ROBERTO IERACI

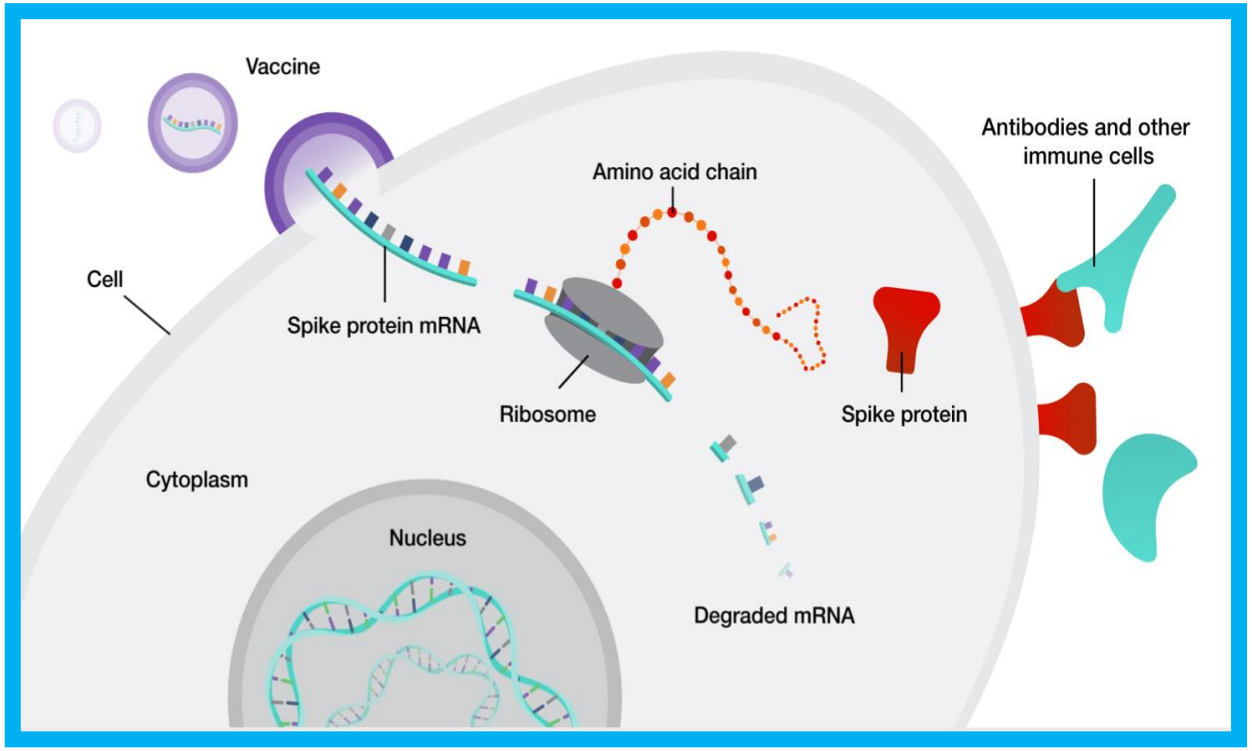
LE DIVERSE APPLICAZIONI DELLA TECNOLOGIA mRNA, COVID-19 E NON SOLO

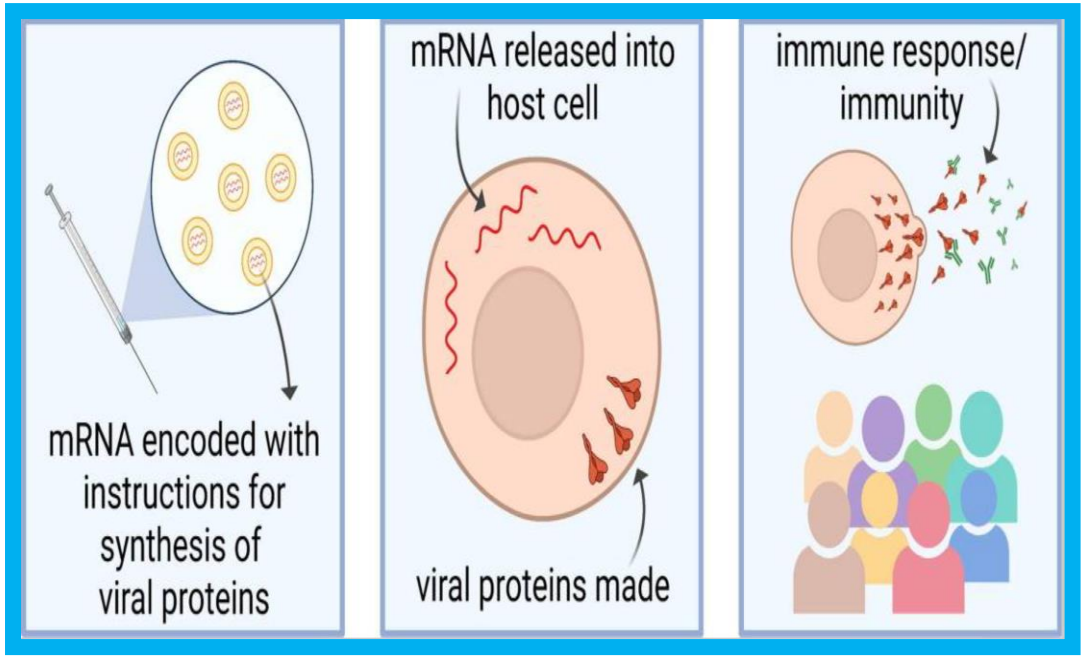
Presiede: *Simone Scarlata (Roma)*

SOCIETÀ ITALIANA
DI GERONTOLOGIA
E GERIATRIA

Roma, 30 novembre - 3 dicembre 2022
UNIVERSITÀ CATTOLICA DEL SACRO CUORE

la tecnologia ad mRNA





Immunity CellPress
2000 Immunity *55*, November 8, 2022

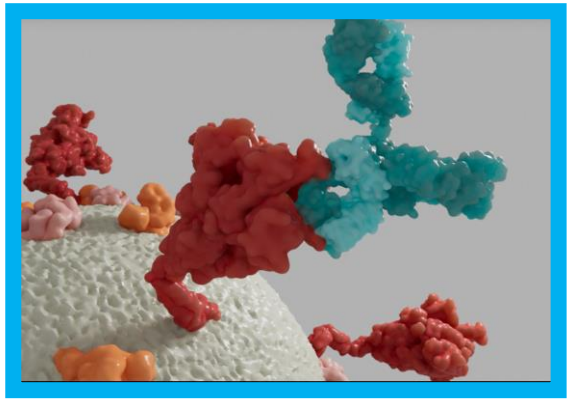
Review

Innate immune mechanisms of mRNA vaccines

Rein Verbeke,[1,2,*] Michael J. Hogan,[3] Karin Loré,[4,5] and Norbert Pardi[6,*]

318 | Nature | Vol 597 | 16 September 2021

THE TANGLED HISTORY OF MRNA VACCINES



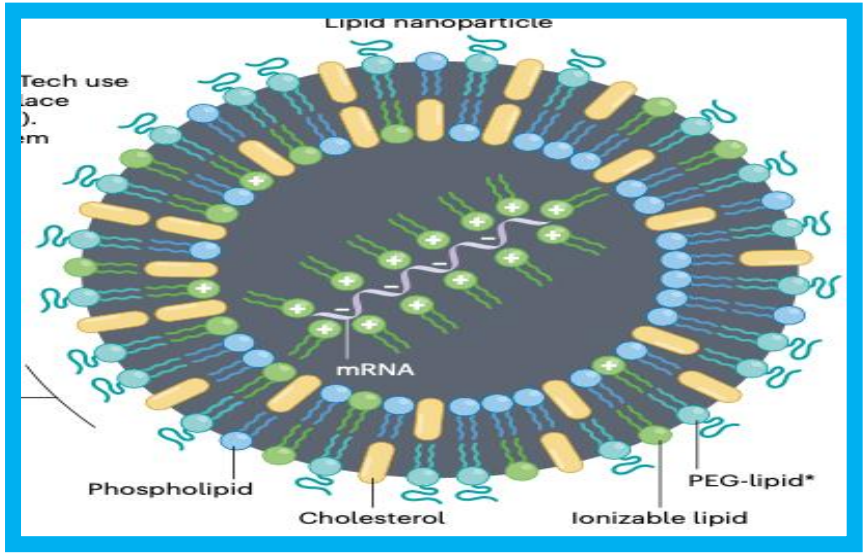
nanomedicina fondamentale per fornire vaccini mRNA

riformulare
- **farmaci esistenti e nuovi**

per curare i pazienti con Covid-19

Nanotechnology versus coronavirus

Nature NaNotechNology | VOL 15 | August 2020 | 617 | www.nature.com/naturenanotechnology



RESEARCH ARTICLE

ADVANCED SCIENCE

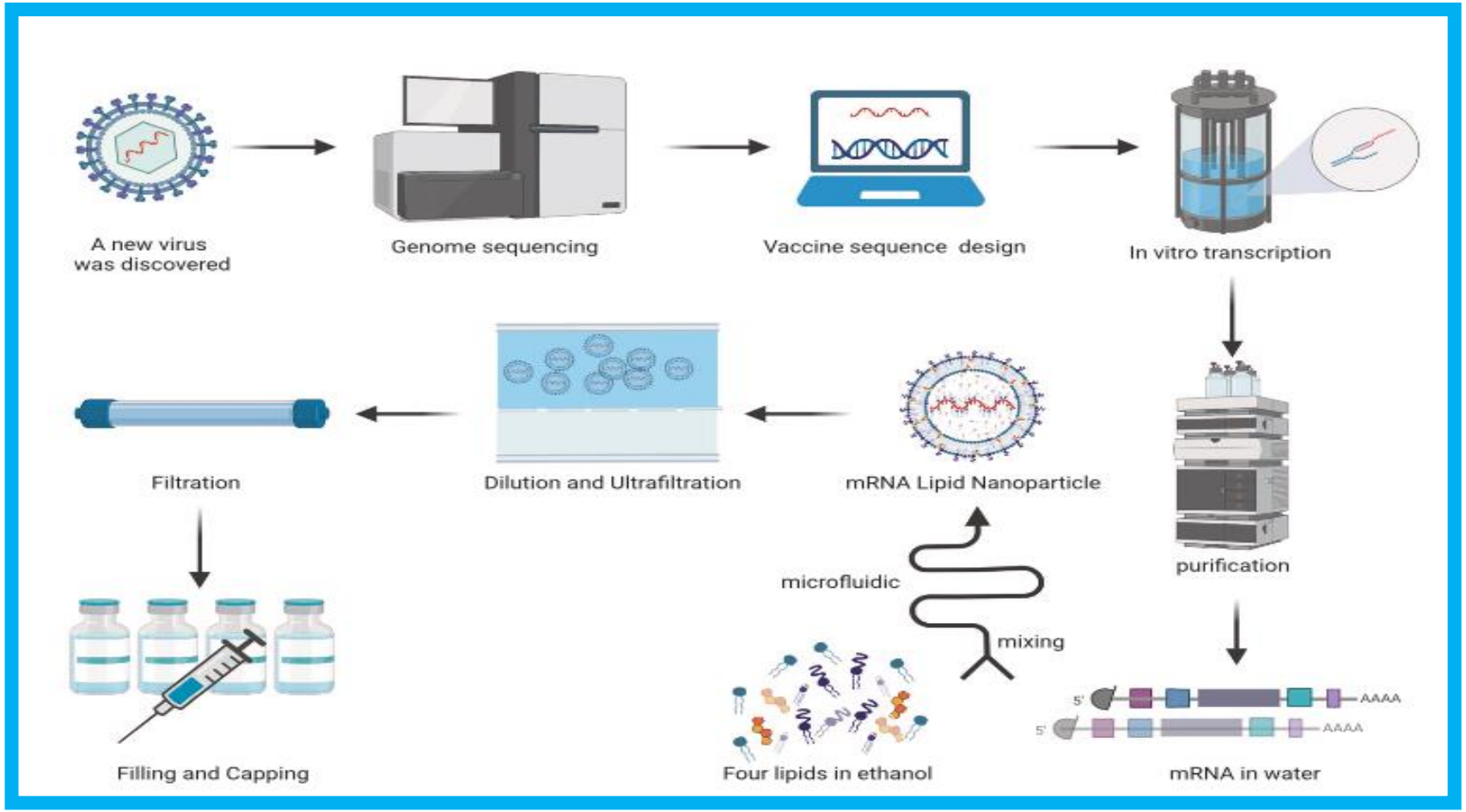
www.advancedscience.com

Rapid Generation of Circulating and Mucosal Decoy Human ACE2 using mRNA Nanotherapeutics for the Potential Treatment of SARS-CoV-2

*Jeonghwan Kim, Antony Jozic, Anindit Mukherjee, Dylan Nelson, Kevin Chiem, Md Siddiqur Rahman Khan, Jordi B. Torrelles, Luis Martinez-Sobrido, and Gaurav Sahay**

vaccini mRNA Covid contengono un adiuvante sotto forma di nanoparticelle lipidiche

production process of mRNA vaccines



Signal Transduction and Targeted Therapy
www.nature.com/sigtrans
Signal Transduction and Targeted Therapy
REVIEW ARTICLE OPEN

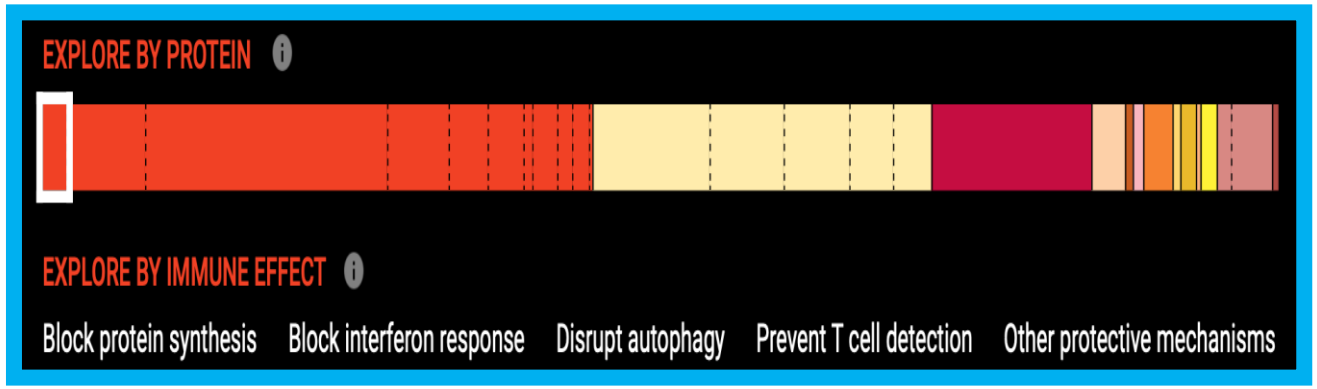
Advances in COVID-19 mRNA vaccine development

Enyue Fang[1,2], Xiaohui Liu[1], Miao Li[1], Zelun Zhang[1], Lifang Song[1], Baiyu Zhu[3], Xiaohong Wu[1], Jingjing Liu[1], Danhua Zhao[1] and Yuhua Li[1]

protezione per:

- **Infezione: transitoria limitata dopo booster**
- **malattie gravi: in gran parte mantenuta**

Science



Further humoral immunity evasion of emerging SARS-CoV-2 BA.4 and BA.5 subvariants

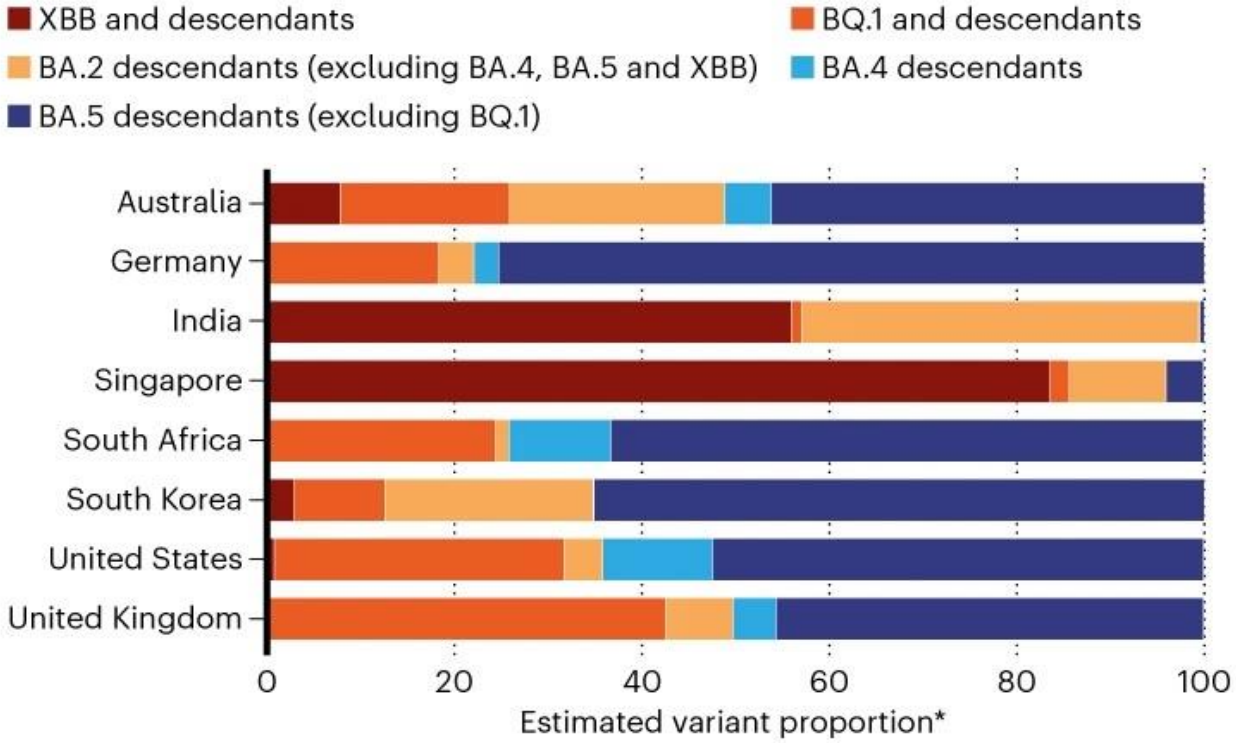
https://doi.org/10.1016/S1473-3099(22)00642-9

inseguiamo sempre le varianti ma non riusciamo mai a superarle

Science

VARIANT SWARM

A menagerie of Omicron sublineages is spreading globally, but some geographic patterns are beginning to emerge.



©nature

*As of 27 October 2022

https://www.nature.com/articles/d41586-022-03445-6

NEWS | 28 October 2022

COVID 'variant soup' is making winter surges hard to predict

COVID-19

Published Online October 13, 2022

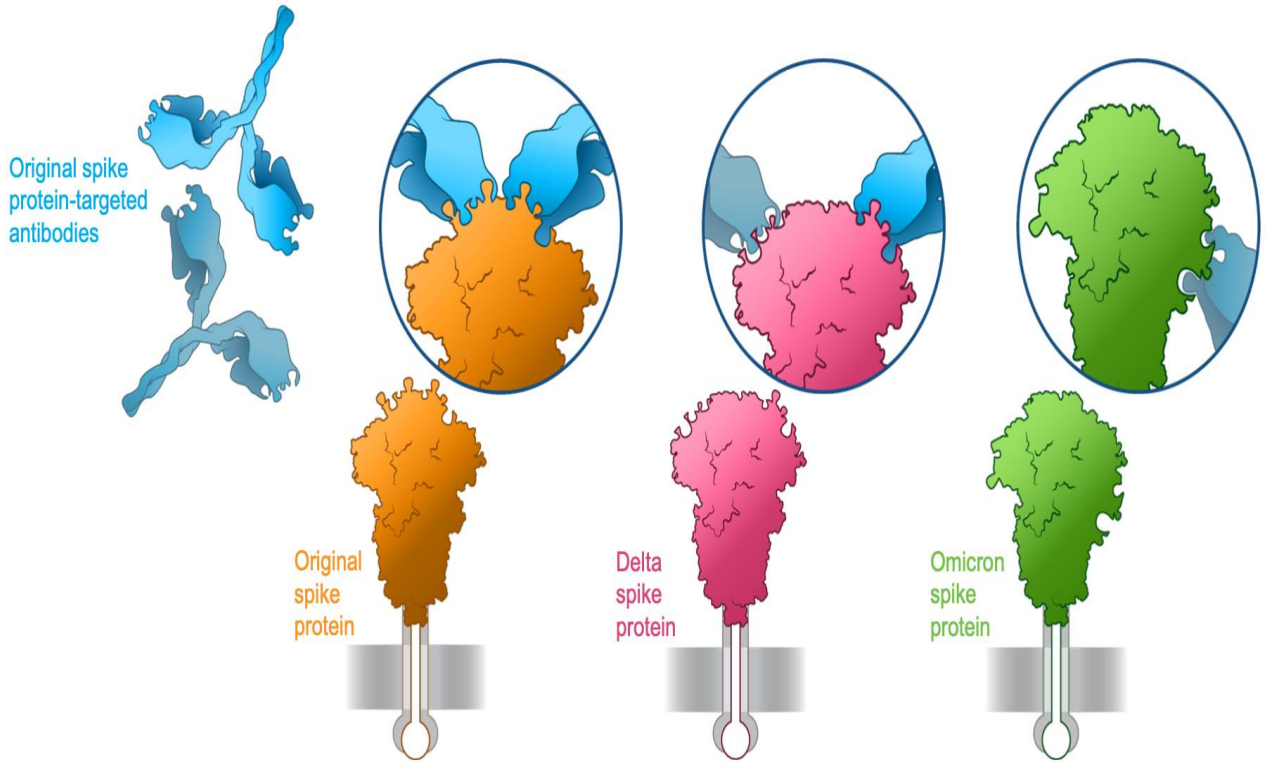
New Omicron strains may portend big COVID-19 waves

Emerging subvariants are more immune evasive than ever

Omicron sublineage BA.2.75.2 exhibits extensive escape from neutralising antibodies

evoluzione omicron → numerose sotto-varianti con un vantaggio di crescita rispetto a BA.5

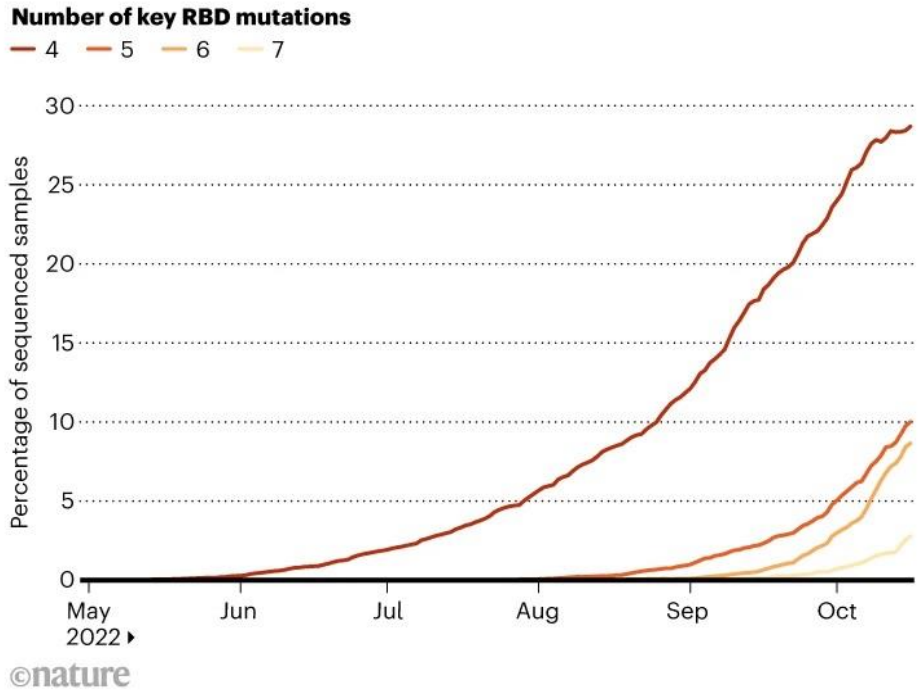
Evaluate Variant-containing Boosters Due to Mutations in the RBD Region of SARS-CoV-2 Spike Protein



RBD, receptor binding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

LEVEL ALERT

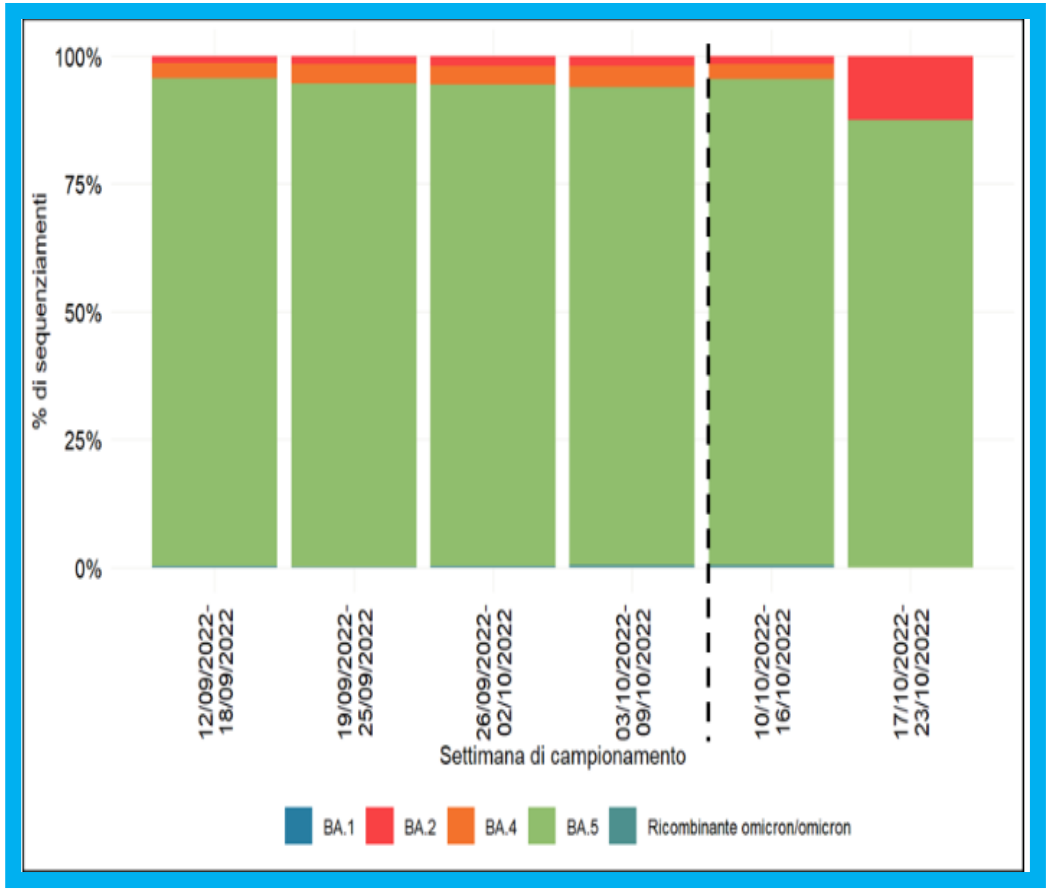
The success of various SARS-CoV-2 sublineages is due to a handful of key changes to the receptor binding domain (RBD) in the viral spike protein. The more of these mutations a variant has, the quicker it seems to grow.



Prevalenza e distribuzione delle varianti di SARS-CoV-2 di interesse per la sanità pubblica in Italia

Rapporto n. 25 del 28 ottobre 2022

Nomenclatura OMS	Lignaggio	N. di sequenze	%
	CC.1	1	0,02%
	CG.1	3	0,07%
	Totale BA.5	*3828*	*94,03%*
	XAZ	6	0,15%
	XBB	2	0,05%
	XBB.1	6	0,15%
	Totale Ricombinanti omicron/omicron	*14*	*0,34%*
	Totale Omicron	***4071***	***100,00%***



prevalenza di BA.5 e una elevata variabilità genomica

domanda chiave:

- **come ottimizzare immunità linfociti T con i vaccini**

Science Immunology | REPORT | FIRST RELEASE

CORONAVIRUS

Sci. Immunol. published First Release 1 November 2022

Durable spike-specific T-cell responses after different COVID-19 vaccination regimens are not further enhanced by booster vaccination

Yacine Maringer[1,2,3], Annika Nelde[1,2,3], Sarah M. Schroeder[1,2,4], Juliane Schuhmacher[1,3], Sebastian Hörber[5], Andreas Peter[5], Julia Karbach[6], Elke Jäger[6], Juliane S. Walz[1,2,3,7]*

cellule T memoria mantengono capacità riconoscere varianti virali Omicron

Cell
https://doi.org/10.1016/j.cell.2022.01.015
Article

SARS-CoV-2 vaccination induces immunological T cell memory able to cross-recognize variants from Alpha to Omicron

- **disconnessione tra infezione e malattia grave**
- **livello sostanziale immunità popolazione con immunità umorale e cellulare**

DOI: 10.1056/NEJMoa2208343

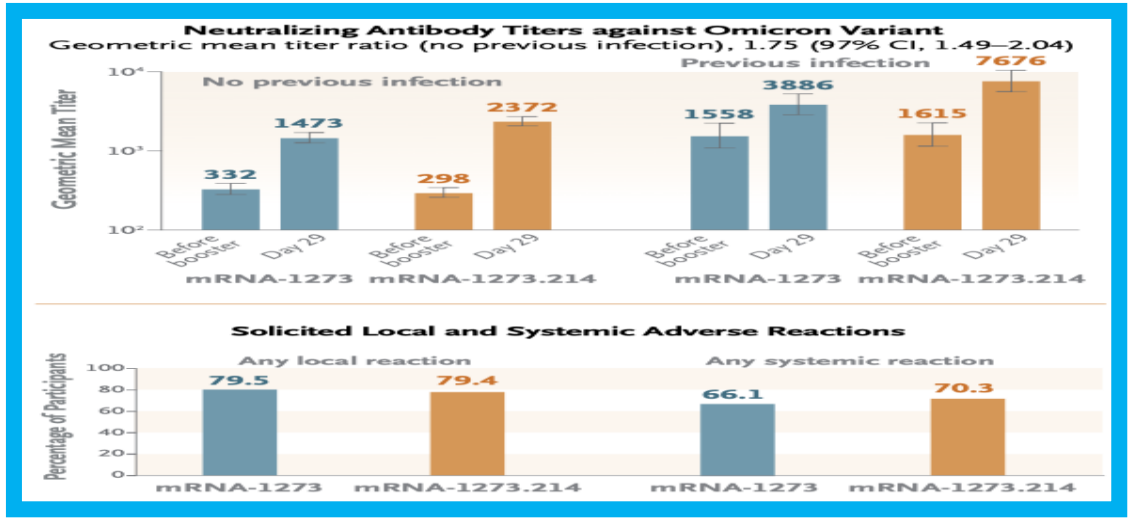
Lancet Infect Dis 2022

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Bivalent Omicron-Containing Booster Vaccine against Covid-19

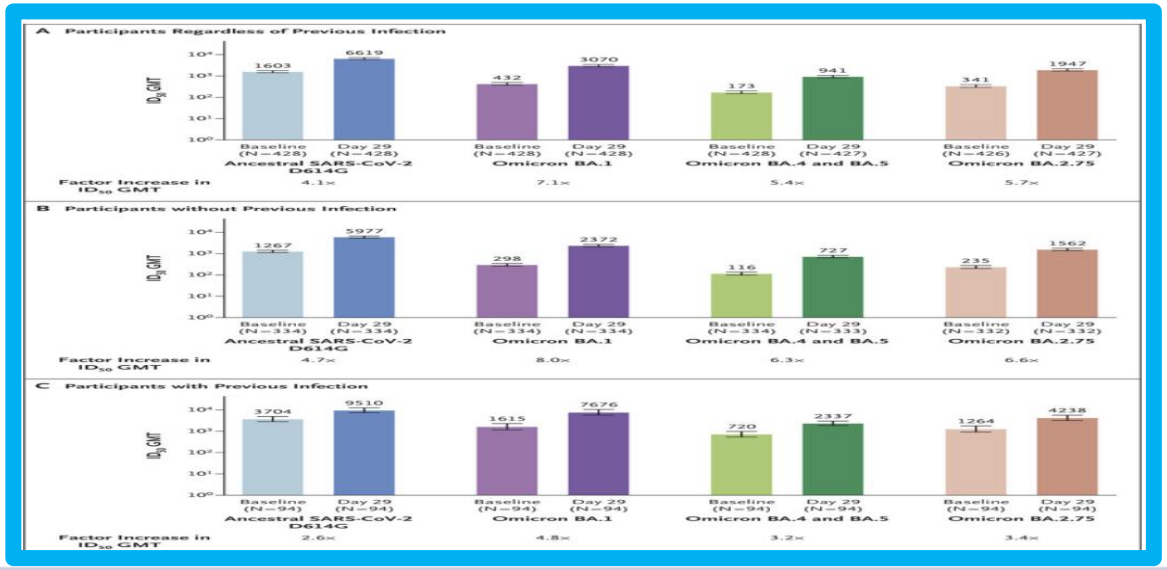
Spyros Chalkias, M.D., Charles Harper, M.D., Keith Vrbicky, M.D., Stephen R. Walsh, M.D., Brandon Essink, M.D., Adam Brosz, M.D., Nichole McGhee, B.S., Joanne E. Tomassini, Ph.D., Xing Chen, Sc.D., Ying Chang, M.S., Andrea Sutherland, M.D., M.P.H., David C. Montefiori, Ph.D., Bethany Girard, Ph.D., Darin K. Edwards, Ph.D., Jing Feng, M.S., Honghong Zhou, Ph.D., Lindsey R. Baden, M.D., Jacqueline M. Miller, M.D., and Rituparna Das, M.D., Ph.D.



The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Neutralization of Omicron Subvariant BA.2.75 after Bivalent Vaccination



7 studi di laboratorio che valutano il booster bivalente BA.5 rispetto al booster originale

Bivalent BA.5 Booster Neutralizing Antibody Lab Assessments

Moderna	Live virus	5 to 6-fold improved	Increased
Suthar	Live virus	4-fold improved	~10-fold increased (vs 1 booster)
Shi	Live virus	3-fold improved	Low, but 3-fold GMT
Pfizer	Live virus	4-fold improved	Not assessed
Ho	Pseudovirus	Minimal difference	Not assessed
Barouch	Pseudovirus	1.3-fold increase	Not assessed
Barouch	Pseudovirus	No difference	Modest ~1.2-fold increase

@erictopol

Moderna's BA.4/BA.5 Targeting Bivalent Booster, mRNA-1273.222, Meets Primary Endpoint of Superiority Against Omicron Variants Compared to Booster Dose of mRNA-1273 in Phase 2/3 Clinical Trial

Antibody responses to Omicron BA.4/BA.5 bivalent mRNA vaccine booster shot

bioRxiv preprint doi https://doi.org/10.1101/2022.10.22.513349

Qian Wang[1,#], Anthony Bowen[2,#], Riccardo Valdez[3], Carmen Gherasim[3], Aubree Gordon[3,*], Lihong Liu[1,*], David D. Ho[1,*]

Substantial Neutralization Escape by the SARS-CoV-2 Omicron Variant BQ.1.1

Jessica Miller, Nicole Hachmann, Ai-ris Collier, Ninaad Lasrado, Camille Mazurek, Robert Patio, Olivia Powers, Nehalee Surve, James Theiler, Bette Korber, Dan H. Barouch

doi: https://doi.org/10.1101/2022.11.01.514722

Immunogenicity of the BA.5 Bivalent mRNA Vaccine Boosters

bioRxiv preprint doi: https://doi.org/10.1101/2022.10.24.513619

Ai-ris Y. Collier, M.D., Jessica Miller, B.S., Nicole P. Hachmann, B.S., Katherine McMahan, M.S., Jinyan Liu, Ph.D., Esther Apraku Bondzie, M.S.N., Lydia Gallup, R.N., Marjorie Rowe, B.S., Eleanor Schonberg, B.A., Siline Thai, B.S., Julia Barrett, B.S., Erica N. Borducchi, Ph.D., Emily Bouffard, B.S., Catherine Jacob-Dolan, B.S., Camille R. Mazurek, M.S., Audrey Mutoni, B.A., Olivia Powers, B.S., Michaela Sciacca, B.S., Nehalee Surve, M.S., Haley VanWyk, B.S., Cindy Wu, B.S., and Dan H. Barouch, M.D., Ph.D.*

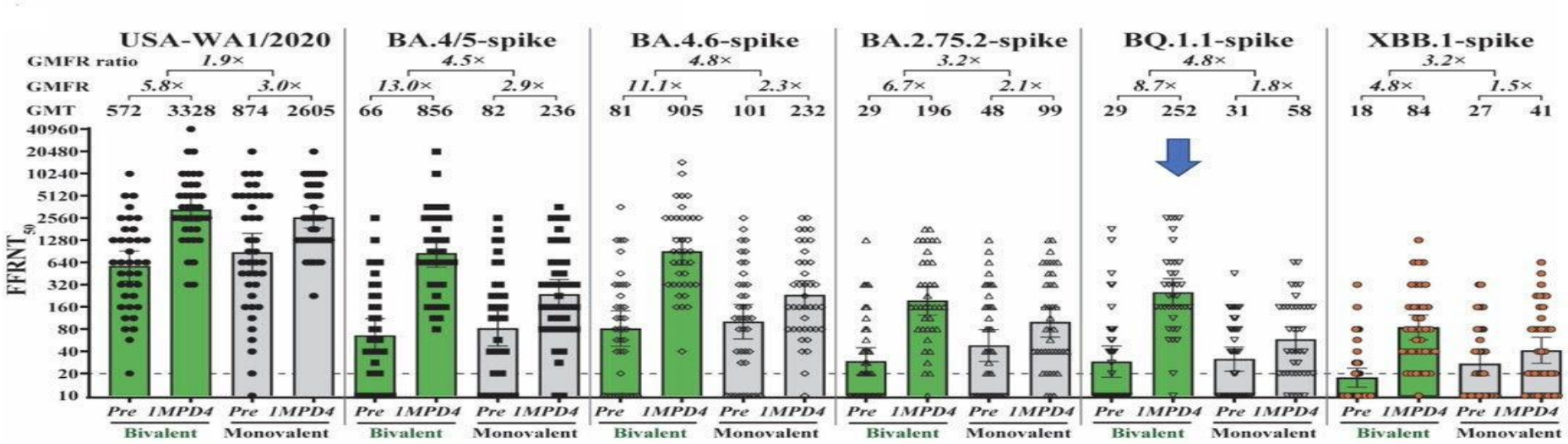
orig/BA/5 amplia immunità umorale contro sottovarianti Omicron

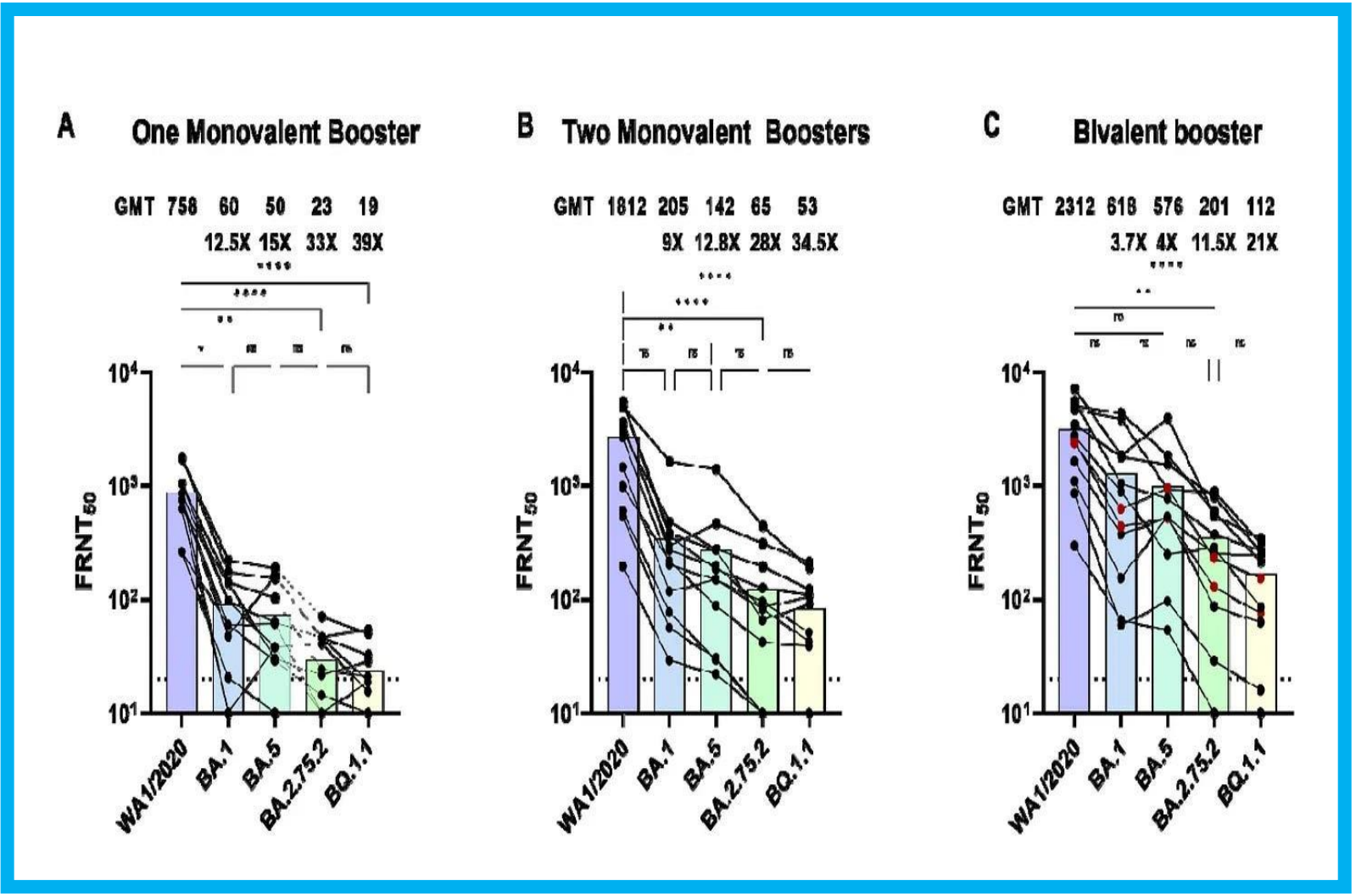
New boosters are here! Who should receive them and when?

Lancet Infect Dis 2022

vaccini covid-19 adattati inducono attività di neutralizzazione incrociata più elevate e ad ampio spettro rispetto ai vaccini originali

The bivalent BA.5 booster induced an 8.7-fold increase in neutralizing antibodies; the original booster only 1.5-fold increase





Cold Spring Harbor Laboratory
bioRχiv
THE PREPRINT SERVER FOR BIOLOGY

mRNA bivalent booster enhances neutralization against BA.2.75.2 and BQ.1.1

Posted November 01, 2022.

Meredith E Davis-Gardner, Lilin Lai, Bushra Wali, Hady Samaha, Daniel Solis, Matthew Lee, Andrea Porter-Morrison, Ian Thomas Hentenaar, Fumiko Yamamoto, Sucheta Godbole, Daniel C Douek, Frances Eun-Hyung Lee, Nadine Rouphael, Alberto Moreno, Benjamin A Pinsky, Mehul S Suthar

doi: https://doi.org/10.1101/2022.10.31.514636

efficacia del bivalente migliore rispetto al booster monovalente

doi.org/10.1016/S2213-2600(22)00361-7

COVID vaccine booster doses for omicron variants

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

7 settembre 2022
EMA/706119/2022

COVID-19: raccomandazioni sull'uso dei vaccini adattati

strategia UE

- **un'ampia gamma di vaccini adattati destinati a diverse varianti di Sars-Cov-2**

Morbidity and Mortality Weekly Report

https://www.cdc.gov/mmwr/volumes/71/wr/mm7148e1.htm

Interim Recommendations from the Advisory Committee on Immunization Practices for the Use of Bivalent Booster Doses of COVID-19 Vaccines — United States, October 2022

bivalenti original/BA.5

- **protezione aggiuntiva significativa per infezione sintomatica SARS-CoV-2**
- **in soggetti con 2, 3 o 4 ds vaccino monovalente**

variant chasing **temporalmente imperfetta** → **vaccini universali a prova di varianti**

Received: 26 November 2021 | Revised: 28 March 2022 | Accepted: 23 April 2022
DOI: 10.1002/jcla.24479

RESEARCH ARTICLE — WILEY

Nucleocapsid protein of SARS-CoV-2 is a potential target for developing new generation of vaccine

Weixu Feng[1] | Yunru Xiang[1] | Lianpeng Wu[2] | Zhuo Chen[1] | Qingfeng Li[1] | Jun Chen[1] | Yanru Guo[1] | Dandan Xia[2] | Na Chen[2] | Lifang Zhang[1] | Shanli Zhu[1] | Kong-Nan Zhao[1,3,4]

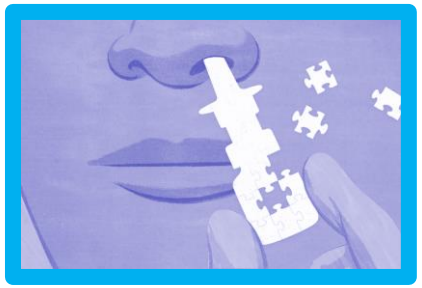
SCIENCE ADVANCES | RESEARCH ARTICLE

CORONAVIRUS

Cell surface SARS-CoV-2 nucleocapsid protein modulates innate and adaptive immunity

Alberto Domingo López-Muñoz, Ivan Kosik, Jaroslav Holly, Jonathan W. Yewdell*

vaccini nasali per immunità mucosa



The NEW ENGLAND JOURNAL of MEDICINE
DOI: 10.1056/NEJMc2209651

CORRESPONDENCE

Anti-Spike Mucosal IgA Protection against SARS-CoV-2 Omicron Infection

240 | Nature | Vol 609 | 8 September 2022

HOW NASAL-SPRAY VACCINES COULD CHANGE THE PANDEMIC

450 | Nature | Vol 609 | 15 September 2022

CHINA AND INDIA APPROVE NASAL COVID VACCINES

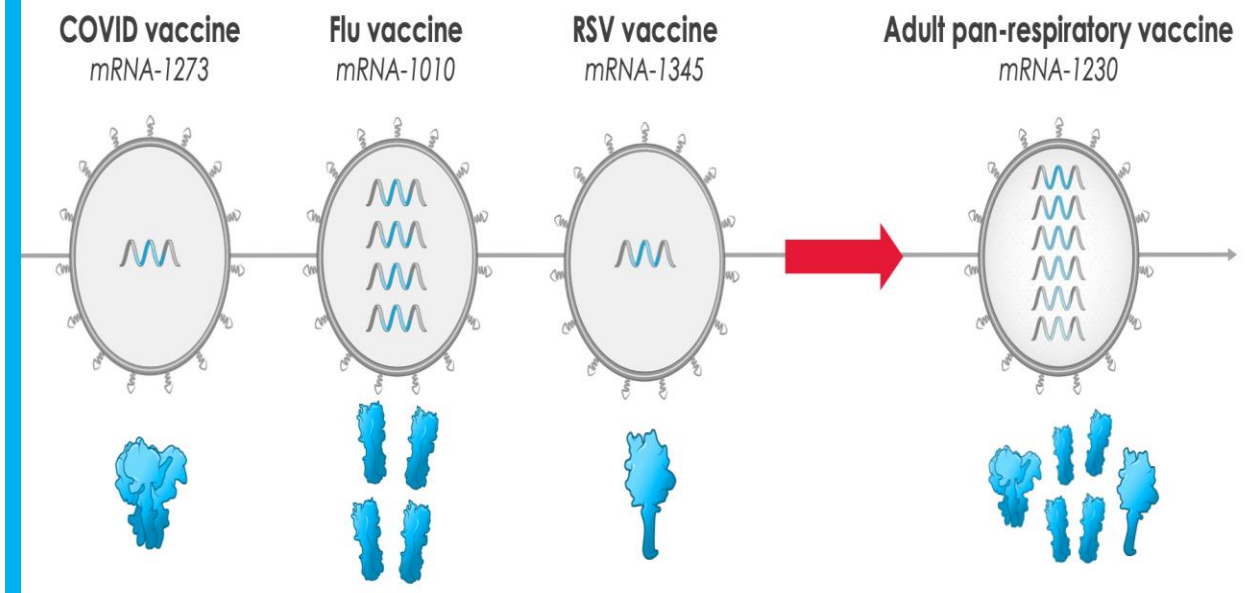
Science — RESEARCH ARTICLES
Cite as: T. Mao *et al.*, *Science* 10.1126/science.abo2523 (2022).

Unadjuvanted intranasal spike vaccine elicits protective mucosal immunity against sarbecoviruses

Tianyang Mao[1†], Benjamin Israelow[1,2*†], Mario A. Peña-Hernández[1], Alexandra Suberi[1], Liqun Zhou[1], Sophia Luyten[1], Melanie Reschke[4], Huiping Dong[1], Robert J. Homer[2], W. Mark Saltzman[3,6,7,8,9], Akiko Iwasaki[1,10*]

significativo bisogno di nuovi vaccini

tecnologia ad mRNA



Sicurezza e immunogenicità di un vaccino antinfluenzale stagionale quadrivalente a base di mRNA (mRNA-1010) negli adulti: risultati ad interim di una sperimentazione clinica randomizzata di fase 1/2

Ivan T. Lee, Raffael Nachbagauer, Lizbeth Carmona, Kristi Schaefers, Andrei Avanesov, Daniel Stadlbauer, Angela Choi, Carole Henry, Ren Chen, Wenmei Huang, Jintanat Ananworanich, Robert Paris

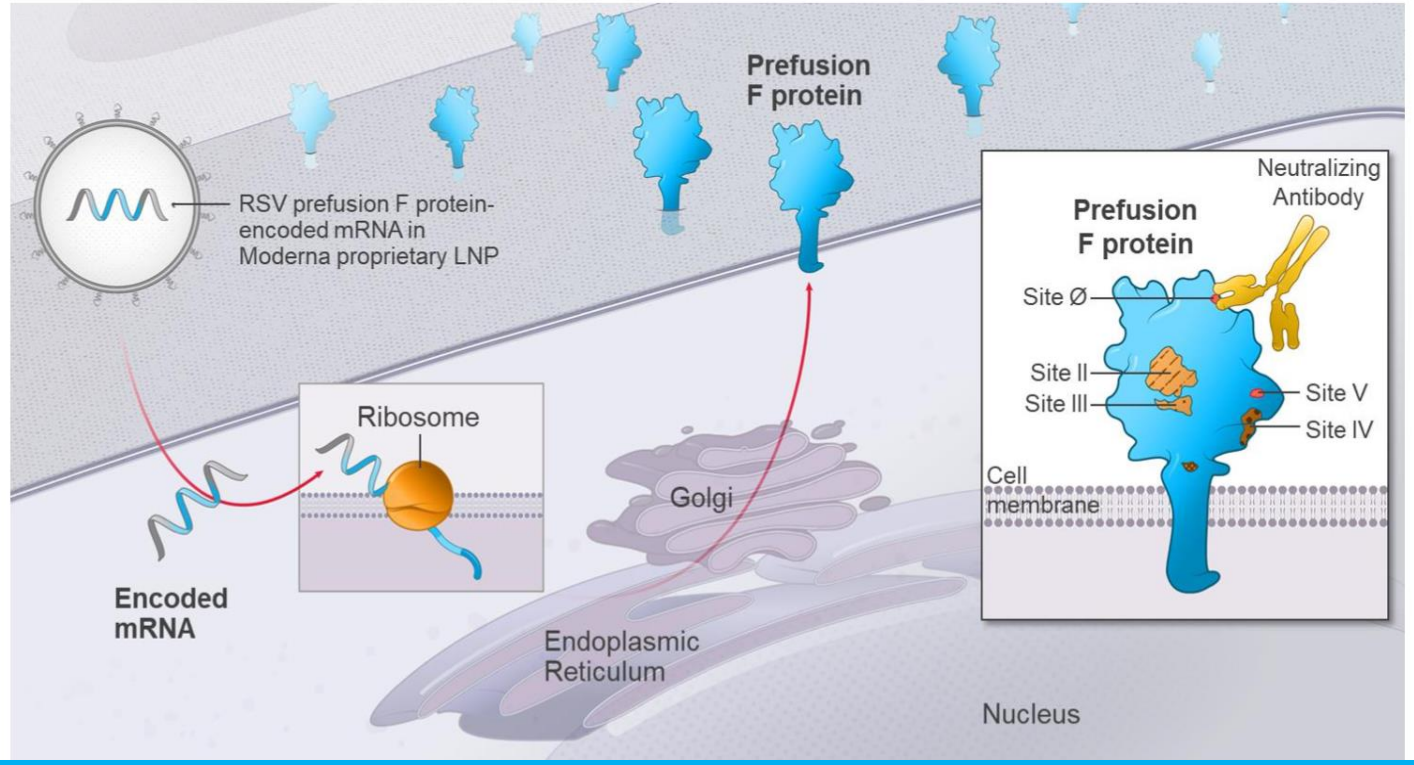
mRNA-1010 contro l'influenza stagionale

piattaforma a mRNA per migliorare efficacia dei flu-vax

WHAT THE LIGHTNING-FAST QUEST FOR COVID VACCINES MEANS FOR OTHER DISEASES

Nature | Vol 589 | 7 January 2021

RSV vaccine (mRNA-1345) encodes for a stabilized prefusion F glycoprotein



vaccino m-RNA-1345 codifica RSV stabilizzato PRE-F

stessa formulazione di nanoparticelle lipidiche

VZV: Vaccine against herpes zoster/shingles (mRNA-1468)

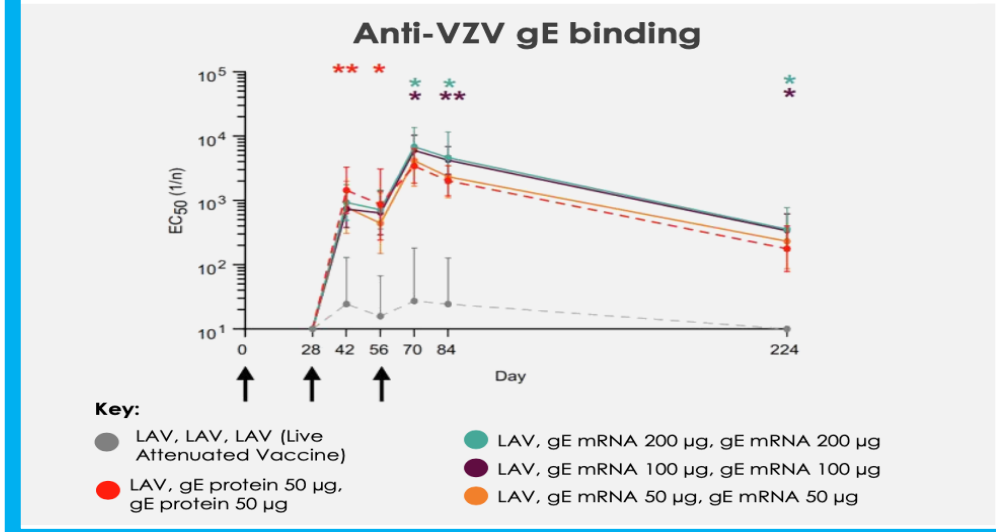
Vaccine
Volume 38, Issue 36, 10 August 2020, Pages 5793-5802

Immunogenicity generated by mRNA vaccine encoding VZV gE antigen is comparable to adjuvanted subunit vaccine and better than live attenuated vaccine in nonhuman primates

Morgan A. Monslow [a] ... Kalpit A. Vora [a]

vaccino mRNA genera titoli anti-gE simili rispetto a un vaccino gE a subunità adiuvato

mRNA vaccine generated similar anti-gE titers compared to an adjuvanted subunit gE vaccine (proxy for Shingrix™)[2] in NHP



Sperimentazione clinica di fase 2 di un vaccino a base di mRNA per il citomegalovirus

fase di sviluppo un vaccino contro il CMV mRNA-1647

KEY MESSAGES

WILL THERE BE A COVID WINTER WAVE? WHAT SCIENTISTS SAY

Nature | Vol 610 | 13 October 2022

la pandemia non è finita ancora

co-circolazione virus influenzali e Sars Cov 2

vaccinare di più contro l'influenza

booster covid forniscono un beneficio sostanziale e inequivocabile per protezione da covid grave

SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

il muro immunitario costruito da vaccini booster e infezioni sembra resistere a una sostanziale evoluzione del virus

Grazie