Covid 19 Aşılarına İmmün Yanıtlar

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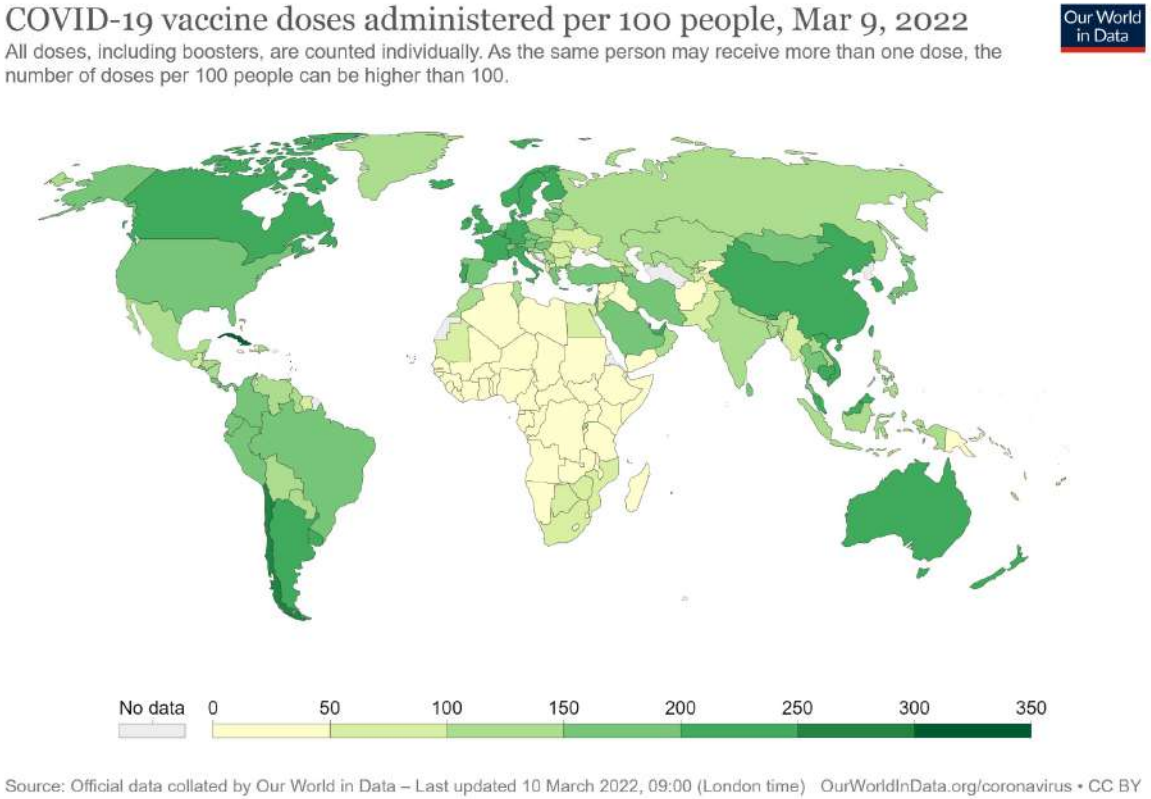
Ankara Üniversitesi Tıp Fakültesi

İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı

12 Aralık 2020 ABD



World Health Organization

R&DBlueprint
Powering research to prevent epidemics

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

4 Mart 2022 Cuma

Summary Information on Vaccine Products in Clinical Development

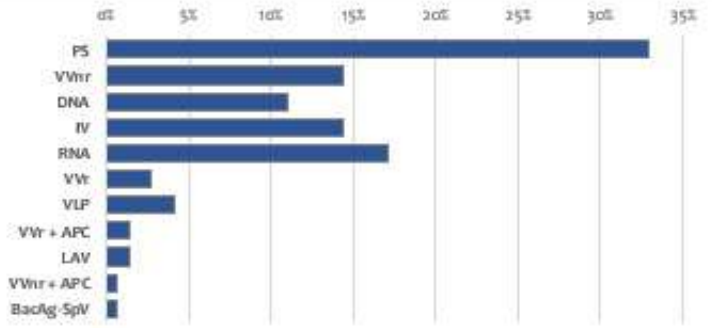
1. - Number of vaccines in clinical development: 147

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

3. - Candidates in clinical phase

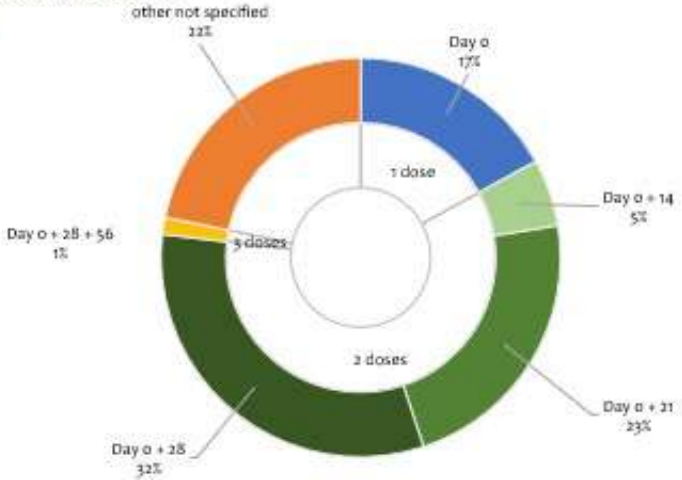
Filter: All — Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	48	33%
VVnr	Viral Vector (non-replicating)	21	14%
DNA	DNA	16	11%
IV	Inactivated Virus	21	14%
RNA	RNA	25	17%
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%
		147	



4. - Number of doses, schedule and route of administration of candidates in clinical phase

Number of doses & schedule		Candidate vaccines (no. and %)	
1 dose		25	17%
Day 0		25	
2 doses		88	60%
Day 0 + 14		8	
Day 0 + 21		33	
Day 0 + 28		47	
3 doses		2	1%
Day 0 + 28 + 56		2	
TBD / No Data (ND)		32	22%
Route of administration			
Oral		4	3%
Injectable		123	84%
SC	Sub cutaneous	5	3%
ID	Intra dermal	6	4%
IM	Intra muscular	110	76%
IN	Intra nasal	8	5%
AE	Aerosol	1	1%
IH	Inhaled	2	1%
TBD / No Data (ND)		20	14%



COVID-19 aşıları, farklı platformlar (farklı mekanizmalar, dağıtım yöntemleri, süreçler) aracılığıyla ve farklı şekillerde çalışır.

mRNA aşıları gibi bazı aşı teknolojileri, COVID-19 için ilk kez kullanım için lisanslanmıştır.

Mevcut COVID-19 aşıları, ciddi hastalık ve ölümlere karşı güçlü koruma sağlamaya devam etmektedir; bununla birlikte aşılar, Omicron varyantına karşı daha az etkilidir.

Enhancing Readiness for Omicron (B.1.1.529): Technical Brief and Priority Actions for Member States (who.int)

COVID19 VACCINE TRACKER

Vaccine platforms designed to train our immune system

TYPES OF COMPONENT VIRAL VACCINES

Protein Subunit

İzole edilmiş ve saflaştırılmış viral proteinler

Virus-like particles (VLP)

Virusun yapısını taklit eden viral proteinler içerir, ancak genetik materyal içermez

DNA-based

RNA-based

Viral proteinlerin yapılması için bilgi sağlayan viral genetik materyali (mRNA gibi) içerir.

Non-Replicating Viral Vector

Replike olamayan başka bir zararsız virusun içinde paketlenmiş viral genetik materyali içerir.

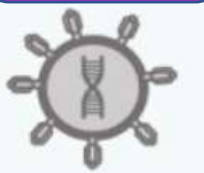
Replicating Viral Vector

Replike olabilen başka bir zararsız virusun içinde paketlenmiş viral genetik materyal içerir.

TYPES OF WHOLE VIRUS VACCINES

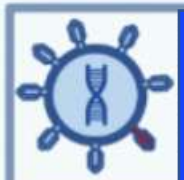
Inactivated

Virusun ölü (inaktive edilmiş) kopyalarını içerir.



Live-Attenuated

Virusun zayıflatılmış kopyalarını içerir.



Sars-CoV2 spike proteini = Antijen

Aşılar, bağışıklık sistemimizi virusları veya antijen adı verilen virus parçalarını tanıması için eğitmenin en iyi yoludur.

Aşılı bir kişi SARS-CoV-2'ye maruz kaldığında, bağışıklık sistemi viral antijenleri tanır ve kontrol altın almak için harekete geçer.

Viral İnfeksiyona Karşı İmmun Yanıt

- Doğal İmmun Yanıt

  Herhangi bir infeksiyona genel yanıt

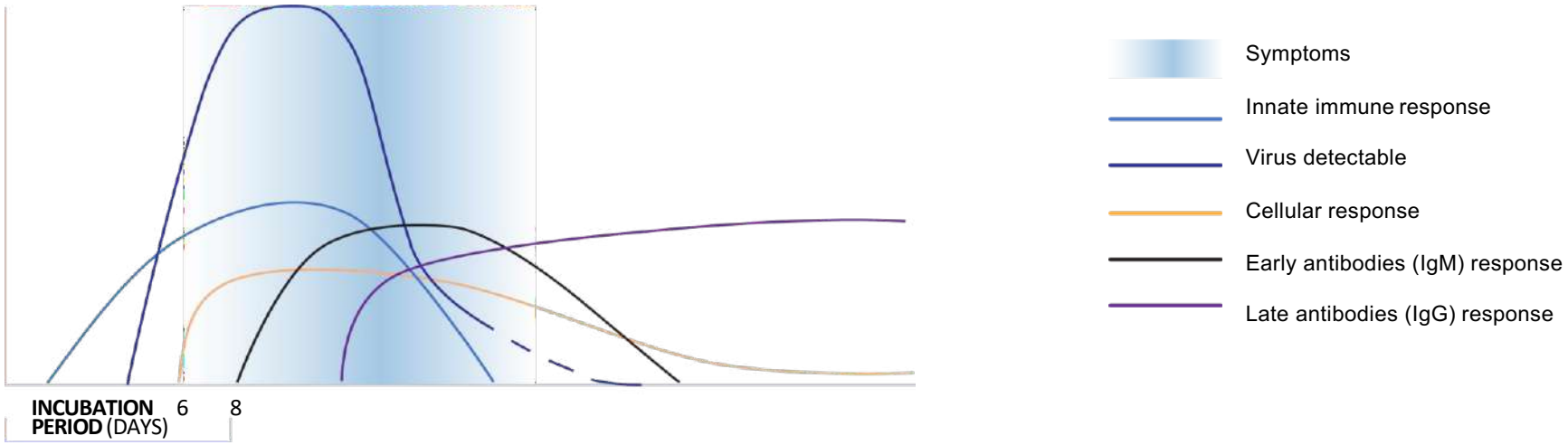
- Adaptif İmmun Yanıt

  Bir infeksiyona spesifik yanıt

  Hücresel yanıtı (T hücreleri) ve antikor yanıtını (B hücreleri) içerir.

- Doğal immun yanıt anında gerçekleşir; hücresel ve antikor yanıtı genellikle 6-8 gün sonra başlar.

Figure. *Immune response to viral infection*

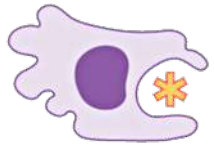


Nature, 580, 576-577 (doi: 10.1038/d41586-020-01221-y)

Doğal İmmun Yanıt

- Bir virus vücuda girdiğinde hücreler virus üzerinde bulunan belirteçleri tanır.
- Bu, spesifik olmayan antiviral aktivite ile sonuçlanır.
- Doğal immun yanıt hücreleri (makrofajlar, nötrofiller, dendritik hücreler ve diğerleri gibi) vücuttan patojenleri ve yabancı hücreleri uzaklaştırmak ve adaptif immun yanıtı uyarmak için aktive edilir.

Doğal immun yanıtta yer alan hücreler

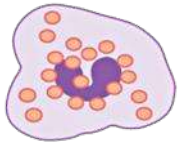


Makrofaj

Yabancı patojenleri tüketen fagositik hücre; Diğer bağışıklık hücrelerinin tepkisini uyarır.

Nötrofil

İnfeksiyon bölgesinde ilk müdahaleci. Mikroorganizmaları öldüren ve diğer bağışıklık hücrelerini infeksiyon bölgesine toplayan toksinleri serbest bırakır.



Natural killer

Virusla infekte hücreleri ve tümör hücrelerini öldürür.

Dendritik Hücre

Yüzeyinde antijen sunar, böylece adaptif bağışıklık tepkisini tetikler.

Nature, 580, 576-577 (doi: 10.1038/d41586-020-01221-y)

Adaptif İmmun Yanıt: T Hücreleri

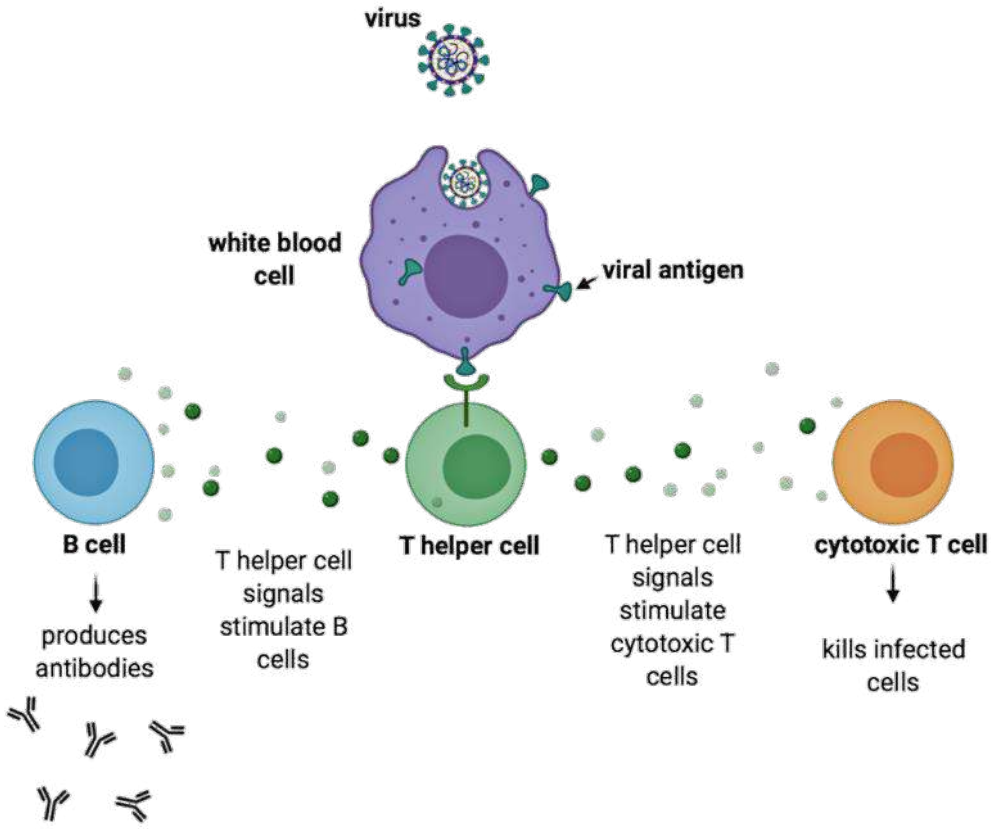
T hücreleri (Hücresel yanıt)

- T hücreleri, belirli bir virusla infekte olan hücreleri tanır ve infeksiyonla mücadele etmek için sayıları hızla artar.

T hücresi türleri:

- CD4+ yardımcı T hücreleri, bağışıklık sisteminin diğer hücrelerini ortama çağırır ve B hücrelerini o virusa özgü antikorlar üretmesi için uyarır.

- CD8+ sitotoksik T hücreleri, virusun çoğaldığı hücreleri öldürür ve infeksiyonu yavaşlatmaya veya durdurmaya yardımcı olur.

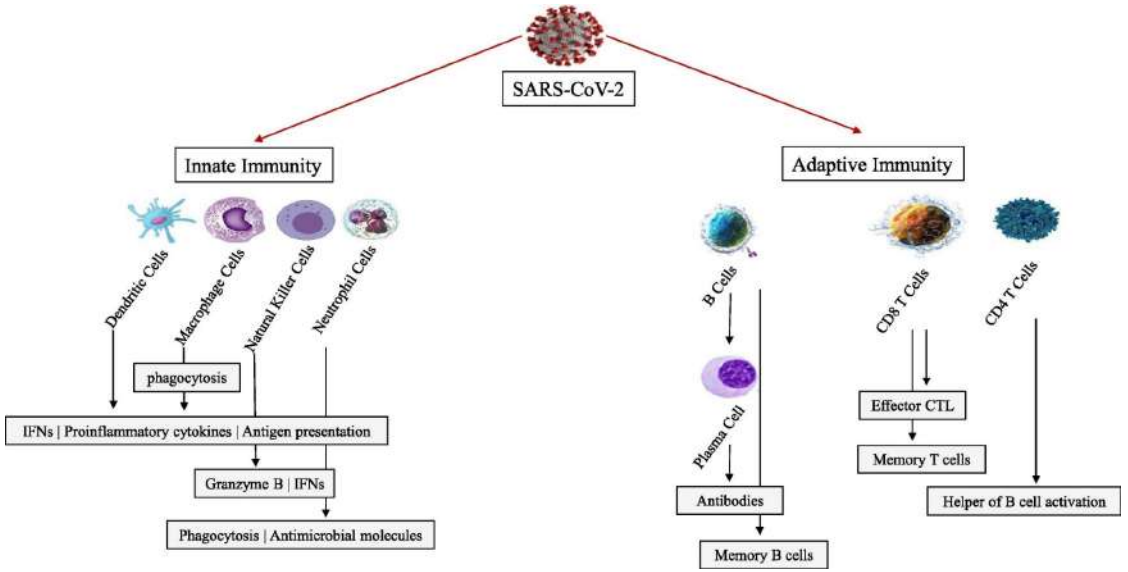


Nature, 580, 576-577 (doi: 10.1038/d41586-020-01221-y)

Adaptif İmmun Yanıt: B Hücreleri

B hücreleri (Antikor yanıtı)

- B hücreleri, virusa özgü antikorlar üretir.
- İlk önce IgM antikorları üretilir ve birkaç hafta sonra kaybolur.
- IgG antikorları aynı anda veya birkaç gün sonra üretilir ve titreler (seviyeler) genellikle aylar veya yıllar boyunca yüksek kalır.



Bellek hücreleri

- İnfeksiyon bittiğinde, T hücreleri ve B hücrelerinin sayısı azalır, ancak bazı hücreler kalır (bellek hücreleri).
- Bellek hücreleri, aynı virusla tekrar temasa geçerlerse hızla yanıt verir, virusu öldürür ve antikor yanıtını hızlandırır.

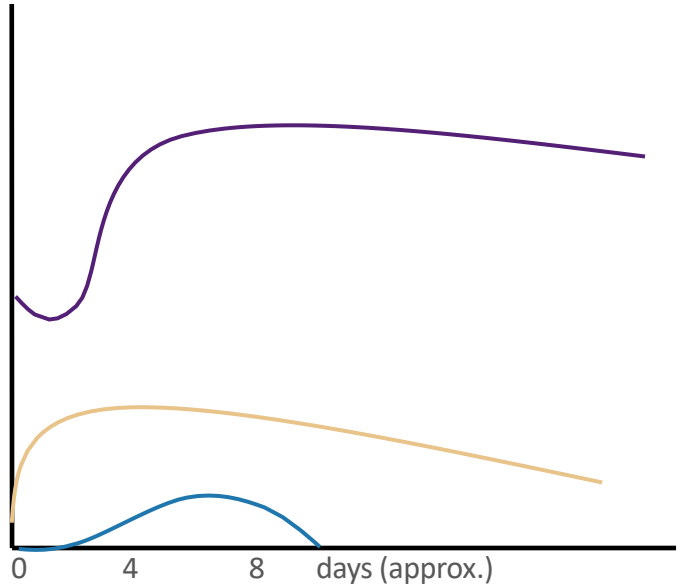
Nature, 580, 576-577 (doi: 10.1038/d41586-020-01221-y)

Bağışık bir kişide immun yanıt

- Adaptif bağışıklık hücreleri (T hücreleri ve B hücreleri) aynı virusla tekrar karşılaştıklarında hızlı tepki verirler ve bağışıklık sistemi bu patojeni hastalığa neden olmadan önce etkili bir şekilde temizleyebilir.

- Bağışıklık belleği, önceki bir infeksiyondan veya etkili bir aşıdan kaynaklanabilir.

Figure. Immune response in an immunized person



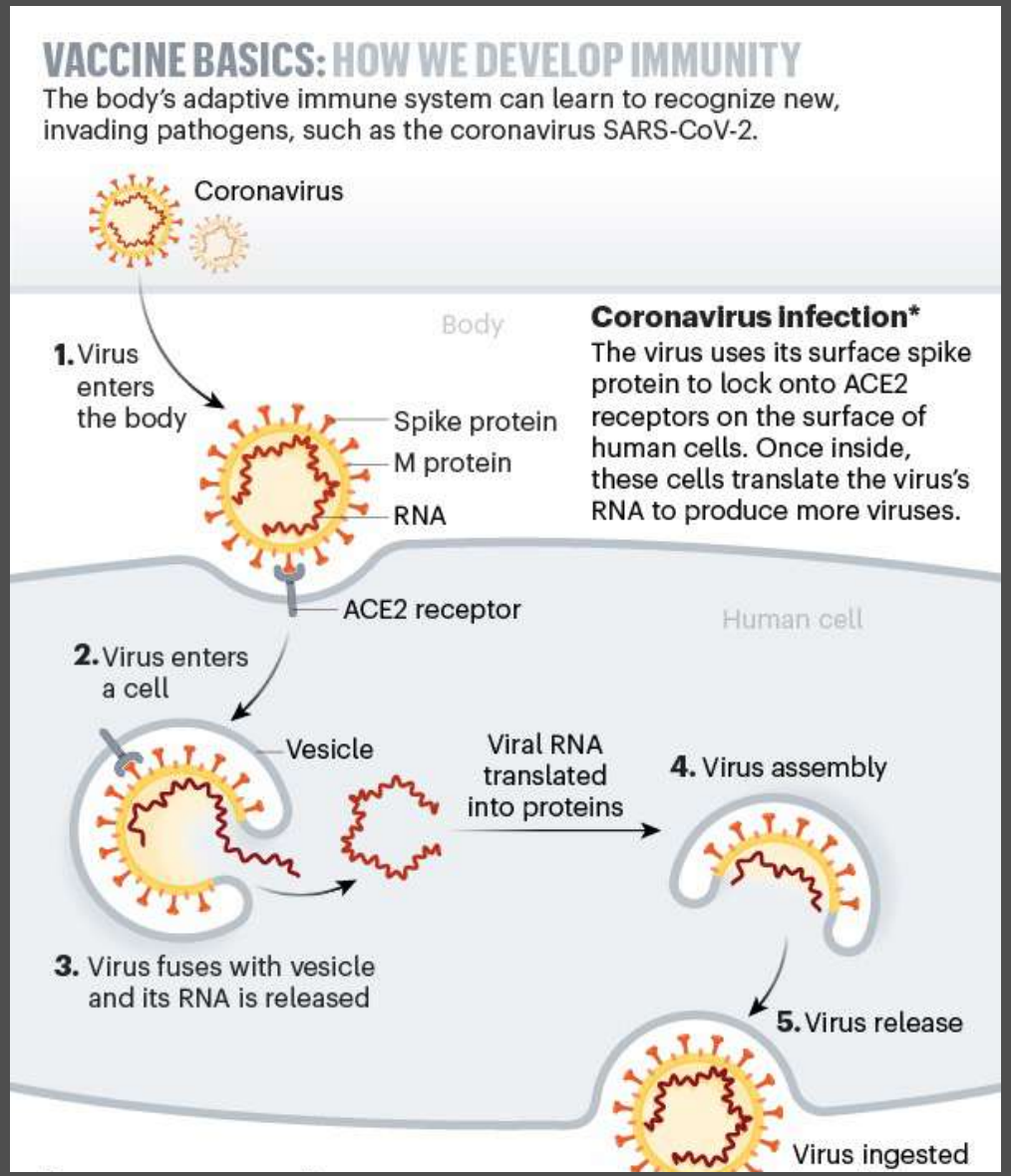
Strong and rapid antibody response

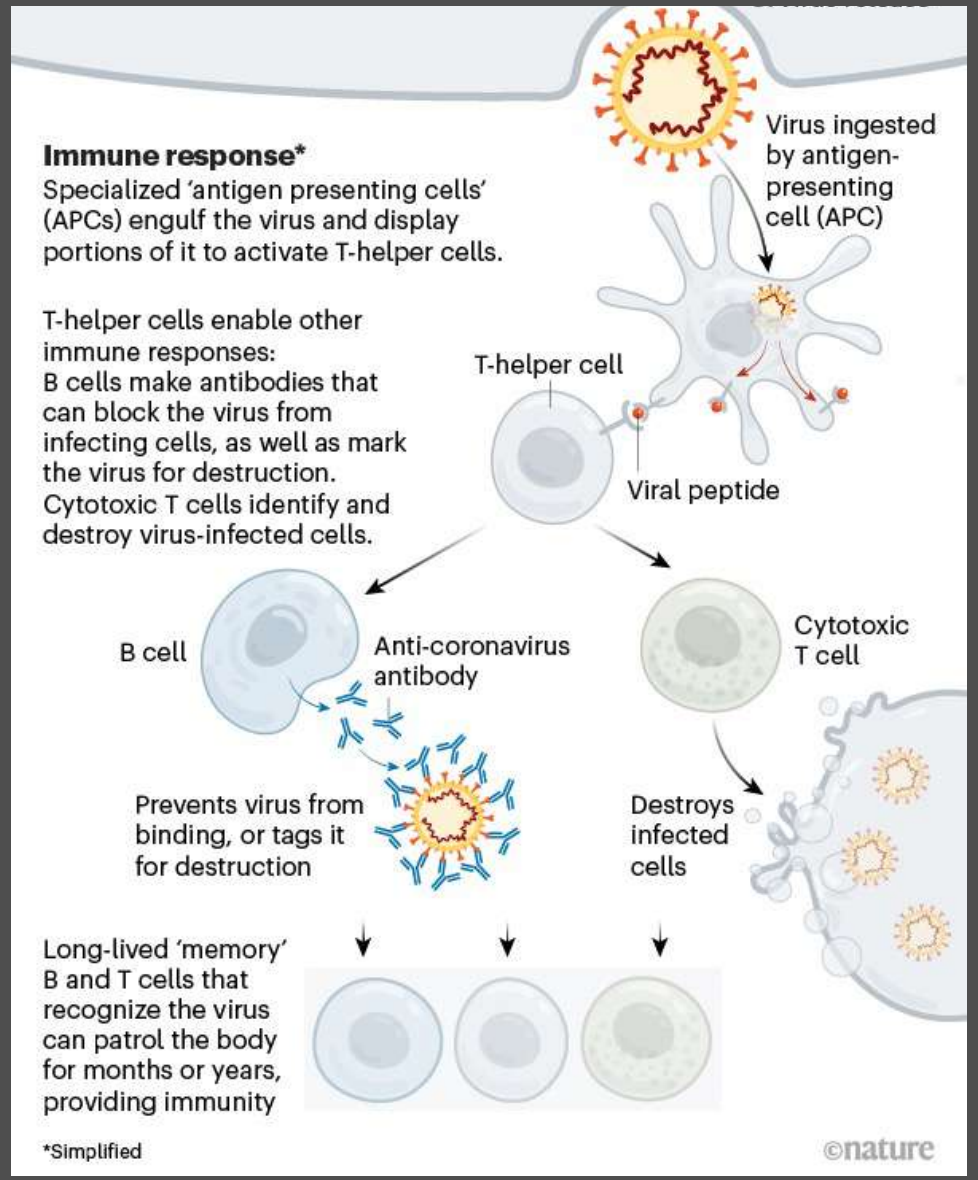
Virus amount

Cellular response

Antibody response

Nature: doi: 10.1038/d41586-020-01221





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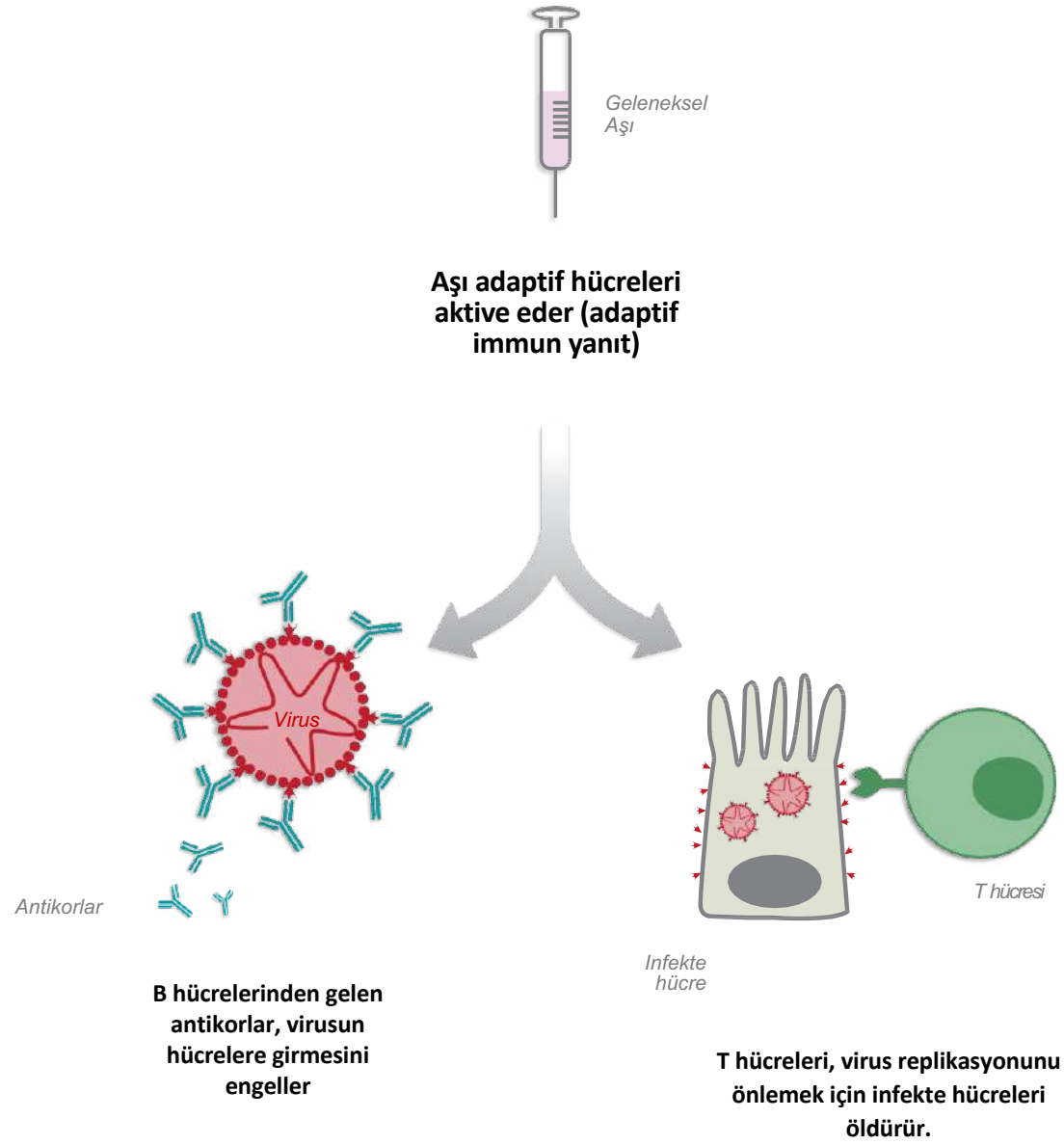
Aşılar tarafından indüklenen immun yanıt

- Aşılar, doğal olarak karşılaşıldığında patojeni tanıması için immun sisteme güvenli bir şekilde bir immünojen sunar:
- CD4+ yardımcı T hücrelerini uyarır.
- Virusa özgü nötralize edici antikorlar üretmek için B-hücreleri
- Virus tarafından infekte olmuş hücreleri tanımak ve öldürmek için CD8+ sitotoksik T hücreleri



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COVID19 VACCINE TRACKER

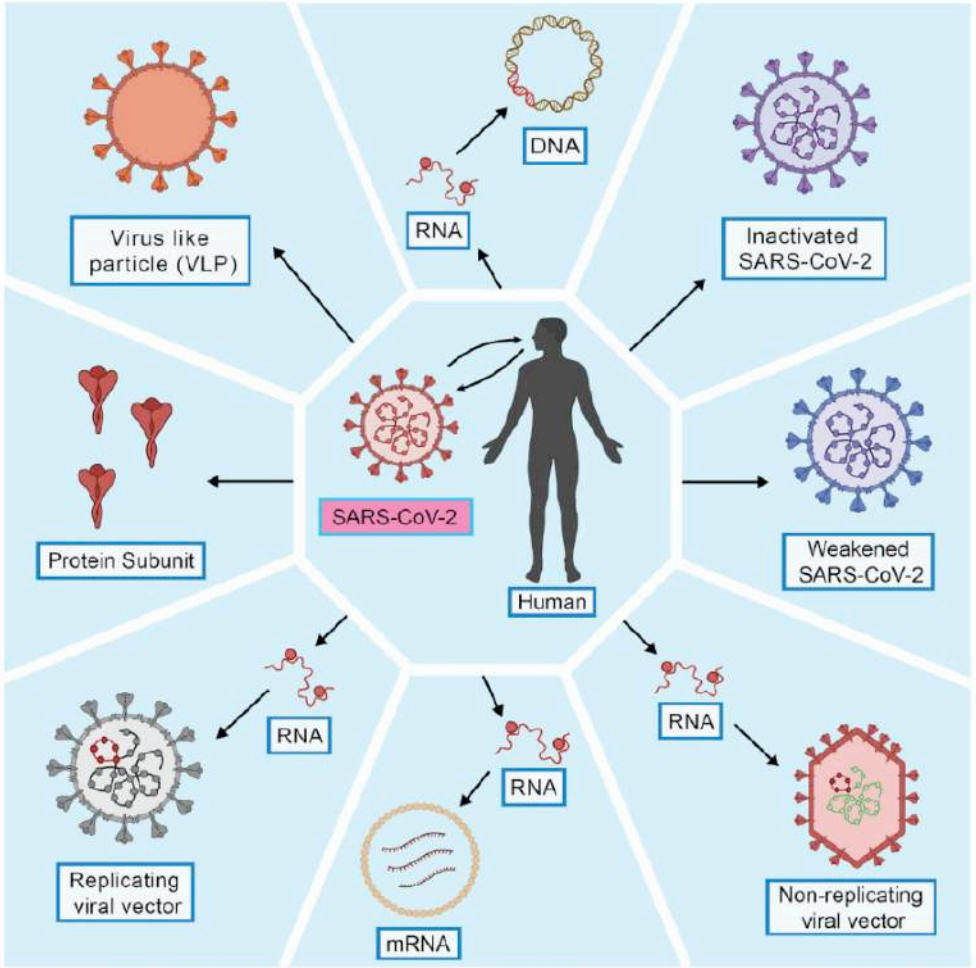
HOME EXPLORE VACCINES ABOUT VACCINES & TRIALS ABOUT

Translate

WORLD HEALTH ORGANIZATION (WHO)

Last Updated 9 March 2022.

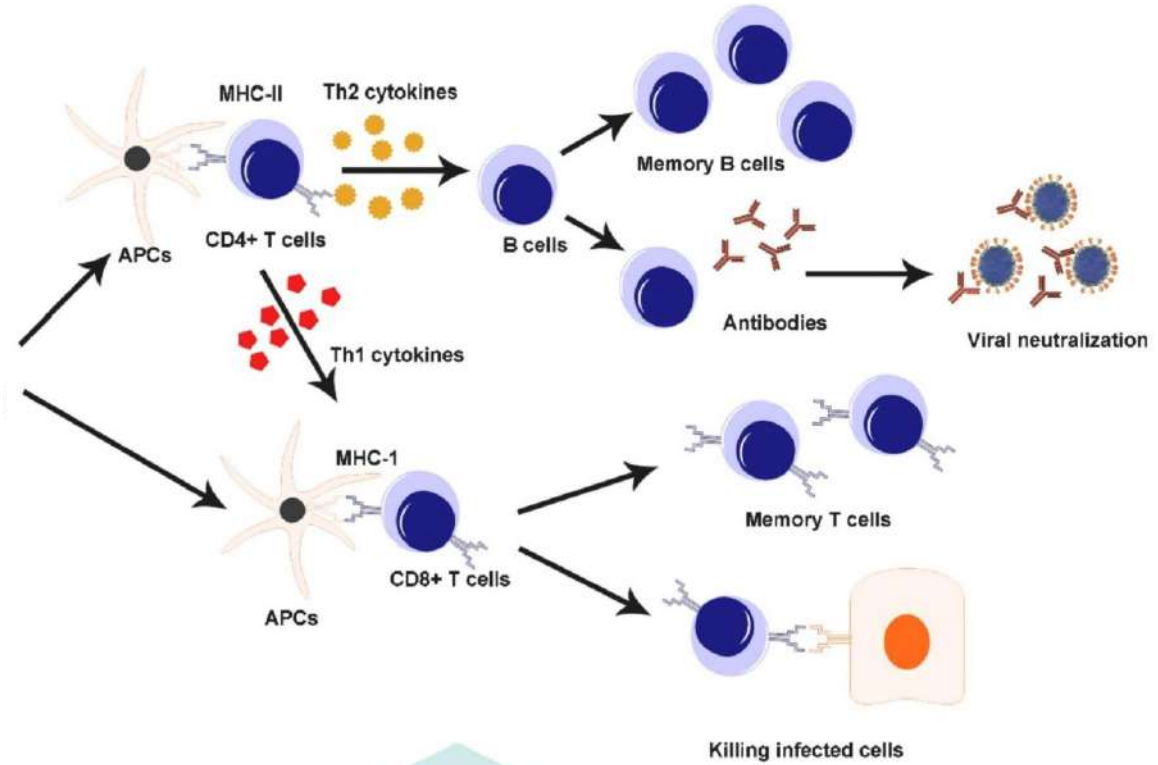
10 Vaccines Granted Emergency Use Listing (EUL) by WHO

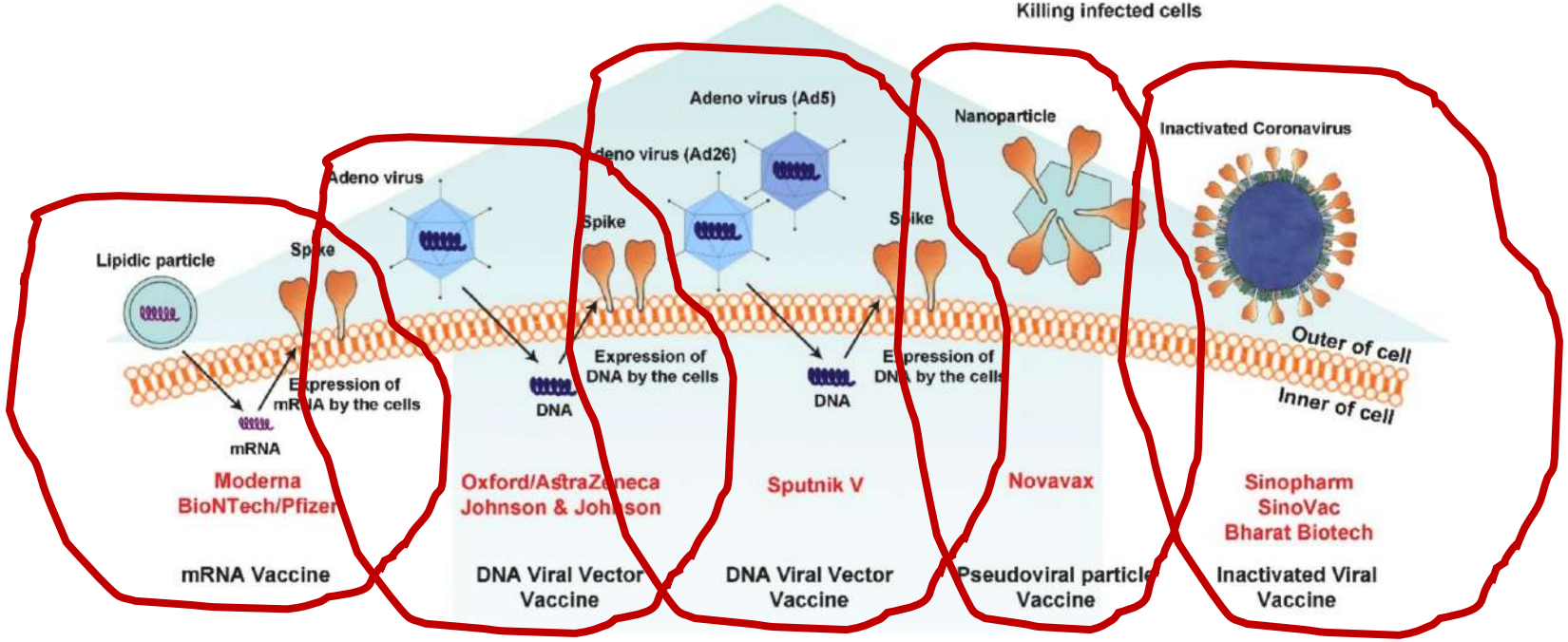


COVID 19 AŞI PLATFORMLARI

AŞI PLATFORMU	ÜRETİCİ&MARKA ADI	TANIM
mRNA	**Comirnaty (Pfizer/BioNtech)**	mRNA aşıları, insan hücrelerine SARS-CoV-2 spike proteininin bir parçasını yapma talimatı verir. Spike protein, alıcının bağışıklık sistemini, gelecekte SARS CoV-2'ye maruz kalma durumunda koruyucu bir yanıt geliştirmesi için tetikler.
	Spikevax (Moderna)	
Nonreplike viral vektör	**Vaxzevria (Oxford/Astra Zeneca)**	COVID 19'a neden olan virüs dışında modifiye edilmiş bir virus (viral vektör), insan hücrelerine SARS-CoV-2 spike proteininin bir parçasını yapma talimatını iletmek için kullanılır. Spike proteini, alıcının bağışıklık sistemini, gelecekte SARS-CoV-2'ye maruz kalma durumunda koruyucu bir yanıt geliştirmesi için tetikler.
	Covishield (Serum Institute of India)	
	Janssen	
İnaktive virus	**Coronavac (Sinovac)**	İnaktive edilmiş bir aşı, immun yanıt ortaya çıkarmak için bağışıklık sistemi tarafından tanınan öldürülmüş virus veya virüs parçacıklardan oluşur.
	Sinopharm	
	Covaxin (Bharat Biotech)	
Subunit **(Rekombinan spike protein nanopartikül)**	**Novavax** **Covovax-Serum Institute of India**	Alt birim aşıları, bu moleküllerin güçlü ve etkili bir bağışıklık tepkisi oluşturması muhtemel kombinasyonlarını üretmek üzere dikkatle seçilmiş olan SARS-CoV-2 spike proteininin spesifik fragmanlarını içerir.

İmmun Yanıt

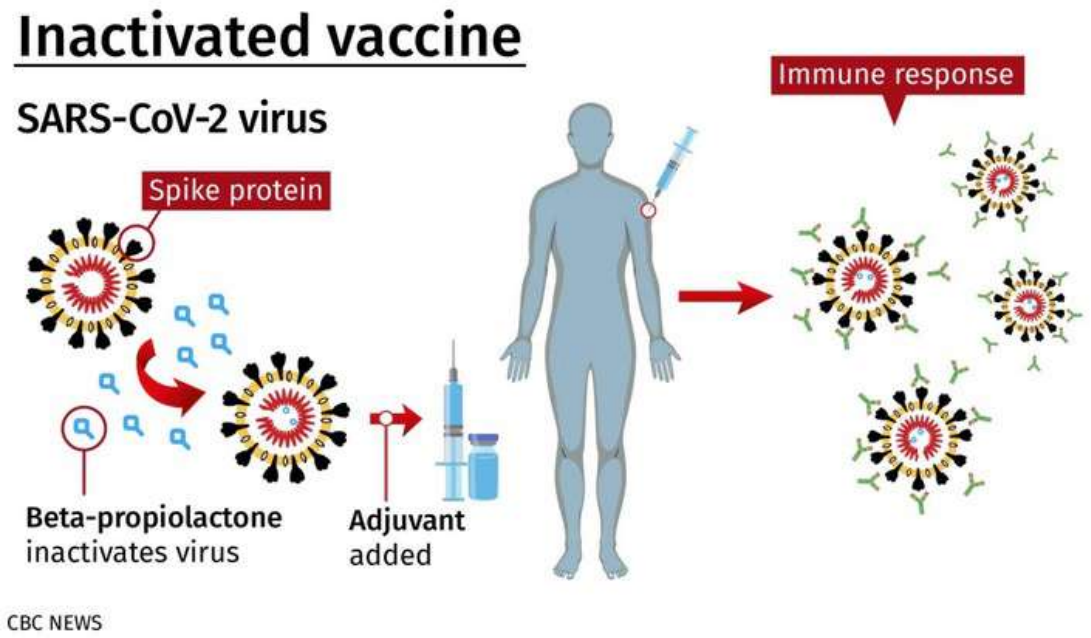




PMID: 34755408

İnaktive Virus Aşıları

- İnaktive virüs aşılarında, hastalık üretme kapasitesini durdurmak için virusun genetik materyali yok edilmiştir.
- İnaktive edilmiş virus vücutta çoğalamaz, bu nedenle daha yüksek dozlara ihtiyaç vardır.
- Bazen, bağışıklık tepkisini güçlendirmeye yardımcı olmak için bir adjuvan (bağışıklık sistemini uyaran moleküller) kullanılır.
- İnaktive virus aşıları genellikle sadece antikor aracılı bağışıklığı indükler.



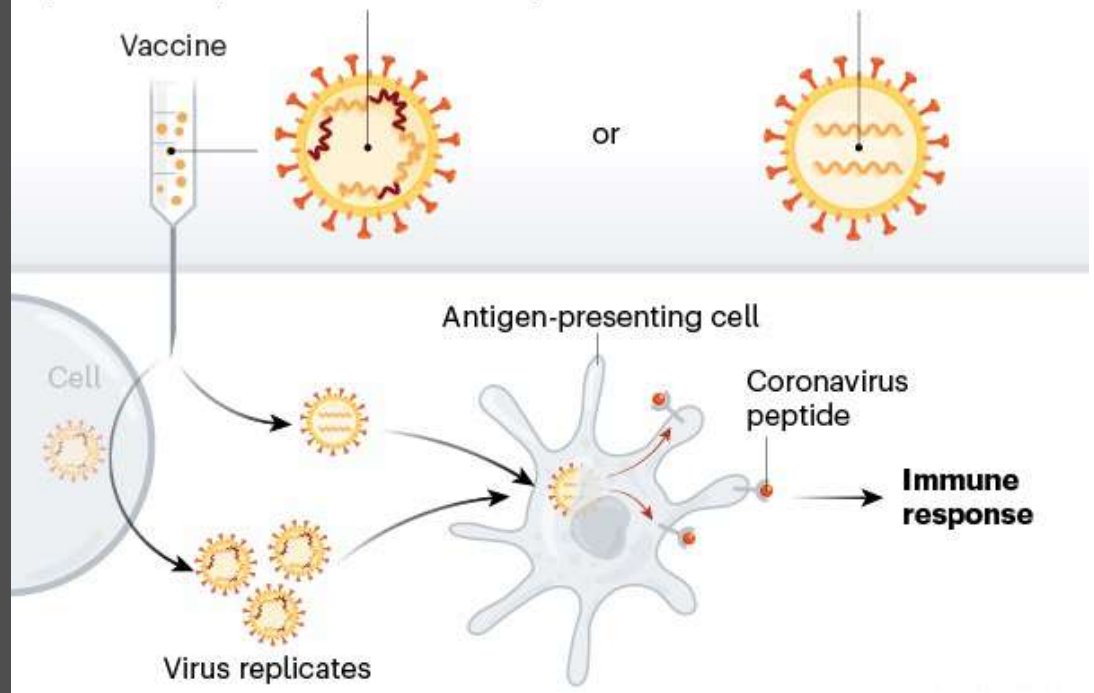
VIRUS VACCINES

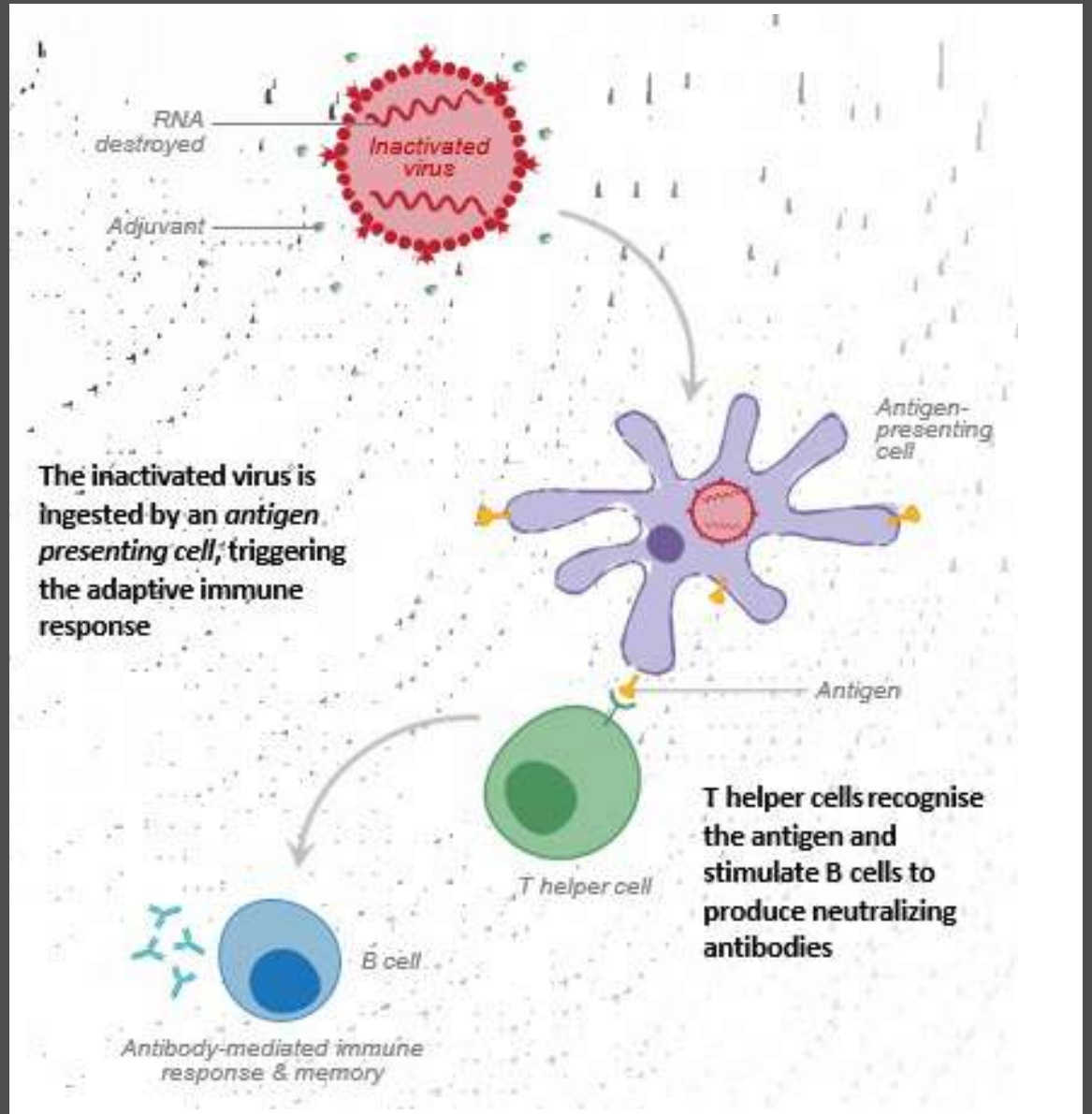
Weakened virus

A virus is conventionally weakened for a vaccine by being passed through animal or human cells until it picks up mutations that make it less able to cause disease. Codagenix in Farmingdale, New York, is working with the Serum Institute of India, a vaccine manufacturer in Pune, to weaken SARS-CoV-2 by altering its genetic code so that viral proteins are produced less efficiently.

Inactivated virus

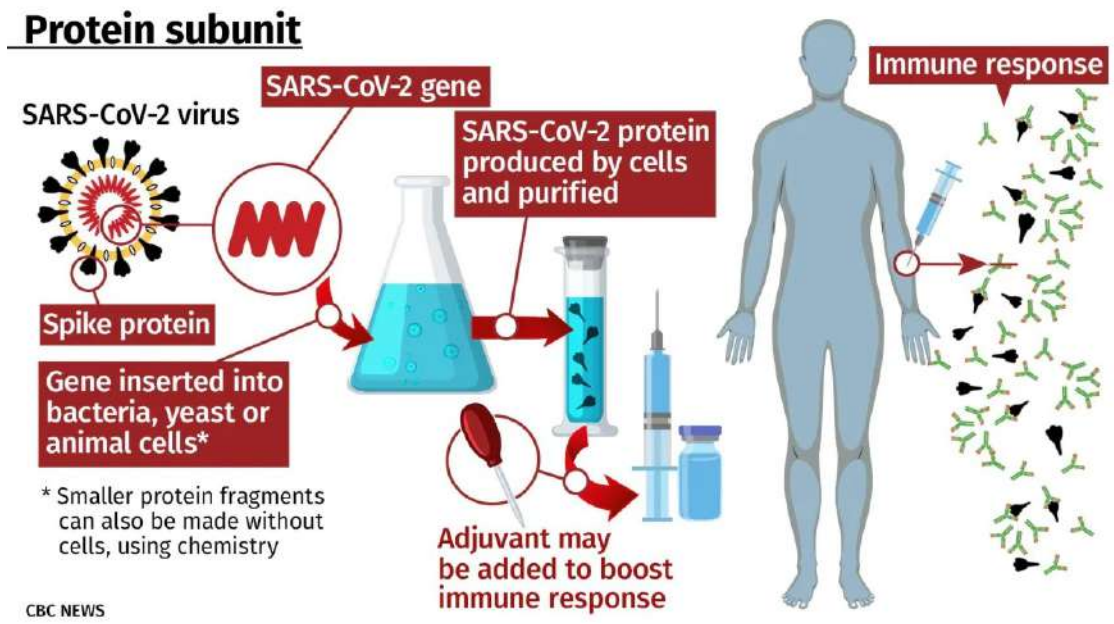
In these vaccines, the virus is rendered uninfectious using chemicals, such as formaldehyde, or heat. Making them, however, requires starting with large quantities of infectious virus.





Subunit Aşıları

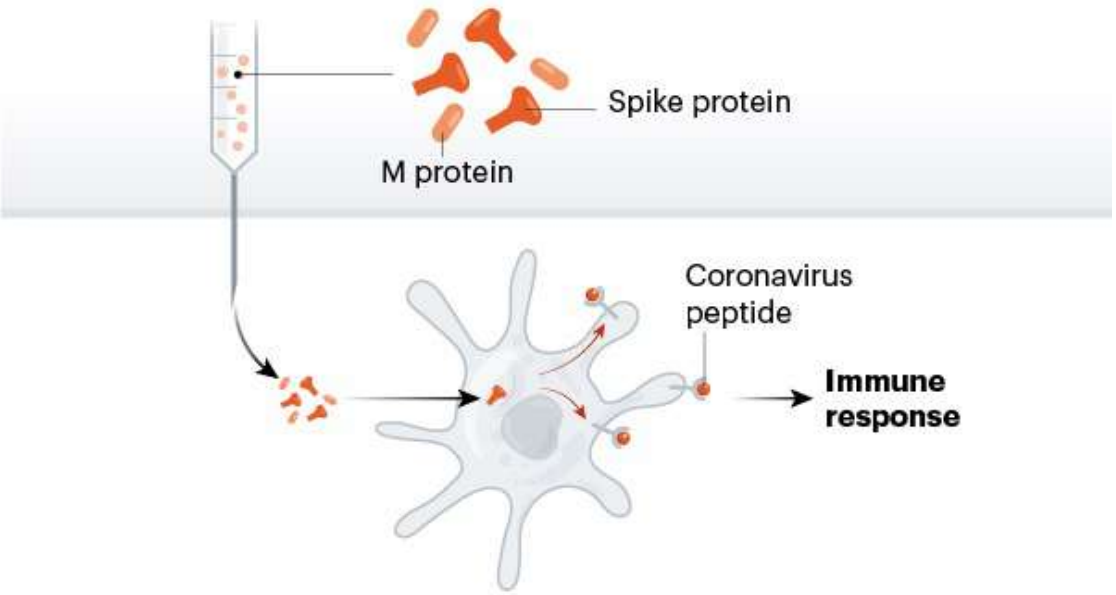
- Daha iyi bir bağışıklık tepkisi vermek için genellikle bir adjuvan ile herhangi bir genetik materyal olmadan virusun antijenini kullanır.
- Genellikle bir rekombinant ekspresyon sistemi kullanılarak yapılır (virüs kullanılmadan bir hücrede yapılır).
- Antijen sunan hücrelerin yardımıyla, antijenler T yardımcı hücreler tarafından gerçek bir viral infeksiyonda olduğu gibi tanınır.
- Alt birim aşılar genellikle antikor aracılı bağışıklığı indükler.

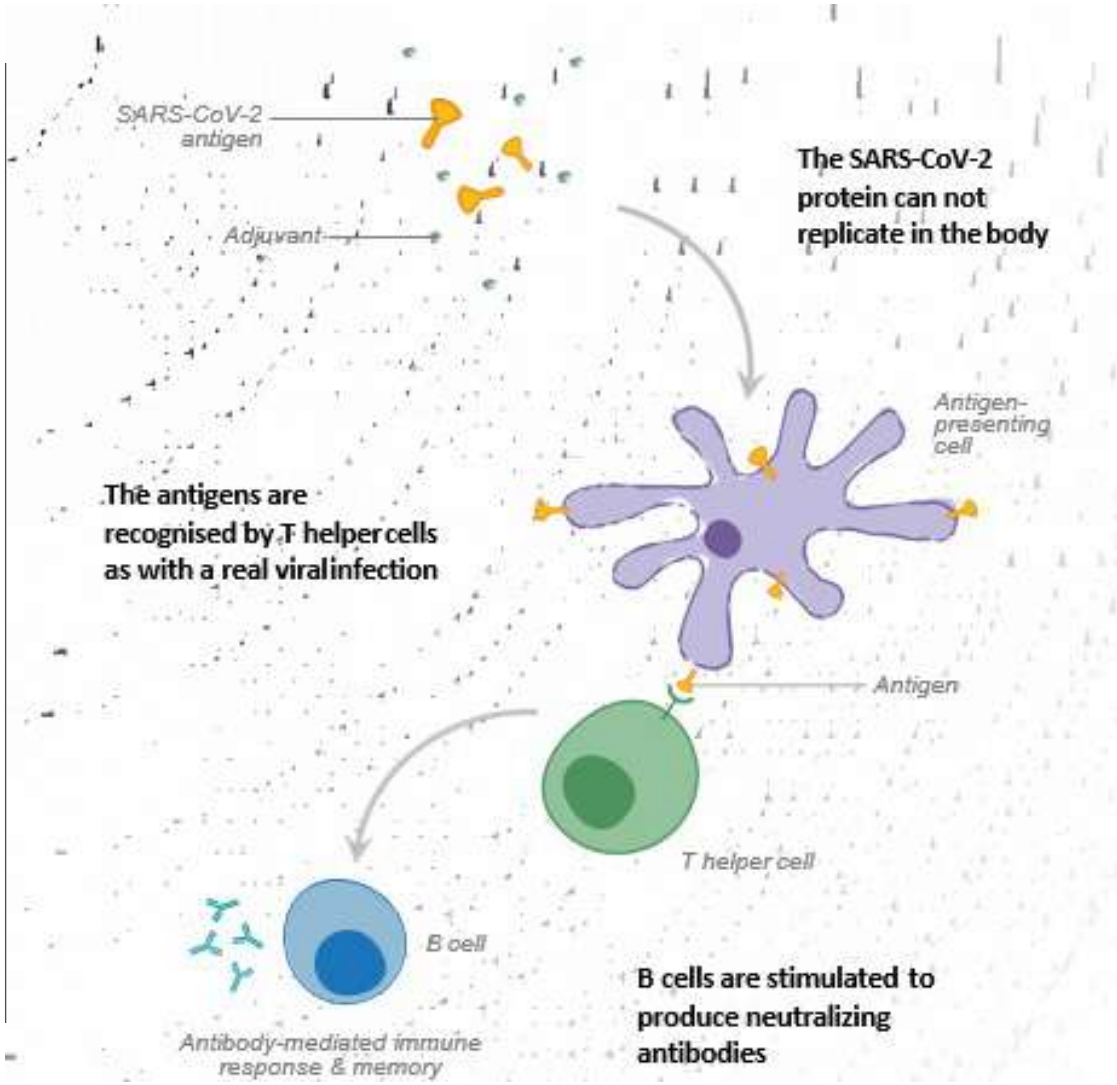


PROTEIN-BASED VACCINES

Protein subunits

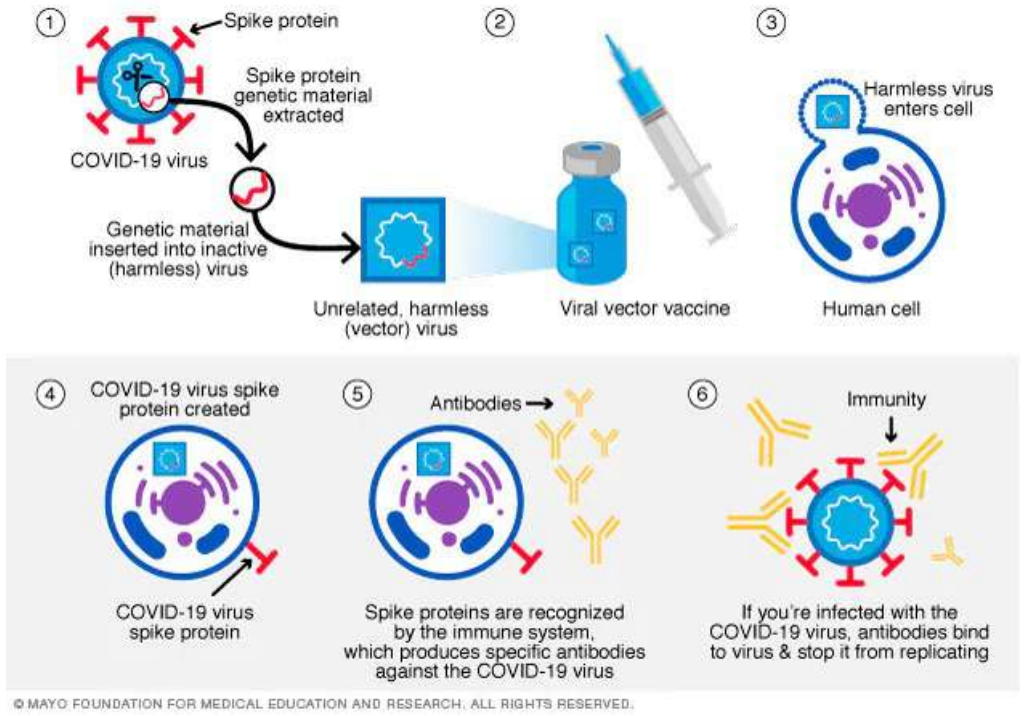
Twenty-eight teams are working on vaccines with viral protein subunits — most are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven't been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.





Viral Vektör Aşıları

- Hedef antijeni kodlayan bir geni içerecek şekilde modifiye edilmiş koronavirus dışı bir vektör (örn. adenovirus) kullanılır.
- Replike olan / Replike olmayan
- Replike olan: İnfeksiyon üzerine, o hücrede SARS-CoV-2 antijeni ve diğer hücreleri infekte eden yeni virus üretir.
- Replike olmayan: Bir hücreyi infekte eder ve o hücrede SARS-CoV-2 antijeni üretir ancak yeni virus üretmez.
- Hücrelerin içindeki SARS-CoV-2 antijeni nedeniyle bu bir SARS-CoV-2 infeksiyonu gibi algılanır ve yardımcı T hücreleri ve sitotoksik T hücreleri indüklenir.



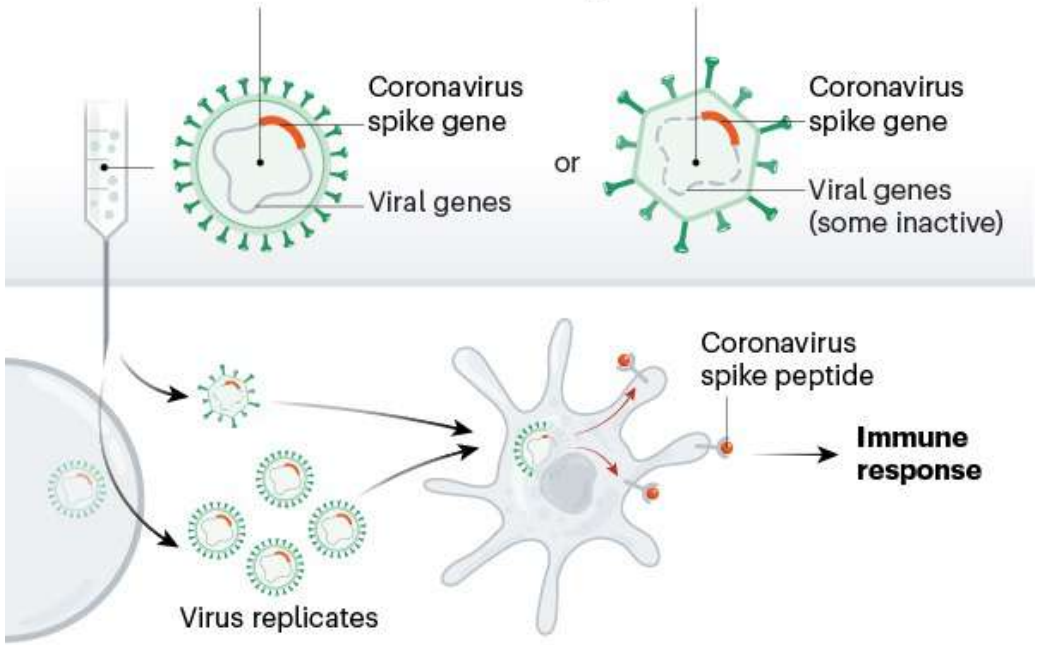
VIRAL-VECTOR VACCINES

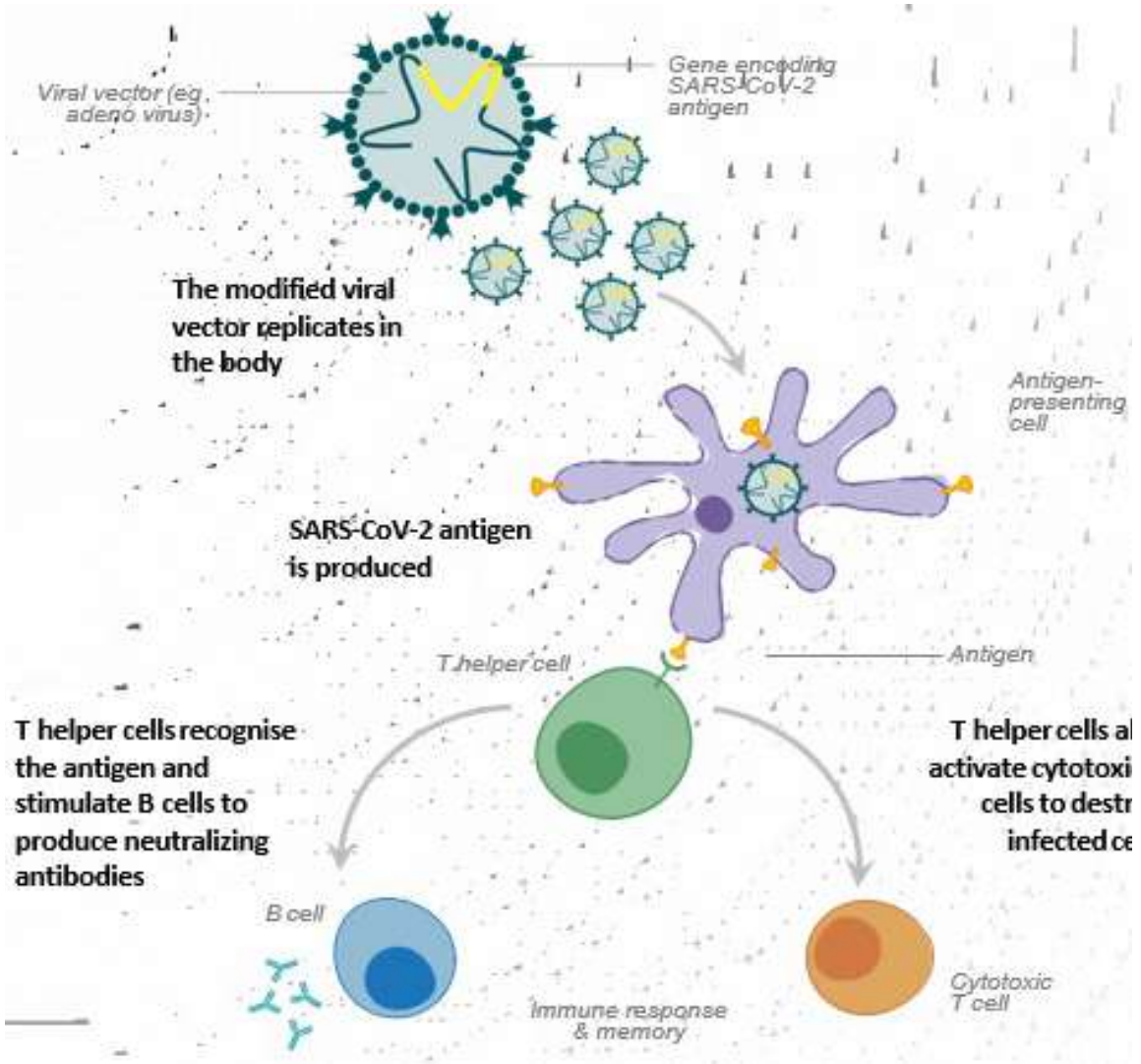
Replicating viral vector (such as weakened measles)

The newly approved Ebola vaccine is an example of a viral-vector vaccine that replicates within cells. Such vaccines tend to be safe and provoke a strong immune response. Existing immunity to the vector could blunt the vaccine's effectiveness, however.

Non-replicating viral vector (such as adenovirus)

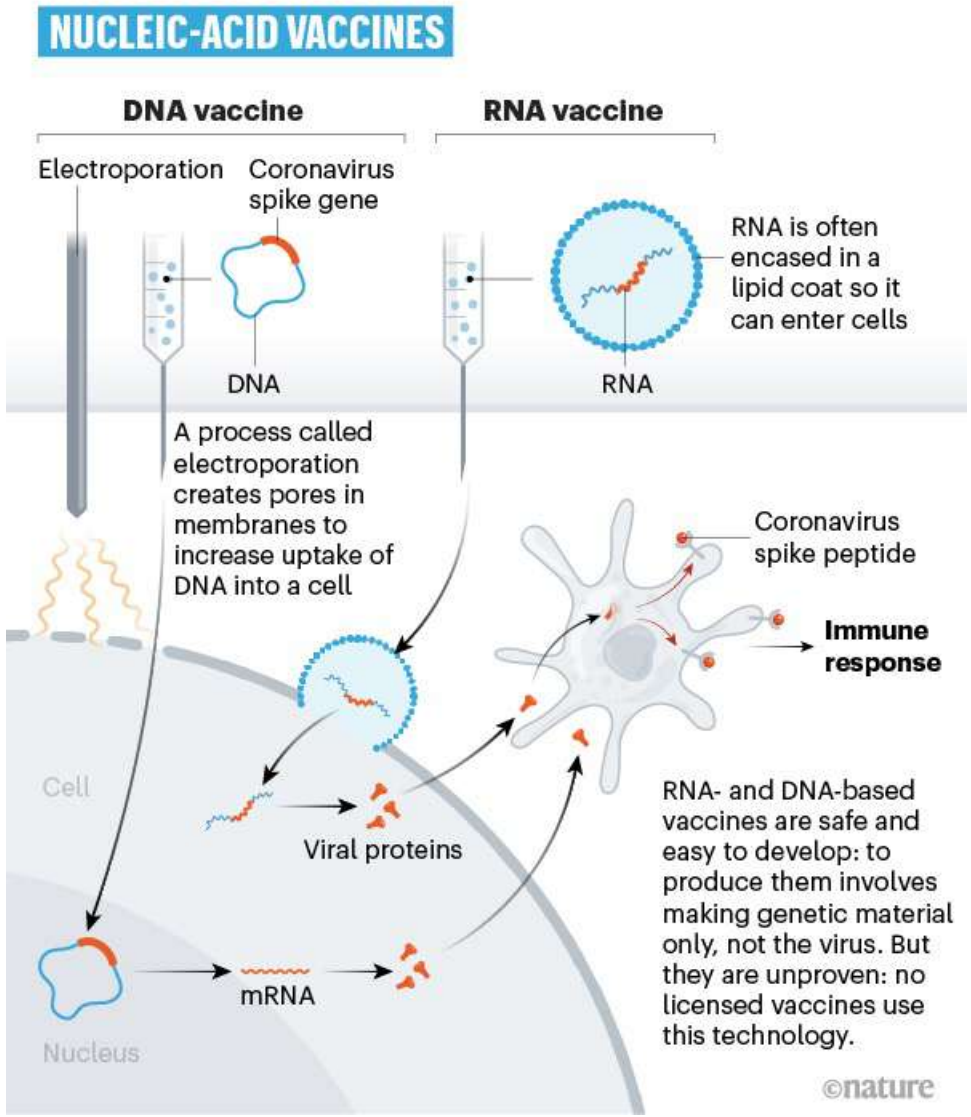
No licensed vaccines use this method, but they have a long history in gene therapy. Booster shots can be needed to induce long-lasting immunity. US-based drug giant Johnson & Johnson is working on this approach.

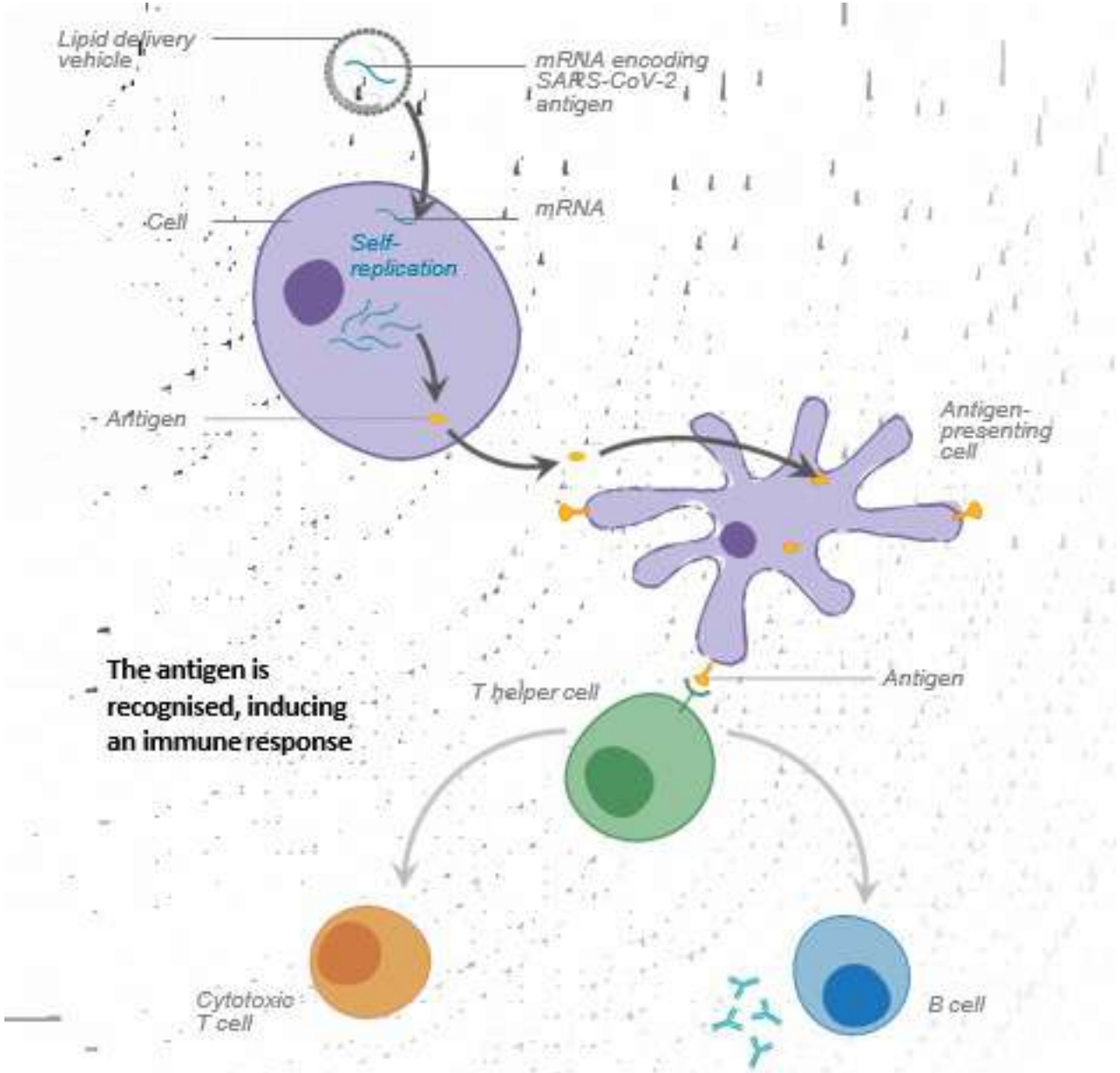




mRNA Aşıları

- mRNA aşıları, bir lipid kaplama içinde iletilen haberci RNA'nın (mRNA) antijen kodlayan zincirleridir.
- Hücrelerin içine girdikten sonra mRNA, protein antijenine çevrilir.
- Antijen tanınır ve bir immün reaksiyonu indükler.
- Vücut tarafından bir hücrenin içinde virus varmış gibi algılanır, yardımcı ve sitotoksik T hücreleri ile antikorlar uyarılır.
- mRNA, hücreler tarafından güçlü bir bağışıklık tepkisini uyaran bir "patojen" olarak tanınır.





UKCIC

British Society for immunology

Immune response after COVID-19 vaccination

One dose of a COVID-19 vaccine is injected into the arm.

The vaccine contents enter our cells at the injection site with the genetic material for the Spike protein.

The Spike protein is produced by our cells and presented on their surfaces. This trains the immune response by activating...

The Spike protein is the part of the virus, SARS-CoV-2, that allows it to enter our cells.

Helper T cells that detect the Spike protein and alert other immune cells.

Killer T cells that seek out the Spike protein.

B cells that create antibodies to specifically recognise the Spike protein.

T and B cells develop immune memory of the Spike protein and will be quick to respond the next time it is encountered.

Antibodies remain in the body for some time, ready to bind to the Spike protein and block the virus from infecting new cells.

B cells can produce more antibodies if needed in future.

A second vaccine dose is administered weeks later. This trains the immune system further, strengthens the response, and creates an immune memory to the virus.

The immune system is now ready to launch a quick and effective response against SARS-CoV-2 if it encounters the virus in future, preventing infection and serious illness.

www.uk-cic.org

www.immunology.org

Table 1 Immunological significances of all vaccine candidates against SARS-CoV-2

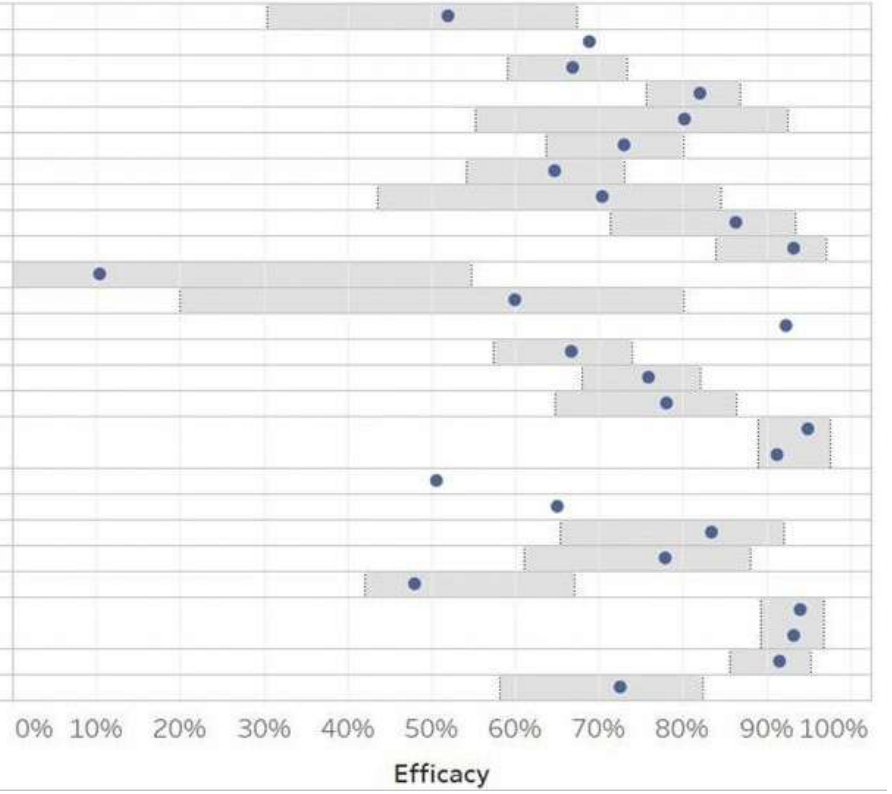
Vaccine platform	Type of antigen	Type of immune response	Neutralizing antibody response	T cell response		Immunogenicity and required dose (s)	References
				CD4 + Th cell	CD8 + T cell		
Inactivated	Inactivated SARS-CoV-2	Antibody and/or cell mediate response	Strong response	Th1 cell or Th2 cell depending on adjuvant	Weak response	Weak; requires two or more doses	[52, 64]
Live attenuated	Weakened SARS-CoV-2	Antibody and/or cell mediate response	Strong response	Th1 cell	Strong response	Strong; requires a single dose	[52, 64]
Protein Subunit	SARS-CoV-2 spike protein	Antibody and/or cell mediate response	Strong response	Th1 cell or Th2 cell depending on adjuvant	Weak response	Weak; requires two or more doses	[52, 64]
Virus-like particles (VLPs)	Multiple proteins of SARS-CoV-2	Antibody mediate response	Strong response	Th1 cell or Th2 cell depending on adjuvant	Weak response	Weak; two or more doses	[52, 64]
Viral vector	Nucleic acid of SARS-CoV-2	Antibody and/or cell mediate response	Depends on pre- existing anti-vector immunity	Th1 cell	Strong/weak response depends on spike protein vaccines (replicating and non-replicating	Strong, weak or moderate; requires two or more doses	[52, 64]
DNA	Nucleic acid of SARS-CoV-2	Antibody and/or cell mediate response	Depends on pre- existing anti-vector immunity	Th1 cell	Moderate response	Weak; requires two or more doses	[52, 64]
RNA	Nucleic acid of SARS-CoV-2	Antibody and/or cell mediate response	Depends on pre- existing anti-vector Immunity	Th1 cell or Th2 cell depending on adjuvant	Strong/weak response depends on the choice of adjuvant and formulation	Strong, weak or moderate; requires two or more doses	[52, 64]

https://doi.org/10.1007/s13337-022-00755-1

Etkinlik

	Sinopharm	Sinovac Biotech	Bharat Biotech	University of Oxford and AstraZeneca	Janssen and Johnson & Johnson	Gamaleya	Moderna and NIAD	Pfizer and BioNTech	Novavax and CEPI
Aşı Tipi	İnaktive virus	İnaktive virus	İnaktive virus	Şempanze adenovirus vektör	İnsan adenovirus vektör	İnsan adenovirus vektör	mRNA	mRNA	Protein subunit
Hedef Antijen	Tam virus	Tam virus	Tam virus	S protein	S protein	S protein	S protein	S protein	S protein
Semptomatik Covid-19'a Karşı Etkinliği	**78.1%**	**50.7%**	**77·8%**	**81.3%**	**66%**	**91.6%**	**94.1%**	**95%**	**96.4%**
Alpha	N.R	N.R	N.R	74.5%	N.R	N.R	100% (Qatar study)	93.7%	86.3%
Beta	N.R	N.R	N.R	10.4%	N.R	N.R	96.4% (Qatar study)	75%	51%
Delta	N.R	59.0%	65.2%	67%	N.R	90%	N.R	88%	N.R

Number of doses	Variant	Vaccine	Country	Author
One dose	Beta	Ad26.COV2.S	South Africa	US FDA [24]
	Not specified	Ad5-nCoV	Pakistan, Mexico, Russia, Chile and Argentina	Cansino [30]
		Ad26.COV2.S	Latin America, South Africa	US FDA [24]
		BNT162b2	Multiple	Polack [14]
		mRNA-1273	USA	Baden [17]
		Sputnik V	Russia	Loguno [26]
	Zeta	Ad26.COV2.S	Latin America	US FDA [24]
Two doses	Alpha	AZD1222	UK	Emary [20]
		NVX-CoV2373	UK	Heath [28]
			USA, Mexico	Novavax [29]
	Beta	AZD1222	South Africa	Mahdi [22]
		NVX-CoV2373	South Africa	Shinde [27]
	Not specified	Abdala	Cuba	Abdala [35]
		AZD1222	UK/Brazil/South Africa	Voysey [21]
			USA	AstraZeneca [23]
		BBIBP-CorV	Bahrain, China, Pakistan and the UAE	Al Kaabi [33]
		BNT162b2	Multiple	Polack [14]
				Thomas [15]
		CoronaVac	Brazil, Chile, Argentina, Colombia, Peru, Mexico, US, South Africa	Sinovac [31]
			Indonesia	Sinovac [31]
			Turkey	Tanriover [32]
		COVAXIN	India	Bharat Biotech [34]
		Curevac	Ten countries	Curevac [19]
		mRNA-1273	USA	Baden [17]
				El Sahly [18]
		Sputnik V	Russia	Loguno [26]
		Wuhan inactivated ..	China	Al Kaabi [33]

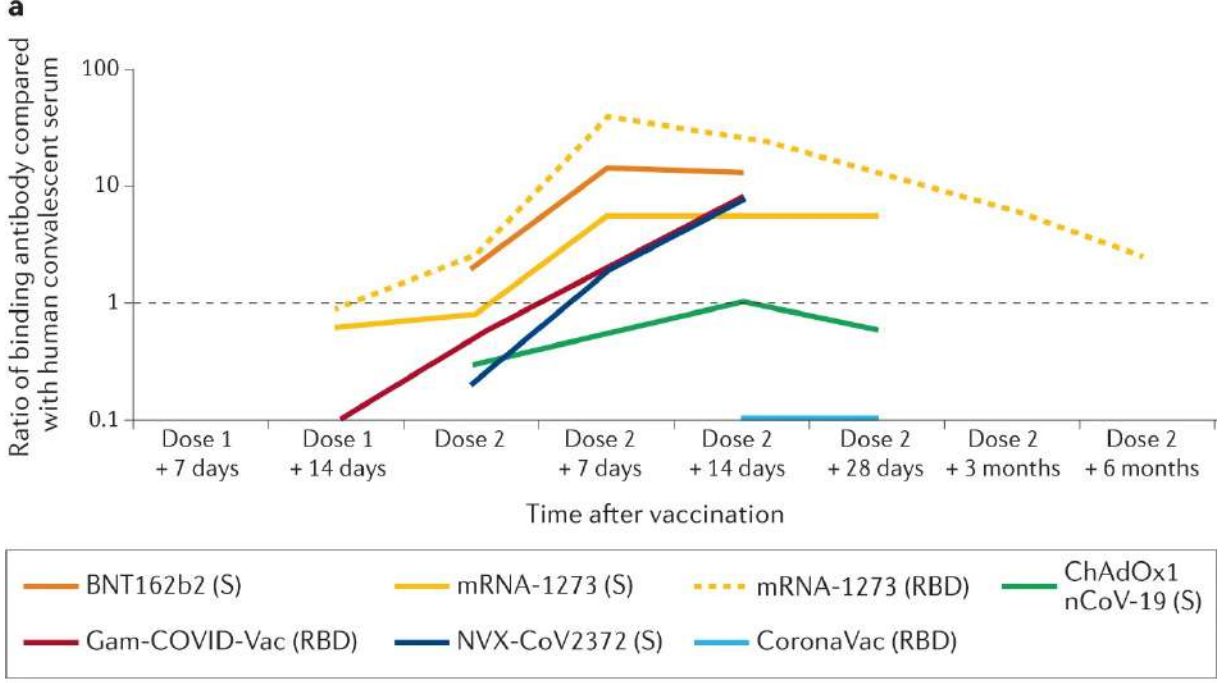


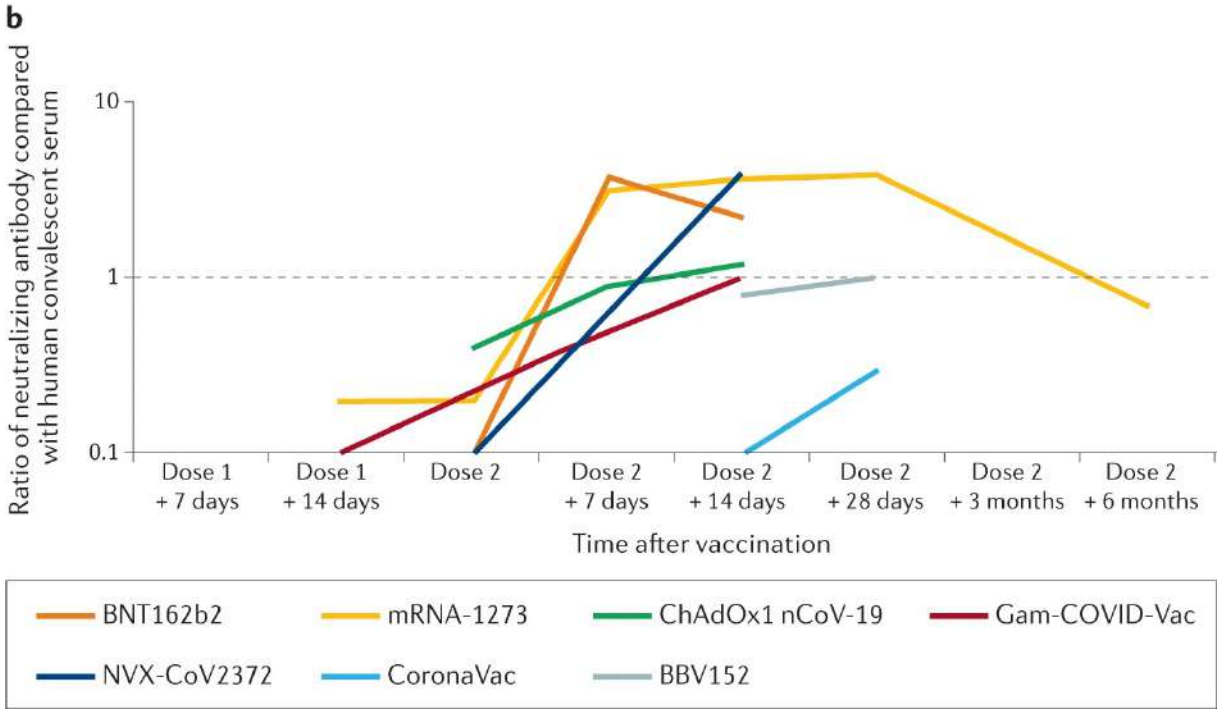
Immunological mechanisms of vaccine-induced protection against COVID-19 in humans

Manish Sadarangani, Arnaud Marchant and Tobias R. Kollmann

Antikor Seviyeleri

Nat Rev Immunol *21, 475–484 (doi: 10.1038/s41577-021-00578-z)*





SinoVac CoronaVac

- İnaktif virüs
- *Vero* hücrelerinde virüs kültürü
- *β-propiolactone* aracılı inaktivasyon
- *Alum* adjuvant

Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey

Mine Durusu Tanriover, Hamdi Levent Doğanay*, Murat Akova*, Hatice Rahmet Güner, Alpay Azap, Sıla Akhan, Şükran Köse, Fatma Şebnem Erdinç, Emin Halis Akalın, Ömer Fehmi Tabak, Hüsnü Pullukçu, Özgür Batum, Serap Şimşek Yavuz, Özge Turhan, Mustafa Taner Yıldırmak, İftihar Köksal, Yeşim Taşova, Volkan Korten, Gürdal Yılmaz, Mustafa Kemal Çelen, Sedat Altın, İlhami Çelik, Yaşar Bayındır, İlkay Karaoğlan, Aydın Yılmaz, Aykut Özkul, Hazal Gür, Serhat Unal*, and the CoronaVac Study Group†*

the second dose, yielding a vaccine efficacy of 83·5% (95% CI 65·4–92·1; p<0·0001).

Effectiveness of inactivated SARS-CoV-2 vaccines against the Delta variant infection in Guangzhou: a test-negative case–control real-world study

Xiao-Ning Li[a*], Yong Huang[a*], Wen Wang[a*], Qin-Long Jing[a*], Chun-Huan Zhang[a*], Peng-Zhe Qin[a*]

single dose of inactivated SARS-CoV-2 vaccine yielded the VE of only 13.8%. After adjusting for age and sex, the overall VE for two-dose vaccination was 59.0% (95% confidence interval: 16.0% to 81.6%) against coronavirus disease 2019 (COVID-19) and 70.2% (95% confidence interval: 29.6–89.3%) against moderate COVID-19 and 100% against severe COVID-19 which might be overestimated due to the small sample size. The VE of two-dose vaccination against

CoronaVac	Inactivated SARS-CoV-2, in vitro production in Vero cells	Whole virus	Mostly humoral response, aluminum adjuvant enhances response more robustly	51% in Brazil, 83.5% in Turkey; 50% (against gamma variant)	2 doses, 2 weeks apart	[58, 128, 143, 145, 152]

VirusDis.https://doi.org/10.1007/s13337-022-00755-1

Oxford-AstraZeneca / ChAdOx1

- Nonreplike adenovirus (şempanze) vektör

ChAdOx1 nCoV-19	Non-replicating viral vector, use recombinant ChAdOx1 adenoviral vector encoding the spike (S) protein of the SARS-CoV-2	Spike protein	Both humoral and cell mediate responses	70.4% (Interim); 79% in US phase 3 study; 74.5% (against Alpha variant); 67% (against Delta Variant); In Canada, 70% (against Delta variant), 72% (against Alpha variant), 50% (against both Beta and Gamma variant)	2 doses, 12 weeks apart	[5, 75, 102, 139]

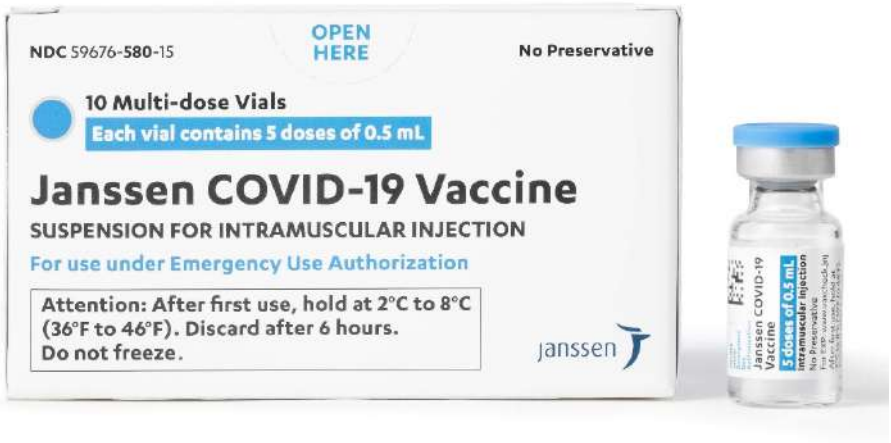
VirusDis.https://doi.org/10.1007/s13337-022-00755-1

Janssen/ Ad26.CoV2.S

- Nonreplike adenovirus (insan) vektör
- Tek doz

Table 2 Globally approved vaccines for COVID-19 until 13 August 2021

Vaccines	Vaccine platform and formulation techniques	Target antigen	Immunogenicity	Efficacy	Dose and time interval	References
BNT162b2	RNA, nucleoside modification of SAS-CoV-2 mRNA	Spike protein	Both humoral and cell mediate responses	95%; 88% (against Delta variant); 93% (against Alpha variant)	2 doses, 3 weeks apart	[75, 97, 111, 139]
mRNA-1273	RNA, encapsulation of SAS-CoV-2 mRNA in lipid nanoparticle (LNP)	Spike protein	Both humoral and cell mediate responses	94.1%; 100% (against Alpha variant); 96.4% (against Beta variant)	2 doses, 4 weeks apart	[7, 33, 63, 98]
Ad26.COV2.S	Non-replicating viral vector, use recombinant and replication incompetent Adenovirus type 26 (Ad26) vector which encodes the SAS-CoV-2 spike (S) protein	Spike protein	Both humoral and cell mediate responses	67% in phase 3 study; 72% in US; 68.1% in Brazil study; 64% in South Africa Study	Single dose	[66, 92, 108, 128, 139]

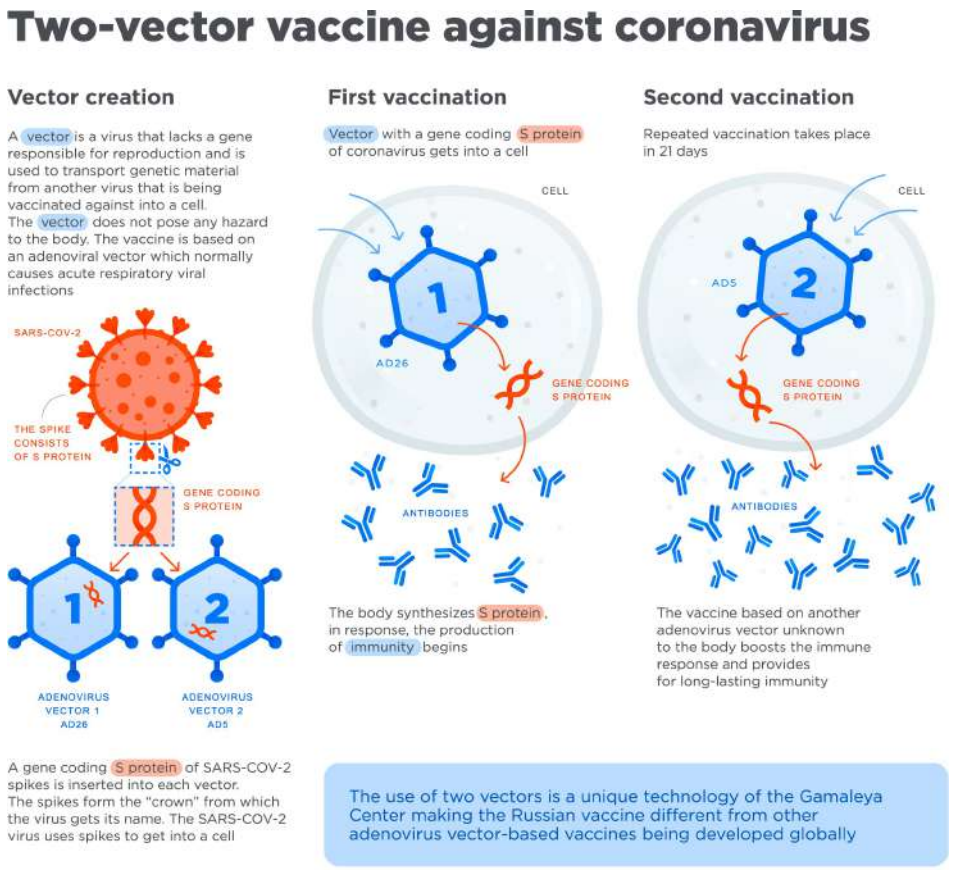


VirusDis. https://doi.org/10.1007/s13337-022-00755-1

Sputnik V

2 adenovirus vektörü

Gam-COVID-Vac	Non-replicating viral Vector, use human Adenovirus type 5 (Ad5) and Adenovirus type 26 (Ad26) vector encoding the spike (S) protein of the SARS-CoV-2	Spike protein	Both humoral and cell-mediated responses	91.6%	2 doses, 3 weeks apart	[73, 74]



VirusDis. https://doi.org/10.1007/s13337-022-00755-1

BioNTech – Pfizer /BNT162b2

Lipid nanopartikül içinde **mRNA**

Tam S proteinini kodluyor

Table 2 Globally approved vaccines for COVID-19 until 13 August 2021

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VirusDis.https://doi.org/10.1007/s13337-022-00755-1

Moderna/mRNA 1273

Lipid nanopartikül içinde **mRNA**

Tam S proteinini kodluyor

Table 2 Globally approved vaccines for COVID-19 until 13 August 2021

Vaccines	Vaccine platform and formulation techniques	Target antigen	Immunogenicity	Efficacy	Dose and time interval	References
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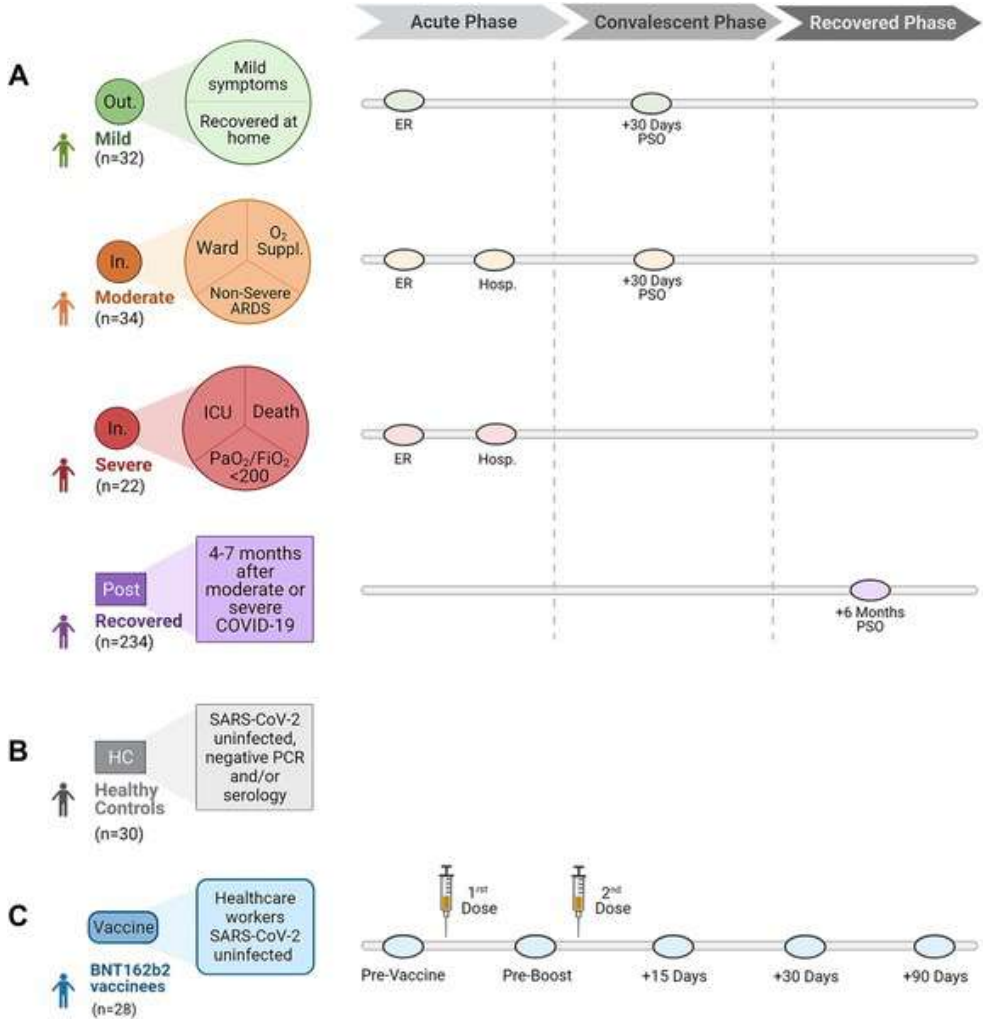
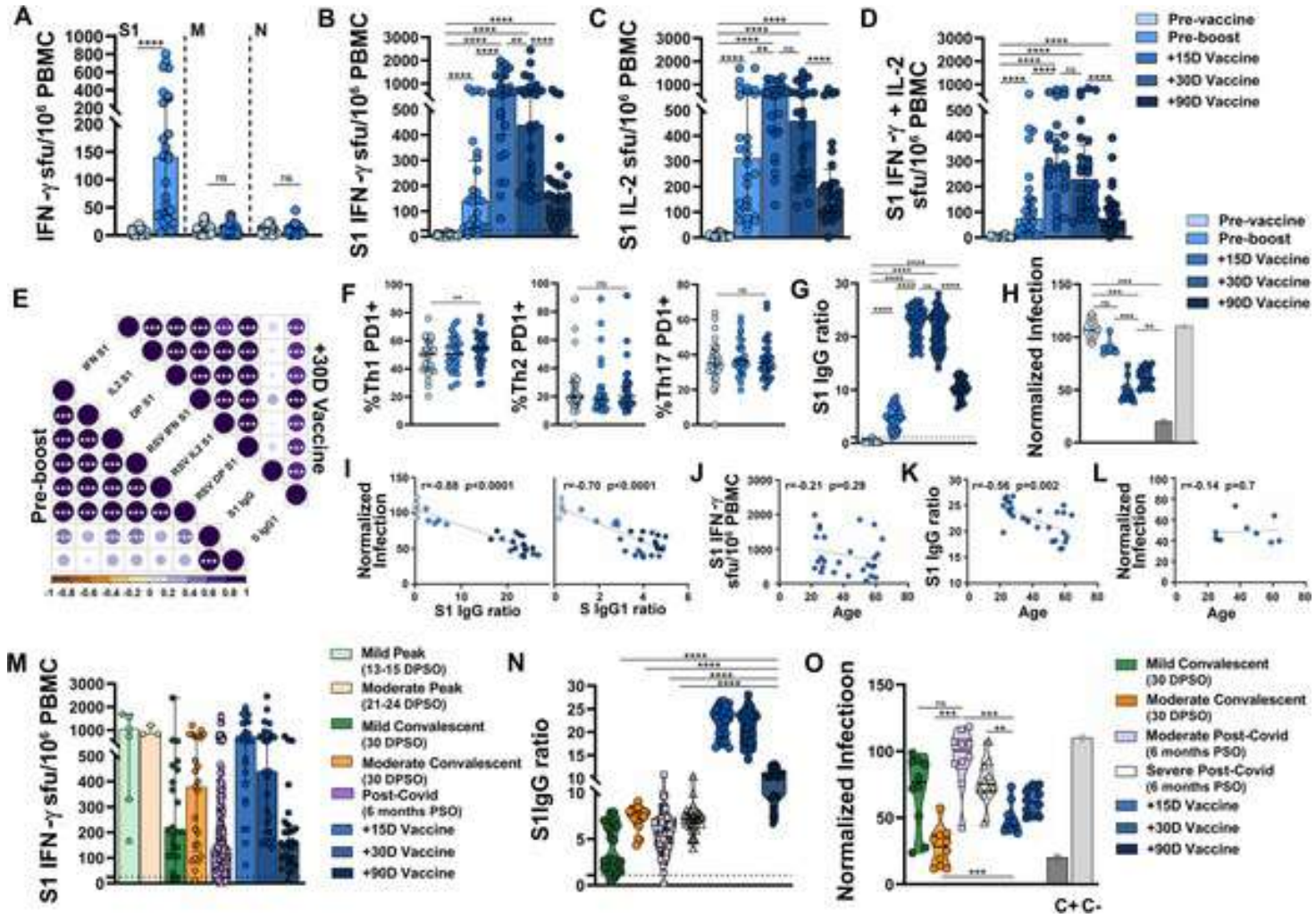
VirusDis.https://doi.org/10.1007/s13337-022-00755-1

Fig 1. Overview of patient cohorts including the time of sample collection.



Almendro-Vázquez P, Laguna-Goya R, Ruiz-Ruigomez M, Utrero-Rico A, Lalueza A, et al. (2021) Longitudinal dynamics of SARS-CoV-2-specific cellular and humoral immunity after natural infection or BNT162b2 vaccination. PLOS Pathogens 17(12): e1010211. https://doi.org/10.1371/journal.ppat.1010211
https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1010211

Fig 7. Development of SARS-CoV-2-specific cellular and humoral immunity after BNT162b2 vaccination.



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https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1010211

Omicron Varyantı'na Karşı Etkinlik

The NEW ENGLAND JOURNAL of MEDICINE

Effectiveness of BNT162b2 Vaccine against Omicron Variant in South Africa

Reduced Neutralization of SARS-CoV-2 Omicron Variant by Vaccine Sera and monoclonal antibodies

Alexander Wilhelm, Marek Widera, Katharina Grikscheit, Tuna Toptan, Barbara Schenk, Christiane Pallas, Melinda Metzler, Niko Kohmer, Sebastian Hoehl, Fabian A. Helfritz, Timo Wolf, Udo Goetsch, Sandra Ciesek

doi: https://doi.org/10.1101/2021.12.07.21267432

A meta-analysis of Early Results to predict Vaccine efficacy against Omicron

David S. Khoury, Megan Steain, James A. Triccas, Alex Sigal, Miles P. Davenport, Deborah Cromer

doi: https://doi.org/10.1101/2021.12.13.21267748

neutralisation titre against Omicron of 9.7-fold (95% CI 5.5-17.1). We use our previously established model to predict that six months after primary immunisation with an mRNA vaccine, efficacy for Omicron is estimated to have waned to around 40% against symptomatic and 80% against severe disease. A booster dose with an existing mRNA vaccine (even though it targets the ancestral spike) has the potential to raise efficacy for Omicron to 86.2% (95% CI: 72.6-94) against symptomatic infection and 98.2% (95% CI: 90.2-99.7) against severe infection.

Protection by 4th dose of BNT162b2 against Omicron in Israel

January 25, 2022
11:30 PM GMT+3
Last Updated 24 days ago

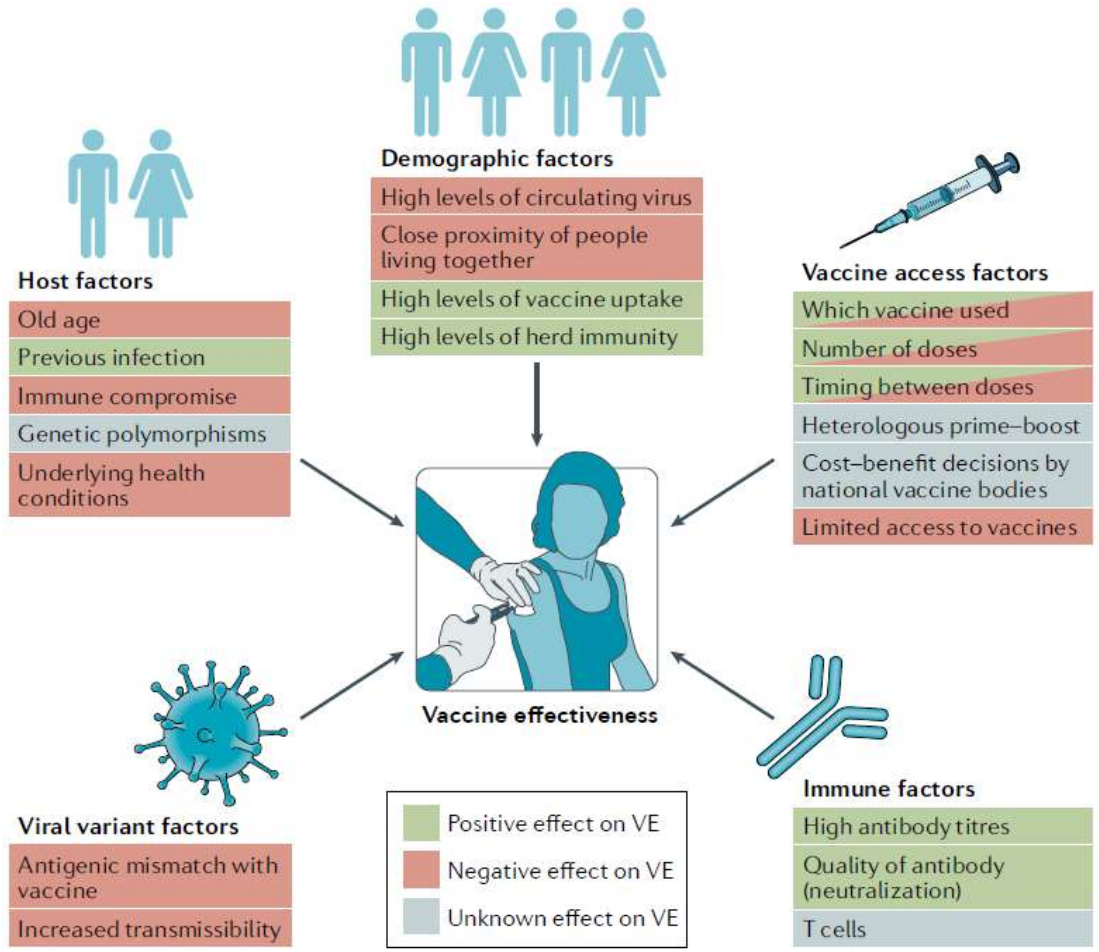
Healthcare & Pharmaceuticals

Pfizer and BioNTech launch trial of Omicron-targeted COVID vaccine

%80'i nden, iki doz yine de ciddi hastalığa karşı korumayı indükleyebilir (5)

[6] The Faculty of Medicine, Tel Aviv University, Israel

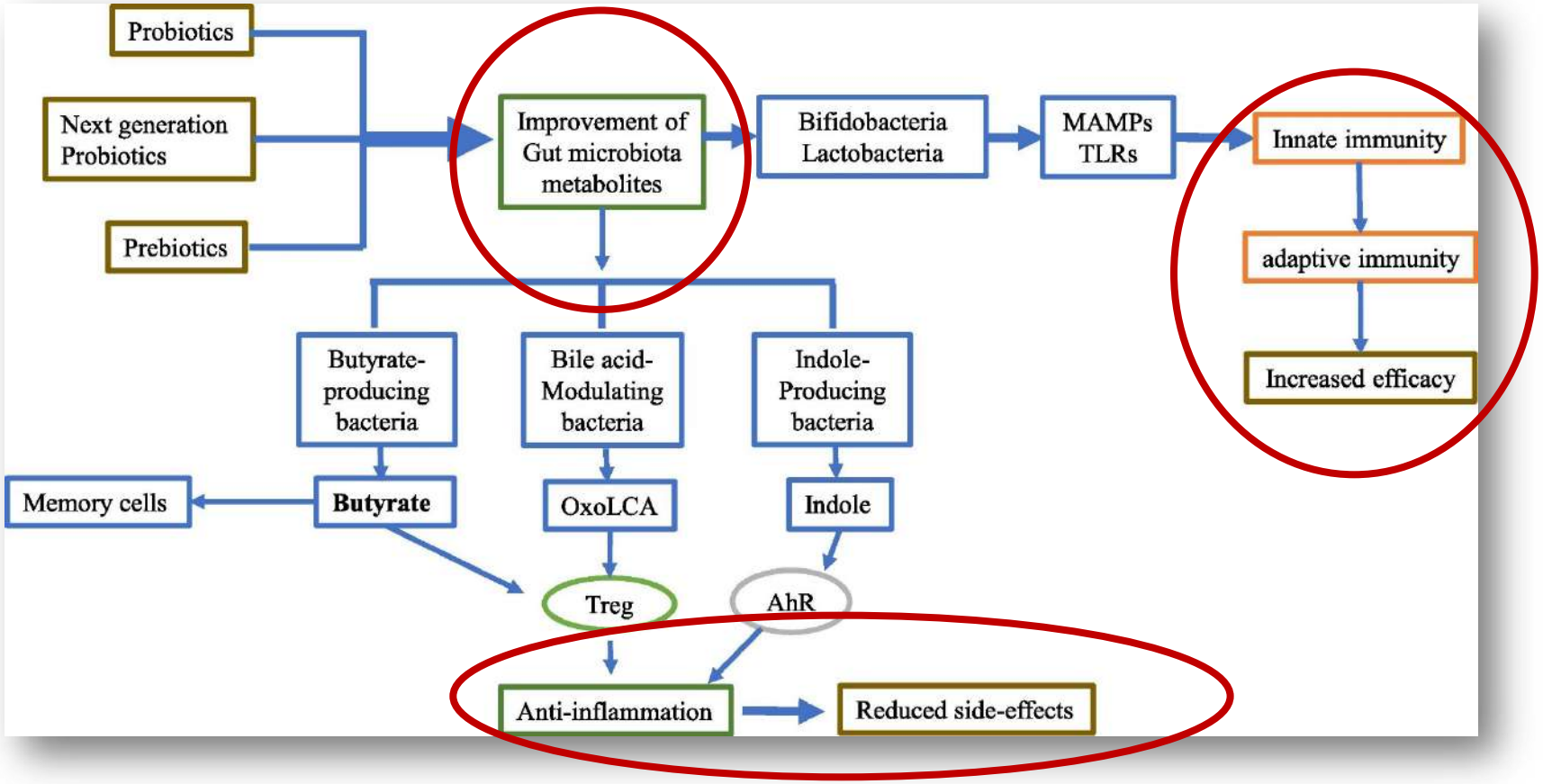
Aşı Etkinliğini Etkileyen Faktörler



The intestinal microbiota and improving the efficacy of COVID-19 vaccinations

Jiezhong Chen [a,*], Luis Vitetta [a,b,*], Jeremy D. Henson [a,c], Sean Hall [a]

[a] *Medlab Clinical, Department of Research, Sydney 2015, Australia*
[b] *The University of Sydney, Faculty of Medicine and Health, Sydney 2006, Australia*
[c] *The University of New South Wales, Faculty of Medicine, Prince of Wales Clinical School, Sydney, Australia*



OPEN ACCESS

Original research

Gut microbiota composition is associated with SARS-CoV-2 vaccine immunogenicity and adverse events

Siew C Ng [1,2,3,4] Ye Peng [5,6] Lin Zhang [1,2,4,7] Chris KP Mok,[3,8] Shilin Zhao,[5,6] Amy Li,[1] Jessica YL Ching [1] Yingzhi Liu,[4,7] Shuai Yan,[4,7] Dream L S Chan,[4] Jie Zhu,[5,6] Chunke Chen,[3,8] Adrian CH Fung,[9] Kenneth KY Wong [9] David SC Hui,[1,10] Francis KL Chan [1,2,3,4] Hein M Tun [5,6]

Bifidobacterium adolescentis - Coronavac (p=0.023)

Roseburia faecis dahil olmak üzere kamçılı ve fimbrialı bakterilerin toplam bolluğu- Biontech (p=0.028)

Prevotella copri ve iki Megamonas türünün bolluğu, aşılardan herhangi birini takiben daha az yan etki

Redox Biology 50 (2022) 102242

Contents lists available at ScienceDirect

Redox Biology

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

Humoral immune response to COVID-19 mRNA vaccination in relation to selenium status

Kamil Demircan [a,b], Thilo Samson Chillon [a], Qian
Georg Jochen Klingenberg [a], Ines Maria Hirschbil-
Joachim Diegmann [e], Manuel Bachmann [e], Arash I

A B S T R A C T

The essential trace element selenium (Se) is of central importance for human health and particularly for a regular functioning of the immune system. In the context of the current pandemic, Se deficiency in patients with COVID-19 correlated with disease severity and mortality risk. Selenium has been reported to be associated with the immune response following vaccination, but it is unknown whether this also applies to SARS-CoV-2 vaccines. In this observational study, adult health care workers (n = 126) who received two consecutive anti-SARS-CoV-2 vaccinations by BNT162b2 were followed for up to 24 weeks, with blood samples collected at the first and second dose and at three and 21 weeks after the second dose. Serum SARS-CoV-2 IgG titres, neutralising antibody potency, total Se and selenoprotein P concentrations, and glutathione peroxidase 3 activity were quantified. All three biomarkers of Se status were significantly correlated at all the time points, and participants who reported supplemental Se intake displayed higher Se concentrations. SARS-CoV-2 IgG titres and neutralising potency were highest three weeks after the second dose and decreased towards the last sampling point. The humoral immune response was not related to any of the three Se status biomarkers. Supplemental Se intake had no effect at any time point on the vaccination response as measured by serum SARS-CoV-2 IgG levels or neutralising potency. Overall, no association was found between Se status or supplemental Se intake and humoral immune response to COVID-19 mRNA vaccination.

International Journal of
Molecular Sciences

MDPI

Review

Putative Role of Vitamin D for COVID-19 Vaccination

Sheng-Kang Chiu [1,2,3,†], Kuo-Wang Tsai [4], Chia-Chao Wu [5,6], Cai-Mei Zheng [7], Chung-Hsiang Yang [8,†], Wan-Chung Hu [4,*], Yi-Chou Hou [9], Kuo-Cheng Lu [10] and You-Chen Chao [11]

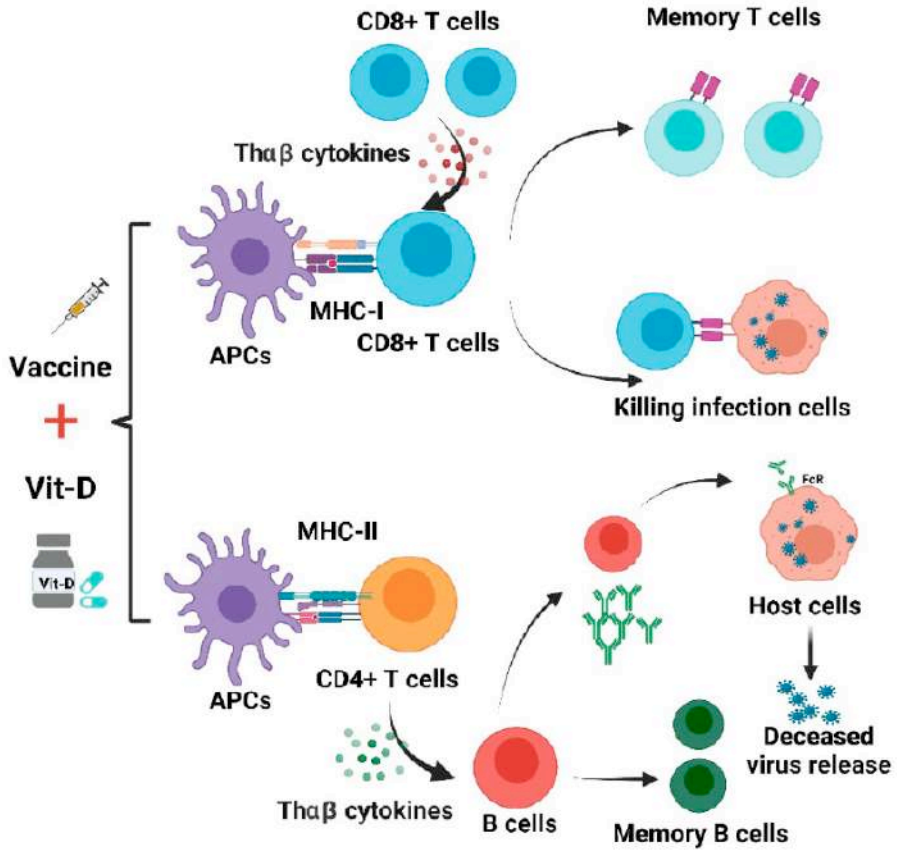


Figure 4. Effects of vitamin D on immune responses induced by COVID-19 vaccines.

biomedicines

MDPI

Article

Relationship between Vitamin D Status and Antibody Response to COVID-19 mRNA Vaccination in Healthy Adults

Thilo Samson Chillon [1], Kamil Demircan [1,2], Raban Arved Heller [1,3,4], Ines Maria Hirschbil-Bremer [5], Joachim Diegmann [5], Manuel Bachmann [5], Arash Moghaddam [6] and Lutz Schomburg [1,*]

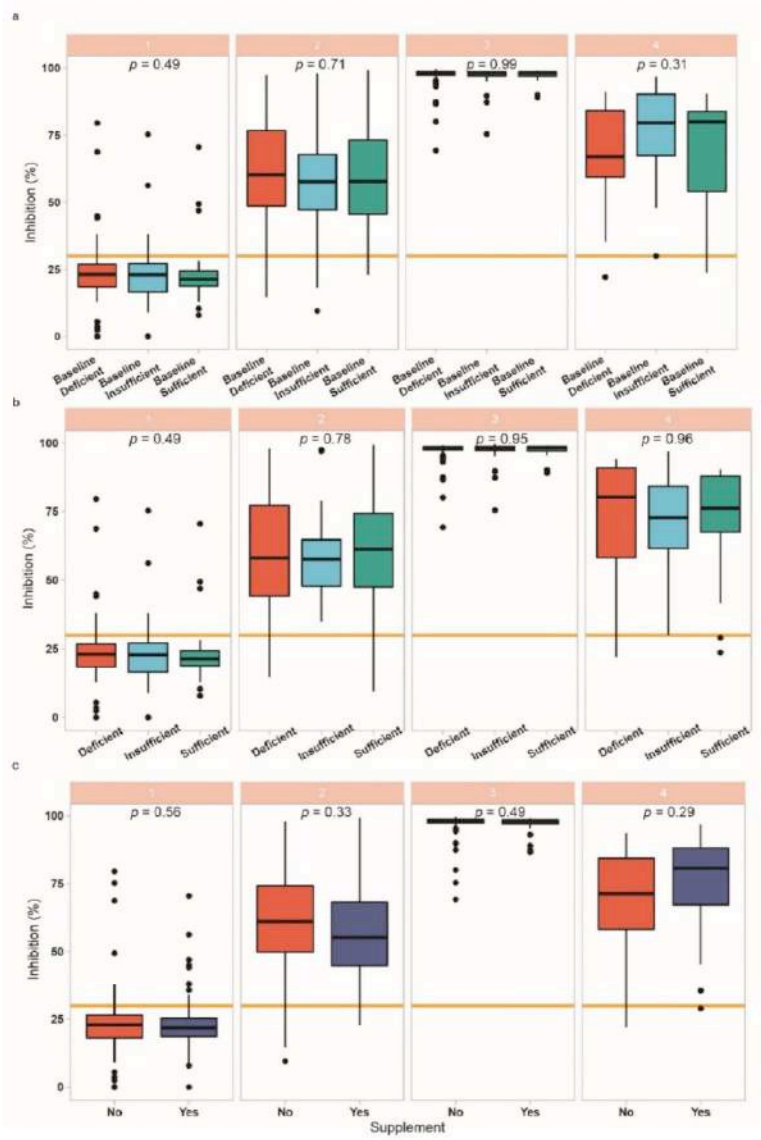


Figure 5. Association of vitamin D status with the neutralising antibody response to BNT162b2 vaccine. Patients were categorized into vitamin D deficient (25(OH)D < 20 ng/mL), insufficient (25(OH)D < 30 ng/mL, or sufficient (25(OH)D > 30 ng/mL). (**a**) Vitamin D status measured at baseline (time point 1) was compared to neutralising antibody levels at each sampling time. No significant differences were observed. (**b**) Vitamin D status was re-evaluated at each sampling time and compared to inhibition. No significant differences were observed. (**c**) Lastly, neutralising antibody titres were compared according to supplement use, without observing significant differences. When comparing three groups, (**c**), and when comparing two groups, Wilcoxon rank-sum test was applied.

Time of Day of Vaccination Affects SARS-CoV-2 Antibody Responses in an Observational Study of Health Care Workers

Wei Wang[*,1], Peter Balfe[†,1], David W. Eyre[‡], Sheila F. Lumley[†,§], Denise O'Donnell[§], Fiona Warren[§], Derrick W. Crook[†,§,||], Katie Jeffery[§,¶], Philippa C. Matthews[†,§], Elizabeth B. Klerman[*,#,2], and Jane A. McKeating[†,**,2,3]

[*]*Division of Sleep and Circadian Disorders and Division of Sleep Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA,* [†]*Nuffield Department of Medicine, University of Oxford, Oxford, UK,* [‡]*Big Data Institute, Nuffield Department of Population Health, University of Oxford, Oxford, UK,* [§]*John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, UK,* [||]*NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK,* [¶]*Radcliffe Department of Medicine, University of Oxford, Oxford, UK,* [#]*Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA, and* [**]*Chinese Academy of Medical Sciences Oxford Institute, University of Oxford, Oxford, UK*

JOURNAL OF BIOLOGICAL RHYTHMS / February 2022

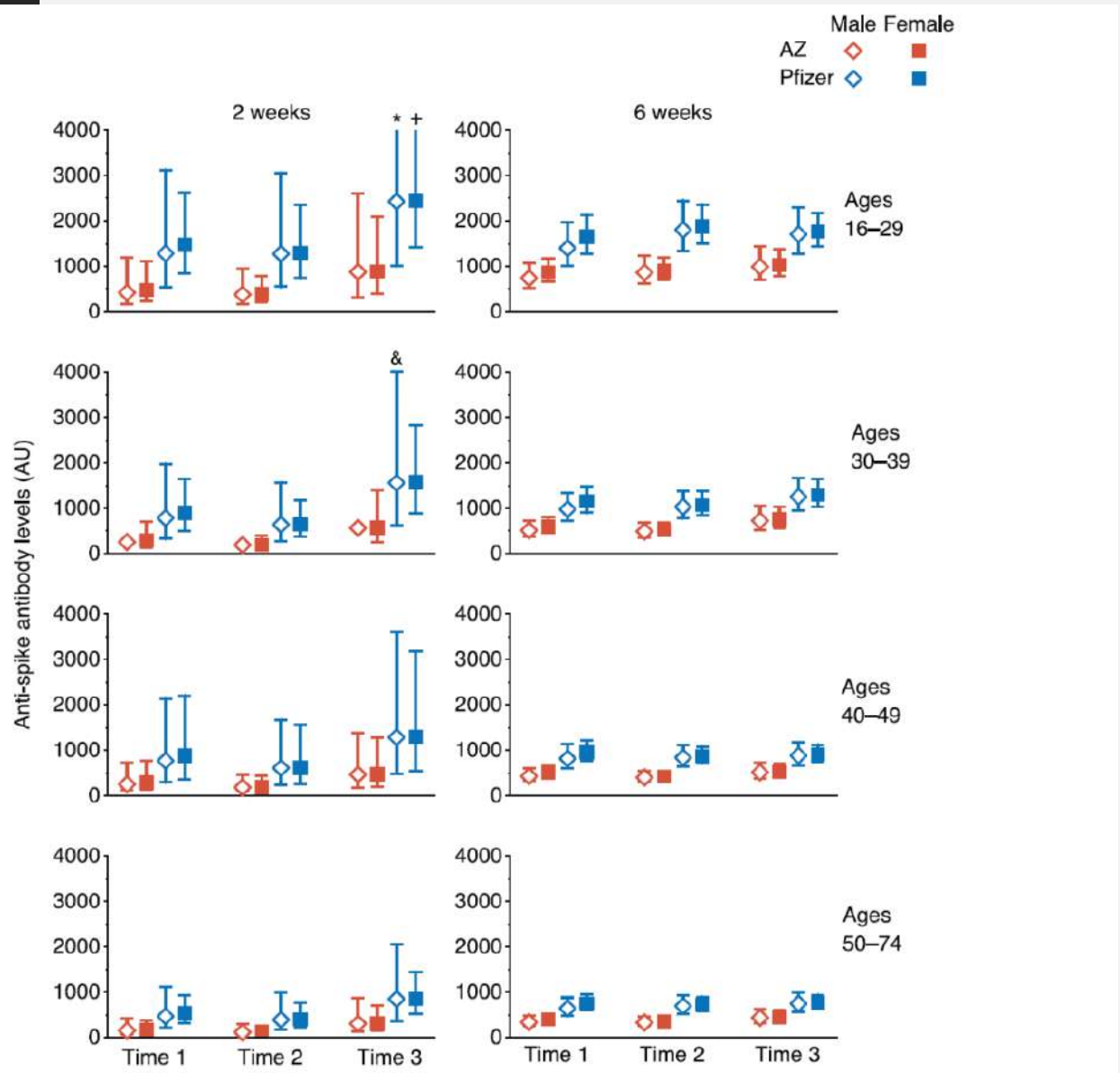
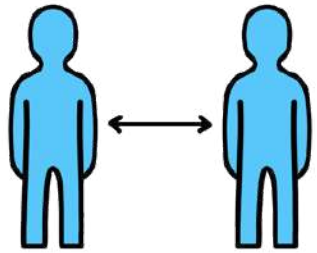


Figure 1. Estimated Anti-Spike antibody levels at 2 and 6 weeks after first SARS-CoV-2 vaccination, partitioned by age, sex, and time of day of vaccination (Time 1, 0700-1059 h; Time 2, 1100-1459 h; Time 3, 1500-2059 h). Mean value (symbol) with 95% confidence values (vertical line). Three confidence intervals extend beyond the Y-axis limits (* = 4275, + = 5996 and & = 4028). Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

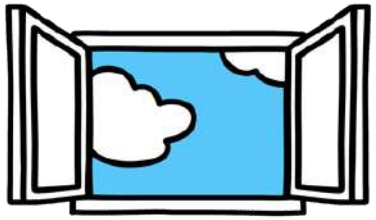
COVID-19 koruyucu önlemleri
Kendinizi&başkalarını koruyun



Mesafe

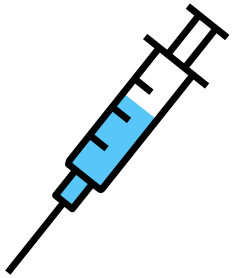
El hijyeni

Ağız kapatılarak öksürme, hapşırma



İyi havalandırma

Maske



Aşılanma