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Mini Review

Inspiring (Intelligent, Informative, Intelligible) Medical Physiology (Imp.)

Part-03[$]: Nobel Prize in Medicine for 2023

S. Narasinga Rao[1]* and R. Sambasiva Rao[2]

1. Dept. of General Medicine, Government medical College, Government General Hospital, Srikakulam, AP, **INDIA**
2. School of Chemistry, Andhra University, Visakhapatnam 530 003, **INDIA**

Email snrnaveen007@gmail.com (+91 ,9848136704) rsr.chem@gmail.com (+91 ,99 85 86 01 82)

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https://en.wikipedia.org/wiki/List_of_Nobel_laureates_in_Physiology_or_Medicine

Conspectus

Alfred Nobel was born in Stockholm on 21st October, 1833. Dr. Alfred was a chemist, manufacturer of explosives, entrepreneur and self-sufficient man. Nobel was fluent in five languages, poet, drama writer and philanthropist. Alfred imbibed fascismand his views were criticized as radical. He has fascination for literature. His expertise and devotion for physics and chemistry resulted inprofessional growth to bag more than 350 patents of different nations. He had kind heart and donated huge funds for medical advancement and growth. He rose in industry and became one of the few richest persons of his time. Dr Nobel never married and had no biological children.

False obituary news and impact on Alfred's endeavours: Ludvig Nobel, one of Alfred Nobel's brothers, passed away in Cannes in the year 1888 and Alfred was in Parisat that time. A Persian journalist mistook Alfred for Ludvig and published it as Alfred Nobel's obituary event. The pungent comments and allegations (viz."The merchant of death is dead", "Nobel was an arms merchant and became rich by finding ways to kill more people faster than ever before") by news-makers spread a black-shadow on his personality and integrity as a human.More strangewas he could follow it all as was alive at that moment. It caused a stir in his brain. He decided to set apart all his personally acquired property, of course in explosives/armoury business, for an organization which should be remembered in serving for welfare of higher order for humankind. He legalized the institution of five awards called "Nobel prizes" after his family name. The disciplines selected were Medicine, Physics, Chemistry, Literature and peace and the prizes have been given since 1901.

[$]Part 1:Nobel Prize in "Physiology or Medicine"for 2021,S. Narasinga Rao* and R. Sambasiva Rao, Journal of Applicable Chemistry, 2021, 10 (6): 827-837.

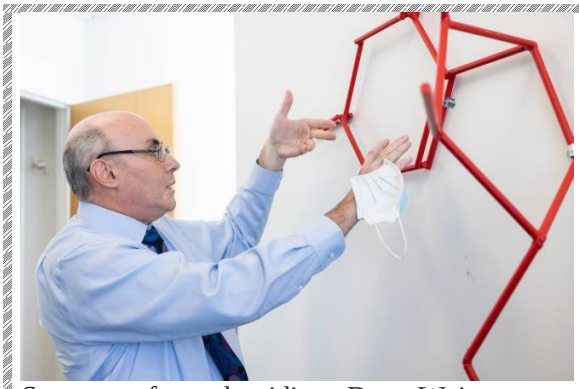
Part 2- Inspiring Medical Professionals (Imp)Maurice Hilleman, S. Narasinga Rao* and R. Sambasiva Rao, JournalApplicable Chemistry, 2022, 11 (3): 331-343.

Nobel Prize in Physiology or Medicine: During the years 1901 to 2023, the numbers of annual Nobel prizes announced in medicine are 115. They are conferred on 228 scientists (who are referred popularly as Nobel Laureatesfrom then on) among whom 13 are women. The prize amount is increased from SEK 10 in yesteryears to 11 million from this year (now equivalent to 1039K US-Dollars).

Nobel prize of 2023 in Medicine is shared by Katalin Karikó and Drew Weissman for their fundamental research in pure science which led to medical applications of m-RNA on vaccine preventing viral diseases. Their concerted efforts along with those of many other investigators resulted in synthetic m-RNA vaccine for SARS-Cov-2virus. U.S. Food and Drug Administration (FDA) approval in August 2021, the vaccine manufactured by Pfizer-BioNTech. The Moderna COVID-19 (COronaVIrus Disease-19 or 2019)vaccine was authorized for emergency use. The covid-19 vaccine saved millions of human lives by preventing from infection putting a stop for catastrophe/pandemic.

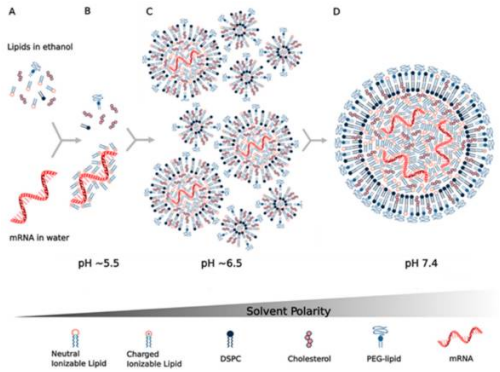
Nobel Future prospects m-RNA as therapeutic drugs and vaccines: The astounding success, proved validity and safety already paving way for re-investigations forcancer. A new dimension is looking for therapeutic drugs for cure of diseases through protein machinery approach.

Graphical Abstract:

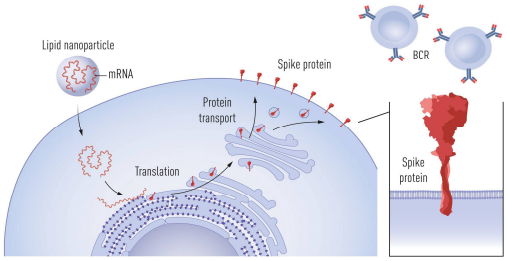


Structure of pseudouridine; Drew Weissman

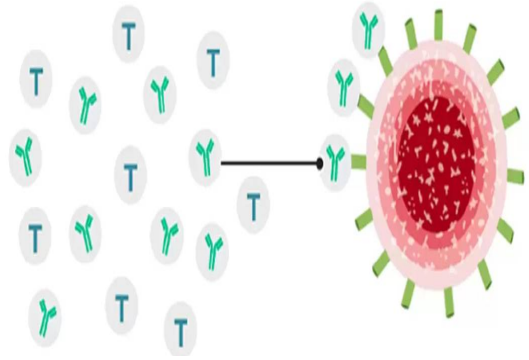
Alfred Nobel



mRNA lipid nanoparticle assembly



- Spike production
- mRNA vaccination recognition of spike by B cells



- ✓ Corona-virus attacks immunized person
- ✓ antibodies and T-cells are triggered to fight against virus with the spike protein

Dr. Katalin Kariko at her UPenn lab in 2005

Keywords: Nobel Prize-2023-Physiology or Medicine; Katalin Karikó; Drew Weissman;FDA approved; Pfizer-BioNTech and Moderna's vaccines; prevent COVID-19 infection; Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); Nucleoside base modifications (uridine (U) by pseudouridine) mRNA;Zika virus; Influenza; prevent herpes, end HIV defeat influenza; stop the next coronavirus and/like pandemic

All figures are from (copyright) literature

	Layout of Review -- NP in Medicine for 2023
1.	**Introduction**
2	**Inspiration for start of Nobel Prize**
	2.1 Start of Nobel prizes
	2.2 Nobel Prize in Physiology or Medicine of 2023
3	**Vaccines**
4	**Katalin Karikó Era**
	4.1 Research contributions of Katalin Karikó prior to 1998
5	**Drew Weissman Era**
	5.1 Research contributions of Drew Weissman prior to 1998
6	**Collaborative Research contributions (1998-)**
7	**Novel performance of m-RNA vaccine for Corona**
	7.1 FDA approval
	7.2 Skeptics' complaints on rapid development of m-RNA vaccine technology for COVID-19 (COronaVIrus Disease-19 or 2019)
8	**Basic Science research (Univ., Labs) to applicable products (vaccines, robotic surgery protocols, Therapeutics)**

1. INTRODUCTION

Alfred (Bernhard) Nobel was born in Stockholm on 21st October, 1833. His mother Carolina Andriette (Ahlsell) Nobel (1805-1889) was a homemaker. She was veryfond of him and very supportive of her husband. Alfred's father, Immanuel Nobel(1801–1872), was an inventor/engineer. Immanueland Carolina married in 1827 and gave birth to eight children. poverty was a curse and only Alfred (third child) and his three brothers survived beyond childhood.

Immanuelhad interest in explosivesdisplacing large amounts of rockseven from riverbed. He planned to build a canal at Suez and his experiments were intrigued by Russian military. On their request, Immanuel developed two systems viz. land mines to defend army bases or towns, and sea mines to protect harbours and docked ships. ÖstraNöbbelöv, is the name of the habitational villagein Scania andNobelius is a Latinized version. Nobel is the shortened form.

Olof Rudbeck the Elder was seventeenth-century Swedish physician, scientist, and scholar, who became the Rector of the University of Uppsala. Peter Olai Nobelius married Rudbeck's daughter.Nobel family descended from this couple and credibility flew into family of Nobels.

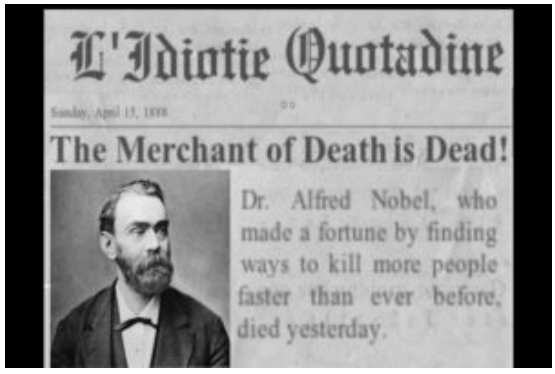
Education: Mr. Nobel learned and was a fluent speaker in five languages by the age of seventeen years. He was interested in engineering, particularly explosives, learning the basic principles from his father at a young age. Alfred Nobel's interest in technology was inherited from his father, an alumnus of Royal Institute of Technology in Stockholm.

Dr Alfred was an intelligent synthetic chemist, shrewd designer, skilled experimentalist, and balanced manufacture of explosives conscious inventor, successful entrepreneur, accomplished businessman and wise philanthropist during last part of nineteen century. He obtained round 350 patents including 58 English and 39 Swedish ones.Dr Nobel successfully marketed dynamite (a detonator), the blasting cap, gelignite, and ballistite. He grew to one of few wealthy men of his time.

Traits and personality: Alfred sustained life-long devotion and respect for physics and chemistry and he used the principles in his inventions and products which brought sanction of patents. He had an inner urge to save mankind from suffering of diseases and promote to keep good health. Dr Nobel was a bibliophile, an author. He wrote poetry and dramain English. It influences culture, human thought processing of experts of all fields, peace mongers and wise inventors. He liked harmony among nations for happier and peaceful society. Nobel was also very much interested in social and peace-related issues. Some of his views were considered radical at that time.He trusted power of dialogue and diplomacy to instil peace in diverse societal frames. Dr Alfred was a fascist and was impressed with expression and writings of contemporary thinkers of that clad in his time.

2 Inspiration for start of Nobel Prize

False news of death of Dr Alfred Nobel: In 1888, Ludvig Nobel, one of Alfred Nobel's brothers, passed away in Cannes. At that time, Alfred was living in Paris. The Parisian newspaper mistook Alfred for Ludvigand published news with eye-catching headline, "Le marchand de la morteest mort" (in English "The merchant of death is dead"). The false obituary column also colored with criticism that 'Alfred Nobel amassed wealth from the invention of explosives'. His inventions--explosive chemicals (including dynamite) and devices, wereportrayed as a destructive force in warfare. Another pungent statement of the journalist was "Nobel was an arms merchant and became rich by finding ways to kill more people faster than ever before".


L'Idiotie Quotadine

The Merchant of Death is Dead!

Dr. Alfred Nobel, who made a fortune by finding ways to kill more people faster than ever before, died yesterday.

(Image Source: shikshanews.com) Fake Obituary

Impact of False (his) obituary news on Alfred Nobel: Alfred was deeply moved by the creation and spread of negative perception of his scientific inventions. In fact, his research outcome also has civilian benefits in construction engineering andrevolutionized industries. Then he decided to make use of all his acquired property for the benefit (health, knowledge, progress, pleasure and peace) of humankind. This act of un-selfish motto may leave positive legacy of Nobels in time to come.


Image of Women packing dynamite cartridges, 1888. Explosives …

Alfred made up his mind to start prizes creating a lasting legacy in ensuing decades. It crystallised intoNobel (after his family name) prizes legalised in Alfred's last will prepared on 27th November, 1895. The awards are unique and will honour the brainy-individuals of higher order in contributing for welfare of generations of man-kind.

Death of Alfred Nobel: Alfred Nobel beathed his last at the age of 63 on 10thDec1996 at his home in San Remo, Italy surrounded only by paid-employees.

2.1Start of Nobel prizes: The award of Nobel prizes started from the year 1901, five years after Alfred Nobel's death. Of several awards /Prizes/ honours on the globe, Nobel Prize finds a niche during these 120 years of time.The prizes were intended to honour and give huge funds toscientists/individuals/organisations who made substantial contributions to humanity.The recipients are hailed in their discipline, institute, community, and country through ages. The annual Nobel prize winners in Medicine, Physics, Chemistry, Literature and peace are honoured on December 10thof every year at a ceremony in Stockholm. Each Nobel Laureate receives a diploma, gold medal and cash. All the Nobel prize winners of that year deliver a lecture narrating salient features culminating into the innovation,

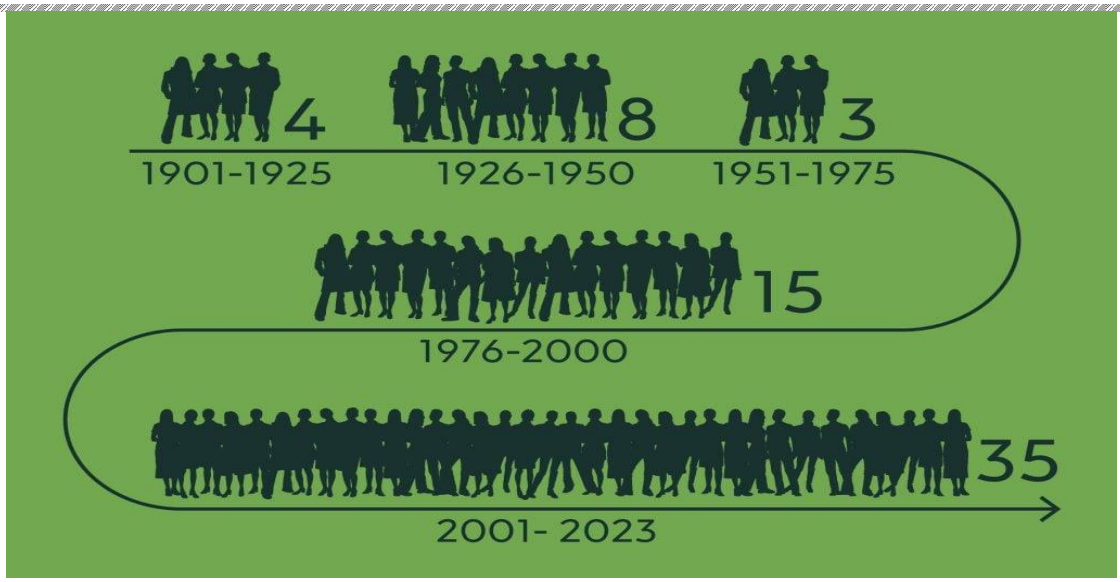
discovery, development of product/instrument/process, cure/ intervention/ prevention of a disease etc. Later, they participate in a lavish banquet dinner meet hosted by the Royal family. The banquet speeches by coveted prize winners are thought-provoking to all.

Greatest Peace for Universe (GPU) -- Non_Life- Life-forms & Energies (NLE)

https://www.nobelprize.org/prizes/medicine/2023/summary/

2.1 Nobel Prize in Physiology or Medicine of 2023

From the year 1901 onwards, Nobel Prize under medicine category was announcedin 115 yearly events [1-11]. Of the 228 laureates till date, 215 are men and 13 are women. During the years, 1915–1918 (during first world war), 1940–1942 (second world warperiod),1921and 1925, the Nobel prizes were not announced.



Nobel Prize awarded women 1901-2023.

© Nobel Prize Outreach

year	Woman Nobel Laureate In Medicine	#	Focal theme	Contribution
1947	Gerty Cori	1	Catalytic conversion of glycogen	Discovery ;
1977	Rosalyn Yalow	2	Radio-immunoassays of peptide hormones	Development
1983	Barbara McClintock	3	Mobile genetic elements	Discovery ;
1986	Rita Levi-Montalcini	4	Growth factors	Discoveries ;
1988	Gertrude B. Elion	5	Important principles for drug treatment	Discoveries ;
1995	Christiane Nüsslein-Volhard	6	Genetic control of early embryonic development	Discoveries
2004	Linda B. Buck	7	Odorant receptors and the organization of the olfactory system	Discoveries
2008	Françoise Barré-Sinoussi	8	Human immunodeficiency virus	Discovery ;
2009	Elizabeth H. Blackburn	9	How chromosomes are protected by telomeres and the enzyme telomerase”	Discovery ;
2009	Carol W. Greider	`		
2014	May-Britt Moser	11	Cells that constitute a positioning system in the brain	Discoveries ;
2015	Tu Youyou	12	Concerning a novel therapy against Malaria	Discoveries
2023	Katalin Karikó	13	Nucleoside base modifications that enabled the development of effective mrna vaccines against COVID-19	Innovation

https://www.nobelprize.org/prizes/lists/nobel-prize-awarded-women/

Katalin Karikó and Drew Weissmanare awarded Nobel Prize in Physiology or Medicine of 2023 byNobel Assembly at the Karolinska Institute,Stockholm (Sweden) for their research outcome (during 2005-2010) in pure science dealing with [nucleotide] base modifications in developing first synthetic m-RNA vaccine (without biological virus or their components) with astounding function (in human beings) in preventing covid-19 viral disease.

https://www.nobelprize.org/prizes/medicine/2022/paabo/facts/

Gold medal for the Nobel Prize in Physiology or Medicine.

Portrait of Alfred Nobel on one side of the medal	**Opposite face of medal relevant to the discipline viz. Medicine**
	

- This medal depicts the “genius of medicine” represented as a woman seated with an open book on her lap.
- The woman is filling a bowl of water from a spring to relieve a suffering girl’s thirst.
- There is a Latin inscription above: “Inventasvitamjuvatexcoluisse per artes” (“Invention enhances life, which is beautified through art”) cited from Virgil’s Aeneid.

- ! There the hero Aeneas is in the underworld and looking upon the spirits of past human beings who made great contributions to the betterment of humankind by their unique creations and discoveries in what we now call artes et scientiae , the arts and sciences.
- ! The original line was ably rendered by William Morris in 1876 as follows:
- ! and they who bettered life on earth by new-found mastery

- The name of the laureate is engraved on the plate below the figure,
- in this case Francis Crick, the co-discoverer of the structure of DNA.
- The lower text "REG. UNIVERSITAS MED. CHIR. CARO." designates the Royal Caroline Institute (Karolinska Institutet).
- Reproduced with permission of the Nobel Foundation. © ® The Nobel Foundation.

The in-vitro prepared m-RNA for surface Spite protein of corona-virus encapsulated in nano-lipid layer technology was adapted by Pfizer-BioNTech and Moderna companies in large scale preparation. The mega-vaccination programs (13 billion doses) saved millions of humans from death/disastrous consequences of pandemic and also reduced the spread of infection in uncountable numbers.

https://www.nobelprize.org/prizes/medicine/2023/summary/

Table 1. Focal theme of Nobel Prize for Physiology or Medicine in 2023

! **Development/Discovery**	☞ Nucleoside base modifications in mRNA
	☞ Developed a delivery technique to package the mRNA in lipid nanoparticles. This made it possible for mRNA to reach the proper part of the body and trigger an immune response to fight disease.
! **Consequence/Outcome**	☞ Development of effective mRNA vaccines against COVID-19
! **Benefit to Humankind**	☞ Reduction of death toll and prevention of morbidity

Professors Drew Weissman (left) and Katalin Kariko

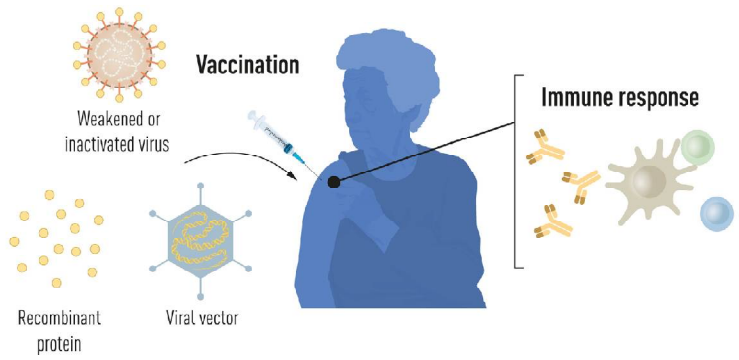
- Roberts Family Professor in Vaccine Research
- Director of Vaccine Research, Infectious Diseases Division
- Director, Institute for RNA Innovation, Univ of Pennsylvania

Department: Medicine

3Vaccines

The goal of any vaccine is to train the immune system of body to recognize virus/ bacterium/germs by producing antibodies and activating immune cells to fight against threats by using fragments/whole of the infectious agent.Cytotoxic T cells with specialised proteins on their surface are instrumental to recognise virally-infected cells.Thus, Vaccines protect people by giving the immune system a preview of an invading microbe so it can prepare a strongdefence.Vaccination triggers immune response when the particular pathogen (virus) attacks the human system. The next sequence of steps iscuring disease in the event of that virus attacks later.

Conventional vaccines: Traditional vaccine technology introduce weakened, dead, or non-infectious parts of aoriginal virus or bacterium into the body. By contrast, mRNA vaccines give the body only instructions for making its own viral or bacterial proteins. The immune system then responds by creating antibodies.



Methods for vaccine production before the COVID-19 pandemic
Currently used vaccines are made from weakened or inactivated whole viruses, recombinant viral protein components (subunit vaccines), or viral vectors delivering antigens of interest (vector vaccines). The vaccination event stimulates antigen-specific immune responses, which provide protection if the vaccinated person is later exposed to the live pathogen

Vaccines from live-weakened or dead virus: These had been available for polio and measles prevention. Max Theiler was awarded Nobel prize in 1951 under medicine category for development of vaccine against yellow-fever.

Individual components of virus as vaccines: Part of viral genetic code which encode proteins on the virus surface are used to develop vaccines for hepatitis B or human papilloma virus. They stimulate the formation of virus blocking antibodies.

Protein subunit as vaccines: Here, the purified pieces of virus are made use in triggering immune response by anti-bodies.

Vectorbased vaccines: Under this category, sub-set of genetic-code is transferred into a harmless virus carrier called vector. The weakened or dead virus when injected into healthy individual for preventing/intervening virus attack, the amount is not enough to make the person sick. But, sufficient to produce/stimulates immune response against targeted virus (for example in the case of Ebola). The antibodies will fight against the virus on attack of the vaccinated person later.

The Oxford-AstraZeneca and Johnson & Johnson vaccines for COVID-19, utilize viral vectors to trigger an immune response against the spike protein of the SARS-CoV-2 virus. The noteworthy advantages are

+ robust immune responses and

+ potential long-term protection

But, some of challenges in creating and manufacturing yester year's vaccines include

Vector-based vaccines

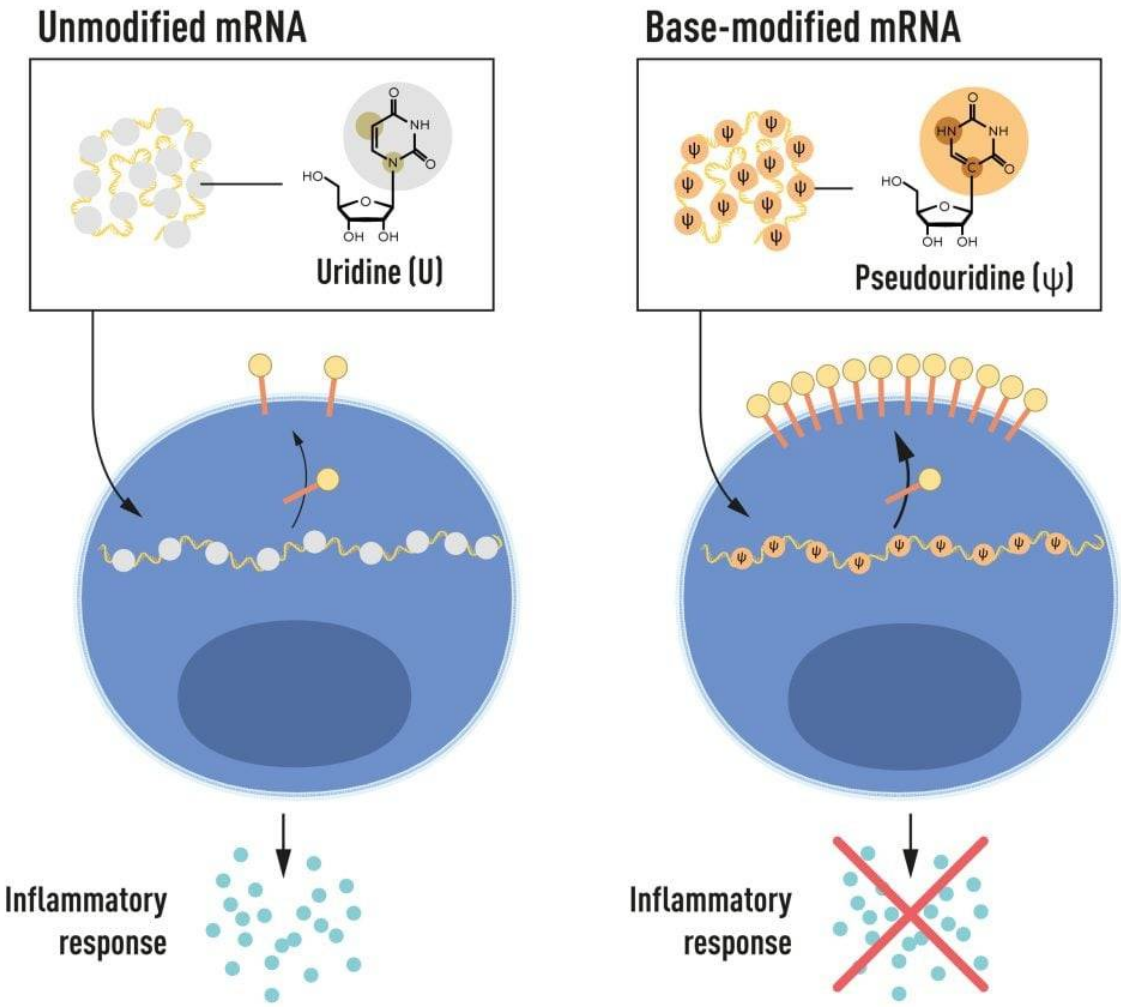
- need for careful vector selection,
- potential immune responses against the viral vector,
- more complex production processes compared to mRNA type.

whole-, protein type of vaccines

- They involve large scale cell culture
- Complicated and intensive process and huge resources requirement
- Time consuming rendering viability of combating with disease load less effective
- Modification of vaccines to be adaptive with mutations of viruses is lengthy and impracticable
- Limited feasibility during out-breaks or pandemic scenarios (like covid-19)

In vitro transcribed m-RNAfor medical use

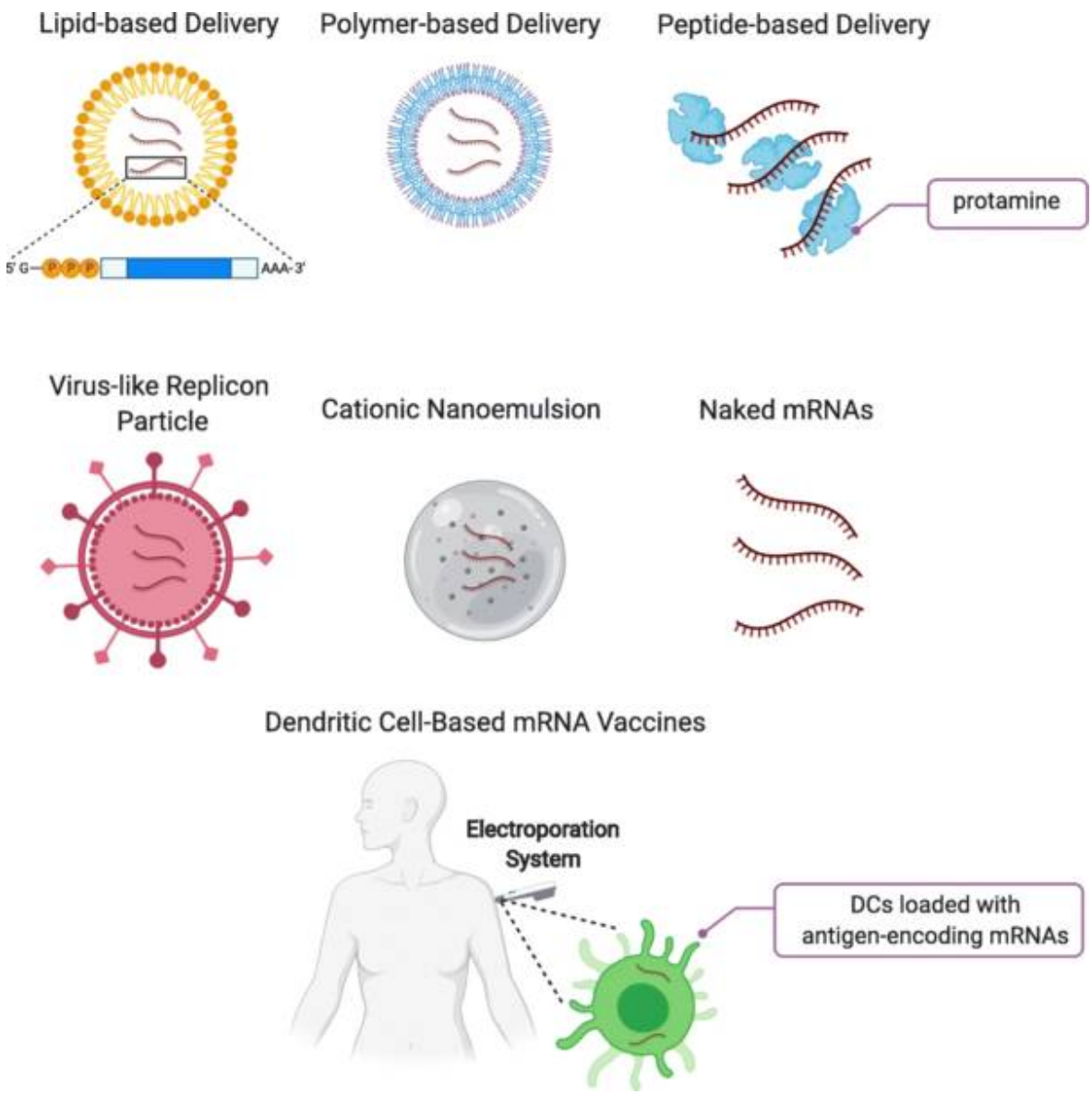
This activity started in early 1980s. The myth was that m-RNA, transcribed in vitro,was unstable and thus cannot have therapeutic function/value. It produced inflammation response making the subjects sick when injected into in-vivo cells of animals. The amount of protein produced was less compared to in-vivo counterpart. Further, it was a challenge to find or develop optimum lipid carrying (delivery) system to encapsulate m-RNA for transfer of in-lab prepared m-RNA into human beings/test animals.



✓ Weissman and Karikó (Nobel Laureates of 2023) found that base-modified mRNA
- Blocks activation of inflammatory reactions (secretion of signaling molecules)
- Increases protein production when mRNA is delivered to cells

📖 mRNA contains four different bases, abbreviated A, U, G, and C

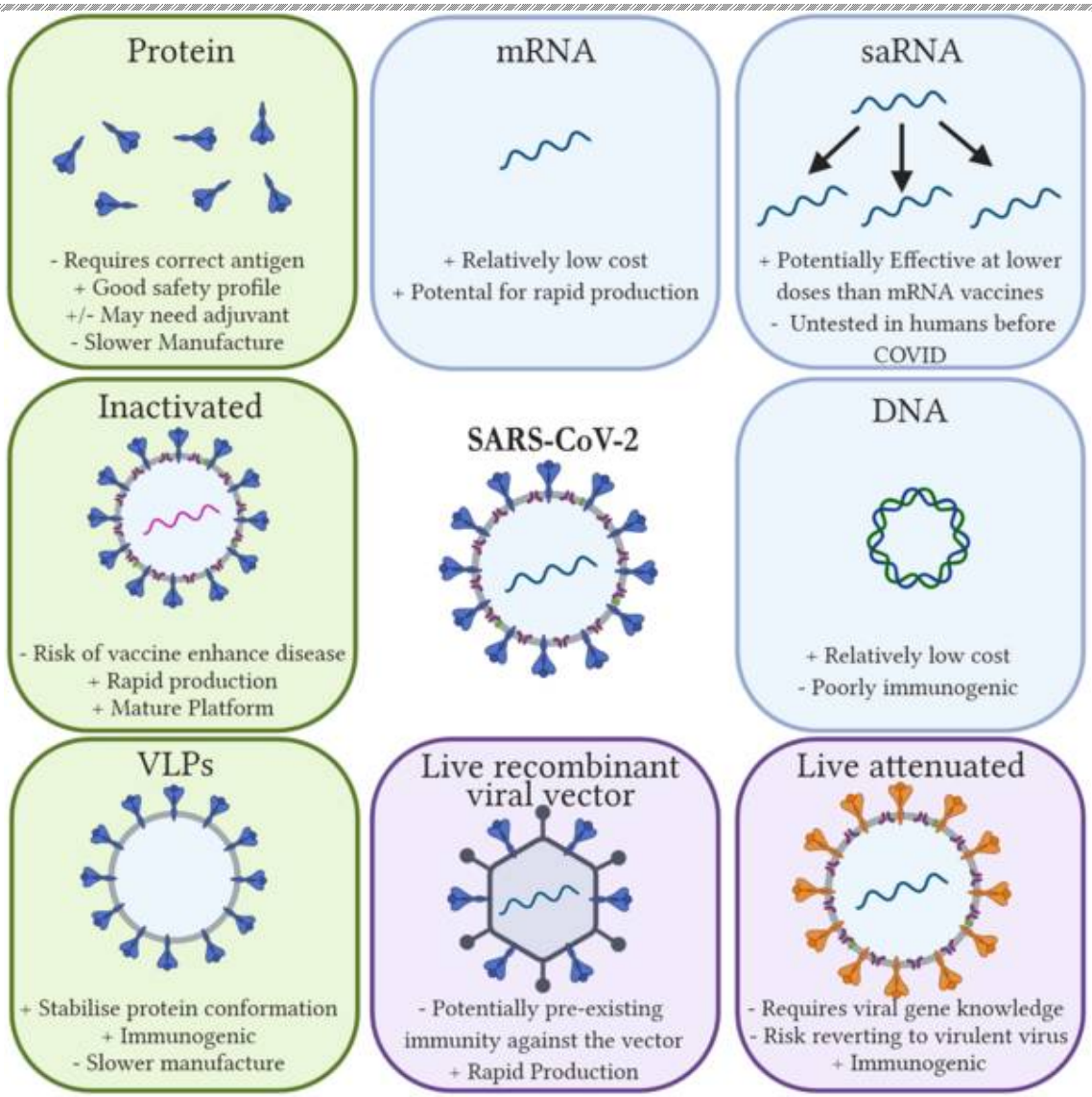
© The Nobel Committee for Physiology or Medicine.



Major delivery methods for mRNA vaccines commonly used delivery methods and carrier molecules for mRNA vaccines are shown:

Source Wang, Y., Zhang, Z., Luo, J. et al. mRNA vaccine: a potential therapeutic strategy. Mol Cancer 20, 33 (2021). https://doi.org/10.1186/s12943-021-01311-z; 16 February 2021

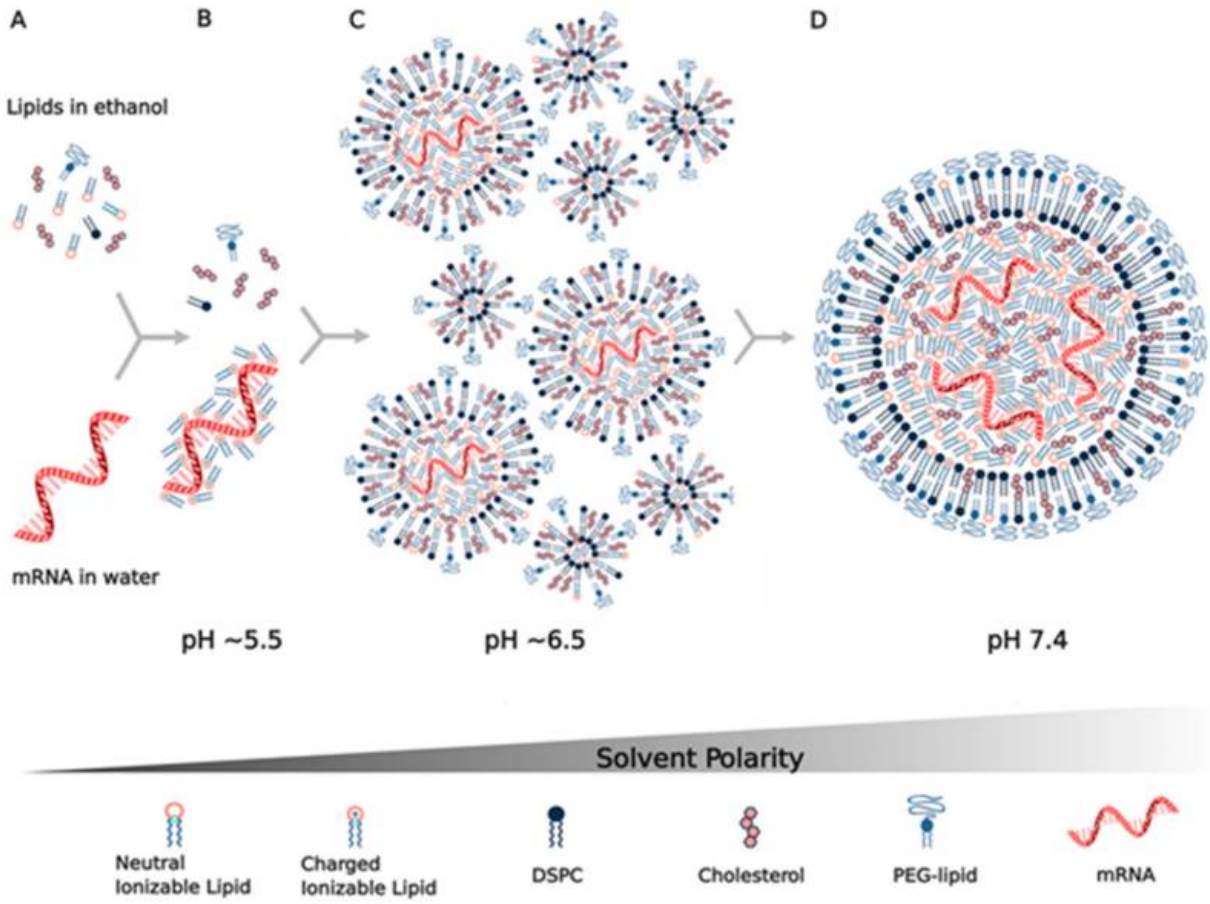
Road-block for m-RNA medical therapeutics: Thus, the initial enthusiasm of prospective advancement of m-RNAs in vaccines and therapeutics was chilled due to the scientific stumble-block (with no immediate solution or way-out to over-come the` hurdle).



Vaccine platforms for Covid-19; Over 200 different vaccines are in development. They loosely group into protein, inactivated, VLP, viral vector, mRNA, self-amplifying RNA, DNA and live attenuated vaccines.

Source Tregoning, J.S., Brown, E.S., Cheeseman, H.M., Flight, K.E., Higham, S.L., Lemm, N.-M., Pierce, B.F., Stirling, D.C., Wang, Z. and Pollock, K.M. (2020), Vaccines for COVID-19. Clin. Exp. Immunol., 202: 162-192. https://doi.org/10.1111/cei.13517 ; 15 September 2020

m-RNA vaccines:In m-RNA vaccines, the temporary genetic code has utility to tell the cells to make protein which is a part of virus.



mRNA lipid nanoparticle assembly

(A) rapid mixing in a microfluidic or T-junction mixer of four lipids (ionizable lipid, DSPC, cholesterol, PEG–lipid) in ethanol with mRNA in an aqueous buffer near pH4.

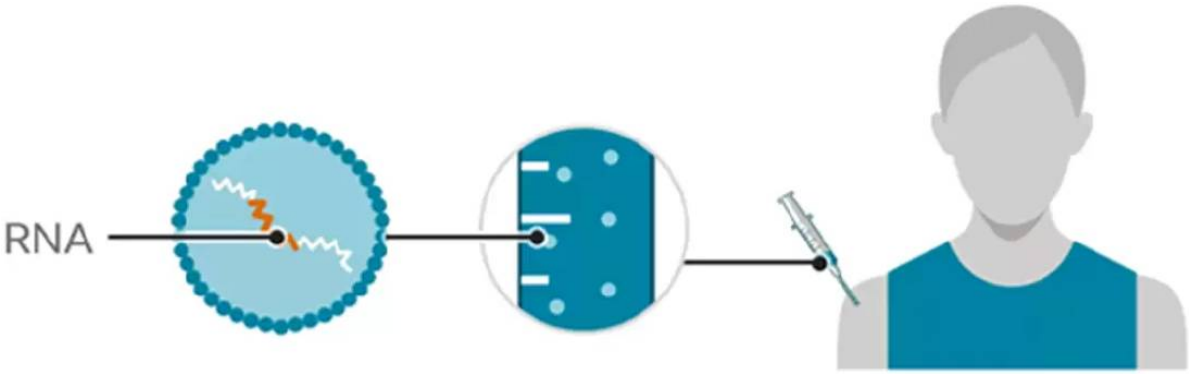
(B) When the ionizable lipid meets the aqueous phase, it becomes protonated at a pH ~5.5, which is intermediate between the pKa of the buffer and that of the ionizable lipid.

(C) The ionizable lipid then electrostatically binds the anionic phosphate backbone of the mRNA while it experiences hydrophobicity in the aqueous phase, driving vesicle formation and mRNA encapsulation.

(D) After initial vesicle formation, the pH is raised by dilution, dialysis or filtration, which results in the neutralization of the ionizable lipid, rendering it more hydrophobic and thereby driving vesicles to fuse and causing the further sequestration of the ionizable lipid with mRNA into the interior of the solid lipid nanoparticles. The PEG–lipid content stops the fusion process by providing the LNP with a hydrophilic exterior, determining its thermodynamically stable size, and the bilayer forming DSPC is present just underneath this PEG–lipid layer.

Source Buschmann, M.D.; Carrasco, M.J.; Alishetty, S.; Paige, M.; Alameh, M.G.; Weissman, D. Nanomaterial

Delivery Systems for mRNA Vaccines. Vaccines 2021, 9, 65. https://doi.org/10.3390/vaccines9010065 19 January 2021;

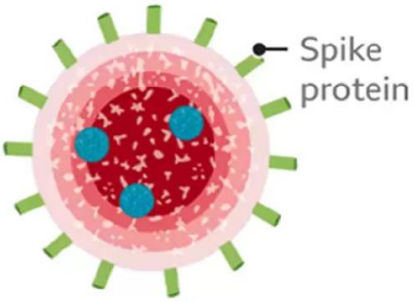


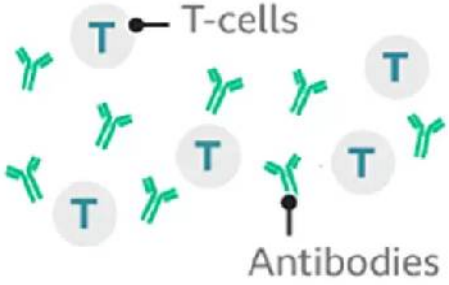
- ✓ part of genetic code of virus is the RNA made into vaccine
- ✓ injected into healthy person for immunization against viral disease

From left: Dr. Graham, **President Biden**, Dr. Francis Collins and Kizzmekia Corbett during a visit to the Viral Pathogenesis Laboratory at the N.I.H. last year

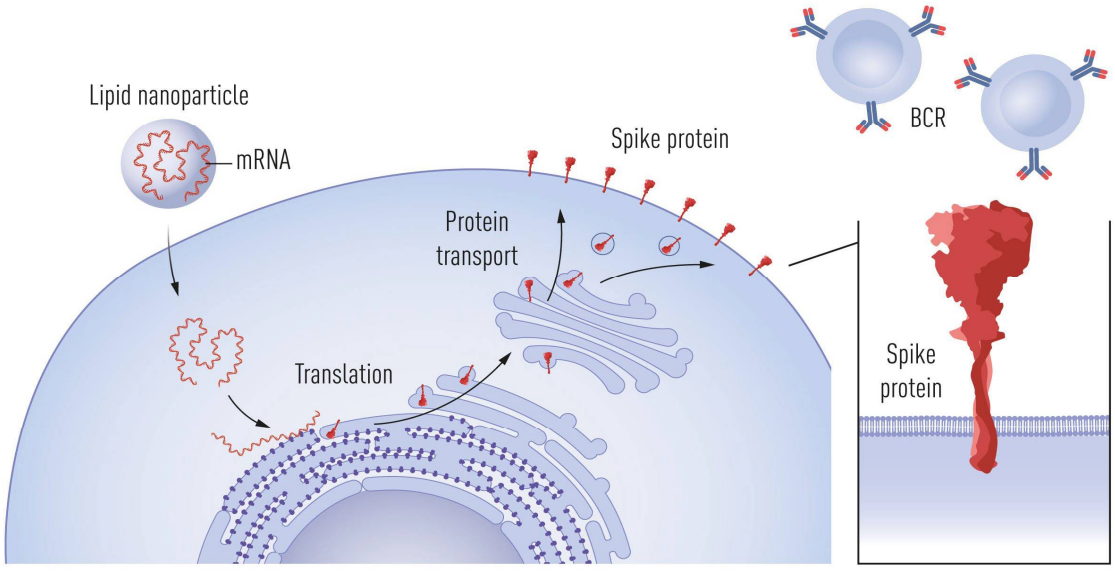
. The scientists were explaining the role of spikeproteins to Mr. Biden

Pete Marovich for The New York Times



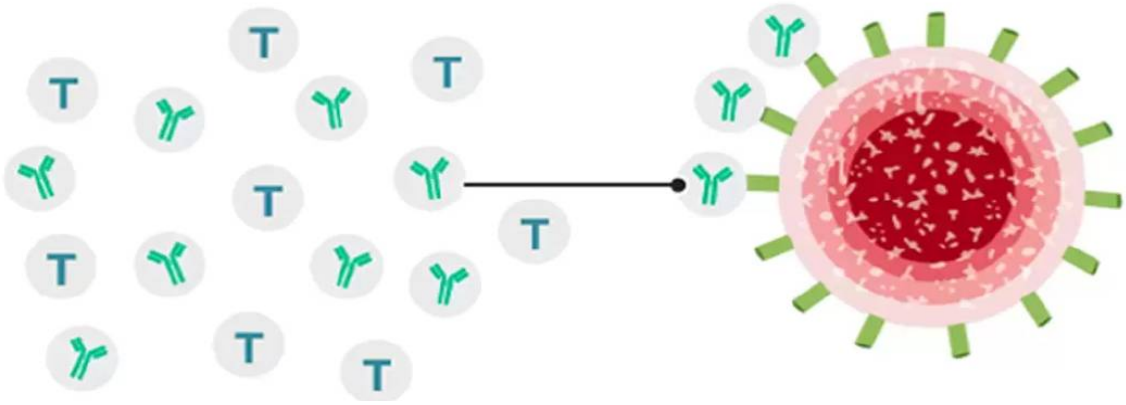


- ✓ Vaccine which entered into the human body tells cells to produce spike protein ofcorona virus
- ✓ The immune system of the body produces antibodies
- ✓ Activates T-cells to destroy cells with spike proteins



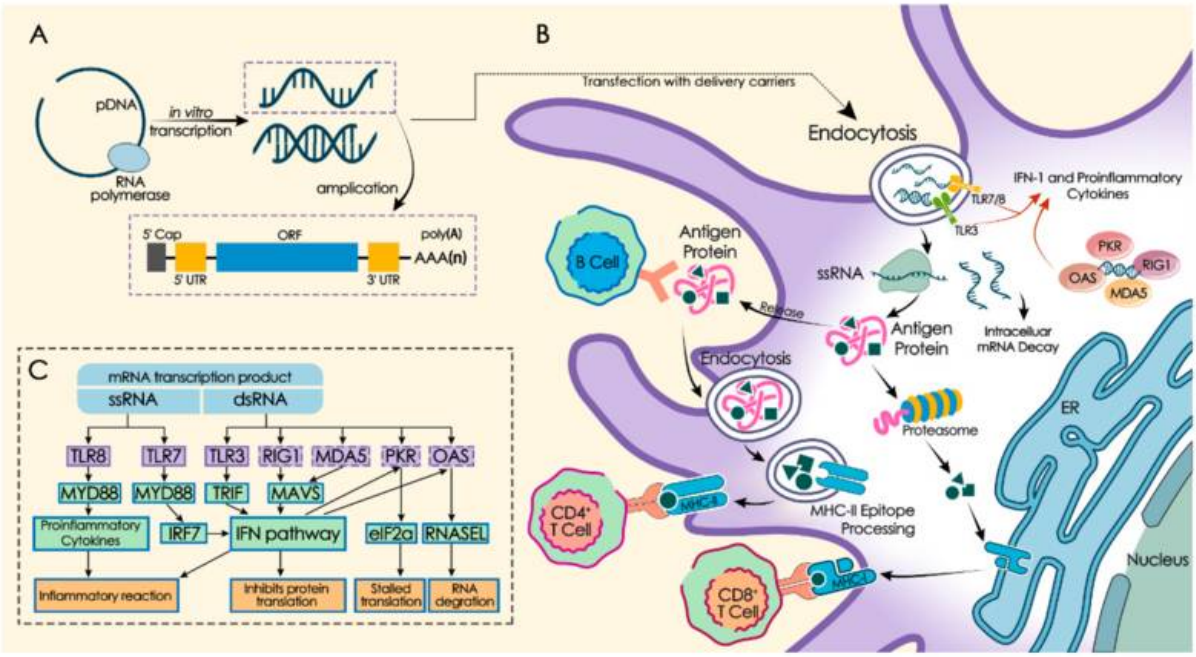
Spike productionfollowing mRNA vaccination recognition of spike by B cells

- ✓ Following uptake of mRNA into cells, facilitated by lipid nanoparticles, the mRNA acts as a template for spike protein production.
- ✓ Spike is then transiently expressed on the cell surface,
- ✓ where it is recognized by B cells via their B cell receptors (BCRs),
- ✓ stimulating the secretion of spike-specific antibodies



✓ If the immunized person Is attacked by Corona-virus, antibodies and T-cells are triggered to fight against virus

The body produces anti bodies and special immunity system cells in response. This knowledge, process-instructions etc. will be there in vaccinated healthy subject's body. Later, when the real virus attacks, the immunity system recognises, fights and kills the virus saving human/animal.Virus-associated molecules (like genomic DNA and RNA or double-stranded RNA) produced in virally infected cells are recognized by host pattern-recognition receptors (PRRs) expressed in innate immune cells such as dendritic cells.

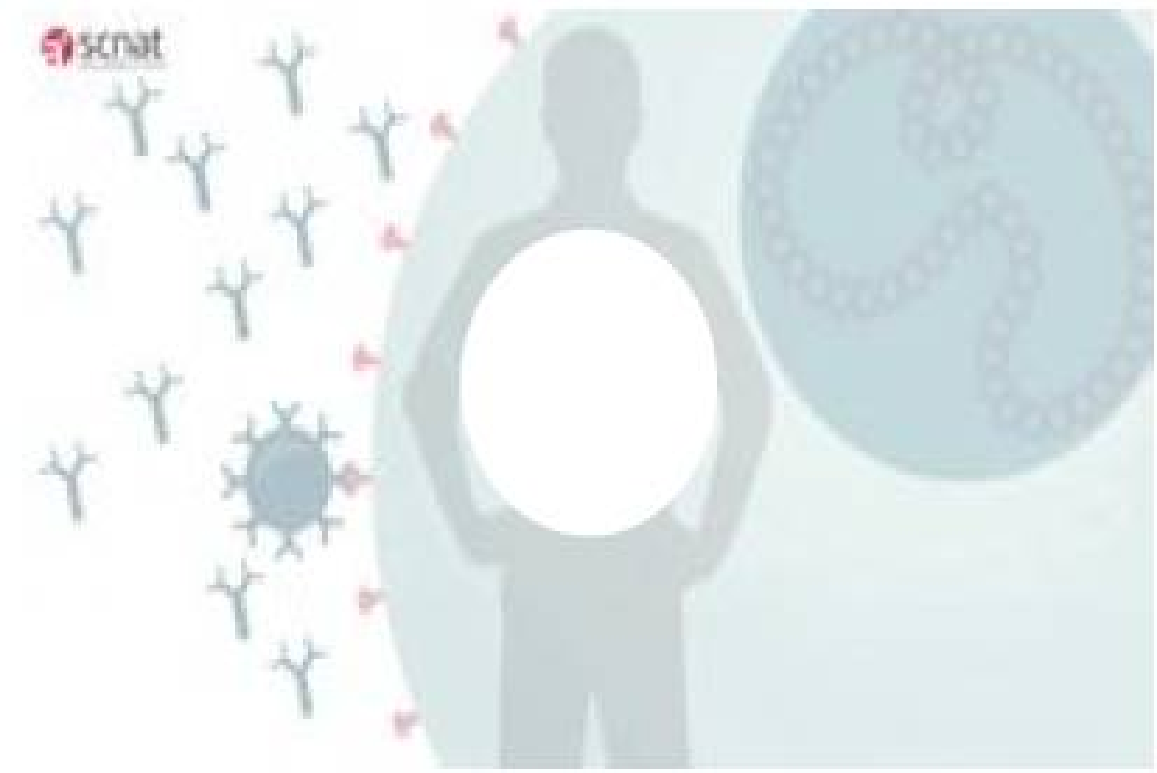


mRNA in vitro transcription and innate immunity activation.

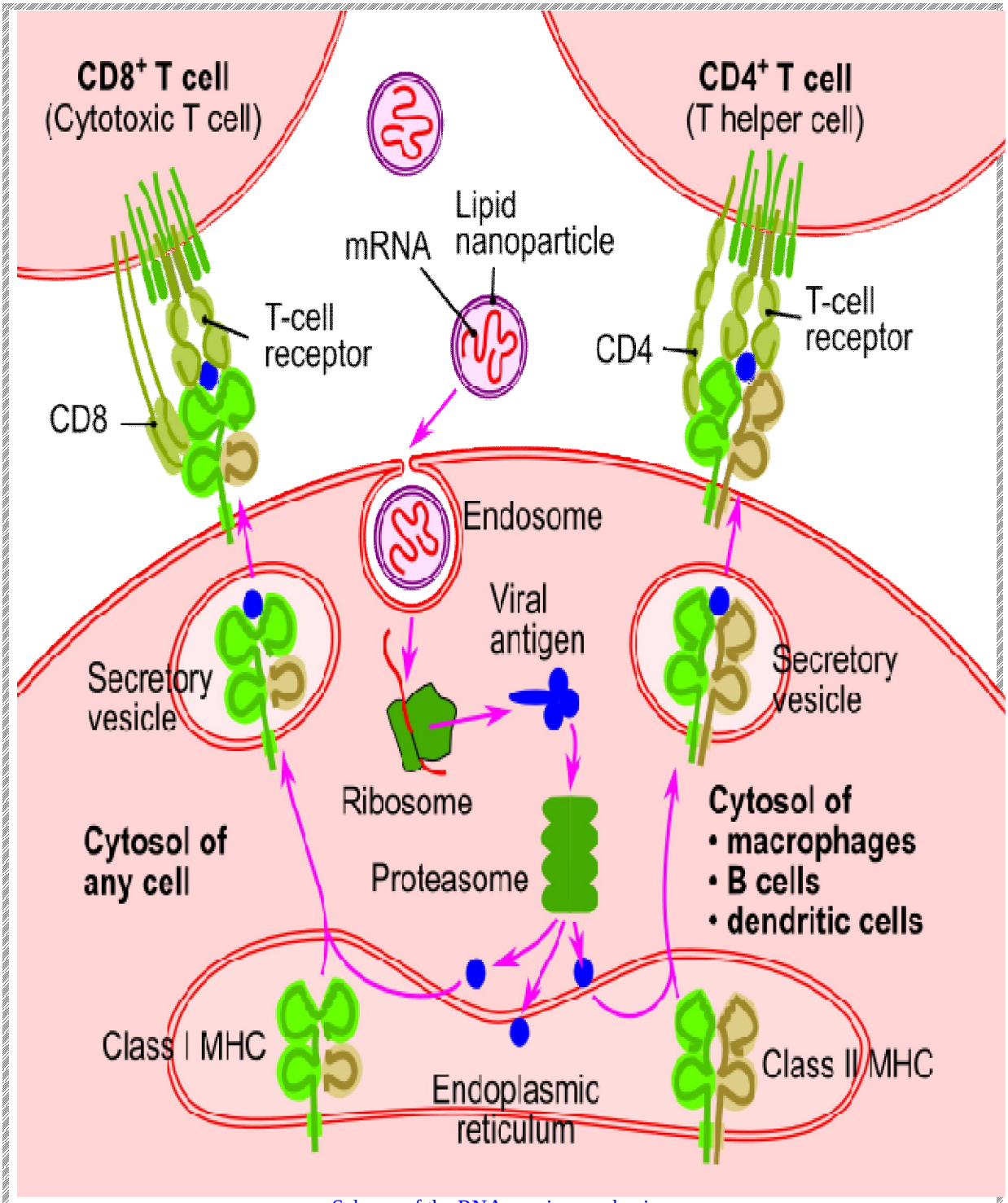
(A) mRNA in vitro transcription. Using DNA with the antigen-encoding sequence as template, mRNA in vitro transcription products contain single-stranded RNA (ssRNA), double-stranded RNA (dsRNA), etc. The ssRNA structure normally includes five-prime cap (5′ cap), five-prime untranslated region (5′ UTR), open reading frame (ORF) region, three-prime untranslated region (3′ UTR), and poly (A) tail structure.
(B) RNA translation and antigen presentation. Through endocytosis, mRNAs enter the cytoplasm. Some mRNAs combine with ribosomes of the host cell and translate successfully. Antigen proteins can be degraded to antigenic peptides by proteasome in the cytoplasm and presented to cytotoxic T lymphocytes (CTLs) via major histocompatibility complex (MHC) I pathway. Or, they can be released out of the host cell and taken up by DCs. Then, they are degraded and presented to helper T cells and B cells via MHC-II pathway. B cells can also recognize released antigen proteins.

(C) Self-adjuvant effect. Various of pattern recognition receptors (PRRs) can recognize mRNA in vitro transcription product. ssRNA can be recognized by endosomal innate immune receptors (e.g., Toll-like receptor 7 (TLR7), TLR8). dsRNA can be recognized by endosomal innate immune receptors (e.g., TLR3) and cytoplasmic innate immune receptors (e.g., protein kinase RNA-activated (PKR), retinoic acid-inducible gene I protein (RIG-I), melanoma differentiation-associated protein 5 (MDA5), and 2′-5′-oligoadenylate synthase (OAS). Based on those, mRNA products can stimulate the secretion of pro-inflammatory cytokines and type I interferon (IFN), which leads to antigen-presenting cells (APCs) activation and inflammatory reaction. However, they can also activate antiviral enzymes that cause stalled mRNA translation and mRNA degradation.9 September 2020

https://upload.wikimedia.org/wikipedia/commons/transcoded/e/e3/MRNA_vaccines_against_the_coronavirus.webm/MRNA_vaccines_against_the_coronavirus.webm.720p.vp9.webm

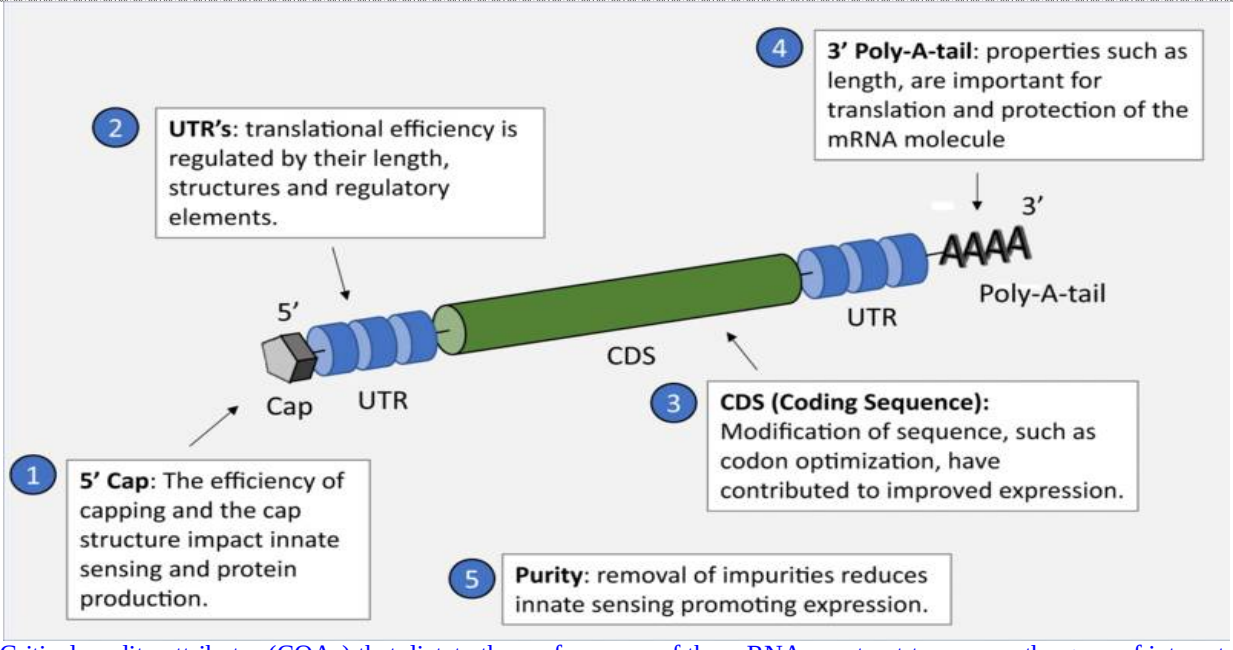


Video showing how vaccination with an mRNA vaccine works



Schema of the RNA vaccine mechanism

Date 13 December 2020



Critical quality attributes (CQAs) that dictate the performance of the mRNA construct to express the gene of interest efficiently.

Five principal CQAs

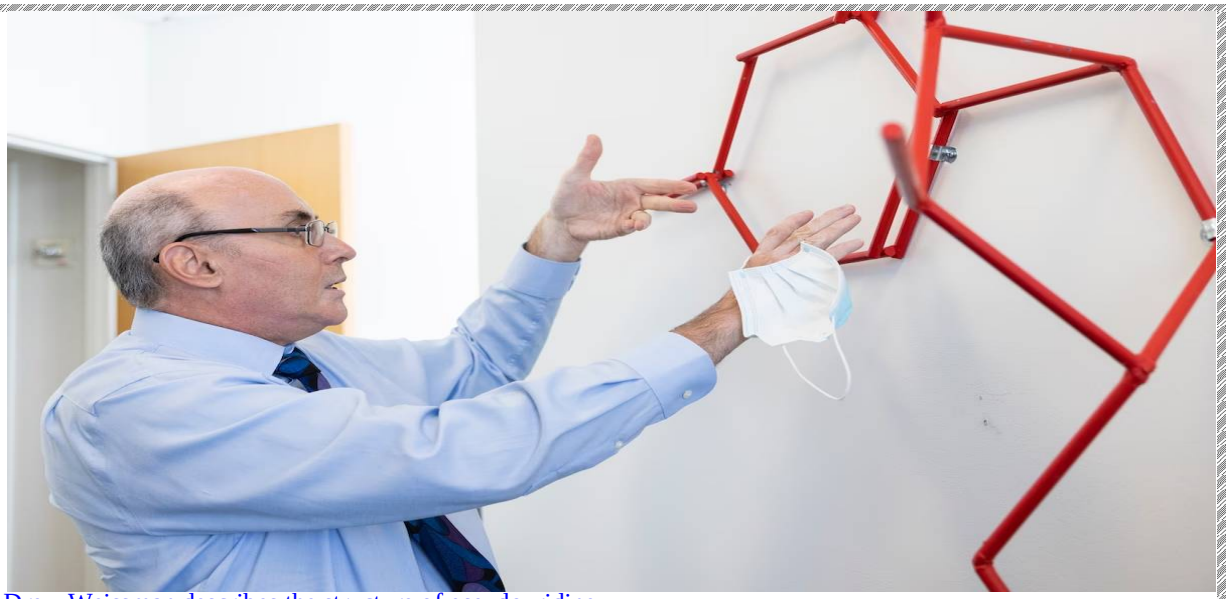
5′ capping efficiency and structure; UTR structure, length, and regulatory elements; modification of coding sequence; poly-A-tail properties; mRNA purity.

Source Jackson, N.A.C., Kester, K.E., Casimiro, D. et al. The promise of mRNA vaccines: a biotech and industrial perspective. npj Vaccines 5, 11 (2020). https://doi.org/10.1038/s41541-020-0159-84 February 2020

mRNA vaccine for COVID-19: Here, no live virus is used.The protein molecule directs the cells too look for harmless spike proteins of Corona, the dreaded virus.The spike protein of the Covid virus was encoded in mRNA molecules.

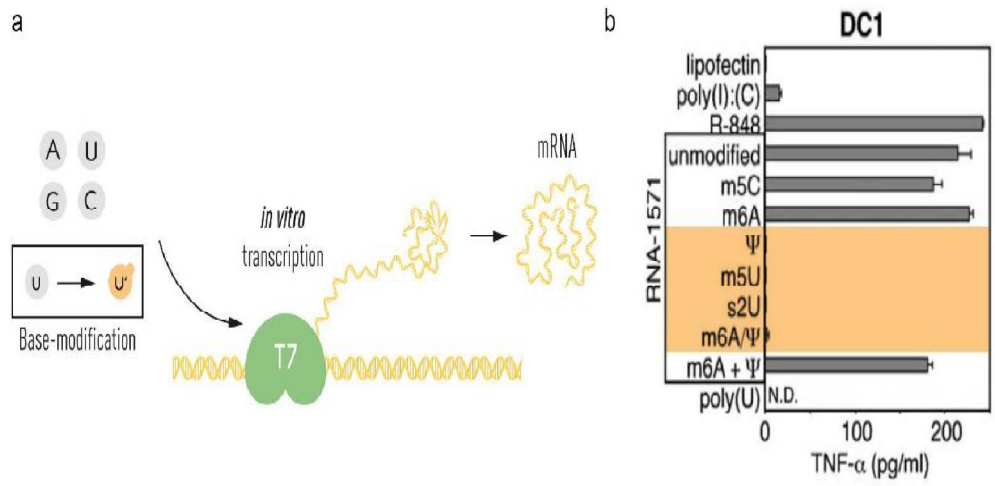
Today, m1Ψ (N1-methylpseudo-uridine (m1Ψ)) is the most common modified base used in mRNA vaccine production, including in the two COVID-19 vaccines approved in late 2020, as discussed below

structure of pseudouridine



Drew Weissman describes the structure of pseudouridine, the molecule that made messenger RNA work,

- ✓ pointing to a sculpture of the molecule
- ✓ welded by his daughter Rachel Weissman for his office
- ✓ at the University of Pennsylvania.
- ✓ (Rachel Wisniewski for The Washington Post)



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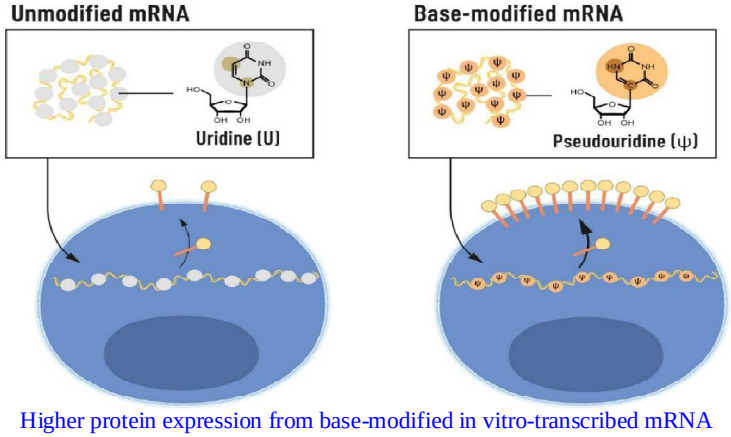
Evaluation of in vitro transcribed mRNA with or without nucleoside base modifications and transfection into primary dendritic cells.

(a) The T7 in vitro transcription system was used to produce mRNA with canonical RNA bases (A, U, G and C) or modified bases.

(b) The bases used for in vitro transcription of RNA-1571 are shown, with those that did not result in TNF-a secretion indicated in orange (modified from Karikó et al. Immunity 2005).



Higher protein expression from base-modified in vitro-transcribed mRNA

- Base-modified in vitro transcribed mRNA was produced where uridines (U) were substituted with pseudouridine (Ψ).
- When base-modified mRNA was introduced into cells, an increased protein production compared to that achieved with unmodified mRNA was observed

Those molecules were wrapped in a protective layer of fat in vaccine. The synthetic mRNA in the vaccine instructs cells in the human body to make their own viral spike protein. Then, the body makes the viral protein.This triggers the immune system to make antibodies to fight the virus. Once the immune system knows how to make these antibodies, italso learns how to destroy them. This gives the vaccinated body the tools to defend against virus.Thus, it can do it again when exposed laterto the SARS-CoV-2 (with) spike protein. This is a warning immune system to kill the virus.In m-RNA vaccines for covid-19, the protein molecule directs the cells too look for harmless spike proteins of Corona, the dreaded virus.The failure/success outcome cycles in the concerted efforts in pure/basic sciences (of Kariko and Weissman) and trans-disciplinary technological innovations through not-easy-to-surmount-hurdles resulted in astounding success. To make long-story-short, the extraordinary knowledge bits/tools in old discoveries plucked from obscurity were put all in one place fulfilled promise of basic scientific research: that was once great.

Advantages and unique features of m-RNA vaccines: m-RNA vaccines excel all traditional counterparts in technology, safety and feasibility.

- \+ no live/attenuated /dead virus is used at any stage in vaccine design/preparation to administration cycle.
- \+ Unlike conventional vaccines, mRNA vaccines are not grown in live cells
  - ✓ only the knowledge of genetic sequence code of full/part of virus or other components (like spite proteins) is used
  - ✓ whole process of product in the in-vitro/ human made-laboratory
  - ✓ no risk of infection by the vaccine
- \+ The flexibility and speed of preparation opened a new platform in vaccine development.
- \+ speed up the manufacturing process. mRNA vaccines also bypass the step of inactivating viruses or isolating the protein, which also makes them quicker to produce
- \+ **Immune to mutation of virus**
  - \+ effective against germs that evolve through mutation
  - \+ RNA vaccines typically trigger an immune response to a part of the virus (the viral stalk) that doesn't mutate easily

- Traditional vaccines typically target a different part of the virus (the globular head), which does mutate easily

+ This novel new paradigm has potential application to deliver therapeutic proteins to treat even certain cancers

4Katalin Karikó Era

Affiliation	Nobel Laureate (Med) Photo Date & place of birth	Share
o Professor o Szeged University, Szeged, Hungary; o University of Pennsylvania, Philadelphia, PA, USA	Katalin Karikó  Born: 17 January 1955, Szolnok, Hungary	1/2

Birth and Family: She was born on 17 January 1955 in Szolnok, Hungary. Her father was an employed butcher and blessed with the skill of playing violine. Also, he excelled in mental maths. Her mother was a book-keeper. The family had a radio and record player in their home and thusKariko's mother developed intense interest in music.The family lived in asmall village of Kisujszallas. The abode was a two-room modest house withno television, no air conditioner, no refrigerator and not even running water.They had a garden. They had pigs. Kariko watched a neighbour's cow give birth. Yet, her parents extended an unwavering support for her academic career. Kariko's mother lived long life and died in the year 2018. She was blessing her daughter year after year to get the Nobel award.

Education: Karikó has interest in nature from childhood and excelled in Science in her academic pursuit. She went on excursions to a nearby forest and remembers being curious about birds, plants, natureetc.. And she was good — and fiercely competitive — at science. It is evident securing a third placein the country in biology in a national contest during her eighth grade. She obtained a bachelor degree in 1978 and Ph.D in 1982 both from university of Szeged, Hungary.

DNAand RNA studies: DNA (Deoxyribonucleic acid) contained in the nucleus of every biological cell (save red blood cells) is a blue print of recipe book/manual with all instructions of life. Nuclear DNA stores the genetic information that speaks about traits of individual, characteristics and overall biology. It contains thousands of genes (sets of instructions) to make proteins and other molecules required for structure and function of cells and continuation of life processes of entire organism. Each of the genes encode the instructions for a specific protein.

There are different of RNAs, namely messenger RNA (mRNA), ribosomal RNA (rRNA) and transfer RNA (tRNA). In gene expression, the information in DNA is transcribed into messenger (m-) RNA (ribonucleic acid). These molecules are called messenger RNA because they carry instructions for producing proteins from one part of the cell to another. m-RNA is a single strand of genetic code that cell can read to prepare protein. This like a hand written copy of recipe is discarded after use. In m-RNA, the bases (adenine (A), uracil (U), cytosine (C) or guanine (G)) are present, while in DNA thymine (T) is there instead of uracil (U). The molecular structure of m-RNA consists of chains of nucleotides with 5'

and 3' poly-A tail. The genetic code specifying the order of amino acids in the protein is in sequence of nitrogenous bases. The ribosomes read the information in the process of translation for synthesis of proteins.

Protein synthesis through mRNA in anin-vivo cell:The transcription makes an RNA copy of a DNA sequence for a proteinmRNA. It is moved from the nucleus (center) of the cell to the ribosomes, which are located in the cell outside. Theribosomes "translate" the instructions in mRNA and synthesize the protein of the nucleus

4.1 Research contributions of Katalin Karikó prior to 1998

Employment in Hungary: She was selected for a position in biological research centre (BRC) where she carried out investigations on anti-viral activity of short segment regions of RNA. Later she focused on studies with modified m-RNAby replacing/altering synthesized or naturally modified nucleotide moieties. In 1970s, m-RNA was new and was a prime field of study focus.

Setback:In 1985, Karico's research program ran out of funds for continuing investigations. This was the first set-back (followed by several severe stumble-blocks, dead-ends and so on) in her academic research career.

Spouse and off spring: Karikó met Bela Francia, an engineer at a disco held as part of an annual biology celebration.He was 17, she 22. Three years later they married. The couple have a daughterSusan Francia, who won two Olympic gold medals in rowing in Beijing and London. Their grandson was born in the U.S. in February 2021 to their daughter and son-in-law, Ryan Amos,anarchitect.

Dr. Kariko and her family in 1985.Credit...via Kati Kariko

Hungarian-born biochemist Katalin Karikó, with her husband Bela Francia and daughter, Zsuzsanna “Susan” Francia, at London 2012 Olympics

Susan Francia's mother, Dr. Katalin Kariko, taught her perseverance. She brought that inherited tenacity to rowing. Matt King/Getty Images

Position in USA: Around the same time, she secured an invitation from Temple University in Philadelphia for a position.

Moving (going away) from Hungary to USA: Katalin moved to US to continue her inner innate urge to continue academic research pursuitof human health improvement. She was accompanied by her husband, who was a consistent supporter during all her hurdles and two-year-old daughter (Susan). They sold their in Hungary for USD 1200 (equivalent) carried in the teddy bear of the baby for safe keeping to meet emergencies whatever.

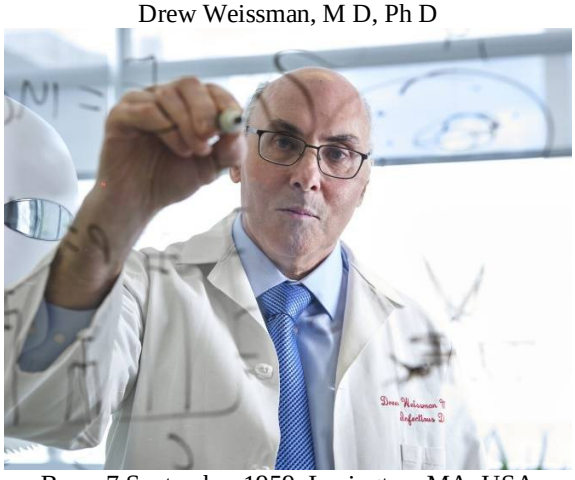
Post-doctoral Fellow in USA: In 1989, Kairko joined as a Post-doctoralresearch Fellow with American cardiologist Elliot Barnathan in the Dept of medicine, University of Pennsylvania (Penn),

Break through observation: Katalin along with a colleague demonstrated that m-RNA sent into a cell directs the production of proteins.

Hope of future medical therapy and intervention: The break-through procedure can be used to study the feasibility of m-RNA based gene therapy. She was convinced that it would be a new paradigmin therapeutics based on proof-of-concept and definitelynot a gut feeling.

Setback:The concept was too novel to attract funds. The hope of a few scientists turned into scepticism and the initial excitement started to fizz out. The therapeutic value was deemed as radical. The financial fund proposalsof Kariko were rejected one after another.In 1995. Dr Kariko was demoted from her position in the Penn university with a remark “she was not of faculty quality”, So, the team fell apart for just lack of sustained financial support. This was another set-back for Kariko in m-RNA research progress. Added to it, she was diagnosed with cancer. Thus, a heap of misfortunes engulfed her.

5Drew Weissman Era

Affiliation	Nobel Laureate (Med) Photo Date & place of birth	Share
o Penn Institute for RNA Innovations, University of Pennsylvania, Philadelphia, PA, USA	Drew Weissman, M D, Ph D  Born: 7 September 1959, Lexington, MA, USA	1/2

Birth and Family: Drew Weissman was born on 7th September, 1959 in Lexington, Massachusettsandwas grown up there. His mother was an Italian and the father a Jew. From childhood, he was a disciplined,

self-possessed and more capable compared to other kids of his age group. Although, he was happy to play sports including martial arts, he was fond of science.Weissman's father was an engineer and his profession was production of optical mirrors for use in satellites. Drew worked in his father's firm from high school stage itself. He was brought up celebrating all Jewish holidays, although his mother was not converted to Judaism, StephenWeissman, his younger sister, mentioned that Drew use to do everything while sailing with cousins which sheds light how he likes to do himself everything in a group.

Education: In 1981, Weissman received B A and M A degrees fromBrandeis University. He worked under the guidance of Gerald Fasman in the Lab during master program specializing in Biochemistry and Enzymology. Drew was curious, clear and with a firm sense that Science was central focus of goals of his academic life. He worked hard compared to his fellow mates and decided to pursue for a medical and science degrees simultaneously. He liked to be a trained medical doctor to become a better scientist in serving humanity suffering with dreadeddeceases. He had sustained inner urge of thinking of what he wants to do and moving towards the direction of happiest niche in his brain. He chose immunology and micro-biology in the studies. He received both M D and Ph D from Boston university in 1987.

Internship: Weissman did residency in internal medicine at Beth Israel Deaconess Medical Center.

5.1 Research contributions of Drew Weissman prior to 1998

Fellowship at NIH: DrDrew Weissman moved to NIH accepting a fellowship to do research in the lab under the supervision of Anthony Fauci ,then director of the National Institute of Allergy and Infectious Diseases. Drew was inspired and committed in the study of dynamic dendric cells which were discovered in the immediate past. The cells use to branch like in a tree under a microscope and were key to how immune system learns to kill/defeat pathogens, by traveling through all limbs in the body searching for foreign/non-self-cells or invaders.

Employment: Harvey Friedman, chief of the infectious-diseases division,recruited Weissman to the medical school at the University of Pennsylvania (Penn), although he wasnot trained as an infectious-disease doctor.It was a tough time for Friedman with the department chairman to induce Dr.Drew in to the department. From 1997, Weissman started his lab and carried out intense research in dendric cells, RNA, and system biology atPerelman School of Medicine of the University of Pennsylvania (Penn) in Philadelphia. It resulted in m-RNA therapeutics and vaccine development during the next two decades. His discoveries, patents, publications etc. were in collaboration with Dr. Katalia Karico, a biochemist fascinated in m-RNA in clinical medicine/vaccine protocol.

Spouse and off spring: Mary Ellen, a graduate studentat Brandeis University was introduced through a friend that Mary has doubts in calculus. He clarified the concept of infinity to her with simplenaïve analogy "if you have all the cloths you wanted that is infinity". After a few years, Mary Ellenbecame his wifeMary EllenWeissman. They have two daughters.

Weissman celebrates Father's Day in 2012 with daughters Rachel Weissman, left, and Allison Weissman at his home near Philadelphia. (Family photo)

Family joke: Dr Weissman was, straight forward, calm and has the habit to talk less in all occasions. The family joke was he used to say without malice even to his wife that "we talked for today"

6Collaborative Research contributions of Katalin Karikó + Drew Weissman (1998-)

Life ambitions ofWeissman:Drew Weissman was an immunologist and was interested in dendric cells research. He had life's goal to develop vaccines for HIV, to relieve human kind (their generations) from wide-spread life-style disease. He also dreamt of at least partially terminate influenza, prevent herpes and cure cancer.

Katalin Karikó

They both started collaboration to study how different RNA types interact with immune system

Set-backs for Weissman and Karikó:Weissman and Karikó could not attract/get financial assistance for medical applications of m-RNA research. The field met with indifference and continuation of activity was frustrating. At that juncture, one should leave the field and look for another area for survival prospects. Yet, these scientists with single laser focussed goal did not want to quit the pursuit, but pursue the investigations with a (baseless) hope of some miraclesturn up/fortune showers on this niche and on them.

Even with small signs of positive experimental results, Kariko use to repeatedly pronounce that “I am not giving up, I am not giving up and I am not giving up” .

Dendric cells play a vital role in immune surveillance. Their function is in activation of in induced immune response.

Break-through in basic science research: m-RNA transcribed in vitro was detected as a foreign molecule by dendritic cells, while those from mammalian cells were not. They inferred that there are some properties and structural details of two types of m-RNAs responsible for the subtle differences.

Dr. Katalin Kariko in 2005 at her UPenn lab.

Her innovative mRNA research laid the foundation for the development of the COVID-19 vaccines being deployed across the globe

The valid knowledge at that time was that the bases in m-RNA from mammalian cells were chemically modified while there was no change in in-vitro prepared m-RNA. The question remains whether absence of altered nucleotides in-vitro could explain the cause of undesirable inflammation reaction.

Experiment: Weissman and Kariko developed m-RNA in-vitroby different variation of nucleotide (U) and delivered it into dendritic cells. With a chemical tweak to one nucleotide (U) of the genetic code, the inflammation vanished and the yield of protein increased. This enabled them to surmount the scientific hurdle in in-vitro prepared RNA to use for protein synthesis in vivo.

Start of new era in Science of Vaccine preparation with m-RNA in a non-traditional way: In 2005, Weissman and Kariko recognised the impact of new understanding how cells recognise and produce proteins to different types m-RNAs. This will pave way to employ m-RNAs in therapeutics and vaccines. They communicated their findings. The journals Nature and Science rejected and it was finally published in Immunity. There was no response or appreciation and Weissman expressed that their phones never rang and nobody recognised. It was a piece of worthwhile knowledge, but ahead of time. So, none cared about it. Top science journals and their contributors were not interested.

Delivery of in-vitro transcribed m-RNAs into in-vivo cells: The outcome of intense studies on delivery of m-RNA obtained in-vitro with modifications in the base (nucleotides) were published in 2008 and 2010. The increase in the yield of protein compared to unmodified m-RNAs was due to reduced activation of an enzyme.

New company for vaccine preparation: Weissman and Kariko founded a pharma company to translate science findings into technology to save lives of humankind suffering/dying with dreaded viral diseases.

Activities of several companies to develop protocols for manufacture of m-RNA medical products: The noteworthy instance was in pursuing a vaccine for Zyka virus and MERS-Cov. As this catastrophe lasted only for a short time period, there were no many significant improvements.

7 Novel performance of m-RNA vaccine for Corona: When covid-19 broke out at a large scale all over the world within a short span of time, several companies plunged into manufacturing activity. The fantastic result was preparation of two-base modified m-RNA vaccines encoding SAR-COv2 surface (spike) proteins within short span of a year.Protective performance of Vaccine against covid-19 was up to 95%.

7.1 FDA approval: The Pfizer-BioNTech COVID-19 vaccine received U.S. Food and Drug Administration (FDA) approvalin August 2021for Americans 6 months and up.

The Moderna COVID-19 vaccine was authorized by the FDA for emergency use.They are the first-ever mRNA-based vaccines which obtained FDA regulatory authorization.More than 13 billion vaccine doses were administered globally by 2023. It saved millions of lives and prevented spread of the worst pandemic during last several decades. It made possible the societies to open-up and return to normalcy, of course at the cost of huge financial crisis and losing the loved ones.

Development of a vaccine against the Zika virus,
Which is spread by Aedes aegypti mosquitoes

? Weissman's family thought his breakthrough moment might arrive

7.2 Skeptics' complaints on rapid development of m-RNA vaccine technology for Covid-19: Skeptics started raising their voice against (false) disadvantages stuffed with apparently convincing lone patient episodes of post-vaccination effects. That was to undermine the public trust in the new technology. In fact, m-RNA method is valid and acceptable on firm scientific background and shrewd survey results. Today's preventive product is a culmination of break-throughs and lessons from failures little by little over decades. The research efforts are diverse from large number of scientists across the globe. The outcome was unthreaded knowledge bits in across trans-disciplines. None ever contemplated that it would result in combining together to be help in saving lives in the covid-19 pandemic, the most disastrous one of the century.

8 Basic Science research (Univ., Labs) to applicable products (vaccines, robotic surgery protocols, Therapeutics):

8.1 State-of-knowledge-m-RNA vaccines and Therapeutics: The real-life tested m-RNA vaccine for Covid-19 with astounding success and low rate of ADRR (adverse drug reaction reporting) is a mile-stone in ensuring the prospects of this approach. This paradigm will bring in new life in curing diseases by delivering the therapeutic proteins in treating certain types of cancers.

9 Future prospects of m-RNA in Medical care

m-RNA therapeutics will bring in a healthier society through vaccination and therapeutic intervention even in an unfortunate emergence of infectious bacterial/viral diseases and pandemics. The abnormal proteins

produced in cancer patient's tumor that are not in healthy tissue will be detected and analyzed in the coming years. m-RNAs of therapeutic functional value will be developed. They will be injected into the patient for curative purposes.

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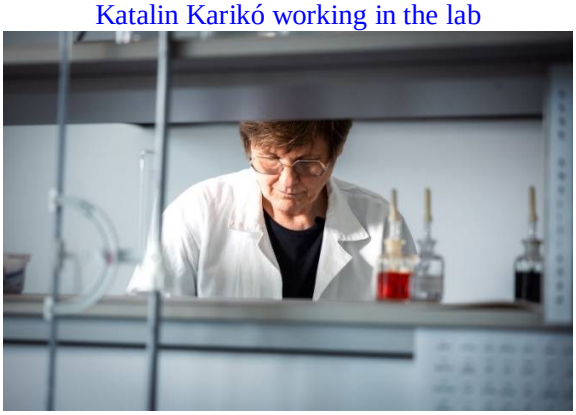
Information Supplementary (Is)

SI.1: First Response of Noble Prize Winners of 2023 in Medicine

Interviewer (Telephonic)	Dr. Adam Smith (AS) Chief Scientific Officer of Nobel Prize Outreach Nobelprize.org, the website of the Nobel Prize

Katalin Karikó working in the lab  Medicine	Nobel Award News (NaN: Not a number) ! I am at my home in a suburb of Philadelphia in Abington township ! Doing actually then (DAT) ! I was sleeping, and actually my husband picked up the phone First action/reaction/expression (Fare) ! AS: first thoughts on hearing this news ! KK: That somebody is just joking ! KK: It was kind of very scientific and too much information was in it that somebody would just make it up. But you never know in these days ! AS: Now you know for sure ! KK: I'm not … [unclear] a hundred percent sure!

Weissman turns on a DNA printing machine in his lab at Penn.

- Nobel Award News (NaN: Not a number)
  - ! AS: It must be very early there, how did you receive the call?
  - ! DW: Yes, I got the call a little while ago, I got a call from Kati a little bit earlier.
  - ! AS: OK, so she actually broke the news to you that you'd been awarded together?
  - ! DW: Yes.
    - Doing actually then (DAT)
  - ! But we weren't sure it was true, we thought that maybe somebody was playing a joke on us.
- First action/reaction/expression (Fare)
  - ! AS: Apart from slight disbelief, what was your first reaction?
  - ! DW: You know, it's a lifetime dream. And this is coming from somebody who doesn't work for or look forward to awards. But you know, the Nobel is the ultimate recognition of work, so it is a wonderful experience
  - ! AS: Have you ever imagined yourself in this moment before?
  - ! DW: You know, starting as a basic scientist doing work in high school it was always a dream but I never imagined it would happen

- ! Katalin Karikó called him early this morning with some incredible news – they had both been awarded the 2023 Nobel Prize in Physiology or Medicine
- ! Dr. Weissman said that he found out about the prize at 4 a.m. when Dr. Karikó texted him, asking if he had heard from Thomas yet.
- ! "No. Who's Thomas?" he replied.
- ! Dr. Kariko told him that Thomas Perlmann was from the Nobel committee.
- ! He was looking for Dr. Weissman's phone number

The technology developed by Karikó and Weissman may also be used to treat other diseases.
Courtesy Penn Medicine

SI2: Noble work-style of Nobel laureates

✓ Typically, as scientists growin their career,their labs get larger and so spend less time running their own experiments.This is just because they do not really get clock hours.
! Kariko was unusually talented atthe benchwork and also loved involvement fully
! Not that she didn't have great success or very big grup

Commitment and Success

- Her academic career looked nothinglike a traditional success.
o But Kariko wasn't done.
o She wanted her work to reach patients.
o She joinedBioNTech, then a little-known start-up that had never created an approved medical product. She wouldlive in Mainz, Germany, for 10 months out of the year.

Self-assessment-respect and expressing truth

🔔 She knows she's brilliant, and she doesn't suffer fools
🔔 A colleague told another scientist, "Kati works for me." She responded as "I don't work for you. Do you think that Saturday, Sunday, I am here for you?"
🔔 Kariko said, "I am herefor me. I am here to learn more and understand."
! Langer, a colloborator said. "And the reality of Americanresearch, which continues today, is pursuit of money is high on the list. Kate's kind of the opposite. Katedoes nothing for money.
! The reality is, she is doing the best science she can do and she has zero political-savvy about how to navigate this world."
! Kariko was obsessed with messenger RNA
! but colleagues say she also knew not to fall too deeply in love with any specific outcome
! She learns from the data — even when it was disappointing. "Experiments never err, your expectations do,"

SI3:Noble words of Nobel laureates

✓ You have to focus on the things you can change, but not
✓ on the things you cannot change

+ When I was terminated, I didn't spend time feeling sorry
+ Or saying things like "Why me?"
+ I focussed all the energy Ihad to spend
+ I tried to seek out, "What next? What I can do."

Funds for science

o Now, Professor Karikó remains convinced of the need for more funding to create the enabling conditions for other revolutionary discoveries
o senior scientists to be permitted to apply their time and energy to exploring unconventional ideas and breaking new ground.

"I would go to meetings and present what I was working on, and people would look at me and say: 'Well, that's very nice, but why don't you do something worthwhile with your time mRNA will never work.'. But

Katie and I kept pushing," Professor Wiseman told the BBC's Newshour programme

Facts in Academic life of Nobel Prize winners

Katalin Karikó

- 10 years ago, I was forced to retire. from Penn Chose the position in BioNTech (Germany)

Drew Weissman

- Nothing distracts me from my work

AS: I know you are very focused on bringing RNA therapeutics to the,and there are so many things you want to do with mRNA vaccines still to come. I guess the Nobel Prize might be a bit of a distraction.

Alfred Nobel, I think, wanted to make things free from distraction for laureates by giving them some money to sort of get on and concentrate on their work, but how do you feel about the prize?

DW: To me, nothing distracts me from my work. With the new notoriety that Kati and I have, we've been traveling around the world for awards or discussions.

Labs-funds---Away from bench work

Mother's confidence in Kariko

- Kariko: My mother listened always the announcement of who gets the Nobel Prize because
- she told me, "Oh next week they will announce, maybe you will get it."
- Kariko: I was laughing, I was not even a professor, no team, and, I told my mom, don't listen,
- Mother: "Yes but you know, you work so hard."
- Kariko: all scientists work very hard
- AS: How wonderful to have a mother who believes you to such an extent

Information Supplementary (Is)

SI4: Awards

Shared awards between Katalin Kariko and Drew Weissman

- (2020) Lewis S. Rosenstiel Award for Distinguished Work in Basic Medical Research
- (2021) Lasker-DeBakey Clinical Medical Research Award
- (2021) Louisa Gross Horwitz Prize

Lewis S. Rosenstiel Award

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Weissman and Kariko received the Lewis S. Rosenstiel Award this year, celebrates medical research, for their work on mRNA vaccines.

(Rachel Wisniewski for The Washington Post

Awards
to Katalin Kariko

- ✓ Breakthrough Prize in Life Sciences
- ✓ Princess of Asturias Award
- ✓ Vilcek Prize for Excellence in Biotechnology

Kariko Katalin with a statue of AlbertSzent-Gyorgyi , a fellow Nobel Prize winner in Medicine
University of Szeged

A mural in Budapest, by "The colorful city" artist group

Captures the likeness of Hungarian-born scientist Katalin Kariko,
whose research on mRNA technology is
backbone of two coronavirus vaccines
(Attila Kisbenedek/AFP/Getty Images)