

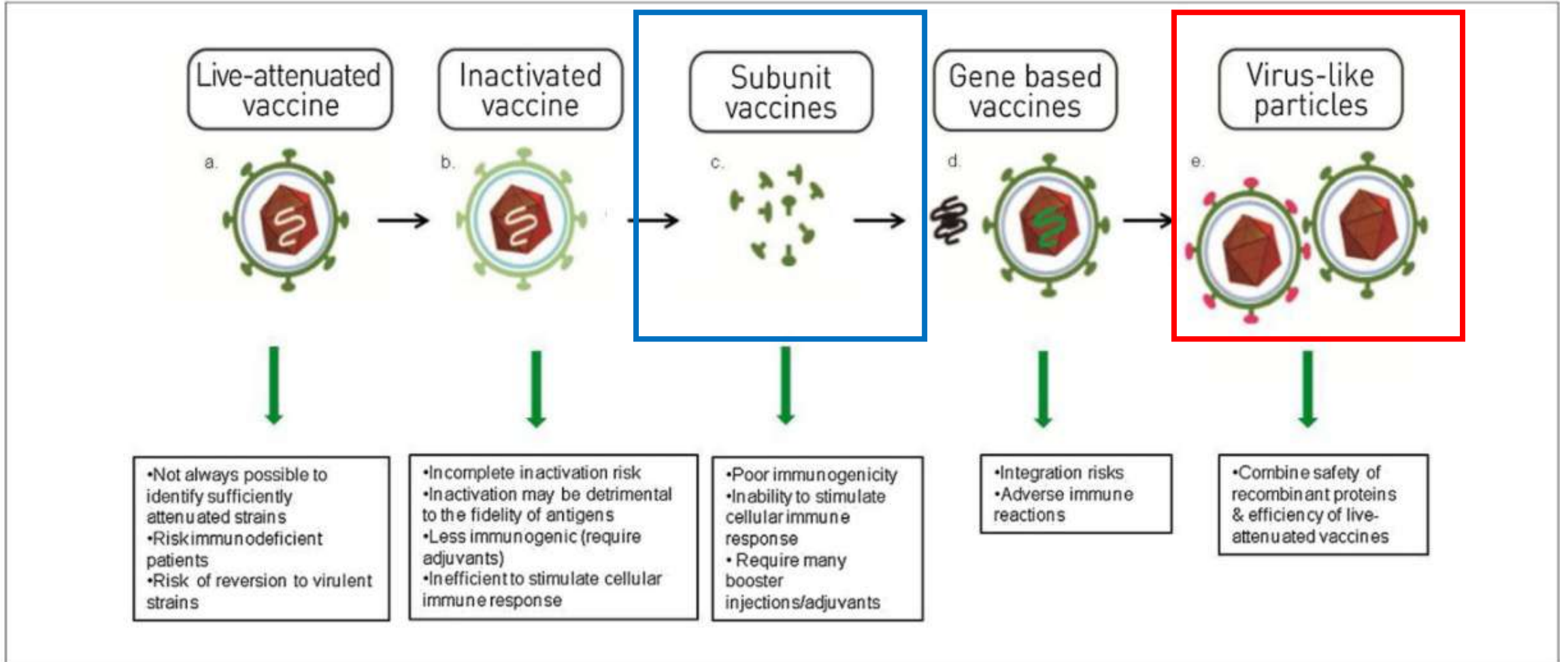
COVID-19 Baęlamında Aşı Geliřtirme Teknolojileri-2

Rekombinant Ařılar

Dr.H.Selçuk Özger

Gazi Üniversitesi Tıp Fakóltesi Enfeksiyon
Hastalıkları Anabilim Dalı

hselcukozger@gazi.edu.tr



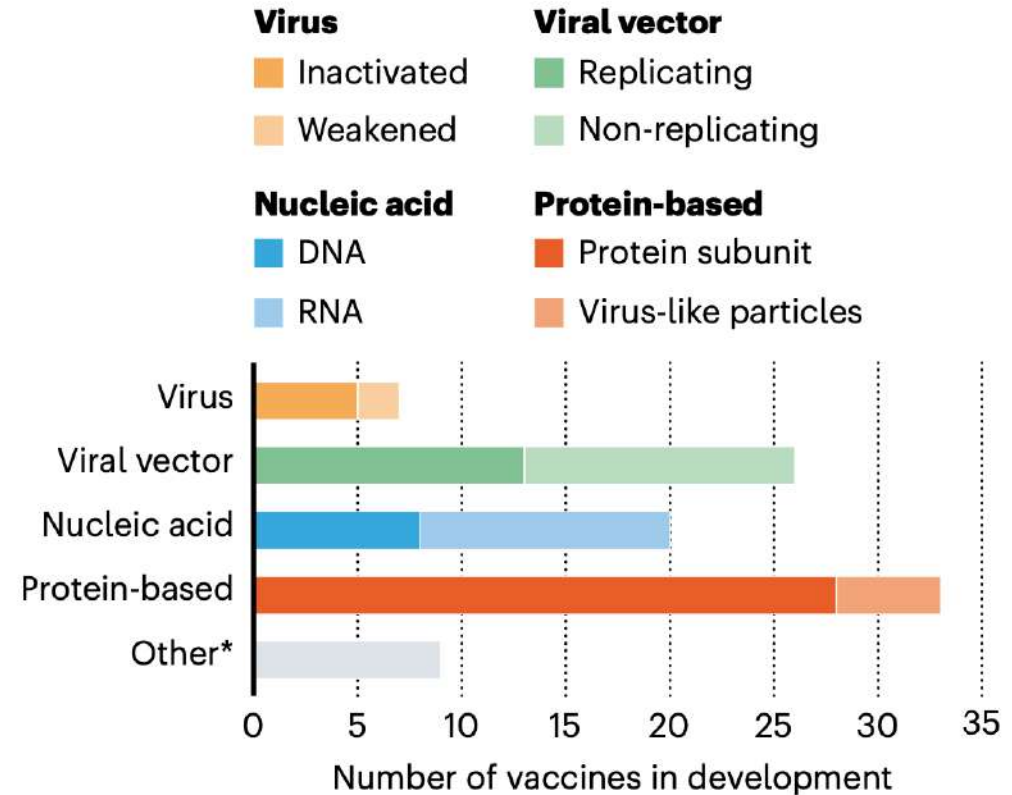
THE RACE FOR CORONAVIRUS VACCINES

By Ewen Callaway;
design by Nik Spencer.

More than 90 vaccines are being developed against SARS-CoV-2 by research teams in companies and universities across the world. Researchers are trialling different technologies, some of which haven't been used in a licensed vaccine before. At least six groups have already begun injecting formulations into volunteers in safety trials; others have started testing in animals. *Nature's* graphical guide explains each vaccine design.

AN ARRAY OF VACCINES

All vaccines aim to expose the body to an antigen that won't cause disease, but will provoke an immune response that can block or kill the virus if a person becomes infected. There are at least eight types being tried against the coronavirus, and they rely on different viruses or viral parts.



* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

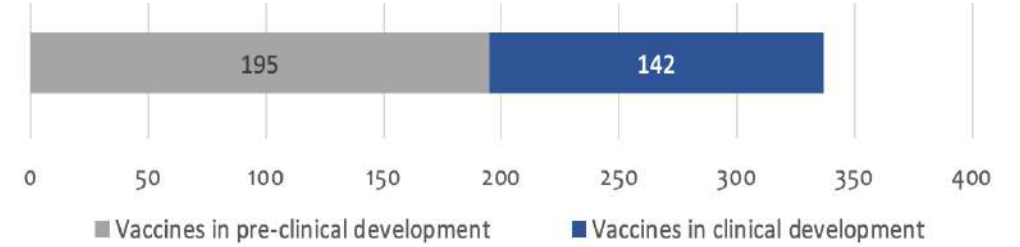
COVID-19 vaccine tracker and landscape, 11.02.2022

1. - Number of vaccines in clinical development

142

2. - Number of vaccines in pre-clinical development

195

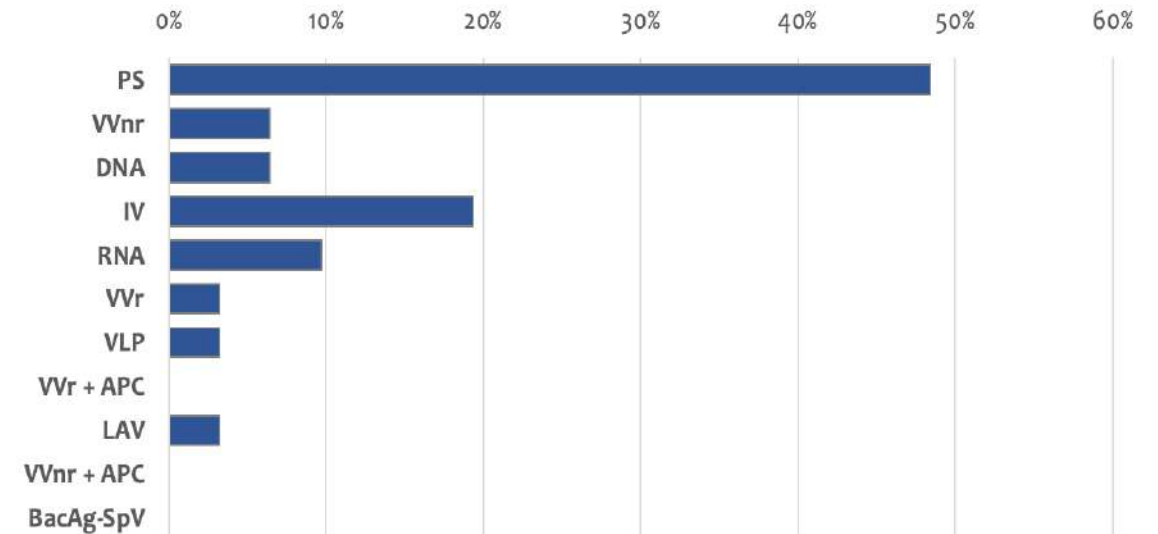


3. - Candidates in clinical phase

Filter Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	15	48%
Wnr	Viral Vector (non-replicating)	2	6%
DNA	DNA	2	6%
IV	Inactivated Virus	6	19%
RNA	RNA	3	10%
VVr	Viral Vector (replicating)	1	3%
VLP	Virus Like Particle	1	3%
Wv + APC	Wv + Antigen Presenting Cell	0	0%
LAV	Live Attenuated Virus	1	3%
Wnr + APC	Wnr + Antigen Presenting Cell	0	0%
BacAg-SpV	Bacterial antigen-spore expression vector	0	0%

31



Protein Subunit aşular

Saflaştırılmış belirli protein

Güvenlik
Ölçeklendirilebilirlik



Daha az immunojenik

Adjuvan

Tekrar doz gereksinimleri



Virüs benzeri partikül aşular

Nanopartikül aşular

Virus benzeri partikül aşıları (VBP)

Rekombinant proteinlerin güvenliği

Canlı-attenué aşıların etkinliği



Viruse benzeyen (biyokimyasal,
morfololojik ve boyut) yapay bir
nanopartikül



Viral kapsid proteinleri
Genomik bir materyal
içermiyor

VBP: bir veya daha fazla yapısal proteininden oluşan multimerik nanoyapılar

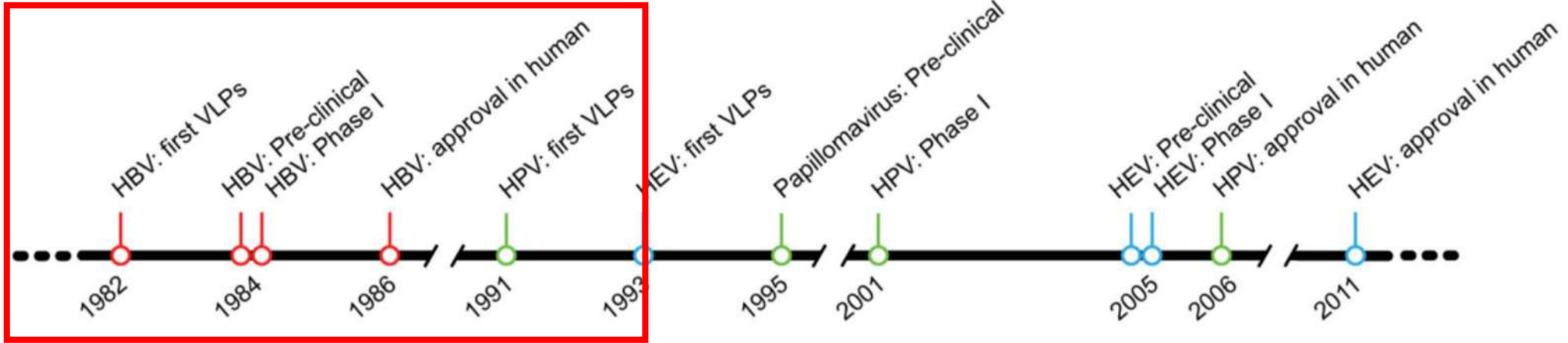
Uygulama alanları Antikor geliştirme, ilaç taşıma, görüntüleme, hedefe yönelik immünoterapi, **aşı geliştirme**

Özellikler

- Artmış immünojenisite
- Hızlı immün yanıt
- Uygun boyut
- Biyouyumluk
- Non-infeksiyöz
- Modifikasyon

Zorluklar

- Stabilizasyon
- Birleşme zorlukları
- Dış koşullara duyarlılık
- Yüksek maliyet

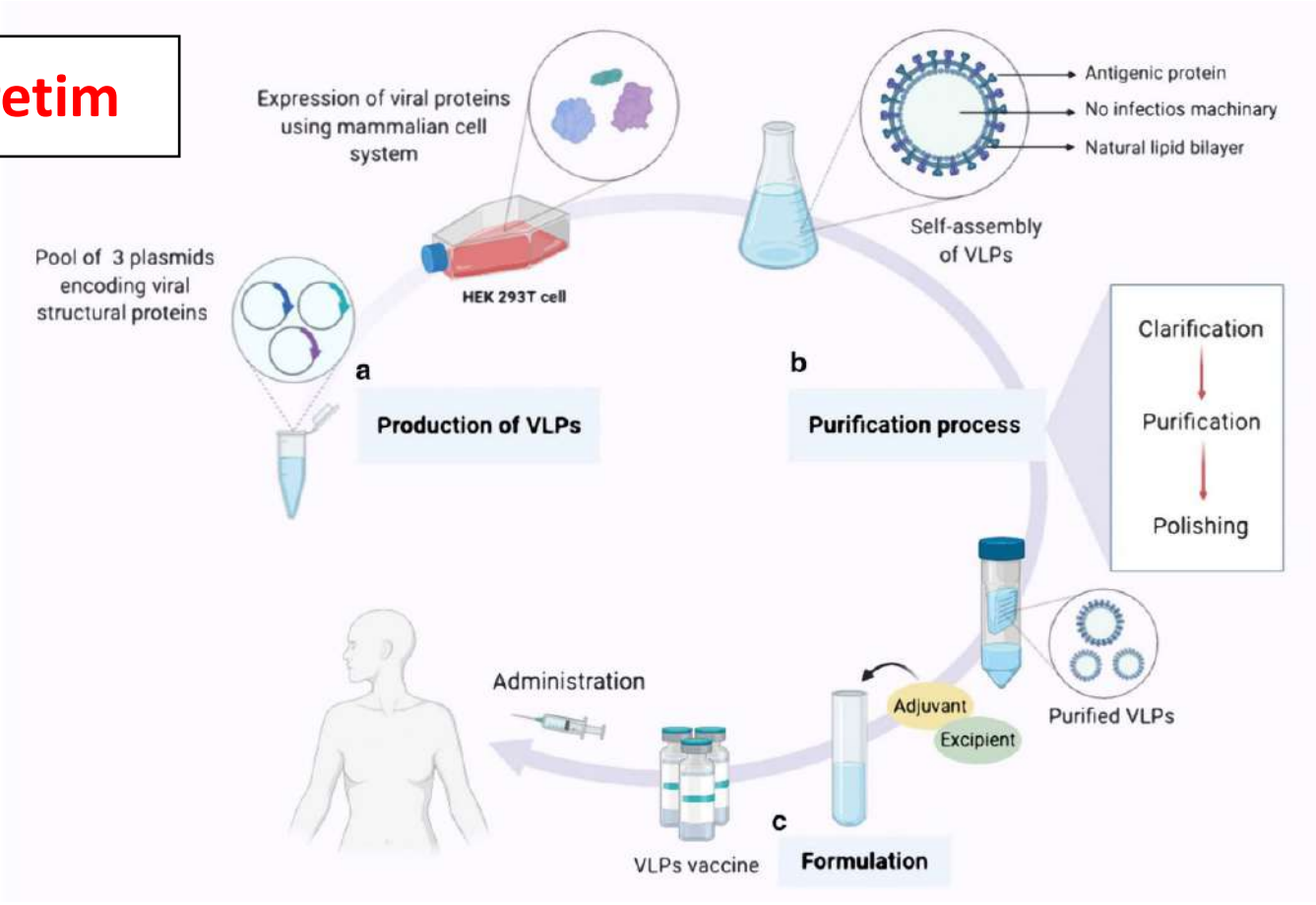


Lisanslı	Klinik çalışma	
HBV HPV HEV <i>P.falciparum</i>	Influenza Norovirus Enterovirus RSV	HMPV Rabies Chikungunya virus Norwalk virus CMV

 COVID-19

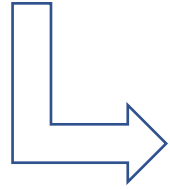
Rekombinant aşı geliştirme basamakları

Üretim



Saflaştırma

Formülasyon

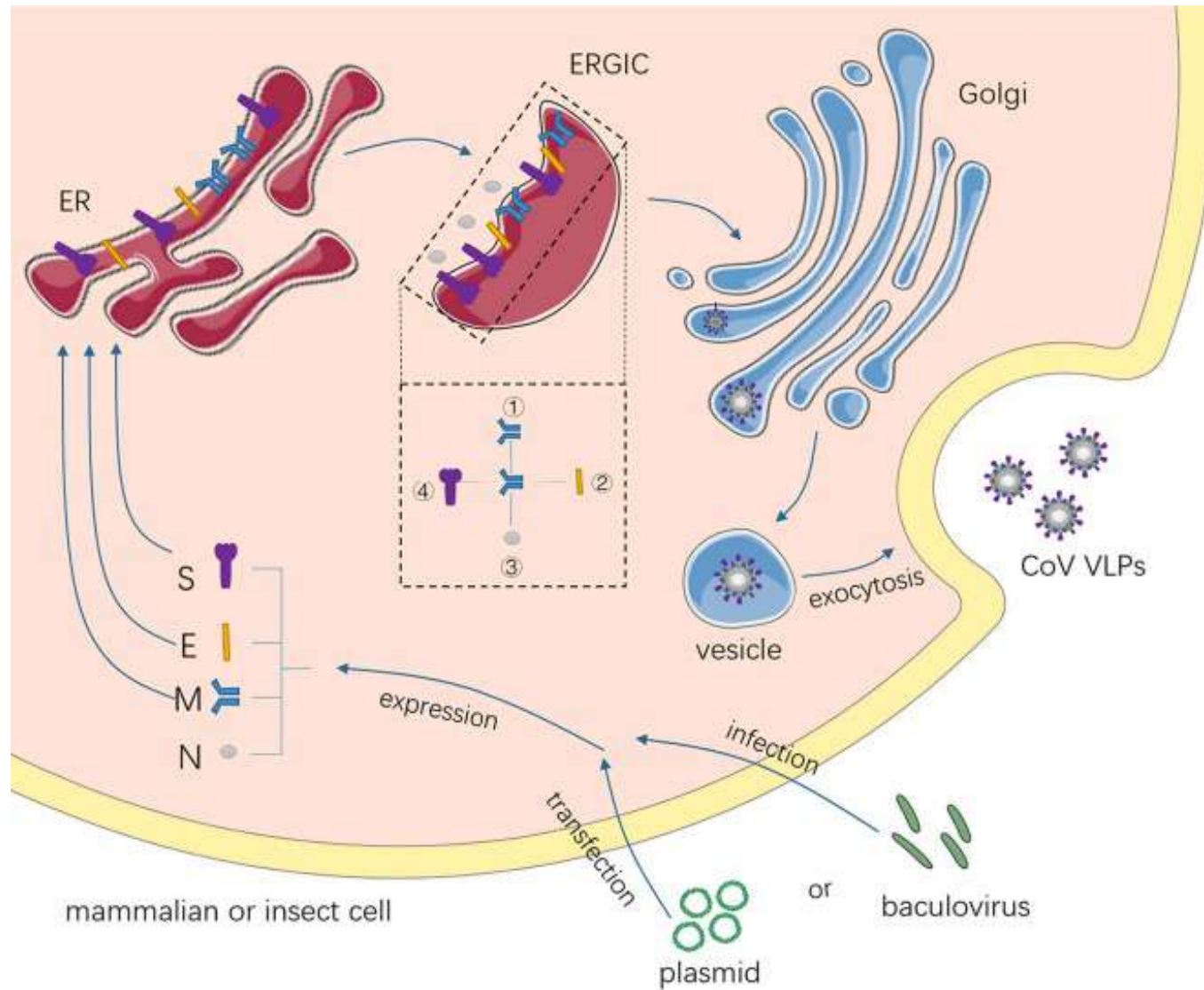


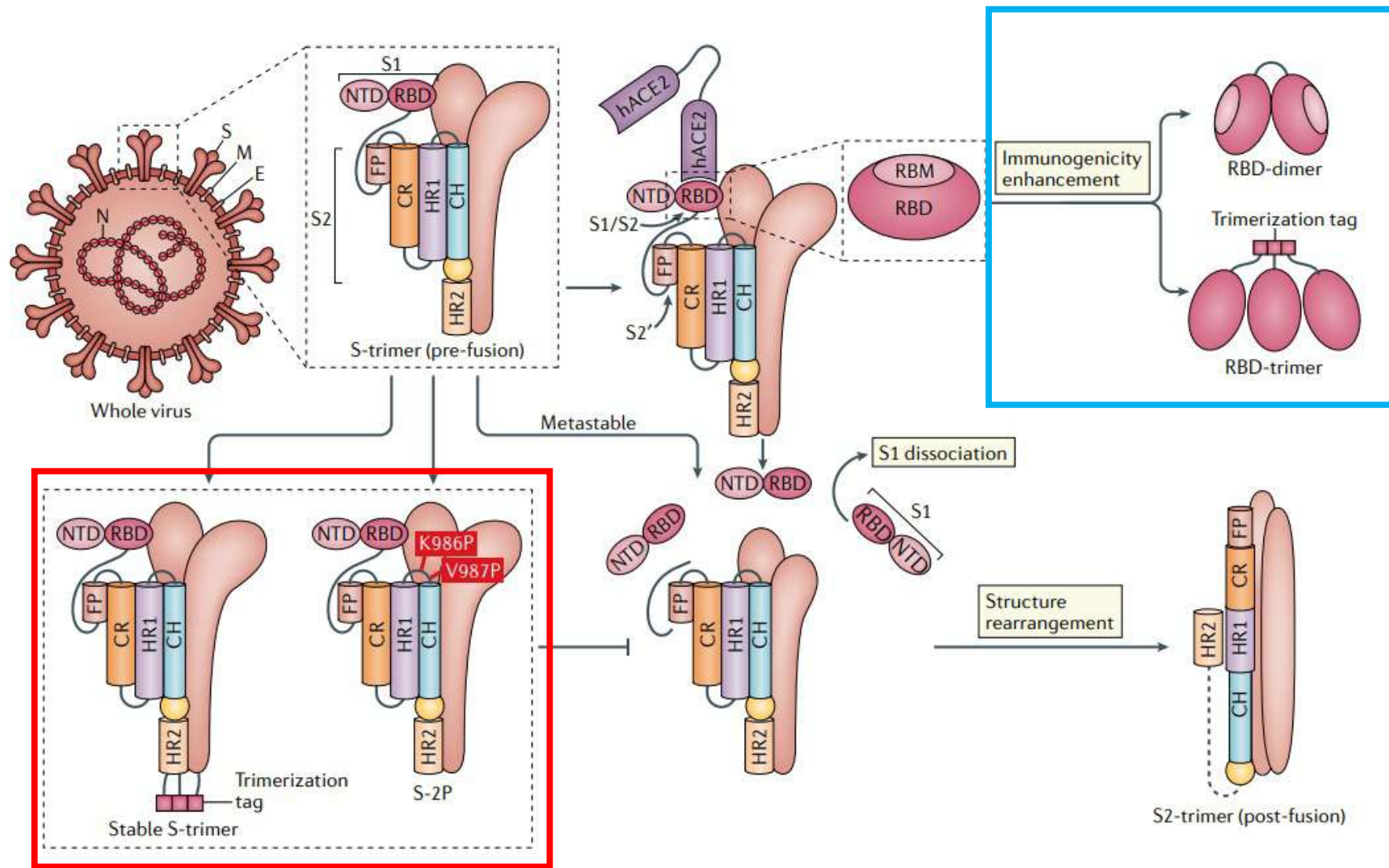
Virus		Parazitler
HPV	RSV	<i>Plasmodium falciparum</i>
HBV	HMPV	<i>Toxoplasma gondii</i>
HEV	Rabies	Leishmania
Influenza	HIV	
Norovirus	Flavivirusler	
Enterovirus	RSV	

Gerekli yapısal proteinleri kodlayan genlerin klonlanması

Table 4 VLPs derived from single- and double-1 stranded DNA viruses

Virus family ^a , structure	Genome properties, structural genes	Expressed genes	Expression system ^b	Example VLPs ^c
<i>Adenoviridae</i> icosahedral T = 25	DsDNA, 35–36 kb, 7 genes for different structural proteins	Penton base and fiber proteins	Insect	Human adenovirus B (type3) Ad3 [154]
<i>Circoviridae</i> icosahedral T = 1	SsDNA, 1.8–2 kb, single CP gene	Coat protein	Bacterial	Porcine circovirus (PCV) [155]
<i>Hepadnaviridae</i> icosahedral T = 4	Partially dsDNA, ~3.2 kb, genes for surface (HBsAg) and core (HBcAg) proteins	HBsAg or HBcAg proteins	Bacterial, yeast, insect, plant	Hepatitis B virus (HBV) [18]
<i>Herpesviridae</i> icosahedral T = 16	Monopartite, dsDNA, 120–240 kb, genes for major (VP5) and minor capsid (VP19C, VP23) proteins and scaffolding protein (pre-VP22a)	VP5, VP19C, V23, pre-VP22a	Insect, mammalian	Herpes simplex virus type 1 (HSV-1) [156]
<i>Papillomaviridae</i> icosahedral T = 7	Circular dsDNA, ~8 kb, genes for structural proteins L1 and L2	L1	Bacterial, yeast, insect, plant	Human papillomavirus (HPV) [45]
<i>Parvoviridae</i> icosahedral T = 1	SsDNA, 4–6 kb, single CP gene	Coat protein	Bacterial, yeast, insect, mammalian	Canine parvovirus(CPV) [157]
<i>Polyomaviridae</i> icosahedral T = 7	Circular dsDNA, ~5 kb, genes for structural proteins VP1, VP2	VP1	Bacterial, yeast, insect	JC polyomavirus [158]



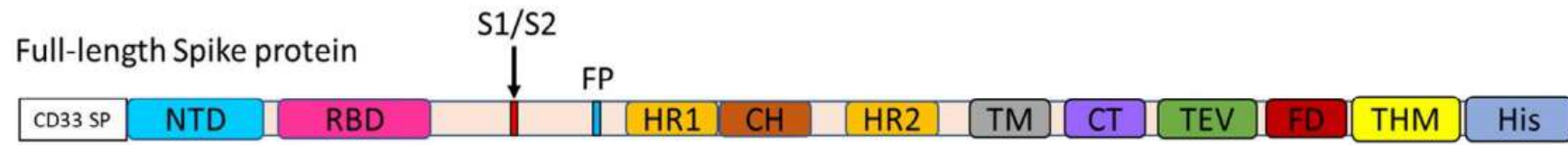


COVID-19 ve Rekombinant aşilar

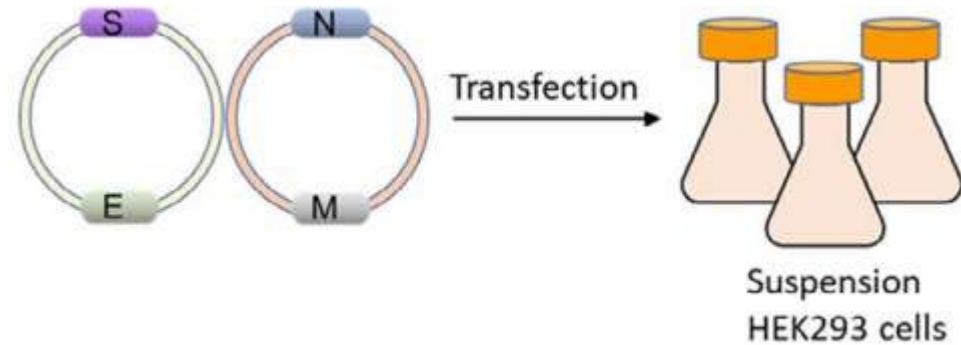
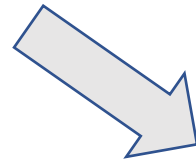
Table 1

Select recombinant protein vaccine candidates in clinical trials for COVID-19 as of December 8, 2020 [5]

Antigen	Vaccine developer	Platform/technology	Adjuvants	Most advanced clinical stage	References
Full-length S-protein based vaccines					
Trimer	Novavax	Insect cells	Matrix M	Phase 3	[6–8]
S-protein	Sanofi Pasteur/GSK	Insect cells	2 different adjuvants (likely variants of AS03)	Phase 1 (to be repeated)	[9]
SCB-2019 trimer	Clover Biopharmaceuticals Inc./GSK/Dynavax	CHO cells	Alum+CpG 1018 or AS03	Phase 1	[10,11]
S-2P (MVC-COV1901)	Medigen Vaccine Biologics Corporation/NIAID/Dynavax	CHO cells	Alum+CpG1018	Phase 1	[12,13]
Covax-19	Vaxine Pty Ltd./Medytox	Insect cells	AdvaxCpG55.2	Phase 1	[14,15]
RBD-based vaccines					
AdimrSC-2I	Adimmune	Baculovirus/Sf9	Alum	Phase 1	[16]
SARS-CoV-2-RBDN1C1	Biological E/BCM	Yeast	Alum+CpG	Phase 1-2	[17–19]
FINLAY-FR-1/2	Instituto Finlay de Vacunas, Cuba			Phase 1	[20,21]
KBP-201	Kentucky Bioprocessing, Inc	Plants		Phase 1-2	[22]
RBD Dimer	Anhui Zhifei Longcom Biopharmaceutical/Institute of Microbiology, Chinese Academy of Sciences	CHO Cells	Aluminum preparation	Phase 3	[23,24]
RBD	West China Hospital, Sichuan University P	Insect Cells	Alum	Phase 2	[25–27]
Multi-epitope vaccines					
Multi-epitope Peptide-based Vaccine (MPV)	COVAXX	Peptides	CpG and alum (AdjuPhos®)	Phase 1	[28,29]
EpiVacCoron	Vektor Laboratories, Russia	Chemical synthesis	Alum	Phase 1	[30]
CoVax-1	University Hospital Tübingen	Peptides	Montanide ISA51	Phase 1	[31,32]



Construct	Sequence at S1/S2 site	Prefusion stabilizing substitutions
WT:	QTQTNSP RR ARSVAS 689	-
S-2P:	QTQT----- IL RSVAS 688	K986P, V987P
S-6P:	QTQTNSP GS ASSVAS 692	F817P, A892P, A899P, A942P, K986P, V987P

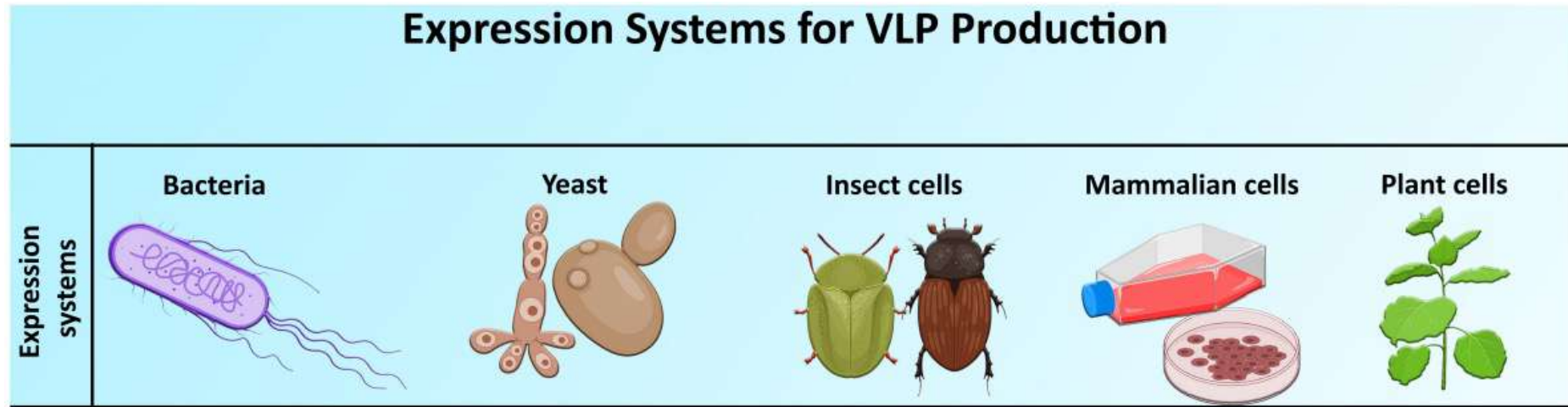


Vaccine	Expression System	Adjuvant	VLP Platform	Antigen	Administration Route	Development Stage	References
Heptavax-B (Merck & Co.)	None (Plasma derived)	Aluminum hydroxide	HBsAg	SHBs	IM	Licensed	[39,40]
Engerix-B® (GSK, Belgium)	Yeast (<i>S. cerevisiae</i>)	Aluminum hydroxide	HBsAg	SHBs	IM	Licensed	[41–43]
Recombivax HB (H-B-Vax®II) (Merck & Co., USA)	Yeast (<i>S. cerevisiae</i>)	Aluminum sulfate	HBsAg	SHBs	IM	Licensed	[43,44]
Sci-B-Vac® (Bio-Hep-B®) (SciGen, Israel)	Mammalian (CHO cells)	Aluminum hydroxide	HBsAg	SHBs, MHBs, LHBs	IM	Licensed	[45–48]
Heplisav-B (Dynavax)	Yeast (<i>H. polymorpha</i>)	1018 ISS	HBsAg	SHBs	IM	Licensed	[49,50]
Fendrix® (GSK, Belgium)	Yeast (<i>S. cerevisiae</i>)	AS04 (Aluminum hydroxide & MPL)	HBsAg	SHBs	IM	Licensed	[51]
Hepavax-Gene® (Crucell)	Yeast (<i>H. polymorpha</i>)	Aluminum hydroxide	HBsAg	SHBs, MHBs	IM	Licensed	[41,52]
Gardasil® (Merck & Co.)	Yeast (<i>S. cerevisiae</i>)	Aluminum hydroxyphosphate sulphate	HPV	HPV6/11/16/18 VLP	IM	Licensed	[53,54]
Cervarix® (GSK)	Insect cells (High Five™ cells)	AS04 (Aluminum hydroxide & MPL)	HPV	HPV16/18 VLP	IM	Licensed	[55,56]
Gardasil-9® (Merck & Co.)	Yeast (<i>S. cerevisiae</i>)	Aluminum hydroxyphosphate sulfate	HPV	HPV6/11/16/18/31/33/45/52/58 VLP	IM	Licensed	[57]
Cecolin® (Innovax)	Bacteria (<i>E. coli</i>)	Aluminum hydroxide	HPV	HPV16/18 VLP	IM	Licensed	[58,59]

Farklı
ekspresyon
sistemleri

Ekspresyon sistemleri

Ekspresyon etkinlikleri, translasyon sonrası modifikasyonlar, kontaminasyon riskleri ve verimlilik açısından farklılıklar



Ekspresyon sistemi		Aşılar
Bakteri	<i>E.coli</i> <i>Bacillus subtilis</i>	HEV, HBV, Influenza, rotavirus, <i>P. falciparum</i> , HCV, Batı Nil virüs, enterovirus
Mayalar	<i>S. cerevisiae</i> <i>Hansenula polymorpha</i> <i>Pichia pastoris</i>	HBV, HPV, <i>Plasmodium falciparum</i> Enterovirus, HIV, deng virüs, Chikungunya virus
Böcek hücreleri (Baculovirus ile infekte)	Spodoptera frugiperda(sf-9) Trichoplusia ni (Tn5)	HPV, Influenza, RSV, Norovirus, RVFV, enterovirus, HEV, toxoplazma, plasmodium
Memeli hücreleri	Ovaryan hücreler (CHO), embroyojenik böbrek hücresi (HEV293), Karaciğer hücresi (huh7 cells)	HBV, HCV, Influenza, HIV, kuduz, kanamalı ateş etkenleri, <i>Plasmodium falciparum</i>
Bitki hücreleri	Nicotiana benthamiana	Influenza, Norovirus, HPV, HBV, HIV,kuduz

Ekspresyon sistemi	Verimlilik	Avantaj	Dezavantajlar
Bakteri (HEV, HPV)	<i>Basit proteinler için yüksek</i>	Hızlı, kolay ve ucuz ekspresyon Kolay manipüle edilebilirlik	Translasyon sonrası modifikasyon yapılamaması Bakteriyel endotoksinler ile kontaminasyon riski Protein katlanma ve çözünürlük problemleri
Mayalar (HBV, HPV, <i>P.falciparum</i>)	Yüksek	Hızlı, kolay ve ucuz ekspresyon Fazla sayıda protein ekspresyonu	Yüksek mannoz glikolizasyonu
Böcek hücreleri (HPV)	Orta- Yüksek	Düşük sıcaklık ve CO2 siz ortamada inkübasyon Baculovirus ile enfekte edildiğinde yüksek ekspresyon düzeyleri Çoklu protein ekspresyonları	Yüksek maliyetli, geliştirme zorlukları Eksprese edilen glikoproteinler için daha basit n-glikolizasyon paterni Baculovirus proteinlerinin uzaklaştırılması

Nooraei et al. J Nanobiotechnol, 2021

Tariq H et al. Front. Microbiol.,2022

Qian C et al. et al., Vaccines,2020

Shin MD et al.Nature Nanotechnology,2020

Ekspresyon sistemi	Verimlilik	Avantaj	Dezavantajlar
Memeli hücreleri (HBV)	Orta- Yüksek	Proteinlerin katlanması, birleştirilmesi ve Translasyon sonrası modifikasyonu için uygun Çoklu protein ekspresyonu	Geliştirme ve ekspresyon maliyeti yüksek Uzun ekspresyon zamanı Memeli patojenleri ile kontaminasyon
Bitki hücreleri	Orta- Yüksek	Ölçeklendirilebilme Yüksek ekspresyon düzeyleri Düşük üreme ve saflaştırma maliyeti İnsan patojenleri ile kontaminasyon riski yok	Sınırlı translasyon sonrası modifikasyon Yeni sistem

Nooraei et al. J Nanobiotechnol, 2021

Tariq H et al. Front. Microbiol.,2022

Qian C et al. et al., Vaccines,2020

Shin MD et al.Nature Nanotechnology,2020

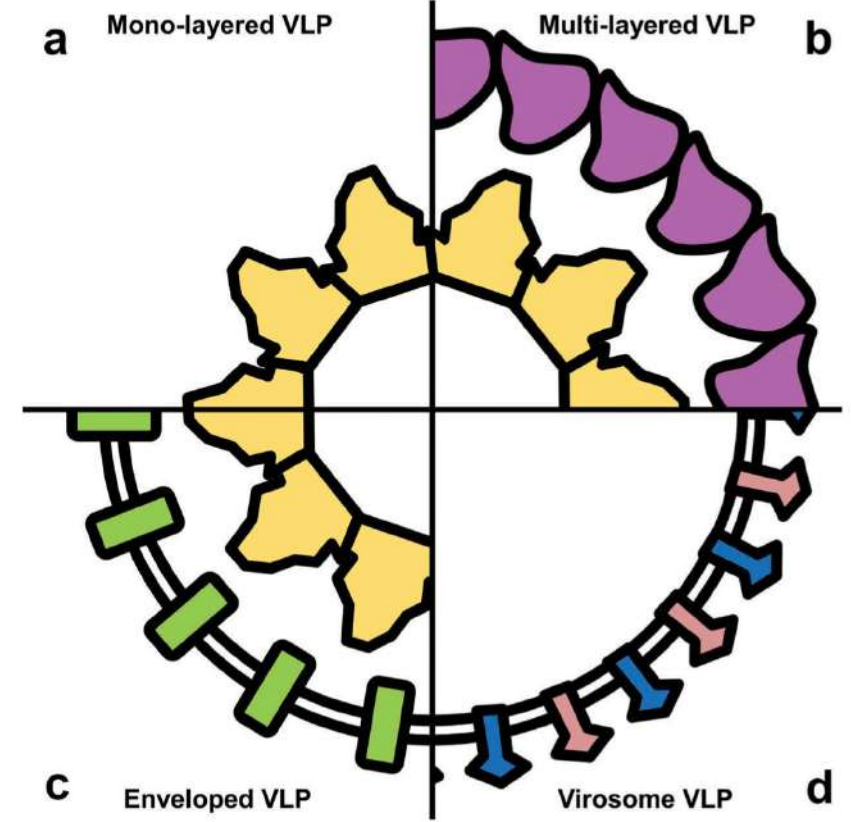
VBP-Biyolojik çeşitlilik

Boyut

Yapısal (basit-kompleks)

Polivalan-mozaik + Modifikasyon

Hedef hastalık (Korunma/tedavi)



Zarfsız VBP: Ekpresyon konakçısına ait membran içermiyor

Tek bir majör kapsid protein

Küçük, üretim kolay

Ökaryotik-prokaryotik hücrelerde eksprese

HBV, HPV

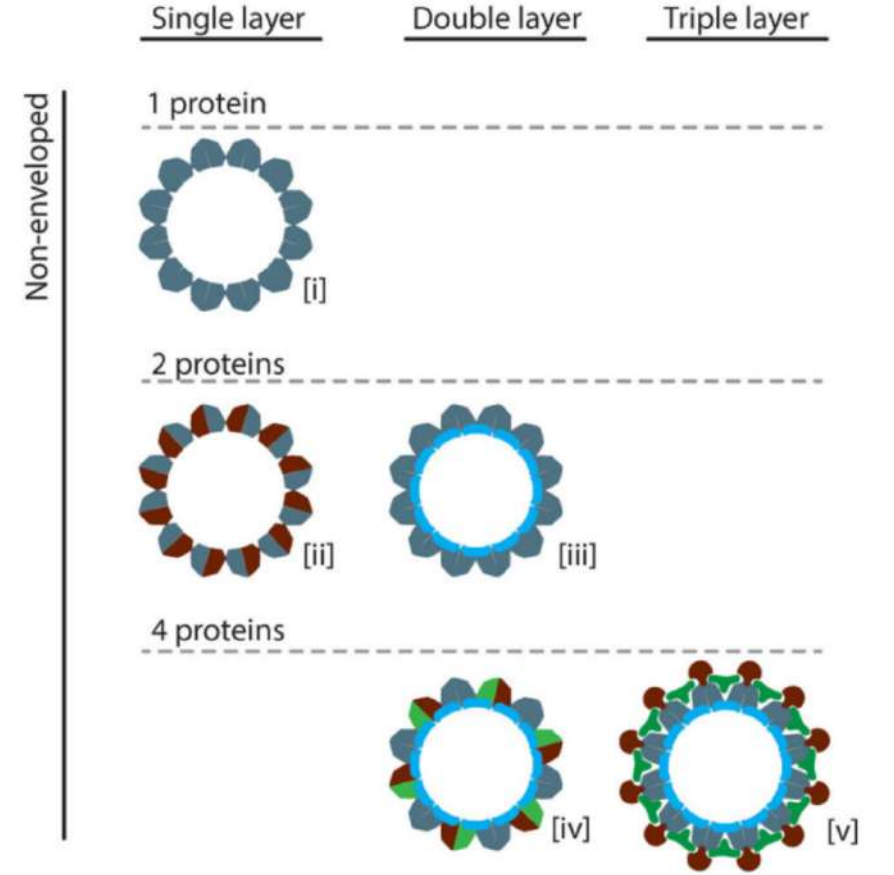
Çoklu kapsid protein

Ökaryotik hücre ekspresyonu

Bir hücre içerisinde birden fazla VBP

ekspresyonu

HPV, Enterovirus, Rotavirus



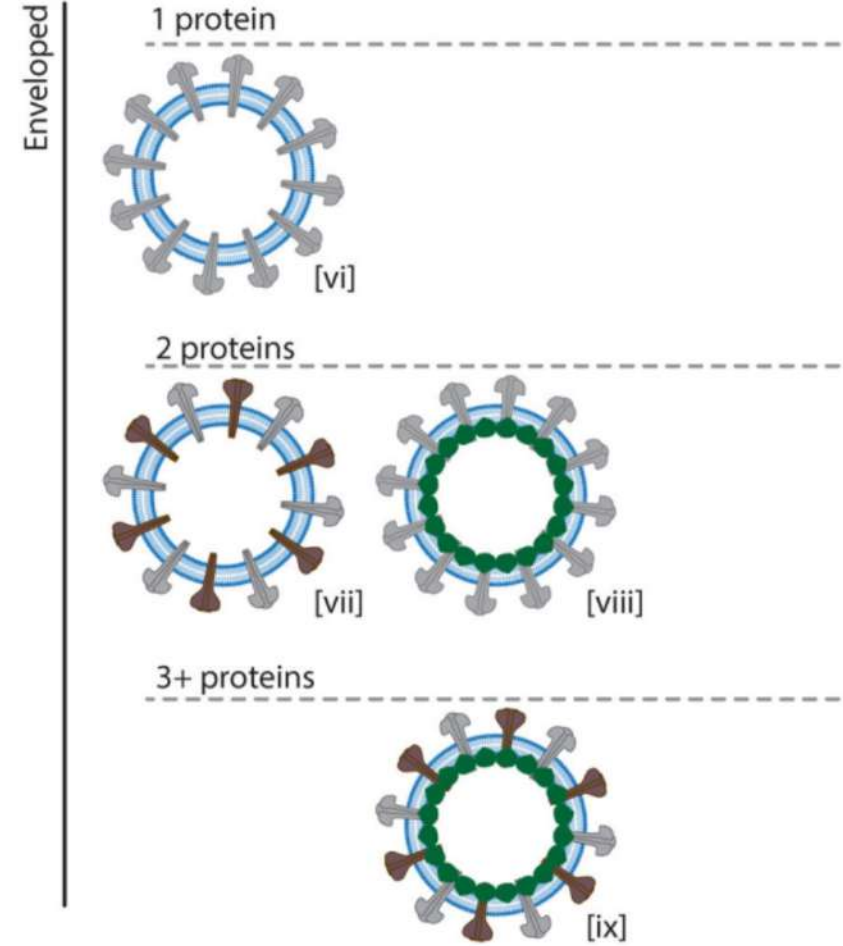
Zarflı VBP: Ekpresyon konakçısına ait lipid membran ve bu membran gömülü glikoproteinler

Daha kompleks yapıda ve büyük

Esneklik daha fazla

Ökaryotik hücre ekspresyonu

Influenza, HIV, Ebola, Chikungunya virus



Antijen: S, RBD

Ekspresyon sistemi:

Bitki hücresi, bakteri hücresi,
memeli hücresi, Böcek hücresi

Zarflı ve zarfsız VBP

Adjuvan;
AS03, Matrix-M, SAS, Alüminyum

Preklinik, Faz 1-2, faz 3

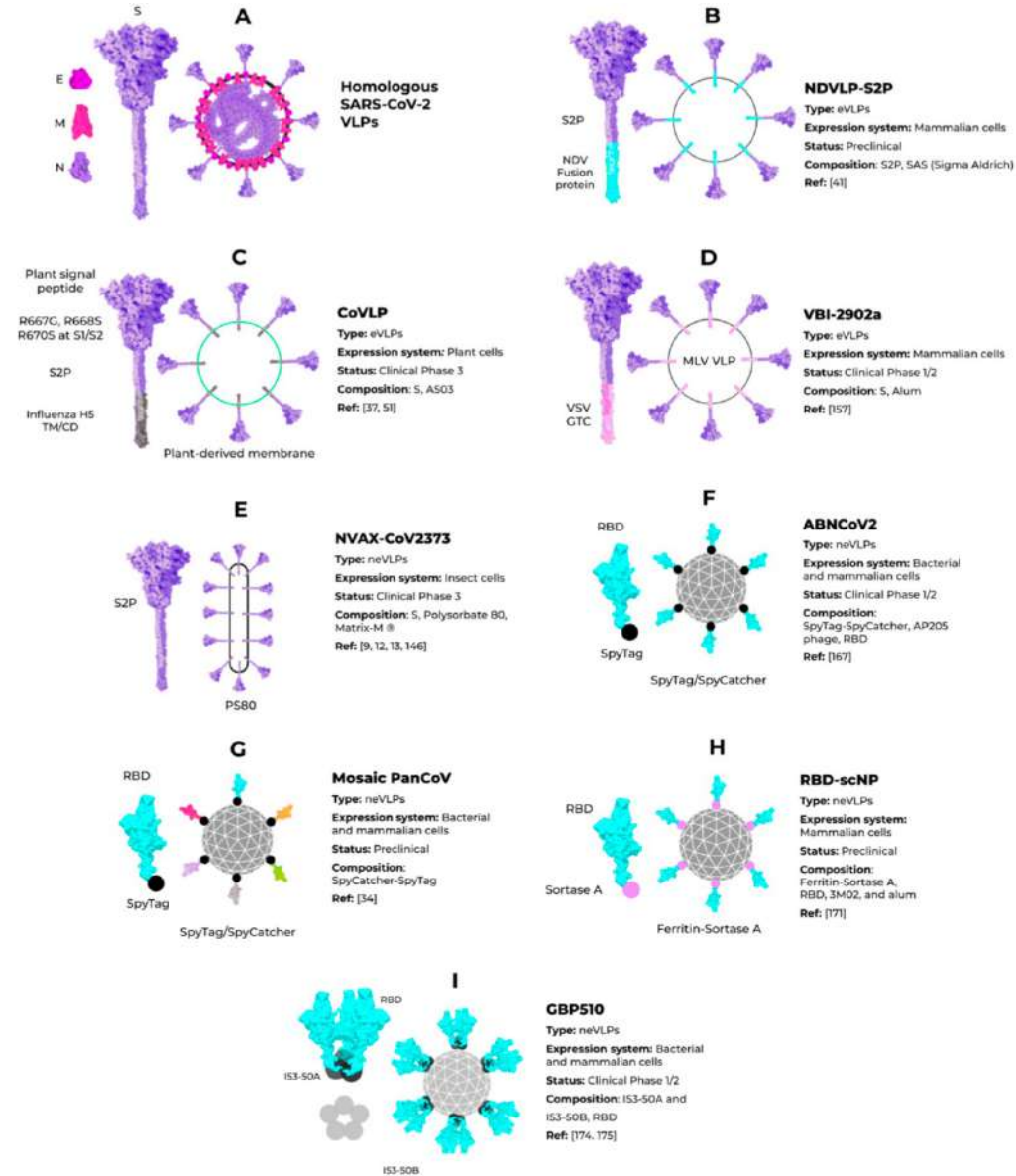


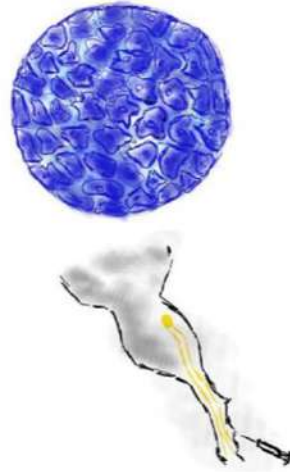
Figure 5. Enveloped and nonenveloped VLPs against SARS-CoV-2.

Modifikasyonlar

İmmünojenitenin artırılması

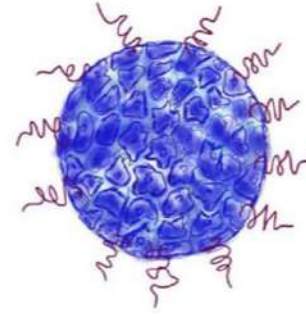
Stabilitenin sağlanması

Size of VLPs



- Size of VLPs range between 20-200 nm allowing VLPs to efficiently reach lymph vessels
- VLPs accumulate in mouse popliteal LN in <10 min post injection in footpad for B and T cell activation

Modifying Exterior Facets of VLPs



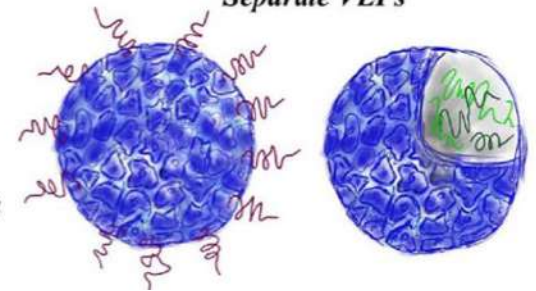
- Chemical Techniques
 - Modification of amino groups
 - Modification of carboxylic groups
 - Modification of sulfhydryl groups
 - Modification of hydroxyl groups
- Genetic Techniques
 - Direct Introduction of amino acids
 - Manipulation of viral structural genes for more efficient introduction of amino acids

Exploiting Interior Facets of VLPs



- Packaging VLPs with TLR Ligands
 - dsRNA, TLR3 ligand
 - ssRNA, TLR7/8 ligand
 - Non-methylated CpGs, TLR9 ligand

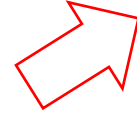
Delivering Adjuvants and Antigens in Separate VLPs



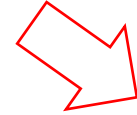
Kimerik VBP: Dięer virüslere ait antijenler yüzeyde ekspresyonu

Dięer virüslere ait antijenik epitoplar
Çoklu protein içeren makro yapılar
Artmış T hücre yanıtı

Influenza, hepatit B , HIV,
Anti-malaryal



Genetik füzyon



Kimyasal bağlama

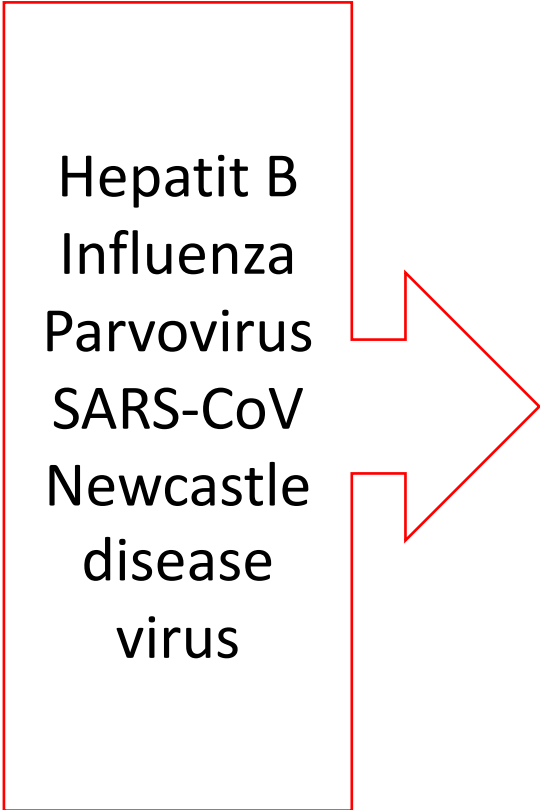
Kimerik VBP- SARS-CoV-2

Table 2

The examples of chimeric VLPs carrying CoV proteins.

VLP platform	Basic composition	Foreign protein	Ref.
MHV	E, M and N	S of SARS-CoV	[87]
SARS-CoV	E and M	S of SARS-like CoV	[41]
Influenza virus	M1 and CT and TM domain of HA	S of SARS-CoV	[95]
Influenza virus	M1 and CT and TM domain of NA	S1 of IBV	[96]
CPV	VP2	RBD of MERS-CoV	[98]
HBV	HBcAg	B-cell epitopes of PEDV	[104,105]
HBV	HBcAg	Immunogenic epitopes of SARS-CoV-2	[106]
NDV	M, NP and CT and TM domain of F	S of SARS-CoV-2	[110]
MLV	Gag	S of SARS-CoV-2	[113]

Hepatit B
Influenza
Parvovirus
SARS-CoV
Newcastle
disease
virus

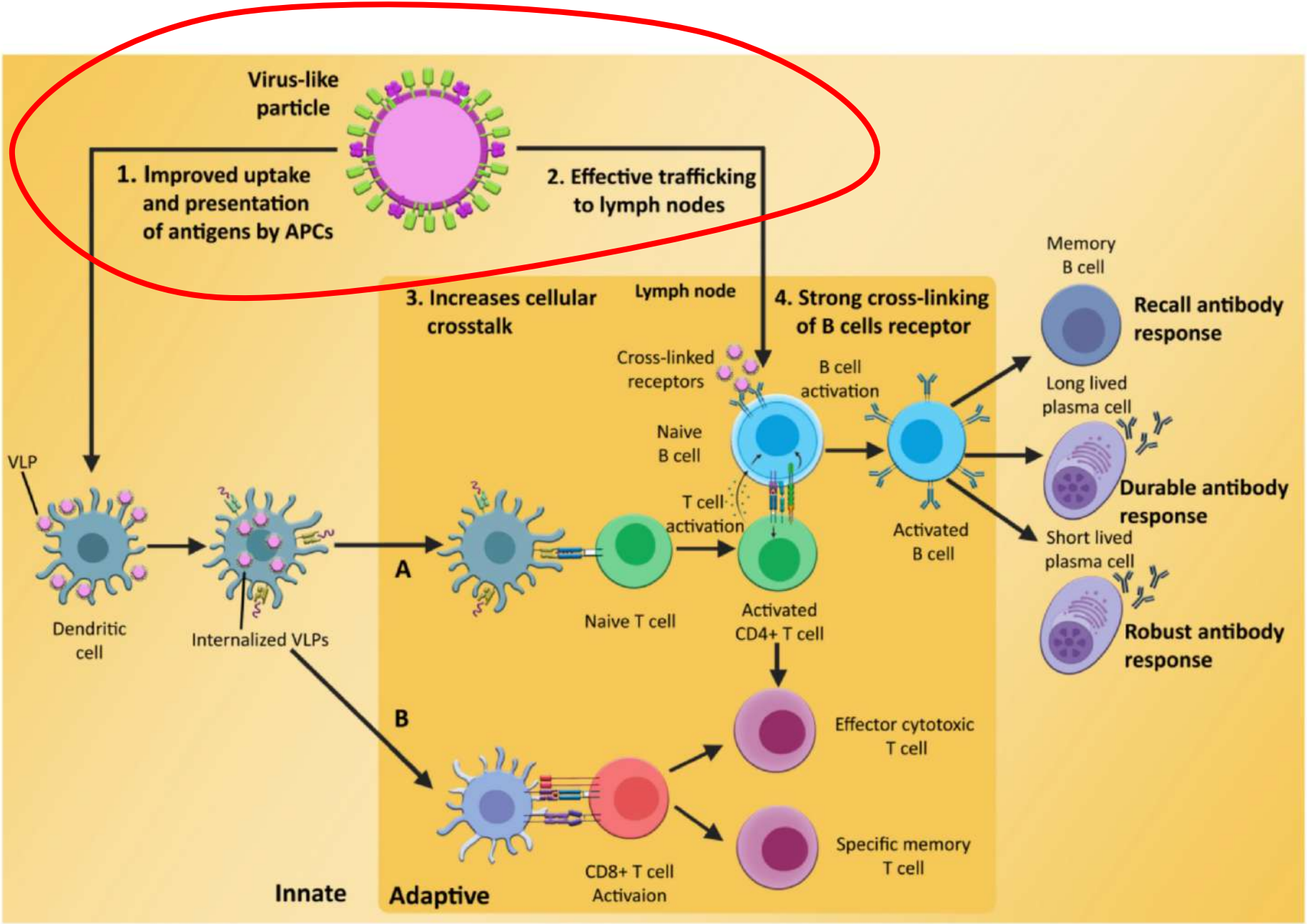


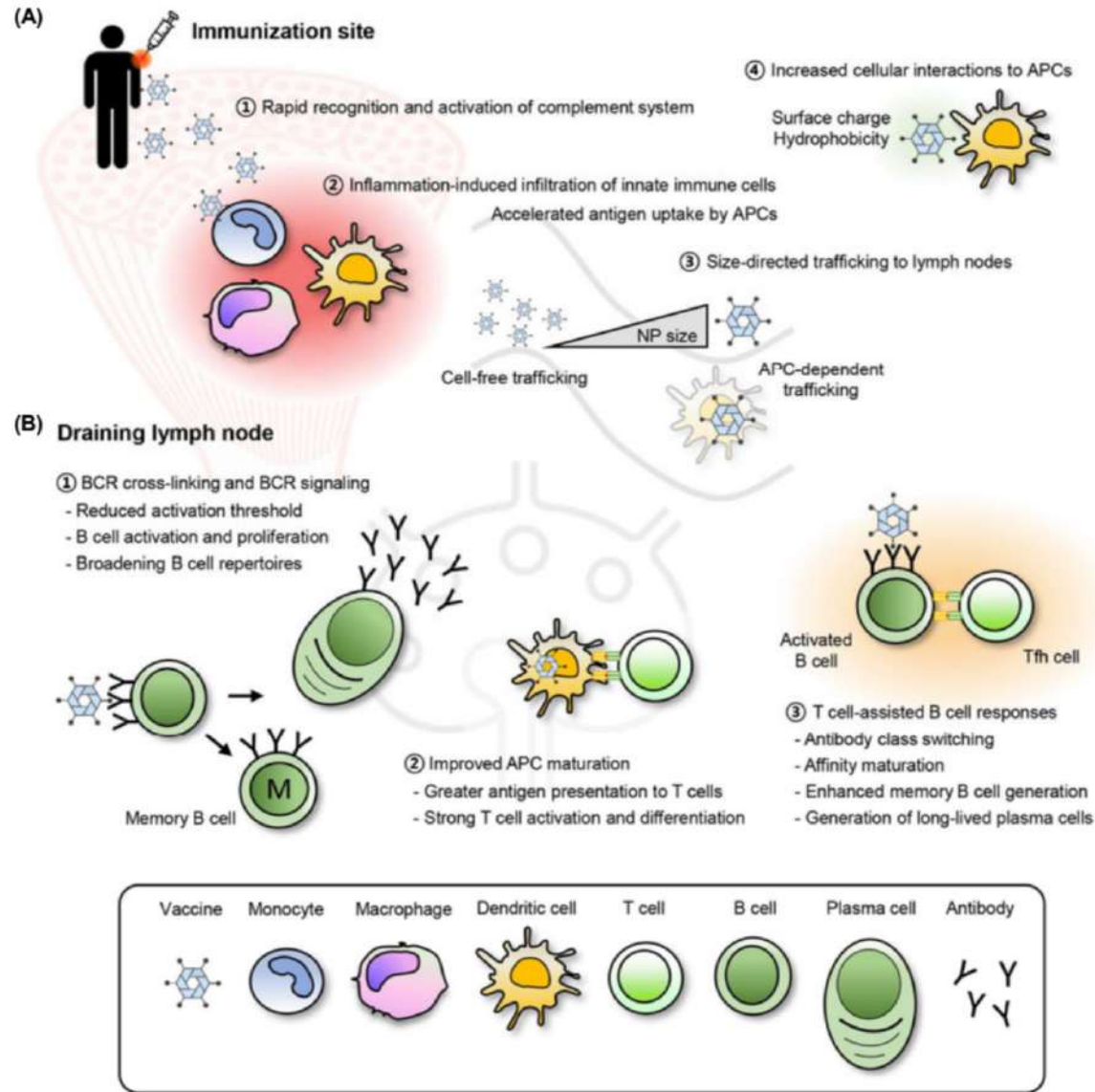
Emilim
Antijen sunum

Lenf nodu erişimi

CD4+ ve CD8+
Aktivasyonu

B hücre
aktivasyonu





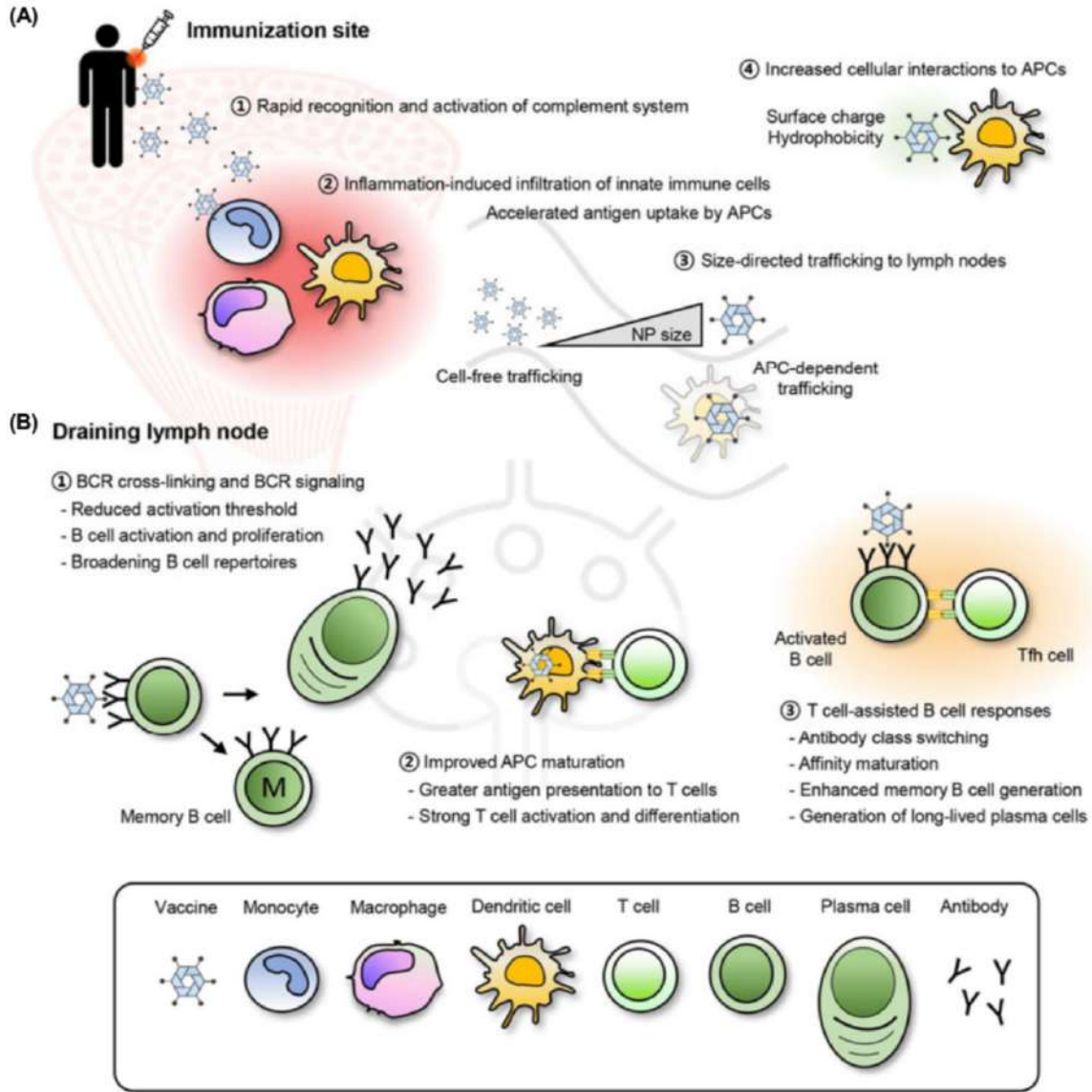
Enjeksiyon bölgesi

Kompleman sisteminin hızlı aktivasyonu

Hızlı antijen sunumu

Lenf nodu ulaşımı

APC'ler ile artmış hücresel etkileşim



Lenf nodu

B hücre aktivasyonun kolaylaşması ve proliferasyonu

APC maturasyonunda artma

Güçlü bir antijen sunumu, T hücre aktivasyonu

T hücre aracılı B hücre aktivasyonu

Artmış bellek hücre oluşumu

Uzun ömürlü plazma hücreleri

VBP-boyut

**Boyut (VBP boyutu 20-200 nm
arasında deęiřiyor)**

- Lenfoid organlara uygun drenaj
- APC sunumunun kolaylařması

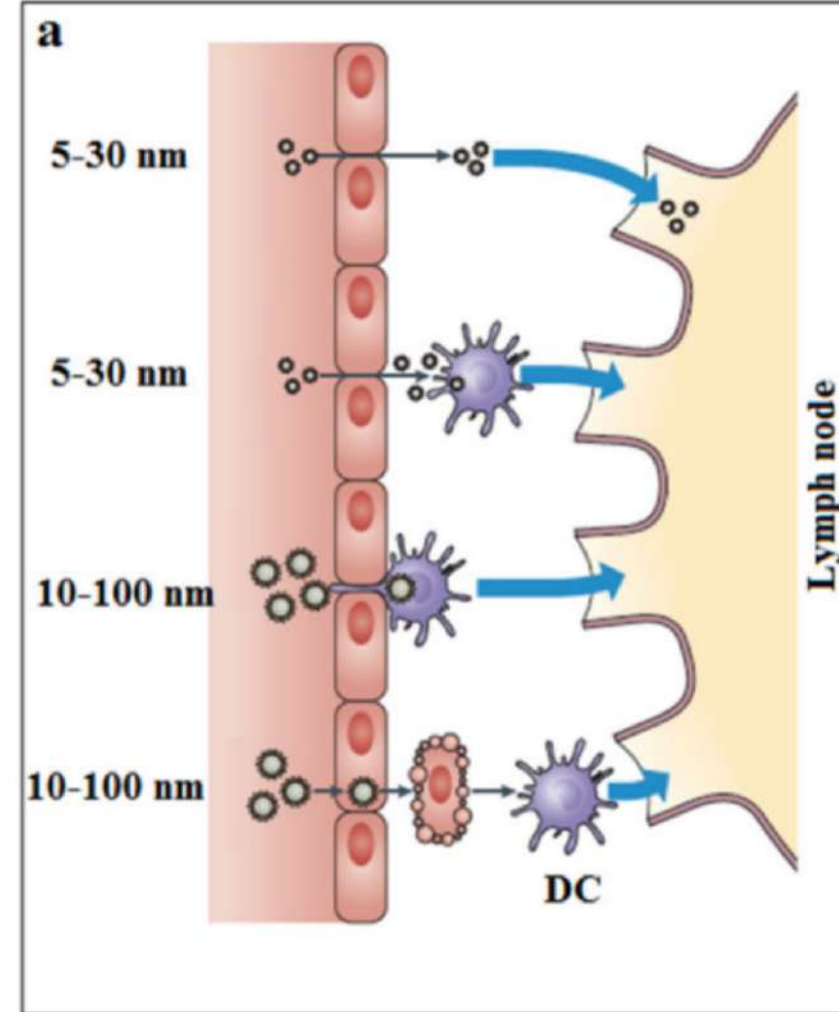
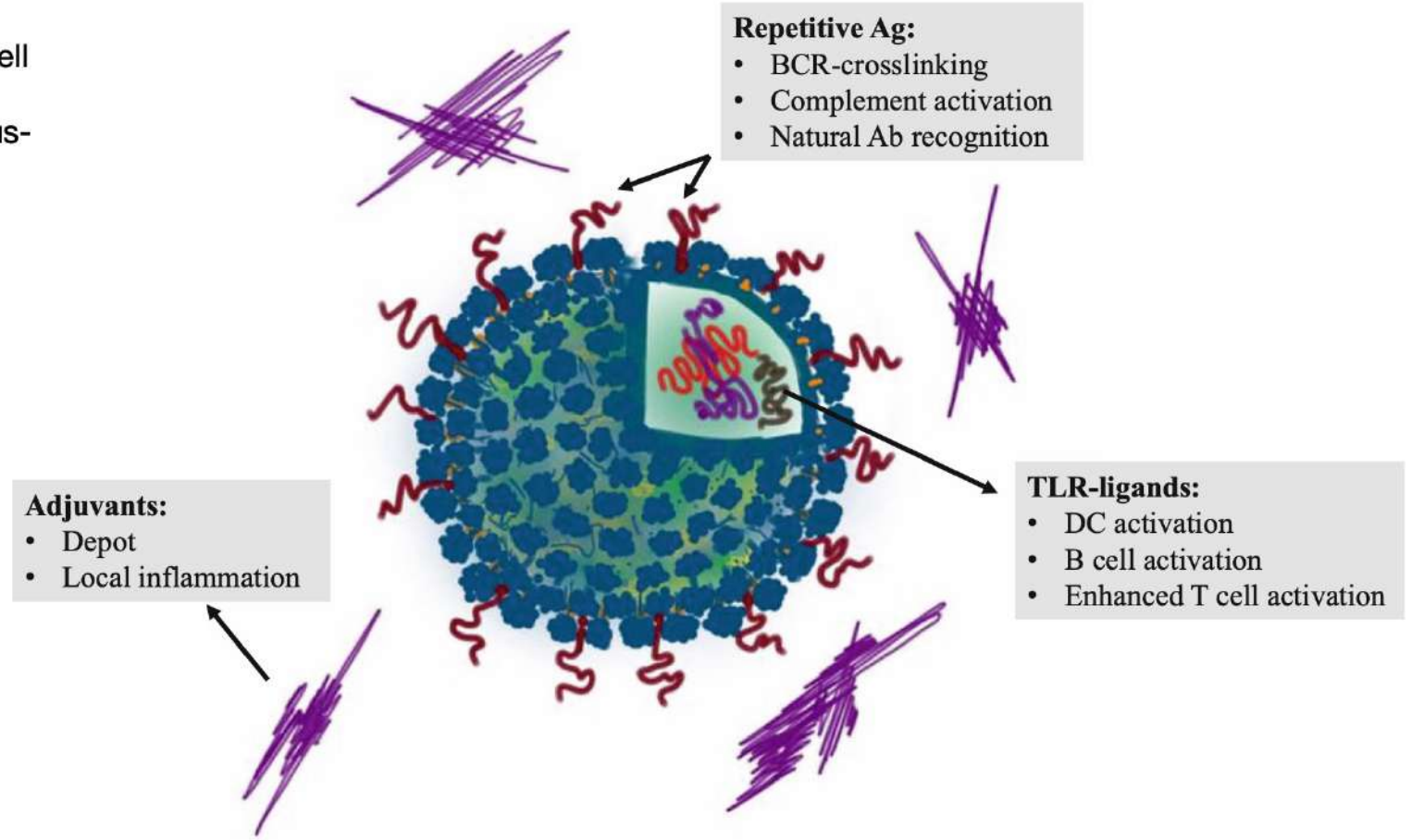


Fig. 2 Immunological mechanisms of VLP-based vaccines. *Ab* antibodies; *BCR* B cell receptor; *DC* dendritic cell; *TLR* Toll-like receptor; *VLP* virus-like particle

-Boyut
-Yüzey kongfigürasyonu
-Epitop yoğunluğu
-TLR



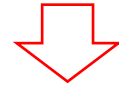
Zapede-Cervantes J et al, *Frontiers in Immunology*, 2020

Mohsen M.O et al., *Vaccines* 2018

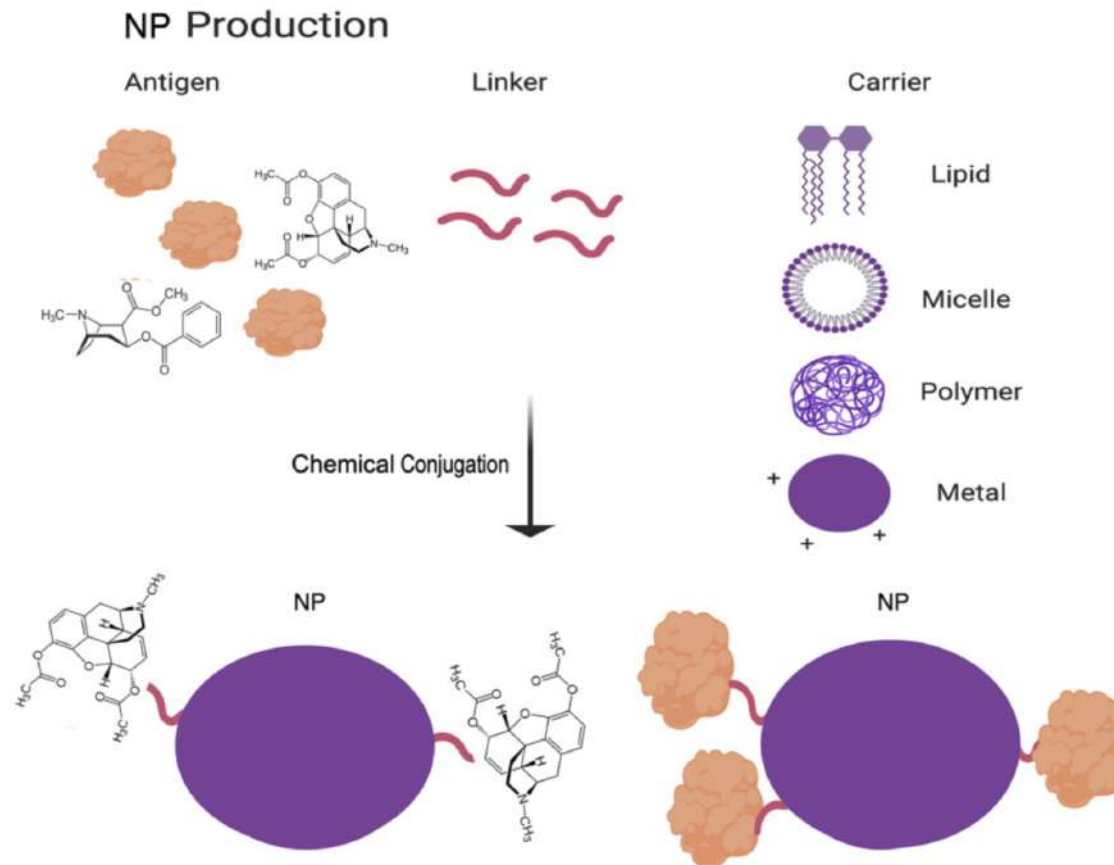
Tariq H et al. *Front. Microbiol.*, 2022

Klimek L et al, *Allergo J Int*, 2018

Sentetik Nanopartiküller

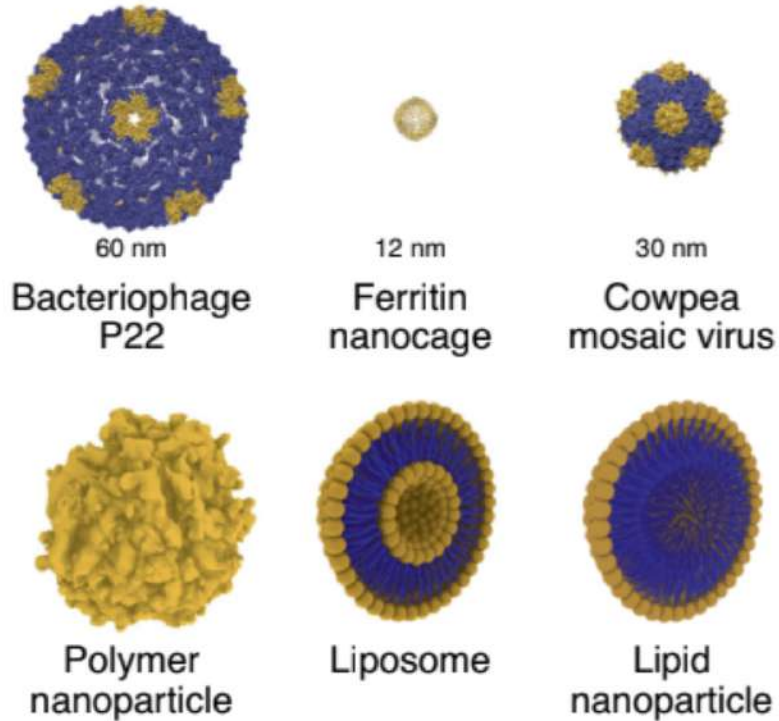


3 temel rol: Antijen sunum, Adjuvan, Taşıyıcı



a

Nanoparticle platform technology



Key attributes for vaccine nanotechnology

- Multivalent peptide/protein display
- Peptide/protein or DNA/mRNA encapsulation
- Structures mimic the multivalent features of pathogens
- Nanoparticles interact efficiently with antigen-presenting cells (APCs)



Multivalanlı
protein/peptit
sunumu

APC ile etkin
etkileşim

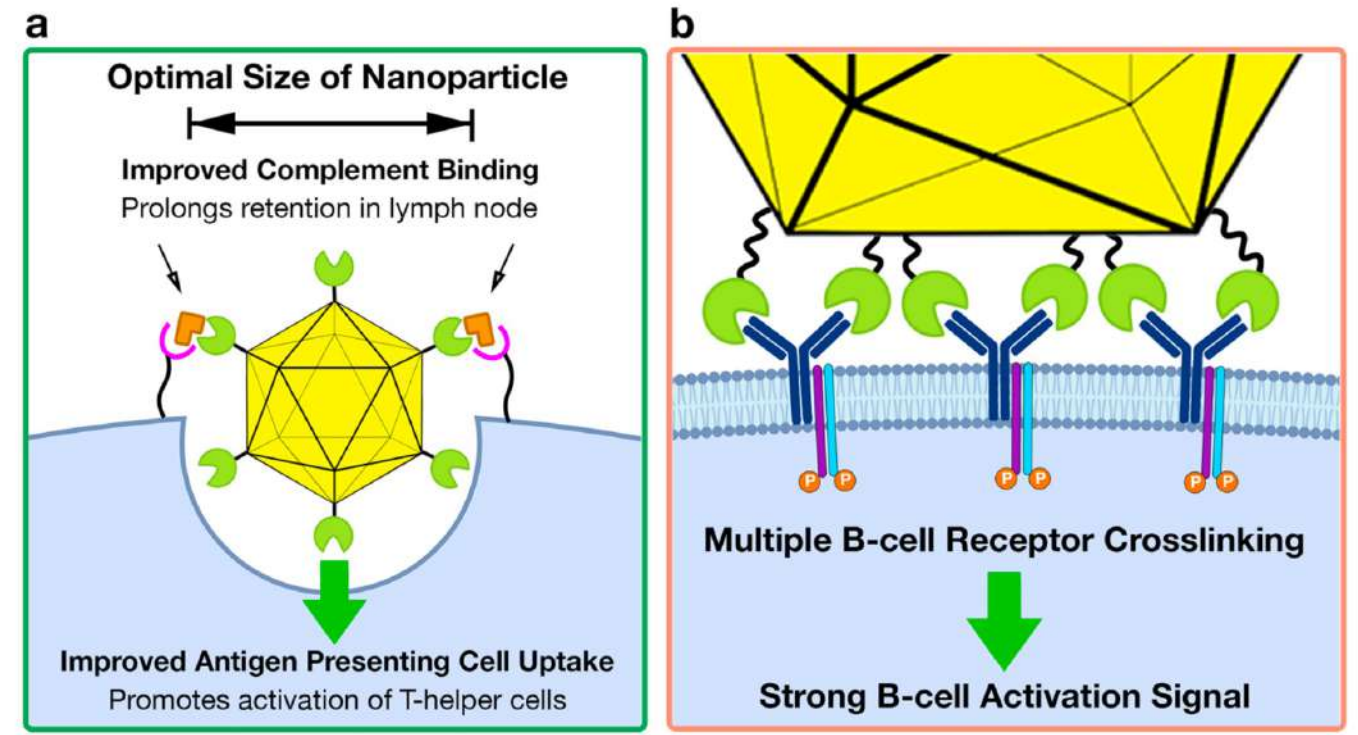


Farklı taşıyıcı
moleküller

Nanopartikül Aşıları

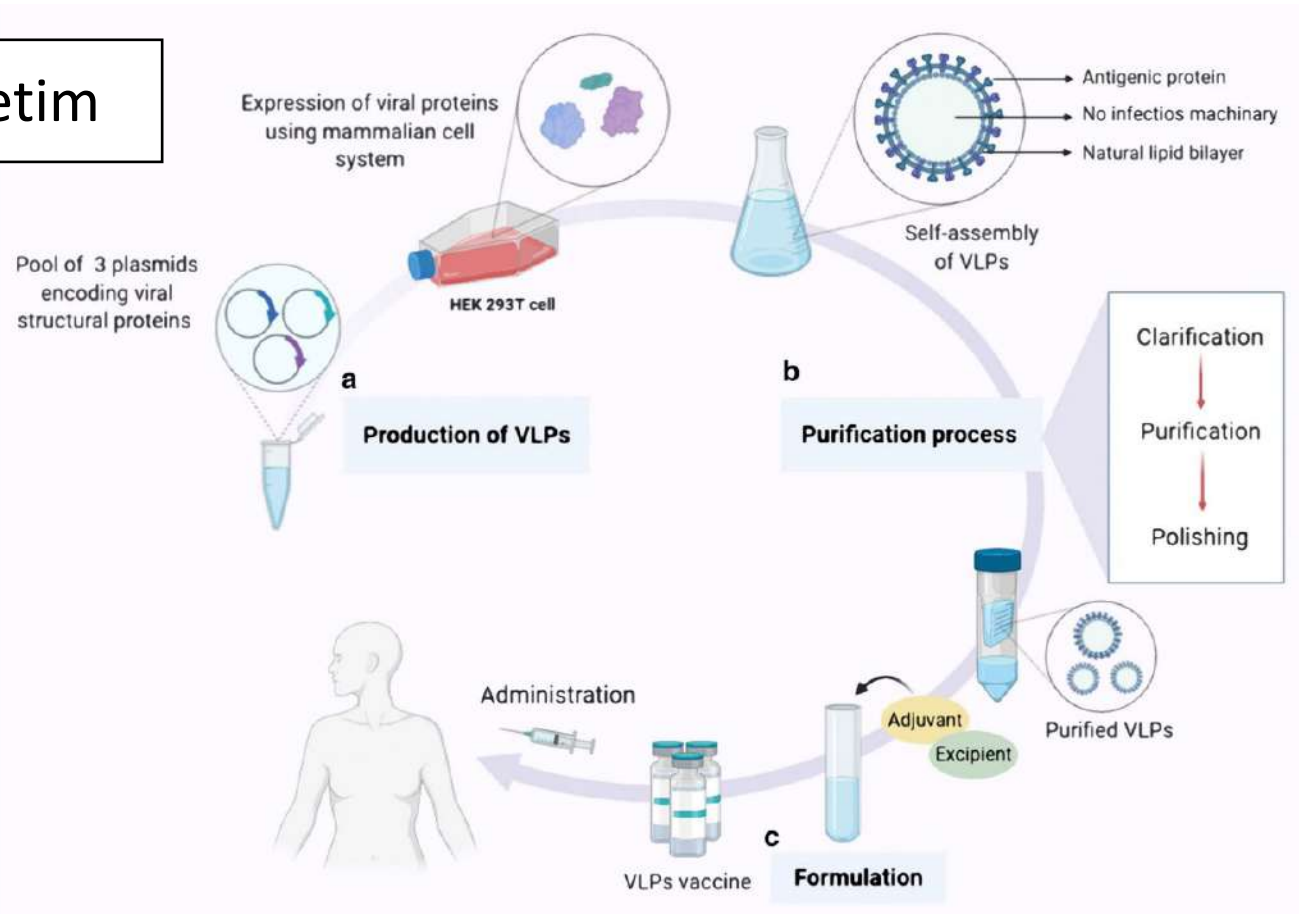
Basit
Kolay üretilebilen
Güvenli

Boyut, temas yüzeyi, şekil, hidrofobik, taşıyıcı molekül



Rekombinant aşı geliştirme basamakları

Üretim



Safılaştırma

Formülasyon

Pürifikasyon

Saflaştırma basamak sayısını ve maliyetleri azaltıyor



Arıtma
Hücre artık ve agregatları uzaklaştırmak

VBP/Hücre oranının artırılması



VBP yakalanması ve konsantrasyonu

DNA ve endotoksin seviyelerinin azaltılması



Santrifüj
(IEC-HIC)

Arıtma
(IEC, ultrafiltrasyon, diyafiltrasyon)

Formülasyon

Uygulanabilir solüsyonun oluşturulması

Protein, Adjuvan, Katkı maddeleri

Etkin, güvenilir, stabil

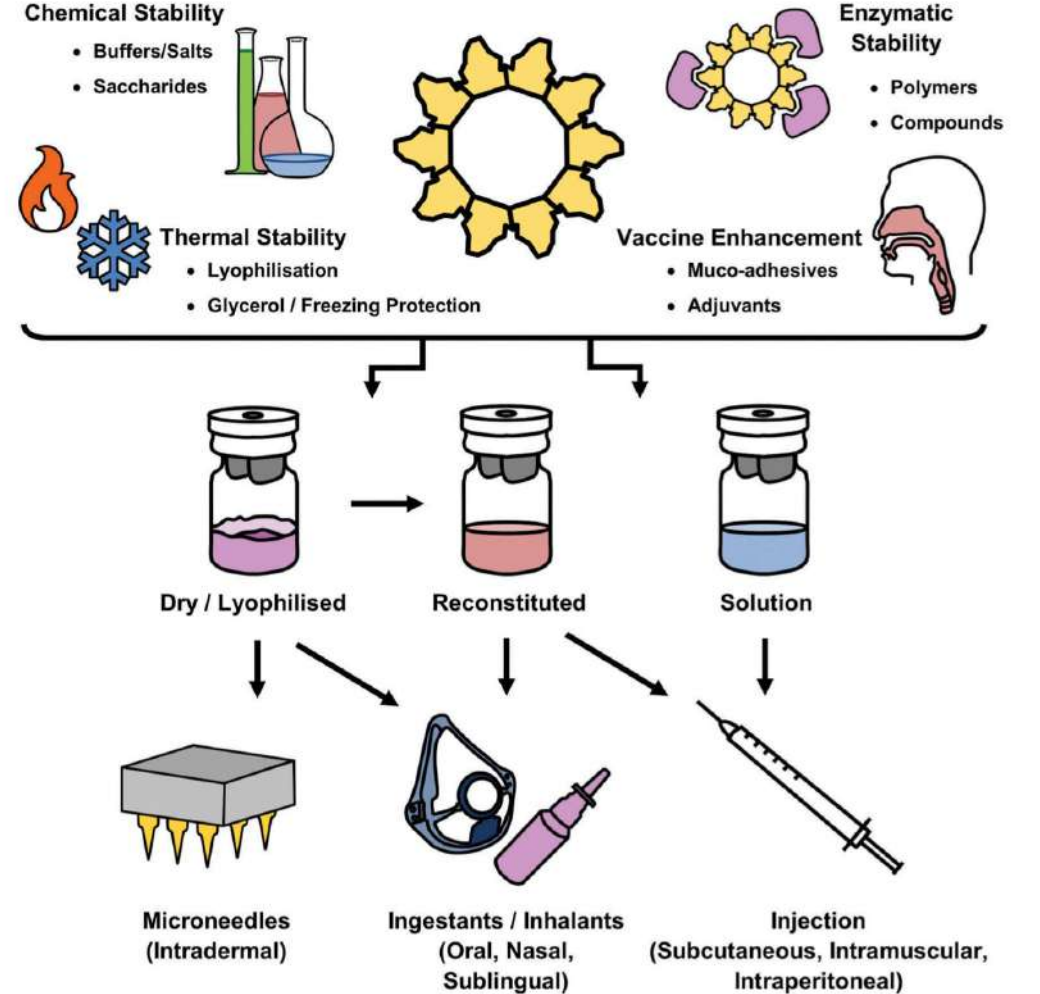
Dozajın azaltılması

İmmunojenitenin artırılması

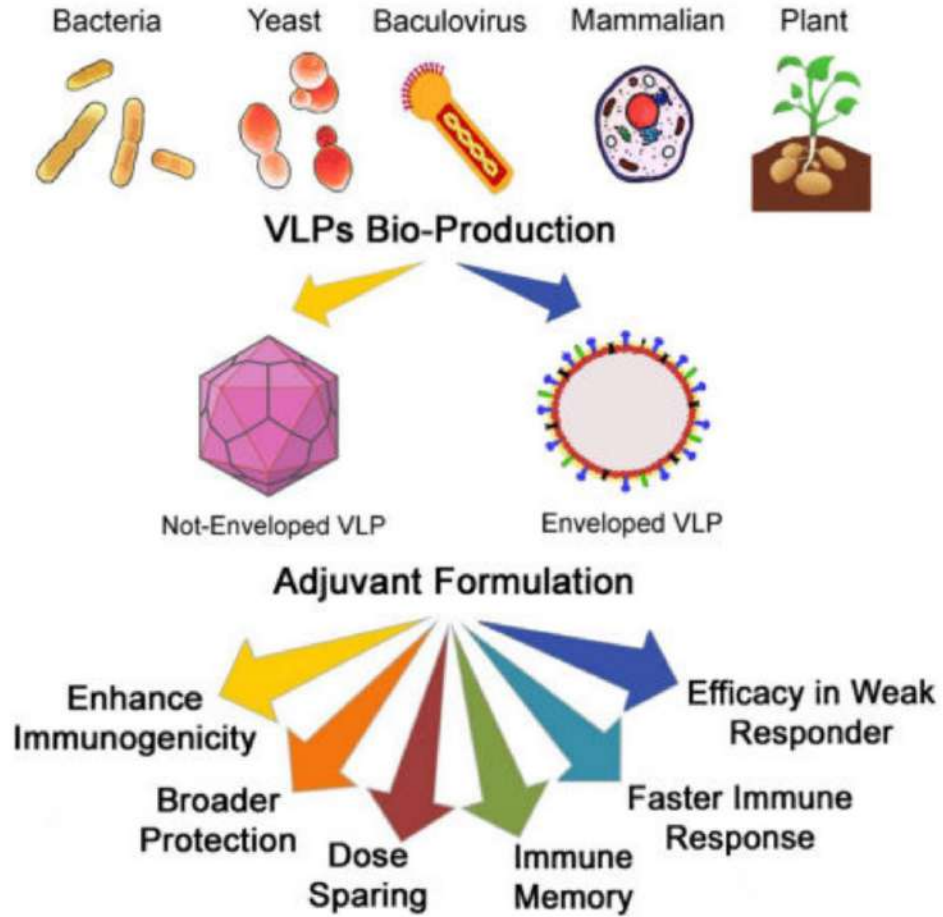
Soğuk zincir gereksiniminin kaldırılması

Uzun dönem depolamada stabilitesinin

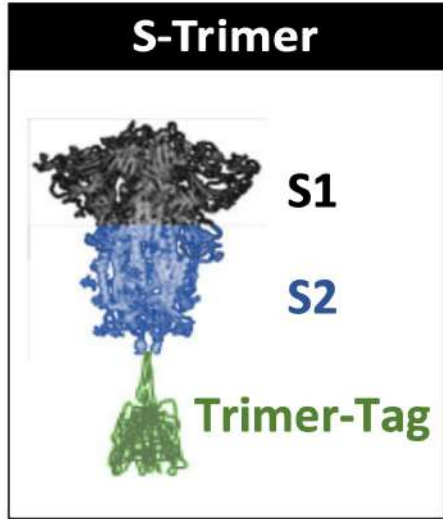
sağlanması



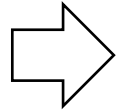
Adjuvanlar



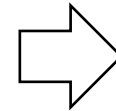
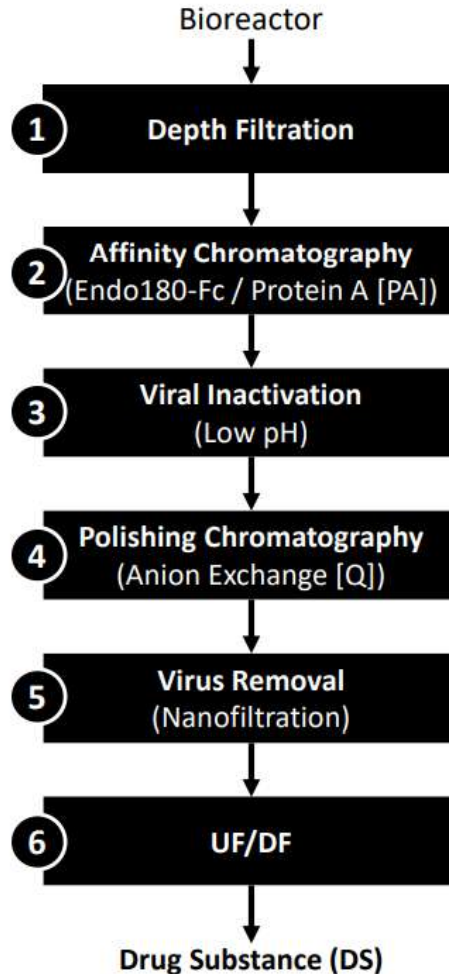
COVID-19 aşıları ve adjuvanlar	
Alüminyum	Alüminyum hidroksit Alüminyum fosfat Alhydrogel
Emülsiyonlar	MF59 AS03
TLR agonistleri	CpG PolyI:C Glukopiranozil lipid A Resikimod AS37
Diğer	Matrix M1 STING agonistleri Advax AS01 _B



Ekspresyon sistemi:
Memeli hücresi (CHO)



**S-Trimer DSP
Purification Process**



Adjuvan
AS03 veya CpG 1018
+ Alm

**S-Trimer, a COVID-19 subunit vaccine candidate, induces protective
immunity in nonhuman primates**

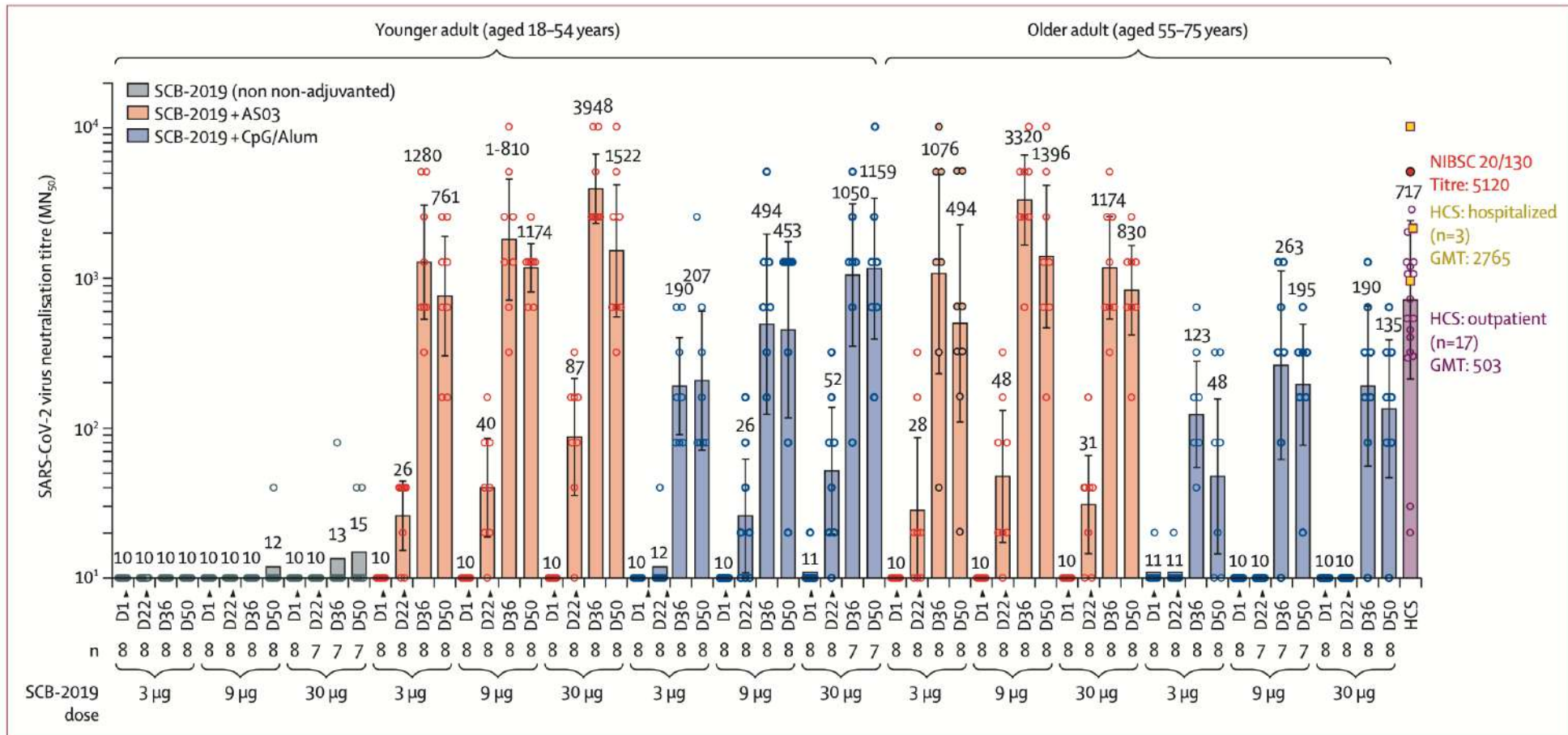
Joshua G. Liang^{1*}, Danmei Su^{1*}, Tian-Zhang Song^{2*}, Yilan Zeng^{3*}, Weijin Huang^{4*}, Jinhua Wu¹,



Safety and immunogenicity of S-Trimer (SCB-2019), a protein subunit vaccine candidate for COVID-19 in healthy adults: a phase 1, randomised, double-blind, placebo-controlled trial

Peter Richmond, Lara Hatchuel, Min Dong, Brenda Ma, Branda Hu, Igor Smolenov, Ping Li, Peng Liang, Htay Htay Han, Joshua Liang, Ralf Clemens

S-trimer Adjuvan; CpG/Alimünyum veya AS03



Efficacy of the adjuvanted subunit protein COVID-19 vaccine, SCB-2019: a phase 2 and 3 multicentre, double-blind, randomised, placebo-controlled trial



Lulu Bravo, Igor Smolenov, Htay Htay Han, Pina Li, Romana Hosain, Frank Rockhold, Sue Ann Costa Clemens, Camilo Roa Jr.

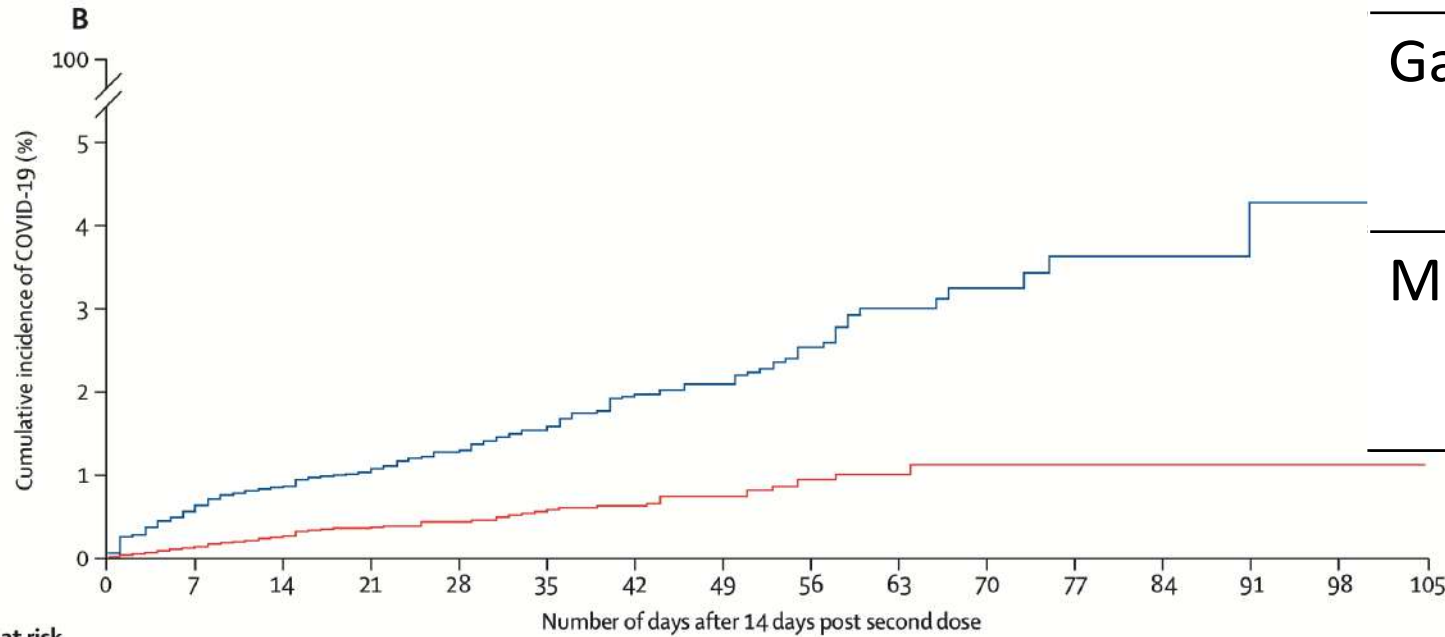
30 µg + 1.50 mg CpG-1018 ve 0.75 mg alüm.

Aşı etkinliği

Delta :78.7% (95% CI 57.3–90.4)

Gamma: 91.8% (95% CI 44.9–99.8)

Mu:58.6% (95% CI 13.3–81.5)



Number at risk
(cumulative number of
COVID-19 cases)

SCB-2019	12153	11018	9558	7295	5418	4463	3773	2960	2060	1040	640	424	315	150	79	10
	(3)	(16)	(30)	(39)	(43)	(50)	(52)	(56)	(61)	(62)	(63)	(63)	(63)	(63)	(63)	(63)
Placebo	11983	10827	9337	7063	5275	4375	3692	2866	1974	1014	646	426	310	149	79	7
	(8)	(74)	(97)	(115)	(128)	(142)	(158)	(162)	(173)	(180)	(182)	(184)	(184)	(185)	(185)	(185)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

C. Keech, G. Albert, I. Cho, A. Robertson, P. Reed, S. Neal, J.S. Plested, M. Zhu, S. Cloney-Clark, H. Zhou, G. Smith, N. Patel, M.B. Frieman, R.E. Haupt, J. Logue, M. McGrath, S. Weston, P.A. Piedra, C. Desai, K. Callahan, M. Lewis, P. Price-Abbott, N. Formica, V. Shinde, L. Fries, J.D. Lickliter, P. Griffin, B. Wilkinson, and G.M. Glenn

(NVX-CoV2373-Novovax)

SARS-CoV-2 spike glikoprotein



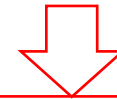
Nukleotit 21563–25384



Stabilizasyon



Ekspresyon sistemi: Böcek hücresi
(Sf9)

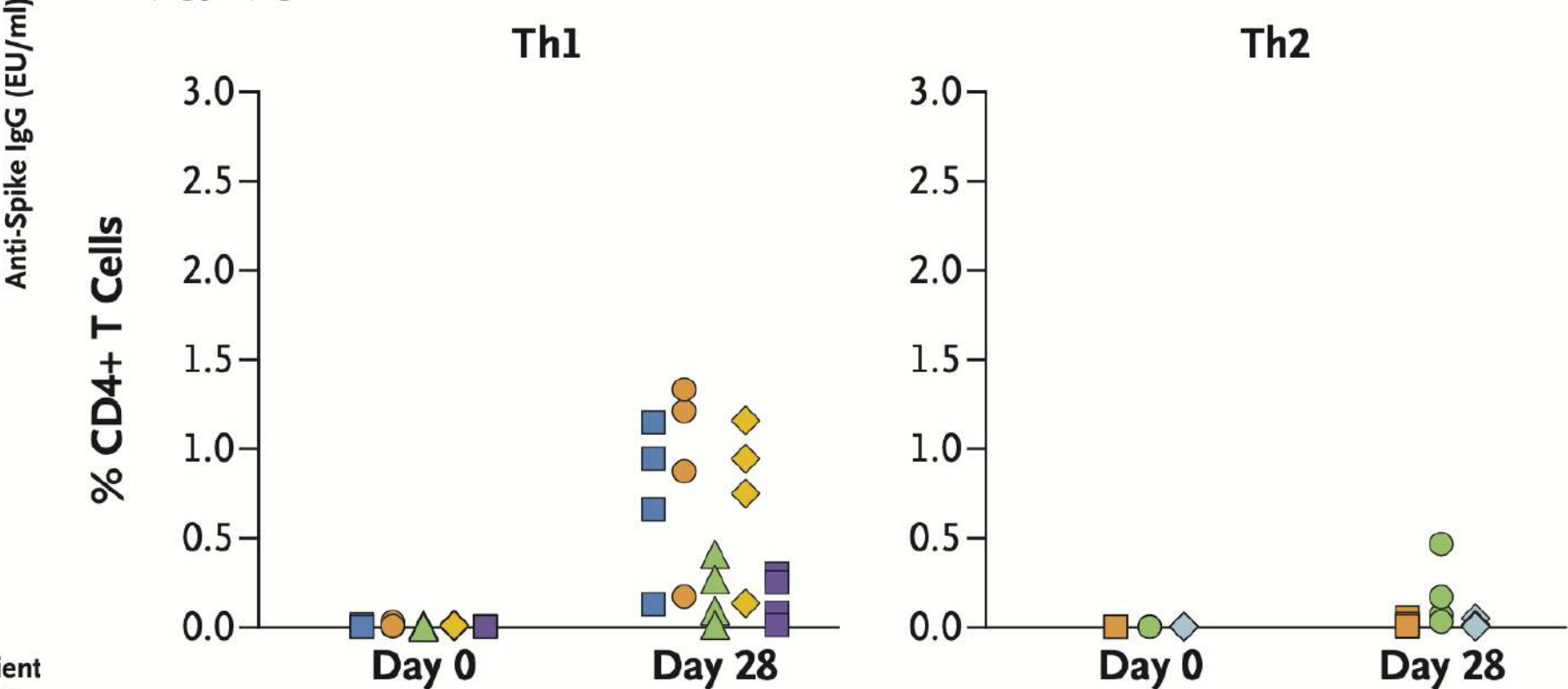


Matrix-M1 adjuvan eklenmesi

Adjuvan etkisi: Antikor yanıtının artırılması ve antijen dozunun azaltılması

A SARS-CoV-2 Anti-Spike IgG ELISA

C 5 µg/5 µg+Matrix-M1



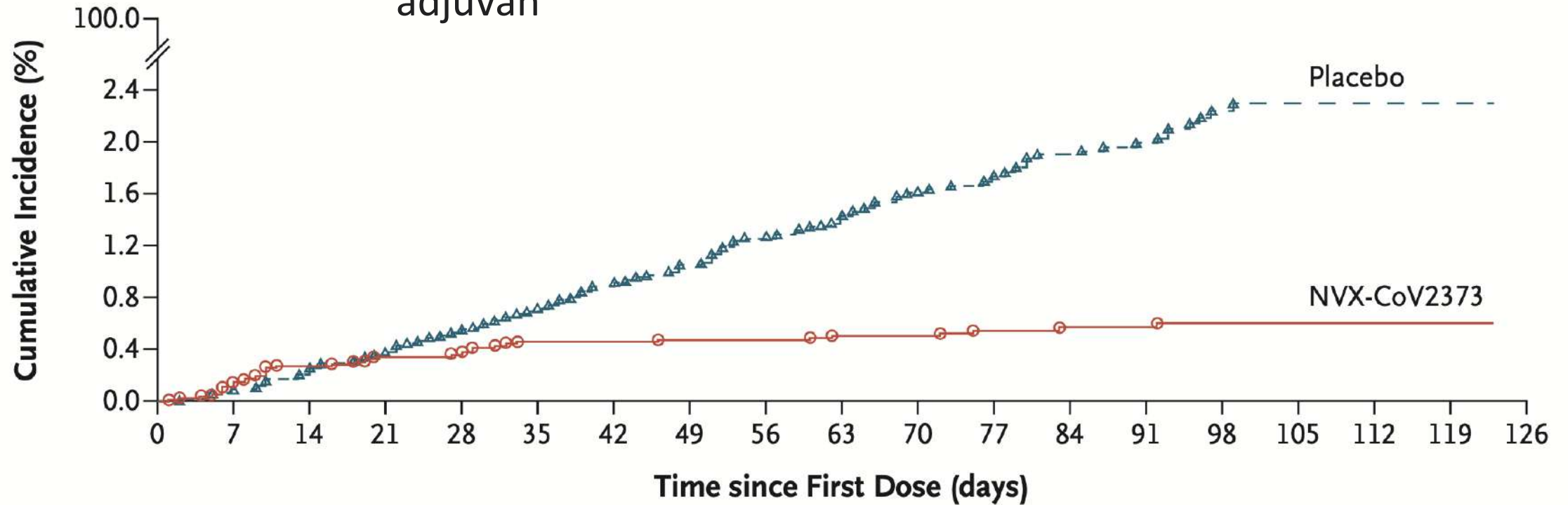
nan
escent
um
ptomatic
atient
tomatic
italized

No. of Patient
(dose 1/dose)

Subgroup	Placebo	NVX-CoV2373	Vaccine Efficacy (95% CI)	
	no. of events/no. at risk		%	
Per-protocol population	96/7019	10/7020	89.7	(80.2 to 94.6)
Intention-to-treat population	141/7570	42/7569	70.4	(58.3 to 79.1)

3 Intention-to-Treat Population

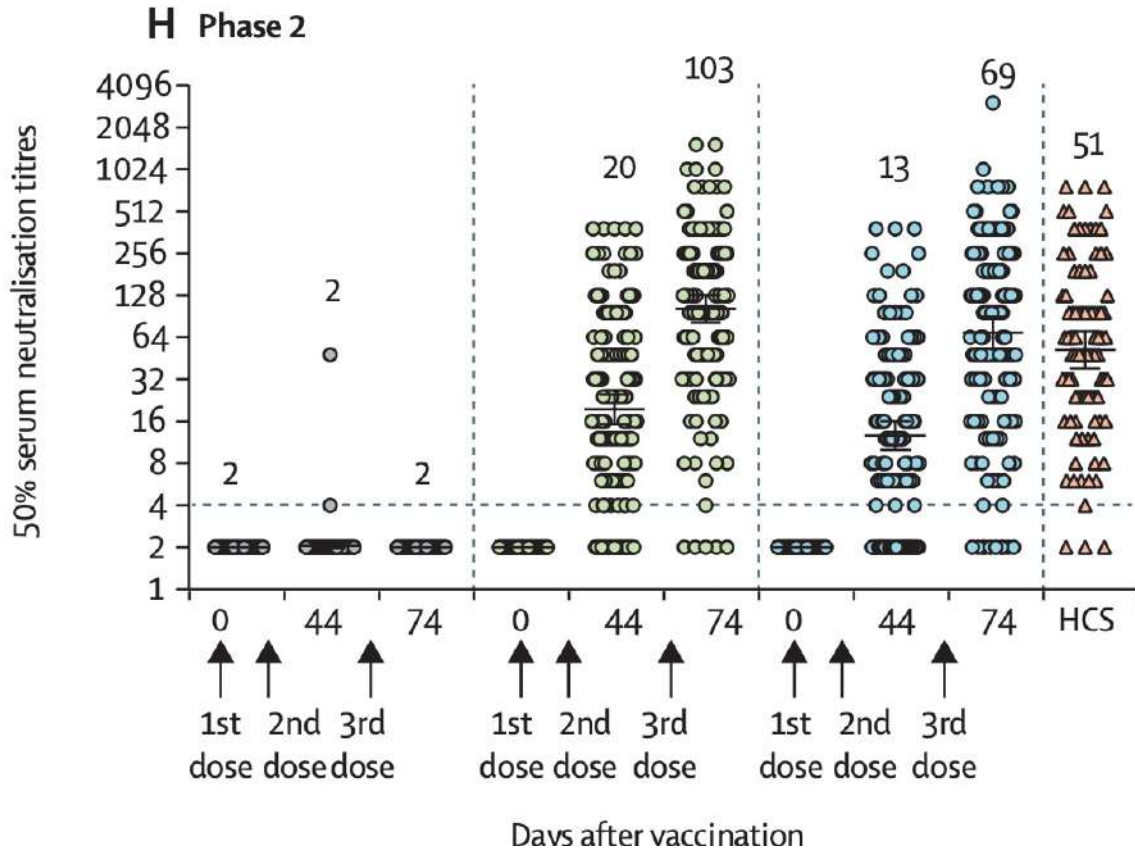
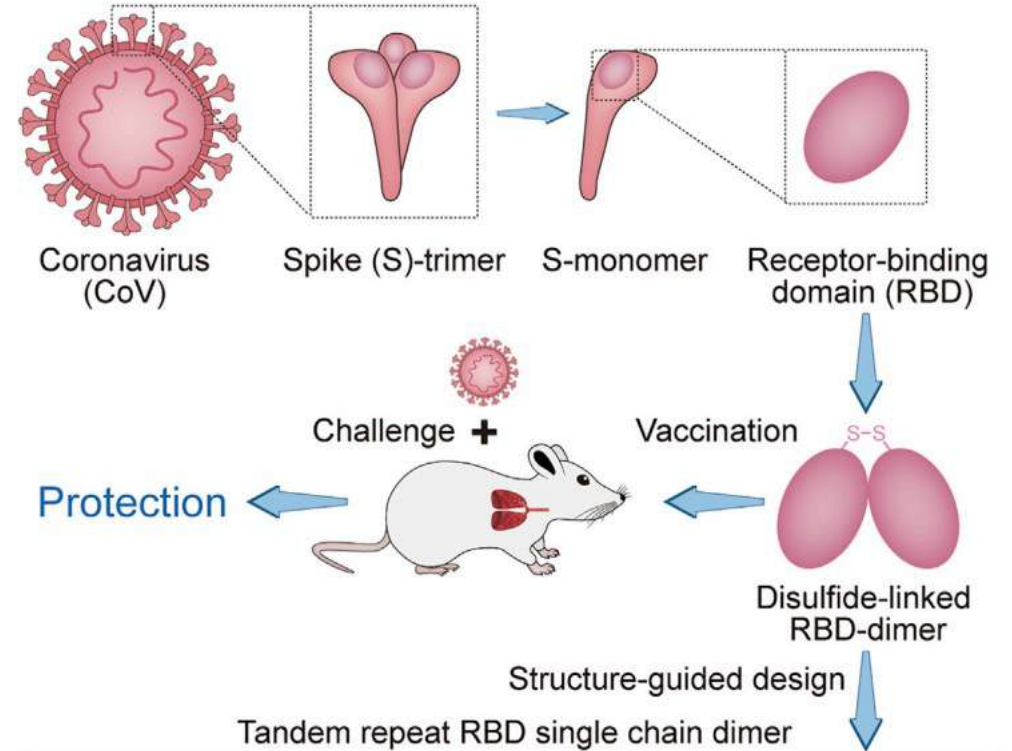
5 µg rekombinant S protein + 50 µg Matrix-M1 adjuvan



Safety and immunogenicity of a recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) against COVID-19 in adults: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials



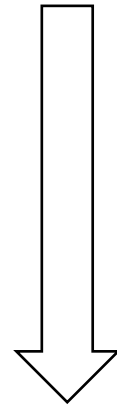
Shilong Yang*, Yan Li*, Lianpan Dai*, Jianfeng Wang*, Peng He*, Changgui Li, Xin Fang, Chenfei Wang, Xiang Zhao, Enqi Huang, Changwei Wu, Zaixin Zhong, Fengze Wang, Xiaomin Duan, Siyu Tian, Lili Wu, Yan Liu, Yi Luo, Zhihai Chen, Fangjun Li, Junhua Li, Xian Yu, Hong Ren, Lihong Liu, Shufang Meng†, Jinghua Yan†, Zhongyu Hu†, Lidong Gao†, George F Gao†



RBD (25 µg or 50 µg)+ Alm

Safety and immunogenicity of SARS-CoV-2 recombinant protein vaccine formulations in healthy adults: interim results of a randomised, placebo-controlled, phase 1–2, dose-ranging study

Paul A Goepfert, Bo Fu, Anne-Laure Chabanon, Matthew I Bonaparte, Matthew G Davis, Brandon J Essink, Ian Frank, Owen Haney, Helene Janosczyk, Michael C Keefer, Marguerite Koutsoukos, Murray A Kimmel, Roger Masotti, Stephen J Savarino, Lode Schuerman, Howard Schwartz, Lawrence D Sher, Jon Smith, Fernanda Tavares-Da-Silva, Sanjay Gurunathan, Carlos A DiazGranados, Guy de Bruyn



S protein

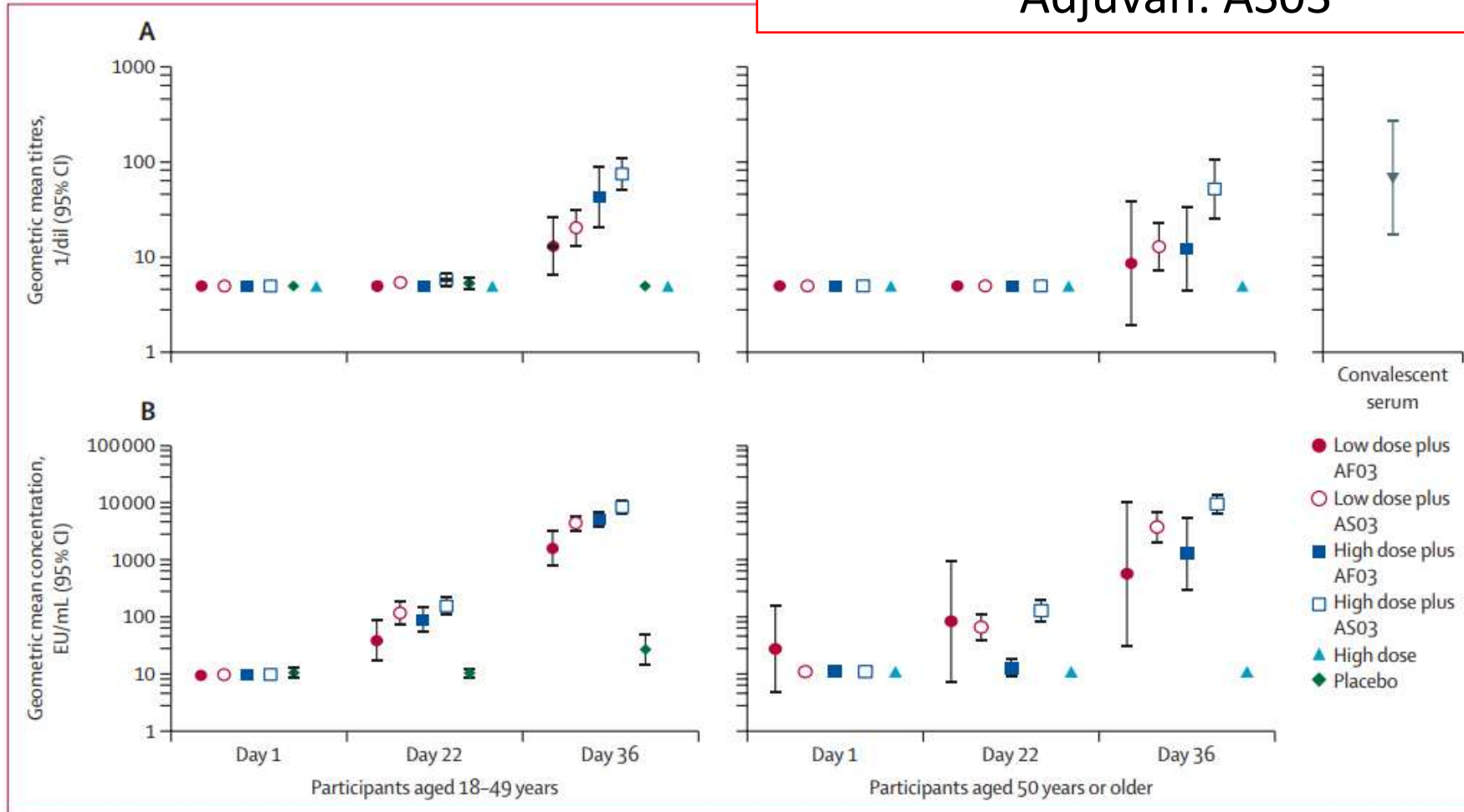
Wuhan Y_P009724390.1 S sekans

Modifikasyon (Prolin mutasyonu)
(Stabilizasyon, pürifikasyon kolaylaşması)

Ekspresyon sistemi: Böcek hücresi
(Baculovirus Spodoptera fruaiperda Sf9)

Adjuvan AF03/AS03

Doz optimizasyonu? Adjuvan: AS03

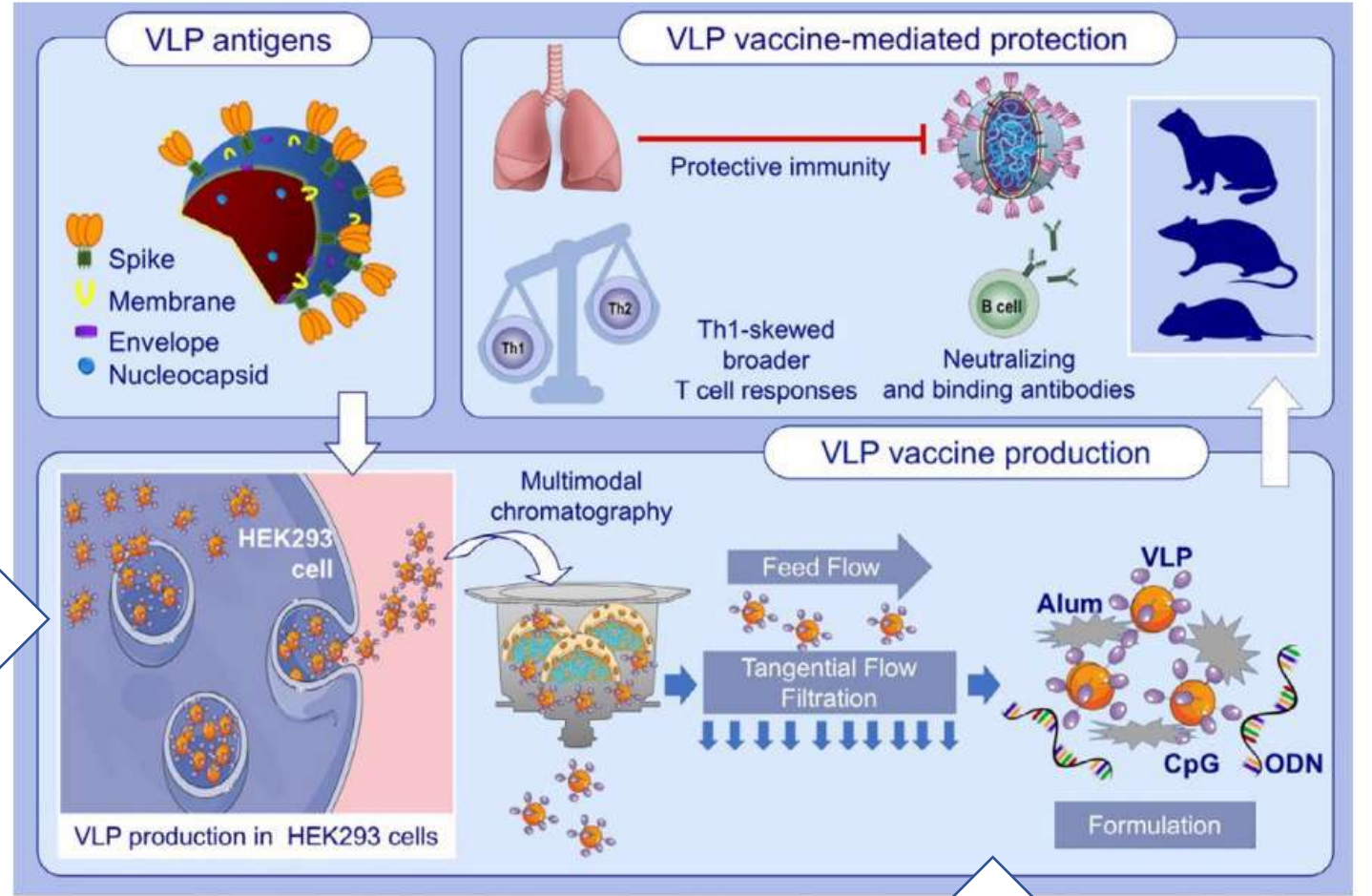


Development and preclinical evaluation of virus-like particle vaccine against COVID-19 infection

Ismail Cem Yilmaz^{1,2} | Emre Mert Ipekoglu¹ | Artun Bulbul² | Nilsu Turay² | Muzaffer Yildirim² | Irem Evcili² | Naz Surucu Yilmaz¹ | Nese Guvencli¹ | Yagmur Aydin¹ | Bilgi Gungor² | Berfu Saraydar² | Asli Gulce Bartan² | Bilgehan Ibibik² | Tugce Bildik² | İlayda Baydemir¹ | Hatice Asena Sanli¹ | Basak Kayaoglu¹ | Yasemin Ceylan² | Tugce Yildirim² | Irem Abras² | Ihsan Cihan Ayanoglu¹ | Sefa Burak Cam³ | Eda Ciftci Dede⁴ | Merve Gizer⁵ | Osman Erganis⁶ | Fahriye Sarac⁷ | Serdar Uzar⁷ | Hakan Enul⁷ | Cumhuri Adiyay⁷ | Gamze Aykut² | Hivda Polat⁸ | Ismail Selim Yildirim⁸ | Saban Tekin⁸ | Gulay Korukluoglu⁹ | Hasan Ersin Zeytin¹⁰ | Petek Korkusuz³ | Ihsan Gursel² | Mayda Gursel¹

S protein (WT, S-2P,2-6P)+ diğer yapısal proteinler

Memeli hücresi
(insan embriyonik böbrek hücre)



Alüminyum ve TLR- 9 ag.

HEK293 hücrelerinde SARS-CoV-2'nin dört yapısal proteinin ekprese eden VBP

Yüksek anti-S, anti-RBD, anti-N IGG yanıtı

Çok fonksiyonlu TH1 yanıtı

Virüs yükünü azalma

Aşıllılarda virüs akciğer patolojisi engellendiği



Study of a Severe Acute Respiratory Syndrome CoV-2 (SARS-CoV-2) Virus-like Particle (VLP) Vaccine in Healthy Adults (COVID-19)

ClinicalTrials.gov Identifier: NCT04818281

[Recruitment Status](#) ⓘ : Recruiting

[First Posted](#) ⓘ : March 26, 2021

[Last Update Posted](#) ⓘ : July 13, 2021

See [Contacts and Locations](#)