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Vaccini, vaccinologia e COVID-19

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COSA È
E COSA DEVE FARE UN VACCINO ?

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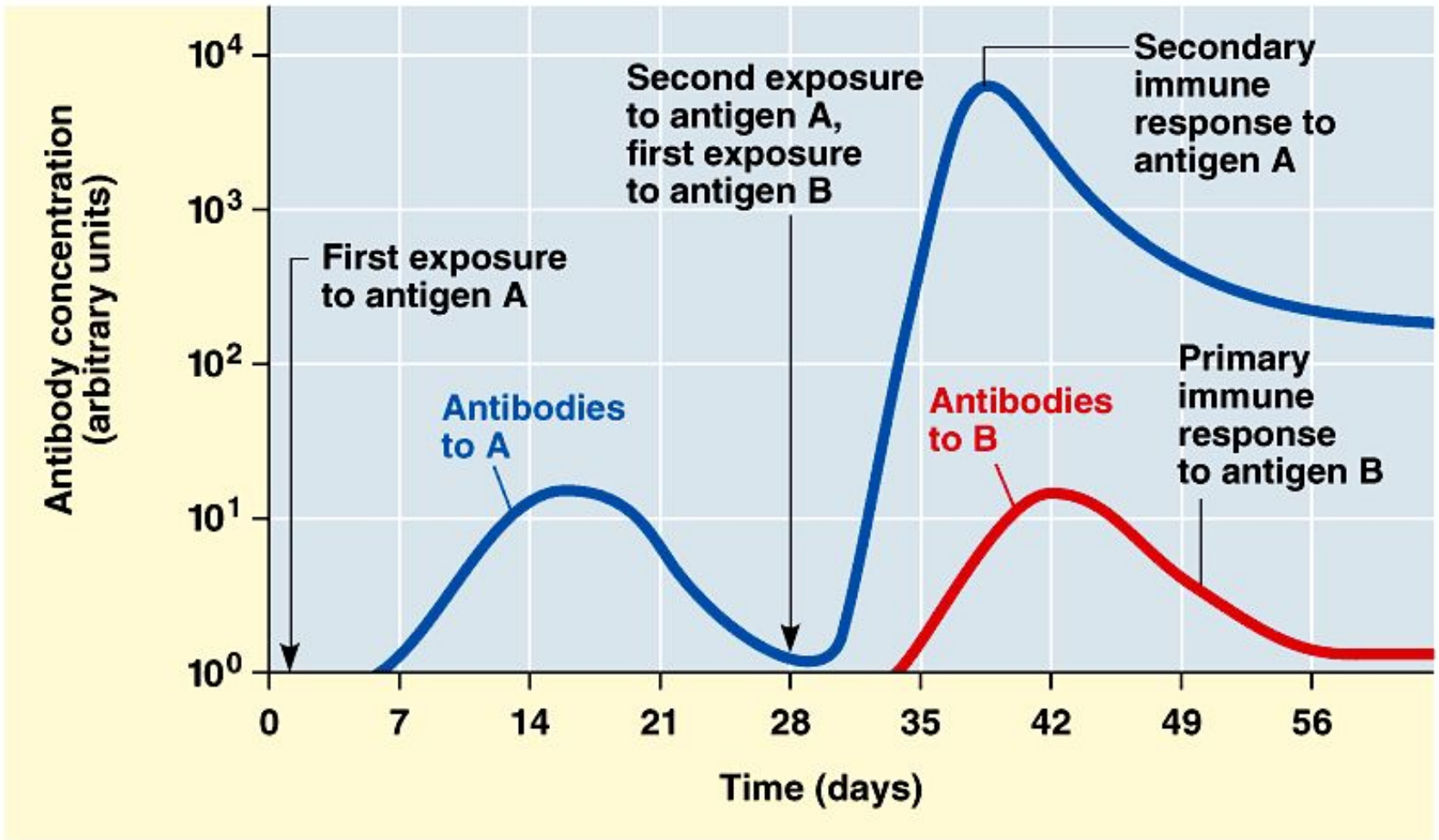
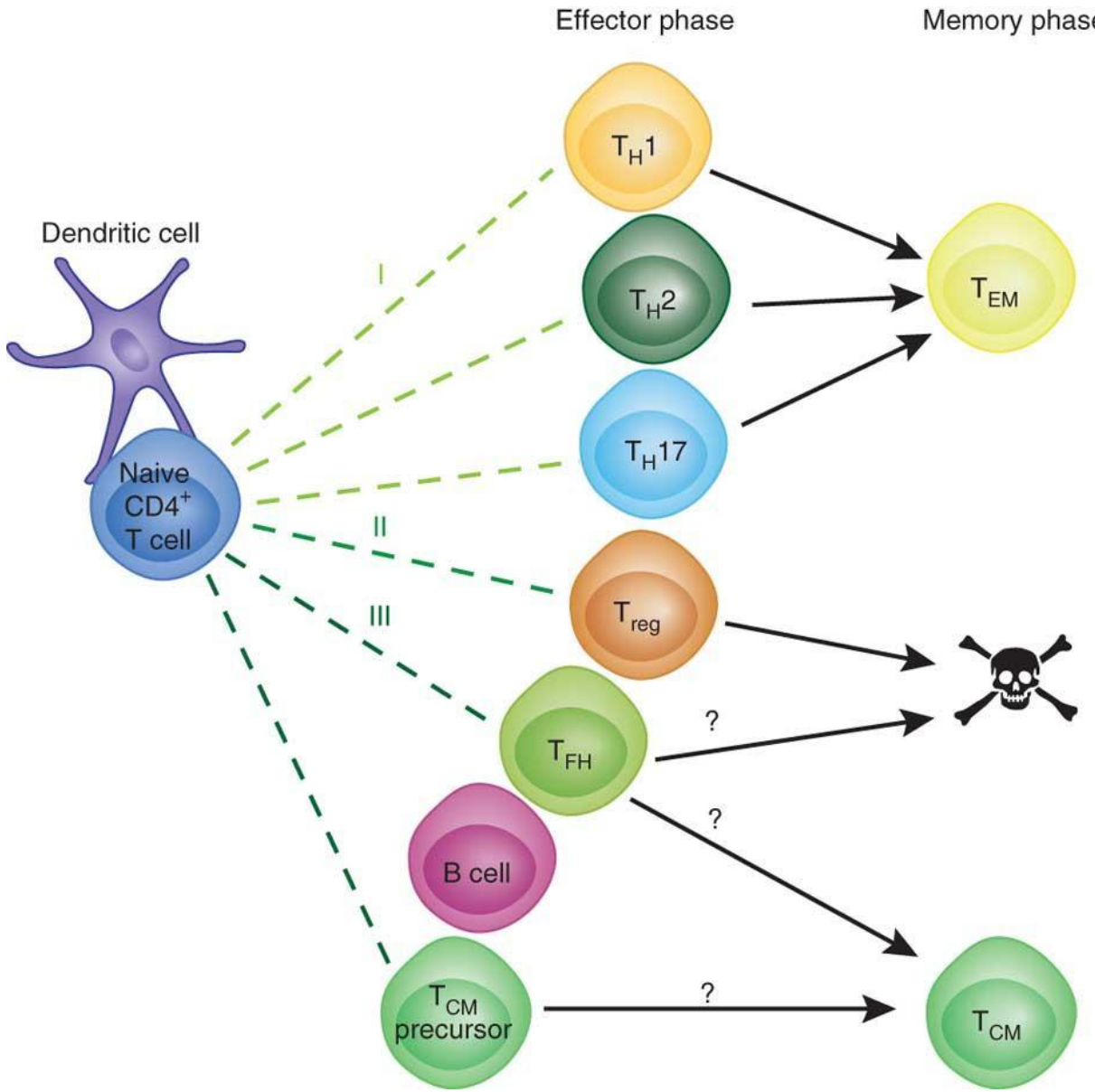
COSA DEVE FARE UN VACCINO?

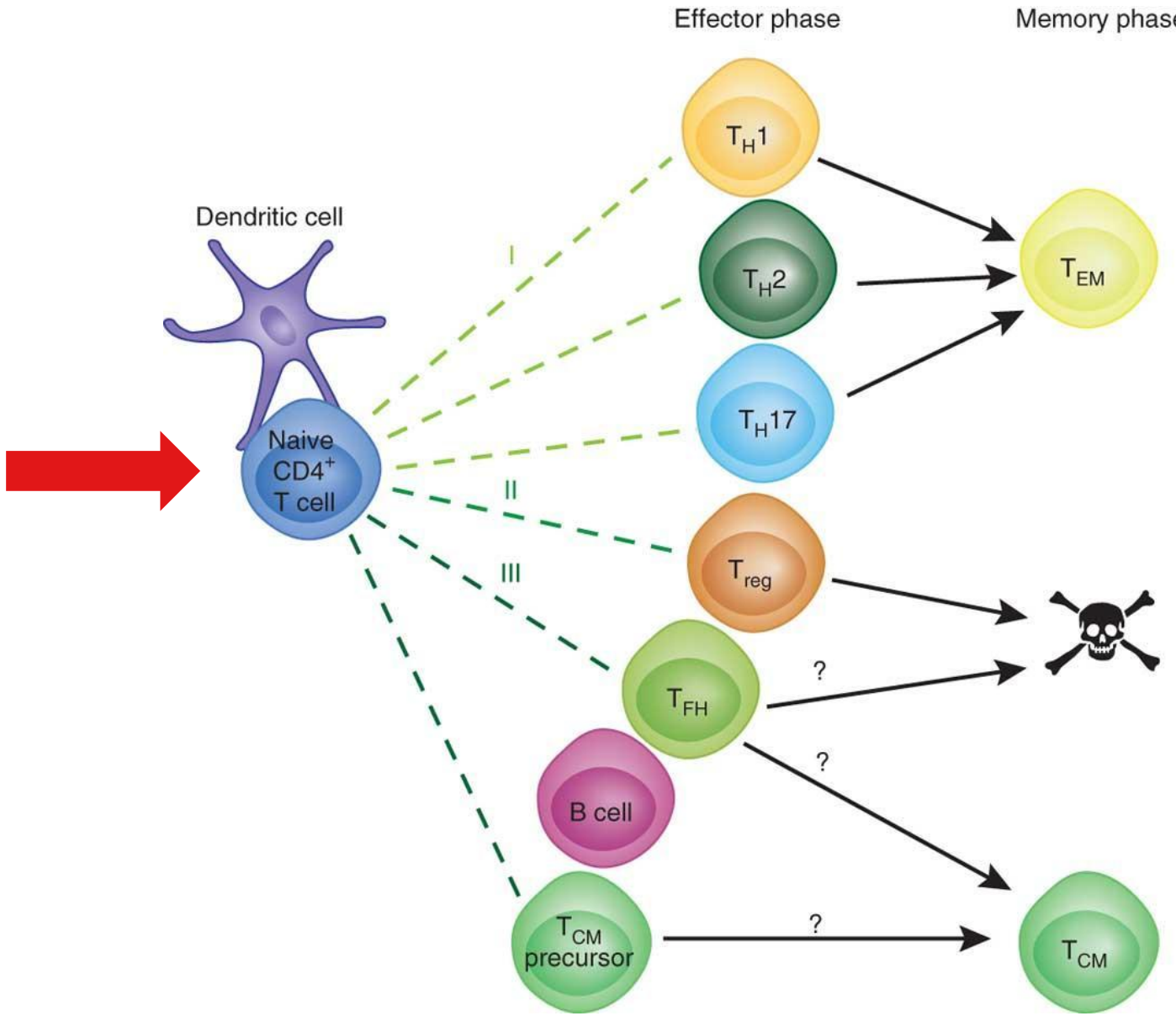
Un vaccino utilizza materiale antigenico (proteine, RNA, etc) del patogeno private della componente di tossicità per indurre il priming dei linfociti vergini e trasformarli in cellule della memoria.

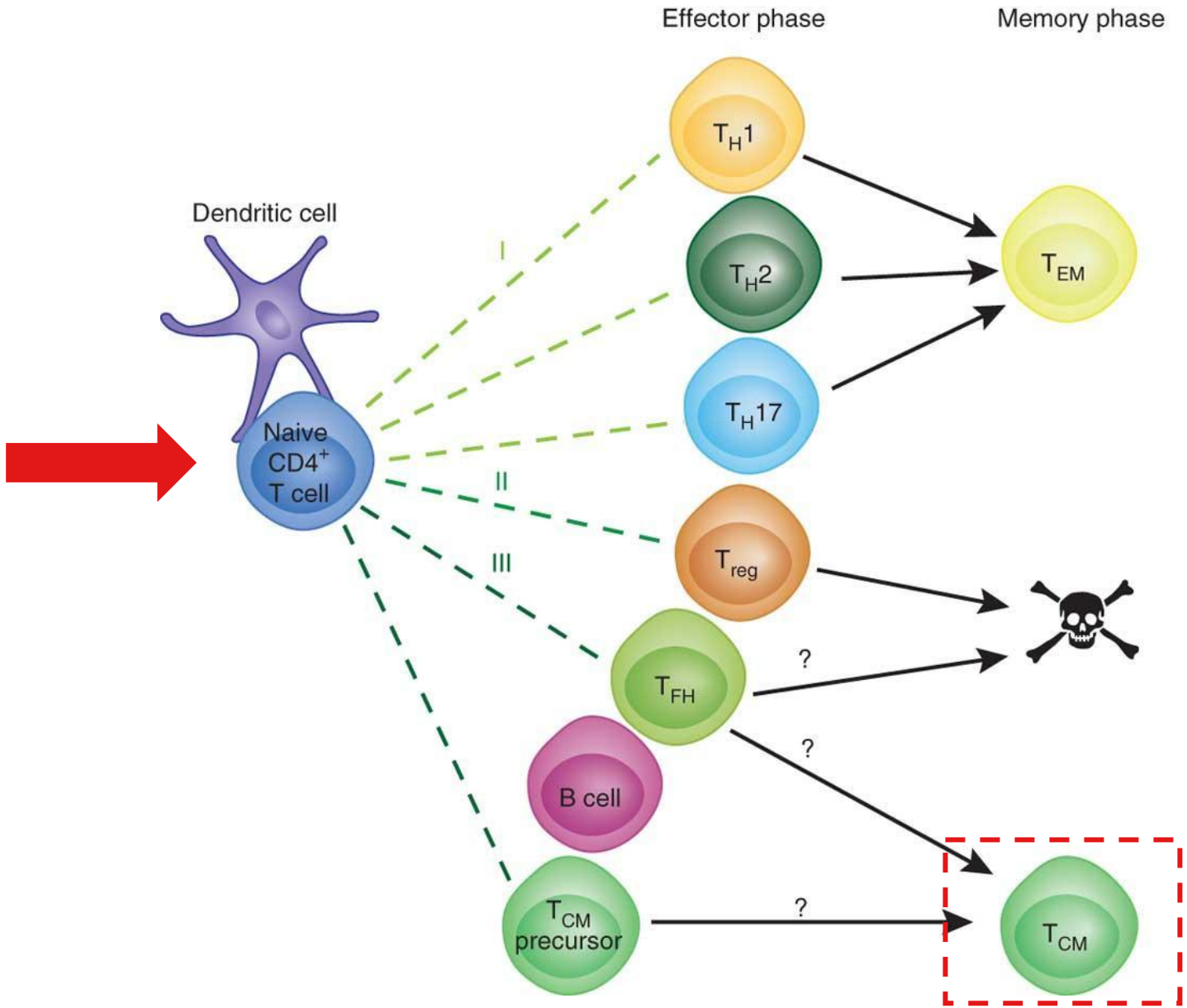
Un vaccino, dunque, trasforma la natura della risposta immune da primaria a secondaria.

RISPOSTA IMMUNE PRIMARIA **RISPOSTA IMMUNE SECONDARIA**

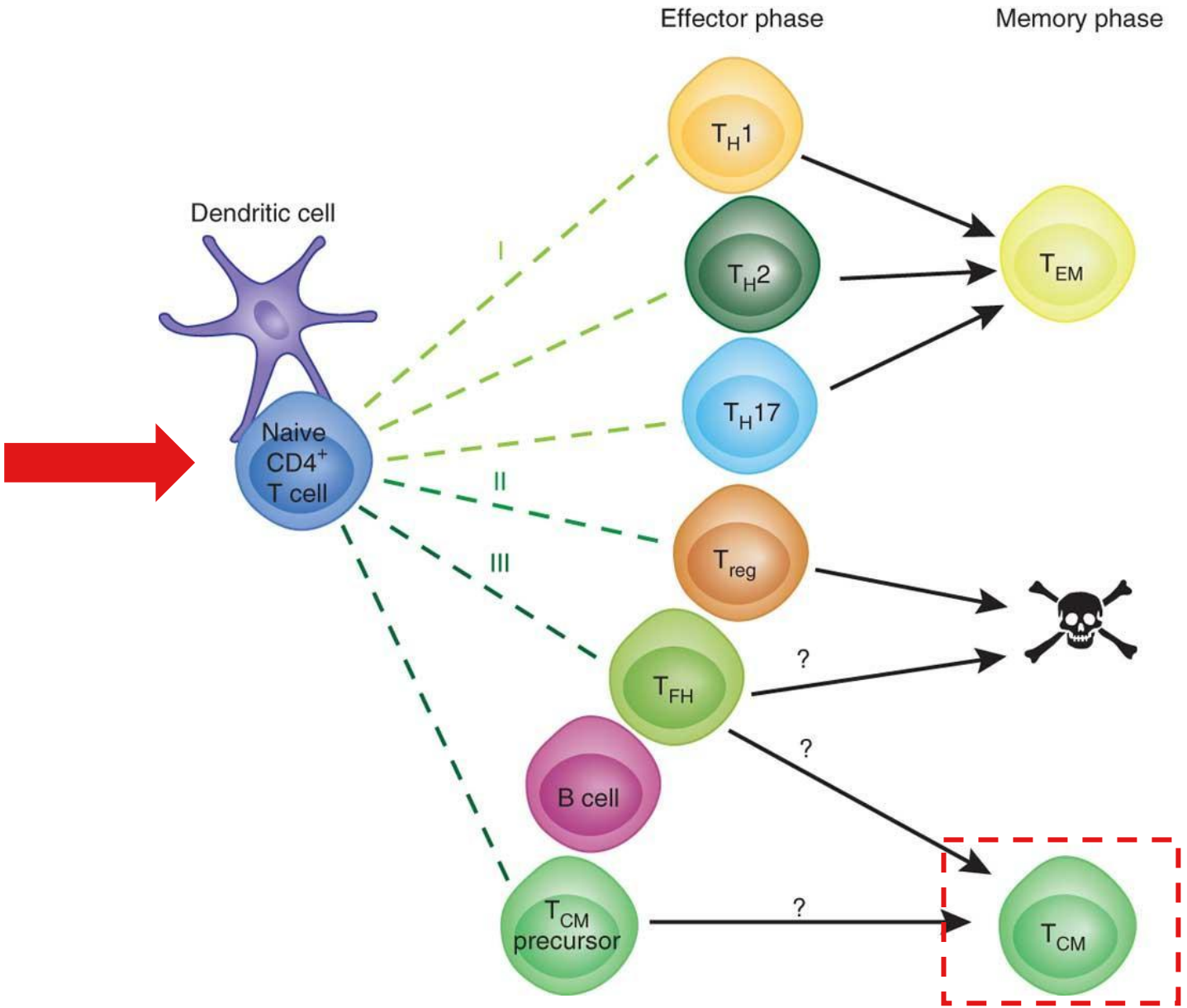








Naive T cell= risposta immune primaria, dopo stimolazione con antigene ho differenziazione in cellule effettrici, che distruggono il patogeno



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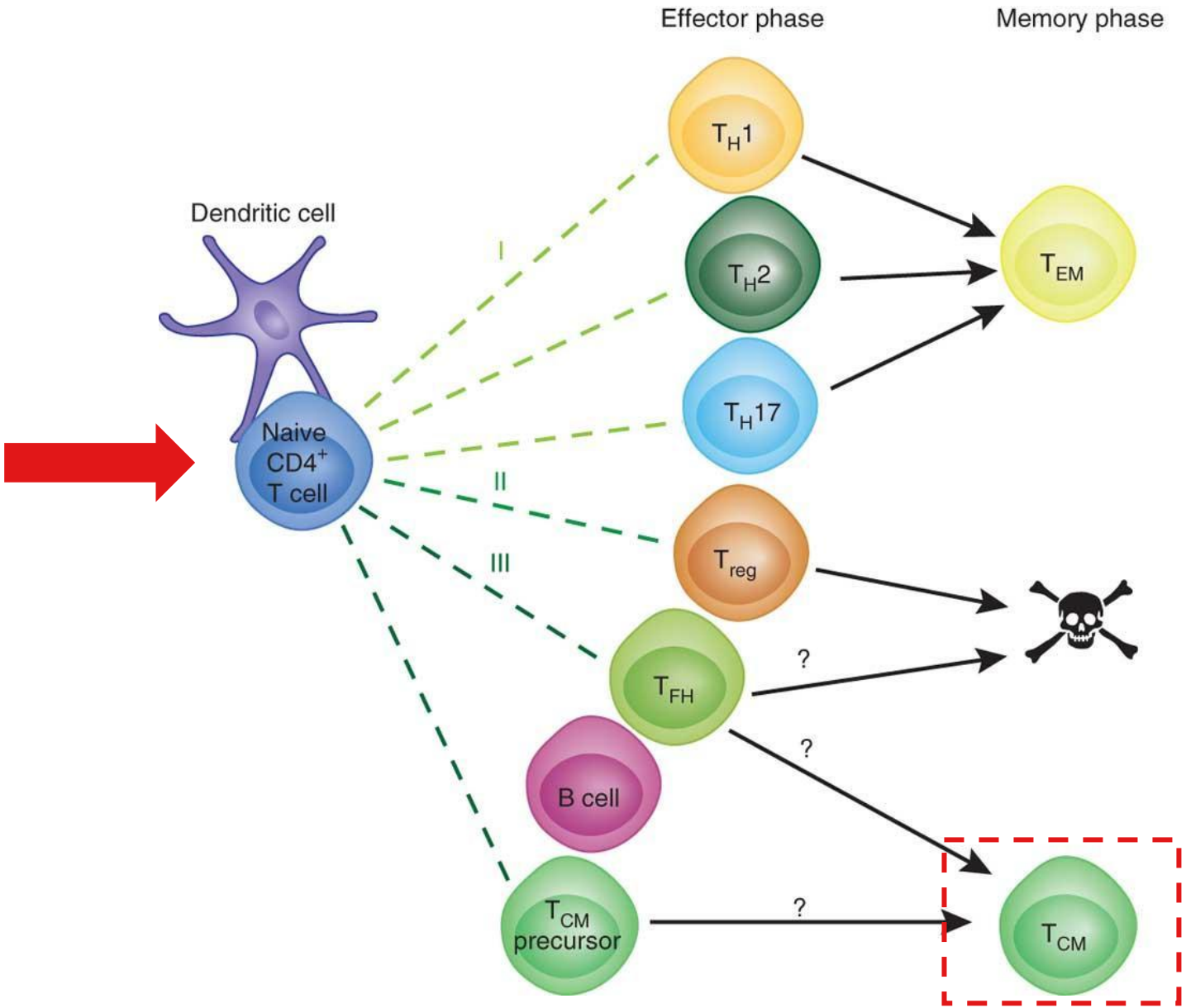
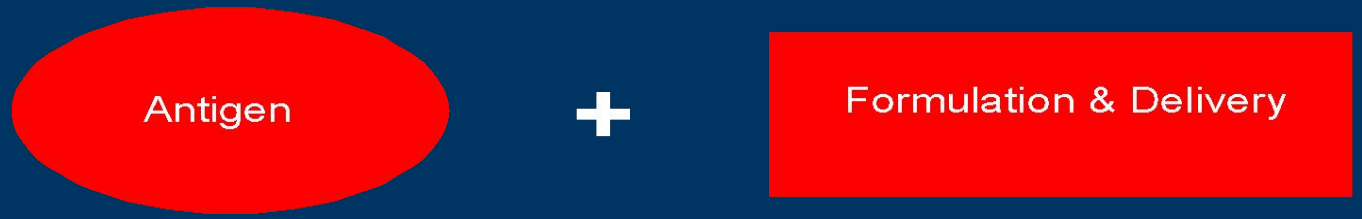


Tcm= T linfociti central memory: cellule della memoria a lunga sopravvivenza che mediano la risposta immune secondaria

Come si costruisce un Vaccino?



Protein and/or
Carbohydrate
and/or DNA/RNA

Specificity

Adjuvant/conjugate
Vaccine vehicle

Magnitude
Composition
Duration
Compartmentalization

ADIUVANTE

ANTIGENE

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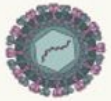
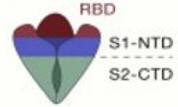
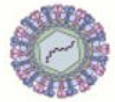
A Licensed for use

Vaccine type	PAMP	Examples (route if not IM/ID)	Adjuvant	Booster
Live attenuated 	Endogenous 	Measles	None	Yes
		Mumps	None	Yes
		Rubella	None	Yes
		Rotavirus (oral)	None	Yes
		Yellow Fever	None	No
		Chicken pox	None	Yes
		Polio Sabin (oral)	None	Yes
		Live zoster	None	No
		BCG	None	No
		Influenza (nasal: FluMist)	None	Annual
Killed 	Intrinsic 	Whole cell pertussis	None	Yes
		Polio Salk	None	Yes
Split 	Intrinsic 	Seasonal influenza	None	Annual
		Fluad for > 65 yr.	MF59	Annual
Virus like particles 	Incorporated*	HPV Guardasil 9	Alum	Yes
		HPV Cervarix	AS04	Yes
Toxoid 	None	Diphtheria	Alum	Yes
		Tetanus	Alum	Yes
Recombinant subunit 	None	Hep A Havrix	Alum	Yes
		Hep A Vaqta	Alum	Yes
		Hep B Engerix-B	Alum	Yes
		Hep B Recombivax	Alum	Yes
		HepA/Hep B Twinrix	Alum	Yes
		Hep B Heplisav-B	CpG	Yes
		Acellular pertussis	Alum	Yes
		Zoster Shingrix	AS01B	Yes
		Influenza Flublock	None	Annual
Conjugate 	None	MenB Bexsero	Alum	Yes
		MenB Trumenba	Alum	Yes
		Pneumococcal Prevnar 13	Alum	Yes
		HiB	Alum	Yes
Polysaccharide	None	Pneumococcal polysaccharide PPSV23	None	Yes

B In clinical trial for COVID-19

Vaccine type	PAMP	Examples (route if not IM/ID)	Adjuvant	Booster
mRNA 	RNA 	Spike mRNA	None	Yes
		RBD mRNA		
DNA 	DNA 	Spike DNA	None	Yes
Recombinant protein 	None	Spike		
		Novavax	Matrix-M	Yes
		Medigen	CpG 1018	Yes
		Vaxine	Advax	Yes
		University of Queensland	MF59	Yes
		Others	Alum	Yes
		RBD	Alum	Yes
Viral vector 	Endogenous 	Chimp Adeno vectored	None	No
		Simian Adeno vectored	None	No
		Adenovirus vectored	None	No
		Adeno-based (rAd26-S+rAd5-S)	None	Yes*
Inactivated 	Intrinsic 	Inactivated virus		
		Sinovac	CpG	Yes
		Wuhan/Sinopharm	Alum	Yes
		Beijing/Sinopharm	Alum	Yes
		Institute of Medical Biology, Chinese Academy of Medical Sciences	None	Yes
		Research Institute for Biological Safety Problems, Rep of Kazakhstan	None	Yes

MECCANISMI IMMUNOLOGICI INDOTTI DAL VACCINO IDEALE

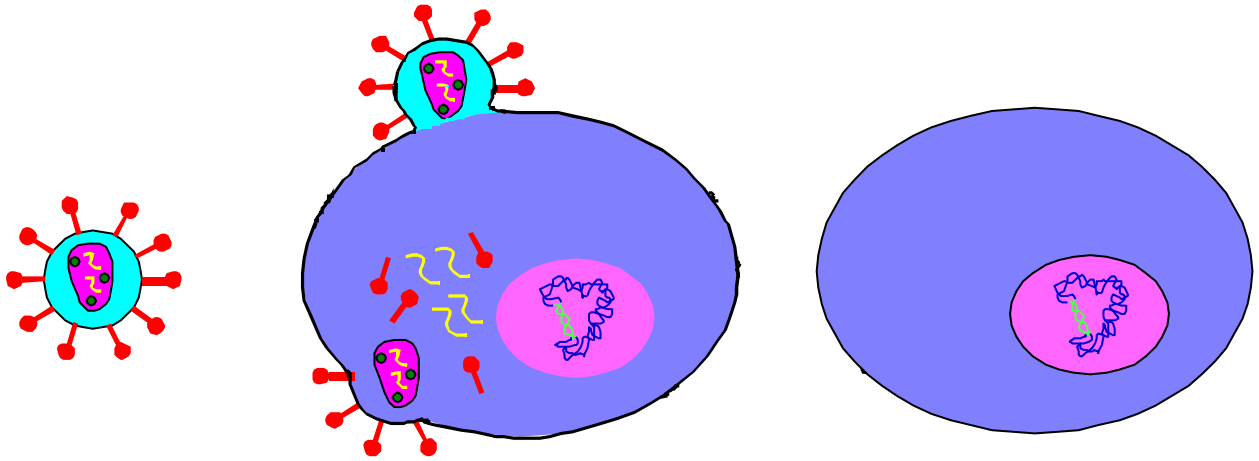
ANTICORPI

- Legano il patogeno;
- ne neutralizzano la infettività e gli impediscono di infettare le cellule;
- contribuiscono alla eliminazione del patogeno

T LINFOCITI CITOTOSSICI (CTL)

- Riconoscono le cellule che sono state infettate e le uccidono

RUOLO DELLE DIVERSE RISPOSTE IMMUNE INDOTTE DA UN VACCINO ANTIVIRALE



Anticorpi	+++	+/-	-
T linfociti	-	+++	-

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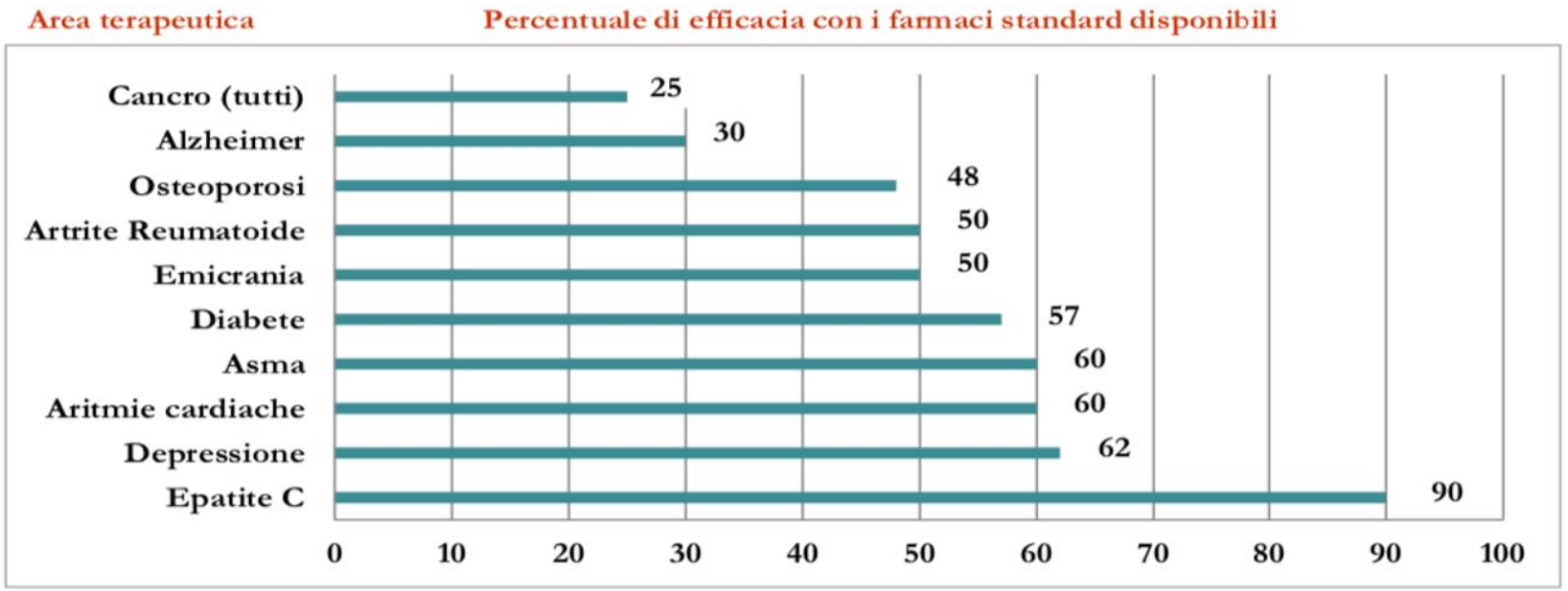
COSA DOVREBBE FARE IL VACCINO IDEALE?

Un vaccino ideale dovrebbe indurre la formazione di anticorpi non solo nel circolo sanguigno ma anche sulle superfici mucose (90% infezioni da HIV sono sessualmente trasmesse; SARS-CoV-2 è trasmesso per via aerea...).

Farmaci efficaci ma non in tutti

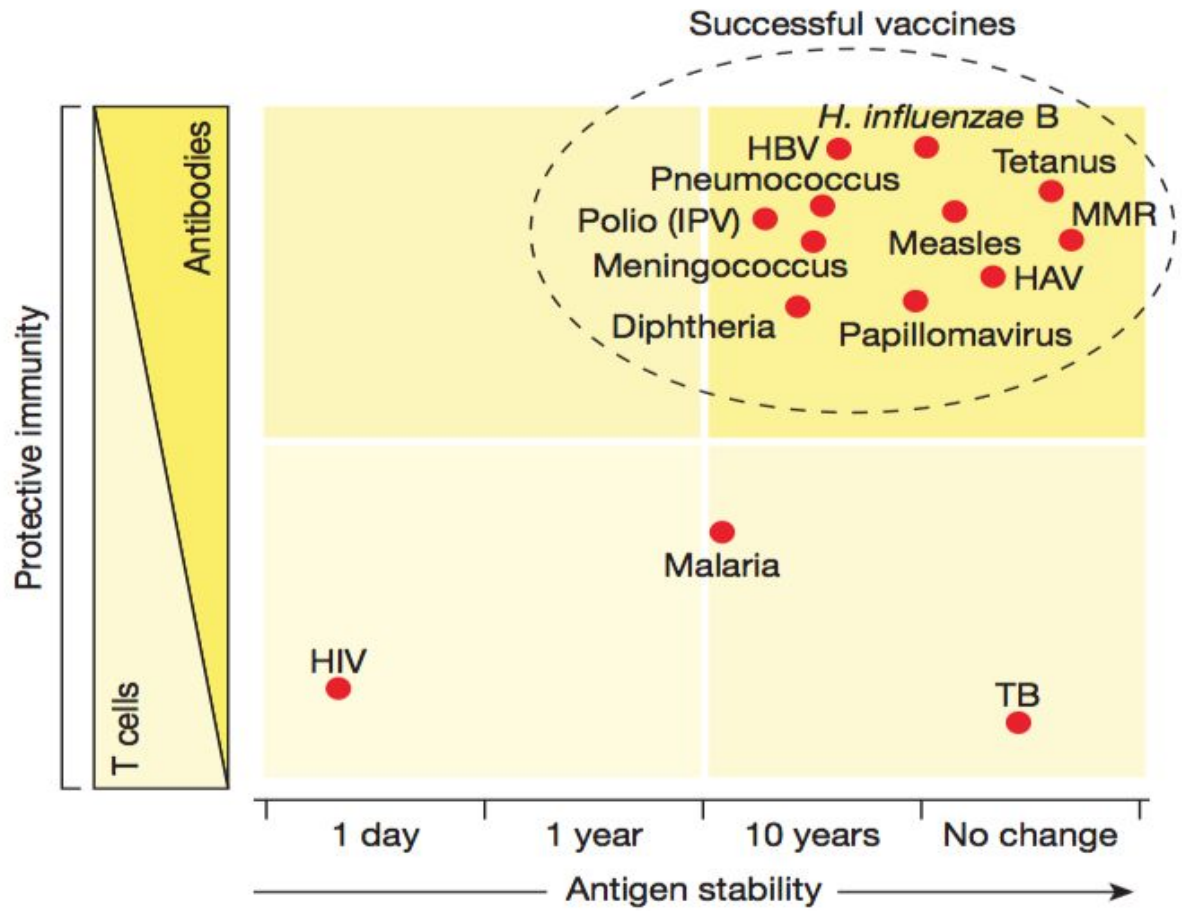


Consigliereste a nessuno di vivere senza vaccinarsi?

Infezione	Efficacia vaccinale (%)
Poliomelite	100 %
Difterite	99.99 %
Morbillo	99.99 %
Rosolia	99.78 %
Parotite	99.86 %
Pertosse	98.20 %
H. *influenzae*	98.79 %
Men B/ Men C	90.40 %
HBV	97 %

Challenging infectious diseases

Historically successful vaccines have been developed mostly against those pathogens that can be treated by antibodies and have a stable antigen repertoire (Box 1 Figure). HIV, malaria and tuberculosis vaccines do not fall within the cluster of successful vaccines in the graph, because of antigenic variability and the requirement of T-cell immunity for protection. Developing vaccines against these pathogens requires novel approaches.



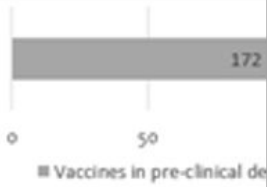
World Health Organization

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

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 p of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or an accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or o responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procu documents.

Summary Information on Vaccine Products in Clinical Development

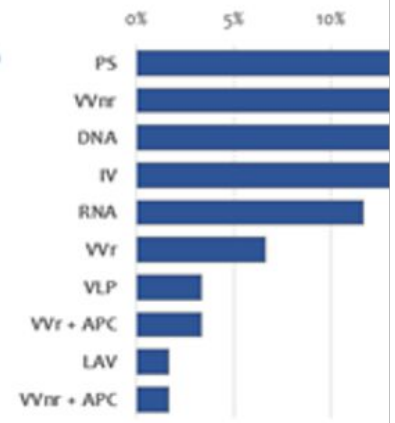
1. - Number of vaccines in clinical development	60
2. - Number of vaccines in pre-clinical development	172



3. - Candidates in clinical phase

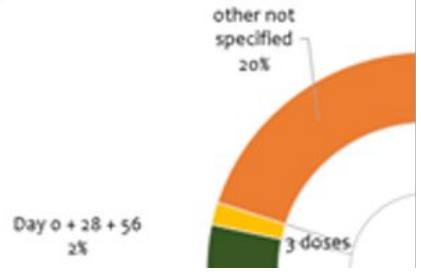
Filter: All — Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	18	30%
VVnr	Viral Vector (non-replicating)	9	15%
DNA	DNA	8	13%
IV	Inactivated Virus	8	13%
RNA	RNA	7	12%
VVr	Viral Vector (replicating)	4	7%
VLP	Virus Like Particle	2	3%
VVr + APC	VVr + Antigen Presenting Cell	2	3%
LAV	Live Attenuated Virus	1	2%
VVnr + APC	VVnr + Antigen Presenting Cell	1	2%
		60	



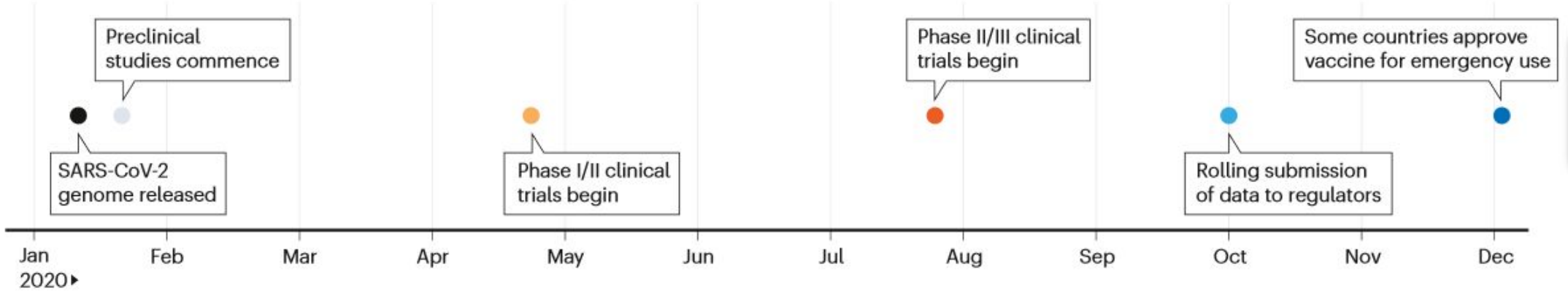
4. - Dosage, schedule and route of admistration of candidates in clinical phase

Dosage & schedule	Candidate vaccines (no. and %)	
1 dose	10	17%
Day 0	10	
2 doses	37	62%
Day 0 + 14	5	
Day 0 + 21	14	
Day 0 + 28	18	
3 doses	1	2%
Day 0 + 28 + 56	1	
TBD / No Data (ND)	12	20%



A VACCINE IN A YEAR

The drug firms Pfizer and BioNTech got their joint SARS-CoV-2 vaccine approved less than eight months after trials started. The rapid turnaround was achieved by overlapping trials and because they did not encounter safety concerns.



tecnologia	produttore	n dosi	efficacia	efficacia 1 dose	efficacia malattia severa	efficacia in pop anziani	confezione
m RNA	**Pfizer/Biontech**	**2**	**95%**	**52.4%**	**66.4-75%**	**93.7%** *>55 anni*	5-6 dosi fiala
	Moderna	**2**	**94.1%**	**69.5 %**	**42.6 %** *(dopo 1 dose)* **100%** *(dopo 2 dose)*	***86,4%-94.1%*** *(dopo 2 dose >65 anni)*	10 dosi fiala
Vettore virale	**Astra Zeneca**	**2**	**70.4%** *(blended) (62.1% base dose standard)*	**64.1%**			10 dosi fiala
	The Gamaleya National Center	**2**	***91.6%***	**73.1%**	**100%**	**91.8%** >60 anni	5 dosi fiala
	Johonson&Johnson	**1**	***66%***	**66%**	**85%** *dopo 28 giorni 100% su ospedalizzazione dopo 28 giorni*		
	CanSino Bio	**1**	***65.7%***		**90,98%**		
Proteina ricombinante	**Novavax**	**2**	**89.3%**				10 dosi fiala
	Bektop	**2**	**100%???**				
Virus inattivato	**Sinopharm**	**2**	**79.4%**				
	Sinovac	**2**	**59.65%**				

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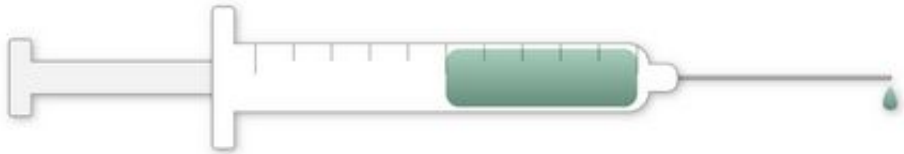
mRNA vaccines (Moderna e Pfizer)

- **mRNA vaccines** contain material from SARS-CoV-2 and gives our cells instructions for how to make a harmless viral protein. After our cells make copies of the protein, they destroy the genetic material from the vaccine. Our bodies recognize that the protein should not be there and build T-lymphocytes and B-lymphocytes that will remember how to fight SARS-CoV-2 if we are infected in the future.

How Moderna's Vaccine Works

By Jonathan Corum and Carl Zimmer Updated Jan. 11, 2021



Moderna, a Massachusetts-based vaccine developer, partnered with the National Institutes of Health to develop and test a coronavirus vaccine known as **mRNA-1273.** A clinical trial demonstrated that the vaccine has an efficacy rate of 94.1 percent in preventing Covid-19.

Pfizer works exactly on the same principle and has an efficacy rate of 95%

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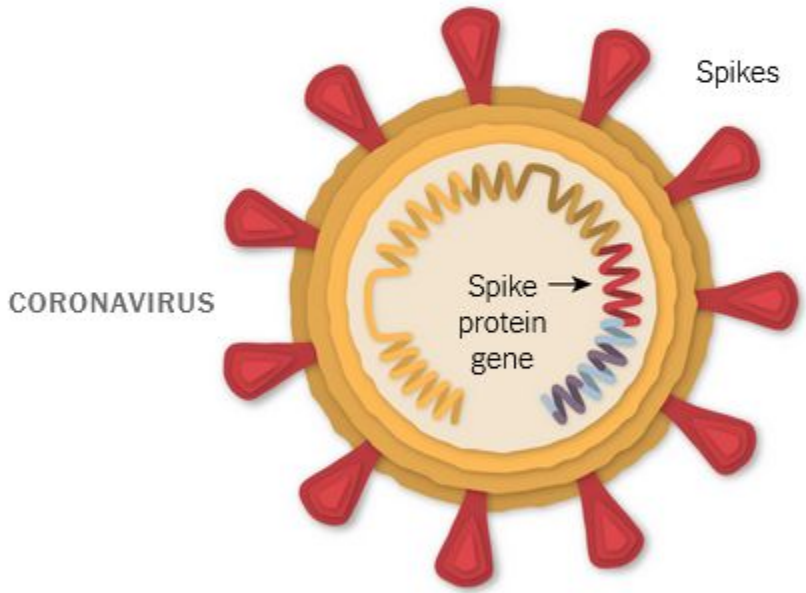
A Piece of the Coronavirus

The SARS-CoV-2 virus is studded with proteins that it uses to enter human cells. These so-called spike proteins make a tempting target for potential vaccines and treatments.



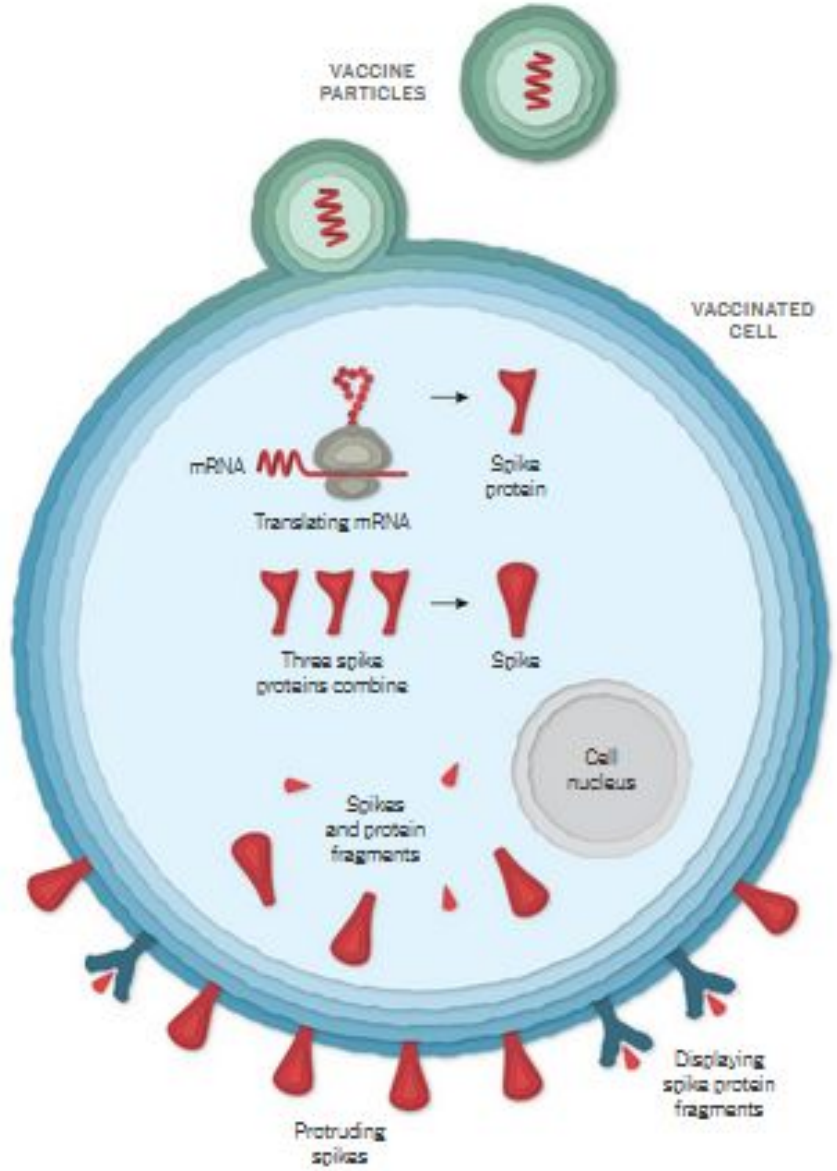
Like the Pfizer-BioNTech vaccine, Moderna's vaccine is based on the virus's genetic instructions for building the spike protein.

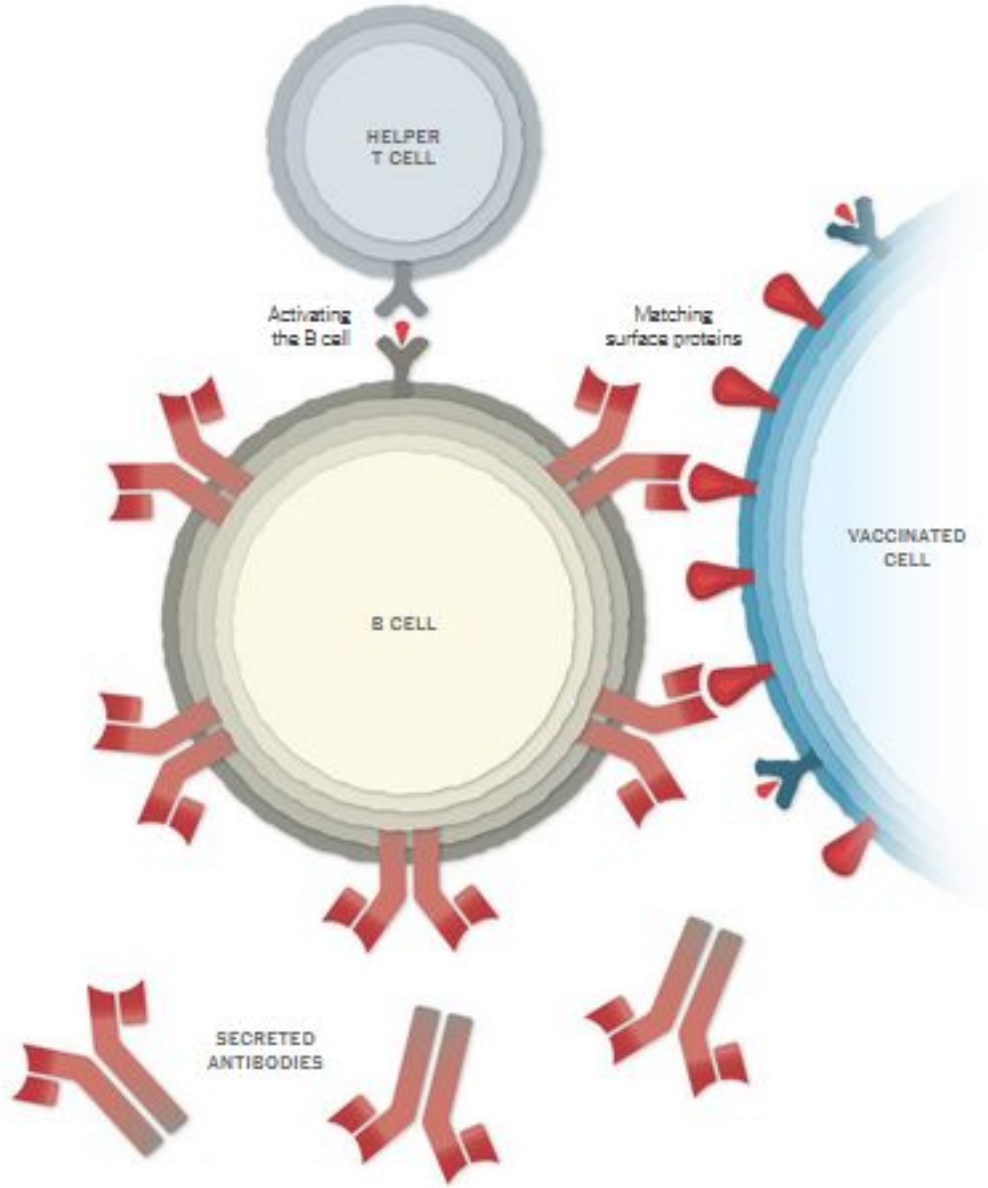
mRNA Inside an Oily Shell

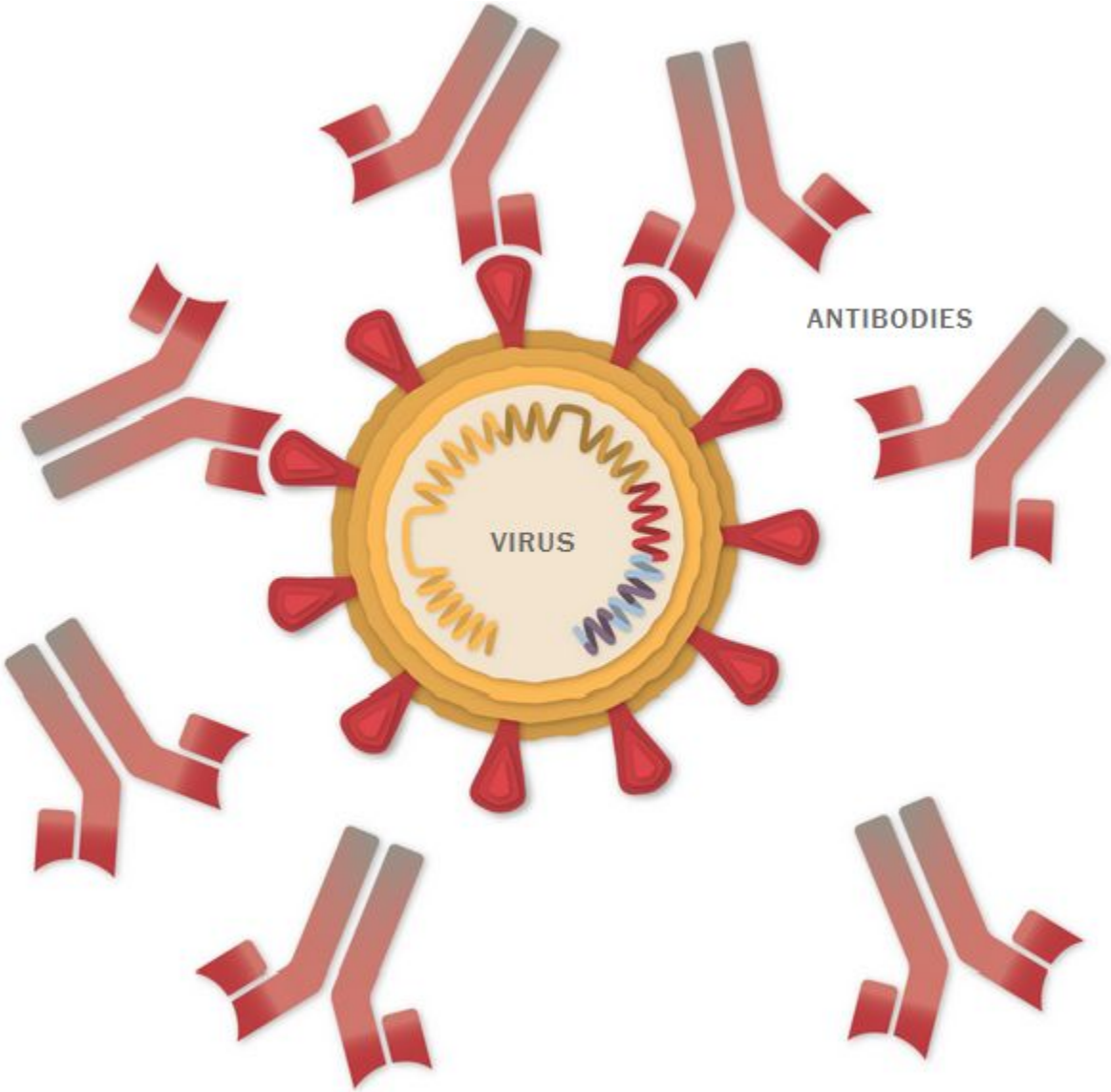
The vaccine uses messenger RNA, genetic material that our cells read to make proteins. The molecule — called mRNA for short — is fragile and would be chopped to pieces by our natural enzymes if it were injected directly into the body. To protect the vaccine, Moderna wraps the mRNA in oily bubbles made of lipid nanoparticles.

Lipid nanoparticles surrounding mRNA

Because of their fragility, the mRNA molecules will quickly fall apart at room temperature. Moderna's vaccine will need to be refrigerated, and should be stable for up to six months when shipped and stored at –4°F (–20°C).

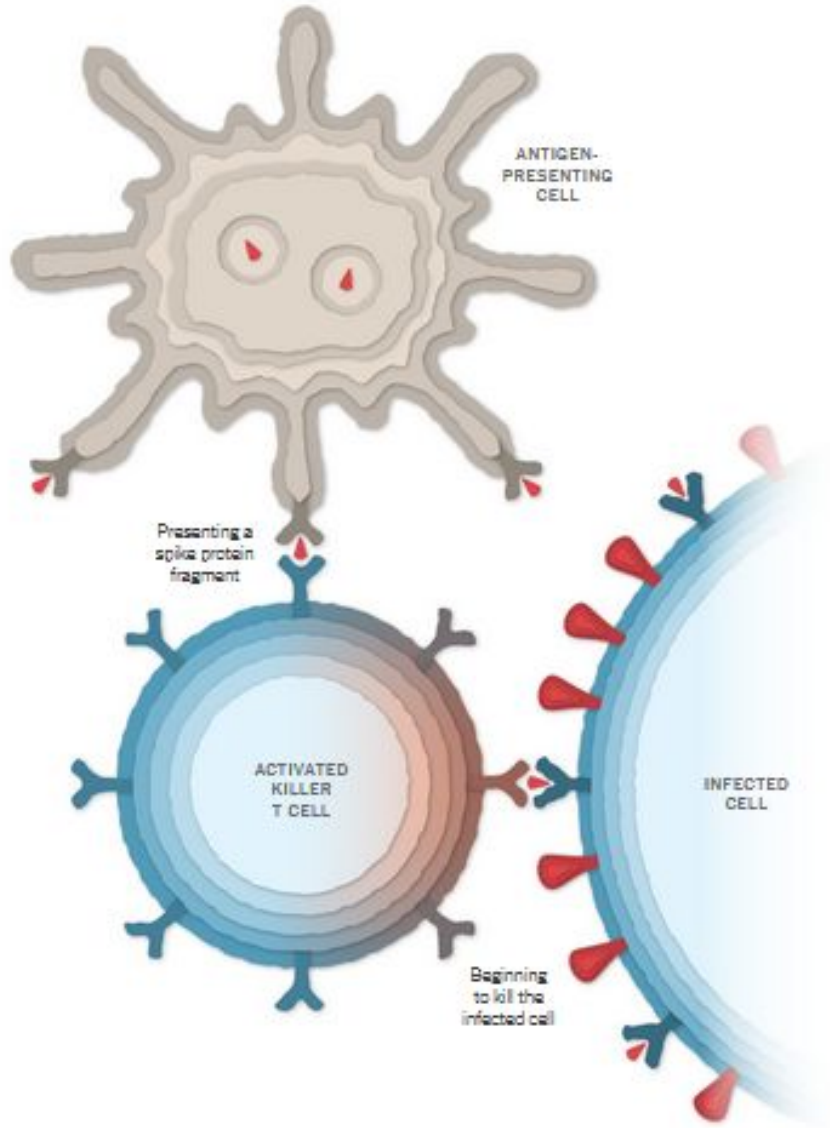




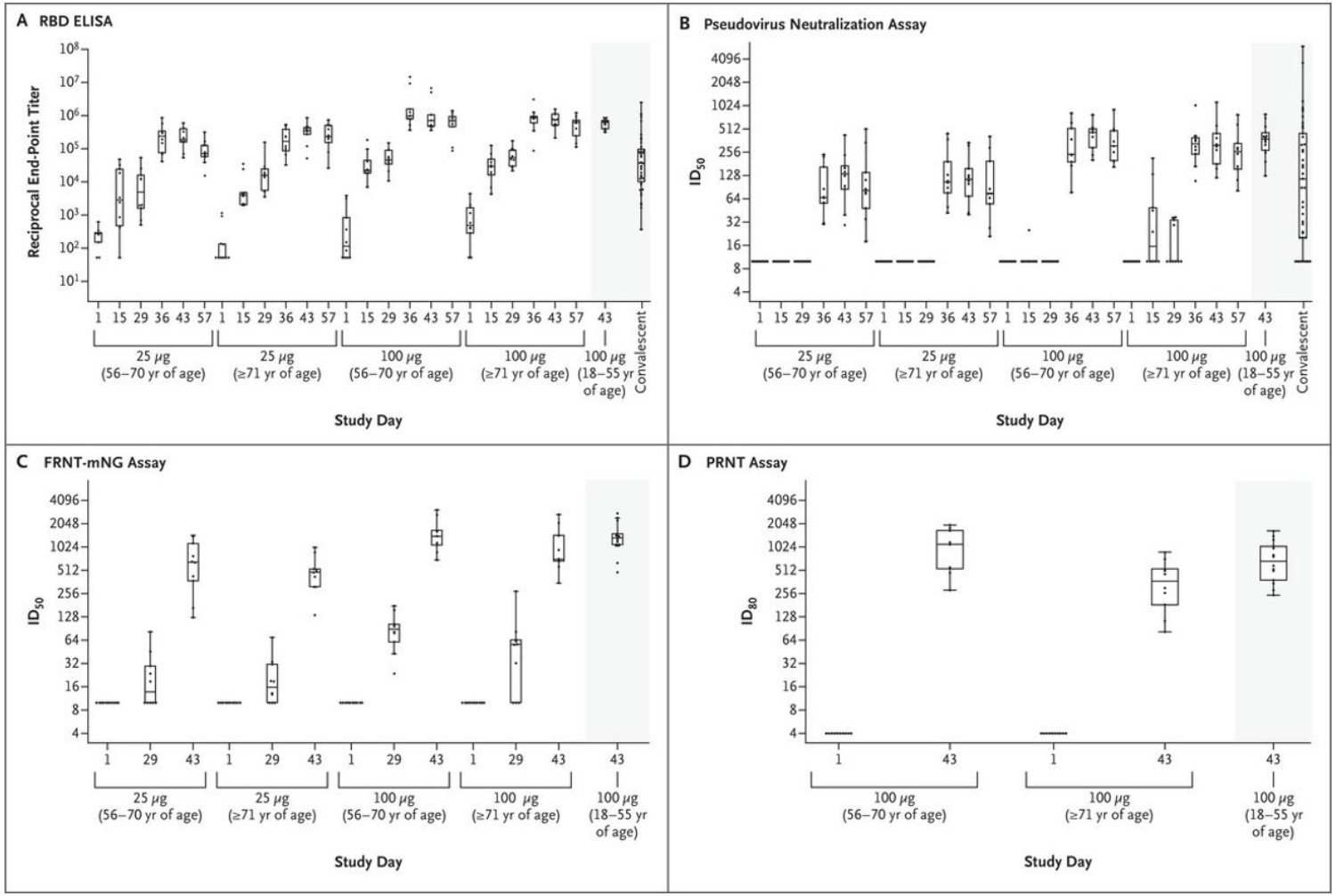


Killing Infected Cells

The antigen-presenting cells can also activate another type of immune cell called a killer T cell to seek out and destroy any coronavirus-infected cells that display the spike protein fragments on their surfaces.



MODERNA SARS-CoV-2 vaccine
SARS-CoV-2 Antibody-Binding and Neutralization Responses.



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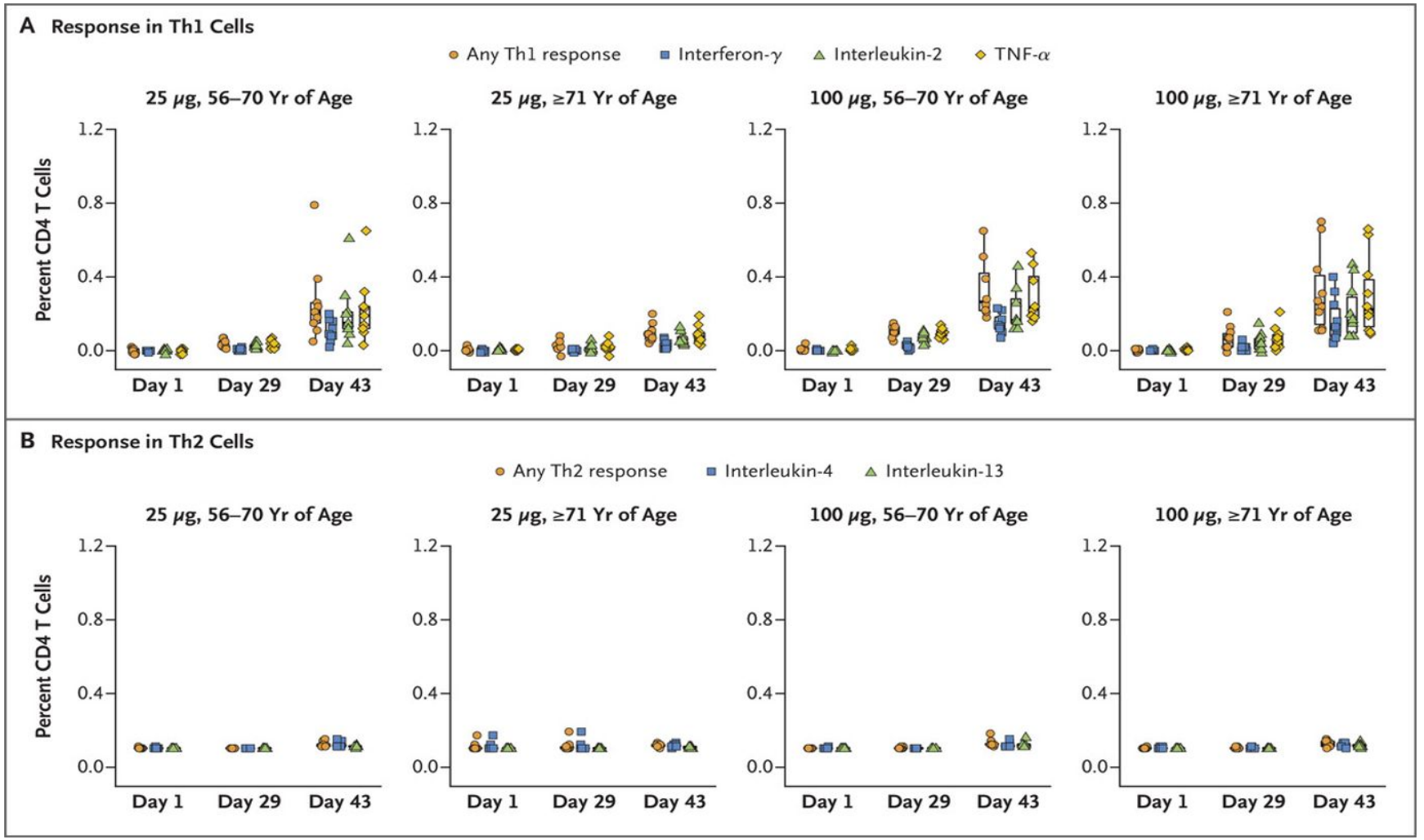
MODERNA SARS-CoV-2 vaccine
SARS-CoV-2 T cell Responses.



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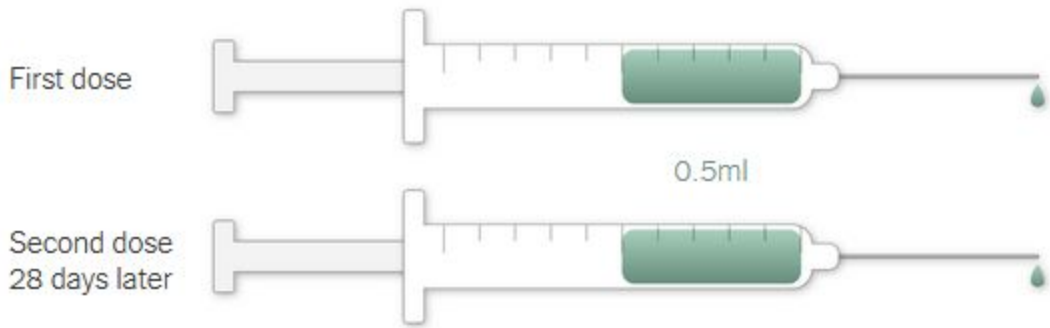
Remembering the Virus

Moderna's vaccine requires two injections, given 28 days apart, to prime the immune system well enough to fight off the coronavirus. But because the vaccine is so new, researchers don't know how long its protection might last.



Vector Vaccines (AZ, Sputnik, JJ)

- **Vector vaccines** use a viral vector that contains genetic material of COVID-19. Once the viral vector is inside our cells, the genetic material gives cells instructions to make viral proteins. This prompts our bodies to build T-lymphocytes and B-lymphocytes that will remember how to fight that virus if we are infected in the future.

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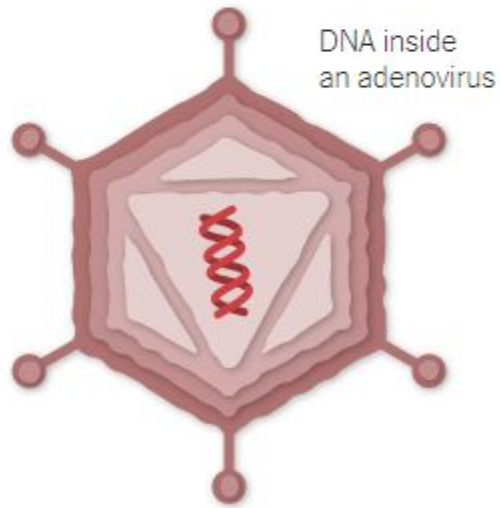
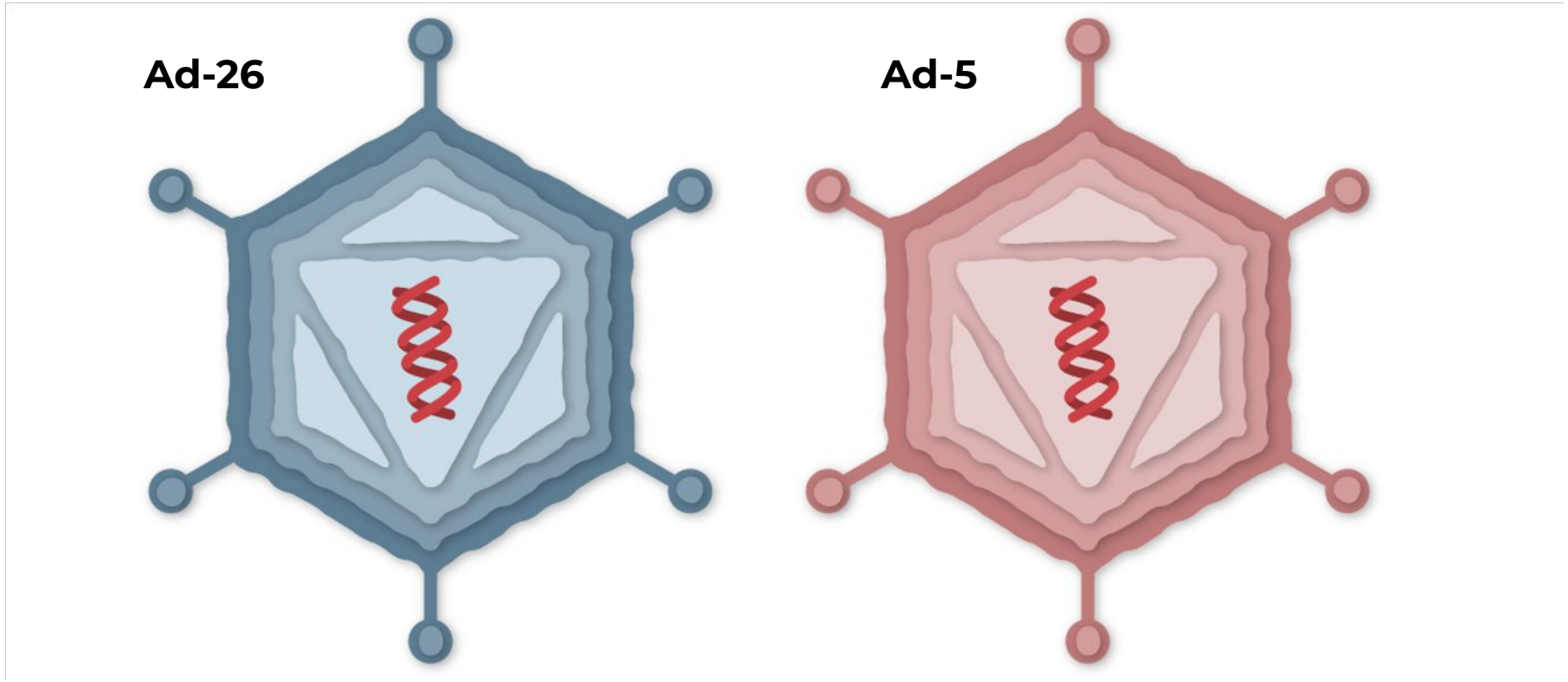
DNA Inside an Adenovirus

The researchers added the gene for the coronavirus spike protein to another virus called an adenovirus. Adenoviruses are common viruses that typically cause colds or flu-like symptoms. The Oxford-AstraZeneca team used a modified version of a chimpanzee adenovirus, known as ChAdOx1. It can enter cells, but it can't replicate inside them.



Sputnik V



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How the Oxford-AstraZeneca Vaccine Works

By Jonathan Corum and Carl Zimmer Updated Jan. 8, 2021

The University of Oxford partnered with the British-Swedish company AstraZeneca to develop and test a coronavirus vaccine known as **ChAdOx1 nCoV-19** or **AZD1222**. A clinical trial revealed the vaccine was 62 to 90 percent effective, depending on the initial dosage. Despite some uncertainty over trial results, Britain authorized the vaccine for emergency use in December, and India authorized a version of the vaccine called **Covishield** on Jan. 3.

Sputnik has an efficacy rate of 91.5%

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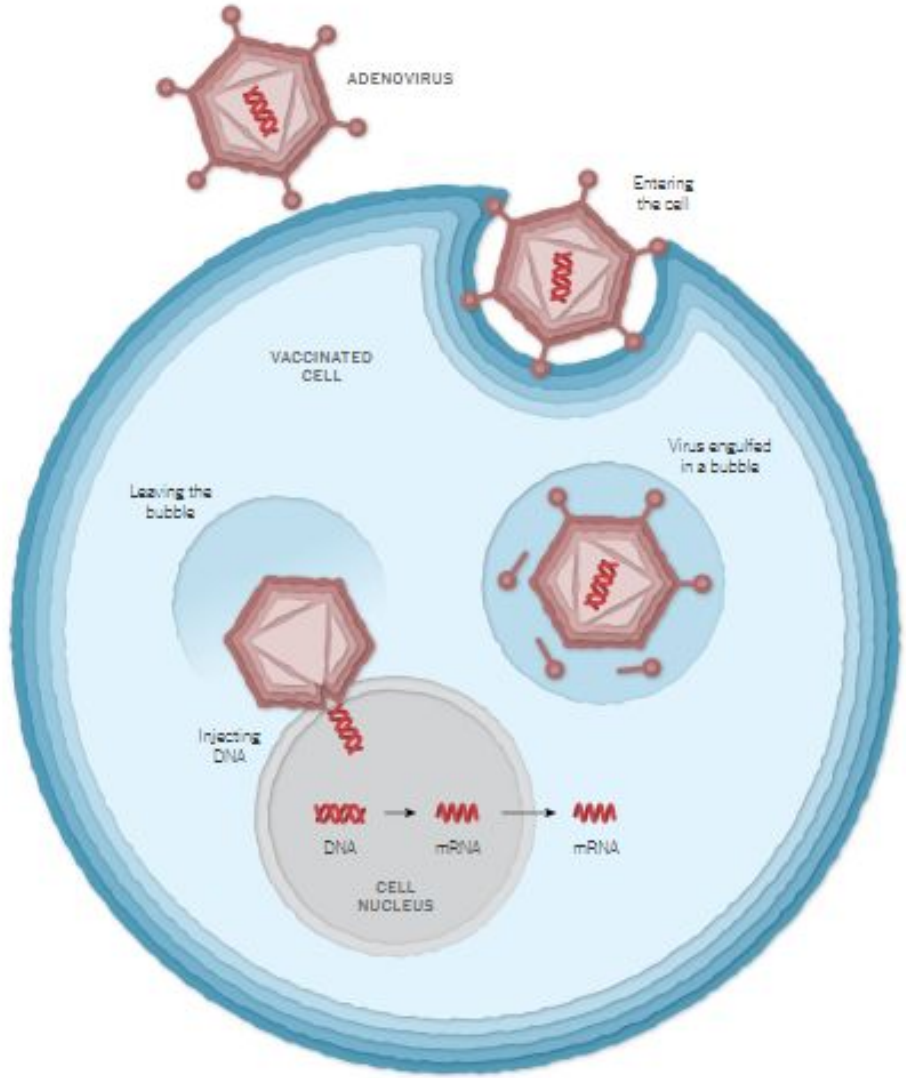
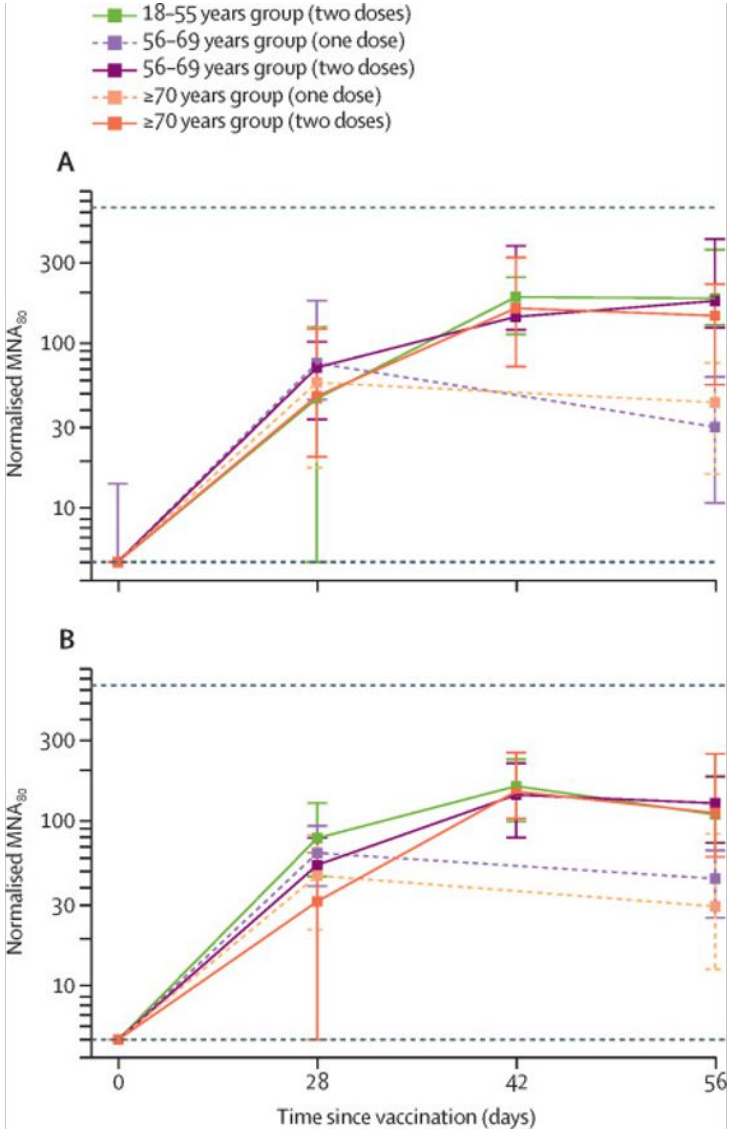


Neutralising antibody titres after prime and boost doses of vaccine in standard-dose groups (A) and low-dose groups (B)(AZ)



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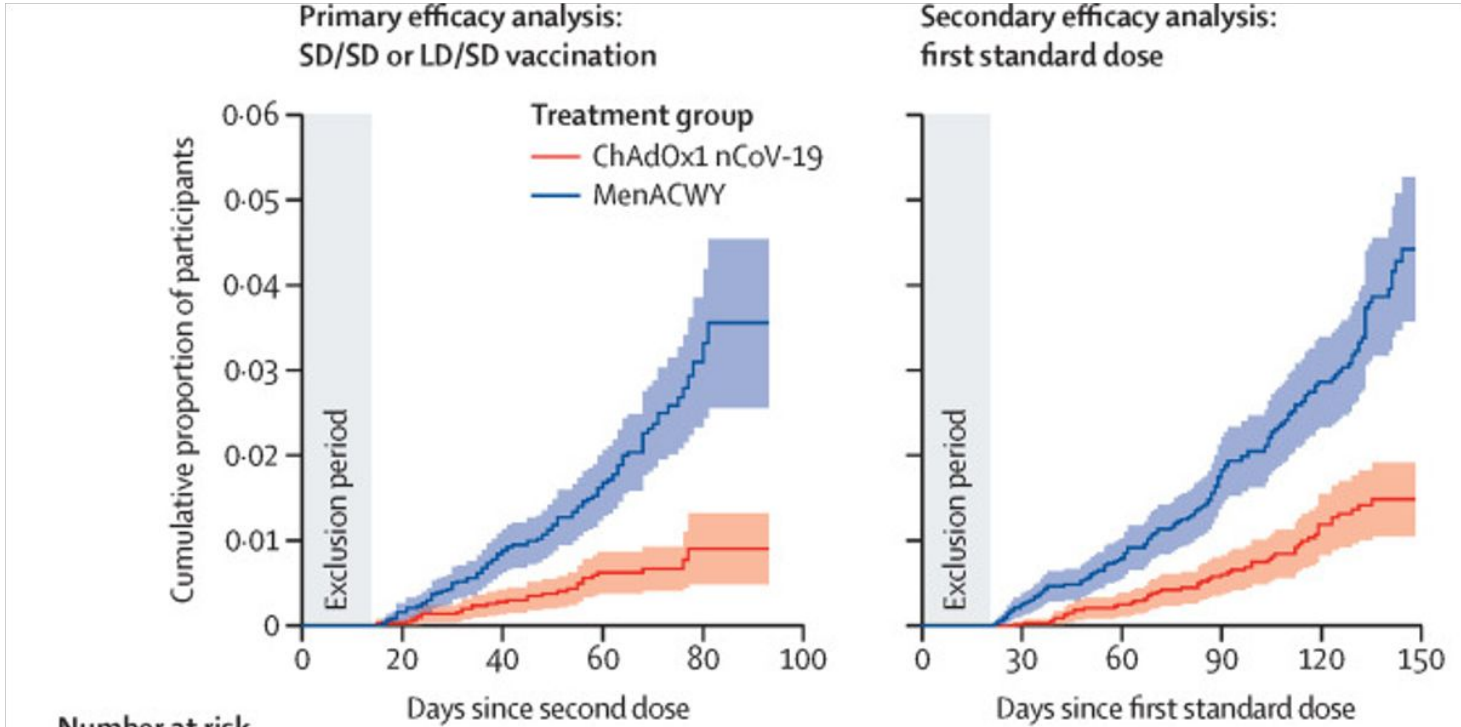
First clinical efficacy results of ChAdOx1 nCoV-19 in a pooled analysis of phase 2/3 trials in the UK and Brazil (AZ)



Number at risk (number censored)												
ChAdOx1 nCoV-19	5807	5639	4779	3181	499	0	6307	5732	4857	3681	2490	0
	(0)	(189)	(1162)	(2620)	(5300)	(5777)	(0)	(645)	(1443)	(2636)	(3811)	(6256)
MenACWY	5829	5657	4765	3146	435	0	6297	5718	4836	3652	2452	0
	(0)	(182)	(1164)	(2636)	(5322)	(5728)	(0)	(639)	(1424)	(2599)	(3760)	(6156)

Vector Vaccines

VACCINE NAME:	**Ad26.COV2.S**
EFFICACY:	**72% in United States, 66% in Latin America, 57% in South Africa**
DOSE:	**1 dose**
TYPE:	**Muscle injection**
STORAGE:	**Up to two years frozen at –4° F (–20° C), and up to three months refrigerated at 36–46° F (2–8° C)**

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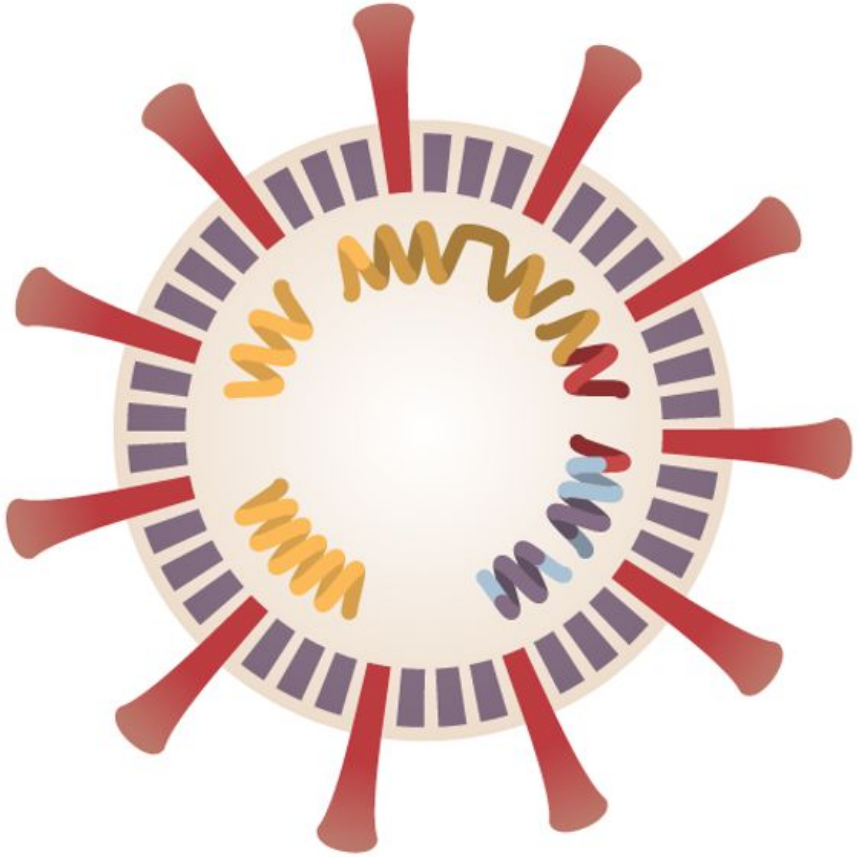
Inactivated Vaccines (Sinovac)

Vaccines created from coronaviruses that have been killed with chemicals.



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Sinopharm

- **BBIBP-CorV**
  EFFICACY: **79.34%**
  DOSE: **2 doses, 3 weeks apart**
  TYPE: **Muscle injection**

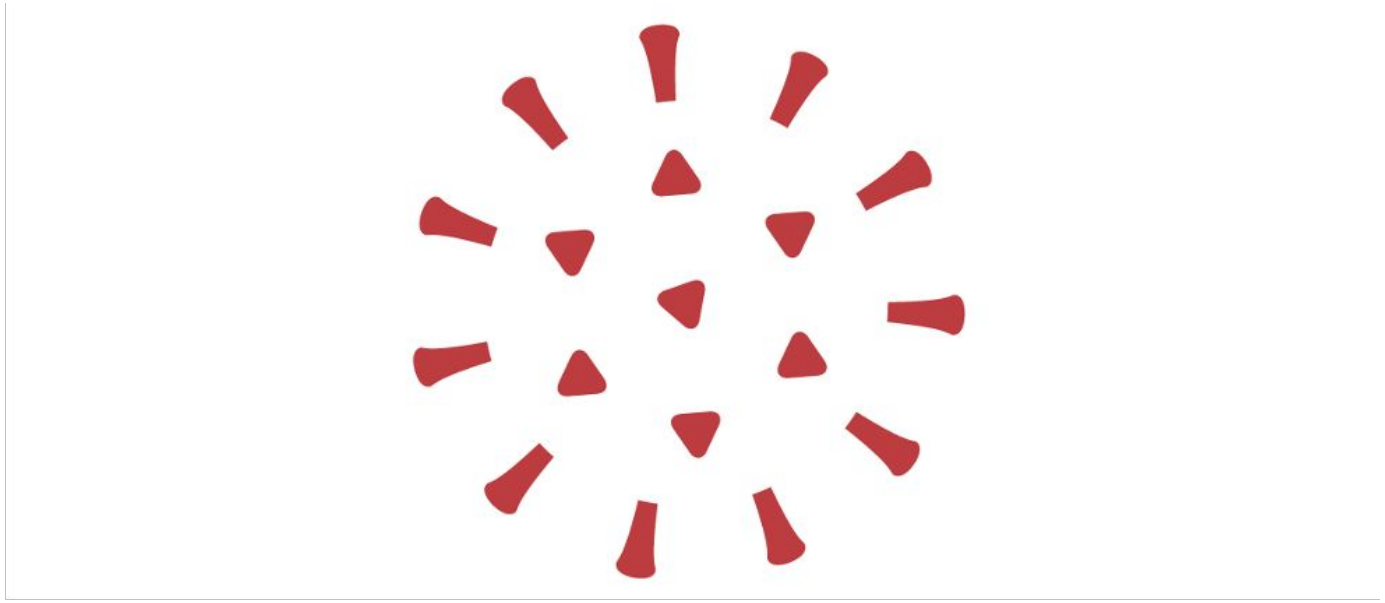
Sinovac

- **CoronaVac (formerly PiCoVacc)**
  EFFICACY: **50.38%**
  DOSE: **2 doses, 2 weeks apart**
  TYPE: **Muscle injection**
  STORAGE: **Refrigerate**

Protein subunit vaccines (Novavax)

- **Protein subunit vaccines** include proteins but not genetic material of the COVID-19 virus. Once vaccinated, our immune system recognizes that the proteins don't belong in the body and begins making T-lymphocytes and antibodies.

Protein subunit vaccines



Each injection includes many spike nanoparticles, along with a compound extracted from the soapbark tree. The compound attracts immune cells to the site of the injection and causes them to respond more strongly to the nanoparticles.

NOVAVAX

Creating Tomorrow's Vaccines Today

VACCINE NAME:	NVX-CoV2373
EFFICACY:	89.3% against most variants
DOSE:	2 doses, 3 weeks apart
TYPE:	Muscle injection
STORAGE:	Stable in refrigerator

Very recent data: efficacy approx 55% in South Africa

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tecnologia	produttore	n dosi	efficacia	efficacia 1 dose	efficacia malattia severa	efficacia in pop anziani	confezione
m RNA	**Pfizer/Biontech**	**2**	**95%**	**52.4%**	**66.4-75%**	**93.7%** *>55 anni*	5-6 dosi fiala
	Moderna	**2**	**94.1%**	**69.5 %**	**42.6 %** *(dopo 1 dose)* **100%** *(dopo 2 dose)*	***86,4%-94.1%*** *(dopo 2 dose >65 anni)*	10 dosi fiala
Vettore virale	**Astra Zeneca**	**2**	**70.4%** *(blended) (62.1% base dose standard)*	**64.1%**			10 dosi fiala
	The Gamaleya National Center	**2**	***91.6%***	**73.1%**	**100%**	**91.8%** >60 anni	5 dosi fiala
	Johonson&Johnson	**1**	***66%***	**66%**	**85%** *dopo 28 giorni 100% su ospedalizzazione dopo 28 giorni*		
	CanSino Bio	**1**	***65.7%***		**90,98%**		
Proteina ricombinante	**Novavax**	**2**	**89.3%**				10 dosi fiala
	Bektop	**2**	**100%???**				
Virus inattivato	**Sinopharm**	**2**	**79.4%**				
	Sinovac	**2**	**59.65%**				

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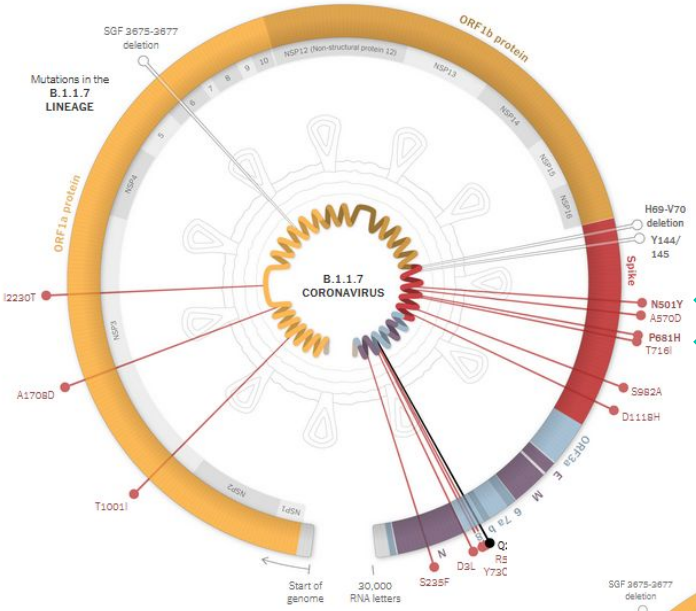
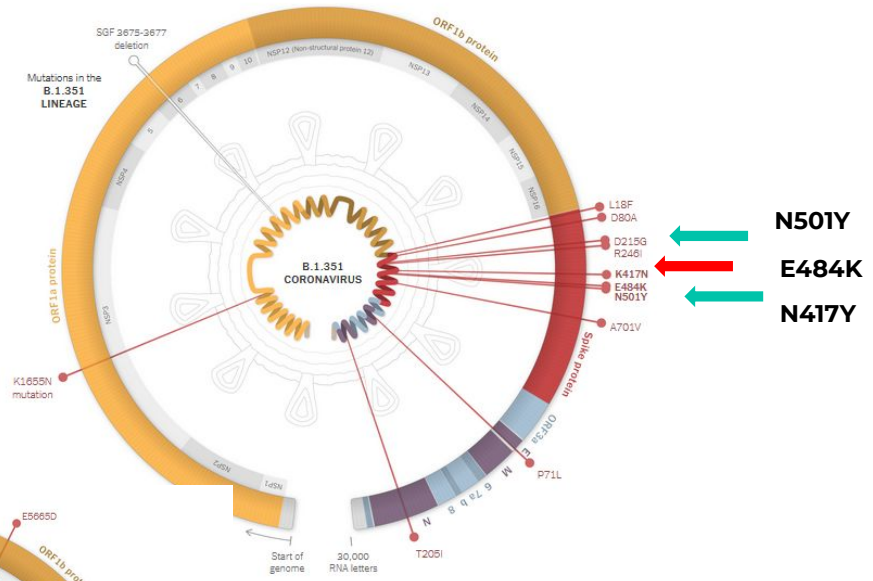
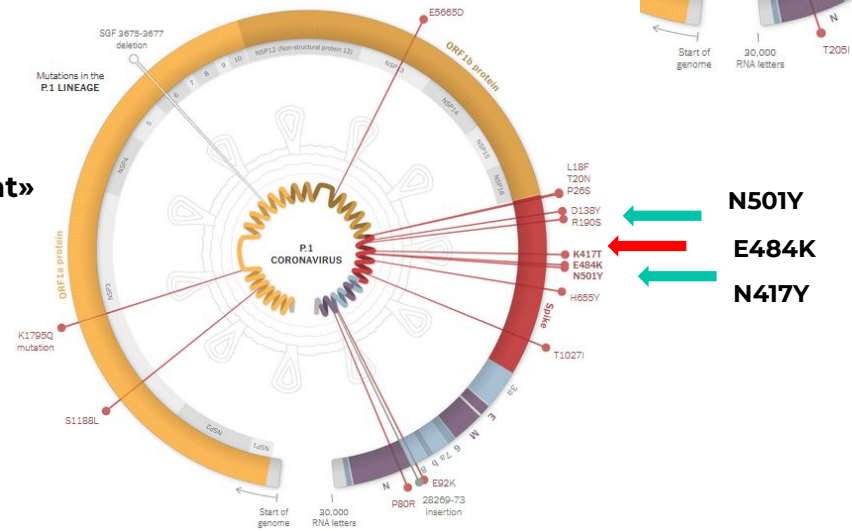
The B.1.1.7 Lineage «UK Variant»



The B.1.351 Lineage »South African variant»



The P.1 Lineage «Brasilian variant»



N501Y and N417 help the virus latch on more tightly to human cells; unlikely to help the virus evade current vaccines

P681H helps infected cells create new spike proteins more efficiently

E484K may help the virus evade some kinds of antibodies

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- **Pfizer vaccine:** studies comparing sera of neutralizing antibody titers from vaccinees show no reduction in neutralization of UK and South African variants.

- **Moderna vaccine:** no significant impact on neutralization against the UK variant. A reduced, but still significant neutralization was measured against the South African variant.

Speed of vaccinations by country

Share of newly vaccinated population by week

COUNTRY	AVG. SINCE VACCINATIONS BEGAN	LAST 7 DAYS	AT THAT RATE, MAJORITY VACCINATED IN ...
Israel	6%	5.2%	4 weeks
United Arab Emirates	3.9%	6.1%	4 weeks
United Kingdom	1.4%	3.7%	3 months
Malta	1.1%	1.9%	6 months
Turkey	1%	0.6%	18 months
United States	1%	1.9%	6 months
Denmark	0.8%	0.2%	55 months
Ireland	0.8%	1%	11 months
Bahrain	0.8%	2.5%	4 months
Spain	0.6%	0.7%	16 months
Slovenia	0.6%	0.3%	34 months
Italy	0.6%	0.2%	59 months
Romania	0.6%	1.2%	9 months
Lithuania	0.6%	0.3%	39 months
Portugal	0.6%	1%	11 months
Estonia	0.5%	0.6%	19 months
Sweden	0.5%	0.7%	17 months
Switzerland	0.5%	1.2%	9 months
Austria	0.5%	0.7%	15 months
Cyprus	0.5%	NA	NA
Czechia	0.5%	0.7%	16 months
Germany	0.4%	0.5%	23 months
Slovakia	0.4%	0.7%	17 months

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