

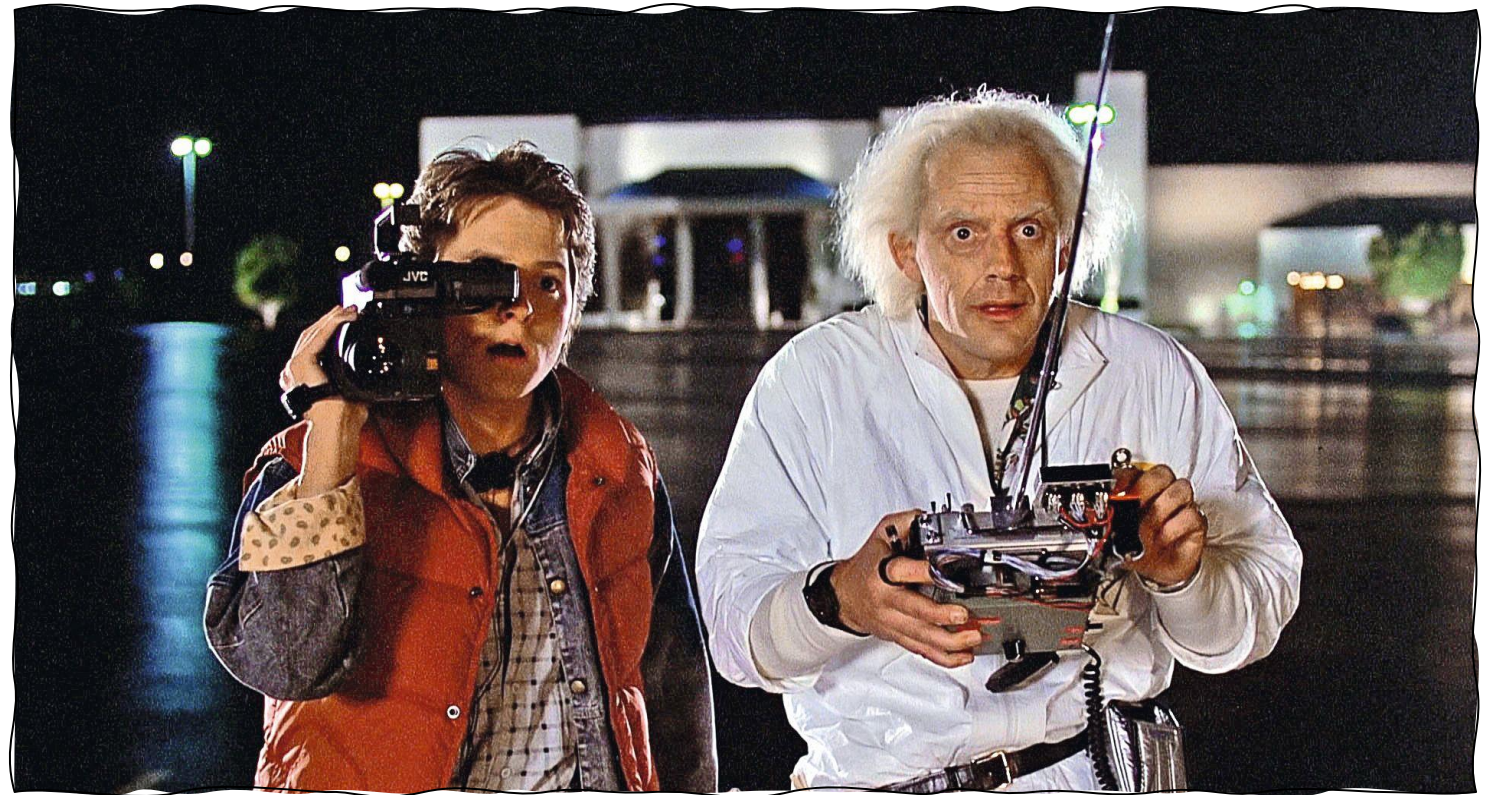
XII JORNADAS DE
VACUNAS

AEP



JORNADAS DIGITALES 15 Y 16 DE ABRIL DE 2021
vacunasaep.org

HAEMOPHILUS INFLUENZAE TIPO B
Rotavirus
SRP
POLIOMIELITIS
HA
HIB
HEPATITIS B
MENB
NEUMOCOCCO
Pas
Tofferina
VAR
VINC
DIPLOMA HUMANO



Regreso al futuro Vacunas del covid

15 de abril de 2021

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vacunasaep.org



Vacunas del covid

Regreso al futuro

Ángel Hernández Merino

Pediatra de Atención Primaria, Madrid
Vocal del CAV-AEP

15 de abril de 2021

@angel_h_merino

Vacunas del covid: regreso al futuro

Ideas clave

Pasado, presente y futuro

- A hombros de gigantes

Las vacunas del covid no son producto de la suerte

- Todo empezó con Kariko

El futuro de la pandemia

- Retos pendientes

La próxima generación de vacunas

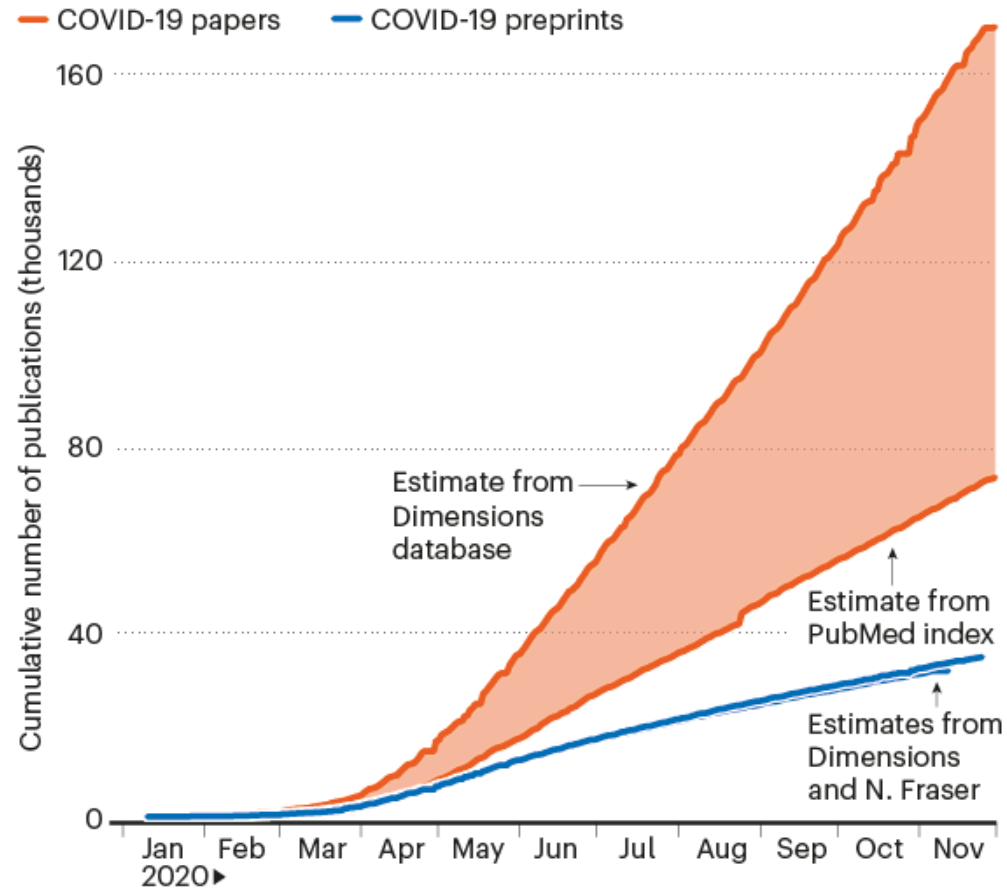
- Esto solo acaba de empezar

Las vacunas de ARNm no son flor de un día

- Las vacunas del covid, un antes y un después

CORONAVIRUS CASCADE

One estimate suggests that more than 200,000 coronavirus-related journal articles and preprints had been published by early December.



*Estimates differ depending on search terms, database coverage, and definitions of what counts as a scientific article; some preprints were posted on multiple sites online.

©nature

H. Else. Nature. 2020;558:553.

¿Cómo hemos llegado hasta aquí?

“A hombros de gigantes”

Pasado,
presente y
futuro

- A hombros de gigantes



1796,
Edward
Jenner



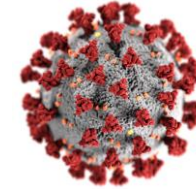
1885,
Louis
Pasteur



1937,
Max
Theiler



1980, R.
Mulligan
y P. Berg



2020, vacunas
del covid de
ARN y
vectores
virales



A. Desmond. N Engl J Med. 2021; 384:1081-3
<https://www.nejm.org/doi/full/10.1056/NEJMp2034334>

Vacunas del covid

El año 2020, ¿solo un año de suerte?

Las vacunas del covid no son producto de la suerte

- Todo empezó con Kariko



Vacunas del covid

Los antecedentes lejanos

Las vacunas del covid no son producto de la suerte

- Todo empezó con Kariko

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Direct gene transfer into mouse muscle in vivo

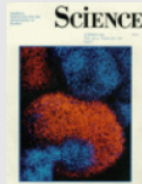
JA Wolff, RW Malone, P Williams, W Chong, G Acsadi, A Jani, PL Felgner
[+ See all authors and affiliations](#)

Science 23 Mar 1990:
Vol. 247, Issue 4949, pp. 1465-1468
DOI: 10.1126/science.1690918

Article Info & Metrics eLetters PDF

Abstract

RNA and DNA expression vectors containing genes for chloramphenicol acetyltransferase, luciferase, and beta-galactosidase were separately injected into mouse skeletal muscle in vivo. Protein expression was readily detected in all cases, and no special delivery system was required for these effects. The extent of expression from both the RNA and DNA constructs was comparable to that obtained from fibroblasts transfected in vitro under optimal conditions. In situ cytochemical staining for beta-galactosidase activity was localized to muscle cells following injection of the beta-galactosidase DNA vector. After injection of the DNA luciferase expression vector, luciferase activity was present in the muscle for at least 2 months.



Science
Vol 247, Issue 4949
23 March 1990
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Vacunas del covid

Katalin y Drew se encuentran

Las vacunas del covid no son producto de la suerte

- Todo empezó con Kariko

Katalin Kariko



Katalin Kariko y Drew Weissman

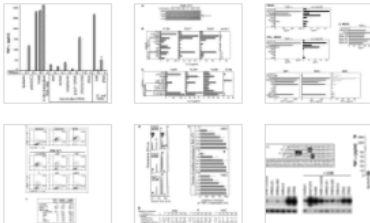




Outline

[Summary](#)[Introduction](#)[Results](#)[Discussion](#)[Experimental Procedures](#)[Acknowledgments](#)[Supplemental Data](#)[References](#)[Show full outline](#)

Figures (6)



Extras (1)

[Document S1. One figure](#)

Immunity

Volume 23, Issue 2, August 2005, Pages 165-175



Article

Suppression of RNA Recognition by Toll-like Receptors: The Impact of Nucleoside Modification and the Evolutionary Origin of RNA

Katalin Karikó¹ , Michael Buckstein², Houping Ni², Drew Weissman²[Show more](#) [+ Add to Mendeley](#) [Share](#) [Cite](#)<https://doi.org/10.1016/j.immuni.2005.06.008>[Get rights and content](#)

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Summary

DNA and RNA stimulate the mammalian **innate immune system** through activation of **Toll-like receptors** (TLRs). DNA containing methylated CpG motifs, however, is not stimulatory. Selected **nucleosides** in naturally occurring RNA are also methylated or otherwise modified, but the immunomodulatory effects of these alterations remain untested. We show that RNA signals through human **TLR3**, **TLR7**, and **TLR8**, but incorporation of modified nucleosides m5C, m6A, m5U, s2U, or **pseudouridine** ablates activity. Dendritic cells (DCs) exposed to such modified RNA express significantly less cytokines and activation markers than those treated with unmodified RNA. DCs and TLR-expressing cells are potently activated by **bacterial and mitochondrial RNA**, but not by mammalian total RNA, which is abundant in modified nucleosides. We conclude that nucleoside modifications suppress the potential of RNA to activate DCs. The innate immune system may therefore detect RNA lacking nucleoside modification as a means of selectively responding to bacteria or necrotic tissue.

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Immunity, Volume 43, Issue 1, 2015, pp. 41-51 [Download PDF](#)[View details](#) [The Emerging Role of *In Vitro*-Transcribed mRN...](#)
Molecular Therapy, Volume 27, Issue 4, 2019, pp. 747-... [Download PDF](#)[View details](#) [1](#) [2](#) [Next](#)

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News Mentions:	6
References:	7

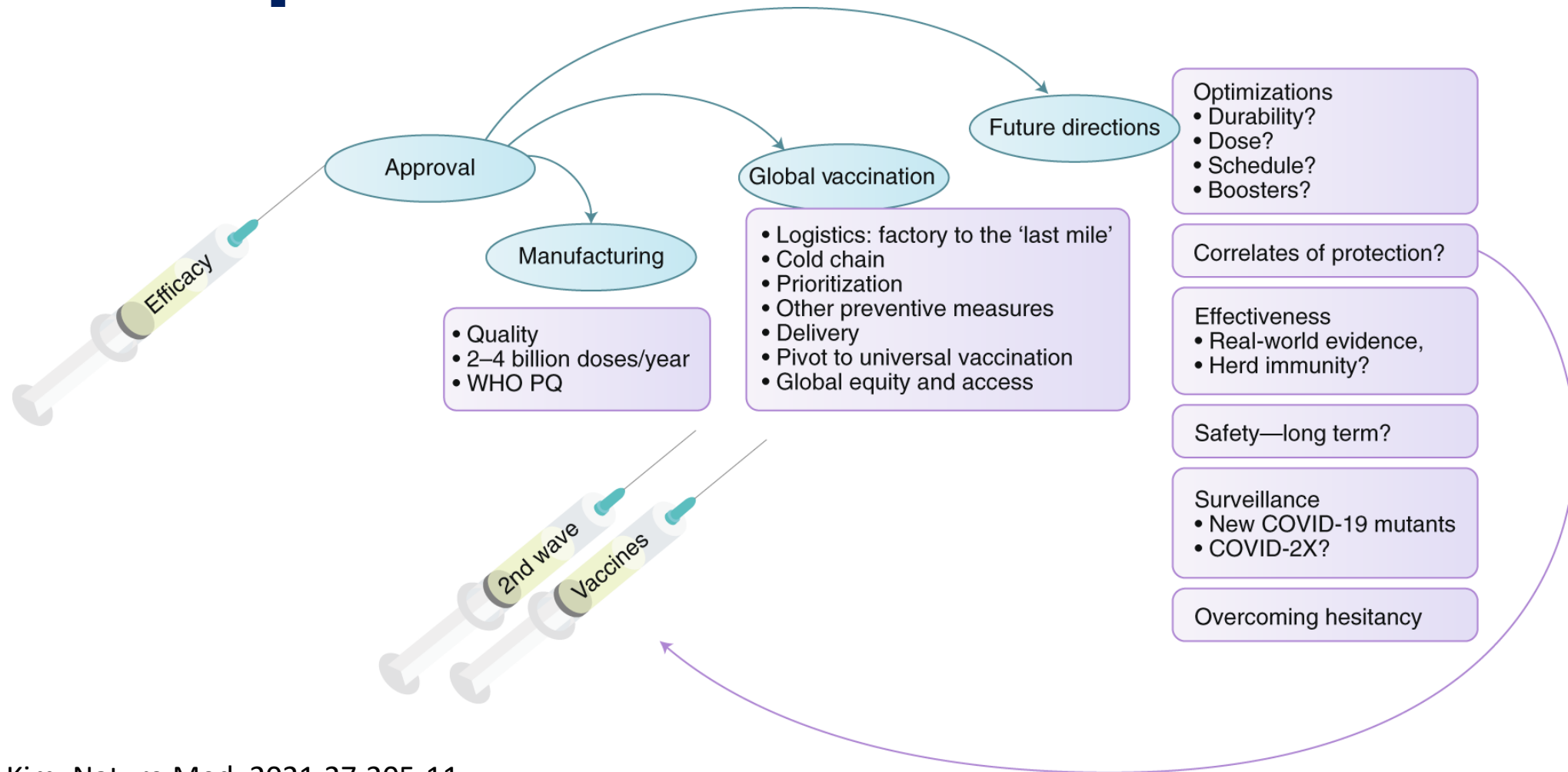
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Shares, Likes & Comments:	90
Tweets:	231

Retos de las vacunas del covid a corto plazo

El futuro de la pandemia

- Retos pendientes



JH. Kim. Nature Med. 2021;27:205-11.

<https://www.nature.com/articles/s41591-021-01230-y>

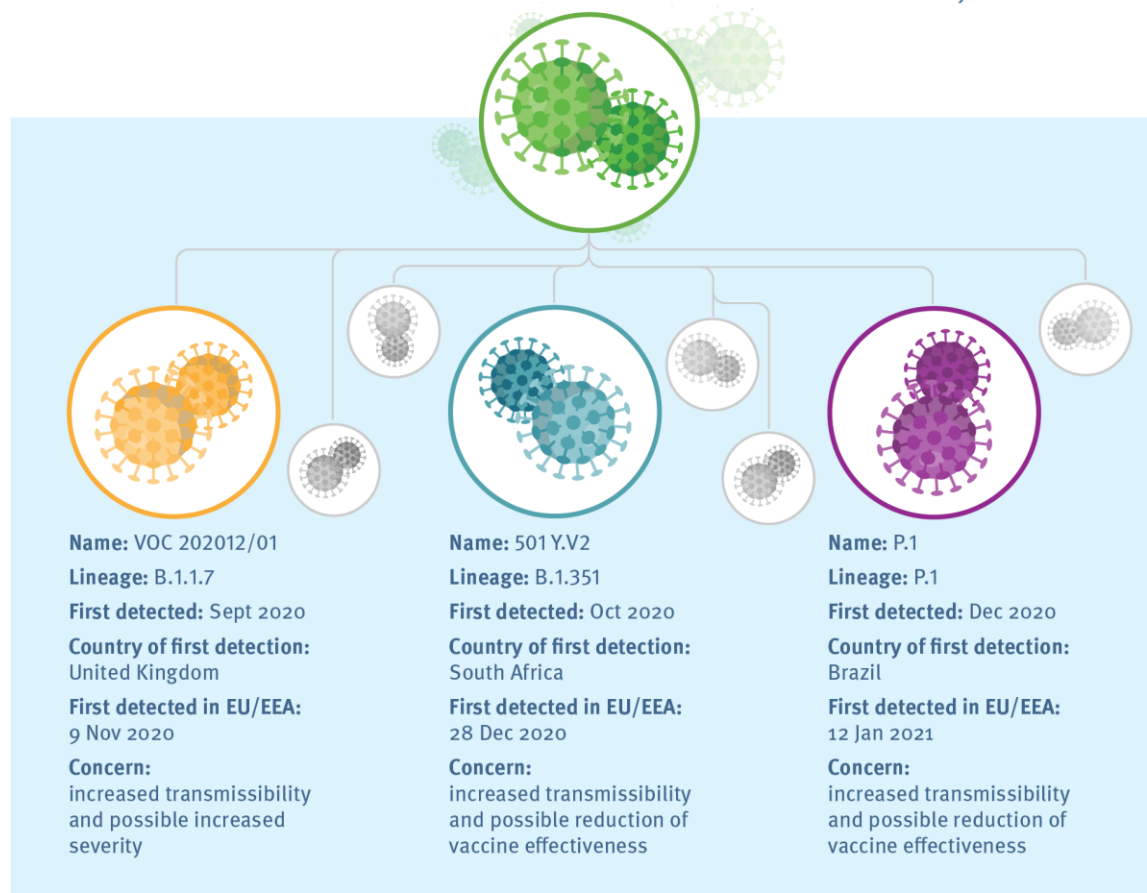
¿Cómo afectarán las variantes del SARS-CoV-2



Mutation of SARS-CoV-2: current variants of concern

8 February 2021

Mutations of SARS-CoV-2 that cause COVID-19 have been observed globally. Viruses, in particular RNA viruses such as coronaviruses, constantly evolve through mutations, and while most will not have a significant impact, some mutations may provide the virus with a selective advantage such as increased transmissibility. Such mutations are cause for concern and need to be monitored closely.



El futuro de la pandemia

- Retos pendientes

#COVID19

Learn more in the latest risk assessment by ECDC on SARS-CoV-2 variants of concern <http://bit.ly/RRAVariants1>



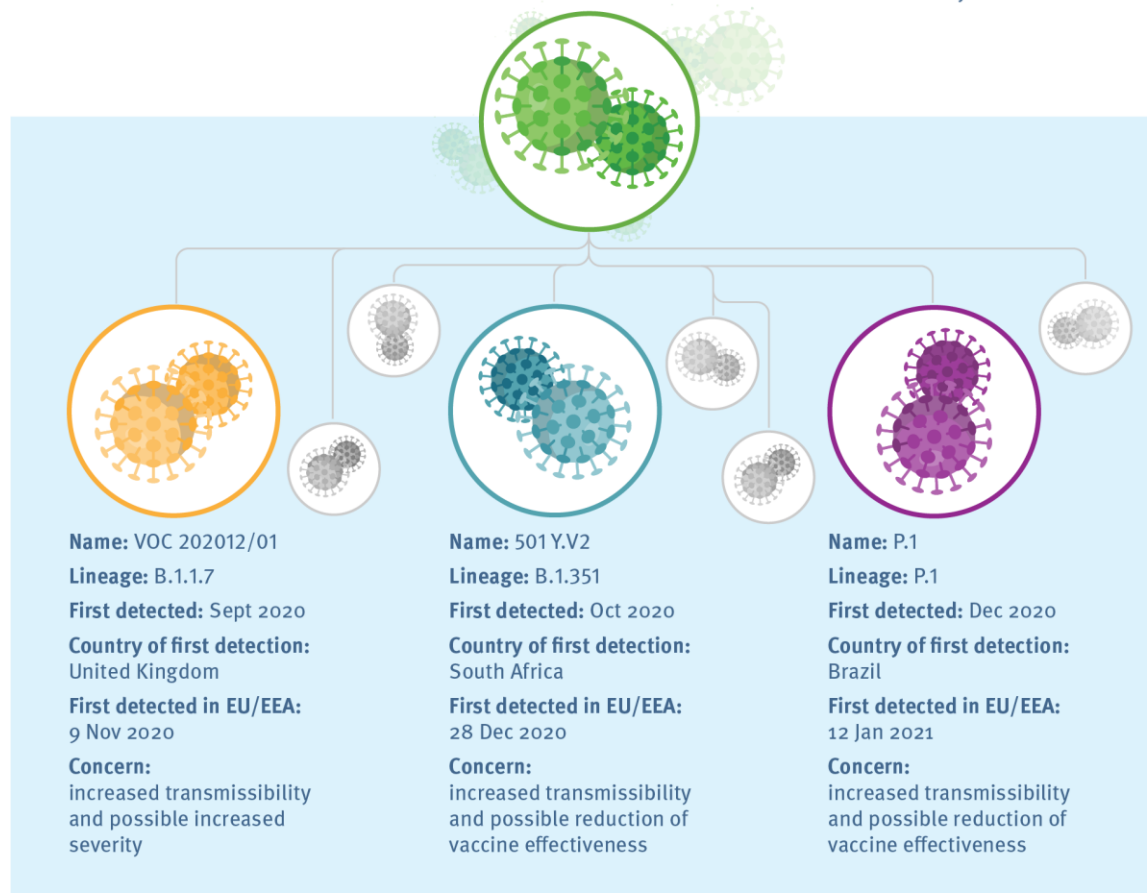
¿Cómo afectará la vacunación a las variantes del SARS-CoV-2



Mutation of SARS-CoV-2: current variants of concern

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El futuro de la pandemia

- Retos pendientes

#COVID19

Learn more in the latest risk assessment by ECDC on SARS-CoV-2 variants of concern <http://bit.ly/RRAVariants1>

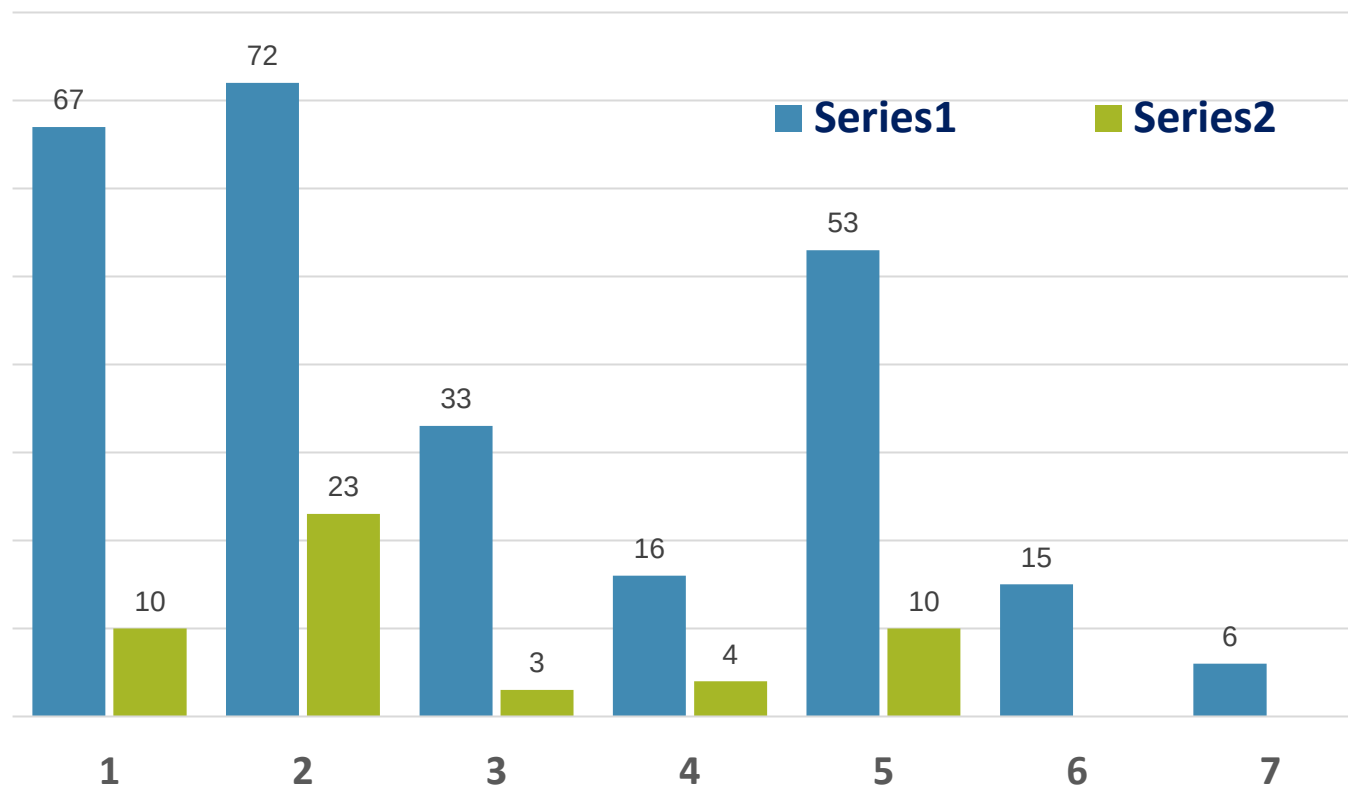


Vacunas del covid

Nuevos productos en investigación

La próxima generación de vacunas

- Esto solo acaba de empezar



OMS, investigación en vacunas en curso

Candidatos en estudio: 272

- 86 en fase clínica
- 186 en fase preclínica

86 candidatos a vacunas en investigación clínica

- 262 estudios registrados
- 50 publicaciones originales revisadas

7/abril de 2021

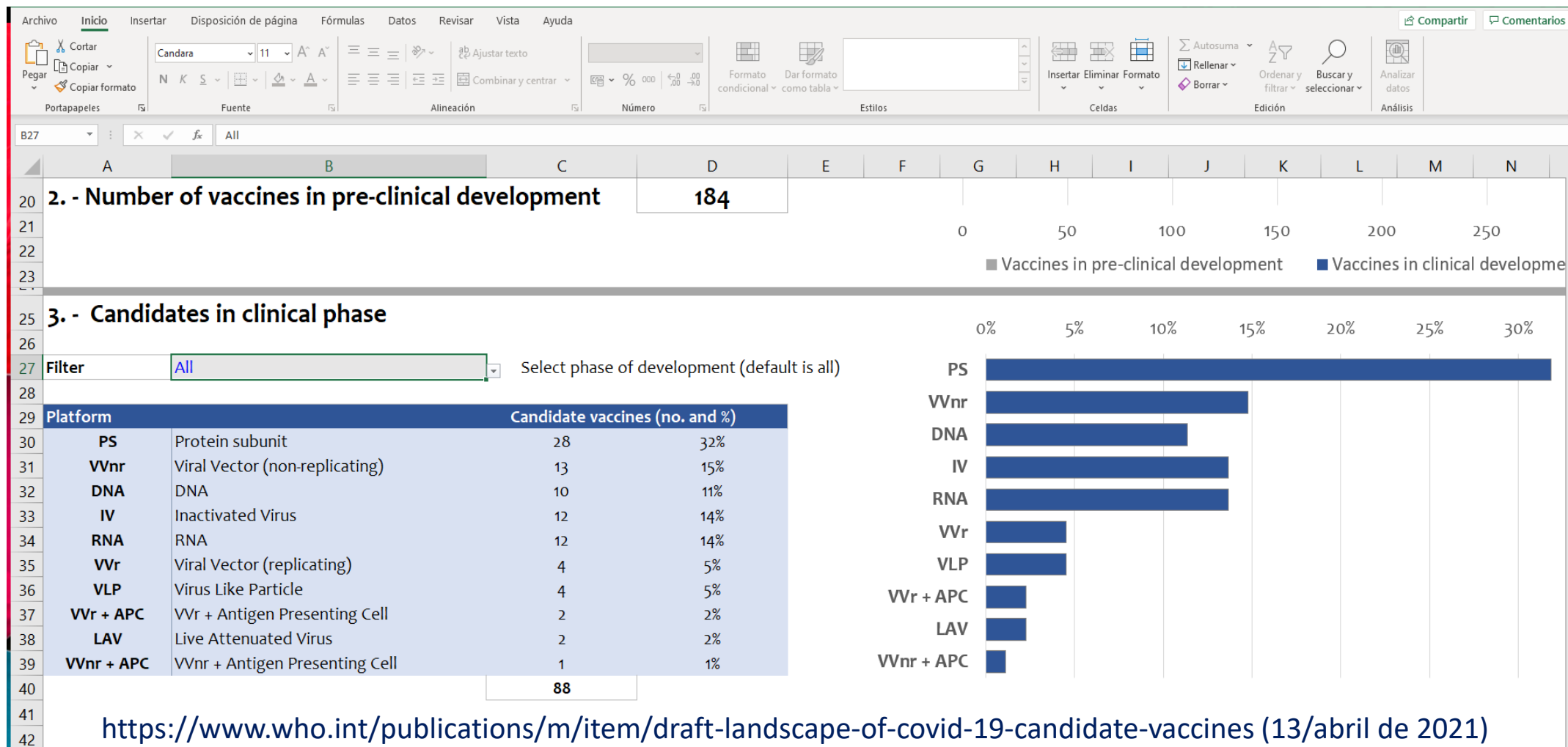
Draft landscape and tracker of COVID-19 candidate vaccines

Vacunas del covid

Nuevos productos en investigación

La próxima generación de vacunas

- Esto solo acaba de empezar



Vacunas del covid futuras

Vacunas de ARNm

La próxima generación de vacunas

- Esto solo acaba de empezar

Campos de investigación

- Cáncer
- Terapia génica
- Terapia celular
- Vacunas terapéuticas
- Vacunas preventivas

Vacunas preventivas

- Zika
- Gripe
- VIH
- Rabia
- Coronavirus

Profilaxis pasiva

- ARNm que codifica anticuerpos específicos (chikunguña)

Ventajas

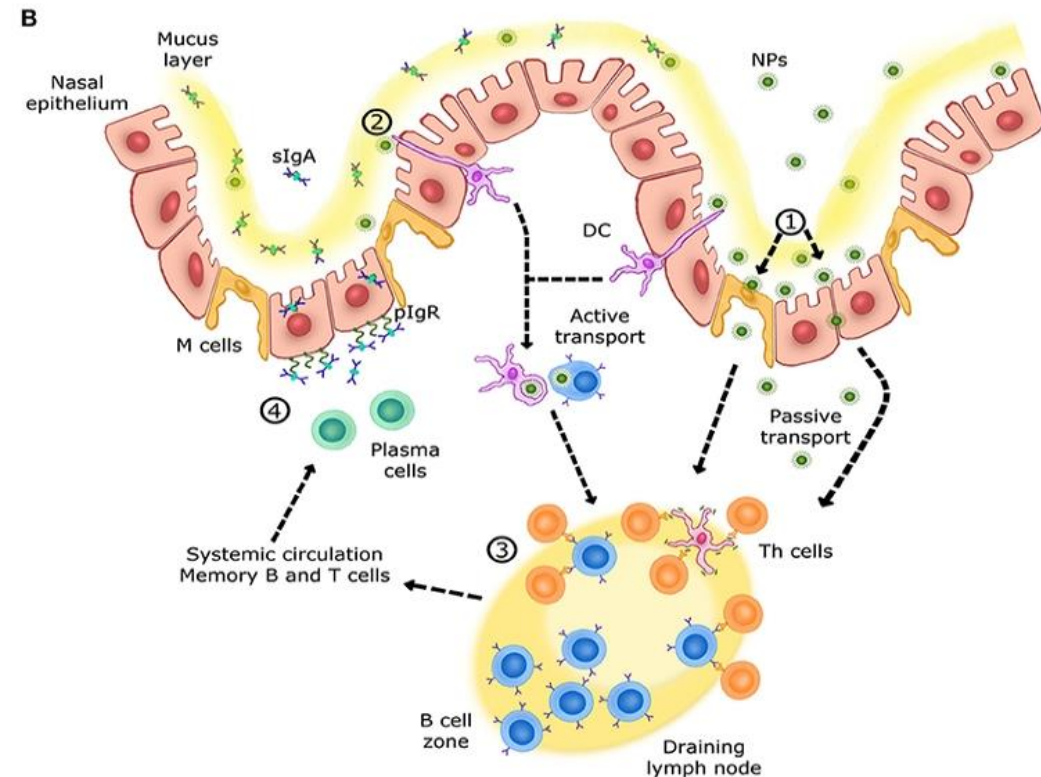
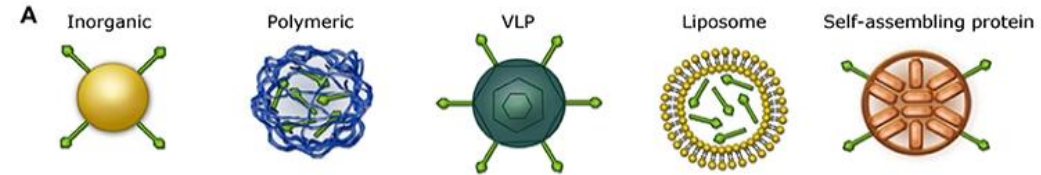
- Abre vías de avance en patologías sin alternativas farmacológicas
- Diseño relativamente sencillo, al alcance de pequeños grupos
- Flexibilidad: adaptación a nuevos objetivos
- Medicina personalizada

Vacunas de ARNm futuras

Retos: **estabilidad**

La próxima generación de vacunas

- Esto solo acaba de empezar



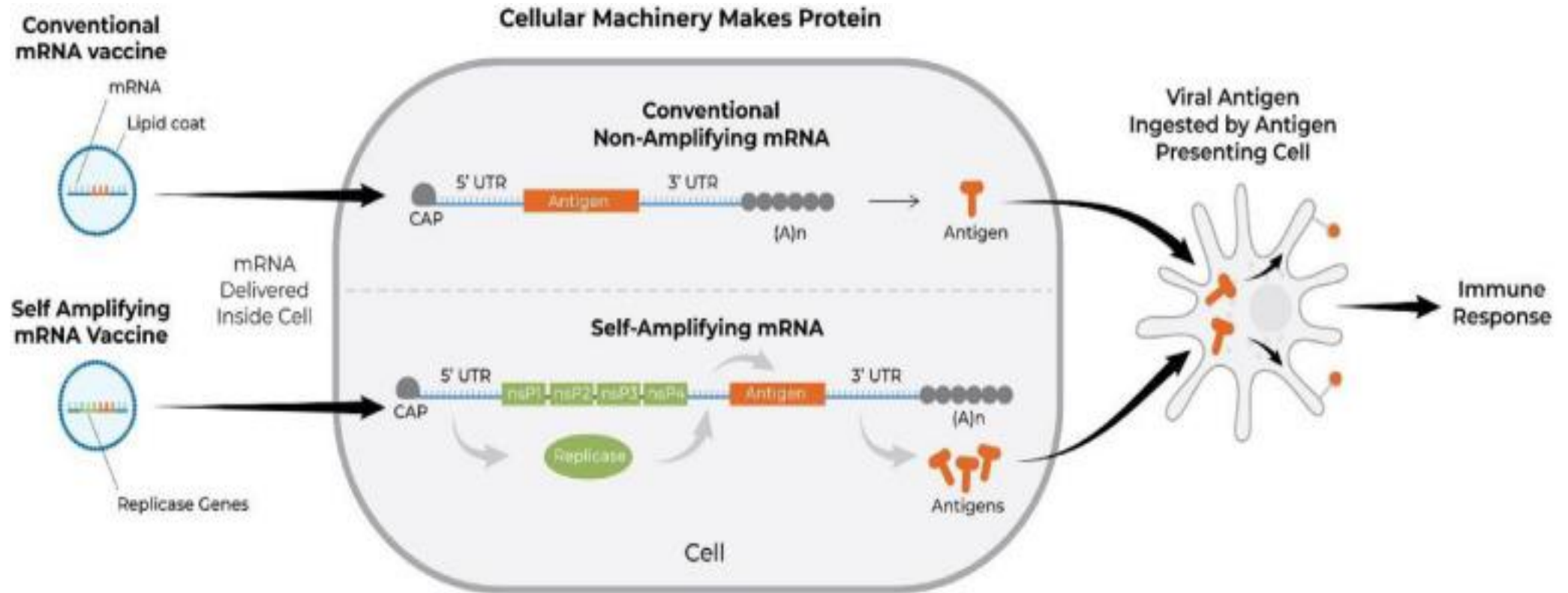
www.1000pensamientospositivos.blogspot.com

Vacunas de ARNm futuras

Retos: **rendimiento**

La próxima generación de vacunas

- Esto solo acaba de empezar

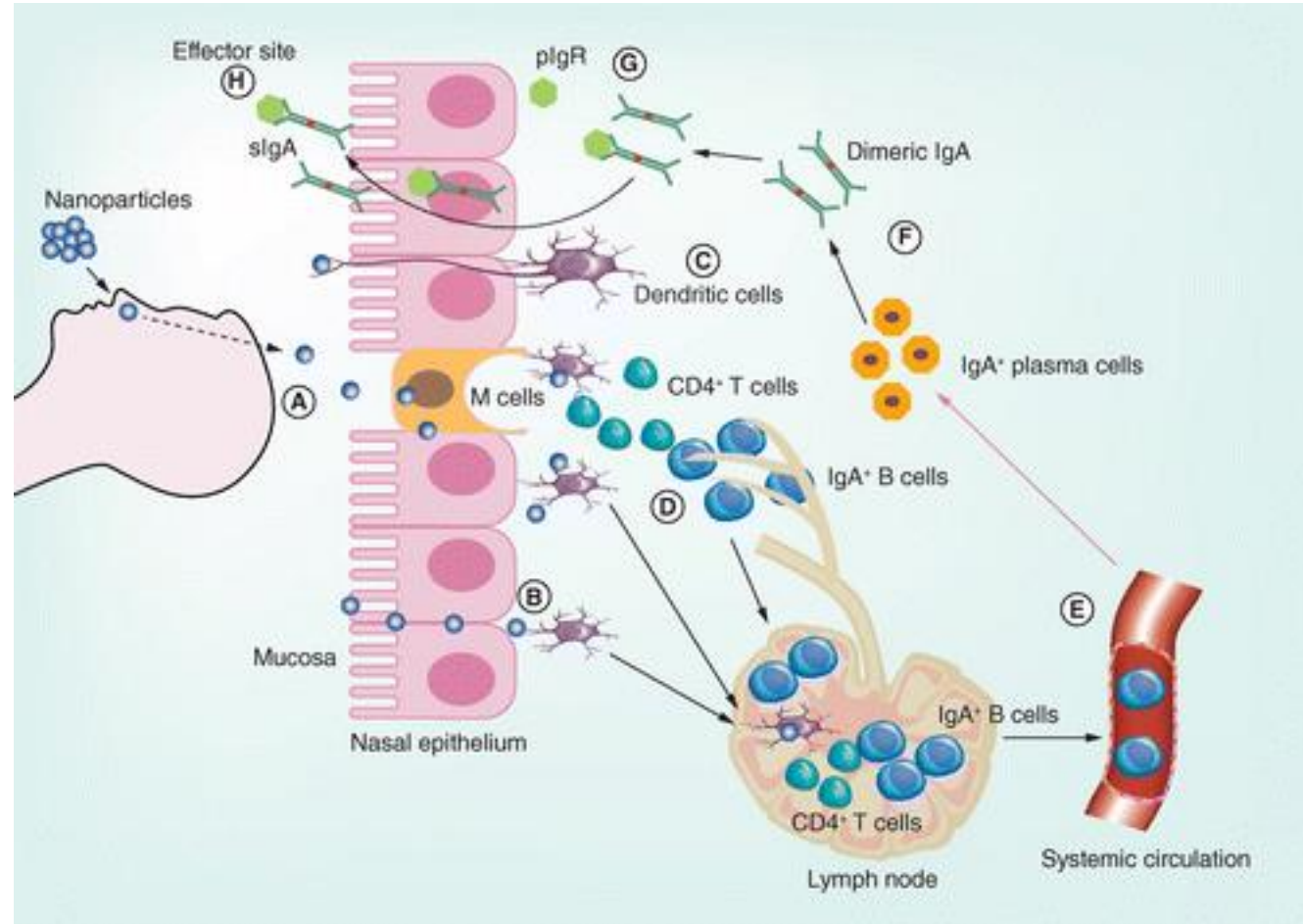


Vacunas de ARNm futuras

Retos: **inmunidad mucosal**

La próxima generación de vacunas

- Esto solo acaba de empezar



Las vacunas de ARNm no son flor de un día

Las vacunas de ARNm no son flor de un día

- Las vacunas del covid, un antes y un después

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Published: 12 January 2018

mRNA vaccines – a new era in vaccinology

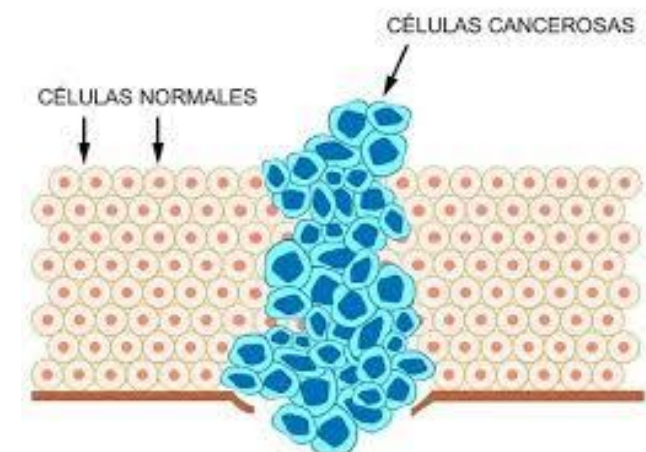
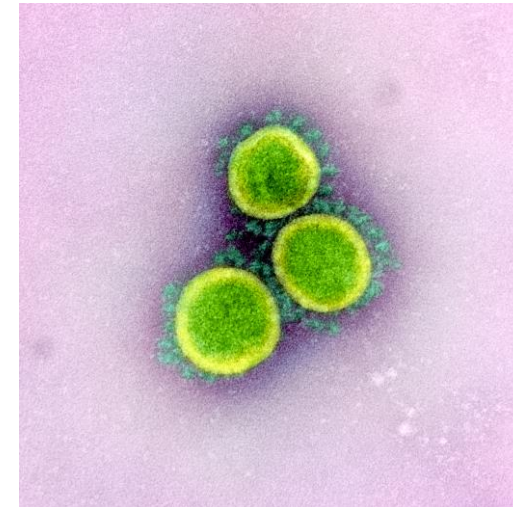
Norbert Pardi, Michael J. Hogan, Frederick W. Porter & Drew Weissman ✉

Nature Reviews Drug Discovery **17**, 261–279(2018) | Cite this article

1.50m Accesses | 523 Citations | 4476 Altmetric | Metrics

Key Points

- Recent improvements in mRNA vaccines act to increase protein translation, modulate innate and adaptive immunogenicity and improve delivery.
- mRNA vaccines have elicited potent immunity against infectious disease targets in animal models of influenza virus, Zika virus, rabies virus and others, especially in recent years, using lipid-encapsulated or naked forms of sequence-optimized mRNA.
- Diverse approaches to mRNA cancer vaccines, including dendritic cell vaccines and various types of directly injectable mRNA, have been employed in numerous cancer



Las vacunas del covid son producto de una combinación de tecnologías usadas por separado antes

PNAS Proceedings of the National Academy of Sciences of the United States of America

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PERSPECTIVE

Vaccinology in the post-COVID-19 era

Rino Rappuoli, Ennio De Gregorio, Giuseppe Del Giudice, Sanjay Phogat, Simone Pe...
+ See all authors and affiliations

PNAS January 19, 2021 118 (3) e2020368118; <https://doi.org/10.1073/pnas.2020368118>

Edited by Diane E. Griffin, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, and approved November 30, 2020 (received for review October 15, 2020)

Article Figures & SI Info & Metrics PDF

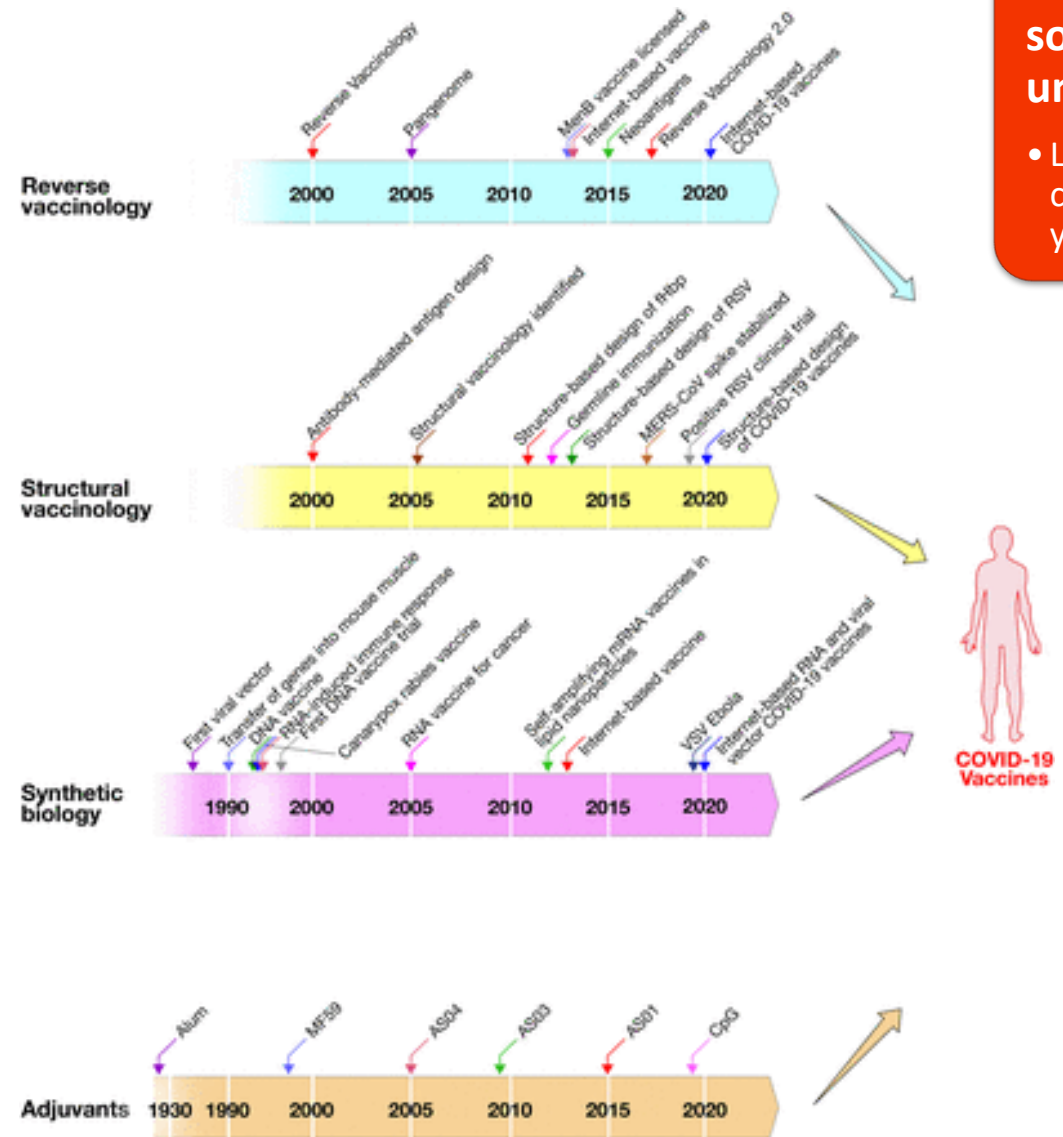
Abstract

The COVID-19 pandemic is a shocking reminder of how our world would look in the absence of vaccination. Fortunately, new technologies, the pace of understanding new and existing pathogens, and the increased knowledge of the immune system allow us today to develop vaccines at an unprecedented speed. Some of the vaccine technologies that are fast-tracked by the urgency of COVID-19 may also be the answer for other health priorities, such as antimicrobial resistance, chronic infections, and cancer, that the post-COVID-19 world will urgently need to face. This perspective analyzes the way COVID-19 is transforming vaccinology and the opportunities for vaccines to have an increasingly important role in health and well-being.

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Las vacunas de ARNm no son flor de un día

- Las vacunas del covid, un antes y un después

R. Rappuoli. PNAS. 2021;118(3):e2020368118

Vacunas del covid: regreso al futuro

Ideas clave

Pasado, presente y futuro

- ¿Cómo hemos llegado hasta aquí?
- “A hombros de gigantes”
- Grandes hitos y personajes en el desarrollo de las vacunas

Las vacunas del covid no son producto de la suerte

- Valor de la investigación básica
- Las vacunas del covid son producto de más de una década de investigación
- Papel de Katalin Kariko y Drew Weissman (entre otros)

El futuro de la pandemia

- Retos pendientes
- Producción y logística
- Condiciones de conservación
- Duración, efectividad, seguridad
- Variantes virales y vacunación

La próxima generación de vacunas

- Esto solo acaba de empezar
- Cientos de productos en investigación
- Ventajas de las plataformas de ARN
- Estabilidad: nanopartículas y otros vehículos
- Rendimiento: ARN autoamplificante
- Inmunidad mucosal

Las vacunas de ARNm no son flor de un día

- Las vacunas del covid, un antes y un después
- La tecnología del ARN abre la puerta a nuevas opciones en patologías sin alternativas válidas hasta ahora

@angel_h_merino



Gracias!

A stylized graphic of the word "Gracias!" in a white, cursive script. The text is set against a background of vibrant, multi-colored paint splashes in shades of green, yellow, orange, and red. The splashes are dynamic and energetic, with some colors bleeding into each other.



GRACIAS

A graphic of the word "GRACIAS" in a bold, blocky, sans-serif font. The letters are filled with a multi-colored, splattered texture, featuring shades of blue, yellow, orange, and red. The overall effect is vibrant and celebratory.



Gracias

A graphic of the word "Gracias" in a cursive script. The letters are filled with a rainbow gradient, transitioning from orange to yellow to green to blue. The text is surrounded by colorful paint splashes and a soft, glowing aura.



gracias

A graphic of the word "gracias" in a cursive script. The text is set against a background of blue and purple paint splashes. The splashes are soft and blended, creating a dreamy, ethereal atmosphere.

@angel_h_merino