

La Real Academia de Medicina de Zaragoza

celebrará **Sesión Científica**,
el próximo 4 de febrero, jueves, a las 19:30 horas,

Impartirá la conferencia el

Ilmo. Sr. D. Carlos Martín Montañés

Académico de Número

con el título

Investigación y desarrollo de nuevas vacunas contra la COVID-19

Zaragoza, febrero 2021

Sesión telemática que, por el contexto sanitario, se accederá vía Zoom en el enlace:

<https://zoom.us/j/5961643232?pwd=bkE5U0huYW05ZF15b1F6b1dJNzh4Zz09>

INVESTIGACION Y DESARROLLO DE NUEVAS VACUNAS CONTRA LA COVID-19



**Real Academia de Medicina
de Zaragoza**

Carlos Martín Montañés

Jueves 4 de Febrero 2021



Rafael Gómez Lus
Fernando Solsona Motrel





REAL ACADEMIA DE MEDICINA DE ZARAGOZA

La Corporación celebrará Sesión Científica el día **20 de febrero de 2020** (jueves) a las **19.30 horas**, en el Salón de Sesiones de la Real Academia de Medicina, Plaza Paraíso, 4 (Edificio Paraninfo), en la que intervendrá el

DR. D. FERNANDO SIMÓN SORIA

Director del Centro de Coordinación de Alertas
Y Emergencias Sanitarias.
Ministerio de Sanidad.

Pronunciará la conferencia titulada:

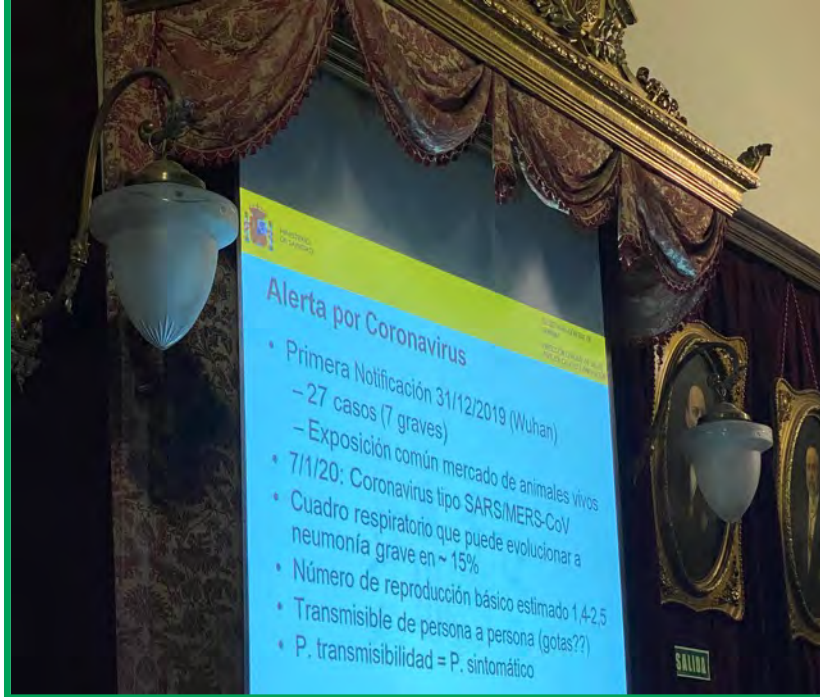
“Cambio global y amenazas sanitarias: ¿estamos preparados?”

Será presentado por el
ILMO. SR. D. FRANCISCO J. CASTILLO GARCÍA
Académico de Número.

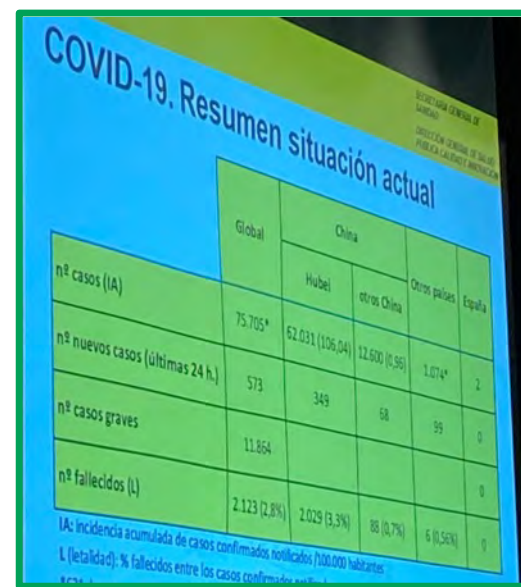
Zaragoza, 6 de febrero de 2020

El Secretario General
MARIANO MATEO ARRIZABALAGA





31 Diciembre 2019 primeros casos Neumonía: SARS en Wuham (China)



75.705 casos, 11.864 graves 2.123 fallecidos (2,8%)

Age Group	Confirmed Cases	Deaths	Case Fatality Rate (%)	Mortality Rate (%)
0-4	0 (0)	0	0	0
5-14	18 (0,1)	0	0	0
15-24	58 (0,2)	0	0	0
25-34	349 (0,1)	0	0	0
35-44	748 (0,2)	0	0	0
45-54	1.071 (0,3)	0	0	0
55-64	1.608 (0,4)	0	0	0
65-74	6.920 (19,2)	28 (0,2)	0,4	0,4
75-79	3.518 (9,8)	70 (0,2)	2,0	2,0
80+	1.408 (3,7)	28 (0,2)	2,0	2,0
Sex				
Male	25.981 (64,4)	60 (0,2)	0,2	0,2
Female	25.891 (68,0)	27 (0,1)	0,1	0,1

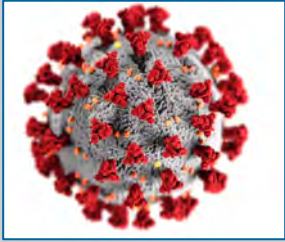
Fuente: Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. CCDC Weekly No. 2020

1-20 años pocos casos Gravedad mayores 60 años

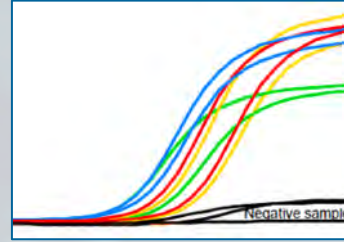


10 Febrero 2020 los casos disminuían

SARS-CoV-2 - COVID-19



SECUENCIACIÓN SARS-COV-2
10 Enero 2020



DIAGNÓSTICO PCR
13 Enero 2020



OMS DECLARA LA PANDEMIA COVID-19
11 Marzo 2020



2020

Febrero 2021

NEUMONÍA WUHAM
8 Diciembre 2019
31 Diciembre
China informa OMS
ENFERMEDAD:
COVID-19

ESPAÑA: 2.9 millones casos COVID-19 más de 60.000 muertes (más de 34 Millones de test diagnósticos)
Aragón: 100.000 casos confirmados 3.000 muertes (más de 600.000 test diagnósticos 14% +)

SARS-CoV-2 - COVID-19



COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins ...



Global Cases

104.389.634

Cases by

Country/Region/Sovereignty

26.554.792 US

10.790.183 India

9.339.420 Brazil

3.882.972 United Kingdom

3.858.367 Russia

3.310.051 France

2.883.465 Spain

2.583.790 Italy

2.501.079 Turkey

Admin0

Last Updated at (M/D/YYYY)

2/4/2021 6:22 a. m.

192

countries/regions

Lancet Inf Dis Article: [Here](#). Mobile Version: [Here](#). Data sources: [Full list](#). Downloadable database: [GitHub](#), [Feature Layer](#).

Lead by [JHU CSSE](#). Technical Support: [Esri Living Atlas team](#) and [JHU APL](#). Financial



Cumulative Cases

Active Cases

Incidence Rate

Case-Fatality Ratio

Testing Rate

+

-

Esri, FAO, NOAA

Global Deaths

2.268.681

450.681 deaths
US

227.563 deaths
Brazil

161.240 deaths
Mexico

154.703 deaths
India

109.547 deaths
United Kingdom

Global Dea...

US State Level

Deaths, Recovered

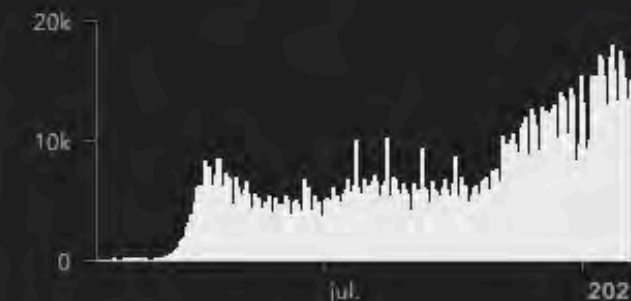
44.148
deaths, **129.378**
recovered

New York US

42.368 deaths,
recovered
California US

38.039
deaths, **2.015.866**
recovered
Texas US

US Deaths,...



Daily Deaths

ESPAÑA: 2.9 millones casos COVID-19 más de 60.000 muertes (más de 34 Millones de test diagnósticos)

Aragón: 100.000 casos confirmados 3.000 muertes (más de 600.000 test diagnósticos 14% +)

HIGIENE, VACUNAS, ANTIBIOTICOS

permiten que hoy podamos vivir en sociedad



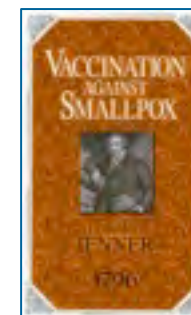
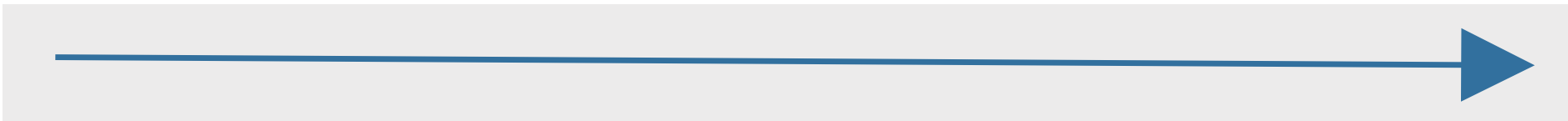
J. Snow Epidemia de Cólera Londres (1854) Broad Street

La HIGIENE:

Ha contribuido enormemente al aumento de la esperanza de vida, saneamiento, agua potable.....

Las VACUNAS:

Controlan las enfermedades infecciosas por largo tiempo sin generar resistencias



E. Jenner (1796) Vacuna viruela . Expedición Vacuna: Distribución Universal (1803-1808)

Los ANTIBIOTICOS:

Generan resistencias, se necesitan nuevos antibióticos.....

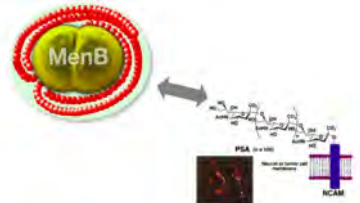


Penicilina (1928)
A. Fleming



Estreptomina (1944)
Waksman /Schatz

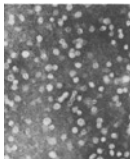
VACUNAS CLÁSICA: Inactivadas, Atenuadas , Subunidades y en los últimos 30 años NUEVAS TECNOLOGÍAS, DNA Recombinante, Vacunas Conjugadas, Vacunología Reversa



Same technology No good for all the problems!
Plosacaride Meningo B is self antigen!
Nort possible use this thecnology

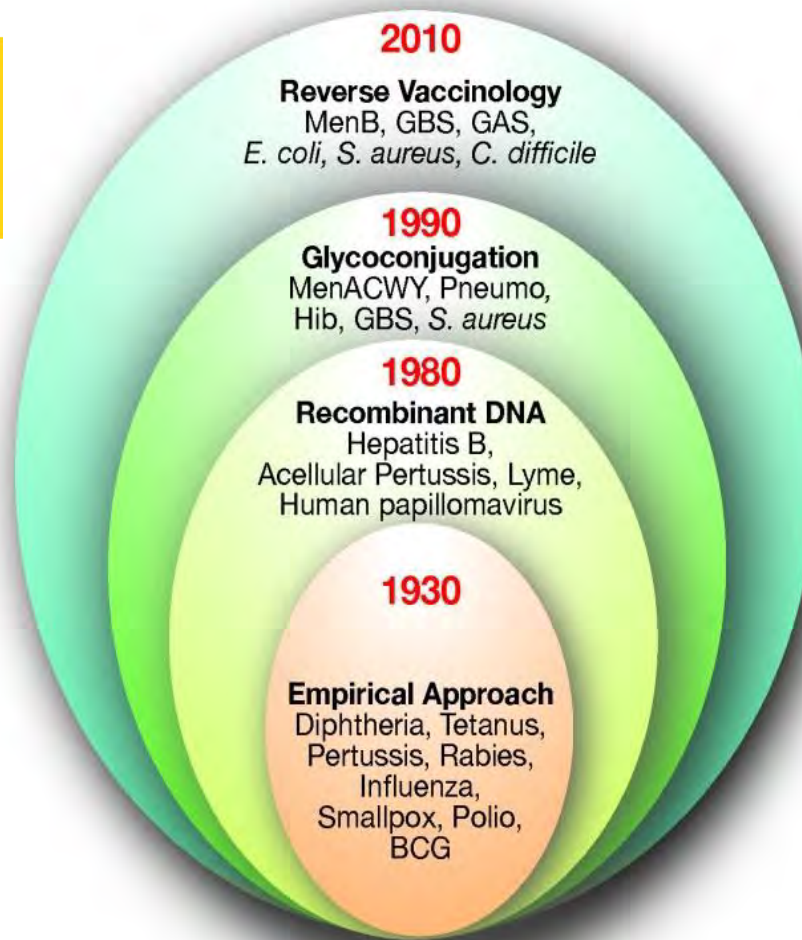
Rino Rappuoli Vaccines, EMI lectures, 2017 UK

Meningococo B⁷



Construcción de un plásmido que expresa HBsAg in levaduras *Saccharomyces cerevisiae*

Hepatitis B¹




Meningococos C y ACWY⁴

***Haemophilus influenzae* tipo b⁴**

Neumococo⁵

VACUNAS CONJUGADAS

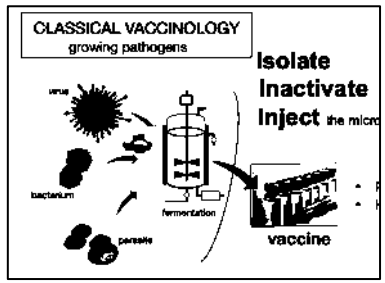
Polisacárido unido a una proteína carrier



Difteria, tétanos y tosferina²

CLASSICAL VACCINOLOGY
growing pathogens

Isolate
Inactivate
Inject the micro



Poliomelitis³

ESPAÑA UNA DE LAS COBERTURAS VACUNALES MAYORES DEL MUNDO



VACUNA	Edad en meses						Edad en años				
	2	4	6	11	12	15	3-4	6	12	14	15-18
Hepatitis B ¹	HB	HB		HB							
Difteria, tétanos y tosferina ²	DTPa	DTPa		DTPa				DTPa/ Tdpa	Tdpa		
Poliomelitis ³	VPI	VPI		VPI				VPI			
<i>Haemophilus influenzae</i> tipo b ⁴	Hib	Hib		Hib							
Neumotoco ⁵	VNC	VNC		VNC							
Rotavirus ⁶	RV	RV	(RV)								
Meningotoco B ⁷	MenB	MenB			MenB						
Meningococos C y ACWY ⁸		MenC			Men ACWY				Men ACWY		
Sarampión, rubeola y parotiditis ⁹					SRP		SRP Var/ SRPV				
Varicela ¹⁰						Var	SRP Var/ SRPV				
Virus del papiloma humano ¹¹								VPH 2 dosis			

<https://vacunasaep.org/>
CALENDARIO VACUNAL 2021

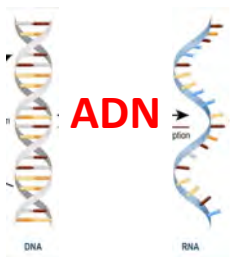
<https://vacunasaep.org/profesionales/calendario-de-vacunaciones-de-la-aep-2021>



NUEVAS TECNOLOGIAS



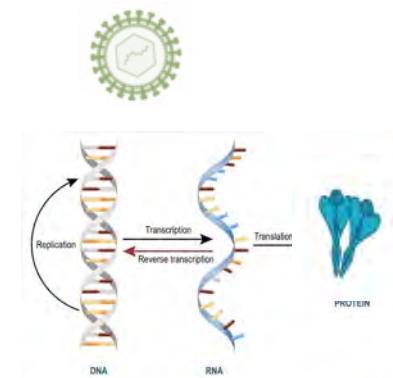
ACIDOS NUCLEICOS



ADN ARN

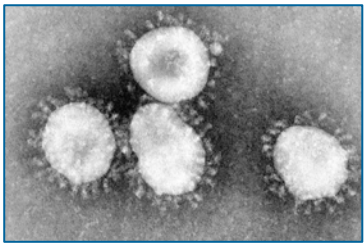
NO EXISTÍAN VACUNAS
LICENCIADAS PARA HUMANOS

VECTORES VIRALES



VIRUS RECOMBINANTES : POXVIRUS (*Vaccinia*) , ADENOVIRUS
ESTOMATITIS,(EBOLA)
NO USO EN VACUNAS DEL CALENDARIO VACUNAL (EBOLA)

NUEVOS ADYUVANTES

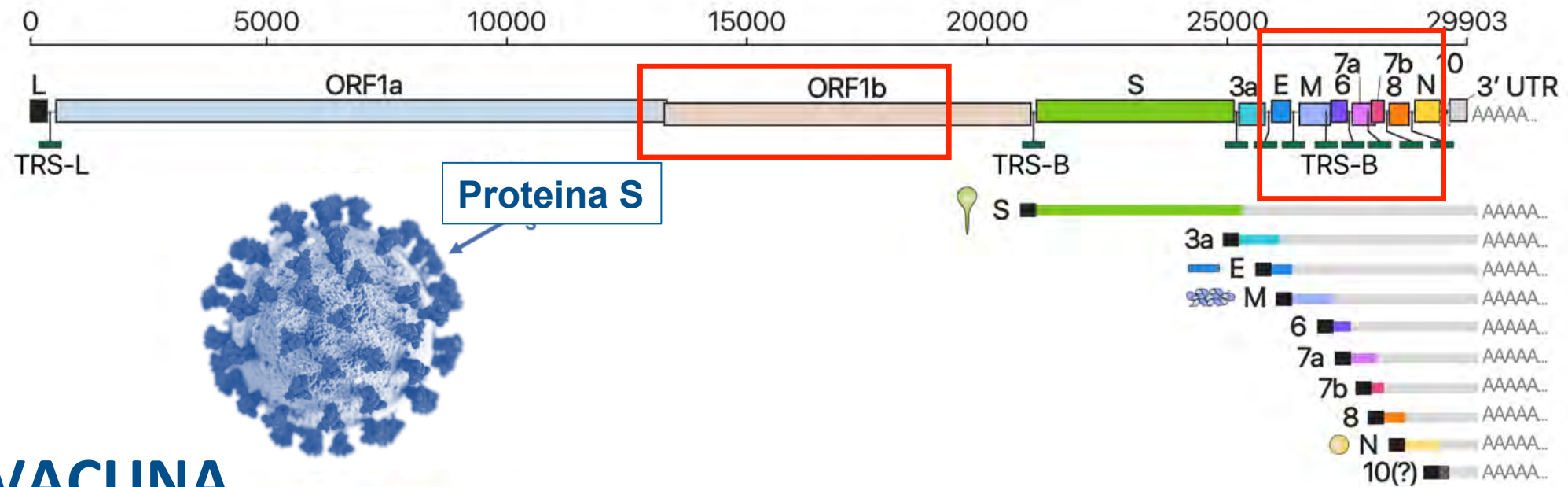


VACUNAS COVID-19 INVESTIGACIÓN DESARROLLO CLÍNICO: COMPOSICIÓN DEL VIRUS SARS-COV-2

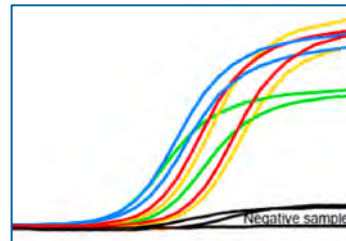
The Architecture of SARS-CoV-2 Transcriptome. Kim et al *Cell* 2020



ARN+



VACUNA

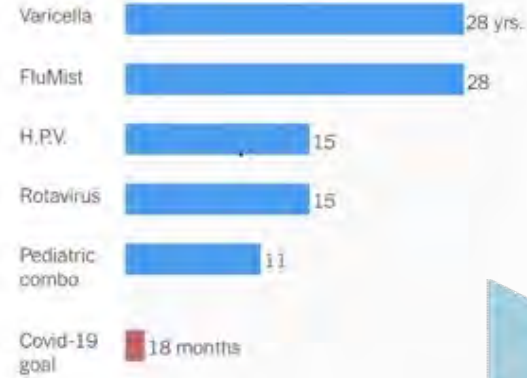


DIAGNÓSTICO POR PCR

DESARROLLO DE UNA NUEVA VACUNA: Media 15-20 años (800-1.000 M\$)

Years and years, at minimum

The vaccine development process has typically taken a decade or longer.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINE HEALTH

CENTENAS DE CANDIDATOS

CLINICA



R&D

PRECLINICA

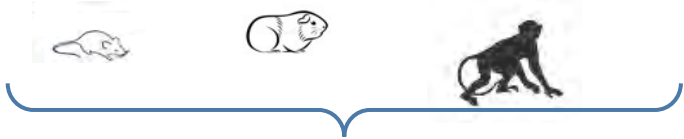
FASE I
SEGURIDAD

FASE II
INMUNIDAD
(seguridad)

FASE III
EFICACIA
(seguridad)

LICENCIA DE USO
FDA, EMA, AEMPS

FASE IV
FARMACO-VIGILANCIA
Seguridad



5-10 años

DECENAS



5 años

CENTENAS



X 10

5 años

MILES



X 100

MILLONES



1.5 años EBOLA



World Health Organization



VACUNAS COVID-19 MAS AVANZAS EN FASE 3 (EFICACIA)



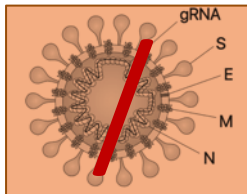
ACIDOS NUCLEICOS (ARN): Pfizer-Biontech, Moderna, CureVac
USA, Alemania



VECTORES VIRALES: Oxford-Astra Zeneca: UK, J&J: USA,
Gamaleya: Rusia, CanSino: China



SUBUNIDAD PROTEICA: Novavax: USA, Sanofi: Francia



INACTIVADAS SARS-CoV-2: Sinopharm, Sinovac: China, Bharat: India



Los equipos o tecnologías de la carrera de las vacunas



Virus inactivado team

Se expone a nuestras células a una versión del virus muerta o que no permite enfermar.



Vector viral team

Se usa otro virus (de catarro, normalmente) para introducir en el cuerpo instrucciones del SARS-CoV2.



ARN o ADN team

Se da a las células el ARN o ADN para fabricar virus o un trozo de él, sin los elementos peligrosos.



Proteína o subunidad team

Se fabrican fuera del organismo partes víricas que quizás sirvan para alertar a las defensas.

Está por verse que funcione en humanos



SINOVAC



AstraZeneca



Sputnik V



Pfizer BIONTECH

moderna



NOVAVAX

Fuente: OMS, Candidatas a vacuna en fase 3, a 3 de noviembre

MARIO VICIOSA: <https://www.newtral.es/escapados-peloton-y-excesos-en-la-carrera-de-la-vacuna-de-covid-19/20200517/>

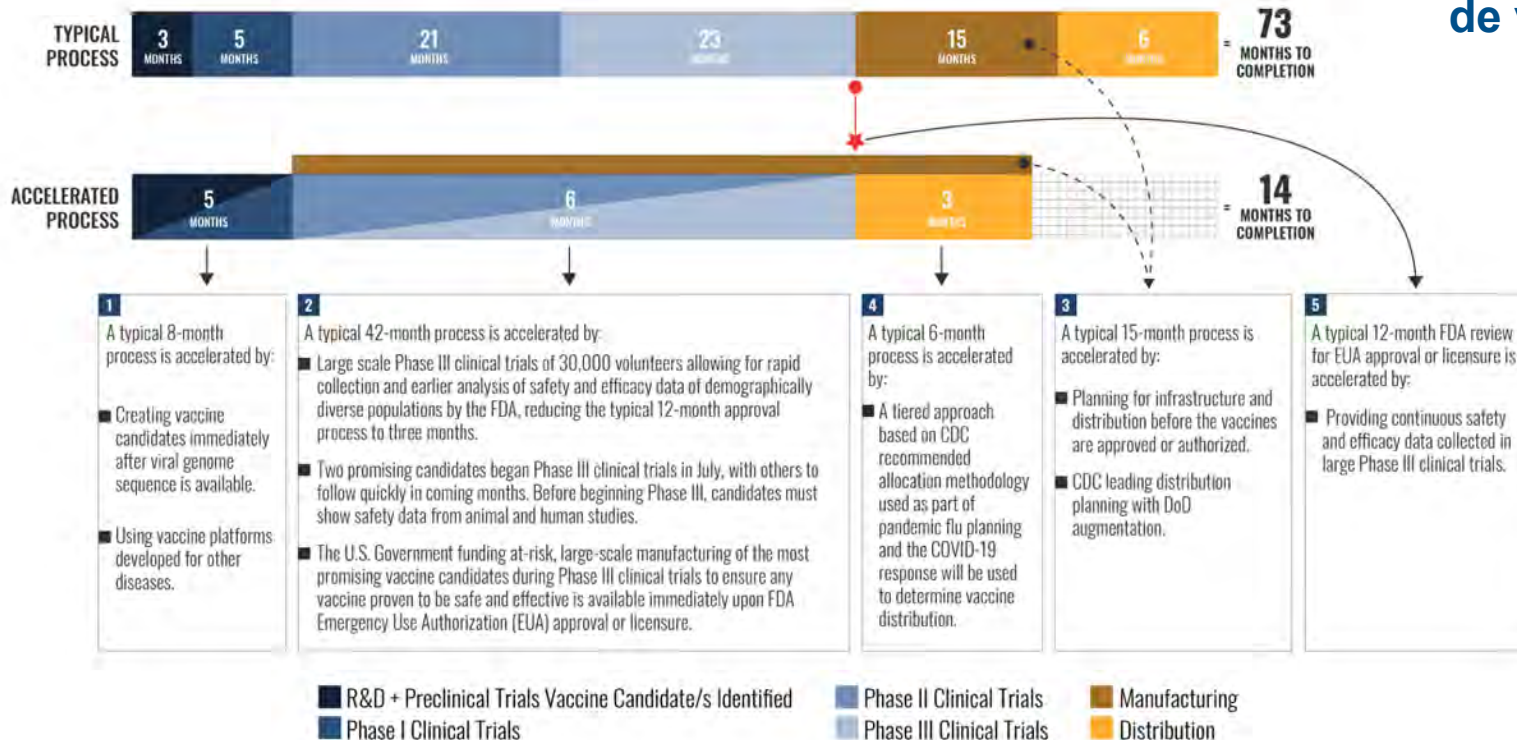
ESTRATEGIA OCCIDENTE

Para el Desarrollo de una Nueva Vacuna contra SARS-CoV-2



OPERATION WARP SPEED ACCELERATED VACCINE PROCESS

MISSION: Deliver 300 million doses of safe and effective vaccine by 1 January 2021.



En Estados Unidos, la administración Trump concedió **10.800 Millones de dólares** “Operation Warp Speed” para acelerar la I+D de vacunas COVID-19

6 VACUNAS FINALISTAS:

2 ARN

2 VECTORES VIRALES

2 SUBUNIDADES PROTEINA

NUEVAS TECNOLOGÍAS

Grandes Compañías Farmacéuticas

(Big Pharma)



**ACIDO NUCLEICO:
ARNm (S)**



<p>Pfizer / BioNTech</p> <p>USA Germany</p>	<p>Comirnaty mRNA that encodes for SARS-CoV-2 spike protein.</p>	<p>mRNA</p>	<p>Pfizer (\$500M) USG (\$1.9M) Warp Speed Finalist</p>	<p>Ph. I/II ongoing: 456/Germany Ph. II planned: 960/China Ph. II/III ongoing: 44K US +5 Authorization: EUA in EU, US, +9; WHO Emergency Validation Approval: Bahrain, Saudi Arabia, Switzerland</p>
<p>Moderna</p> <p>USA</p>	<p>mRNA-1273 Synthetic messenger RNA that encodes for SARS-CoV-2 spike protein.</p>	<p>mRNA</p>	<p>USG (\$2.48B) CEPI/GAVI (Undisclosed) Warp Speed Finalist COVAX Portfolio</p>	<p>Ph. I ongoing: 155/US Ph. II ongoing: 600/US; 3000/US (planned) Ph. III ongoing: 30,000/US Authorization: EUA in Canada, EU, Israel, US Approval: None</p>

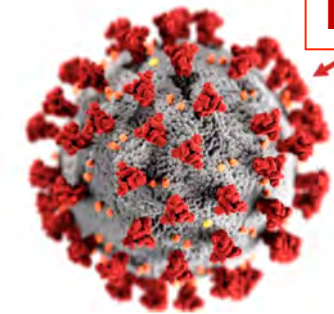
**6 FINALISTAS
WARP SPEED
“Velocidad de la Luz”**

**VECTOR VIRAL :
ADENOVIRUS
(gen S)**



<p>U. of Oxford AstraZeneca</p> <p>UK</p>	<p>AZD1222 Chimpanzee Adeno vector expressing SARS-CoV-2 spike protein.</p>	<p>Viral vector</p>	<p>USG (\$1.2B) CEPI/GAVI (\$750M) EU (\$923M) Warp Speed* Finalist COVAX** Portfolio</p>	<p>Ph. I/II ongoing: Japan, Kenya, RSA, UK Ph. II/II ongoing: 12,390 vols/UK; 1700/India Ph. III ongoing: 40K /US+; 10K/Brazil Authorization: EUA in Argentina, India, UK Approval: None</p>
<p>Johnson & Johnson</p> <p>USA</p>	<p>JNJ-78436735 Ad26 vector expressing SARS-CoV-2 spike protein.</p>	<p>Viral vector</p>	<p>J&J investment (~\$500M) USG (\$1.45B) Warp Speed Finalist</p>	<p>Ph. I and I/II ongoing: 250/Japan; 1045/Belgium, US Ph. II ongoing: 550/Germany, Netherlands, Spain Ph. III ongoing: 30K (2 dose)/France, Germany, RSA+6; 60K(1 dose)/Argentina, Brazil, Chile+7</p>

**5 Hoy en Fase 3 de
Eficacia**



Proteína S

**PROTEÍNA “S”
/ ADYUVANTE**



<p>Novavax</p> <p>USA</p>	<p>NVX-COV2373 Full-length recombinant SARS-CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M.</p>	<p>Protein Subunit</p>	<p>CEPI (\$388M) USG (\$1.6B) Warp Speed Finalist COVAX Portfolio</p>	<p>Ph. I ongoing: 130/Australia Ph. II ongoing: 2900/ RSA Ph. III ongoing: 15,000/ UK; 30K/US, Mexico</p>
<p>Sanofi / GSK</p> <p>France</p>	<p>DNA from the surface protein of the SARS-CoV-2 virus is inserted into insect cells, which express antigen that is then purified and combined with GSK's pandemic AS03 adjuvant.</p>	<p>Subunit</p>	<p>USG (\$2.1B) Warp Speed Finalist</p>	<p>Ph. I/II ongoing: 440/US Ph. III planned: 30K/US+ (Delayed)</p>



The push for a COVID-19 vaccine

Credits +

CEPI



COVAX: colaboración para un acceso equitativo mundial a las vacunas contra la COVID-19

CEPI: The Coalition for Epidemic Preparedness Innovations

COVID-19 current vaccine clinical development pipeline – confirmed commencement of dosing

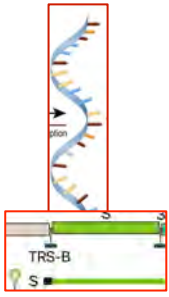


	Phase I	Phase I/II	Phase II	Phase II/III	Phase III		
 Viral vectors	Shenzhen GIMI - aAPC	Merck – TMV-083	Shenzhen GIMI - LV		Gamaleya rAd5, rAd26 ³	AstraZeneca AZD1222	
	ReiThera Srl - GRAd-COV2	Wantai / U.HK LAIV DelNS1 ¹				Cansino Ad5 ²	Janssen Ad26.COV2-S
 RNA		Walvax Biotech mRNA	Imperial saRNA	CureVac CVnCoV	Moderna mRNA-1273	Pfizer BNT162	
			Arcturus ARCT-021				
 DNA			Genexine GX-19	Inovio INO-4800			
			Osaka / AnGes - AG0301	Cadila ZyCoV-D			
 Protein-based	VLP Medicago	Sichuan RBD	Vaxine Covax-19	FBRI SRC EpiVacCorona	SpyBio / SII VLP-Spycatcher	Anhui Zhifei Recombinant	
	Queensland Sclamp	Clover SCB-2019	Finlay Soberana 01	Sanofi / GSK VLP-Spycatcher		Novavax NVX-CoV2373	
 Inactivated			IMB CAMS			CNBG, WIBP ⁴	Sinovac Biotech
						CNBG, BIBP ⁴	Bharat BBV 152

¹ Distinct from CEPI-funded programme
² Cansino has been approved for military use in China
³ Gamaleya (rAd5, rAd26) has been conditionally registered in Russia.
⁴ Emergency use approval in China and UAE

The Coalition for Epidemic Preparedness Innovations (CEPI)
 global partnership launched in 2017 to develop vaccines to stop future epidemics
 New vaccines for a safer world





VACUNAS COVID-19 ACIDOS NUCLEICOS ARN: ARN mensajero

Proteína "S" de SARS-CoV-2:

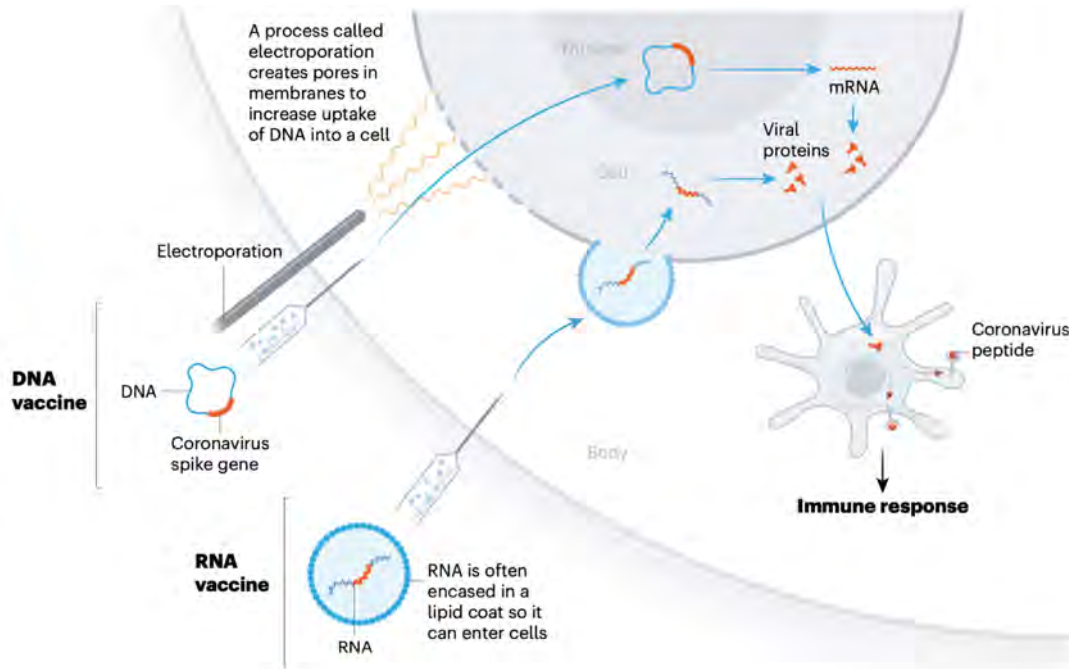
2 CANDIDATOS FASE 3: Aprobados Uso Emergencia FDA y EMA

ARNm prot "S"

NUCLEIC-ACID VACCINES

At least 20 teams are aiming to use genetic instructions (in the form of DNA or RNA) for a coronavirus protein that prompts an immune response. The nucleic acid is inserted into human cells, which then churn out copies of the virus protein; most of these vaccines encode the virus's spike protein.

RNA- and DNA-based vaccines are safe and easy to develop: to produce them involves making genetic material only, not the virus. But they are unproven: no licensed vaccines use this technology.



 	BNT162b2 <i>mRNA that encodes for SARS-CoV-2 spike protein.</i>	mRNA (x4)
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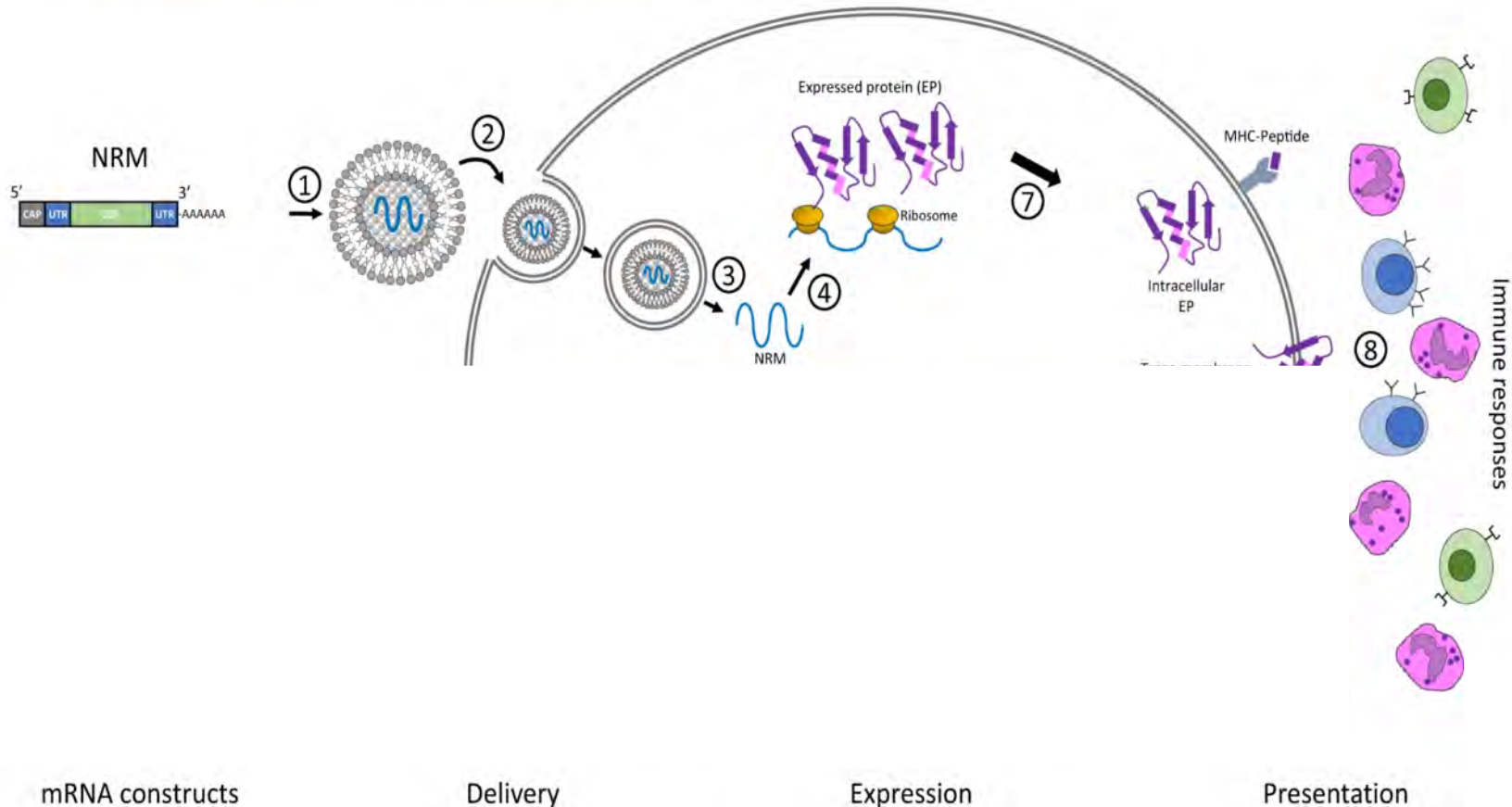
 	mRNA-1273 <i>Synthetic messenger RNA that encodes for SARS-CoV-2 spike protein.</i>	mRNA
------	---	----------

 	CVnCoV <i>mRNA vaccine that encodes for the spike protein formulated with lipid nanoparticles.</i>	mRNA 	CEPI (\$8.3M) EU (\$\$421M) USG. (Undisclosed) COVAX Portfolio	Ph. I ongoing: 284/Belgium, Germany Ph. II ongoing: 691/Panama, Peru
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VACUNAS COVID-19 ACIDOS NUCLEICOS ARNm

From: The promise of mRNA vaccines: a biotech and industrial perspective



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ARN induce una fuerte respuesta celular inmunogénica

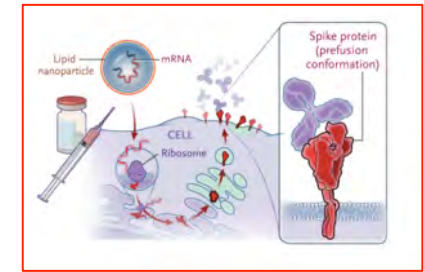
Investigación básica anterior: [Kariko y col. \(2008\)](#) y [Durbin y col. \(2016\)](#),

Nucleósidos modificados
 1-metil-3'-pseudouridina
No inducen respuesta inmunogénica contra el RNA

Además aumenta la capacidad de traducción!!

Jackson *et al.* The promise of mRNA vaccines: a biotech and industrial perspective. *npj Vaccines* 5, 11 (2020). <https://doi.org/10.1038/s41541-020-0159-8>

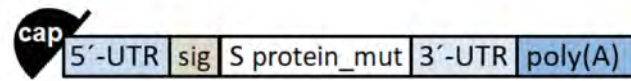
VACUNAS COVID-19 ACIDOS NUCLEICOS ARNm



NEJM Polack et al Dic 2020

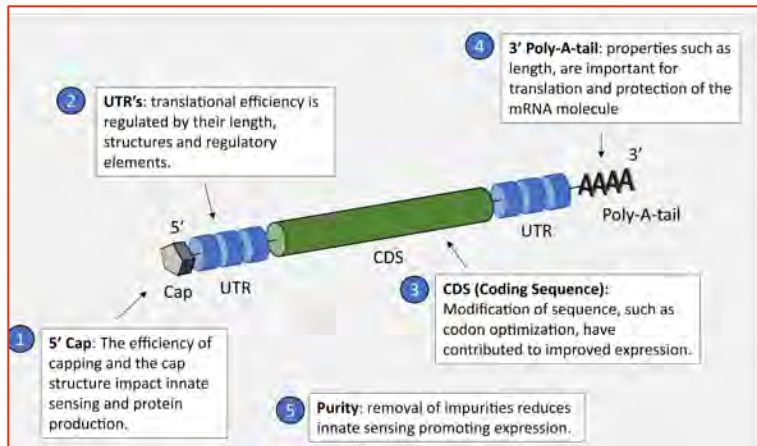
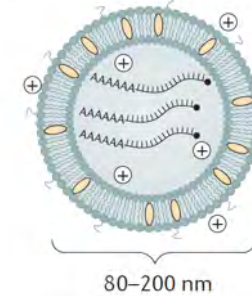
Messenger RNA encoding the full-length SARS-CoV-2 spike glycoprotein.

Schematic

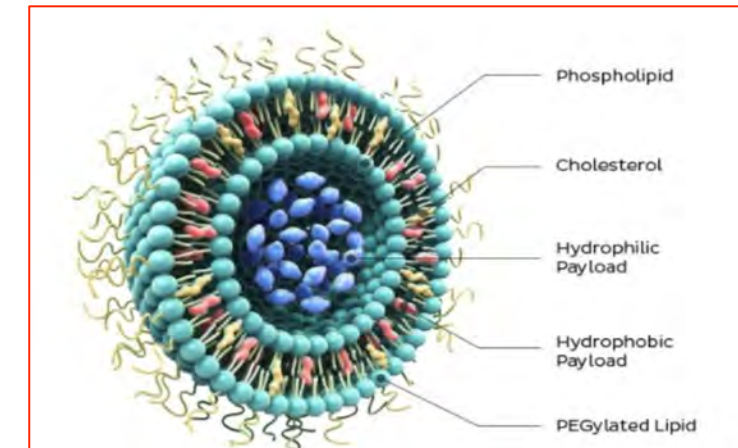


UTR = Untranslated region; sig = extended signal sequence of the S glycoprotein; S protein_mut = S glycoprotein sequence containing mutations K986P and V987P; poly(A) = polyadenylate signal tail.

Cationic lipid, cholesterol, PEG nanoparticle



Secuencia original
1273 Aminoácido codifica glicoproteína S
K (lisina) y V (valina) se mutaron a P (prolina)
conformación de la proteína S
antigenicidad óptima
[Wrapp y col. \(2020\).](#)



CONSTRUCCION mRNA:
 Traducción a Proteína S

CONFIGURACIÓN OPTIMA
 Proteína S

Administración
 LIPOSOMAS

	Comirnaty mRNA that encodes for SARS-CoV-2 spike protein. *** **	mRNA 	Pfizer (\$500M) USG (\$1.9M) Warp Speed Finalist	Ph. I/II ongoing: 456/Germany Ph. II planned: 960/China Ph. II/III ongoing: 44K US +5 Authorization: EUA in EU, US, +9; WHO Emergency Validation Approval: Bahrain, Saudi Arabia, Switzerland
---	---	--	--	--

	mRNA-1273 Synthetic messenger RNA that encodes for SARS-CoV-2 spike protein. *** **	mRNA 	USG (\$2.48B) CEPI/GAVI (Undisclosed) Warp Speed Finalist COVAX Portfolio	Ph. I ongoing: 155/US Ph. II ongoing: 600/US; 3000/US (planned) Ph. III ongoing: 30,000/US Authorization: EUA in Canada, EU, Israel, US Approval: None
--	--	--	--	---

BNT162B2 (Comimnaty) DE BIONTECH Y PFIZER

NEJM Polack et al <http://doi.org/10.1056/NEJMoa2034> Dec 2020

AUTORIZACIÓN EUA: FDA 14 Dic 2020

EMA: 21 DICIEMBRE 2020



MRNA-1273 DE MODERNA

NEJM Baden et al. <http://doi.org/10.1056/NEJMoa2035389> Dec 2020

AUTORIZACIÓN EUA: FDA 19 Dic 2020

EMA: 6 ENERO 2021

2 dosis, 21 días días intervalo (30 µg)

(-80°C)

1:1 randomización placebo

n= 43.538 participantes (+38.955 recibieron 2 dosis)

95% eficacia (+94% >65yrs)

(basados en 170 casos) 8 casos en vacunados

Target: 162 cases 7 días 2nd dosis

Seguridad : Similar ambos grupos 4 Meses

DURACIÓN ESTUDIO: 2 AÑOS

2 dosis, 28 días intervalo (100 µg)

(-20°C)

1:1 randomización placebo

n = 30.420 participantes(15.210 recibieron 2 dosis)

94.1% eficacia

(basada en 185 casos) 11 casos en vacunados

Target: 151 cases 14 días 2nd dosis

Seguridad : Similar ambos grupos 4 Meses

DURACIÓN ESTUDIO: 2 AÑOS

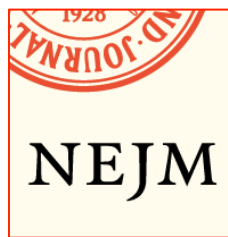
BIONTECH **Pfizer**

Comirnaty
mRNA that encodes for SARS-CoV-2 spike protein.

mRNA

Pfizer (\$500M)
USG (\$1.9M)
Warp Speed Finalist

Ph. I/II ongoing: 456/Germany
Ph. II planned: 960/China
Ph. III ongoing: 44K US +5
Authorization: EUA in EU, US, +9; WHO
Emergency Validation
Approval: Bahrain, Saudi Arabia, Switzerland



moderna

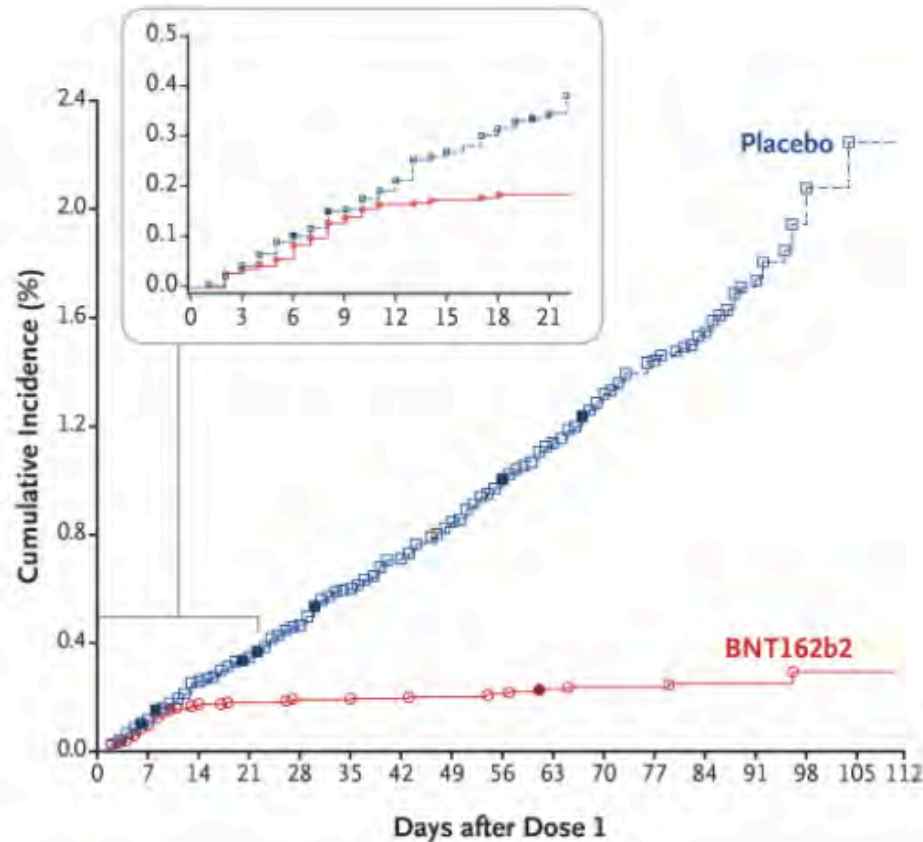
mRNA-1273
Synthetic messenger RNA that encodes for SARS-CoV-2 spike protein.

mRNA

USG (\$2.48B)
CEPI/GAVI (Undisclosed)
Warp Speed Finalist
COVAX Portfolio

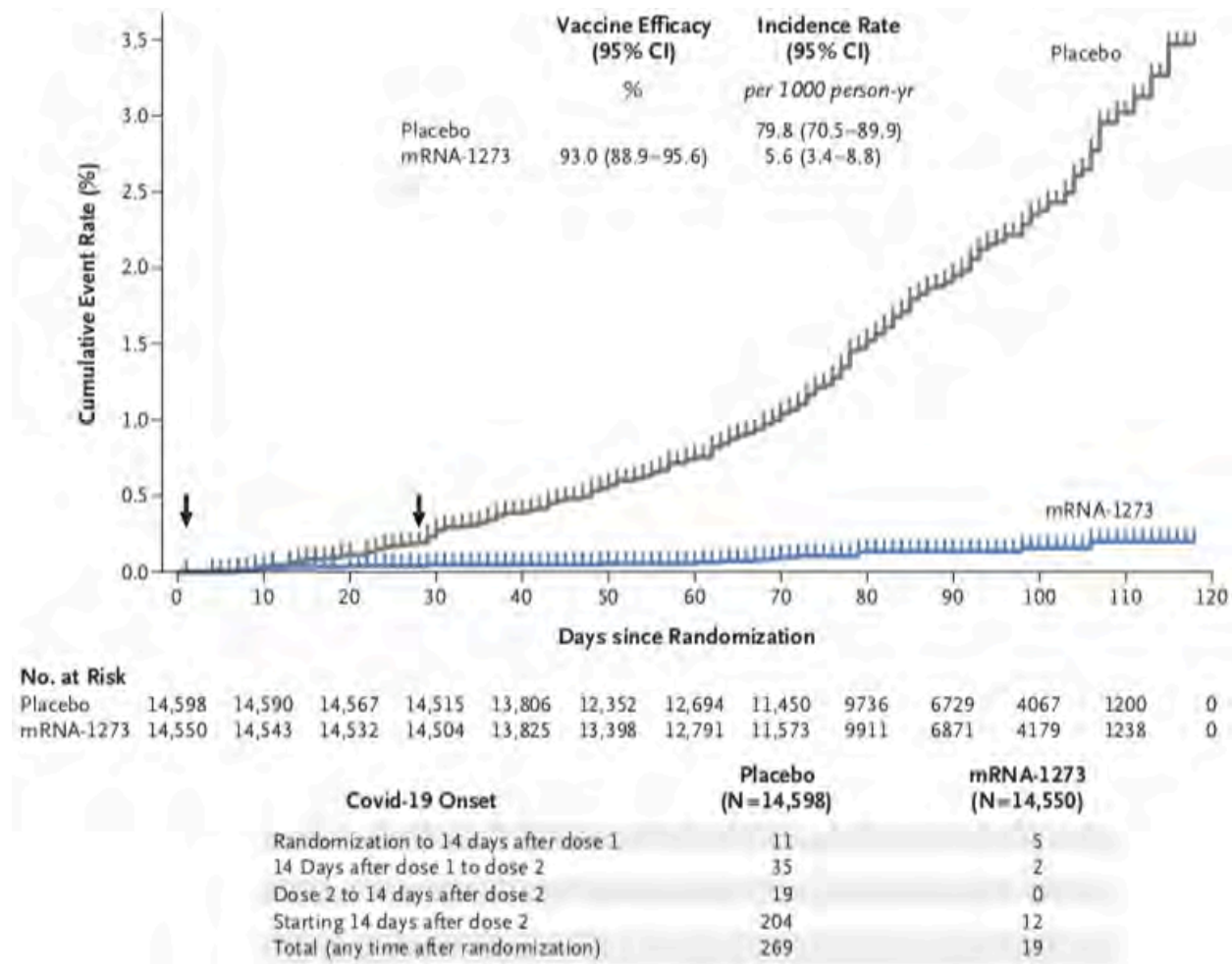
Ph. I ongoing: 155/US
Ph. II ongoing: 600/US; 3000/US (planned)
Ph. III ongoing: 30,000/US
Authorization: EUA in Canada, EU, Israel, US
Approval: None

BNT162B2 (Comirnaty) DE BIONTECH Y PFIZER



Efficacy of BNT162b2 against Covid-19 after the First Dose.

MRNA-1273 DE MODERNA



Cumulative incidence of Covid-19 events

Microbial dispersal in wildfire smoke p. 1408

Quantum advantage with light p. 1460

Alpine plants and herbivores in a changing climate p. 1469

Science

\$15
18 DECEMBER 2020
SPECIAL ISSUE
sciencemag.org

AAAS

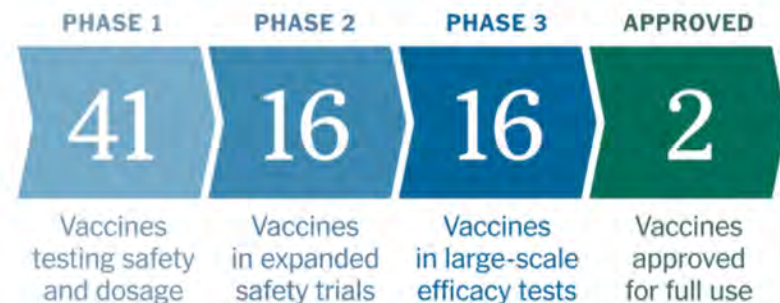


INVESTIGACION Y DESARROLLO: VACUNAS COVID-19 MAYOR AVANCE DE LA CIENCIA AÑO 2020

Coronavirus Vaccine Tracker

A look at all the vaccines that have reached trials in humans.

Coronavirus vaccines in human trials:



31 Enero 2021 The world has now administered almost as many vaccine shots as confirmed covid-19 infections, ~100 M ! Only 7.700 M to go! @EricTopol

Publicado en *Comité Asesor de Vacunas de la AEP* (<https://vacunasaep.org>)

25 noviembre 2020

Fuente: Ministerio de Sanidad

El Ministerio de Sanidad da a conocer la estrategia de vacunación frente a la covid

Vacunas de la covid incluidas en la estrategia europea		
Plataforma	Tipo	Fabricante
Vector viral no replicante (adenovirus) que vehiculiza la proteína S	Adenovirus de chimpancé	AstraZeneca / Oxford
	Adenovirus humano 26	J&J / Janssen
ARNm	ARNm que codifica la proteína S en una nanopartícula lipídica	BioNTech / Pfizer
		Moderna
		Curevac
Vacuna inactivada (Vacuna Subunidad)	Proteína S con adyuvante AS03	Sanofi / GSK
	Nanopartícula con proteína S y adyuvante Matrix	Novavax



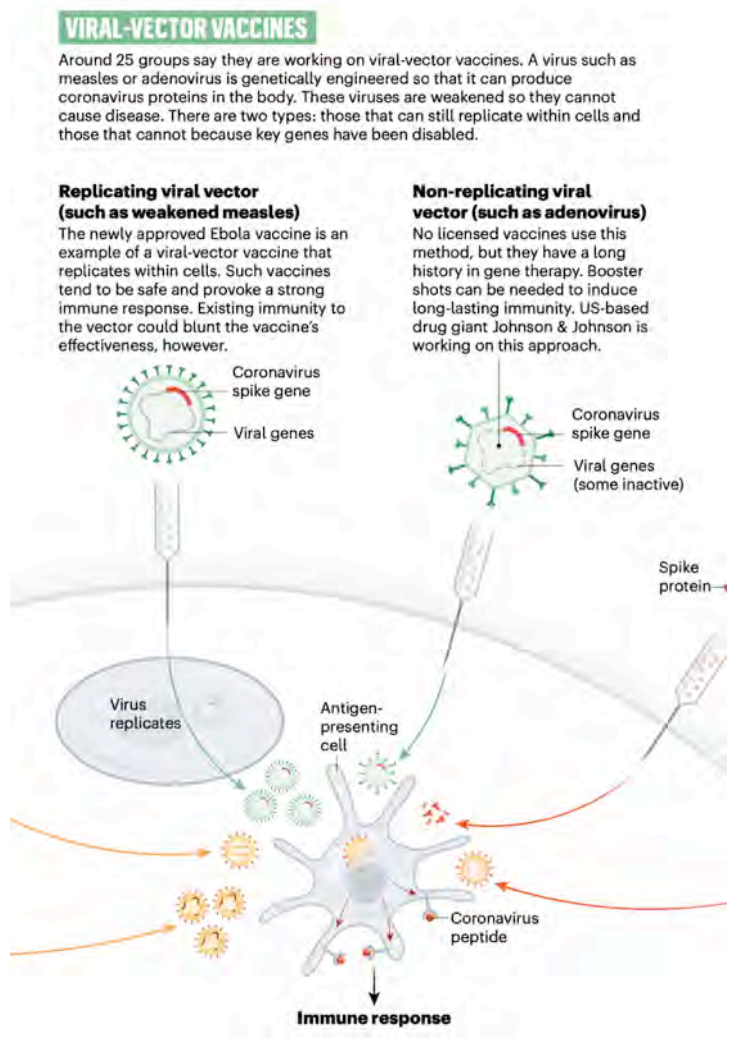
La Unión Europea ya ha firmado contratos de compra anticipados con AstraZeneca/Oxford, BioNTech/Pfizer, J&J/Janssen y Sanofi/GSK, un acuerdo previo con Curevac y está en negociación con Moderna y Novavax.



VACUNAS COVID-19 VECTORES VIRALES: ADENOVIRUS gen que codifica **PROTEÍNA S** de SARS-CoV-2: 4 CANDIDATOS FASE 3

Adenovirus

Gen proteína "S"



VIRAL-VECTOR VACCINES

Around 25 groups say they are working on viral-vector vaccines. A virus such as measles or adenovirus is genetically engineered so that it can produce coronavirus proteins in the body. These viruses are weakened so they cannot cause disease. There are two types: those that can still replicate within cells and those that cannot because key genes have been disabled.

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.

	AZD1222 Chimpanzee Adeno vector expressing SARS-CoV-2 spike protein.	Viral vector
--	--	--------------



ChAdOx1
CHIMPANCE RECOMBINANTE

10^{11} viral particles vector rChAd / 2 dosis

	Sputnik V Combination Ad5 and Ad26 vector expressing the SARS-CoV-2 spike glycoprotein.	Viral vector
--	---	--------------



rAd5 / rAd26
HUMANO RECOMBINANTE

10^{10} viral particles VECTORES rAd5 / rAd26
2 dosis

	JNJ-78436735 Ad26 vector expressing SARS-CoV-2 spike protein.	Viral vector
--	---	--------------



rAd26
HUMANO RECOMBINANTE

5×10^{10} viral particles rAd26 / 1 dosis

	Convidecia Ad5 vector expressing SARS-CoV-2 spike glycoprotein.	Viral vector
--	---	--------------



rAd5
HUMANO RECOMBINANTE

x viral particles rAd26 / 2 dosis

	<p>AZD1222 Chimpanzee Adeno vector expressing SARS-CoV-2 spike protein.</p> 	<p>Viral vector</p> 
---	--	---

VECTOR VIRAL: ADENOVIRUS ChAdOx1

CHIMPANCE RECOMBINANTE gen que codifica **PROTEÍNA S**



Ph. I/II ongoing: Japan, Kenya, RSA, UK
Ph. II/II ongoing: 12,390 vols/UK; 1700/India

Ph. III ongoing: 40K /US+; 10K/Brazil

Authorization: EUA in Argentina, India, UK

Approval: None


Immunogenicity: Ph. III interim analysis shows vaccine was safe and well-tolerated, efficacy averaged 70.4% (62 - 90% depending on dose).

Manufacturing/delivery: Adeno vector vaccines can be manufactured quickly and at scale (capacity to produce 2B doses has been secured).

Platform history: Vaccine utilizing the Ad26 platform (Ad26.ZEBOV) has been approved for use against Ebola Virus Disease.



<https://vacunasaep.org/profesionales/noticias/covid-vacunas-vector-viral-ChAdOx1-Oxford-AstraZeneca>

 	<p>Sputnik V Combination Ad5 and Ad26 vector expressing the SARS-CoV-2 spike glycoprotein</p> 	<p>Viral vector</p> 
--	--	---

Ph. I complete: 38/Russia; 38/Russia
Ph. II/III planned: 1600/India
Ph. III ongoing: 40K/Russia
Ph. III planned: 100/Belarus; 1000/UAE; 2000/ Venezuela
Authorization: EUA in Argentina; Early/limited use in Belarus, Russia
Approval: None

Immunogenicity: Ph. III analysis shows vaccine was safe and well-tolerated; efficacy averaged 91.4% and >90% in individuals over 60.
Manufacturing/delivery: Adeno vector vaccines can be manufactured quickly and at scale (Russia has orders for 1.2 billion doses from 50 countries).
Platform history: Vaccine utilizing the Ad26 platform (Ad26.ZEBOV) has been approved for use against Ebola Virus Disease.

VECTORES VIRALES: ADENOVIRUS rAd5 / rAd26 RECOMBINANTE gen que codifica **PROTEÍNA S**

www.thelancet.com Published
online December 8, 2020 (interim analysis)



Adenovirus ChAdOx1 vector (full length S GP)
5x10¹⁰ virus particles / standard dose
(low dose 2x10¹⁰ virus particles)

1 o 2 dosis, 28 días intervalo

1:1 randomización

Vacuna meningococo ACWY
grupo control!

n= 23.848 + 11.636 Participantes

70.4% Eficacia

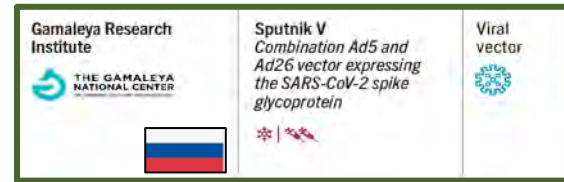
62% (1d&1d standard dose)

90% (1/2d&1d first dose low)

(basado en 131 casos) 30 casos en vacunados

Duración estudio: 1 año

www.thelancet.com Published
online February 2, 2021 (interim analysis)



Adenovirus rAd 26 and rAd 5
(full S GP)
10¹¹ viral particles / dose

2 dosis, 21 días de intervalo

3:1 randomización(20.000 recibieron 1 dosis,
16.000 2 dosis)placebo n= 40.000 participantes

91,6% Eficacia

21 días 1ª dosis

Basados en 4.902 casos placebo y 62 en
vacunados

Duración estudio : 6 meses

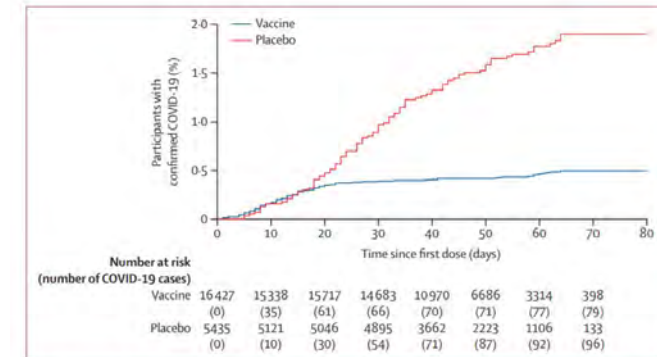


Figure 2: Kaplan-Meier cumulative incidence curves for the first symptomatic, PCR-positive COVID-19 after dose 1, in participants who received at least one dose of vaccine or placebo

PCR+



CONDITIONAL MARKETING AUTHORISATION

The European Commission will now FAST-TRACK the decision-making process to grant a decision on the conditional marketing authorisation for COVID-19 Vaccine AstraZeneca,

Medicines ▾

Human regulatory ▾

Veterinary regulatory ▾

Committees ▾

News & events ▾

Partners & networks

EMA recommends COVID-19 Vaccine AstraZeneca for authorisation in the EU

News 29/01/2021



The safety and effectiveness of the vaccine will continue to be monitored as it is used across the EU, through the EU pharmacovigilance system and additional studies by the company and by European authorities.

EMA has recommended granting a conditional marketing authorisation for COVID-19 Vaccine AstraZeneca to prevent coronavirus disease 2019 (COVID-19) in people from 18 years of age. This is the third COVID-19 vaccine that EMA has recommended for authorisation.

These showed a 59.5% reduction in the number of symptomatic COVID-19 cases in people given the vaccine (64 of 5,258 got COVID-19 with symptoms) compared with people given control injections (154 of 5,210 got COVID-19 with symptoms).

This means that the vaccine demonstrated around a **60% efficacy in the clinical trials.**

studies were between **18 and 55 years old**

as two injections into the arm, the **second between 4 to 12 weeks** after the first



The NEW ENGLAND JOURNAL of MEDICINE

8 Dicembre

N ENGL J MED NEJM.ORG

The New England Journal of Medicine

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The members of the WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation

Perspective

Placebo-Controlled Trials of Covid-19 Vaccines — Why We Still Need Them

WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation

Recent announcements that some Covid-19 vaccines are estimated to have high short-term efficacy provide new hope that vaccination will soon contribute to controlling the pandemic.

IMPORTANCIA DE QUE LOS ESTUDIOS DOBLE CIEGO EN MARCHA DEBEN CONTINUAR PARA CONOCER LA EFICACIA Y SEGURIDAD A LARGO PLAZO

VACUNAS Y NUEVAS VARIANTES SARS-CoV2

<https://jamanetwork.com/journals/jama/fullarticle/2775006>

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NEWS · 07 JANUARY 2021

Could new COVID variants undermine vaccines? Labs scramble to find out

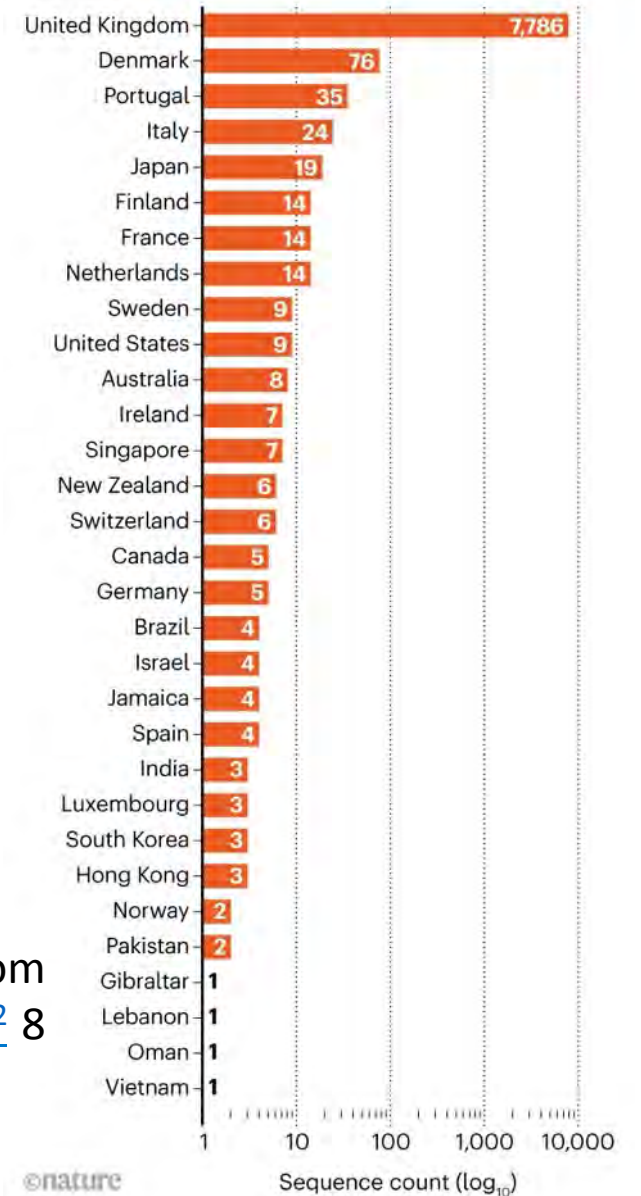
Researchers race to determine why variants identified in Britain and South Africa spread so quickly and whether they'll compromise vaccines.

Epidemiologists studying the growth of  **UK B.1.1.7 variant** in the United Kingdom have [estimated](#) that it is around **50% more transmissible** than existing viruses in circulation². 8 changes that affect the spike protein, and several more in other genes; samples of the  **South African 501Y.V2** variant carry up to 9 changes to the spike protein.

RAMZ Carlos Martín 4 Febrero 2021

VIRAL SEQUENCES

Genome-sequencing efforts are crucial to understanding how the SARS-CoV-2 coronavirus is mutating. A fast-spreading variant, called B.1.1.7, was identified by a UK-wide COVID-19 genomics effort, and 31 countries or regions have now uploaded sequence data to the GISAID website.



©nature

Sequence count (log₁₀)

jueves, 7 de enero de 2021 Ignacio Lopez Goñi

La complejidad de las nuevas variantes del coronavirus

¿Variantes o cepas?



<https://microbioun.blogspot.com/>

Variante implica diferencias en la secuencia del genoma, debido a mutaciones.

Cepa es una variante en la que se demuestran cambios en su biología (antigenicidad, transmisibilidad, virulencia, ...). **Por e momento, variantes.**

Mutación D614G, Mutación N453Y (DK visones), Mutación N501Y (UK 28% casos), Mutación 501.V2 (SA)

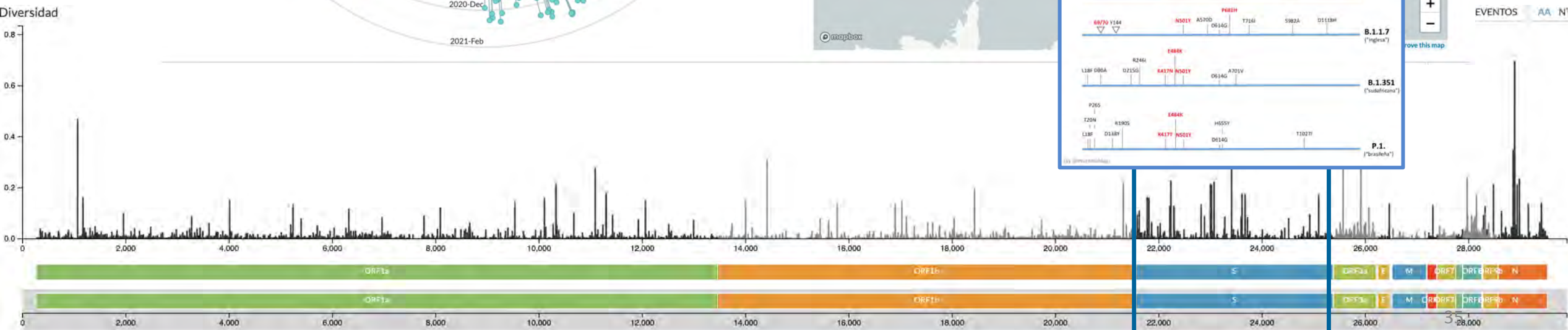
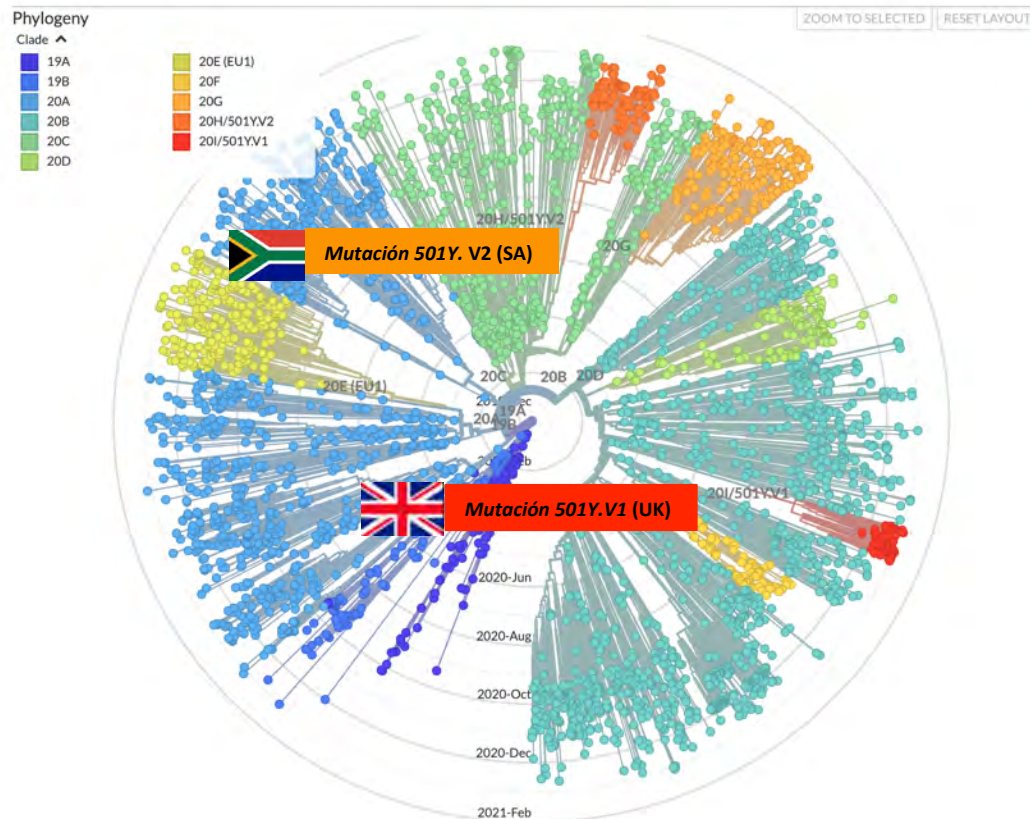
614: aspártico (D) por una glicina (G) / **453:** asparragina (N) por una tirosina (Y) / **501:** asparragina (N) por una tirosina (Y)

Genomic epidemiology of novel coronavirus - Global subsampling

Maintained by the Nextstrain team. Enabled by data from GISAID

Showing 4022 of 4022 genomes sampled between Dec 2019 and Jan 2021.

<https://nextstrain.org/ncov/global?l=radial>



29 Enero 2021

- 1 L@EMA_News aprueba la vacuna de #AstraZeneca (Oxford)
- 2 1 dosis de #Johnson and Johnson muestra una eficacia del 60-70% en fase III
- 3 La vacuna de # Novavax muestra una eficacia del 90% en fase III

2 Febrero 2021

- **Publicación Lancet Sputnik V : 92%**

66% PROTECCION:

72% en USA

57% Sudáfrica



Johnson & Johnson

VECTOR VIRAL

ADENOVIRUS rAd26

gen que codifica PROTEÍNA S



Johnson & Johnson Announces Single-Shot Janssen COVID-19 Vaccine Candidate Met Primary Endpoints in Interim Analysis of its Phase 3 ENSEMBLE Trial

Vaccine Candidate 72% Effective in the US and 66% Effective Overall at Preventing Moderate to Severe COVID-19, 28 Days after Vaccination

85% Effective Overall in Preventing Severe Disease and Demonstrated Complete Protection Against COVID-19 related Hospitalization and Death as of Day 28

Protection Against Severe Disease Across Geographies, Ages, and Multiple Virus Variants, including the SARS-CoV-2 Variant from the B.1.351 Lineage^[1] Observed in South Africa

Single-shot compatible with standard vaccine distribution channels provides important tool in pandemic setting

[1] The B.1.351 lineage also known as 501Y.V2 variant and 2011/501Y.V2 (formerly 20C/501Y.V2) is a variant of SARS-CoV-2, the virus that causes COVID-19

NEW BRUNSWICK, N.J., January 29, 2021 – Johnson & Johnson (NYSE: JNJ) (the Company) today announced topline efficacy and safety data from the Phase 3 **ENSEMBLE** clinical trial, demonstrating that the investigational single-dose COVID-19 vaccine in development at its Janssen Pharmaceutical Companies met all primary and key secondary endpoints. The topline safety and efficacy data are based on 43,783

VACUNAS SUBUNIDAD PROTEÍNA "S" + ADJUVANTE

NOVAVAX

Creating Tomorrow's Vaccines Today

29 Enero 2021



Novavax COVID-19 Vaccine Demonstrates 89.3% Efficacy in UK Phase 3 Trial

Jan 28, 2021 at 4:05 PM EST



First to Demonstrate Clinical Efficacy Against COVID-19 and Both UK and South Africa Variants

- *Strong efficacy in Phase 3 UK trial with over 50% of cases attributable to the now-predominant UK variant and the remainder attributable to COVID-19 virus*
- *Clinical efficacy demonstrated in Phase 2b South Africa trial with over 90% of sequenced cases attributable to prevalent South Africa escape variant*
- *Company to host investor conference call today at 4:30pm ET*

Análisis 62 casos COVID-19 (61 medio o moderado 1 grave):

56 Placebo/ en NVX-CoV2373

Eficacia 89.3% (95% CI:75.2-95.4)



Eficacia 50% Variante Sudáfricana



Novavax Press Release

The first interim analysis is based on 62 cases, of which 56 cases of COVID-19 were observed in the placebo group versus 6 cases observed in the NVX-CoV2373 group, resulting in a point estimate of vaccine efficacy of 89.3% (95% CI: 75.2 – 95.4). Of the 62 cases, 61 were mild or moderate, and 1 was severe (in placebo group).

BRIEF COMMUNICATION OPEN

Experimental and in silico evidence suggests that SARS-CoV-2 spike protein variants are unlikely to be affected by D614G mutation

Alexander J. McAuley¹, Michael J. Kim¹, Kim Blasdell¹, Mary Tachedjian¹, Sue L. Sarag¹, Sarah-Jane Riddell¹, Trevor W. Drew¹

January 6, 2021

JAMA

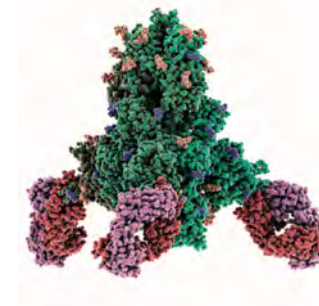
Genetic Variants of SARS-CoV-2—What Do They Mean?

Adam S. Luring, MD, PhD¹; Emma B. Hodcroft, PhD²

► Author Affiliations | Article Information

JAMA. Published online January 6, 2021. doi:10.1001/jama.2020.27124

Variabilidad proteína S SARS-CoV-2 VIGILAR MUY DE CERCA



bioRxiv preprint doi: <https://doi.org/10.1101/2021.01.07.425740>; this version posted January 7, 2021. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

bioRxiv January 7, 2021. ; <https://doi.org/10.1101/2021.01.07.425740>doi:
bioRxiv preprint
Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera

nature

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nature > news > article

NEWS · 21 JANUARY 2021

Fast-spreading COVID variant can elude immune responses

Evidence that a variant of the coronavirus identified in South Africa might compromise immunity sparks concerns about vaccine effectiveness.

Ewan Collinge

nature

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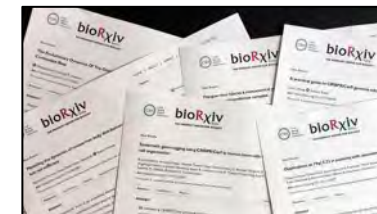
nature > news > article

NEWS · 29 JANUARY 2021

How to redesign COVID vaccines so they protect against variants

Lineages that can evade immunity are spurring vaccine makers to explore ways to redesign their shots.

Ewan Collinge & (left) Ledford



- ¿ CAMBIOS EN LA PRODUCCIÓN ?
- ¿ AUTORIZACION USO : FASE 3?
- ¿ INMUNIDAD PREVIA OTRAS VACUNAS?

Lancet Respir Med 2021

Published Online
January 29, 2021
[https://doi.org/10.1016/S2213-2600\(21\)00075-8](https://doi.org/10.1016/S2213-2600(21)00075-8)

For the WHO COVID-19
Dashboard see covid19.who.int.

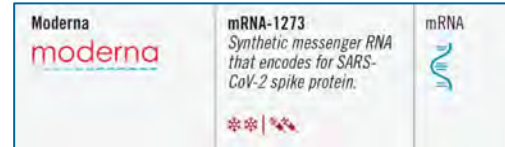
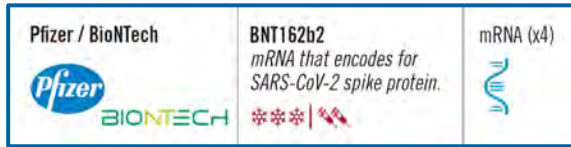
Comment

Lancet Respiratory Medicine 29 Enero 2021

SARS-CoV-2 evolution and vaccines: cause for concern?



PREVISIÓN DE PRODUCCIÓN



2020
50 millones dosis

2020
20 millones dosis

2020
50 millones dosis

2020
10 millones dosis

2021
1.3 Mil millones dosis

2021
1 Mil millones dosis

2021
500 millones dosis

2021
500 millones
/ Mil millones dosis
(fabricación fuera de Rusia)

2.0 Mil millones dosis

+ 125 M (Sanofi, Frankfurt), Alemania

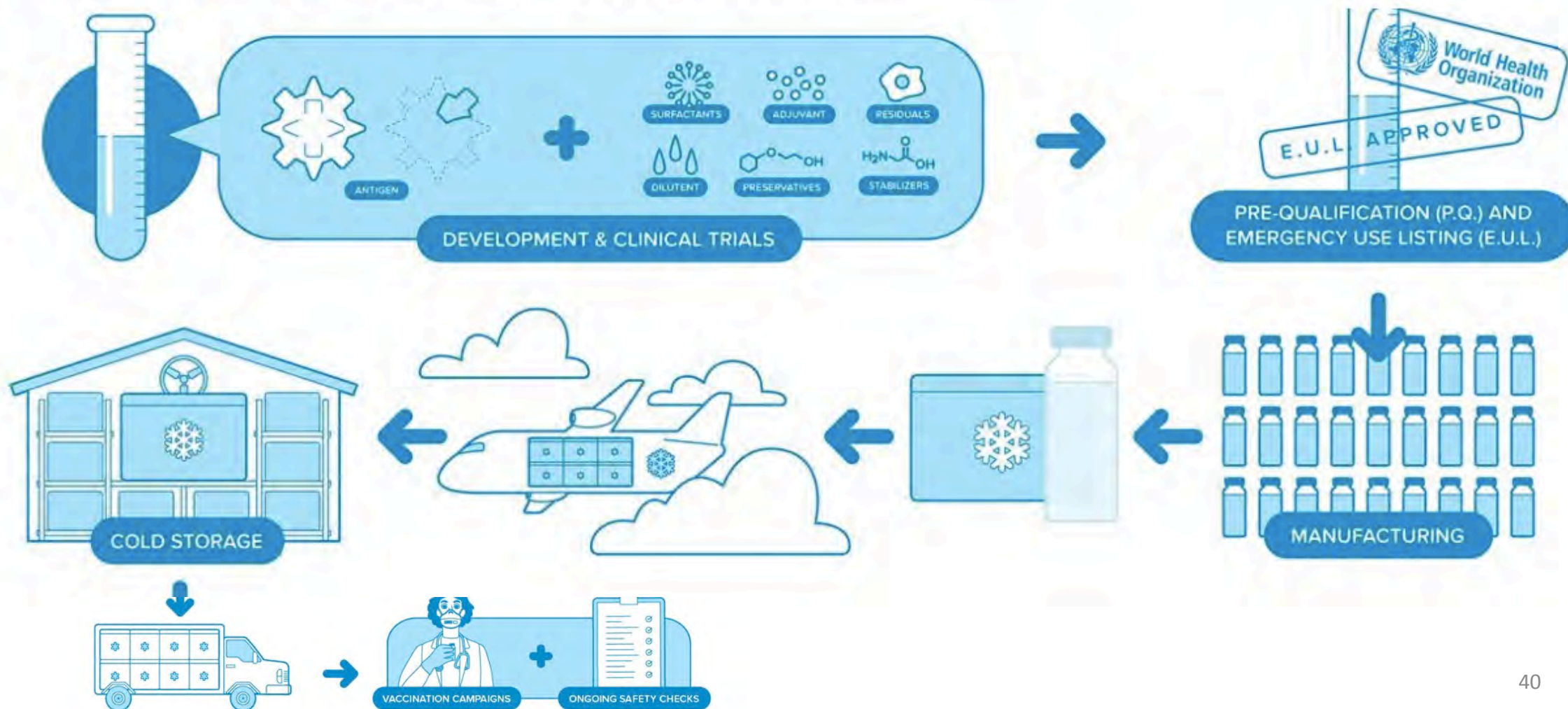
+ Novartis (Stein, Suiza)

+ Nueva planta Malbourn Alemania

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ENORME RETO DE PLANIFICACION ESTRATEGIA DE VACUNACIÓN



What are our experiences and learnings? - a snapshot from regional discussions -

Targeted Population	Learn from past vaccine introduction and regional experiences survey of regions.	Delivery considerations
Health & social workers	Experiences mostly from influenza vaccination, HepB, MCV (more limited); H1N1 pandemic vaccination	Hospital, health centres, health care offices
Older people	Most information from influenza EURO from 53 countries: 49 – have vaccination programs for adults 42 - issued recommendations for vaccination of residents of long-term care facilities	House to house screening to find the eligible people Health Facilities or community outreach clinics for EPI as done in other SIAs
Medical risk groups	Overall limited experience (except pregnancy) EURO: 48/53 countries have influenza vaccination policies for adults with high-risk chronic conditions	House to house screening to find the eligible people Specialized clinics from where they get treatment

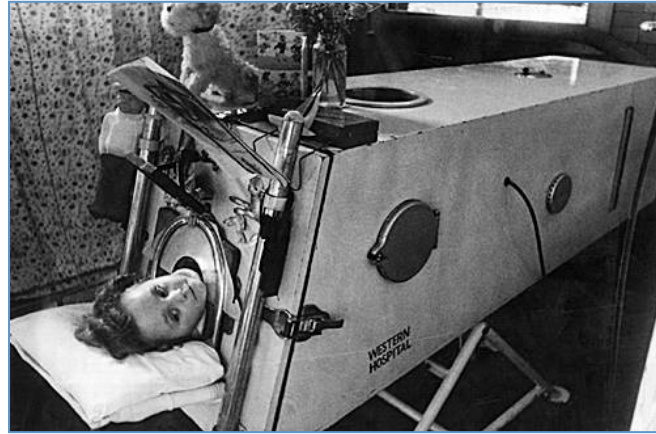
SEGÚN DISPONIBILIDAD DE LA VACUNA

Epidemiologic Setting Scenario: <u>Community Transmission</u>	
Overall public health strategy for epidemiologic setting: Initial focus on direct reduction of morbidity and mortality and maintenance of most critical essential services; also, reciprocity. Expand to reduction in transmission to further reduce disruption of social and economic functions.	
Vaccine supply scenario	Priority populations
Stage I (very limited vaccine availability, ranging from 1-10%)	Stage Ia (Initial Launch) <ul style="list-style-type: none"> - Health workers at <u>high to very high risk</u> of acquiring and transmitting infection Stage Ib <ul style="list-style-type: none"> - Older adults defined by age-based risk specific to country/region, specific age cut-off to be decided at the country level
Stage II (limited vaccine availability, ranging from 11-20%)	<ul style="list-style-type: none"> - Older adults not covered in Stage I - Individuals with comorbidities or health states determined to be at significantly higher risk of severe disease or death. - Sociodemographic groups at significantly higher risk of severe disease or death - Health workers engaged in immunization delivery (routine programme-specific and COVID-19) - High priority teachers and school staff
Stage III (moderate vaccine availability, ranging from 21-50%)	<ul style="list-style-type: none"> - Remaining teachers and school staff - Other essential workers outside health and education sectors - Pregnant women (see accompanying text on pregnant women) - Health workers at <u>low to moderate risk</u> of acquiring and transmitting infection - Personnel needed for vaccine production and other high-risk lab staff - Social/employment groups at <u>elevated risk</u> of acquiring and transmitting infection because they are unable to effectively physically distance

Experiencia Gripe

Joachim Hombach, Immunization, Vaccines & Biologicals WHO Nov 2020


ESTRATEGIA DE ERRADICACIÓN: POLIO



1957 Sabin
Vacuna Polio
Atenuada
(Via oral) OPV



1952 Salk
Vacuna polio inactivada (via intramuscular) IPV

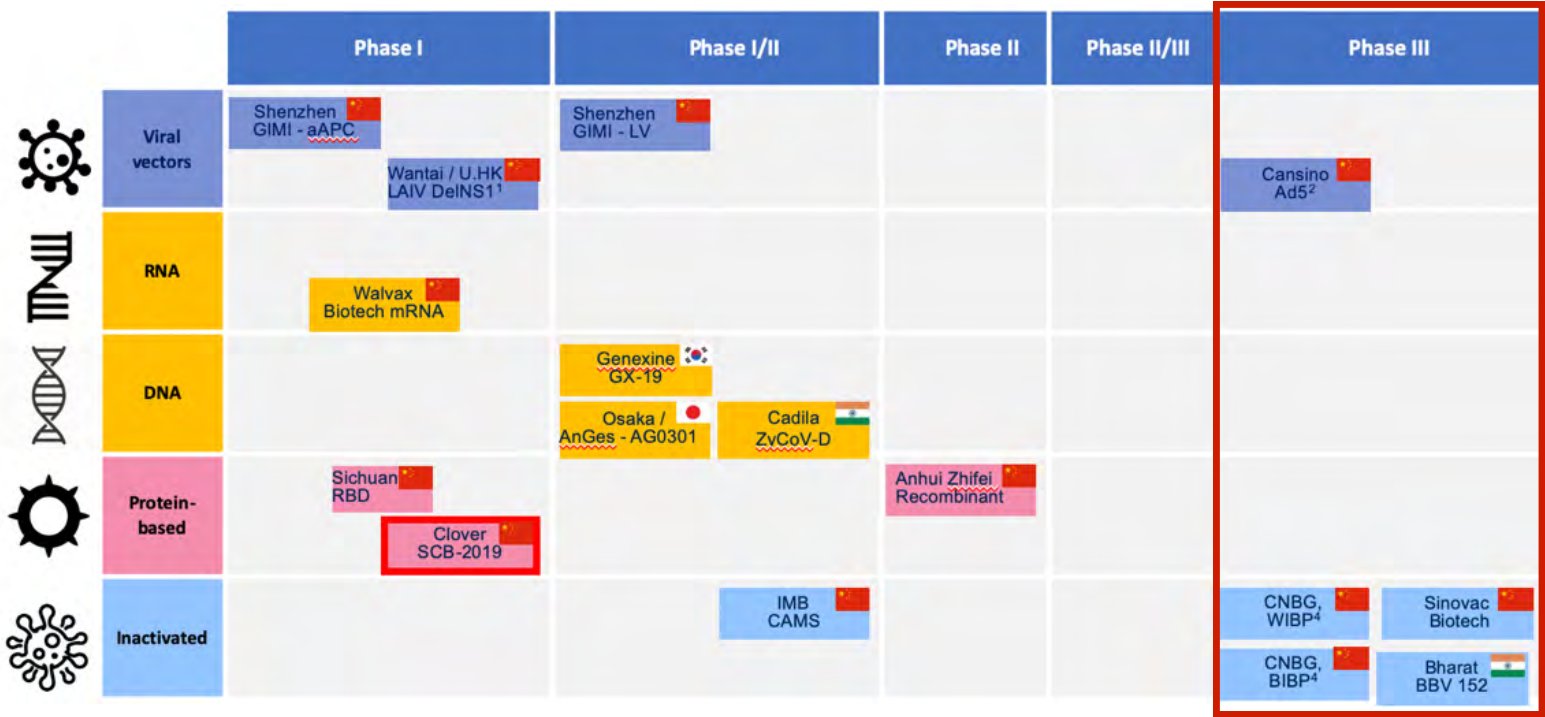


Years of effort and billions of dollars have driven polio to just a few impoverished corners of the world. The campaign is intensifying, but the virus is tenaciously resisting

Polio: The Final Assault?

ESTRATEGIA DE ORIENTE

Para el desarrollo de una nueva vacuna contra SARS-CoV-2



CHINA 12 VACUNAS EN CLINICA



China ha empleado ya al menos dos vacunas experimentales contra la covid-19 en «cientos de miles de chinos», EFE

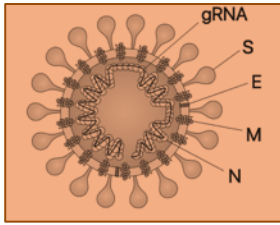


4 CANDIDATOS FASE 3

- VECTORES VIRALES 4 (1)
- RNA 1
- SUBUNIDADES PROTEINA 3
- INACTIVADAS 4 (3)

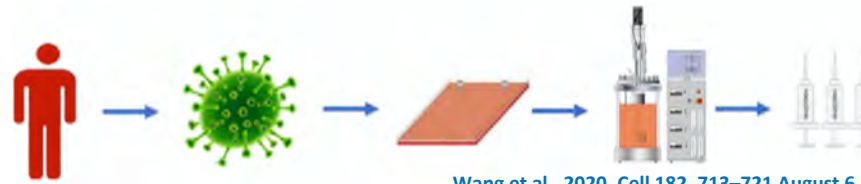
VACUNAS COVID-19 SARS-CoV-2

VIRUS COMPLETO: INACTIVADO: 4 CANDIDATOS FASE 3



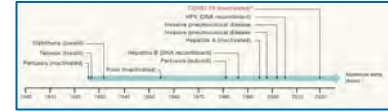
VIRUS VACCINES

At least seven teams are developing vaccines using the virus itself, in a weakened or inactivated form. Many existing vaccines are made in this way, such as those against measles and polio, but they require extensive safety testing. Sinovac Biotech in Beijing has started to test an inactivated version of SARS-CoV-2 in humans.



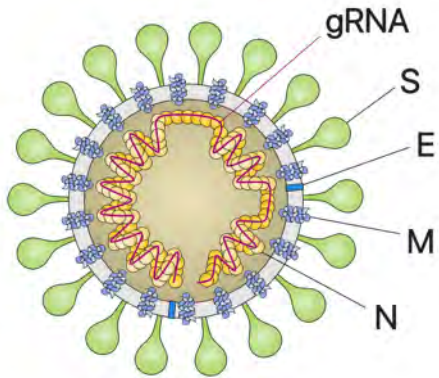
Wang et al., 2020, Cell 182, 713–721 August 6, 2020

Virus Inactivado



Inactivated virus

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



Callaway E. Nature 2020

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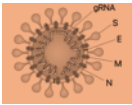
<p>Sinopharm / Beijing Institute of Biologic Products / Wuhan Institute</p>	<p>BBIBP-CorV x 2</p>	<p>Whole inactivated</p>	<p>No Funding Disclosed</p>
<p>Sinovac Biotech</p>	<p>CoronaVac</p>	<p>Whole inactivated</p>	<p>No Funding Disclosed</p>
<p>Bharat Biotech/ Indian Council of Medical Research</p>	<p>Covaxin</p>	<p>Whole inactivated</p>	<p>No funding disclosed</p>



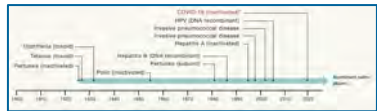
China's vaccine road trip

With few COVID-19 cases at home, Chinese vaccinemakers have had to test the worth of their candidates abroad and four are in efficacy trials in 15 countries.

SCIENCE
 By [Jon Cohen](#) Nov. 25, 2020
 doi:10.1126/science.abf8838



SARS-CoV-2 INACTIVADO
 (beta propiolactone)
 +
ADJUVANTE
 (Sales de Aluminio)



Ad5 virus expresando "S" SARS-Cov-2

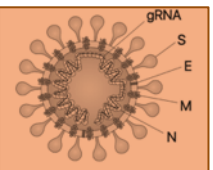
Manufacturer	Country	Start date	Size
Sinovac Biotech 	Brazil	2 July	13,060
	Indonesia	10 Aug.	600
	Turkey	14 Sept.	15,000
	Peru	10 Sept.	6000
Sinopharm / Beijing Institute of Biologic Products / Wuhan Institute 	Bahrain, Egypt, Jordan, UAE	16 July	45,000
	Argentina	16 Sept.	3000
	Morocco	13 Oct.	600
	Peru	10 Sept.	6000
CanSino Biologics 	Russia	11 Sept.	500
	Pakistan, Mexico, Argentina, Chile	15 Sept.	40,000
	Peru	10 Sept.	6000

*Two branches of the China National Biotec Group (CNBG) are developing similar, but distinct, vaccines.




<https://www.nytimes.com/2020/12/08/world/chinese-vaccine-is-86-percent-effective-says-uae-where-trials-were-held.html?referringSource=articleShare>

A Chinese vaccine wins its first approval in the U.A.E., which says it is 86 percent effective. 

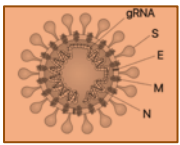




VIRUS COMPLETO: INACTIVADO

<p>Sinopharm / Beijing Institute of Biologic Products / Wuhan Institute</p> 	<p>Ph. I/II: ongoing: 640/China Ph III ongoing: 45K/UAE. Bahrain, Jordan, Egypt; 3K/Argentina; 6K/Peru Authorization: EUA in Egypt Approval: Bahrain, China, UAE</p>	<p>Immunogenicity: Ph. III interim analysis showed an efficacy of 86%. Manufacturing/delivery: Inactivated vaccines may require booster doses; relatively shelf-stable compared to other platforms. Platform history: Numerous whole inactivated vaccines, including polio, Hep A and rabies.</p>
<p>Sinovac Biotech</p> 	<p>Ph. I/II ongoing: 1166/China Ph III ongoing: 8K/Brazil, 1600/ Indonesia, 4K/Bangladesh, 13K/Turkey, 1K/China Authorization: EUA for limited use in China Approval: None</p>	<p>Immunogenicity: Preliminary data showed the vaccine elicited neutralizing antibodies. Manufacturing/delivery: Inactivated vaccines may require booster doses; relatively shelf-stable compared to other platforms. Platform history: Numerous whole inactivated vaccines, including polio , Hep A, and rabies.</p>
<p>Bharat Biotech/ Indian Council of Medical Research</p> 	<p>Ph. I/II ongoing: 755/ India Ph. III ongoing: 25.8K/ India Authorization: EUA in India; still pending final Ph. III efficacy data Approval: None</p>	<p>Immunogenicity: Ph. I/II trial data showed the vaccine was safe and triggered an antibody response. Manufacturing/delivery: Inactivated vaccines may require booster doses; relatively shelf-stable compared to other platforms. Covaxin is stable at room temperature for atleast a week. Platform history: Numerous whole inactivated vaccines, including polio, Hep A and rabies.</p>

No Antibody-dependent enhancement (ADE) detected



VIRUS COMPLETO: INACTIVADO

COVAXIN™ - India's First indigenous COVID-19 Vaccine



COVAXIN™, India's indigenous COVID-19 vaccine by Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV).

The indigenous, inactivated vaccine is developed and manufactured in Bharat Biotech's BSL-3 (Bio-Safety Level 3) *high containment facility*.

The vaccine is developed using *Whole-Virion Inactivated Vero Cell* derived platform technology. Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects. They contain dead virus, incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection.

Why develop Inactivated Vaccine? Conventionally, inactivated vaccines have been around for decades. Numerous vaccines for diseases such as Seasonal Influenza, Polio, Pertussis, Rabies, and Japanese Encephalitis use the same technology to develop inactivated vaccines with a safe track record of >300 million doses of supplies to date. It is the *well-established*, and *time-tested platform* in the world of vaccine technology.

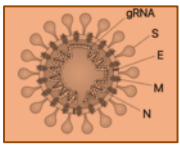
Key Attributes:

- COVAXIN™ is included along with immune-potentiators, also known as vaccine adjuvants, which are added to the vaccine to increase and boost its immunogenicity.
- It is a 2-dose vaccination regimen given 28 days apart.
- It is a vaccine with no sub-zero storage, no reconstitution requirement, and ready to use liquid presentation in multi-dose vials, stable at 2-8°C.
- Pre-clinical studies: Demonstrated strong immunogenicity and protective efficacy in animal challenge studies conducted in hamsters & non-human primates. For more information about our animal study, please visit <https://www.bharatbiotech.com/blog/vaccines/covaxin-animal-study-results>

Bharat Biotech/
Indian Council of
Medical Research



COVAXIN™



VIRUS COMPLETO: INACTIVADO

CONTACT EN | FR Q



About Us Products R&D Investors Media Careers

COVID-19 - VLA2001



<https://valneva.com/research-development/covid-19-vla2001/>

COVID-19 is the infectious disease caused by the new coronavirus (SARS-CoV-2) identified in late 2019. COVID-19 is affecting many countries globally and has been declared a pandemic by the World Health Organization (WHO).

“The partnership with the UK government validates our inactivated vaccine approach and recognizes the strong track record and capabilities we have built in the last fifteen years both in the UK and beyond.”

Thomas Lingelbach, CEO of Valneva

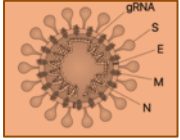
About the vaccine candidate VLA2001

- Inactivated
- Adjuvanted with Alum and CpG 1018
- Highly-purified
- Whole virus candidate
- Vero-cell based
- Using the manufacturing platform of Valneva's commercial Japanese encephalitis (JE) vaccine



[Valneva initiated Phase 1/2 clinical study in December 2020](#)





VIRUS COMPLETO: INACTIVADO



In September 2020, Valneva announced a partnership with the UK government for its inactivated COVID-19 vaccine, VLA2001. Under the agreement, if vaccine development is successful, Valneva will provide the UK government with 60 million doses in the second half of 2021. UK Government then has options over an additional 130 million doses, across 2022 to 2025. UK government is also investing up-front in the scale up and development of the vaccine.

In January 2021, Valneva announced it is in advanced discussions with the European Commission (EC) for the supply of up to 60 million doses of VLA2001.





INDUSTRIA FARMACEUTICA (BIG PHARMA): MEDIOS FINANCIEROS !!!

Investigación Pública, pequeñas industrias farmacéuticas, tratan de conseguir candidatos diferentes,

THE UNDERDOG COVID-19 VACCINES THAT THE WORLD MIGHT NEED

Small developers struggle to get their candidates noticed, but they'll be crucial if front runners stumble.

By Ewen Callaway

When it comes to developing vaccines, Peter Palese is no slouch. A virologist at Icahn School of Medicine at Mount Sinai in New York City, he pioneered genetics techniques that are used to make some of the billions of influenza vaccine doses produced annually, and his team has won millions of dollars to develop a universal flu jab. Palese is developing a COVID-19 vaccine, too. It consists of a bird virus that has been genetically modified to make a protein found on the surface of SARS-CoV-2. The vaccine fully protects mice from an experimental model of COVID-19, according to a preprint (the research has not yet been peer reviewed). It also grows in chicken eggs, like other vaccines, so manufacturing could be up using tried-and-tested techniques. Despite its potential, Palese struggled to gain the needed to progress thought this sliced by our de-

companies rush their COVID-19 vaccines through clinical trials and eye up fast-track regulatory authorization, dozens of underdog vaccines such as Palese's have stalled, or are advancing along a slower, more conventional path. Scientists acknowledge that it's a waste of resources to take every clinical trial. But they argue to have a diverse selection in development fail, confer only poorly in other b-run. University up using tried-and-tested techniques. Despite its potential, Palese struggled to gain the needed to progress thought this sliced by our de-

Candidates
more than 320 COVID-19 vaccines in development, according to a tally by the Coalition for Epidemic Preparedness Innovation (CEPI) in Oslo, a fund created to finance

Las vacunas desfavorecidas contra el coronavirus que el mundo necesitará

"We don't have a billion dollars, but we are moving the programme forward and making sure we don't lose time."



There are more than 320 COVID-19 vaccines in development, but only a handful are in final-stage clinical trials. Credit: Joe Raedler/Getty

CANDIDATOS A VACUNA contra SARS-CoV-2 : Evaluación Preclínica

Investigación en vacunas contra SARS-CoV-2 en España



CANDIDATOS A VACUNA contra SARS-CoV-2 :
EVALUACIÓN PRECLÍNICA: preparando Fase 1



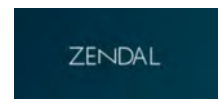
Investigación en vacunas contra SARS-CoV-2 en España

VACUNAS DNA

DNA codifica para proteínas de SARS-CoV-2
Vicente Larraga CIB/ CSIC



DNA
Codifica para proteína
SARS-CoV-2





CANDIDATOS A VACUNA contra SARS-CoV-2 : Evaluación Preclínica

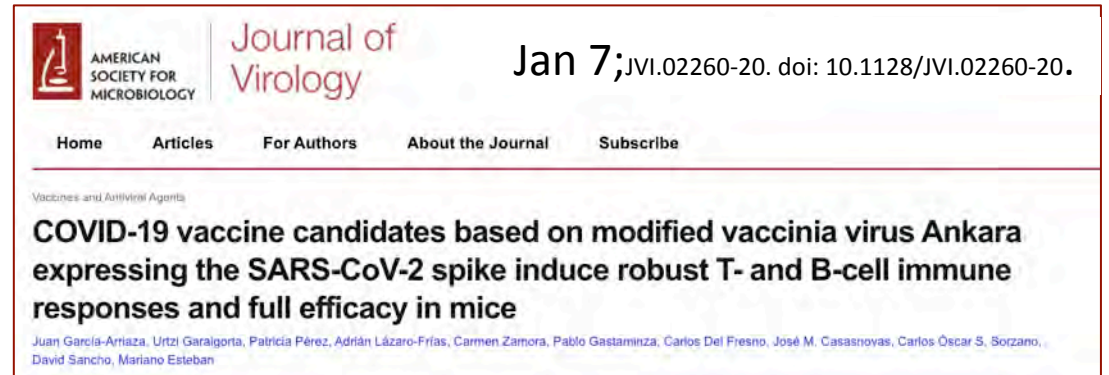
Investigación en vacunas contra SARS-CoV-2 en España



VECTORES VIRALES

VACUNA SUBUNIDAD Virus de la Vacuna (MVA VIRUS DE LA VACUNA) expresando proteínas de SARS-CoV-2

MARIANO ESTEBAN, CSIC/CNB.

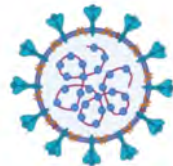


Juan Garcia Arriaza



CANDIDATOS A VACUNA contra SARS-CoV-2 : Evaluación Preclínica

Investigación en vacunas contra SARS-CoV-2 en España



VIVA- ATENUADA

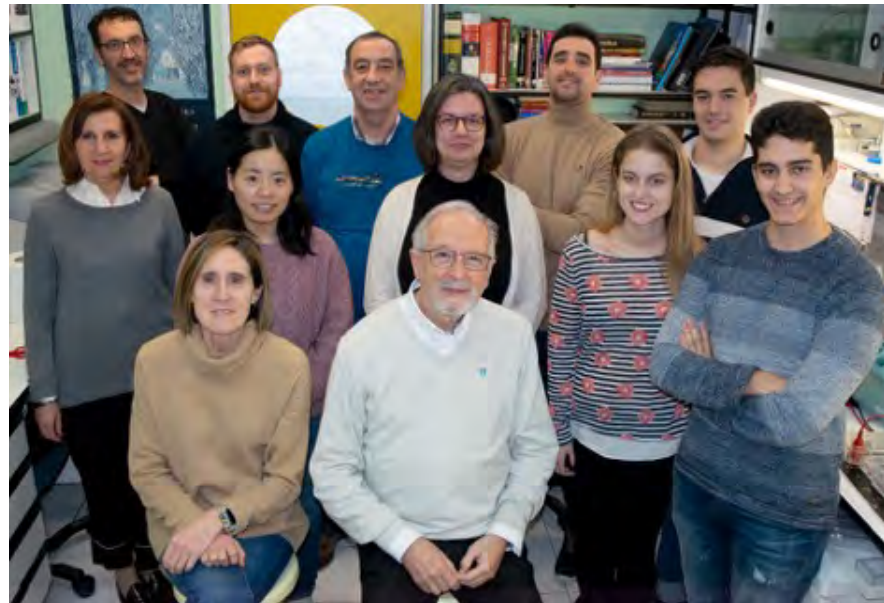
VIRUS ATENUADO SARS-CoV-2

genéticamente modificado.

LUIS ENJUANES,
CSIC/CNB.

Delección en el gen E + delecciones otros genes estructurales (seguridad)

SARS-Cov-1
MERS



¿ ADMINISTRACIÓN MUCOSAL ?

Isabel Sola
Sonia Zuñiga

ACTUALIDAD Santander pierde 8.771 millones en 2020 y volverá a pagar dividendo »

Compañías

INDUSTRIA FARMACÉUTICA

BioNTech y CSIC sondean el desarrollo conjunto de una vacuna española del Covid-19



ALFONSO
SIMÓN
RUIZ

- La alemana ha mostrado interés en la investigación liderada por Enjuanes
- La belga Univercells y la valenciana PTS, también en conversaciones



Luis Enjuanes, virólogo del Centro Nacional de Biotecnología-CSIC.

3 FEB 2021 - 09:35 CET



VICENTE LARRAGA

TALENTO Tres veteranos virólogos 'rescatados' de la jubilación

Los 'Space Cowboys' de la vacuna española

Uno desarrolló una vacuna canina en 2003, otro ha reconstruido versiones del coronavirus no infecciosas y el tercero, el mayor con 76 años, trabaja con un virus atenuado de la viruela. Son la prueba de que no falta talento. Como en la película 'Space Cowboys' con un grupo de jubilados, ellos han sido rescatados para un verdadero reto. Y sólo cobran su pensión

MARIANO ESTEBAN



LUIS ENJUANES

Planeta Calleja 4:
Especial COVID-19

Antes de que la pandemia llegara oficialmente y el reloj de las muertes empezara a correr desbocado, ellos ya habían dado un paso al frente para ir a la guerra que estaba al caer. Se llaman Mariano Esteban (76 años), Luis Enjuanes (75) y Vicente Larraga (72). TRES JUBILADOS que valen oro. TRES MENTES MARAVILLOSAS.

**LA CIENCIA NOS HA DADO LAS VACUNAS,
ENTRE TODOS HAREMOS QUE SEAN EFICACES**

https://www.aeped.es/sites/default/files/20201229_manifiesto_vacunascovid19.pdf

La Asociación Española de Pediatría, a través de su Comité Asesor de Vacunas (CAV-AEP), la Asociación Española de Vacunología (AEV), la Sociedad Española de Inmunología (SEI), la Sociedad Española de Microbiología (SEM) y la Sociedad Española de Virología (SEV) firmantes de este comunicado, consideran que su apoyo y asesoramiento en las decisiones gubernamentales y de las autoridades sanitarias, es fundamental para mantener la aceptación social que España tiene de la vacunación.

- La vacunación masiva es la única forma aceptable de conseguir la inmunidad de grupo.
- Las vacunas de la COVID-19 muestran hasta ahora un elevado nivel de eficacia y seguridad.
- Es fundamental que se confíe en la ciencia.
- Es importante buscar información en fuentes fiables, difundir información contrastada y contribuir a evitar los bulos en las redes sociales.

INICIO VACUNACION ESPAÑA: 5 Enero 2021

GIV COVID-19

Gestión integral de la vacunación COVID-19

Informe de actividad

Periodo de los datos: 27/12/2020 - 05/01/2021
Fecha del informe: 05/01/2021

Informe para comunicación

Informe de actividad del proceso de vacunación Periodo de los datos: 27/12/2020 - 05/01/2021
Fecha del informe: 05/01/2021

Datos globales agregados

Dosis entregadas en CC.AA	Dosis administradas	Nº Personas con pauta completa
743.925	139.339	0
	18,7% dosis recibidas	- % dosis administradas

Distribución por tipo de vacuna

	Dosis entregadas en CC.AA	Dosis administradas	Nº Personas con pauta completa
Pfizer / BioNtech	743.925	139.339	-
Moderna			
AstraZeneca / Celgene			
Johnson & Johnson			
Otras			

(*) Fuentes: AEMPS y REGVACU (datos reportados por las CC.AA). Se incluyen los datos de las dosis entregadas el día 5/1/2021.

Ministerio de Sanidad ✓ @sanidadgob · Jan 5

Actualización del informe de actividad de vacunación en España

...

- ◆ 743.925 dosis distribuidas
- ◆ 139.339 dosis administradas

mscbs.gob.es/profesionales/...

#YoMeVacuno

VACUNACIÓN COVID-19 EN ESPAÑA

Martes, 5 de enero de 2021

DOSIS
DISTRIBUIDAS

743.925

DOSIS
ADMINISTRADAS

139.339

#YoMeVacuno

Datos consolidados a las 17:00 horas de hoy

VACUNAS COVID-19 INFORME DE FARMACOVIGILANCIA



FIGURA 1

Distribución de personas vacunadas por grupo de edad y sexo

Sexo: ● **Mujer** ● **Hombre**

Mayor de 65 años

56.169

123.987

18 - 64 años

79.774

210.068

- ▶ No se ha identificado en España o en la Unión Europea ninguna posible reacción adversa hasta ahora desconocida que pueda ser motivo de preocupación.
- ▶ A la fecha de cierre de este informe (12 de enero), se habían vacunado en España 494.799 personas, habiéndose recibido 374 notificaciones de acontecimientos adversos. Los más frecuentes incluían acontecimientos relacionados con trastornos generales (fiebre, malestar), sistema nervioso central (cefalea, mareos) y aparato digestivo (náuseas, diarrea).



SALUD PÚBLICA

Rafael Nájera, primer director del Instituto de Salud Carlos III

“La aceleración de vacunas es pura política, no tiene que ver con la ciencia.”

El virólogo y médico del Cuerpo de Sanidad Nacional fue el artífice de la campaña de vacunación contra la polio en España y una figura clave en la investigación del VIH-sida. Este experto en investigación y gestión sanitaria es muy crítico con los anuncios de líderes como Trump y Putin que, con intenciones electoralistas, prometen una inmunización rápida, algo que por ahora no se ha conseguido.

The impact of coronavirus on stock markets since the start of the outbreak



Source: Bloomberg, 4 January 2020, 12:55 GMT



Stocks were boosted by news that the Covid-19 vaccine being developed by drugmaker Pfizer and Germany's BioNTech had been found to be more than 90 per cent effective © FT montage: Reuters

Stock Prices Performance of Vaccine Developers

The charts below illustrate the stock prices performance for seven companies currently in the 3rd phase of vaccine development. Highlighted are dates of result reports to the WHO about each phase.

Stock Price Performance of COVID-19 Vaccine Developers

% of base period December 2, 2019 (logarithmic scale is applied)



NOVAVAX

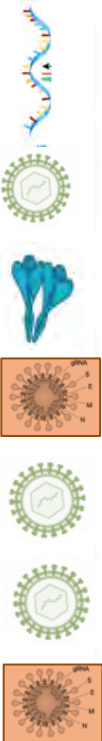
MODERNA

BHARAT

PFZIER

- Novavax Inc
- Moderna Inc
- Pfizer Inc
- AstraZeneca PLC ADR
- SINOPHARM GROUP CO LTD ADR
- Bharat Immunologicals and Biologicals Corporation Ltd
- Cansino Biologics Inc.
- Stock Market Performance Indices, Daily update-SPX

RESUMEN DE LOS ESTUDIOS DE EFICACIA DE LAS NUEVAS VACUNAS COVID-19 a 31 Enero 2021:



Vaccine	Type	Doses	Efficacy			
			Overall	US	UK	South Africa
Pfizer/BioNTech*	mRNA	2	95%	95%	-	-
Moderna*	mRNA	2	94%	94%	-	-
Gameleya (Sputnik V)	Viral vector	2	92%	-	-	-
Novavax	Protein/adjuvant	2	89%	-	89%	49%***
Sinopharm	Inactivated	2	79%-86%	-	-	-
J&J Janssen	Viral vector	1	66%	72%	-	57%
AZ/Oxford*	Viral vector	2	62%**	-	60%**	-
Sinovac	Inactivated	2	50%-91%	-	-	-

*Peer-reviewed. **Standard dose. ***Phase 2b trial.



The NEW ENGLAND JOURNAL of MEDICINE

LA CONFIANZA EN LAS VACUNAS DEPENDE DE LA CONFIANZA:

- *En la seguridad y eficacia de los productos mismos*
- *La confianza en los fabricantes de vacunas*
- *En los médicos que administran las vacunas, y*
- *La confianza en quien formula las **políticas de vacunación** que deben:*
 - *Garantizar la evidencia científica y*
 - *Promulgar las recomendaciones de vacunación*

Perspective

FEBRUARY 4, 2021

A HALF-CENTURY OF PROGRESS IN HEALTH: THE NATIONAL ACADEMY OF MEDICINE AT 50

Vaccine Innovations — Past and Future

Julie L. Gerberding, M.D., M.P.H., and Barton F. Haynes, M.D.

Vaccination is a powerful method of disease prevention that is relevant to people of all ages and in all countries, as the Covid-19 pandemic illustrates. Vaccination can improve peo-

Vaccine confidence depends on trust in the safety and efficacy of the products themselves, trust in vaccine manufacturers and the clinicians who administer vaccines, and trust in policymakers who assess the scientific evidence and promulgate vaccination recommendations.



3 Diciembre 2020 Los Expresidentes-Obama-Bush-y-Clinton-se-ofrecen-como voluntarios-para-vacunarse-contr-el-coronavirus-publicamente



26 de Marzo , 1953:
Jonas Salk anuncia

El descubrimiento de la vacuna de la polio y empiezan las campañas de vacunación masivas



DR. D. FERNANDO SIMÓN



REAL ACADEMIA DE MEDICINA DE ZARAGOZA

**“Cambio global y amenazas sanitarias:
¿estamos preparados?”**

**¿ESTAMOS APRENDIENDO DE ESTA PANDEMIA?
¿NOS ESTAMOS PREPARANDO PARA OTRA POSIBLE PANDEMIA?**



MUCHAS GRACIAS

