

MRNA vaccine

This is an **old revision** of this page, as edited by **OAbot** ([talk](#) | [contribs](#)) at **00:25, 14 June 2021** (**Open access bot**: [pmc](#) added to citation with [#oabot.](#)). The present address (URL) is a **permanent link** to this revision, which may differ significantly from the **current revision** .

([diff](#)) ← [Previous revision](#) | [Latest revision](#) ([diff](#)) | [Newer revision](#) → ([diff](#))

A **ribonucleic acid (RNA) vaccine** or **messenger RNA (mRNA) vaccine** is a type of [vaccine](#) that uses a copy of a natural molecule called [messenger RNA](#) (mRNA) to produce an immune response.^[1] The vaccine [transfects](#) molecules of [synthetic RNA](#) into [immunity cells](#). Once inside the immune cells, the vaccine's RNA functions as mRNA, causing the cells to build the foreign [protein](#) that would normally be produced by a [pathogen](#) (such as a virus) or by a cancer cell. These protein molecules stimulate an [adaptive immune response](#) which teaches the body how to identify and destroy the corresponding pathogen or cancer cells.^[1] The [delivery](#) of mRNA is achieved by a co-formulation of the molecule into [lipid nanoparticles](#) which protect the RNA strands and helps their absorption into the cells.^{[2][3]}

[Reactogenicity](#), the property of a vaccine of being able to produce common, expected adverse reactions, is similar to that of conventional non-RNA vaccines.^[4] People susceptible to an [autoimmune response](#) may have an adverse reaction to RNA vaccines.^[4] The advantages of RNA vaccines over traditional protein vaccines are superior design and production speed, lower cost of production,^{[5][4]} and the induction of both [cellular](#) as well as [humoral immunity](#).^[6] The [Pfizer–BioNTech COVID-19 vaccine](#) requires [ultracold storage](#) before distribution,^[1] but other mRNA vaccines do not, such as the COVID-19 vaccines by [Moderna](#), [CureVac](#) and [Walvax](#).

In [RNA therapeutics](#), mRNA vaccines have attracted considerable interest as [COVID-19 vaccines](#). By December 2020, there were two novel mRNA vaccines for COVID-19 that had completed the required eight-week period post-final human trials and were awaiting [emergency use authorization](#) (EUA): the [Moderna COVID-19 vaccine](#) (mRNA-1273) and the [Pfizer–BioNTech COVID-19 vaccine](#) (BNT162b2).^[1] On 2 December 2020, the UK's [Medicines and Healthcare products Regulatory Agency](#) (MHRA) became the [first medicines regulator](#) to approve an mRNA vaccine, authorizing the Pfizer–BioNTech COVID-19 vaccine (Comirnaty) for widespread use.^{[7][8][9]} On 11 December 2020, the US [Food and Drug Administration](#) (FDA) issued an EUA for the Pfizer-BioNTech COVID-19 vaccine and the US [Centers for Disease Control and Prevention](#) (CDC) recommended its use in those aged 16 and older on 12 December 2020.^{[10][11]} On 19 December 2020, the CDC recommended the use of the Moderna COVID-19 vaccine in adults after the FDA granted an EUA.^{[12][13]}

The use of [RNA](#) in a vaccine has been the basis of substantial [misinformation](#) circulated via social media, wrongly claiming that the use of RNA alters a person's [DNA](#) (a biologically impossible occurrence).^[14]

History

In 1989, Robert W. Malone, P. Felgner, et. al. developed a high-efficiency in-vitro and in-vivo RNA transfection system using cationic liposomes, which were used "to directly introduce RNA into whole tissues and embryos", as well as various cells types. The term and idea of "RNA as a drug" is first described in this paper.^[15] Then, in 1990, Jon A. Wolff, Robert W Malone, et. al. demonstrated the idea of nucleic acid-encoded drugs by direct injecting in vitro transcribed (IVT) mRNA or plasmid DNA (pDNA) into the skeletal muscle of mice which expressed the encoded protein in the injected muscle. These studies were the first evidence that in vitro transcribed (IVT) mRNA could deliver the genetic information to produce proteins within living cell tissue.^{[16][17]}

The first mRNA vaccine experiments were carried out by P. Felgner, J. Wolff, G. Rhodes, R.W. Malone and D. Carson. P. They completed a number of mRNA vaccination studies that resulted in nine patents on mRNA vaccination with a shared priority date of March 21, 1989. One experiment documented that NEF (an HIV protein) mRNA vaccination in mice, followed by HIV challenge reduced positively stained cells by 2-fold and p24 expression was reduced by 50% at eight weeks.^{[18][19][20]}

In 1993, Martinon demonstrated that liposome-encapsulated RNA could stimulate [T-cells](#) in vivo, and in 1994, Zhou & Berglund published the first evidence that RNA could be used as a vaccine to elicit both humoral and cellular immune response against a pathogen.^{[21][22]}

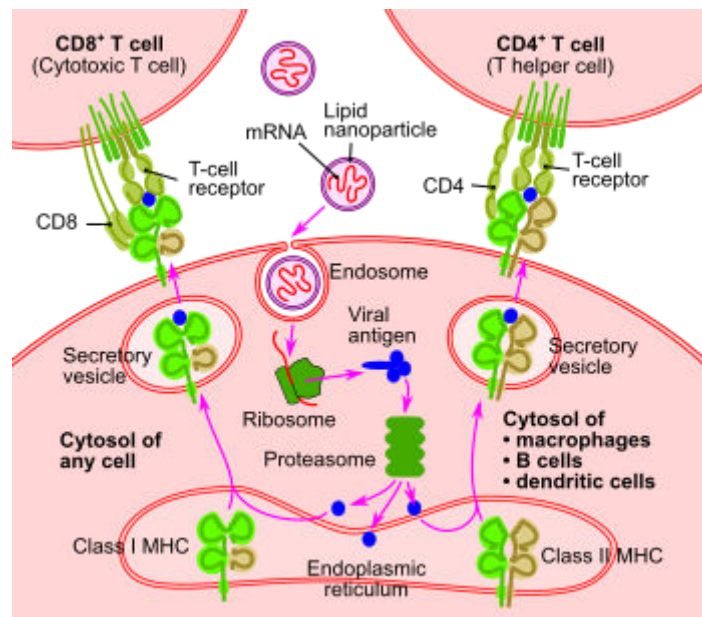
[Hungarian biochemist Katalin Karikó](#) attempted to solve some of the main technical barriers to introducing mRNA into cells in the 1990s. Karikó partnered with American immunologist [Drew Weissman](#), and by 2005 they published a joint paper that solved one of the key technical barriers by using [modified nucleosides](#) to get mRNA inside cells without setting off the body's defense system.^[23] [Harvard stem cell biologist Derrick Rossi](#) (then at Stanford) read Karikó and Weissman's paper and recognized that their work was "groundbreaking",^[23] and in 2010 founded the mRNA-focused biotech [Moderna](#) along with [Robert Langer](#), who also saw its potential in vaccine development.^[23] In 2013, [DARPA](#), the US government organization responsible for emerging technologies for use by the military, saw the potential of the technology for defense against pandemics and invested \$25 million in the company.^[24] Like Moderna, [BioNTech](#) also licensed Karikó and Weissman's work.^[23]

Up until 2020, these mRNA biotech companies had poor results testing mRNA drugs for cardiovascular, metabolic and renal diseases; selected targets for cancer; and [rare diseases](#) like [Crigler–Najjar syndrome](#), with most finding that the side-effects of the mRNA delivery methods

were too serious.^{[25][26]} mRNA vaccines for human use have been developed and tested for the diseases [rabies](#), [Zika](#), [cytomegalovirus](#), and [influenza](#), although these mRNA vaccines have not been licensed.^[27] Many large pharmaceutical companies abandoned the technology,^[25] while some biotechs re-focused on the less profitable area of vaccines, where the doses would be at lower levels and side-effects reduced.^{[25][28]}

At the onset of the [COVID-19 pandemic](#), no mRNA drug or vaccine had been licensed for use in humans. In December 2020, both Moderna and Pfizer–BioNTech obtained emergency use authorization for their mRNA-based COVID-19 vaccines, which had been funded by [Operation Warp Speed](#) (directly in the case of Moderna and indirectly for Pfizer–BioNTech).^[23] On 2 December 2020, seven days after its final eight-week trial, the UK's [Medicines and Healthcare products Regulatory Agency](#) (MHRA), became the first global medicines regulator [in history](#) to approve an mRNA vaccine, granting emergency authorization for Pfizer–BioNTech's BNT162b2 COVID-19 vaccine for widespread use.^{[7][8][29]} MHRA CEO [June Raine](#) said "no corners have been cut in approving it",^[30] and that, "the benefits outweigh any risk".^{[31][32]} On 11 December 2020 the [FDA](#) gave emergency use authorization for the Pfizer–BioNTech COVID-19 vaccine.^[33]

Mechanism



An illustration of the [mechanism of action](#) of the RNA vaccine

The goal of a vaccine is to stimulate the [adaptive immune system](#) to create [antibodies](#) that precisely target that particular [pathogen](#). The markers on the pathogen that the antibodies target are called [antigens](#).^[34]

mRNA vaccines operate in a very different manner from a traditional [vaccine](#).^[1] Traditional vaccines stimulate an [antibody](#) response by injecting [antigens](#), an [attenuated virus](#) (weakened or harmless virus), or a recombinant antigen-encoding [viral vector](#) (carrier virus engineered to have

antigens) into muscles. These antigen-containing ingredients are prepared and grown outside the body.

In contrast, mRNA vaccines introduce a short-lived^[35] [synthetically created fragment of the RNA sequence](#) of a virus into the vaccinated individual. These mRNA fragments are taken up by [dendritic cells](#) – a type of immune system cell – by [phagocytosis](#).^[36] The dendritic cells use their own internal machinery ([ribosomes](#)) to read the mRNA and produce the viral antigens that the mRNA encodes before destroying the mRNA.^[4] Although non-immune cells can potentially absorb vaccine mRNA, manufacture spikes, and display spikes on their surfaces, dendritic cells absorb the mRNA globules much more readily.^[37]

Once the viral antigens are produced by the host cell, the normal adaptive immune system processes are followed. Antigens are broken down by [proteasomes](#), then class I and class II [MHC molecules](#) attach to the antigen and transport it to the cellular membrane, "activating" the dendritic cell.^[38] Once the dendritic cells are activated, they migrate to [lymph nodes](#), where the [antigen is presented](#) to [T cells](#) and [B cells](#).^[39] This eventually leads to the production of antibodies that are specifically targeted to the antigen, resulting in immunity.^[34]

The benefit of using mRNA to have host cells produce the antigen is that mRNA is far easier for vaccine creators to produce than antigen proteins or attenuated virus.^{[38][1][4]} Another benefit is speed of design and production. Moderna designed their [mRNA-1273](#) vaccine for COVID-19 in 2 days.^[40] Another advantage of RNA vaccines is that since the antigens are produced inside the cell, they stimulate [cellular immunity](#), as well as [humoral immunity](#).^{[6][41]}

mRNA vaccines do not affect or reprogram DNA inside the cell. The synthetic mRNA fragment is a copy of the specific part of the viral RNA that carries the instructions to build the antigen of the virus (a protein spike, in the case of the main coronavirus mRNA vaccines), and is not related to human DNA. This misconception was circulated as the COVID-19 mRNA vaccines came to public prominence, and is a debunked [conspiracy theory](#).^{[42][43]}

The mRNA should [degrade](#) in the cells after producing the foreign protein. However, because the specific formulation (including the exact composition of the lipid nanoparticle drug delivery coating) is kept confidential by the manufacturers of the mRNA vaccines, details and timings have not been researched yet by third parties.^[44]

Delivery

The method of vaccine delivery can be broadly classified by whether the RNA transfer to cells happens within (*in vivo*) or outside (*ex vivo*) the organism.^[3]

Ex vivo

Dendritic cells are a type of immune cells that display antigens on their **surfaces**, leading to interactions with **T cells** to initiate an immune response. Dendritic cells can be collected from patients and programmed with the desired mRNA. Then, they can be re-administered back into patients to create an immune response.^[45]

In vivo

Since the discovery that introducing *in vitro* transcribed mRNA leads to the expression *in vivo* following direct administration, *in vivo* approaches have become more and more attractive.^[46] They offer some advantages over *ex vivo* methods, particularly by avoiding the cost of harvesting and adapting dendritic cells from patients, and by imitating a regular infection. There are still obstacles for these methods to overcome for RNA vaccination to be a potent procedure. **Evolutionary mechanisms** that prevent the infiltration of unknown **nucleic material** and promote degradation by **RNases** need to be circumvented to initiate translation. In addition, RNA is too heavy to move around on its own inside the cell via **diffusion**, making it vulnerable to being discovered and eliminated by the host cell.

Naked mRNA injection

A naked injection means that the **delivery** of the vaccine is simply held in a **buffer**.^[47] This mode of mRNA uptake has been known for since the 2000s. The first worldwide clinical studies (Tübingen, Germany) used **intra-dermal injections** of naked mRNA for vaccination.^{[48][49]}

The use of RNA as a vaccine tool was discovered in the 1990s in the form of self-amplifying mRNA.^{[50][51]} The two main categories of mRNA vaccines are non-amplifying (conventional, viral delivery), and molecular self-amplifying mRNA (non-viral delivery). When mRNA is delivered non-virally it enters the cell's cytoplasm and can amplify and express the antigenic protein.^{[52][53]}

It has also emerged that the different routes of **injection**, such as **into the skin, blood** or to **muscles**, resulted in varying levels of mRNA uptake, making the choice of administration route a critical aspect of delivery. One study showed, in comparing different routes, that **lymph node** injection leads to the largest T cell response.^[54]

The mechanisms and consequently the evaluation of self-amplifying mRNA may be different, as self-amplifying mRNA is fundamentally different by being a much bigger molecule in size.^[3]

Polyplex vector

Cationic polymers can be mixed with mRNA to generate protective coatings called **polyplexes**. These protect the recombinant mRNA from **ribonucleases** and assist its penetration in cells.

Protamine is a natural cationic **peptide** and has been used to encapsulate mRNA for vaccination.^[55]

Lipid nanoparticle vector

The first time the FDA approved the use of **lipid nanoparticles** as a drug delivery system was in 2018, when the agency approved the first **siRNA** drug, **Onpattro**.^[56] Encapsulating the mRNA molecule in lipid nanoparticles was a critical breakthrough for producing viable mRNA vaccines, solving a number of key technical barriers in delivering the mRNA molecule into the host cell.^{[56][57]} Research into using lipids to deliver siRNA to cells became a foundation for similar research into using lipids to deliver mRNA.^[58] However, new lipids had to be invented to encapsulate mRNA strands, which are much longer than siRNA strands.^[58]

Principally, the **lipid** provides a layer of protection against degradation, allowing more robust translational output. In addition, the customization of the lipid's outer layer allows the targeting of desired cell types through **ligand** interactions. However, many studies have also highlighted the difficulty of studying this type of delivery, demonstrating that there is an inconsistency between *in vivo* and *in vitro* applications of nanoparticles in terms of cellular intake.^[59] The nanoparticles can be administered to the body and transported via multiple routes, such as **intravenously** or through the **lymphatic system**.^[56]

One issue with lipid nanoparticles is that several of the breakthroughs leading to the practical use of that technology involved the use of **microfluidics**. Microfluidic reaction chambers are difficult to scale up since the entire point of microfluidics is to exploit the microscale behaviors of liquids. The only way around this obstacle, as of 2021, is to conduct the process in a massively parallel fashion by building a great many microfluidic reaction chambers to run in parallel, a novel task requiring custom-built equipment. As of February 2021, this was thought to be the primary bottleneck in the manufacturing of mRNA vaccines.^{[60][61]} Pfizer later revealed that it had utilized the massively parallel approach to solve this problem. After verifying that impingement jet mixers could not be directly scaled up,^[62] Pfizer made about 100 of the little mixers (each about the size of a **U.S. half-dollar coin**), connected them together with pumps and filters with a "maze of piping,"^{[63][64]} and set up a computer system to regulate flow and pressure through the mixers.^[62]

Another issue is the availability of the novel lipids used to create lipid nanoparticles, especially ionizable cationic lipids. Before 2020, such lipids were manufactured in small quantities measured in grams or kilograms, and they were used for medical research and a handful of drugs for rare conditions. As the safety and efficacy of RNA vaccines became clear by late 2020, the few companies able to manufacture the requisite lipids were confronted with the challenge of scaling up production to respond to orders for several tons of lipids.^{[61][65]}

Viral vector

In addition to non-viral delivery methods, [RNA viruses](#) have been [engineered](#) to achieve similar immunological responses. Typical RNA viruses used as vectors include [retroviruses](#), [lentiviruses](#), [alphaviruses](#) and [rhabdoviruses](#), each of which can differ in structure and function.^[66] Clinical studies have utilized such viruses on a range of diseases in [model animals](#) such as [mice](#), [chicken](#) and [primates](#).^{[67][68][69]}

Side effects and risks

[Reactogenicity](#) is similar to that of conventional, non-RNA vaccines. However, those susceptible to an [autoimmune response](#) may have an adverse reaction to RNA vaccines.^[4] The mRNA strands in the vaccine may elicit an unintended immune reaction. To minimize this, mRNA sequences in mRNA vaccines are designed to mimic those produced by host cells.^[5]

Strong but transient reactogenic effects were reported in trials of novel COVID-19 RNA vaccines; most people will not experience severe side effects which include fever and fatigue. Severe side effects are defined as those that prevent daily activity.^[70]

General

Before 2020, no mRNA technology platform (drug or vaccine) had been authorized for use in humans, so there was a risk of unknown effects.^[41] The 2020 coronavirus pandemic required faster production capability of mRNA vaccines, made them attractive to national health organisations, and led to debate about the type of initial authorization mRNA vaccines should get (including [emergency use authorization](#) or [expanded access authorization](#)) after the eight-week period of post-final human trials.^{[71][72]}

Storage

Because mRNA is fragile, some vaccines must be kept at very low temperatures to avoid degrading and thus giving little effective immunity to the recipient. Pfizer–BioNTech's [BNT162b2](#) mRNA vaccine has to be kept between -80 and -60 °C (-112 and -76 °F).^{[73][74]} Moderna says their [mRNA-1273](#) vaccine can be stored between -25 and -15 °C (-13 and 5 °F),^[75] which is comparable to a home freezer,^[74] and that it remains stable between 2 and 8 °C (36 and 46 °F) for up to 30 days.^{[75][76]} In November 2020, *Nature* reported, "While it's possible that differences in LNP formulations or mRNA secondary structures could account for the thermostability differences [between Moderna and BioNtech], many experts suspect both vaccine products will ultimately prove to have similar storage requirements and shelf lives under various temperature

conditions."^[4] Several platforms are being studied that may allow storage at higher temperatures.^[4]

Advantages

Traditional vaccines

RNA vaccines offer specific advantages over traditional [protein vaccines](#).^[5]^[4] Because RNA vaccines are not constructed from an active pathogen (or even an inactivated pathogen), they are non-infectious. In contrast, traditional vaccines require the production of pathogens, which, if done at high volumes, could increase the risks of localized outbreaks of the virus at the production facility.^[5] RNA vaccines can be produced faster, cheaper, and in a more standardized fashion (with fewer error rates in production), which can improve responsiveness to serious outbreaks.^[4]^[5] For example, the Pfizer-BioNTech vaccine originally required 110 days to produce (before Pfizer began to optimize the manufacturing process to only 60 days), but this was still far faster than traditional flu and polio vaccines.^[63] Within that larger timeframe, the actual production time is only about 22 days: two weeks for molecular cloning of DNA plasmids and purification of DNA, four days for DNA-to-RNA [transcription](#) and purification of mRNA, and four days to encapsulate mRNA in lipid nanoparticles followed by [fill and finish](#).^[77] The majority of the days needed for each production run are allocated to rigorous quality control at each stage.^[63]

DNA vaccines

In addition to sharing the advantages of theoretical [DNA vaccines](#) over established traditional [protein vaccines](#), RNA vaccines also have additional advantages over DNA vaccines. The [mRNA](#) is [translated](#) in the [cytosol](#), so there is no need for the RNA to enter the [cell nucleus](#), and the risk of being integrated into the host [genome](#) is averted.^[3] [Modified nucleosides](#) (for example, [pseudouridines](#), 2'-O-methylated nucleosides) can be incorporated to mRNA to suppress [immune response](#) stimulation to avoid immediate degradation and produce a more persistent effect through enhanced translation capacity.^[78]^[79]^[80] The [open reading frame \(ORF\)](#) and [untranslated regions \(UTR\)](#) of mRNA can be optimized for different purposes (a process called sequence engineering of mRNA), for example through enriching the [guanine-cytosine content](#) or choosing specific UTRs known to increase translation.^[81]

An additional ORF coding for a [replication](#) mechanism can be added to amplify antigen translation and therefore immune response, decreasing the amount of starting material needed.^[51]^[82]

Vaccine hesitancy

There is misinformation implying that mRNA vaccines could alter DNA in the nucleus.^[14] mRNA in the **cytosol** is very rapidly degraded before it would have time to gain entry into the cell nucleus. (mRNA vaccines must be stored at very low temperature to prevent mRNA degradation.) **Retrovirus** can be single-stranded RNA (just as **SARS-CoV-2** vaccine is single-stranded RNA) which enters the cell nucleus and uses **reverse transcriptase** to make DNA from the RNA in the cell nucleus. A retrovirus has mechanisms to be imported into the nucleus, but other mRNA lack these mechanisms. Once inside the nucleus, creation of DNA from RNA cannot occur without a **primer**, which accompanies a retrovirus, but which would not exist for other mRNA if placed in the nucleus.^{[83][84]} Thus, mRNA vaccines cannot alter DNA because they cannot enter the nucleus, and because they have no primer to activate reverse transcriptase.

In November 2020, *The Washington Post* reported on novel mRNA vaccine hesitancy amongst healthcare professionals in the United States, citing surveys that "some did not want to be in the first round, so they could wait and see if there are potential side effects".^[85]

Efficacy of mRNA vaccines for COVID-19

It is unclear why the novel mRNA COVID-19 vaccines from Moderna and Pfizer–BioNTech have shown potential efficacy rates of 90 to 95 percent when the prior mRNA drug trials on pathogens other than COVID-19 were not so promising and had to be abandoned in the early phases of trials.^[86] **Physician-scientist Margaret Liu** stated that it could be due to the "sheer volume of resources" that went into development, or that the vaccines might be "triggering a nonspecific inflammatory response to the mRNA that could be heightening its specific immune response, given that the **modified nucleoside technique** reduced inflammation but hasn't eliminated it completely", and that "this may also explain the intense reactions such as aches and fevers reported in some recipients of the mRNA SARS-CoV-2 vaccines". These reactions though severe were transient and another view is that they were believed to be a reaction to the lipid drug delivery molecules.^[86]

Unlike DNA molecules, the mRNA molecule is a very fragile molecule that degrades within minutes in an exposed environment, and thus mRNA vaccines need to be transported and stored at very low temperatures.^[87] Outside the cell, or its drug delivery system, the mRNA molecule is also quickly broken down by the host.^[5] This fragility of the mRNA molecule is a hurdle to the **efficacy** of any mRNA vaccine due to bulk disintegration before it enters the cells, which could lead people to believe, and act as if they are immune when they are not.^{[87][5]}

Self-amplifying RNA

Self-amplifying RNA (saRNA) is a technology similar to mRNA, except the saRNA produces multiple copies of itself in the cell before producing proteins like mRNA does. This allows smaller

quantities to be used and has other potential advantages.^{[88][89]} saRNA vaccines are being researched, including development of a [malaria vaccine](#).^[90]

See also

- [ARCT-021](#)
- [CureVac COVID-19 vaccine](#)
- [Walvax COVID-19 vaccine](#)
- [DNA vaccine](#)
- [Nucleoside-modified messenger RNA](#)
- [RNA therapeutics](#)
- [Timeline of human vaccines](#)

References

1. Park KS, Sun X, Aikins ME, Moon JJ (December 2020). "Non-viral COVID-19 vaccine delivery systems" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7744276>) . *Advanced Drug Delivery Reviews*. **169**: 137–51. doi:10.1016/j.addr.2020.12.008 (<https://doi.org/10.1016%2Fj.addr.2020.12.008>) . PMC 7744276 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7744276>) . PMID 33340620 (<https://pubmed.ncbi.nlm.nih.gov/33340620>) .
2. Kowalski PS, Rudra A, Miao L, Anderson DG (April 2019). "Delivering the Messenger: Advances in Technologies for Therapeutic mRNA Delivery" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6453548>) . *Mol Ther*. **27** (4): 710–28. doi:10.1016/j.ymthe.2019.02.012 (<https://doi.org/10.1016%2Fj.ymthe.2019.02.012>) . PMC 6453548 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6453548>) . PMID 30846391 (<https://pubmed.ncbi.nlm.nih.gov/30846391>) .
3. Verbeke R, Lentacker I, De Smedt SC, Dewitte H (October 2019). "Three decades of messenger RNA vaccine development" (<https://biblio.ugent.be/publication/8628303>) . *Nano Today*. **28**: 100766. doi:10.1016/j.nantod.2019.100766 (<https://doi.org/10.1016%2Fj.nantod.2019.100766>) .
4. Pardi N, Hogan MJ, Porter FW, Weissman D (April 2018). "mRNA vaccines – a new era in vaccinology" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5906799>) . *Nature Reviews. Drug Discovery*. **17** (4): 261–79. doi:10.1038/nrd.2017.243 (<https://doi.org/10.1038%2Fnrdr.2017.243>) . PMC 5906799 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5906799>) . PMID 29326426 (<https://pubmed.ncbi.nlm.nih.gov/29326426>) .
5. PHG Foundation (2019). "RNA vaccines: an introduction" (<https://www.phgfoundation.org/briefing/rna-vaccines>) . *University of Cambridge*. Retrieved 18 November 2020.

6. Kramps T, Elders K (2017). "Introduction to RNA Vaccines". *RNA Vaccines: Methods and Protocols*. Methods in Molecular Biology. Vol. 1499. pp. 1–11. doi:10.1007/978-1-4939-6481-9_1 (https://doi.org/10.1007%2F978-1-4939-6481-9_1) ↗. ISBN 978-1-4939-6479-6. PMID 27987140 (https://pubmed.ncbi.nlm.nih.gov/27987140) ↗.
7. "UK authorises Pfizer/BioNTech COVID-19 vaccine" (https://www.gov.uk/government/news/uk-authorises-pfizer-biontech-covid-19-vaccine) ↗ (Press release). Department of Health and Social Care. 2 December 2020.
8. Boseley S, Halliday J (2 December 2020). "UK approves Pfizer/BioNTech Covid vaccine for rollout next week" (https://www.theguardian.com/society/2020/dec/02/pfizer-biontech-covid-vaccine-wins-licence-for-use-in-the-uk) ↗. *The Guardian*. Retrieved 2 December 2020.
9. "Conditions of Authorisation for Pfizer/BioNTech COVID-19 Vaccine" (https://www.gov.uk/government/publications/regulatory-approval-of-pfizer-biontech-vaccine-for-covid-19/conditions-of-authorisation-for-pfizerbiontech-covid-19-vaccine) ↗ (Decision). Medicines & Healthcare Products Regulatory Agency. 8 December 2020.
10. "FDA Takes Key Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for First COVID-19 Vaccine" (https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19) ↗. *U.S. Food and Drug Administration (FDA)* (Press release). 11 December 2020. Retrieved 6 February 2021.
11. Oliver SE, Gargano JW, Marin M, Wallace M, Curran KG, Chamberland M, et al. (December 2020). "The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine – United States, December 2020" (https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6950e2-H.pdf) ↗ (PDF). *MMWR Morb Mortal Wkly Rep.* **69** (50): 1922–24. doi:10.15585/mmwr.mm6950e2 (https://doi.org/10.15585%2Fmmwr.mm6950e2) ↗. PMC 7745957 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7745957) ↗. PMID 33332292 (https://pubmed.ncbi.nlm.nih.gov/33332292) ↗.
12. "FDA Takes Additional Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for Second COVID-19 Vaccine" (https://www.fda.gov/news-events/press-announcements/fda-takes-additional-action-fight-against-covid-19-issuing-emergency-use-authorization-second-covid) ↗. *U.S. Food and Drug Administration (FDA)* (Press release). 18 December 2020.
13. Oliver SE, Gargano JW, Marin M, Wallace M, Curran KG, Chamberland M, et al. (January 2021). "The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Moderna COVID-19 Vaccine – United States, December 2020" (https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm695152e1-H.pdf) ↗ (PDF). *MMWR Morb Mortal Wkly Rep.* **69** (5152): 1653–56. doi:10.15585/mmwr.mm695152e1 (https://doi.org/10.15585%2Fmmwr.mm695152e1) ↗. PMID 33382675 (https://pubmed.ncbi.nlm.nih.gov/33382675) ↗. S2CID 229945697 (https://api.semanticscholar.org/CorpusID:229945697) ↗.
14. Carmichael F, Goodman J (2 December 2020). "Vaccine rumours debunked: Microchips, 'altered DNA' and more" (https://www.bbc.co.uk/news/54893437) ↗ (Reality Check). BBC.

15. Malone RW, Felgner PL, Verma IM (1 August 1989). "Cationic liposome-mediated RNA transfection" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC297778>) ↗. *PNAS*. **86** (16): 6077–6081. doi:10.1073/pnas.86.16.6077 (<https://doi.org/10.1073/pnas.86.16.6077>) ↗. PMC 297778 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC297778>) ↗. PMID 276315 (<https://pubmed.ncbi.nlm.nih.gov/276315>) ↗.
16. Wolff JA, Malone RW, Williams P, Chong W, Acsadi G, Jani A, Felgner PL (March 1990). "Direct gene transfer into mouse muscle in vivo". *Science*. **247** (4949 Pt 1): 1465–8. Bibcode:1990Sci...247.1465W (<https://ui.adsabs.harvard.edu/abs/1990Sci...247.1465W>) ↗. doi:10.1126/science.1690918 (<https://doi.org/10.1126/science.1690918>) ↗. PMID 1690918 (<https://pubmed.ncbi.nlm.nih.gov/1690918>) ↗.
17. Sahin U, Karikó K, Türeci Ö (October 2014). "mRNA-based therapeutics--developing a new class of drugs" (<https://doi.org/10.1038/nrd4278>) ↗. *Nature Reviews. Drug Discovery*. **13** (10): 759–80. doi:10.1038/nrd4278 (<https://doi.org/10.1038/nrd4278>) ↗. PMID 25233993 (<https://pubmed.ncbi.nlm.nih.gov/25233993>) ↗. S2CID 27454546 (<https://api.semanticscholar.org/CorpusID:27454546>) ↗.
18. USA 5,589,466 (<https://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&p=1&u=/netachtml/PTO/srchnum.html&r=1&f=G&l=50&d=PALL&s1=5589466.PN>) ↗, Felgner, Phillip; Wolff, Rhoades & Malone, Robert et al., "Induction of a protective immune response in a mammal by injecting a DNA sequence", published Dec 31, 1996, issued March 21, 1989, assigned to Vical, Inc. and WARF
19. USA expired 5,703,055 (<https://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&p=1&u=/netachtml/PTO/srchnum.html&r=1&f=G&l=50&d=PALL&s1=5703055.PN>) ↗, Felgner, Phillip; Wolff, Rhoades & Malone, Robert et al., "Generation of antibodies through lipid mediated DNA delivery", published Dec 30, 1997, issued March 21, 1989, assigned to Vical, Inc. and WARF
20. USA expired 6,867,195 (<https://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&p=1&u=/netachtml/PTO/srchnum.html&r=1&f=G&l=50&d=PALL&s1=6867195.PN>) ↗, Felgner, Phillip; Wolff, Rhoades & Malone, Robert et al., "Lipid-mediated polynucleotide administration to reduce likelihood of subject's becoming infected", published March 15, 2005, issued March 21, 1989, assigned to Vical, Inc. and WARF
21. Pascolo S (August 2004). "Messenger RNA-based vaccines". *Expert Opinion on Biological Therapy*. **4** (8): 1285–94. doi:10.1517/14712598.4.8.1285 (<https://doi.org/10.1517/14712598.4.8.1285>) ↗. PMID 15268662 (<https://pubmed.ncbi.nlm.nih.gov/15268662>) ↗. S2CID 19350848 (<https://api.semanticscholar.org/CorpusID:19350848>) ↗.
22. Kallen KJ, Theß A (January 2014). "A development that may evolve into a revolution in medicine: mRNA as the basis for novel, nucleotide-based vaccines and drugs" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3991152>) ↗. *Therapeutic Advances in Vaccines*. **2** (1): 10–31. doi:10.1177/2051013613508729 (<https://doi.org/10.1177/2051013613508729>) ↗. PMC 3991152 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3991152>) ↗. PMID 24757523 (<https://pubmed.ncbi.nlm.nih.gov/24757523>) ↗.
23. Garade D (10 November 2020). "The story of mRNA: How a once-dismissed idea became a leading technology in the Covid vaccine race" (<https://www.statnews.com/2020/11/10/the-story-of-mrna-how-a-once-dismissed-idea-became-a-leading-technology-in-the-covid-vaccine-race/>) ↗. *Stat*. Retrieved 16 November 2020.

24. "DARPA Awards Moderna Therapeutics A Grant For Up To \$25 Million To Develop Messenger RNA Therapeutics" (<https://www.prnewswire.com/news-releases/darpa-awards-moderna-therapeutics-a-grant-for-up-to-25-million-to-develop-messenger-rna-therapeutics-226115821.html>) ↗. 2 October 2013. Retrieved 31 May 2021.
25. Garde D (10 January 2017). "Lavishly funded Moderna hits safety problems in bold bid to revolutionize medicine" (<https://www.statnews.com/2017/01/10/moderna-trouble-mrna/>) ↗. *Stat*. Archived (<https://web.archive.org/web/20201116154151/https://www.statnews.com/2017/01/10/moderna-trouble-mrna/>) ↗ from the original on 16 November 2020. Retrieved 19 May 2020. "struggling to get mRNA into cells without triggering nasty side effects"
26. Garade D (13 September 2016). "Ego, ambition, and turmoil: Inside one of biotech's most secretive startups" (<https://www.statnews.com/2016/09/13/moderna-therapeutics-biotech-mrna/>) ↗. *Stat*. Archived (<https://web.archive.org/web/20201116154313/https://www.statnews.com/2016/09/13/moderna-therapeutics-biotech-mrna/>) ↗ from the original on 16 November 2020. Retrieved 18 May 2020. "because it's exceedingly hard to get RNA into cells without triggering nasty side effects"
27. "COVID-19 and Your Health" (<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html>) ↗. *Centers for Disease Control and Prevention*. 11 February 2020.
28. Kuznia R, Polglase K, Mezzofiore G (1 May 2020). "In quest for vaccine, US makes 'big bet' on company with unproven technology" (<https://edition.cnn.com/2020/05/01/us/coronavirus-moderna-vaccine-invs/index.html>) ↗. *CNN Investigates*. Archived (<https://web.archive.org/web/20201116154315/https://edition.cnn.com/2020/05/01/us/coronavirus-moderna-vaccine-invs/index.html>) ↗ from the original on 16 November 2020. Retrieved 1 May 2020.
29. Roberts M (2 December 2020). "Covid Pfizer vaccine approved for use next week in UK" (<https://www.bbc.com/news/health-55145696>) ↗. *BBC News*. Retrieved 2 December 2020.
30. "UK regulator says it did not cut any corners to approve Pfizer vaccine" (<https://www.reuters.com/article/uk-health-coronavirus-britain-vaccine-re/uk-regulator-says-it-did-not-cut-any-corners-to-approve-pfizer-vaccine-idUSKBN28C1AB>) ↗. *Reuters*. 2 December 2020. Retrieved 2 December 2020.
31. "The benefits of the Pfizer/BioNTech vaccine "far outweigh any risk", says Dr June Raine from UK regulator MHRA" (<https://twitter.com/BBCNews/status/1334084332500226049>) ↗. *BBC News Twitter*. 2 December 2020. Retrieved 2 December 2020.
32. Guarascio F (2 December 2020). "EU criticises 'hasty' UK approval of COVID-19 vaccine" (<https://www.reuters.com/article/uk-health-coronavirus-britain-eu/eu-lawmaker-warns-of-risks-from-uk-hasty-approval-of-pfizer-covid-vaccine-idUKKBN28C12X>) ↗. *Reuters*. Retrieved 2 December 2020.
33. Commissioner, Office of the (18 December 2020). "Pfizer-BioNTech COVID-19 Vaccine" (<https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine>) ↗. *FDA*.

34. Batty CJ, Heise MT, Bachelder EM, Ainslie KM (December 2020). "Vaccine formulations in clinical development for the prevention of severe acute respiratory syndrome coronavirus 2 infection" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7733686>) . *Advanced Drug Delivery Reviews*. **169**: 168–89. doi:10.1016/j.addr.2020.12.006 (<https://doi.org/10.1016%2Fj.addr.2020.12.006>) . PMC 7733686 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7733686>) . PMID 33316346 (<https://pubmed.ncbi.nlm.nih.gov/33316346>) .
35. Hajj KA, Whitehead KA (12 September 2017). "Tools for translation: non-viral materials for therapeutic mRNA delivery" (<https://doi.org/10.1038%2Fnatrevmats.2017.56>) . *Nature Reviews Materials*. **2** (10): 17056. Bibcode:2017NatRM...217056H (<https://ui.adsabs.harvard.edu/abs/2017NatRM...217056H>) . doi:10.1038/natrevmats.2017.56 (<https://doi.org/10.1038%2Fnatrevmats.2017.56>) .
36. Schlake T, Thess A, Fotin-Mleczek M, Kallen KJ (November 2012). "Developing mRNA-vaccine technologies" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3597572>) . *RNA Biology*. **9** (11): 1319–30. doi:10.4161/rna.22269 (<https://doi.org/10.4161%2Frna.22269>) . PMC 3597572 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3597572>) . PMID 23064118 (<https://pubmed.ncbi.nlm.nih.gov/23064118>) .
37. Goldman, Bruce (22 December 2020). "How do the new COVID-19 vaccines work?" (<https://scopeblog.stanford.edu/2020/12/22/how-do-the-new-covid-19-vaccines-work/>) . *Scope*. Stanford Medicine. Retrieved 28 January 2021.
38. "Seven vital questions about the RNA Covid-19 vaccines emerging from clinical trials" (<https://wellcome.org/news/seven-vital-questions-about-rna-covid-19-vaccines-pfizer-biontech-moderna>) . *Wellcome Trust*. 19 November 2020. Retrieved 26 November 2020.
39. Fiedler K, Lazzaro S, Lutz J, Rauch S, Heidenreich R (2016). "mRNA Cancer Vaccines". *Recent Results in Cancer Research. Fortschritte der Krebsforschung. Progres dans les Recherches Sur le Cancer*. Recent Results in Cancer Research. **209**: 61–85. doi:10.1007/978-3-319-42934-2_5 (https://doi.org/10.1007%2F978-3-319-42934-2_5) . ISBN 978-3-319-42932-8. PMID 28101688 (<https://pubmed.ncbi.nlm.nih.gov/28101688>) .
40. Neilson S, Dunn A, Bendix A (26 November 2020). "Moderna's groundbreaking coronavirus vaccine was designed in just 2 days" (<https://www.businessinsider.com/moderna-designed-coronavirus-vaccine-in-2-days-2020-11?r=US&IR=T>) . *Business Insider*. Retrieved 28 November 2020.
41. Dolgin E (November 2020). "COVID-19 vaccines poised for launch, but impact on pandemic unclear" (<https://www.nature.com/articles/d41587-020-00022-y>) . *Nature Biotechnology*. doi:10.1038/d41587-020-00022-y (<https://doi.org/10.1038%2Fd41587-020-00022-y>) . PMID 33239758 (<https://pubmed.ncbi.nlm.nih.gov/33239758>) . S2CID 227176634 (<https://api.semanticscholar.org/CorpusID:227176634>) .
42. Carmichael F (15 November 2020). "Vaccine rumours debunked: Microchips, 'altered DNA' and more" (<https://www.bbc.com/news/54893437>) . *BBC News*. Retrieved 17 November 2020.
43. Rahman G (30 November 2020). "RNA Covid-19 vaccines will not change your DNA" (<https://fullfact.org/online/rna-vaccine-covid/>) . *Full Fact*. Retrieved 1 December 2020.

44. Vallejo J (18 November 2020). "'What is Covid vaccine made of?' trends on Google as Pfizer and Moderna seek FDA approval" (<https://www.independent.co.uk/news/world/americas/covid-vaccine-ingredients-pfizer-moderna-fda-b1729324.html>) ↗. *The Independent*. Retrieved 3 December 2020.
45. Benteyn D, Heirman C, Bonehill A, Thielemans K, Breckpot K (February 2015). "mRNA-based dendritic cell vaccines". *Expert Review of Vaccines*. **14** (2): 161–76. doi:10.1586/14760584.2014.957684 (<https://doi.org/10.1586/14760584.2014.957684>) ↗. PMID 25196947 (<https://pubmed.ncbi.nlm.nih.gov/25196947/>) ↗. S2CID 38292712 (<https://api.semanticscholar.org/CorpusID:38292712>) ↗.
46. Wolff JA, Malone RW, Williams P, Chong W, Acsadi G, Jani A, Felgner PL (March 1990). "Direct gene transfer into mouse muscle in vivo". *Science*. **247** (4949 Pt 1): 1465–68. Bibcode:1990Sci...247.1465W (<https://ui.adsabs.harvard.edu/abs/1990Sci...247.1465W>) ↗. doi:10.1126/science.1690918 (<https://doi.org/10.1126/science.1690918>) ↗. PMID 1690918 (<https://pubmed.ncbi.nlm.nih.gov/1690918/>) ↗.
47. "Vaccine components" (<https://www.immune.org.nz/vaccines/vaccine-development/vaccine-components>) ↗. *Immunisation Advisory Centre*. 22 September 2016. Retrieved 20 December 2020.
48. Probst J, Weide B, Scheel B, Pichler BJ, Hoerr I, Rammensee HG, Pascolo S (August 2007). "Spontaneous cellular uptake of exogenous messenger RNA in vivo is nucleic acid-specific, saturable and ion dependent" (<https://doi.org/10.1038/sj.gt.3302964>) ↗. *Gene Therapy*. **14** (15): 1175–80. doi:10.1038/sj.gt.3302964 (<https://doi.org/10.1038/sj.gt.3302964>) ↗. PMID 17476302 (<https://pubmed.ncbi.nlm.nih.gov/17476302/>) ↗.
49. Lorenz C, Fotin-Mleczek M, Roth G, Becker C, Dam TC, Verdurmen WP, et al. (July 2011). "Protein expression from exogenous mRNA: uptake by receptor-mediated endocytosis and trafficking via the lysosomal pathway" (<https://doi.org/10.4161/rna.8.4.15394>) ↗. *RNA Biology*. **8** (4): 627–36. doi:10.4161/rna.8.4.15394 (<https://doi.org/10.4161/rna.8.4.15394>) ↗. PMID 21654214 (<https://pubmed.ncbi.nlm.nih.gov/21654214/>) ↗.
50. Zhou X, Berglund P, Rhodes G, Parker SE, Jondal M, Liljeström P (December 1994). "Self-replicating Semliki Forest virus RNA as recombinant vaccine". *Vaccine*. **12** (16): 1510–14. doi:10.1016/0264-410x(94)90074-4 ([https://doi.org/10.1016/0264-410x\(94\)90074-4](https://doi.org/10.1016/0264-410x(94)90074-4)) ↗. PMID 7879415 (<https://pubmed.ncbi.nlm.nih.gov/7879415/>) ↗.
51. Berglund P, Smerdou C, Fleeton MN, Tubulekas I, Liljeström P (June 1998). "Enhancing immune responses using suicidal DNA vaccines". *Nature Biotechnology*. **16** (6): 562–65. doi:10.1038/nbt0698-562 (<https://doi.org/10.1038/nbt0698-562>) ↗. PMID 9624688 (<https://pubmed.ncbi.nlm.nih.gov/9624688/>) ↗. S2CID 38532700 (<https://api.semanticscholar.org/CorpusID:38532700>) ↗.
52. Deering RP, Kommareddy S, Ulmer JB, Brito LA, Geall AJ (June 2014). "Nucleic acid vaccines: prospects for non-viral delivery of mRNA vaccines". *Expert Opin Drug Deliv*. **11** (6): 885–99. doi:10.1517/17425247.2014.901308 (<https://doi.org/10.1517/17425247.2014.901308>) ↗. PMID 24665982 (<https://pubmed.ncbi.nlm.nih.gov/24665982/>) ↗. S2CID 33489182 (<https://api.semanticscholar.org/CorpusID:33489182>) ↗.

53. Geall AJ, Verma A, Otten GR, Shaw CA, Hekele A, Banerjee K, Cu Y, Beard CW, Brito LA, Krucker T, O'Hagan DT, Singh M, Mason PW, Valiante NM, Dormitzer PR, Barnett SW, Rappuoli R, Ulmer JB, Mandl CW (September 2012). "Nonviral delivery of self-amplifying RNA vaccines" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3437863>) ↗. *Proc Natl Acad Sci U S A*. **109** (36): 14604–09. Bibcode:2012PNAS..10914604G (<https://ui.adsabs.harvard.edu/abs/2012PNAS..10914604G>) ↗. doi:10.1073/pnas.1209367109 (<https://doi.org/10.1073%2Fpnas.1209367109>) ↗. PMC 3437863 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3437863>) ↗. PMID 22908294 (<https://pubmed.ncbi.nlm.nih.gov/22908294>) ↗.
54. Kreiter S, Selmi A, Diken M, Koslowski M, Britten CM, Huber C, et al. (November 2010). "Intranodal vaccination with naked antigen-encoding RNA elicits potent prophylactic and therapeutic antitumoral immunity" (<https://doi.org/10.1158%2F0008-5472.can-10-0699>) ↗. *Cancer Research*. **70** (22): 9031–40. doi:10.1158/0008-5472.can-10-0699 (<https://doi.org/10.1158%2F0008-5472.can-10-0699>) ↗. PMID 21045153 (<https://pubmed.ncbi.nlm.nih.gov/21045153>) ↗.
55. Weide B, Pascolo S, Scheel B, Derhovanesian E, Pflugfelder A, Eigentler TK, Pawelec G, Hoerr I, Rammensee HG, Garbe C (June 2009). "Direct injection of protamine-protected mRNA: results of a phase 1/2 vaccination trial in metastatic melanoma patients". *J Immunother*. **32** (5): 498–507. doi:10.1097/CJI.0b013e3181a00068 (<https://doi.org/10.1097%2FCJI.0b013e3181a00068>) ↗. PMID 19609242 (<https://pubmed.ncbi.nlm.nih.gov/19609242>) ↗. S2CID 3278811 (<https://api.semanticscholar.org/CorpusID:3278811>) ↗.
56. Cooney E (1 December 2020). "How nanotechnology helps mRNA Covid-19 vaccines work" (<https://www.statnews.com/2020/12/01/how-nanotechnology-helps-mrna-covid19-vaccines-work/>) ↗. *Stat*. Retrieved 3 December 2020.
57. Reichmuth AM, Oberli MA, Jaklenec A, Langer R, Blankschtein D (May 2016). "mRNA vaccine delivery using lipid nanoparticles" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5439223>) ↗. *Therapeutic Delivery*. **7** (5): 319–34. doi:10.4155/tde-2016-0006 (<https://doi.org/10.4155%2Ftde-2016-0006>) ↗. PMC 5439223 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5439223>) ↗. PMID 27075952 (<https://pubmed.ncbi.nlm.nih.gov/27075952>) ↗.
58. Cross, Ryan (6 March 2021). "Without these lipid shells, there would be no mRNA vaccines for COVID-19" (<https://cen.acs.org/pharmaceuticals/drug-delivery/Without-lipid-shells-mrna-vaccines/99/i8>) ↗. *Chemical & Engineering News*. American Chemical Society. Retrieved 6 March 2021.
59. Paunovska K, Sago CD, Monaco CM, Hudson WH, Castro MG, Rudoltz TG, et al. (March 2018). "A Direct Comparison of in Vitro and in Vivo Nucleic Acid Delivery Mediated by Hundreds of Nanoparticles Reveals a Weak Correlation" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6054134>) ↗. *Nano Letters*. **18** (3): 2148–57. Bibcode:2018NanoL..18.2148P (<https://ui.adsabs.harvard.edu/abs/2018NanoL..18.2148P>) ↗. doi:10.1021/acs.nanolett.8b00432 (<https://doi.org/10.1021%2Facs.nanolett.8b00432>) ↗. PMC 6054134 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6054134>) ↗. PMID 29489381 (<https://pubmed.ncbi.nlm.nih.gov/29489381>) ↗.
60. Lowe, Derek (3 February 2021). "Opinion: A straightforward explanation why more COVID-19 vaccines can't be produced with help from 'dozens' of companies" (<https://www.marketwatch.com/story/lets-stick-to-facts-about-covid-19-vaccines-there-arent-dozens-of-drug-companies-who-can-step-in-to-produce-more-11612363386>) ↗. *MarketWatch*. Retrieved 5 February 2021.

61. King, Anthony (23 March 2021). "Why manufacturing Covid vaccines at scale is hard" (<https://www.chemistryworld.com/news/why-manufacturing-covid-vaccines-at-scale-is-hard/4013429.article#/>) ↗. *Chemistry World*. Royal Society of Chemistry. Retrieved 26 March 2021.
62. Sealy, Amanda (2 April 2021). "Manufacturing moonshot: How Pfizer makes its millions of Covid-19 vaccine doses" (<https://www.cnn.com/2021/03/31/health/pfizer-vaccine-manufacturing/index.html>) ↗. *CNN*.
63. Weise, Elizabeth; Weintraub, Karen (7 February 2021). "Race to the Vaccine: A COVID-19 vaccine life cycle: from DNA to doses" (<https://www.usatoday.com/in-depth/news/health/2021/02/07/how-covid-vaccine-made-step-step-journey-pfizer-dose/4371693001/>) ↗. *USA Today*. Gannett. Retrieved 24 February 2021.
64. Hopkins, Jared S.; Eastwood, Joel; Moriarty, Dylan (3 March 2021). "mRNA Covid-19 Vaccines Are Fast to Make, but Hard to Scale" (<https://www.wsj.com/articles/mrna-covid-19-vaccines-are-fast-to-make-but-hard-to-scale-11614776401>) ↗. *The Wall Street Journal*.
65. Rowland, Christopher (18 February 2021). "Why grandparents can't find vaccines: Scarcity of niche biotech ingredients" (<https://www.washingtonpost.com/business/2021/02/18/vaccine-fat-lipids-supply/>) ↗. *The Washington Post*.
66. Lundstrom K (March 2019). "RNA Viruses as Tools in Gene Therapy and Vaccine Development" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6471356>) ↗. *Genes*. **10** (3): 189. doi:10.3390/genes10030189 (<https://doi.org/10.3390%2Fgenes10030189>) ↗. PMC 6471356 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6471356>) ↗. PMID 30832256 (<https://pubmed.ncbi.nlm.nih.gov/30832256>) ↗.
67. Huang TT, Parab S, Burnett R, Diago O, Ostertag D, Hofman FM, et al. (February 2015). "Intravenous administration of retroviral replicating vector, Toca 511, demonstrates therapeutic efficacy in orthotopic immune-competent mouse glioma model" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4326030>) ↗. *Human Gene Therapy*. **26** (2): 82–93. doi:10.1089/hum.2014.100 (<https://doi.org/10.1089%2Fhum.2014.100>) ↗. PMC 4326030 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4326030>) ↗. PMID 25419577 (<https://pubmed.ncbi.nlm.nih.gov/25419577>) ↗.
68. Schultz-Cherry S, Dybing JK, Davis NL, Williamson C, Suarez DL, Johnston R, Perdue ML (December 2000). "Influenza virus (A/HK/156/97) hemagglutinin expressed by an alphavirus replicon system protects chickens against lethal infection with Hong Kong-origin H5N1 viruses". *Virology*. **278** (1): 55–59. doi:10.1006/viro.2000.0635 (<https://doi.org/10.1006%2Fviro.2000.0635>) ↗. PMID 11112481 (<https://pubmed.ncbi.nlm.nih.gov/11112481>) ↗.
69. Geisbert TW, Feldmann H (November 2011). "Recombinant vesicular stomatitis virus-based vaccines against Ebola and Marburg virus infections" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3218670>) ↗. *The Journal of Infectious Diseases*. **204** (Suppl 3): S1075–81. doi:10.1093/infdis/jir349 (<https://doi.org/10.1093%2Finfdi%2Fjir349>) ↗. PMC 3218670 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3218670>) ↗. PMID 21987744 (<https://pubmed.ncbi.nlm.nih.gov/21987744>) ↗.
70. Wadman M (November 2020). "Public needs to prep for vaccine side effects" (<https://doi.org/10.1126%2Fscience.370.6520.1022>) ↗. *Science*. **370** (6520): 1022. doi:10.1126/science.370.6520.1022 (<https://doi.org/10.1126%2Fscience.370.6520.1022>) ↗. PMID 33243869 (<https://pubmed.ncbi.nlm.nih.gov/33243869>) ↗.

71. Thomas K (22 October 2020). "Experts Tell F.D.A. It Should Gather More Safety Data on Covid-19 Vaccines" (<https://www.nytimes.com/2020/10/22/health/covid-vaccine-fda-advisory-committee.html>)[[][↗](#)[]]. *New York Times*. Retrieved 21 November 2020.
72. Kuchler H (30 September 2020). "Pfizer boss warns on risk of fast-tracking vaccines" (<https://www.ft.com/content/1a91c897-66d5-4bd5-ae9b-0b3be185dac8>)[[][↗](#)[]]. *Financial Times*. Retrieved 21 November 2020.
73. "Pfizer-BioNTech COVID-19 Vaccine Vaccination Storage & Dry Ice Safety Handling" (<https://www.cvdvaccine-us.com/product-storage-and-dry-ice>)[[][↗](#)[]]. Pfizer. Retrieved 17 December 2020.
74. Simmons-Duffin S. "Why Does Pfizer's COVID-19 Vaccine Need To Be Kept Colder Than Antarctica?" (<https://www.npr.org/sections/health-shots/2020/11/17/935563377/why-does-pfizers-covid-19-vaccine-need-to-be-kept-colder-than-antarctica>)[[][↗](#)[]]. *NPR.org*. Retrieved 18 November 2020.
75. "Fact Sheet for Healthcare Providers Administering Vaccine" (<https://www.fda.gov/media/144637/download>)[[][↗](#)[]] (PDF). ModernaTX, Inc.
76. "Moderna Announces Longer Shelf Life for its COVID-19 Vaccine Candidate at Refrigerated Temperatures" (<https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-longer-shelf-life-its-covid-19-vaccine>)[[][↗](#)[]]. *NPR.org*.
77. Rabson, Mia (27 February 2021). "From science to syringe: COVID-19 vaccines are miracles of science and supply chains" (<https://www.ctvnews.ca/health/coronavirus/from-science-to-syringe-covid-19-vaccines-are-miracles-of-science-and-supply-chains-1.5327003>)[[][↗](#)[]]. *CTV News*. Bell Media.
78. Karikó K, Buckstein M, Ni H, Weissman D (August 2005). "Suppression of RNA recognition by Toll-like receptors: the impact of nucleoside modification and the evolutionary origin of RNA". *Immunity*. **23** (2): 165–75. doi:10.1016/j.immuni.2005.06.008 (<https://doi.org/10.1016%2Fj.immuni.2005.06.008>)[[][↗](#)[]]. PMID 16111635 (<https://pubmed.ncbi.nlm.nih.gov/16111635>)[[][↗](#)[]].
79. Karikó K, Muramatsu H, Ludwig J, Weissman D (November 2011). "Generating the optimal mRNA for therapy: HPLC purification eliminates immune activation and improves translation of nucleoside-modified, protein-encoding mRNA" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3241667>)[[][↗](#)[]]. *Nucleic Acids Research*. **39** (21): e142. doi:10.1093/nar/gkr695 (<https://doi.org/10.1093%2Fnar%2Fgkr695>)[[][↗](#)[]]. PMC 3241667 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3241667>)[[][↗](#)[]]. PMID 21890902 (<https://pubmed.ncbi.nlm.nih.gov/21890902>)[[][↗](#)[]].
80. Pardi N, Weissman D (17 December 2016). "Nucleoside Modified mRNA Vaccines for Infectious Diseases". *RNA Vaccines*. Methods in Molecular Biology. Vol. 1499. Springer New York. pp. 109–21. doi:10.1007/978-1-4939-6481-9_6 (https://doi.org/10.1007%2F978-1-4939-6481-9_6)[[][↗](#)[]]. ISBN 978-1-4939-6479-6. PMID 27987145 (<https://pubmed.ncbi.nlm.nih.gov/27987145>)[[][↗](#)[]].
81. Schlake T, Thess A, Fotin-Mleczek M, Kallen KJ (November 2012). "Developing mRNA-vaccine technologies" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3597572>)[[][↗](#)[]]. *RNA Biology*. **9** (11): 1319–30. doi:10.4161/rna.22269 (<https://doi.org/10.4161%2Frna.22269>)[[][↗](#)[]]. PMC 3597572 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3597572>)[[][↗](#)[]]. PMID 23064118 (<https://pubmed.ncbi.nlm.nih.gov/23064118>)[[][↗](#)[]].

82. Vogel AB, Lambert L, Kinnear E, Busse D, Erbar S, Reuter KC, et al. (February 2018). "Self-Amplifying RNA Vaccines Give Equivalent Protection against Influenza to mRNA Vaccines but at Much Lower Doses" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5835025>) ↗. *Molecular Therapy*. **26** (2): 446–55. doi:10.1016/j.ymthe.2017.11.017 (<https://doi.org/10.1016%2Fj.ymthe.2017.11.017>) ↗. PMC 5835025 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5835025>) ↗. PMID 29275847 (<https://pubmed.ncbi.nlm.nih.gov/29275847>) ↗.
83. Skalka AM (2014). "Retroviral DNA Transposition: Themes and Variations" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4383315>) ↗. *Microbiology Spectrum*. **2** (5): 1101–23. doi:10.1128/microbiolspec.MDNA3-0005-2014 (<https://doi.org/10.1128%2Fmicrobiolspec.MDNA3-0005-2014>) ↗. ISBN 9781555819200. PMC 4383315 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4383315>) ↗. PMID 25844274 (<https://pubmed.ncbi.nlm.nih.gov/25844274>) ↗.
84. Nirenberg, Edward (24 November 2020). "No, Really, mRNA Vaccines Are Not Going To Affect Your DNA" (<https://www.deplatformdisease.com/blog/no-really-mrna-vaccines-are-not-going-to-affect-your-dna>) ↗. *Vaccines, Immunology, COVID-19*. deplatformdisease.com. Retrieved 28 January 2021.
85. Rowland C (21 November 2020). "Doctors and nurses want more data before championing vaccines to end the pandemic" (<https://www.washingtonpost.com/business/2020/11/21/vaccines-advocates-nurses-doctors-coronavirus/>) ↗. *Washington Post*. Retrieved 22 November 2020.
86. Kwon D (25 November 2020). "The Promise of mRNA Vaccines" (<https://www.the-scientist.com/news-opinion/the-promise-of-mrna-vaccines-68202>) ↗. *The Scientist*. Retrieved 27 November 2020.
87. Jaffe-Hoffman M (17 November 2020). "Could mRNA COVID-19 vaccines be dangerous in the long-term?" (<https://www.jpost.com/health-science/could-an-mrna-vaccine-be-dangerous-in-the-long-term-649253>) ↗. *The Jerusalem Post*. Retrieved 17 November 2020.
88. Bloom, Kristie; van den Berg, Fiona; Arbuthnot, Patrick (22 October 2020). "Self-amplifying RNA vaccines for infectious diseases" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7580817>) ↗. *Gene Therapy*. **28** (3–4): 117–29. doi:10.1038/s41434-020-00204-y (<https://doi.org/10.1038%2Fs41434-020-00204-y>) ↗. PMC 7580817 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7580817>) ↗. PMID 33093657 (<https://pubmed.ncbi.nlm.nih.gov/33093657>) ↗.
89. "saRNA Biology | About Self-Amplifying RNA Genome & How It Works" (<https://www.chimeron.com/sa-rna-biology/>) ↗. *Chimeron Bio | Transforming RNA Therapy*.
90. Lowe, Derek (1 March 2021). "A Malaria Vaccine Candidate" (<https://blogs.sciencemag.org/pipeline/archives/2021/03/01/a-malaria-vaccine-candidate>) ↗. *Science Translational Medicine*. Retrieved 7 May 2021.

External links



Scholia has a profile for **RNA vaccine (Q85795487)**.

- Roberts J (April 2020). "Five things you need to know about: mRNA vaccines" (<https://horizon-magazine.eu/article/five-things-you-need-know-about-mrna-vaccines.html>) ↗. *Horizon*.

- Blackburn L (October 2020). "RNA vaccines: an introduction" (<https://www.phgfoundation.org/briefing/rna-vaccines>)^[c]. *PHG Foundation*. University of Cambridge.
- "Understanding mRNA COVID-19 Vaccines" (<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html>)^[c]. Centers for Disease Control and Prevention.
- "Understanding and Explaining mRNA COVID-19 Vaccines" (<https://www.cdc.gov/vaccines/covid-19/hcp/mrna-vaccine-basics.html>)^[c]. *Centers for Disease Control and Prevention*.

Portals:  **Medicine**  **Viruses**  **COVID-19**