77]
Bacterium-vectored vaccine		M and N proteins	ID or IN, (2)	Hamsters[78]
	LP18:RBD	RBD	IN (2)	Mice[79]
Protein subunit vaccine		RBD protein	IN, IM or ID, (3)	Mice[34]
		S1 protein	IM (3) or IN (4)	Rhesus macaques[73]
		RBD protein	IN or IM, (3)	Mice[69]
		S1 protein	IN (3)	Mice[70]
		Trimeric or monomeric S protein	IN (1)	Mice[71]
DNA vaccine	pQAC—CoV; MVA-CoV	S and N proteins	IN or IM, (3), or IN (2)	Mice[81]
		S protein	IN	Mice[80]

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YENİ COVID-19 AŞILARI

İNTRANAZAL AŞILAR

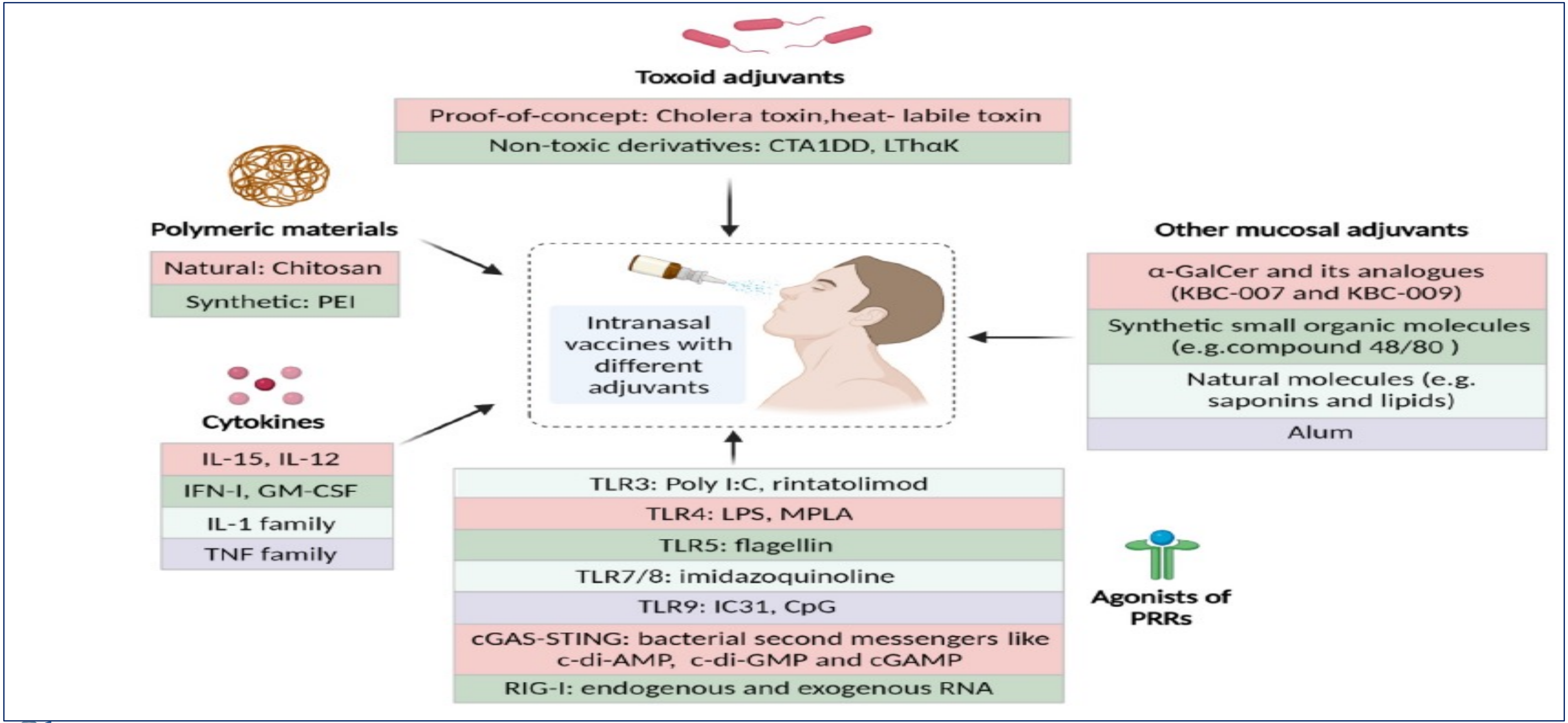
Type	Vaccine	Developer/manufacturer	Nasal delivery device	Phase	Status	Enrollment	Clinical trial No.	Route
Ad-vectored vaccine	Ad5-nCoV	CanSino/Beijing Institute of Biotechnology	Aerogen Ultra Device	I	Active, not recruiting	149	NCT04552366	IN, IM or IN+IM
				I/II	Recruiting	840	NCT04840992	IM or IN
	ChAdOx1	AstraZeneca/University of Oxford	MAD Nasal™ Intranasal Mucosal Atomization Device	I	Enrolling by invitation	54	NCT04816019	IN
	BBV154	Bharat Biotech International Limited	N/A	I	Active, not recruiting	175	NCT04751682	IN
	SC-Ad6−1	Tetherex Pharmaceuticals Corporation	N/A	I	Recruiting	80	NCT04839042	IM or IN
	AdCOVID	Altimmune, Inc.	Pipette droppers	I	Not processing	180	NCT04679909	IN
NDV-vectored vaccine	AVX/COVID-12-HEXAPRO	Laboratorio Avi-Mex, S.A. de C.V.	An automatic syringe (Prima mist sprayer)	I	Recruiting	90	NCT04871737	IN, IM or IN+IM
LAIV-vectored vaccine	DelNS1−2019-nCoV-RBD-OPT1	University of Hong Kong, Xiamen University and Beijing Wantai Biological Pharmacy	Spray devices	I	Complete	60	ChiCTR2000037782	IN
				II	Complete	720	ChiCTR2000039715	IN
				III	−	40,000	ChiCTR2100051391	IN
PIV5-vectored vaccine	CVXGA1	CyanVac LLC	Spray devices	I	Not recruiting	80	NCT04954287	IN
RSV-vectored vaccine	MV-014−212	Meissa Vaccines, Inc.	Droppers or spray devices	I	Recruiting	130	NCT04798001	IN
Protein subunit vaccine	CIGB-669	CIGB	Syringe-based spray devices	I/II	Pending	88	RPCEC00000345	IN alone or IN + IM
	Razi Cov Pars	Razi Vaccine and Serum Research Institute	Spray devices	I	Complete	133	IRCT20201214049709N1	IM + IN
				II	Complete	500	IRCT20201214049709N2	IM + IN
				III	−	41,128	IRCT20210206050259N3	IM + IN
Live attenuated vaccine	COVI-VAC	Codagenix, Inc.	Droppers	I	Active, not recruiting	48	NCT04619628	IN

***Table 2*: Clinical trials of IN COVID-19 vaccines.**

NDV: Newcastle disease virus; LAIV: live attenuated influenza virus; PIV: parainfluenza virus; RSV: respiratory syncytial virus; N/A: Not available. Data from https://clinicaltrials.gov/, https://www.chictr.org.cn/index.aspx and https://covid-19.cochrane.org/.

YENİ COVID-19 AŞILARI

İNTRANAZAL AŞILAR



YENİ COVID-19 AŞILARI

CellPress
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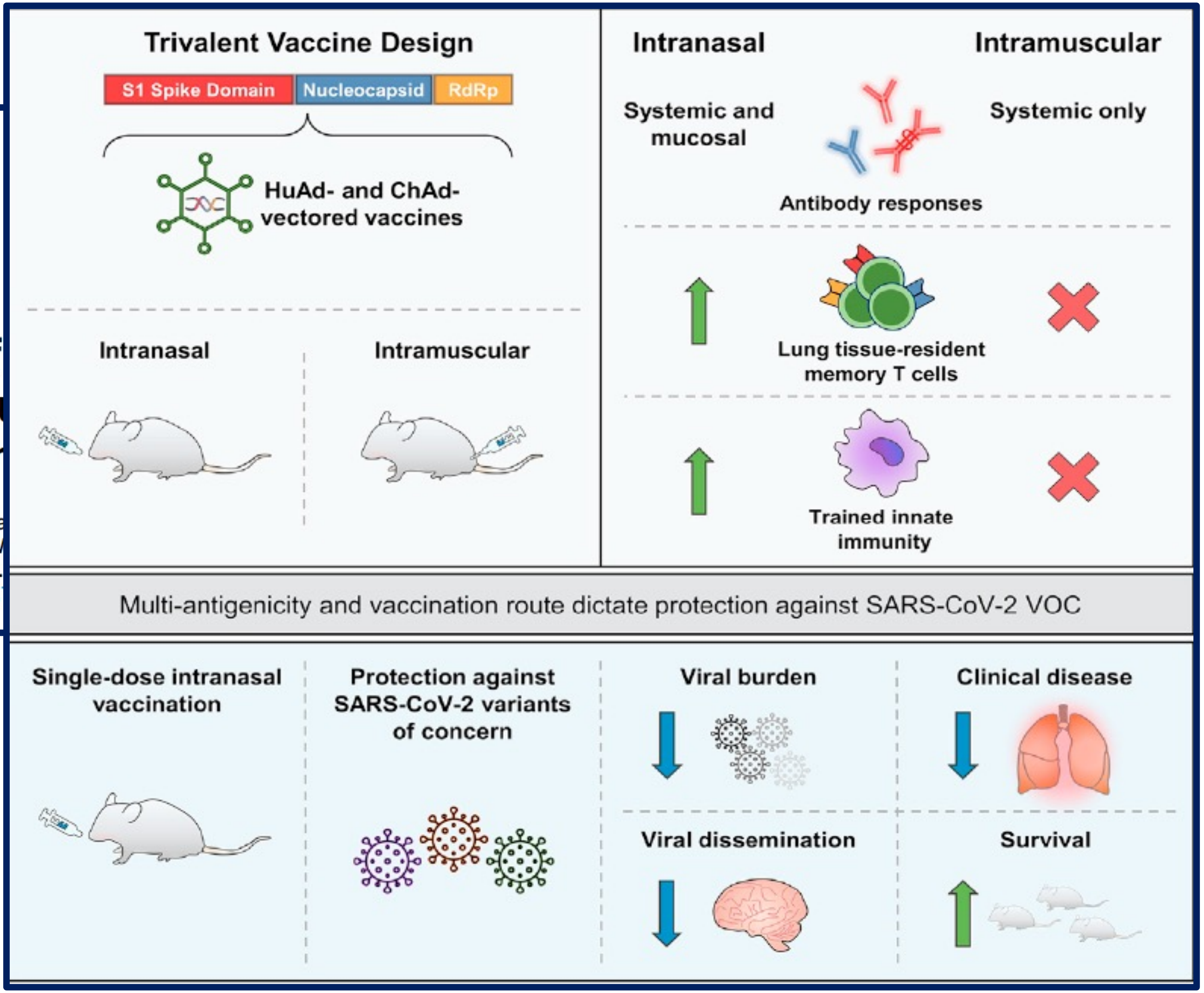
Article

Respiratory mucosal delivery of COVID-19 vaccine provides robu both ancestral and variant strain

Sam Afkhami,[1,5] Michael R. D'Agostino,[2,5] Ali Zhang,[2] Hannah D. Sta
Jegarubee Bavananthasivam,[1] Gluke Ye,[1] Xiangqian Luo,[1,3] Fuan W
Natallia Kazhdan,[1] Joshua F.E. Koenig,[1] Allyssa Phelps,[1] Steven F.
Yonghong Wan,[1] Karen L. Mossman,[1] Mangalakumari Jeyanathan,[1]
Brian D. Lichty,[1,*] Matthew S. Miller,[2,*] and Zhou Xing[1,6,*]



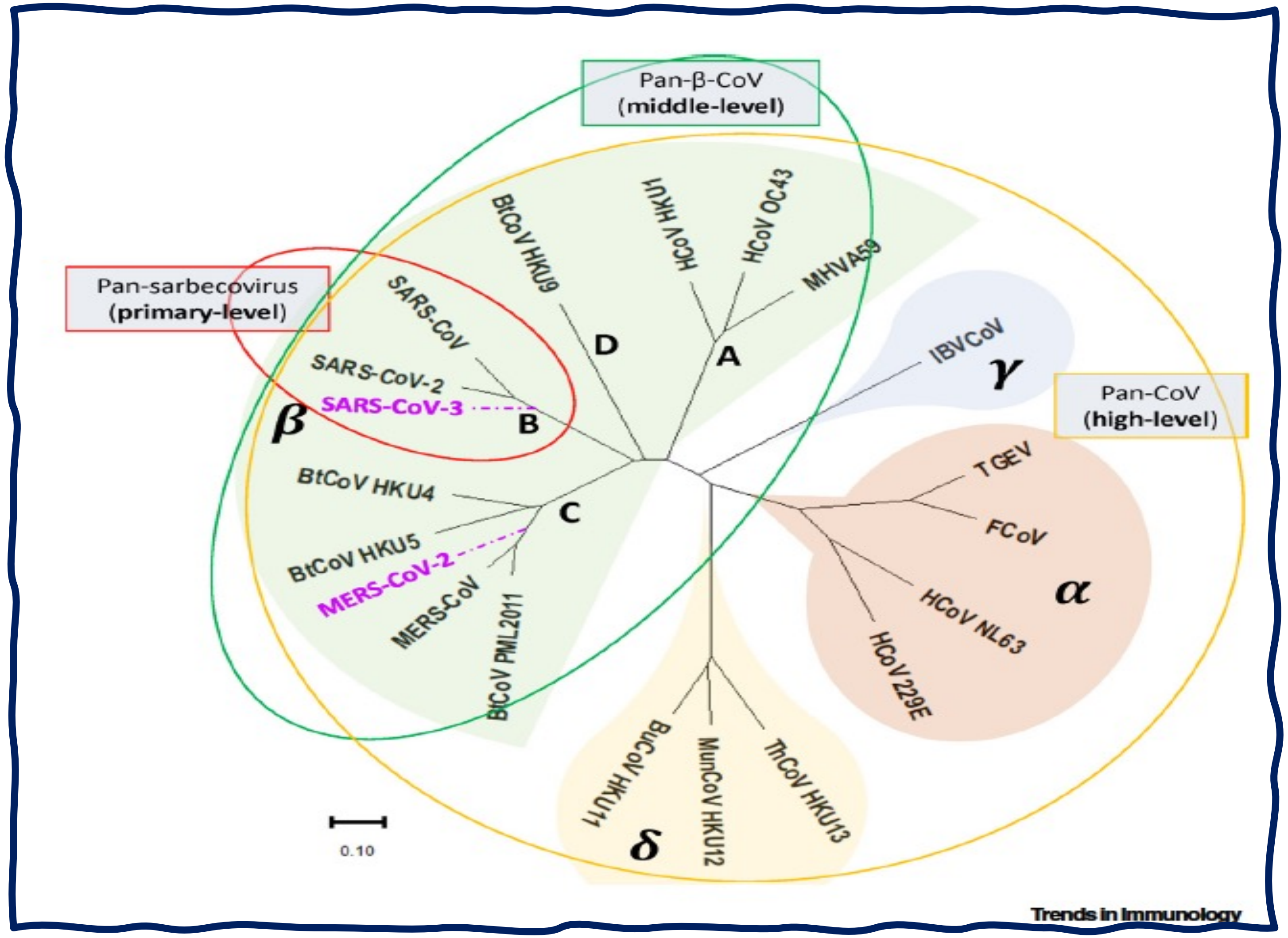
Cell *185*, 896–915, March 3, 2022

YENİ COVID-19 AŞILARI

pan-beta-Coronavirus

Developing pan-β-coronavirus vaccines against emerging SARS-CoV-2 variants of concern

Shan Su,[1] Weihua Li,[2] and Shibo Jiang[1,2,*]

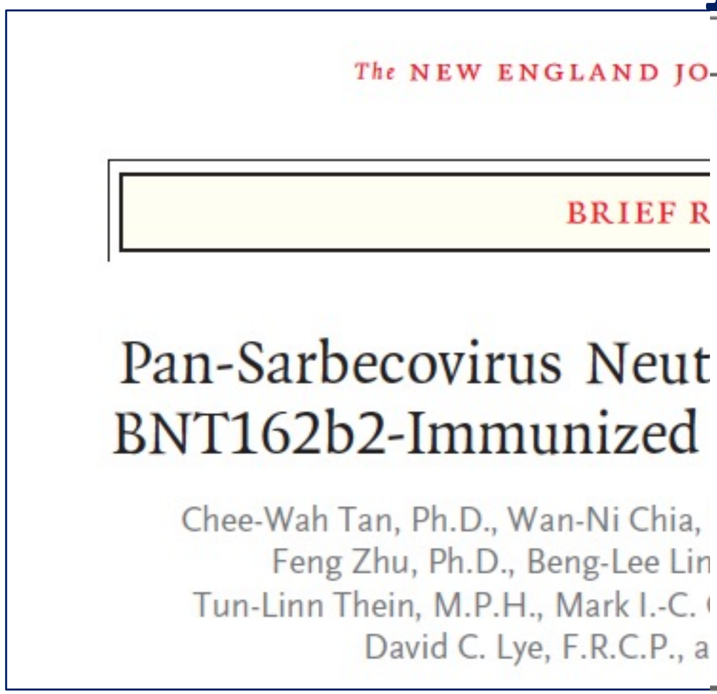


Trends in Immunology, March 2022, Vol. 43, No. 3

Trends in Immunology

YENİ COVID-19 AŞILARI

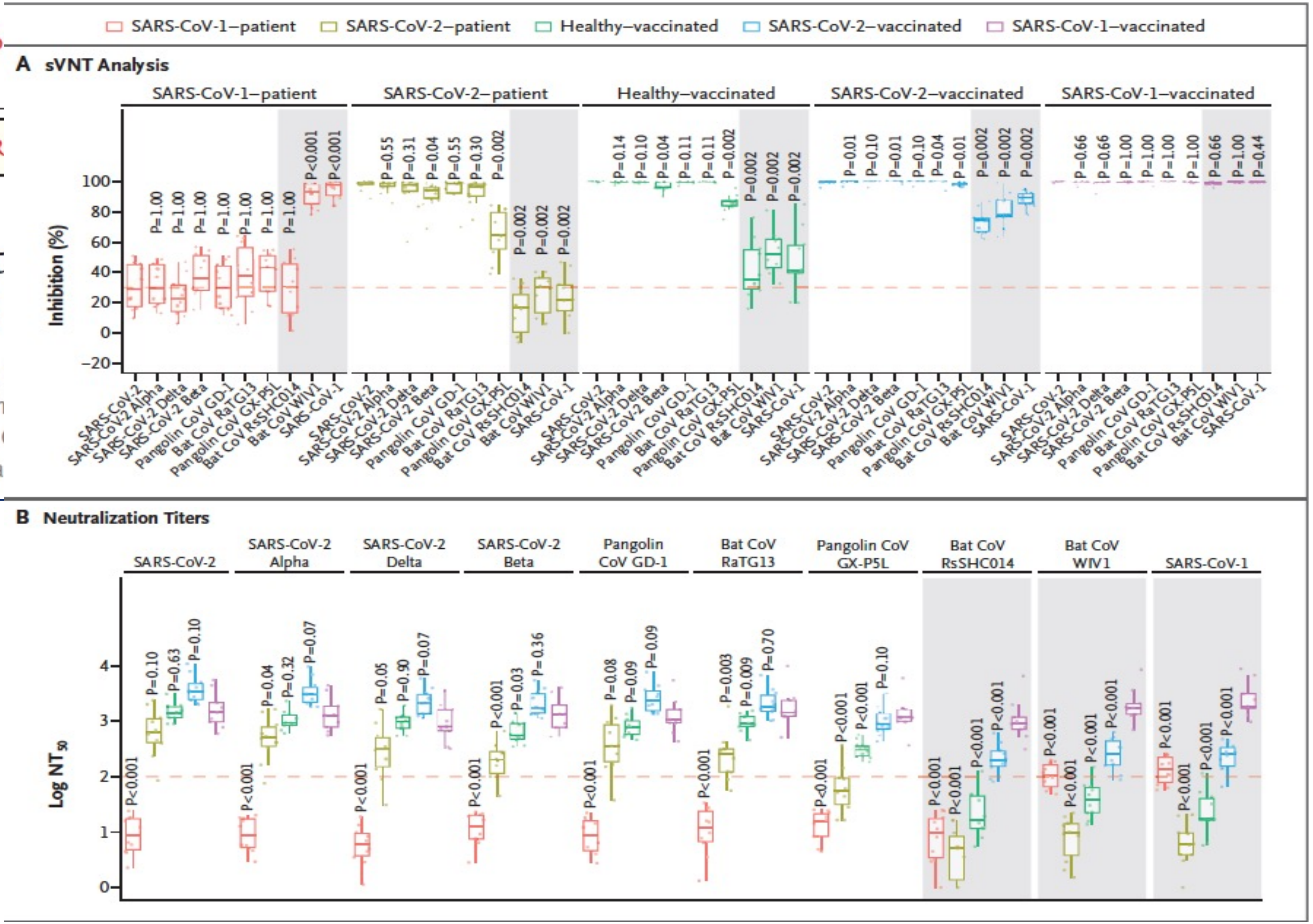
pan-beta-Coronavirus


The NEW ENGLAND JO

BRIEF R

Pan-Sarbecovirus Neut
BNT162b2-Immunized

Chee-Wah Tan, Ph.D., Wan-Ni Chia,
Feng Zhu, Ph.D., Beng-Lee Lin
Tun-Linn Thein, M.P.H., Mark I.-C.
David C. Lye, F.R.C.P., a



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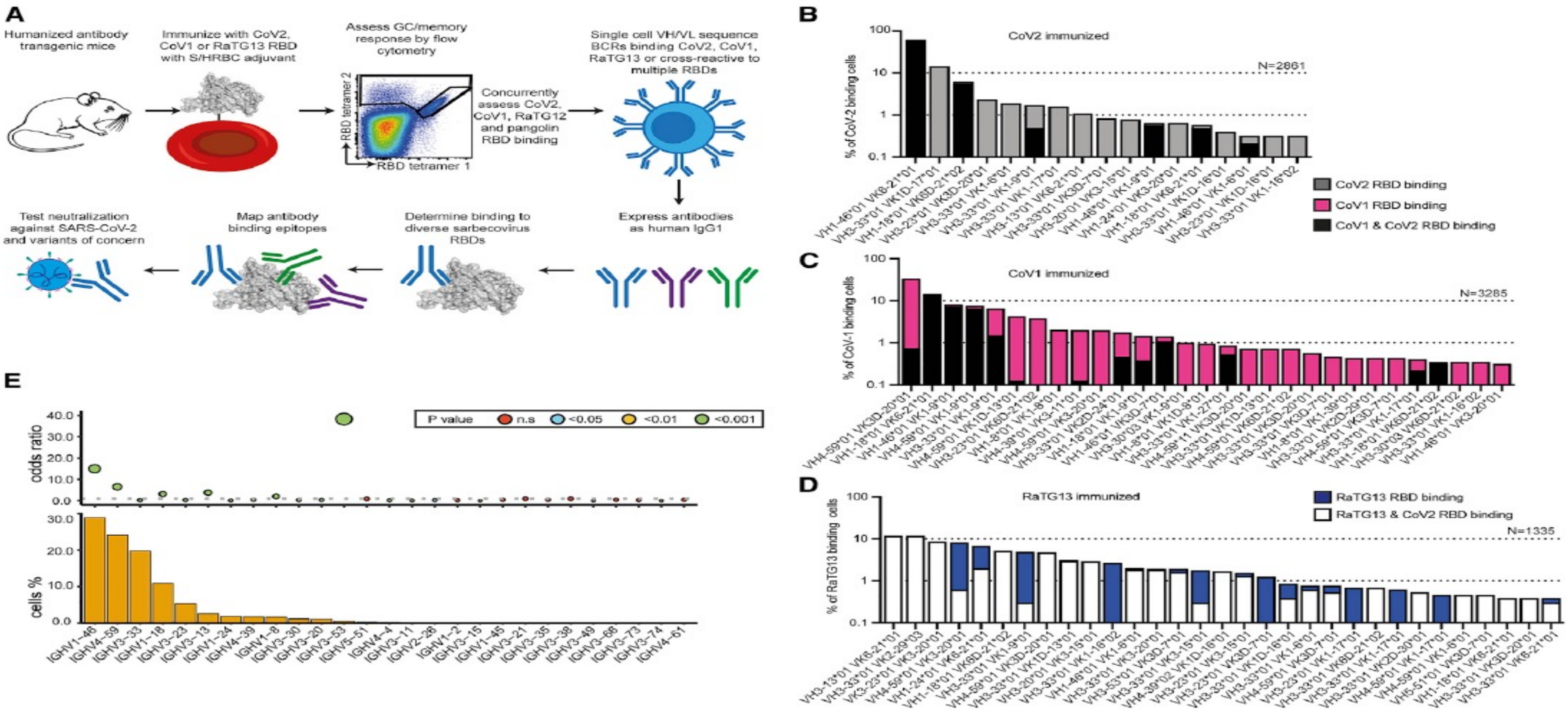
pan-beta-Coronavirus



Immunity 54, 2908–2921, December 14, 2021

YENİ COVID-19 AŞILARI

pan-beta-Coronavirus

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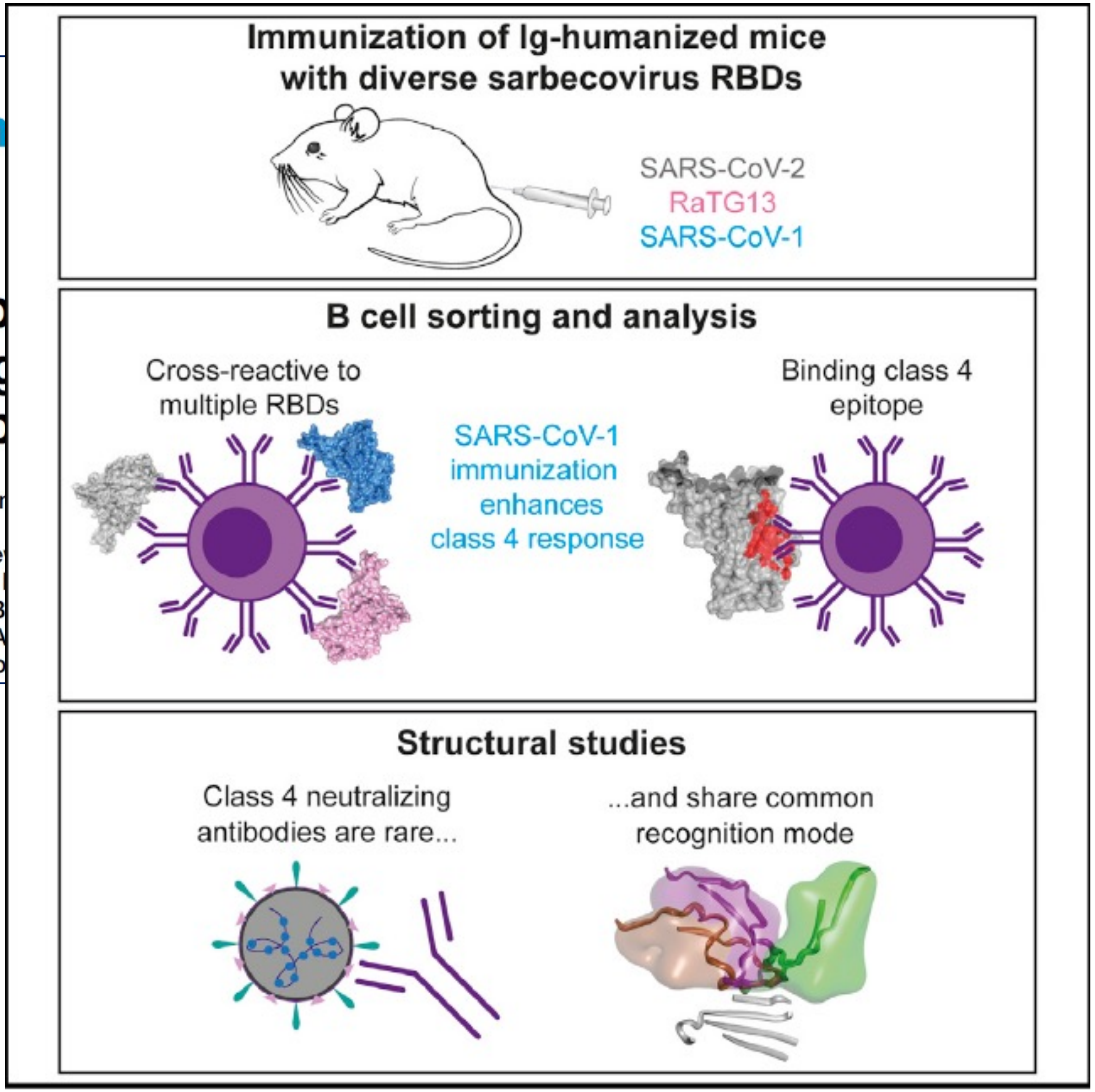
Article

Immunizations with diverse sarbecovirus recep binding domains elicit SARS-CoV-2 neutralizing antibodies against a conserved site of vulnerab

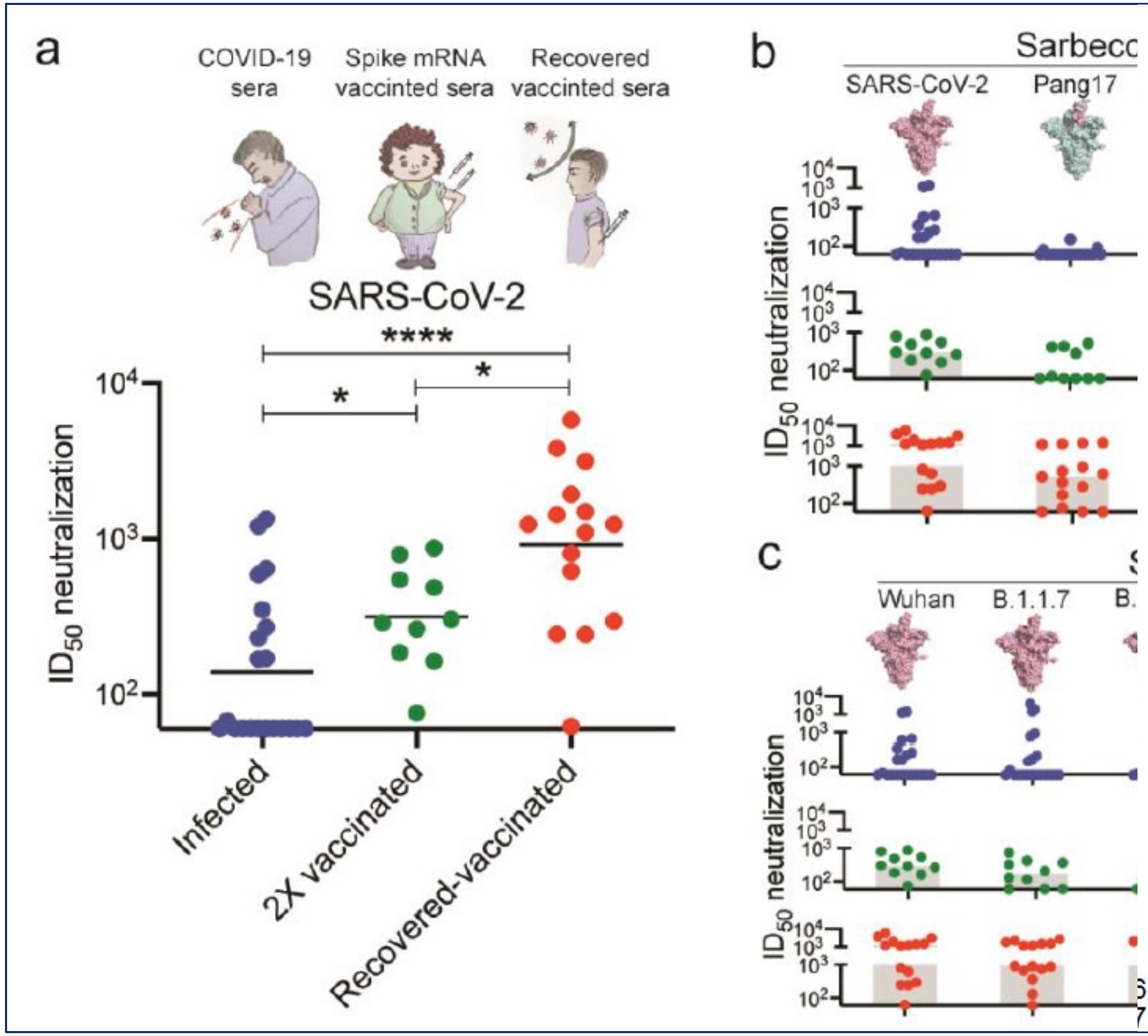
Deborah L. Burnett,[1,2,13,*] Katherine J.L. Jackson,[1] David B. Langley,[1] Anupria Aggrawal,[3] Alberto Ospi
Matt D. Johansen,[4] Harikrishnan Balachandran,[3] Helen Lenthall,[1] Romain Rouet,[1,2] Gregory Walker,[2]
Bernadette M. Saunders,[4] Mandeep Singh,[1,2] Hui Li,[3] Jake Y. Henry,[1] Jennifer Jackson,[1] Alastair G. Ste
Franka Witthauer,[7] Matthew A. Spence,[8] Nicole G. Hansbro,[4] Colin Jackson,[8] Peter Schofield,[1,2] Claire
Marianne Martinello,[3] Sebastian R. Schulz,[7] Edith Roth,[7] Anthony Kelleher,[3] Sean Emery,[3] Warwick J. B
William D. Rawlinson,[2,6] Rudolfo Karl,[9] Simon Schäfer,[9] Thomas H. Winkler,[9] Robert Brink,[1,2] Rowena A
Philip M. Hansbro,[4] Hans-Martin Jäck,[7] Stuart Turville,[2,3] Daniel Christ,[1,2,12] and Christopher C. Goodno



ener çağrı dinleyici

YENİ COVID-19 AŞILARI

pan-beta-Coronavirus



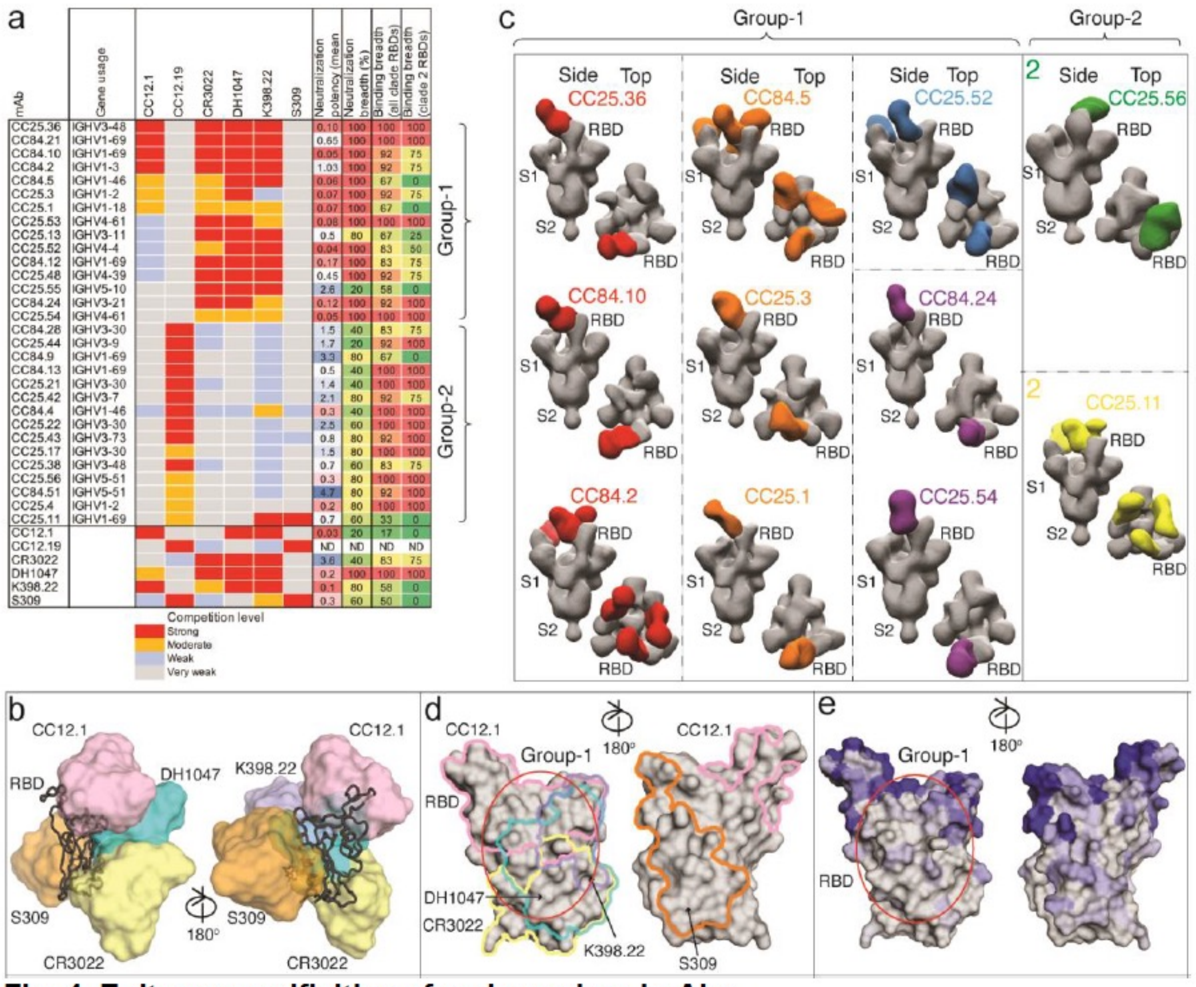
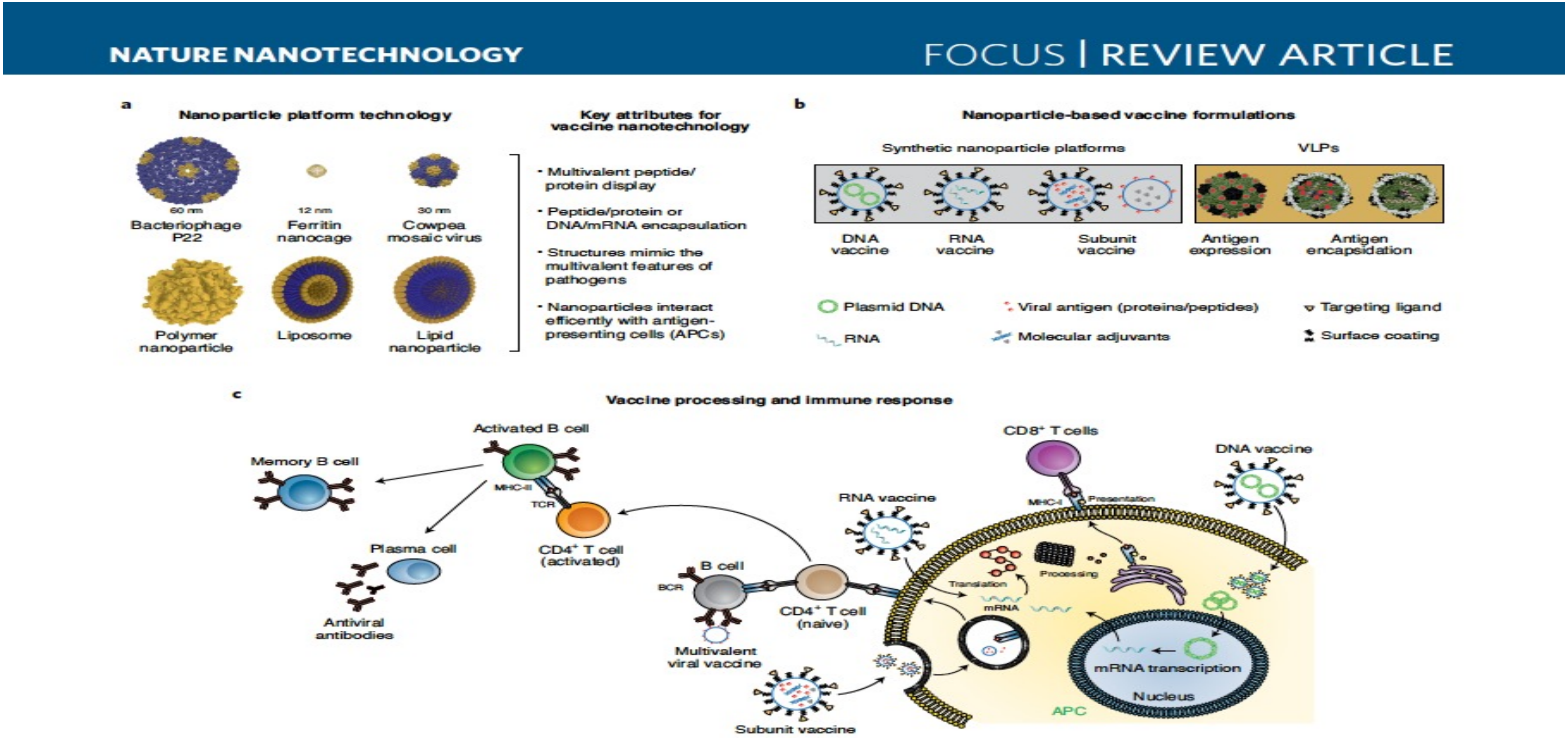


Fig. 4. Epitope specificities of sarbecovirus bnAbs.

WinTeng He et al. BioXriv 2022

YENİ COVID-19 AŞILARI

NANOTEKNOLOJİ



Shin et al. Nature Nanontechnology 2020

YENİ COVID-19 AŞILARI

STRUCTURAL VACCINOLGY

MABS
2022, VOL. 14, NO. 1, e2021601 (13 pages)
https://doi.org/10.1080/19420862.2021.2021601

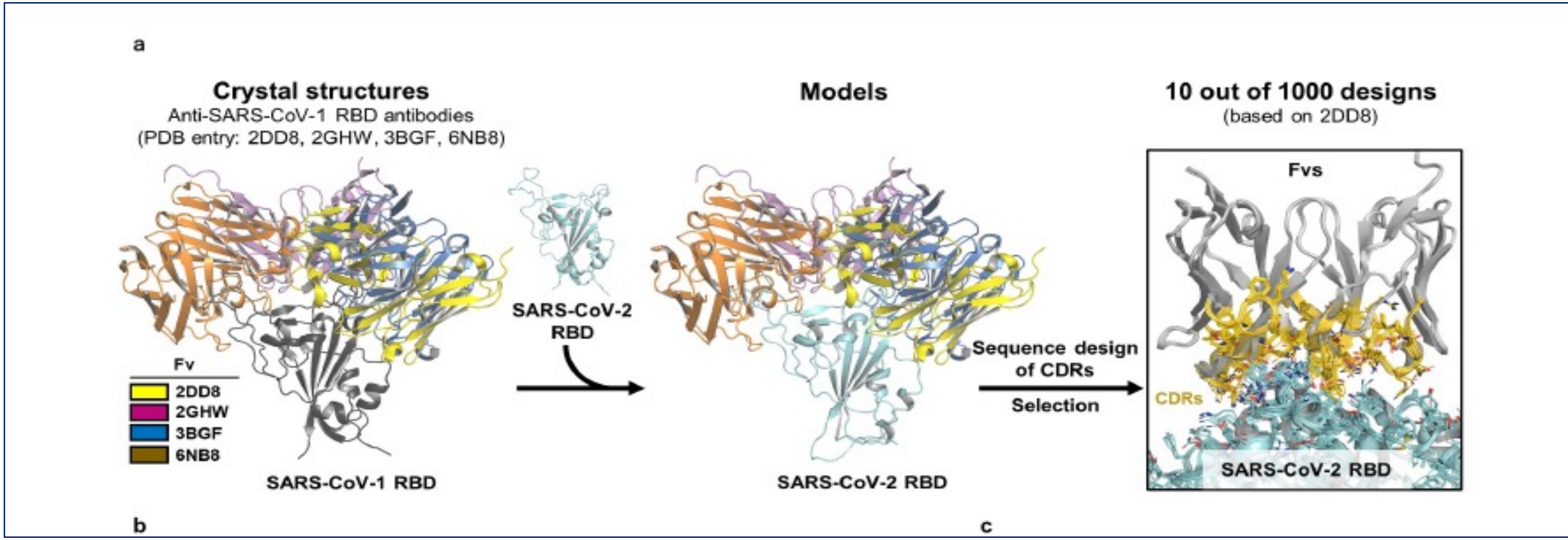
Taylor & Francis
Taylor & Francis Group

REPORT

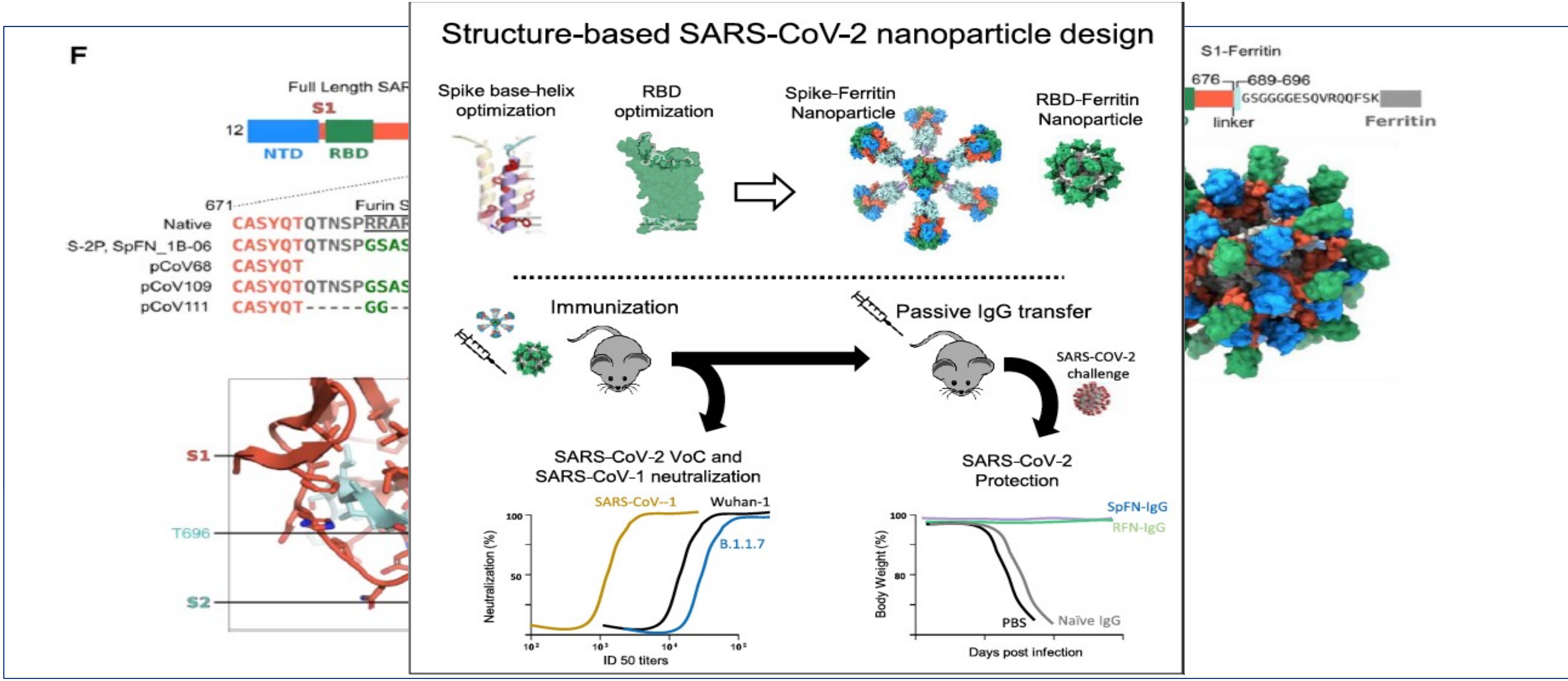
OPEN ACCESS Check for updates

Computational design of a neutralizing antibody with picomolar binding affinity for all concerning SARS-CoV-2 variants

Bo-Seong Jeong[a], Jeong Seok Cha[b,*], Insu Hwang[c,*], Uijin Kim[b], Jared Adolf-Bryfogle[d,e], Brian Coventry[f], Hyun-Soo Cho[b], Kyun-Do Kim[c], and Byung-Ha Oh[a]



YENİ COVID-19 AŞILARI



Cell Reports 37, 110143, December 21, 2021

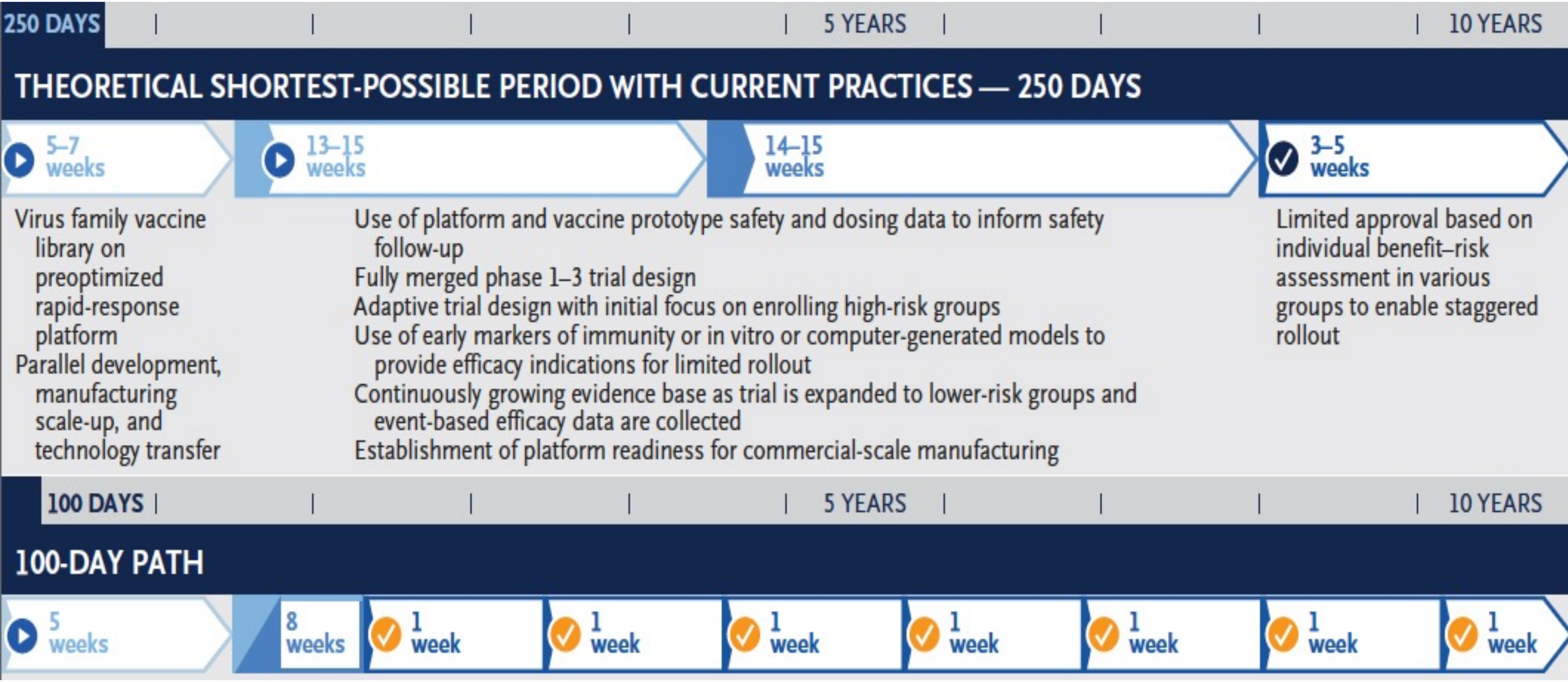
The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Delivering Pandemic Vaccines in 100 Days — What Will It Take?

Melanie Saville, M.B., B.S., Jakob P. Cramer, M.D., Matthew Downham, Ph.D., Adam Hacker, Ph.D.,
Nicole Lurie, M.D., M.S.P.H., Lieven Van der Veken, M.D., Mike Whelan, Ph.D., and Richard Hatchett, M.D.

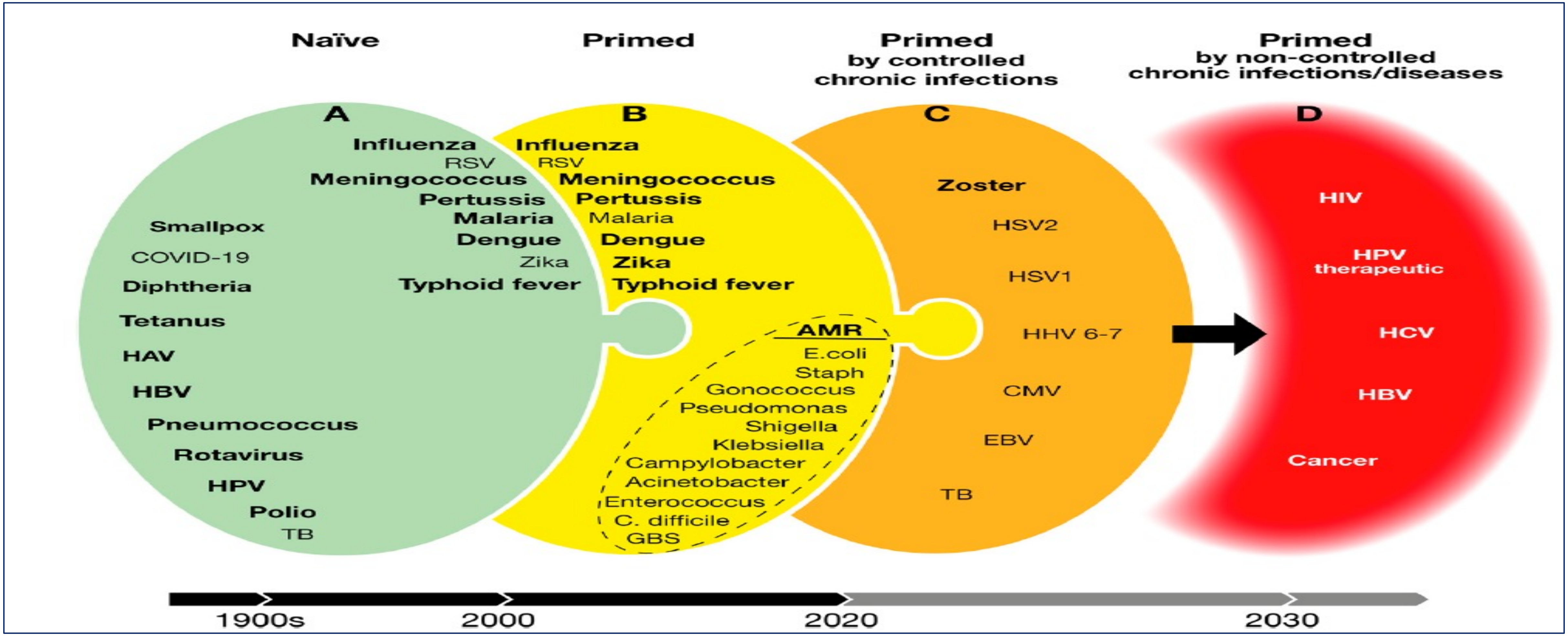
This article was published on March 2, 2022, at NEJM.org.



This article was published on March 2, 2022, at NEJM.org.


ALL
BAD THINGS
MUST COME
TO AN
END.

YENİ AŞILAR



Rappuoli et al. PNAS 2021

YENİ AŞILAR

Modality	Program Indication	ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Core modalities								
Adults	COVID-19 vaccine	mRNA-1273/Spikevax®						Worldwide
	COVID-19 vaccine	mRNA-1273.351	Beta variant					Worldwide
	COVID-19 vaccine	mRNA-1273.617	Delta variant					Worldwide
	COVID-19 vaccine	mRNA-1273.211	Beta variant + wild-type					Worldwide
	COVID-19 vaccine	mRNA-1273.213	Beta+Delta variant					Worldwide
	COVID-19 vaccine	mRNA-1273.529	Omicron variant					Worldwide
	COVID-19 vaccine	mRNA-1283	Next generation (2-5 °C)					Worldwide
	Flu vaccine	mRNA-1010	Phase 3 prep					Worldwide
	Flu vaccine	mRNA-1011						Worldwide
	Flu vaccine	mRNA-1012						Worldwide
	Flu vaccine	mRNA-1020						Worldwide
	Flu vaccine	mRNA-1030						Worldwide
	COVID + Flu vaccine	mRNA-1073	mRNA-1273 mRNA-1010					Worldwide
	Older Adults RSV vaccine	mRNA-1345						Worldwide

YENİ AŞILAR

Adolescents & Pediatrics	COVID-19 (adolescents)	**mRNA-1273**	TeenCOVE	Worldwide
	COVID-19 vaccine (pediatrics)	**mRNA-1273**	KidCOVE	Worldwide
	Pediatric RSV vaccine	**mRNA-1345**		Worldwide
	Pediatric hMPV+PIV3 vaccine	**mRNA-1653**		Worldwide
	Pediatric RSV + hMPV vaccine	**mRNA-1365**		Worldwide
Latent Vaccines	CMV vaccine	**mRNA-1647**		Worldwide
	EBV vaccine (to prevent infectious mononucleosis)	**mRNA-1189**		Worldwide
	EBV vaccine (to prevent EBV sequelae)	**mRNA-1195**		Worldwide
	HSV Vaccine	**mRNA-1608**		Worldwide
	VZV Vaccine	**mRNA-1468**		Worldwide
Prophylactic Vaccines	HIV vaccine	**mRNA-1644**		Worldwide ***IAVI/others*** *funded*
	HIV vaccine	**mRNA-1574**		Worldwide ***IAVI/BMGF/NIAID and others*** *funded*
Public Health Vaccines	Zika vaccine	**mRNA-1893**		Worldwide ***BARDA*** *funded*
	Nipah vaccine	**mRNA-1215**		Worldwide ***NIH*** *funded*

ener çağrı dinleyici

YENİ AŞILAR

Systemic Secreted & Cell Surface Therapeutics	IL-2 *Autoimmune disorders*	mRNA-6231		Worldwide
	Relaxin	mRNA-0184		Worldwide
	PD-L1 *Autoimmune hepatitis*	mRNA-6981		Worldwide
Cancer Vaccines	Personalized cancer vaccine (PCV)	mRNA-4157		50-50 global profit sharing with **Merck**
	KRAS vaccine	mRNA-5671		Worldwide
	Checkpoint Vaccine	mRNA-4359		Worldwide
Intratumoral Immuno-Oncology	OX40L/IL-23/IL-36γ (Triplet) *Solid tumors/lymphoma*	mRNA-2752		Worldwide
	IL-12 *Solid tumors*	MEDI1191		50-50 U.S. profit sharing; **AZ** to pay royalties on ex-U.S. sales
Localized Regenerative Therapeutics	VEGF-A *Myocardial ischemia*	AZD8601		**AZ** to pay milestones and royalties
Systemic Intracellular Therapeutics	PCCA/PCCB *Propionic acidemia (PA)*	mRNA-3927		Worldwide
	MUT *Methylmalonic acidemia (MMA)*	mRNA-3705		Worldwide
	G6Pase *Glycogen Storage Disease Type 1a (GSD1a)*	mRNA-3745	Open IND	Worldwide
	PAH *Phenylketonuria (PKU)*	mRNA-3283		Worldwide
	Crigler-Najjar Syndrome Type 1 (CN-1)	mRNA-3351		Provided to **ILCM**, Institute for Life Changing Medicines free of charge
Inhaled Pulmonary Therapeutics	Cystic Fibrosis (CF)	VXc0522		**Vertex** to pay milestones and royalties

YENİ AŞILAR

Drug Class	Product Candidate	Indication (*Targets*)	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Rights/Collaborator
mRNA	BNT162b2	COVID-19						Fosun Pharma (China), Pfizer (Global, except China)
	BNT161	Influenza						Pfizer
	Un-named program	Shingles						Pfizer
	Un-named program	Malaria						Fully-owned
	Un-named program	Tuberculosis[4]						Bill & Melinda Gates Foundation
	Un-named program	HSV 2						Fully-owned
	Un-named program	HIV[4]						Bill & Melinda Gates Foundation
	Undisclosed programs	Additional mRNA vaccine programs[5]						Fully-owned
	Undisclosed programs	Precision antibacterials						Fully-owned

YENİ AŞILAR

Name		Therapeutic Area	Preclinical	Phase 1	Phase 2	Phase 3	Marketed
NVX-CoV2373	Matrix-M	Coronavirus					
NanoFlu™ - Seasonal Influenza Vaccine (Adults Aged 65+ Years)	Matrix-M	Seasonal Influenza					
ResVax™ - RSV F Vaccine (Infants via Maternal Immunization)		Respiratory Syncytial Virus (RSV)					
RSV F Vaccine (Older Adults 60+ Years)	Matrix-M	Respiratory Syncytial Virus (RSV)					
RSV F Vaccine (Pediatrics 6 Months to 5 Years)		Respiratory Syncytial Virus (RSV)					
Combination Seasonal Influenza/RSV F Vaccine (Older Adults 60+ Years)	Matrix-M	Combination Seasonal Influenza/Respiratory Syncytial Virus					
Ebola GP Vaccine	Matrix-M	Ebola Virus					
Middle East Respiratory Syndrome (MERS) Vaccine		Middle East Respiratory Syndrome (MERS)					

- COVID-19 “**AŞILARININ**” GELECEĞİ

a. Dünyada yaygın olarak kullanılan COVID-19 aşılarına rağmen yeni aşılara ya da yeni aşı teknolojilerine gereksinim var mı?
b. Mevcut yeni varyantlar ve olası yeni endişe verici varyantlar için yeni nesil aşılar mümkün mü (Panbetacoronavirus vaccine?)
c. Solunum yolu virüslerinde kombine aşılama stratejileri mevcut mu?
d. Pandemi aşılaması sonrası: Endemik solunum yolu virüslerinde aşılama?

- COVID-19 “**AŞILAMASININ**” GELECEĞİ

a. COVID-19 aşılarının tüm dünyada yüksek risk gruplarına eşit ve adil dağıtımı
b. COVID-19 pandemisinin rutin aşılama üzerine etkileri
c. Pandemi aşılamasının geleceği

- “**AŞILAMANIN**” GELECEĞİ

PANDEMİ AŞILAMASI

International Journal of Infectious Diseases 112 (2021) 300–317

Contents lists available at ScienceDirect

International Journal of Infectious Disease

journal homepage: www.elsevier.com/locate/ijid

ELSEVIER

Table 1
Features of 20th and 21st century influenza pandemics

Pandemic	Dates	Influenza virus	No. waves
Spanish influenza	1918–1920	A/H1N1	3(Barry, 2005)
Asian influenza	1957–1958	A/H2N2	2(Rogers 2020)
Hong Kong influenza	1968–1969	A/H3N2	2(Cockburn et al., 1969, Saunders-Hastings and K
Russian influenza	1977–1979	A/H1N1	1(Gregg et al., 1978)
Swine influenza	2009–2010	A/H1N1pdm09	2 or 3 depending on location(Jhung et al., 201 Saunders-Hastings and K

SCIENCE

FRIDAY, MAY 30, 1919

CONTENTS

MSS. intended for publication and books, etc., intended for review should be sent to The Editor of Science, Garrison-on-Hudson, N. Y.

THE LESSONS OF THE PANDEMIC

THE pandemic which has just swept round the earth has been without precedent. There have been more deadly epidemics, but they have been more circumscribed; there have been epidemics almost as widespread, but they have been less deadly. Floods, famines, earthquakes and volcanic eruptions have all written their stories in terms of human destruction almost too terrible for comprehension, yet never before has there been a catastrophe at once so sudden, so devastating and so universal.

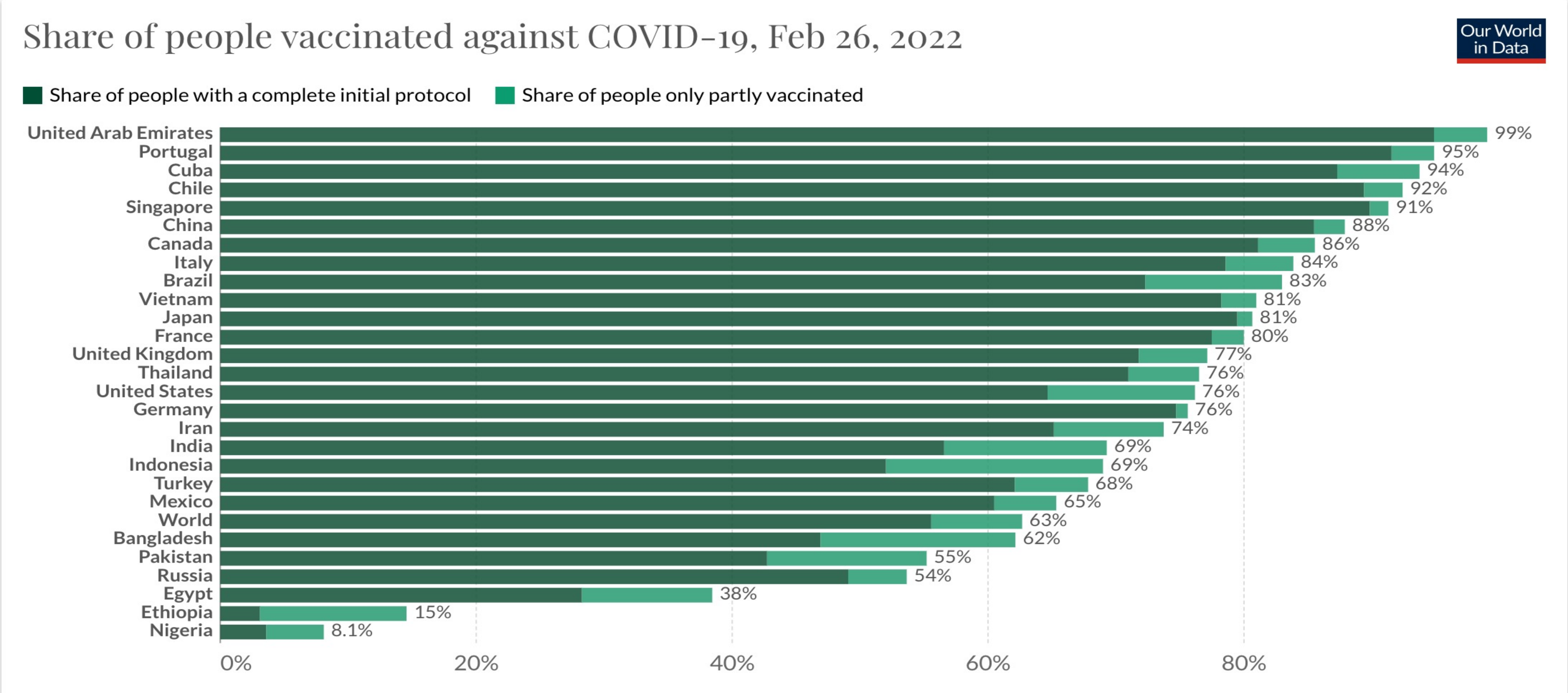
The most astonishing thing about the pandemic was the complete mystery which surrounded it. Nobody seemed to know what the disease was, where it came from or how to stop it. Anxious minds are inquiring to-day whether another wave of it will come again.

The fact is that although influenza is one of the oldest known of the epidemic diseases, it is the least understood. Science, which by patient and painstaking labor has done so much to drive other plagues to the point of extinction has thus far stood powerless before it. There is doubt about the causative agent and the predisposing and aggravating factors. There has been a good deal of theorizing about these matters, and some good research, but no common agreement has been reached with respect to them.

The measures which were introduced for the control of the pandemic were based upon the slenderest of theories. It was assumed that the influenza could be stopped by the employment of methods which it was assumed would stop the other respiratory diseases. This double assumption proved to be a weak reed to lean upon. The respiratory diseases as a class are not under control. They constitute the most frequent cause of death, yet it is not known how they can be prevented.

Three main factors stand in the way of pre-

COVID-19 AŞILAMASI



COVID-19 AŞILAMASI

ener çağrı dinleyici

COVID-19 AŞILAMASI

	Lottery with non-cash prize
Example	Chance to win a truck
Principles	
Receipt is certain	○
Delivered immediately	○
Valued by recipient	◉
Likely impact	○

implemented well. A systematic review of vaccine promotion interventions recommends guaranteed cash payments, with an estimate that they increase uptake of vaccines by 8%.[2] A trial in Sweden found guaranteed payments provided by researchers increased COVID-19 vaccination uptake by 4%.[3] In the United States (U.S.), North Carolina offered $25 incentives for adult vaccination or driving someone to get COVID-19 vaccine, a program that bolstered vaccine uptake.[4] Guaranteed cash incentive programs elsewhere have included Ukraine and Serbia, though these programs' impact has not been evaluated. Employers and insurers have also offered guaranteed cash payments, although these may be less effective because they are unlikely to be provided directly after vaccination.

***Table 1*: Behavioral principles for effective vaccination incentives.**
• = Stronger if program is implemented well; ◉ = Moderate; ○ = Weaker.

Incentives for COVID-19 vaccination

COVID-19 AŞILAMASI

	Incentive Type			
	Guaranteed cash	Guaranteed non-	Lottery with cash	Lottery with non-cash prize
Example	$			ce to win a truck
Principles				
Receipt is certain				○
Delivered immediately				○
Valued by recipient				◉
Likely impact				○

Another promising option is guaranteed non-cash rewards, which may be the most common COVID-19 incentive globally. These rewards are available soon after vaccination, but the value people assign to them may vary substantially or not be enough to motivate the hesitant. For this reason, they may be less effective than guaranteed cash payments. Offers have included free eggs in China, hummus in Israel, and blenders in India. This and the remaining options remain largely unevaluated for COVID-19 vaccination.

***Table 1*: Behavioral principles for effective vaccination incentives.**

• = Stronger if program is implemented well; ◉ = Moderate; ○ = Weaker.

Incentives for COVID-19 vaccination

COVID-19 AŞILAMASI

	Incentive Type	
	Guaranteec paymer	ith non- ›rize
Example	$25 paym	o win a ck
Principles		
Receipt is certain	●	
Delivered immediately	●	
Valued by recipient	●	
Likely impact	●	

A less promising option is lotteries with cash prizes. Lottery incentives fail two of our criteria by being probabilistic rather than guaranteed and being awarded well after vaccination. People prefer sure things over gambles when receiving a benefit according to Prospect Theory. Lotteries can have some effect, however, if people overestimate their slim chances. In the U.S., Ohio offered a million-dollar lottery but evaluations have found null, mixed, or at best a small benefit early on.[5,6] High-value lotteries in Canada, Latvia, and the Philippines have largely not been evaluated.

***Table 1*: Behavioral principles for effective vaccination incentives.**
● = Stronger if program is implemented well; ◉ = Moderate; ○ = Weaker.

ener çağrı dinleyici

Incentives for COVID-19 vaccination

COVID-19 AŞILAMASI

	Incentive Type			
	Guaranteed c payment			n-
Example	$25 paymer			a
Principles				
Receipt is certain	●			
Delivered immediately	●			
Valued by recipient	●			
Likely impact	●	◉	◉	○

The least promising option is lotteries with non-cash prizes. These likely have the smallest impact of all the incentive options, given that they fail all our criteria. They have the weaknesses of cash lotteries as well as having a perceived value that varies considerably among members of the public. For example, Hong Kong's lottery prizes of an apartment may have wide appeal but free motorcycles in the Philippines may not appeal to some residents.

***Table 1*: Behavioral principles for effective vaccination incentives.**
● = Stronger if program is implemented well; ◉ = Moderate; ○ = Weaker.

Incentives for COVID-19 vaccination

PANDEMİ ÖNCESİ DÖNEMDE RUTİN AŞILAMA

Measuring routine childhood vaccination coverage in 204 countries and territories, 1980–2019: a systematic analysis for the Global Burden of Disease Study 2020, Release 1

*GBD 2020, Release 1, Vaccine Coverage Collaborators**

www.thelancet.com Vol 398 August 7, 2021

PANDEMİ ÖNCESİ DÖNEMDE RUTİN AŞILAMA

	DTP3	MCV1	Pol3	HepB3	Hib3	MCV2	RCV1	PCV3	RotaC	Any	All
Global, 2010 (n=204)	59	59	57	48	44	35	47	9	2	67	0
Global, 2019 (n=204)	53	61	53	50	50	35	56	31	14	68	5
Central Europe, eastern Europe, and central Asia, 2010 (n=29)	83	90	79	66	52	79	90	3	0	90	0
Central Europe, eastern Europe, and central Asia, 2019 (n=29)	66	69	69	55	59	55	69	21	3	83	3
High income, 2010 (n=36)	86	75	92	53	72	44	72	17	0	92	0
High income, 2019 (n=36)	89	89	92	75	89	61	86	69	14	97	6
Latin America and Caribbean, 2010 (n=33)	61	64	55	52	52	18	61	3	12	76	0
Latin America and Caribbean, 2019 (n=33)	36	58	39	36	36	27	55	18	6	64	3
North Africa and Middle East, 2010 (n=21)	67	62	62	67	52	57	43	33	0	71	0
North Africa and Middle East, 2019 (n=21)	62	57	57	62	62	52	57	52	24	62	24
South Asia, 2010 (n=5)	40	40	60	40	20	20	20	0	0	60	0
South Asia, 2019 (n=5)	40	80	60	40	40	20	60	20	0	80	0
Southeast Asia, east Asia, and Oceania, 2010 (n=34)	59	53	56	53	32	35	35	6	0	62	0
Southeast Asia, east Asia, and Oceania, 2019 (n=34)	56	65	59	56	38	35	50	12	15	65	6
Sub-Saharan Africa, 2010 (n=46)	22	28	17	20	20	4	2	2	0	28	0
Sub-Saharan Africa, 2019 (n=46)	26	33	17	26	26	2	28	24	24	41	0

Percentage

0% 25% 50% 75% 100%

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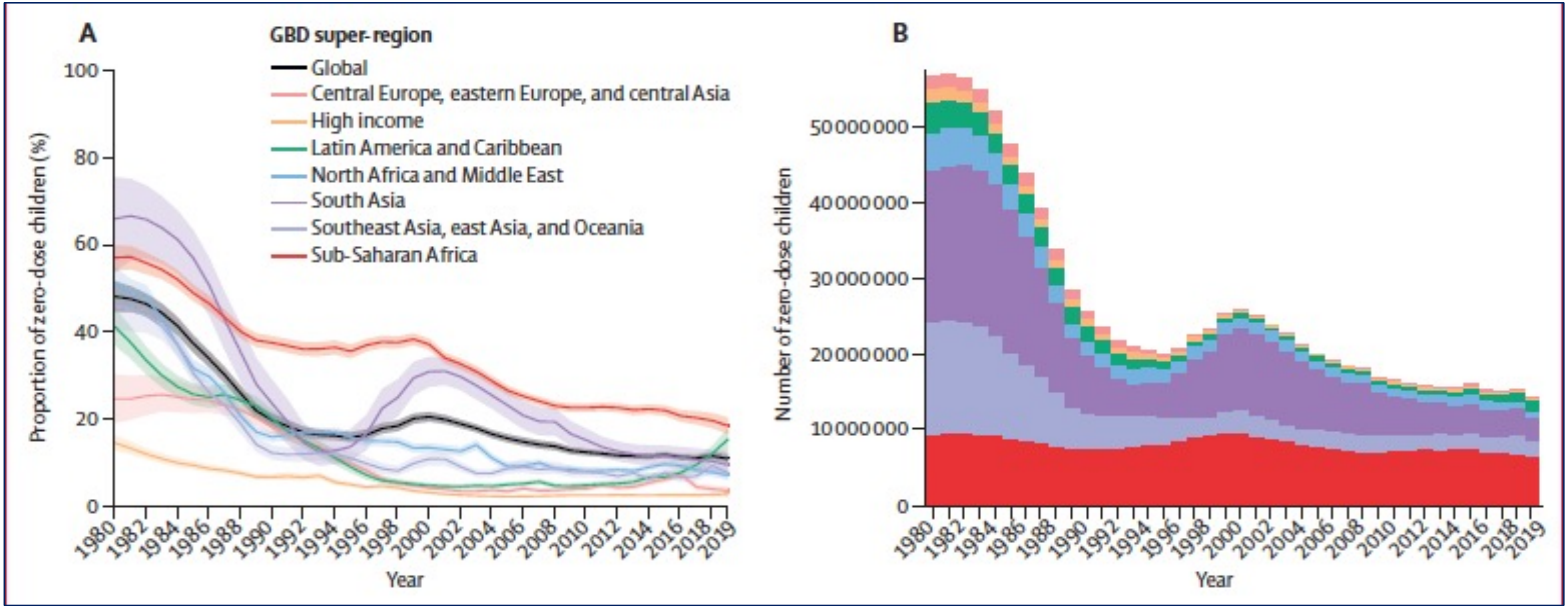

HİÇ AŞILANMAMIŞ ÇOCUKLAR

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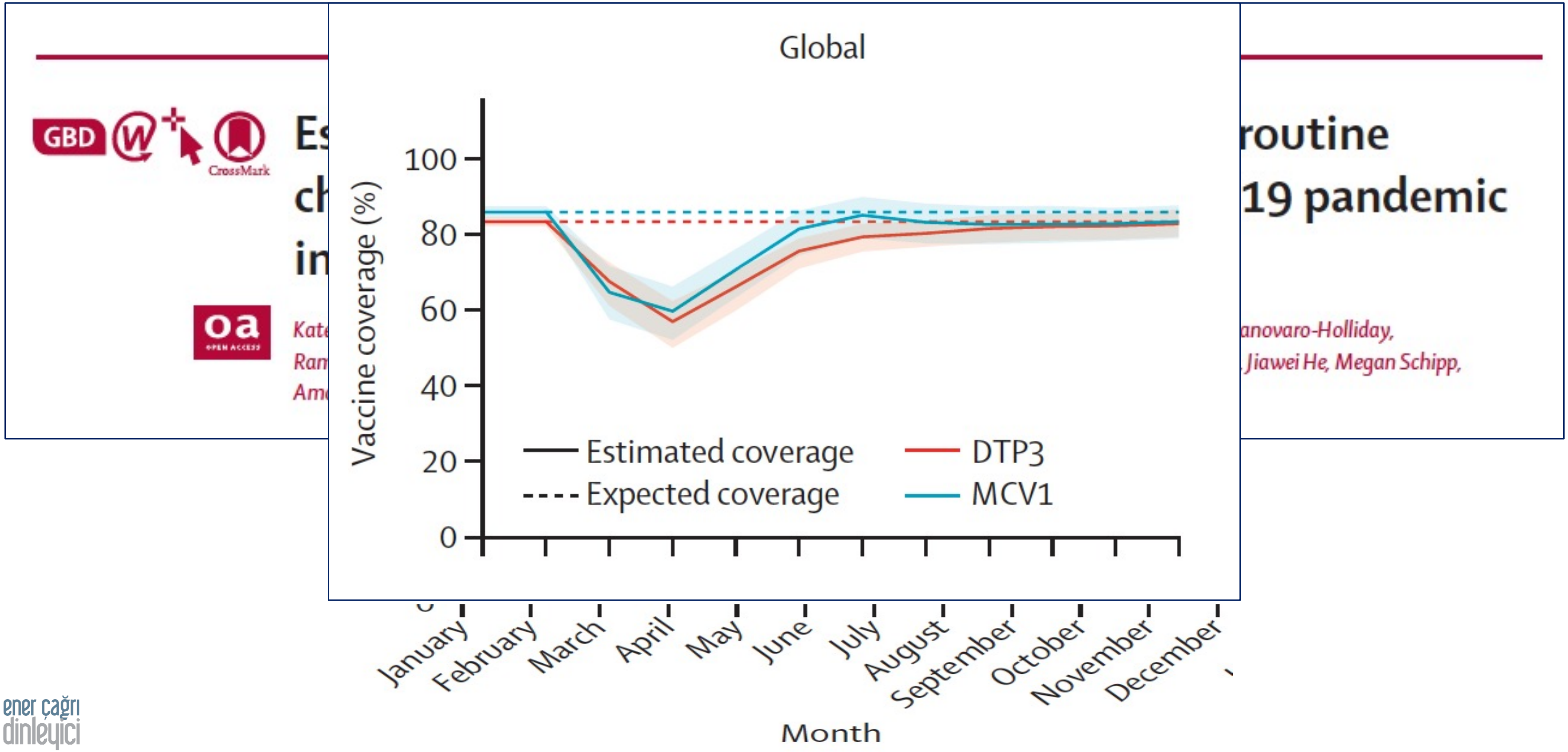
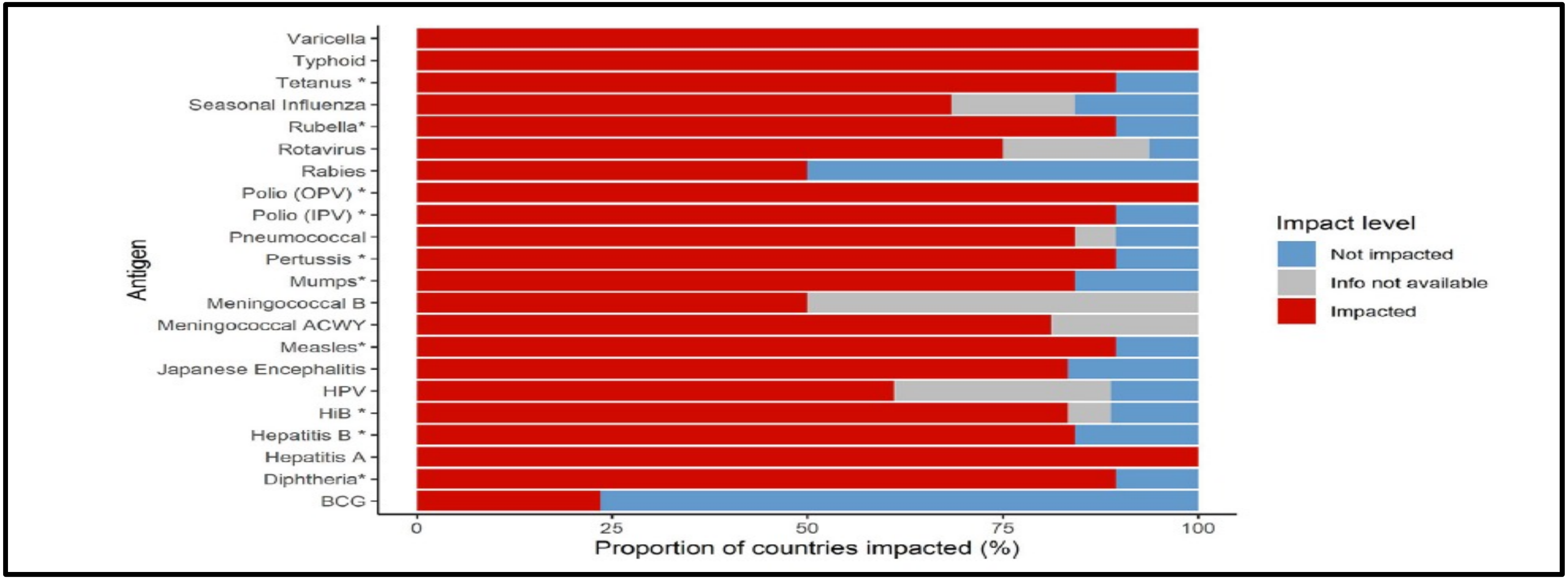
COVID19 PANDEMİSİ

RUTİN AŞILAMA



COVID19 PANDEMİSİ

RUTİN AŞILAMA



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COVID19 PANDEMIC

ROUTINE IMMUNIZATION
MASS CAMPAIGN

Vaccine xxx (xxxx) xxx

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Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Modelling the spread of serotype-2 vaccine derived-poliovirus outbreak in Pakistan and Afghanistan to inform outbreak control strategies in the context of the COVID-19 pandemic

Natalia A Molodecky [a,b,c,e,*], Hamid Jafari [d], Rana M Safdar [c,f], Jamal A Ahmed [b,c,e], Abdirahman Mahamud [b,c,e], Ananda S Bandyopadhyay [g], Hemant Shukla [d], Arshad Quddus [e], Michel Zaffran [e], Roland W Sutter [e], Nicholas C Grassly [a], Isobel M Blake [a]

AFGHANISTAN-PAKISTAN

SEROTYPE 2 POLIOVIRUS

COVID19 PANDEMIC

NEWS → NEWS STORIES → GPEI STATEMENT ON WPV1 IN MALAWI

17/02/2022

At-risk countries, Eradication, GPEI partners, Surveillance

GPEI Statement on WPV1 in Malawi

Wild poliovirus type 1 detected in Lilongwe, Malawi

17 February 2022 As a result of ongoing disease surveillance, the Global Polio Laboratory Network (GPLN) has confirmed the presence of type 1 wild poliovirus (WPV1) in a child suffering from paralysis in Tsabango, Lilongwe, Malawi. Analysis shows that the virus is genetically linked to WPV1 that was detected in Pakistan's Sindh province in October 2019.

The three-year-old girl in Malawi experienced onset of paralysis on 19 November 2021, and stool specimens were collected for testing on 26 and 27 November. Sequencing of the virus conducted in February by the National Institute for Communicable Diseases in South Africa and the U.S. Centers for Disease Control and Prevention confirmed this case as WPV1.

ener çağrı dinleyici

COVID19 PANDEMİSİ

RUTİN AŞILAMA
PERU

Peru

March: Cancellation of outpatient care (immunization, prenatal, obstetric, contraception, pediatric, adult, nutrition), health promotion activities, and home visits (for example, to administer meningococcal vaccines to people over 60 years of age in peri-urban areas of Lima due to lack of personal protective equipment). Maintenance of emergency services. Maintenance of response services to family and gender violence, with a specific line for violence against children, with a communication campaign to alert the population about these services.

UNDP LAC C19 PDS Nº. 19

Challenges posed by the COVID-19 pandemic in the health of women, children, and adolescents in Latin America and the Caribbean

ERİŞKİN AŞILAMA

COVID19 PANDEMİSİ

RUTİN AŞILAMA
KANADA

Vaccine 39 (2021) 5532–5537

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Continuity of routine immunization programs in Canada during the COVID-19 pandemic

Hannah Sell [a,b], Ali Assi [b], S. Michelle Driedger [c], Ève Dubé [d], Arnaud Gagneur [e], Samantha B. Meyer [f], Joan Robinson [g], Manish Sadarangani [h], Matthew Tunis [i], Shannon E. MacDonald [b,*]

Conclusions: Canadian routine immunization programs faced some disruptions due to the COVID-19 pandemic, particularly the school, adult, and older adult programs. Further research is needed to determine the measurable impact of the pandemic on routine vaccine coverage levels.

ERİŞKİN AŞILAMA

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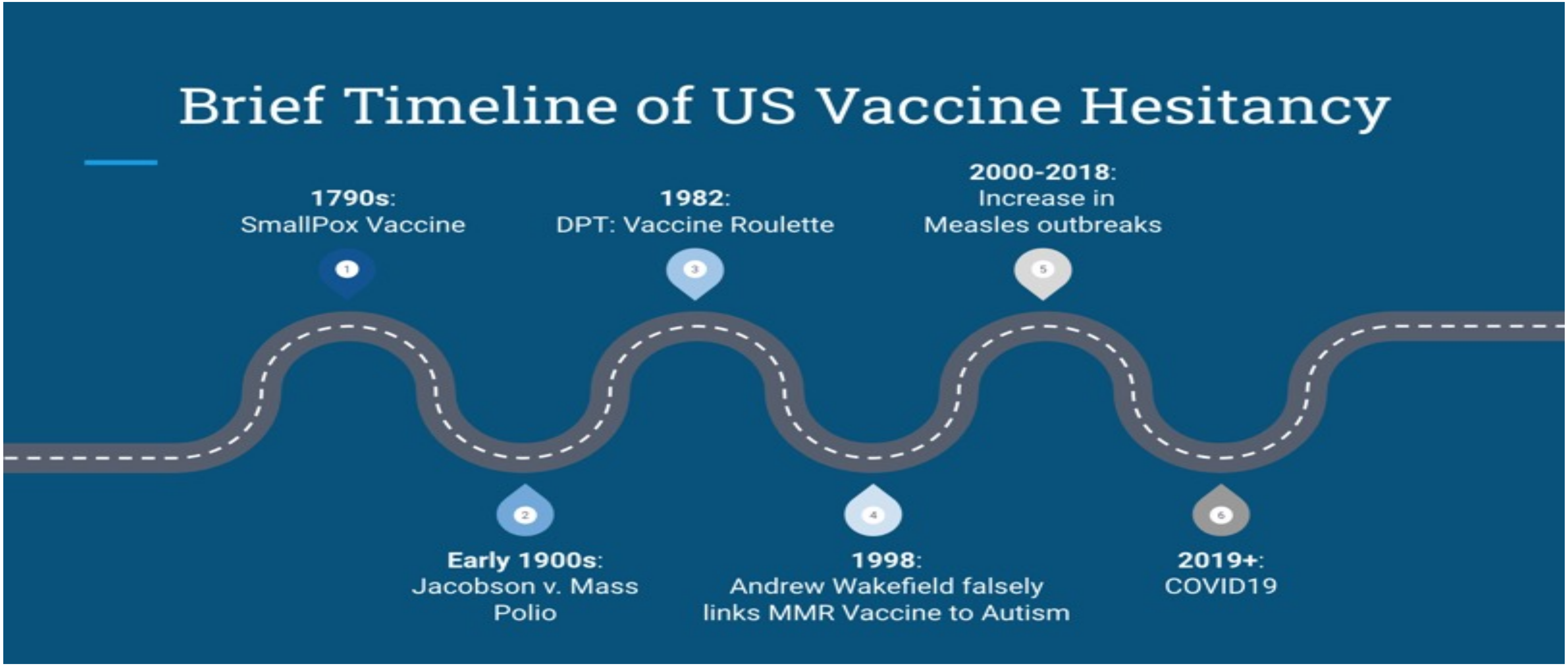
AŞI KARARSIZLIĞI/AŞI REDDİ



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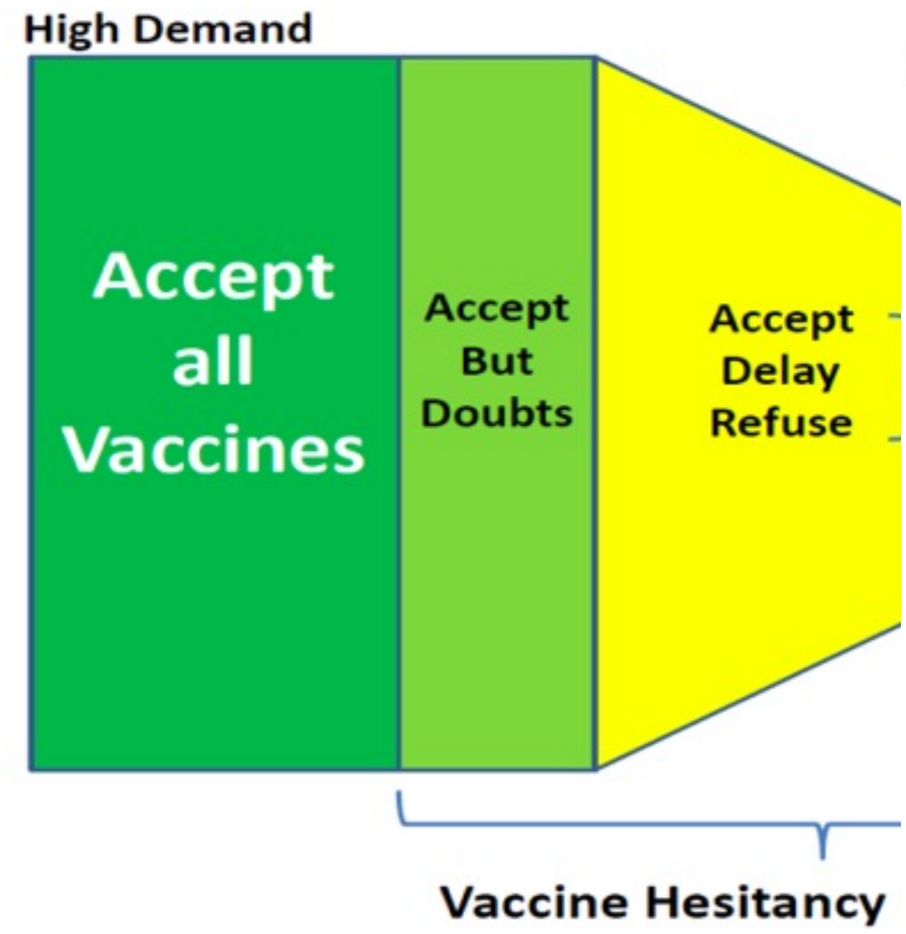
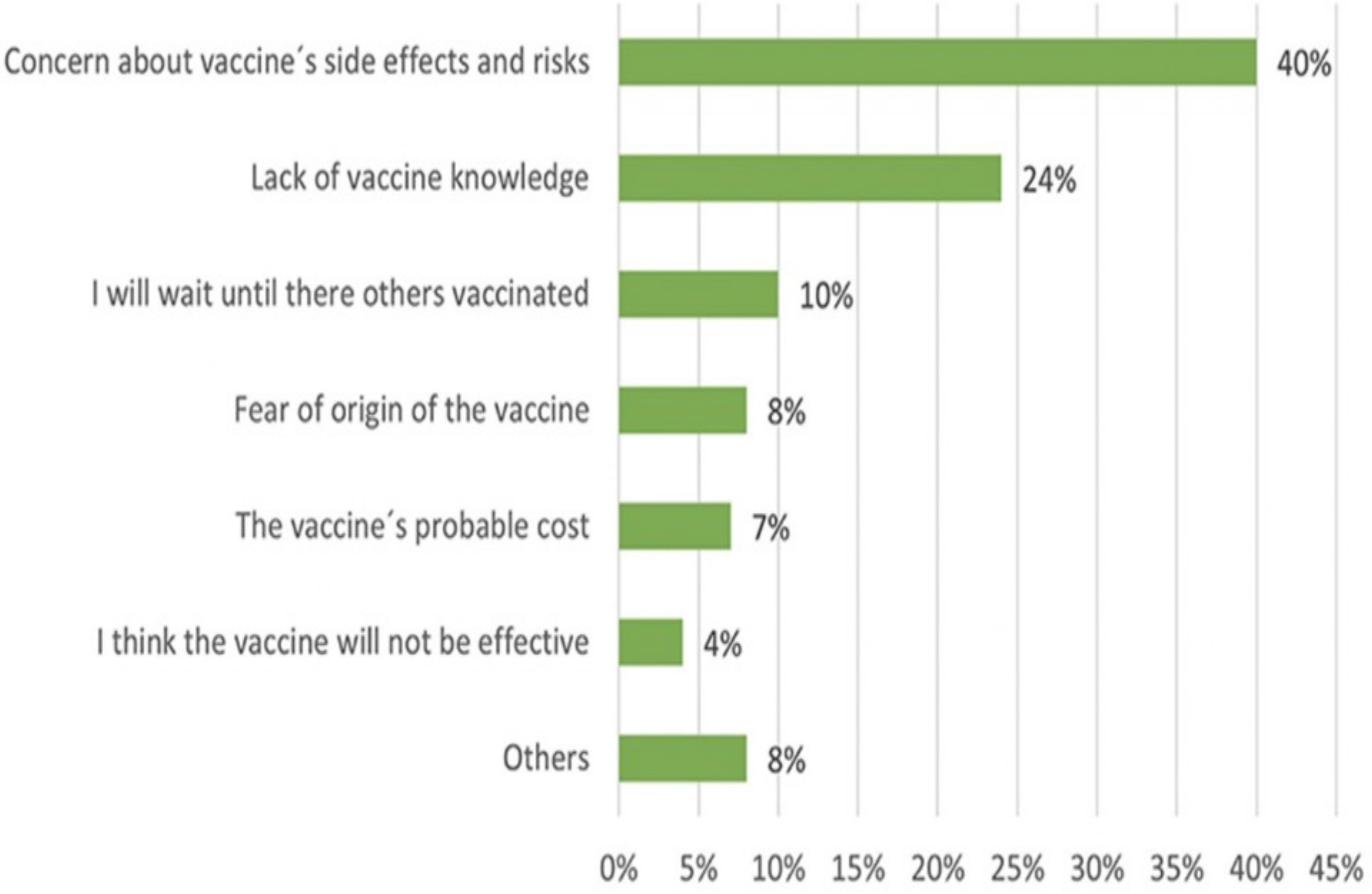
AŞI KARARSIZLIĞI/AŞI REDDİ





ener çağrı dinleyici

COVID-19 PANDEMİSİ MİTLER…

MYTH

The ingredients in COVID-19 vaccines are dangerous

FACT

- "Nearly all the ingredients in COVID-19 vaccines are also ingredients in many foods – fats, sugars, and salts."
- "COVID-19 vaccines do NOT contain ingredients like preservatives, tissues (like aborted fetal cells), antibiotics, food proteins, medicines, latex, or metals."

SOURCE CDC U.S. Centers for Disease Control and Prevention, "Myths and Facts about COVID-19 Vaccines"
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

MYTH

COVID-19 vaccines cause variants

FACT

- "COVID-19 vaccines do not create or cause variants of the virus that causes COVID-19. Instead, COVID-19 vaccines can help prevent new variants from emerging."
- "New variants of a virus happen because the virus that causes COVID-19 constantly changes through a natural ongoing process of mutation (change). As the virus spreads, it has more opportunities to change. High vaccination coverage in a population reduces the spread of the virus and helps prevent new variants from emerging."

SOURCE CDC U.S. Centers for Disease Control and Prevention, "Myths and Facts about COVID-19 Vaccines"
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

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COVID-19 PANDEMİSİ MİTLER…

MYTH

COVID-19 vaccines contain microchips

FACT

- "COVID-19 vaccines do not contain microchips. Vaccines are developed to fight against disease and are not administered to track your movement."
- "Vaccines work by stimulating your immune system to produce antibodies, exactly like it would if you were exposed to the disease. After getting vaccinated, you develop immunity to that disease, without having to get the disease first."

SOURCE CDC U.S. Centers for Disease Control and Prevention, "Myths and Facts about COVID-19 Vaccines"
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

MYTH

Natural immunity from the actual infection is better than immunity from the COVID-19 vaccination

FACT

- "Getting a COVID-19 vaccination is a safer and more dependable way to build immunity to COVID-19 than getting sick with COVID-19."
- "Getting a COVID-19 vaccination is also a safer way to build protection than getting sick with COVID-19. COVID-19 vaccination helps protect you by creating an antibody response without you having to experience sickness. Getting vaccinated yourself may also protect people around you, particularly people at increased risk for severe illness from COVID-19."

SOURCE CDC U.S. Centers for Disease Control and Prevention, "Myths and Facts about COVID-19 Vaccines"
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

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COVID-19 PANDEMİSİ MİTLER…

MYTH

Receiving a COVID-19 vaccine can make me magnetic

FACT

- “Receiving a COVID-19 vaccine will not make you magnetic, including at the site of vaccination which is usually your arm.”
- “COVID-19 vaccines do not contain ingredients that can produce an electromagnetic field at the site of your injection. All COVID-19 vaccines are free from metals.”

SOURCE CDC U.S. Centers for Disease Control and Prevention, “Myths and Facts about COVID-19 Vaccines”
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

MYTH

COVID-19 vaccines can shed virus in the body

FACT

- “Vaccine shedding is the release or discharge of any of the vaccine components in or outside of the body and can only occur when a vaccine contains a live or weakened version of the virus.”
- “None of the vaccines authorized for use in the U.S. contain a live virus.”

SOURCE CDC U.S. Centers for Disease Control and Prevention, “Myths and Facts about COVID-19 Vaccines”
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

COVID-19 PANDEMİSİ MİTLER…

MYTH

COVID-19 vaccines can alter my DNA

FACT

- "COVID-19 vaccines do not change or interact with your DNA in any way."
- "COVID-19 vaccines work by delivering instructions (genetic material) to our cells to start building protection against the virus that causes COVID-19."
- "After the body produces an immune response, it discards all the vaccine ingredients just as it would discard any information that cells no longer need. This process is a part of normal body functioning."

SOURCE CDC U.S. Centers for Disease Control and Prevention, "Myths and Facts about COVID-19 Vaccines"
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

MYTH

A COVID-19 vaccine can make me sick with COVID-19

FACT

- "Because none of the authorized COVID-19 vaccines in the United States contain the live virus that causes COVID-19, the vaccine cannot make you sick with COVID-19."
- "COVID-19 vaccines teach our immune systems how to recognize and fight the virus that causes COVID-19. Sometimes this process can cause symptoms, such as fever. These symptoms are normal and are signs that the body is building protection against the virus that causes COVID-19."

SOURCE CDC U.S. Centers for Disease Control and Prevention, "Myths and Facts about COVID-19 Vaccines"
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

COVID-19 PANDEMİSİ MİTLER…

MYTH

COVID-19 vaccines will affect my fertility

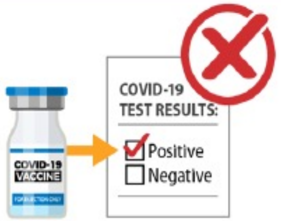
FACT

- "Currently no evidence shows that any vaccines, including COVID-19 vaccines, cause fertility problems (problems trying to get pregnant) in women or men."
- "COVID-19 vaccination is recommended for people who are pregnant, trying to get pregnant now, or might become pregnant in the future, as well as their partners."

SOURCE CDC U.S. Centers for Disease Control and Prevention, "Myths and Facts about COVID-19 Vaccines"
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
Updated by CDC Dec. 15, 2021. Accessed by ACG Jan. 20, 2022.

MYTH

Getting a COVID-19 vaccine will cause me to test positive on a viral test



FACT

- "None of the authorized and recommended COVID-19 vaccines can cause you to test positive on viral tests, which are used to see if you have a ***current infection***."
- If your body develops an immune response to vaccination, which is the goal, you may test positive on some antibody tests. Antibody tests indicate you had a ***previous infection*** and that you may have some level of protection against the virus."

SOURCE CDC U.S. Centers for Disease Control and Prevention, "Myths and Facts about COVID-19 Vaccines"
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/facts.html
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SCIENCE

FRIDAY, MAY 30, 1919

CONTENTS

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THE LESSONS OF THE PANDEMIC

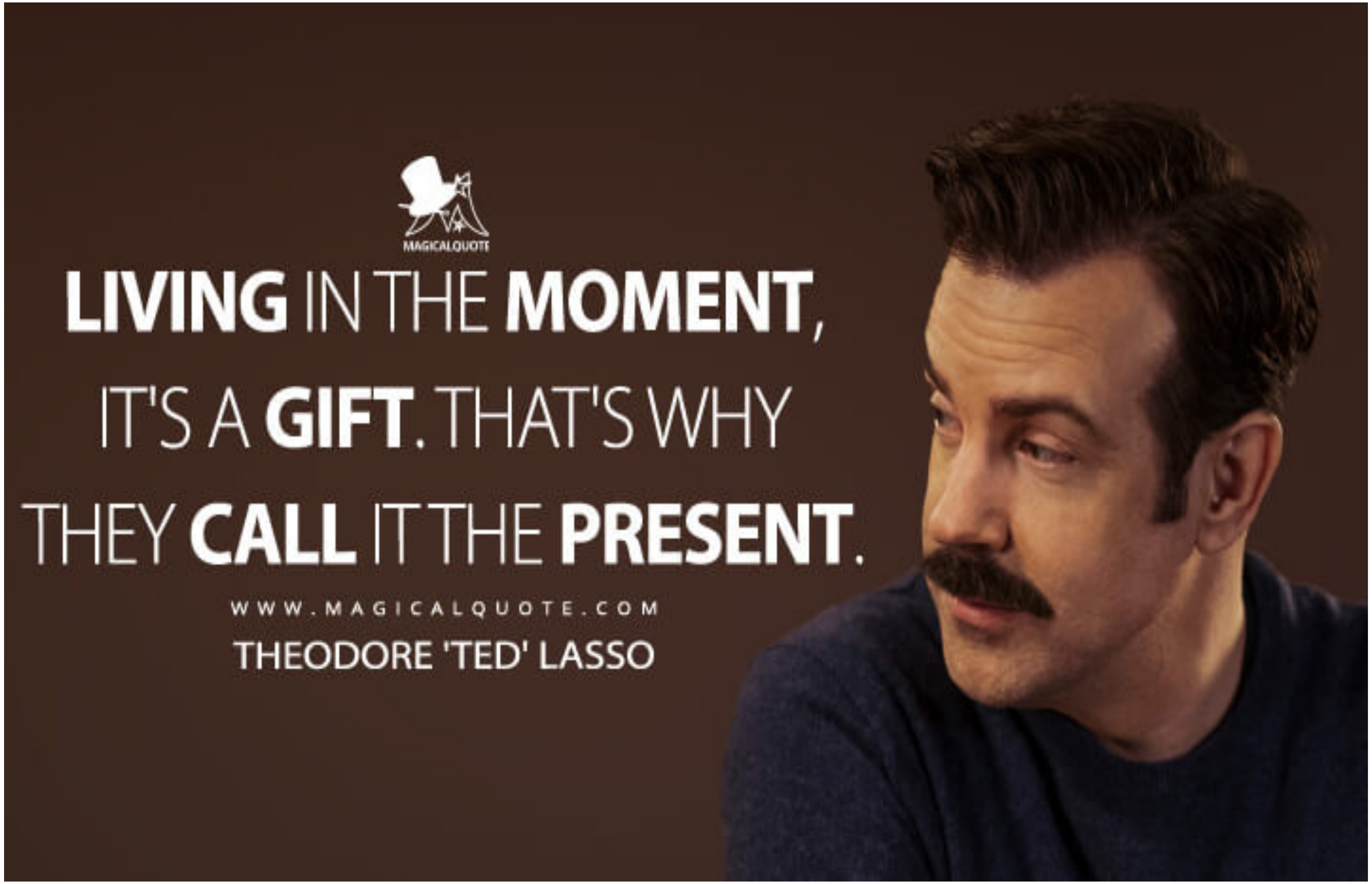
THE pandemic which has just swept round the earth has been without precedent. There have been more deadly epidemics, but they have been more circumscribed; there have been epidemics almost as widespread, but they have been less deadly. Floods, famines, earthquakes and volcanic eruptions have all written their stories in terms of human destruction almost too terrible for comprehension, yet never before has there been a catastrophe at once so sudden, so devastating and so universal.

The most astonishing thing about the pandemic was the complete mystery which surrounded it. Nobody seemed to know what the disease was, where it came from or how to stop it. Anxious minds are inquiring to-day whether another wave of it will come again.

The fact is that although influenza is one of the oldest known of the epidemic diseases, it is the least understood. Science, which by patient and painstaking labor has done so much to drive other plagues to the point of extinction has thus far stood powerless before it. There is doubt about the causative agent and the predisposing and aggravating factors. There has been a good deal of theorizing about these matters, and some good research, but no common agreement has been reached with respect to them.

The measures which were introduced for the control of the pandemic were based upon the slenderest of theories. It was assumed that the influenza could be stopped by the employment of methods which it was assumed would stop the other respiratory diseases. This double assumption proved to be a weak reed to lean upon. The respiratory diseases as a class are not under control. They constitute the most frequent cause of death, yet it is not known how they can be prevented.

Three main factors stand in the way of pre-



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Excellence is a road, not a destination

Cont'd, 2022, Ener Cagri Dinleyici