

Review Article

<https://doi.org/10.20546/ijcmas.2025.1412.002>

RNA-DNA-Based Vaccines for Infection Diseases and Mass Vaccination Appear an Uncertain Experimentation

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ABSTRACT

The present paper deals with a general biological evaluation on the use of RNA-DNA based sequences as vaccines. This analysis briefly considers the unique properties of RNA and DNA in comparison to those of any other organic molecule so far utilized as drug. After the indicated pre-biotic origin of RNA, proteins and DNA, these biomolecules progressively gave rise to cells and multicellular organisms of various complexity. This evolution occurred by trials and errors and the latter were eliminated. In contrast, human scientific knowledge examines nature empirically and progressively discovers some of its principles and mechanisms. Science investigates complex natural phenomena already established while evolution progressed sequentially from molecules to organism communities. Nucleic acids are different from any type of chemical drugs utilized so far because are the fundamental genetic molecules of life, not alien chemicals as most of previously used drugs. Despite the present deep knowledge on RNA and DNA, many of their effects when injected into complex multicellular organisms are unknown. Manipulations of nucleic acids and their applications to people are experimental and the consequences uncertain. Gene transfer or editing for gene therapies, cure of cancer or other diseases is also experimental but aims to fix human genes. These therapies derive from personal requests with no impositions but accepting possible risks. RNA-DNA-based vaccines instead introduce functional alien viral proteins in the body for immunization but also carrying potential pathological effects. To state that RNA-DNA based vaccines are “safe” is an incorrect scientific statement because of incomplete knowledge of their interactions with our body functions.

Keywords

Genetic vaccines,
experimentation,
Science,
Scientism,
Health risks

Article Info

Received:
05 October 2025
Accepted:
22 November 2025
Available Online:
10 December 2025

Introduction

The Theory of biological evolution should guide any study in Biology, including the content of the present brief paper dealing with genetic vaccines (RNA- or DNA-based). It is believed that during organic evolution, the origin of nucleotides and eventually nucleic acids was

a landmark, perhaps never created before in planets of the Universe (Tagami and Li, 2022; Kalambokidis and Trivisano, 2024). The origin of RNA, proteins and DNA formed the base from which life evolved since at least 4.0-3.5 billion years. The chemical formation of RNA was a key cosmic event that created molecules gifted with self-replication and recombination properties with

unpredictable and unleashed potentials. RNA and DNA, by governing the functionality of proteins, gave rise to millions of species during biological evolution, and proceeded step by step led by consequential chemical-physical and organizational principles. New processes and life forms derived from a continuous addition of complexity in which occasional (genetic) or environmental-induced (epigenetic) novelties gave rise to new viable forms, sometimes fitter than the previous ones.

These unique organic molecules called nucleic acids, more than others generated during pre-biotic evolution, possess the capacity to replicate by themselves (RNAs first, and later using proteins and DNA). These molecules broke and mixed in an “unpredictable re-combination numbers” and relative “unpredictable effects”, from long time they “traveled” among simple or more complex living creatures, especially by viruses that can integrate their genomes in the host DNA. The complementarity of uracyl-adenine or thymidine-adenine and of cytosine-guanine appears a simple and amazing chemical property of organic molecules, capable to build polymers that replicate, change (mutate), and recombine in uncountless ways. Nucleic acids are a fantastic sort of molecules but basically “out of control in their potentials”, especially outside laboratory conditions when their integrity is preserved inside carriers and free in the environment. It is rational to think that only the process of evolution during million years, progressing by trial and errors and erasing unfit molecular processes, could “controlled” such molecules. This is testimonial from the fact that they successfully originated millions of different extinct and living biological species (Wiens, 2023; Kalambokidis and Travisano, 2024).

During biological evolution any new process had to be functionally integrated in the pre-existing ones, therefore building an invariant sequence of events from interacting biomolecules, organizing a metabolism in single cells, interacting cells into multicellular communities or bodies, and evolving developmental processes that (re-)generated these multicellular bodies. This is not the case for biotech humans-made RNAs or DNAs after few decades of gene manipulation, incomplete information gained by empiric, random, and sometimes unpredictable but brilliant discoveries that occurred in different but however short historical periods (Simonetta, 2003). In particular, the greater and faster progress in cell and molecular biology essentially occurred in the last 100 years. Therefore, one hundred years is an un-comparable

time and mode to obtain biological information and control on biological processes with respect to the biological evolution that evolved in about four billion years, and that also gave rise to the human body. Even at the present time where an enormous scientific knowledge has been built and research has become less and less empiric, it is rationale thinking that we still insufficiently know many genetic and cellular processes and their integration within complex organisms. Consequently, the applications of this broad but incomplete knowledge to create useful medical cures based on RNA or DNA are scientifically uncertain and remains, by definition, experimental. This in particular considering the potential effects of non-genetic drugs so far created in the last 100-150 years (antibiotics, sulfonamides, antihypertensive drugs, antidepressants, cardiotoxic drugs, anti-inflammatory, traditional vaccines etc.) in comparison to the unpredictable reactivity of genetic molecules nowadays utilized as drugs for genetic cures, creation of transgenes or OGMs, intervention to promote medical therapies, and lately also for vaccines (Khalil, 2020; Gambacorti-Passerini and Aroldi, 2022; Kim *et al.*, 2022; Sarvananda *et al.*, 2023; Inagaki, 2024).

Genetic manipulations were, are, and will remain experimental

It is evident that gene therapies or cancer therapies using RNA and/or DNA are experimental procedures and that they have a limited utilization on specific requests from genetically impaired people or for cancer patients. Genomic editing is an engineering manipulation whereas the defective region of the DNA of a patient can be removed, replacing this sequence with a correct nucleotide sequence that codes for a functional protein of the patient. The defective gene is removed in specific sites by endonucleases coupled to a guide RNA sequence and the correct DNA-sequences can be inserted to replace the previous one using, for instance, the CRISPR/Cas9 procedure (Khalil, 2020).

Likewise, RNA- or DNA-based vaccines against viral infections are also experimental, but differently from gene and cancer therapies, they induce the production not of functional proteins of the patient, but instead of active viral proteins inside the body of vaccinated people. If we reflect, this is a big difference between gene therapy versus the genetic vaccination, since the former fix physiological genes-proteins of the patients while the latter introduce viral proteins that are not physiological but potentially pathogen for the patient.

Science cannot predict the activity of free viral proteins that are alien to our organism, such as the spike of Sars-Cov19, inside the complex environment of a human body. The manufacturers of RNA or DNA vaccines simply focused on the production of the spike protein as an immunogen that elicits some form of immune response with no consideration on other effects. This simplification of the pharmacological action of these vaccines considered the human body as a test tube, not evaluating possible other effects and pathological consequences (Fig. 1). The latter became evident on numerous patients only later, shortly after vaccination or later on, although this is largely denied from the official narration (Gambacorti-Passerini and Aroldi, 2022; Seneff *et al.*, 2022; Acevedo-Whitehouse and Bruno, 2023; Bellavite *et al.*, 2023; Thoene, 2024). It is dismaying that most scientists, physicians and official medical Institutions and internet sites only report this simplistic idea of immunization derived from RNA-DNA-based vaccines, without a larger vision on possible other actions of the active RNA and derived spike protein inside the human body. Even more, it is unbelievable that the official narrations from all these Institutions in 2020-2025 report that the genetic vaccination is “safe” and that genetic vaccination had a long experimental evidence, like the other RNA-DNA manipulations for gene transfer, gene therapies, cancer treatments or else.

As a consequence of this official narration, unproved safe treatments with RNA-DNA-based vaccine have been labeled as “safe” and utilized or even imposed on billions of people. The rational and wise scientific reasoning here appears obscured by scientific superficiality, faith, irrationality, careless or, more likely, from “scientistic” reasons. In fact, while Science use the scientific methods only to enquire and explains natural phenomena, “scientism” uses the Scientific knowledge for non-scientific purposes, political (health politics and mass manipulation), economical (Pharma and Biotech companies), and religious (creationism). To state that RNA-DNA-based vaccines are safe, without a complete knowledge of their actions inside the body, is not a scientific statement and can generate problematic medical applications (Seneff *et al.*, 2022; Acevedo-Whitehouse and Bruno, 2023; Bellavite *et al.*, 2023; Boros *et al.*, 2023).

Rational or Faith in some genetic manipulations

I used to believe that some rational wisdom in scientists indicated that the “wonders and perils” of genetic

engineering were basically understood and that a potential danger, even higher of atomic energy usage and out of any control, was predicted in case of the indiscriminate manipulation and utilization of nucleic acids and their carriers, plasmids and viruses. The latter are also useful for experiments of all sorts, for their capacity to carry and deliver genes/nucleotide sequences to different cells and organisms, and to immune cells in particular since the end of the 70ies. Viruses can also be manipulated through experiments of gain or loss of function, studies carried out for scientific and non-scientific but instead often for scientific purposes (Casadevall *et al.*, 2024; Zhuo, 2024; Fig. 1).

While molecular biologists demonstrate remarkable technical expertise, analytical skill, and research achievements, many remain deeply focused on the specialized aspects of their work. As a result, some may underappreciate the broader biological complexity of the systems they study, occasionally leading to overconfidence in the extent to which these systems can be fully understood or controlled. Maintaining scientific humility is therefore essential when navigating the vast and intricate nature of biological processes. They forget that we have an incomplete knowledge of cell functions, metabolic and genetic pathways in a single cell and even less information on tissue and organ interactions within complex bodies. Stating the contrary is an untenable scientific belief, resembling a religious faith, a concept outside of Science. While test tube experiments are controlled and informative, the delivery of genetic material such as RNA or DNA inside human bodies remains experimental and unpredictable due to its interactions with not completely known body functions. This is just to speak about academic scientists, not to tackle those working in industries, particularly in the Pharma and Biotech sectors where the profit anticipates Science, and is the first “natural goal” of these enterprises. It would be non-scientific to state that we know enough for using RNA-DNA based vaccines, that this knowledge is sufficient for some medical applications, and even a more non-scientific attitude that we can control all our genetic manipulations for various applications.

It is important to recognize that the complexity of cellular systems, viral evolution, and whole-organism biology is the result of millions of years of evolutionary processes (or, for those who hold such beliefs, the work of a higher creative force). Human scientific knowledge, while advancing rapidly, remains inherently incomplete.

Therefore, it is essential to approach modern genetic manipulation technologies with humility and caution, rather than assuming parity with evolutionary mechanisms that have shaped life over vast timescales. The remarkable molecules we manipulate—RNA and DNA—operate within biological networks that are still only partially understood. Accordingly, current assessments of the “safety” of RNA- and DNA-based interventions rely on present scientific understanding, which itself will continue to evolve. A reflective and measured perspective is thus critical when interpreting emerging biotechnological advances.

It is essential to discriminate between research experiments, academic information and their possible medical applications, specifically between viral cycles and viral diseases and their immunological contrast. Rationally speaking we do not know the consequences of inoculated genetic molecules as vaccines, and this is derived for our limits of knowledge and from the fact that we did not create/generate our complex cells, tissues and bodies, but the biological evolution did. We can only carry out experiments in-vitro and in-vivo using these genetic drugs and see what happens, but this has not been done for the genetic vaccines. In fact, serious experimental trials using genetic molecules should take many years of testing and also checking whether these molecules or their effects can be transmitted to next generations.

Potential other effects of RNA-based vaccines

A modification of mRNAs as a drug for different purposes is the introduction of numerous mutated nucleotide bases such as pseudouridine and methyl-pseudouridine in mRNAs, a molecule that usually contains no or few of these bases localized in some polynucleotide regions that likely evolved for specific but still incompletely known cell mechanisms (Kariko and Weissman, 2007; Kim *et al.*, 2022; Wang *et al.*, 2023; Boros *et al.*, 2023). Modified nucleotide bases are also more commonly present in specific regions of mature tRNAs, rRNAs, ncRNAs, but many details on the role of these unusual bases are still unknown or are purely academics. These modified nucleotide bases present important and specific roles for the function of different RNAs and, from present-day knowledge, these appear generally related to transcription and protein synthesis efficiency. The use of modified nucleotide bases in mRNAs derived from studies that showed how mRNAs containing base modifications did not trigger an

immunologic reaction in-vitro and after injection into experimental animals (Kariko and Weissman, 2007; Kim *et al.*, 2022; Wang *et al.*, 2023). In test tube experiments, mRNAs containing modified bases also increased the translational efficiency in comparison to their natural counterparts. These experiments opened-up the use of synthetic mRNAs for the inoculation into the organism, a useful technology for different gene therapies, cancer treatments and, later, they also served for the development of mRNA vaccines.

The latter application as vaccines for infectious diseases has been made in the last 5-6 years, not from long time as reported from the official narration that refers to vaccines a long experience as that for cancer treatments or other diseases. As a matter of fact, the effects of these genetic vaccines for covid19 were unknown, are still under examination today and will be monitored in the future, representing an ongoing experiment. One of the problems with RNAs utilized as vaccines is that while the modified mRNA should not be immunogenic (Kariko and Weissman, 2007), they code for the production of immunogenic but also active viral proteins (spike) that elicit unknown or even pathological effects on the organism (Seneff *et al.*, 2022; Acevedo-Whitehouse and Bruno, 2023; Bellavite *et al.*, 2023; Boros *et al.*, 2023; Alibardi, 2025; Fig. 1). Furthermore, these alien RNAs might also interact with unpredictable mechanisms with cellular RNAs, can insert as cDNAs randomly into the genome as some viruses do, and interfere or alter the basic cellular and immune functions of the organism (Gambacorti-Passerin and Aroldi, 2022). These problems can even be enhanced using the recently commercialized self-replicating RNA vaccines that extend the presence and unknown concentration of RNAs and spike proteins in the human body. Biotech-made RNAs and their coded proteins, e.g. spike for the Sars-Cov2 virus, after reaching the cell cytoplasm can penetrate and interact with the genomic DNA during and after mitosis, when the nuclear membrane disappears for 1-3 hours (Gambacorti-Passerini and Aroldi, 2022; Alibardi, 2023, 2025; Fig. 1). The consequences of these alterations might even be passed onto next generations after reproduction, but we cannot predict these possibilities.

Some experiments, contrasted, retracted from the journal where they were initially published, and which further investigation was discontinued for unknown reasons, indicated a dangerous interference of the spike protein with the mechanism of DNA-repair (Jang and Mey, 2021; Fig. 1). If this is true, the mutation may generate

different pathological consequences including cancers in different organs (Fig. 1) and alteration of the gene re-shuffling mechanisms that generates many immune cell clones and antibodies, lowering our immune responses (Fig. 1). These initial studies could be confirmed or denied from following independent researches, but the latter have not been carried out for unclear reasons. Despite the above reasonable scientific considerations, the alteration of mRNA sequences, mainly in the 5'- and 3'-positions of mRNAs, and introducing modified nucleotide bases, is an active research trend that tries to improve natural mRNAs and use these biotech-designed mRNAs for future medical application, in particular as vaccines (Kim *et al.*, 2022; Wang *et al.*, 2023).

Unpredictability of genetic vaccines

While inventing non-genetic chemical drugs has little to do with the evolution of cellular functions, the empiric inoculation of alien biotech-modified genetic material into an organism may have unpredictable effects. Experimenting with organic molecules that are the basal stuff of ourselves should be carefully evaluated. In fact, aside the specific sequence, the injected material possesses the same nucleotide bases of our own RNA and DNA, to which it might interact and recombine, giving rise to altered and unstable polynucleotides or defective proteins (Gambacorti-Passerini and Aroldi, 2022; Seneff *et al.*, 2022; Acevedo-Whitehouse and Bruno, 2023; Boros *et al.*, 2023). The likeliness of negative effects produced from these potential interactions, derives from the notion that small gene defects produce macroscopic pathological effects that the present scientific knowledge cannot predict but only describe (e.g. progeria for alteration of nuclear lamins, dystrophy due to defects of dystrophin-based muscle junctions, progressive muscle atrophy due to mutations in SMN1 and related genes, Down syndrome or autism for chromosome unbalancing etc.).

The inability of present-day human Science to predict macroscopic effects due to tiny molecular alterations of DNA, derives from its empirical acquisition of knowledge, evidencing again the difference with biological evolution where instead any new innovation had to be consequential and functional with previous mechanisms. In fact, differently from largely empiric or derived scientific discoveries, biological evolution produced, step by step, mRNAs that function and optimally interact with other RNAs, DNA and other biomolecules in the cellular environment. Natural cell

processes, for the way they have evolved to construct these functions and later macroscopic bodies, have determined what we consider as a “normal” rate of growth and aging, “normal” muscle-skeletal movements, a “normal” somatic and neuro-cerebral development etc., resulting in viable and efficient organisms, including humans. We do not grasp how apparently minor genetic defects or alteration of the genome that are naturally introduced, for example, by viruses, chemicals or from transmitted gene defects can affect macroscopic functions such as development, growth, respiration, circulation, contraction and movement, digestion, reproduction, and even behavior. Consequently, how can we pretend to know for sure if and for how long a biotech modified RNA lasts in a body based on what we know in a test tube or even after short-terms tests on animals? A body with a much more complex compositions shows different reactivity from that derived from the known composition of a test tube, not to consider species-specific and individual reactivities. A human body cannot be equalized to a test tube but the mass vaccination with still experimental RNA or DNA-based vaccines has treated millions of people like test-tubes.

These few examples are testimonial of the limitation of present scientific knowledge to predict and explain how small molecular alterations can produce broad anatomical, physiological, neurological, and cancerogenic consequences. This awareness should made scientists more cautioned on the unpredictable effects of biotech-constructed genetic material that is inoculated as drugs into a healthy person for vaccination, especially for low lethal diseases such as influence or covid-19, varying from 0.03-0.5% average mortality for children, young and middle age people with no health problems; Prompetchara *et al.*, 2020; Bhopal *et al.*, 2021; Alibardi, 2023).

Science or scientism in using RNA or DNA-based vaccines

In my following argumentations I initially state the obvious: vaccination has been an amazing reach of mankind, and has saved un-countless people lives for really dangerous or deadly virus diseases such as smallpox, polio, rabies, hepatitis, ebola and others (Brock and Madigan, 1991; Tobin *et al.*, 2011). On that ground, for dangerous infections with indicatively lethality above 5% and/or producing serious health consequences, it is reasonable to take vaccination for these life-threatening diseases, for the individual and for the collectivity.

Fig.1 Few examples illustrating potential problems generated using RNA-DNA vaccines, fragmentation of injected RNAs or DNAs, and unknown vaccine-RNA interactions with cellular RNAs and DNA are outlined. **A**, humans and test tubes are different in relation to the genetic vaccination. **B**, experiments on gain and loss of functions; **C**, nuclear penetration of vaccine-RNA and derived spike proteins during the cell division (the nuclear membrane disappears for 1-3 hours) that might generate autoimmunity or RNA-DNA alterations. Autoimmunity derives from the exposition of the spike or its peptide fragments on cell surface of different organs. Cytoplasmic interactions with cellular RNAs are unpredictable. Nuclear interaction with the DNA might incur in genomic alterations. **D**, interference of the spike protein with DNA-repair mechanisms, and their possible fall-out in cancer and immune-depletion. **E**, non-repaired mutation within proto-oncogenes can lead to cancer. **F**, non-repaired mutations determining alterations in the "re-shuffling mechanism" of activated lymphocytes after immune stimulation (recombination after DNA-elimination of some immune genes, producing a potentially enormous variety of clones and antibodies). The consequences are weakness in immune responses against internal (teratomas, tumors) and external (viral and bacterial) challenges.

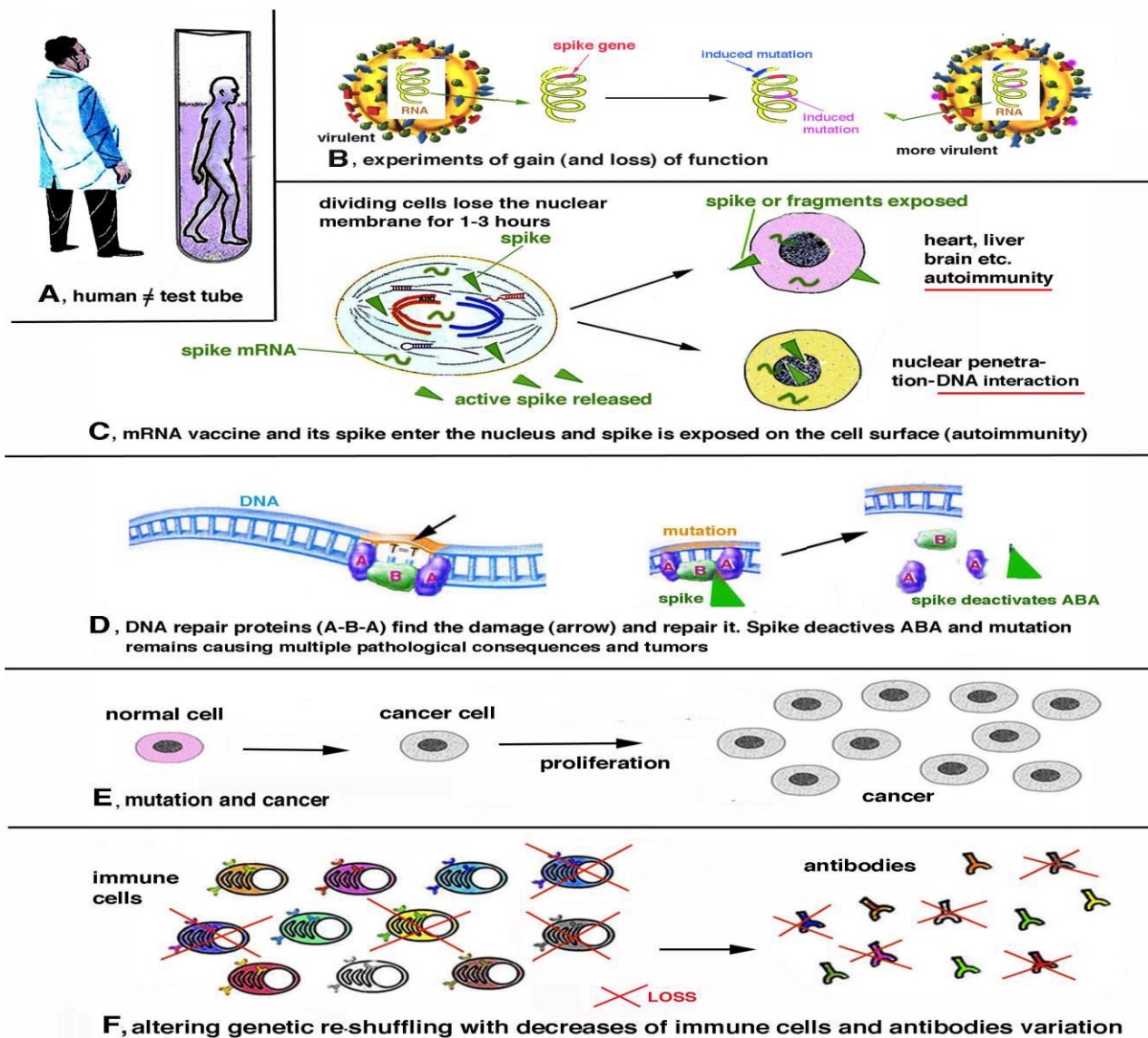

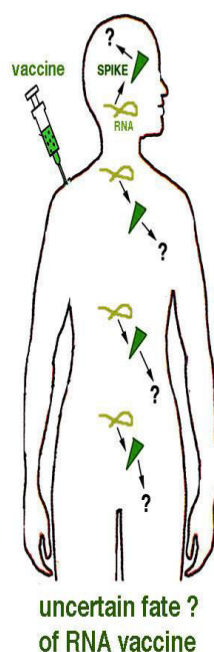


Fig.2 Comparison between scientific (violet color) and Scientific (green color) opinions about the effects of the covid-19 vaccination using mRNA delivery by liposomes or DNAs delivery through a viral vector. Aside from basic immunological and scientific principles known from long time, also the information collected during the pandemic (few official and other non-official narration) using these genetic vaccines have determined the different opinions between scientism and Science (Alibardi, 2023, 2025). Care should be exerted by scientists about the potential fate of genetic material introduced in the human body.

Scientism or Science in the DNA-RNA (genetic) vaccines ?

	<u>Scientism</u>	<u>Science</u>
		
Scientist or ? Scientismist		
-types of vaccines	RNA or DNA	others were available
- genetic vaccine	safe	not safe (no experimentation)
-does RNA penetrate into the nucleus ?	no	yes (during mitosis absent nucl. membr.)
- DNA interactions	no	possible (and detected)
-adverse reactions	few	higher than traditional vaccines
- lethality	very low	higher than traditional vaccines
- Immunization	high and lasting	variable and temporaneous
-vaccination for a naturally healed person	to be done	not necessary (already well immunized)
-degree of immunity between RNA-vaccinated vs naturally healed	better immunization	lower immunization because monovalent
-protection and block of infection transmission	high & efficient	variable and similar to no-vax
-mutagen / Cancerogenic consequences	none	unknown
-future consequences	none	unknown
-use necessity of vaccines	yes for urgency	not as uncertain
-therapeutic alternatives	none	some effective
-origin of the pandemic	natural	uncertain but possible spillover
- number deaths for covid	numerous millions	should be re-counted/evaluated



However, in case of low or neglect lethality, such as measles, rubella, influenza and covid19, the above assumption is not valid, and other less invasive but effective medical treatments are more desirable, also to stop the spreading of the infection.

An imposed vaccination using RNA or DNA likely incurs in deleterious health consequences on millions of people as official and non-official reports are showing.

It is evident that Biomedical Sciences and their modern applications, including developing new types of RNA-DNA-based vaccines, have arisen tremendously in the last 10-30 years, together with interests that are not eminently medical or scientific but instead appear prevalently guided from economical goals of the Pharma sector. The latter, in some cases are sustained by political health measures in the materialistic western society where money has replaced most of religious, educational or ideological values (Muzikante and Skuskovnika, 2018).

Therefore, Science that deals with social, political and economic interests, even more than in the past has actually degenerated into scientism, the use of Science for non-scientific purposes. When scientific information are issued through media and newspapers controlled by the owners or the political establishment, they largely influence and direct most of the large mass of people. More than in the past, the covid19-pandemic has made evident how easily Science can be turned into scientism these days, and how the latter has manipulated most people minds, either ideologically or influencing them through ignorance, fake news and scare (Alibardi, 2023, 2025; Thoene, 2024). I wonder why and how this could happen in modern times despite the high level of scientific knowledge and western societies democracy. Some of the different opinions between scientism and Science applied to the covid19 pandemic are listed (Fig. 2).

Future RNA-based vaccines, planned for other infection diseases of next predicted pandemics, can also generate active viral proteins with unknown interactions within the human body, similar or worse than those of the covid-19 spike protein (Alibardi, 2025). To state that these vaccines obey to scientific principles without complete knowledge on the consequences is therefore wrong and misleading. One of the problems of these injected biotech constructed nucleotide sequences is that they partially mimic viral activities but not the complete

viral cycle, giving rise to free, active and alien proteins circulating inside the body such as the spike, proteins that are pathogens. This is a substantial difference from gene therapies aiming to fix genes and derived proteins of the same individual, not introducing functional proteins from viruses or other alien species. A serious and independent scientific discussion should distinguish between useful gene therapies and cancer therapies with RNAs or DNAs, from uncertain vaccinations using viral RNA or DNA. The complexity of genes and their proteins interactions in a developing, growing or adult body that are only incompletely known by present-day Science, indicates that pretending to state that RNA-DNA vaccines are "safe" is an irrational and non-scientific driven procedure, but fits well with scientific goals (Fig. 2).

Acknowledgments

Self-supported opinion study with no conflict of interest.

Author contribution

The author has entirely planned, analyzed and written the MS.

Data availability

I have no other data to present in the MS.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest There are no conflict of interest in the MS.

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How to cite this article:

Lorenzo ALIBARDI. 2025. RNA-DNA-Based Vaccines for Infection Diseases and Mass Vaccination Appear an Uncertain Experimentation. *Int.J.Curr.Microbiol.App.Sci*. 14(12): 15-24.

doi: <https://doi.org/10.20546/ijcmas.2025.1412.002>