



Title: SARS-CoV-2 and Uncertainty on its: Initial Origin; Vaccination's Feasibility; but proposing Novel Approach in Drug-Vaccine Findings against such Viruses

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abstract

Infectious diseases are still one of the mass killers. Among them the COVID-19, which caused by a virus SARS-CoV-2 (but yet not well investigated its nature), is a new respiratory infectious disease. This pandemic already took around 1.5 million lives, destructing the socio-economic structure of the globe. To combat it world is trying the possible-impossible measures. For instance, at the beginning of the pandemic, around hundred research sites were announced about their engagement in drug-vaccine discovery activities. Today, using the Media as a battle of field, developed countries change the vaccine discovery issue into business and political oriented race. Certainly vaccines as one of prevention based prophylaxis measures are used earlier and now too. However, world do not have not only feasible but even a nominal vaccine against this virus. Yes, when Media announced as if tomorrow will be developed vaccine to this COVID-19 pandemic, since March 29 2020, we are twitting that for such type of virus and moreover within this short of time frame, it is impossible to have practicable vaccine. Furthermore, we tried to broaden this postulation through our two published articles by writing: the cheapest, fastest but effective ways of prevention measures (not to be infected and or not to infect others) are: scaling up the public's awareness on the nature of SARS-CoV-2; guiding nations on how to use properly the sanitation-hygiene based prophylaxis measures; and we tried to caution that a vaccine discovery hope can idle the public and make him negligent for the pandemic. As a result people do not seriously take into account the two decisive prevention measures: "stay at home" and "face masking". Therefore, after awaiting the results of vaccine discovery duel for 9 months, we decided to publish our biochemistry-physiologyanatomy and literature review based research work, which point out the suspiciousness-doubt of its nature and vaccine findings for this corona. In this our work: in a chart form, we showed more than 13 possible varieties that give clue on how to identify SARS-CoV-2's and others future pathogens' initial sources; we have elaborate 5+1 groups reasons, why vaccination for this type of virus may not be feasible; and as a potential solution, we hypothesize how better to direct the drug-vaccine discovery's activities for such type of pathogens.

Biography. Dessalegn Temesgen Leye is a pedagogic-biochemist (PhD) and an assistant professor. Recently, he is highly concerning on COVID-19 issues. He has three published articles regarding to COVID pandemic. He believes that instead of vaccination, more feasible options in battling with this pandemic are: "Stay at home", "face masking", "distance keeping", and properly performing all "sanitation-hygiene prophylactic measures"!! Presenting

1. Introduction

Among human progresses in fighting against disease - discovering vaccination is comparatively new approach of healing. Vaccine idea: start dated to 18th century, transferred into using live attenuated vaccines, further grown into using genetic materials as DNA-RNA, and recently, switching into protein combination techniques become a front line [1,2,3,4]. Nonetheless, still there are failures and successes in vaccination development, for instance, vaccination against tuberculosis [5,6]. Yes, if there is no try and error, no achievement in any field. Medicine too is not an exceptional. Though, we should have proud of vaccine development for instance against smallpox [7] is the pioneer in vaccination's victory. However,

1.1 Statement of the problem (study)

1.1.1 Today, we are afraid that vaccine discovery changes its nature into a net source of business and political achievements [8]. For instance, 3 years ago, we have had encountered about vaccination project as if it is not only possible but also as the main prophylaxis measure against malaria infection! [9].

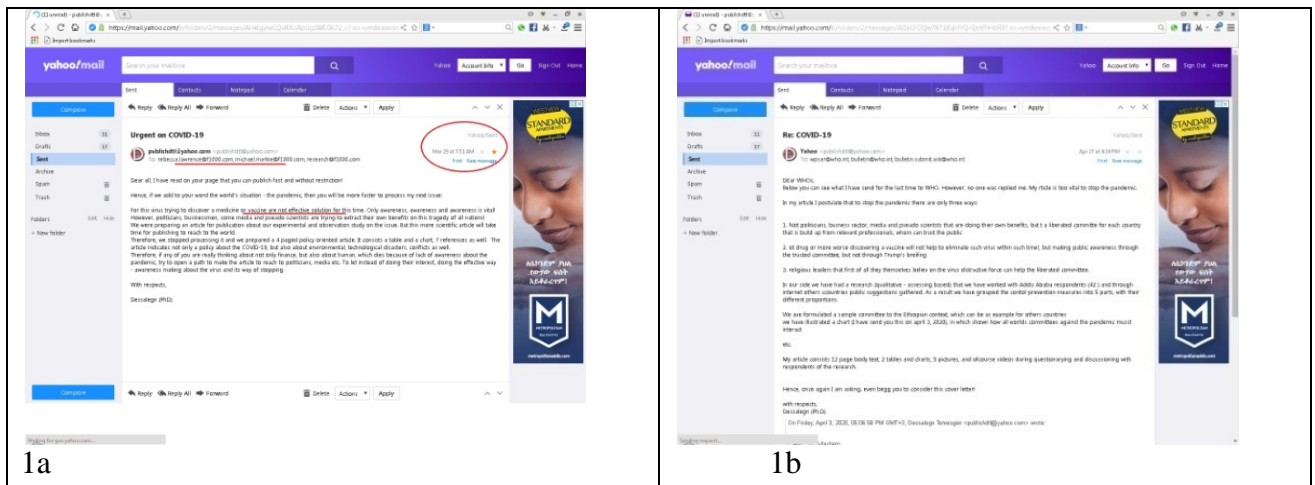
1.1.2 The issue is complicating, when business oriented scientists and politicians are aggressively feed the media with their biased (if oriented to financial and political benefits) attitude:

During the March-April 2020 of such race, there were 115 vaccines projects [10]. At that time, we were anxiety for what is going on the globe. Together such race, there were information as if face masking is not help to protect from being infected. Moreover, inform us that WHO itself opposing face masking for those, who are not health worker and infected. What was aggressively adverting – only hand washing, as if it is the only proper prevention based prophylaxis measures (PPPM). In such battle, the Media become the field of duel: The issue is worsening, when journalists do not want to have scientific reference for what they are talking or writing about. Furthermore, public in such problem (like this pandemic) tends to follow the social media than what science says. Accordingly, we have negative assumption on how the media behaves during this COVID-19's pandemic [11].

Since March 29, 2020, we tried to forward our thoughts (refere to picture 1a-c) that Based on this in our earlier two works, we tried to address to the globe through publication [11,12}

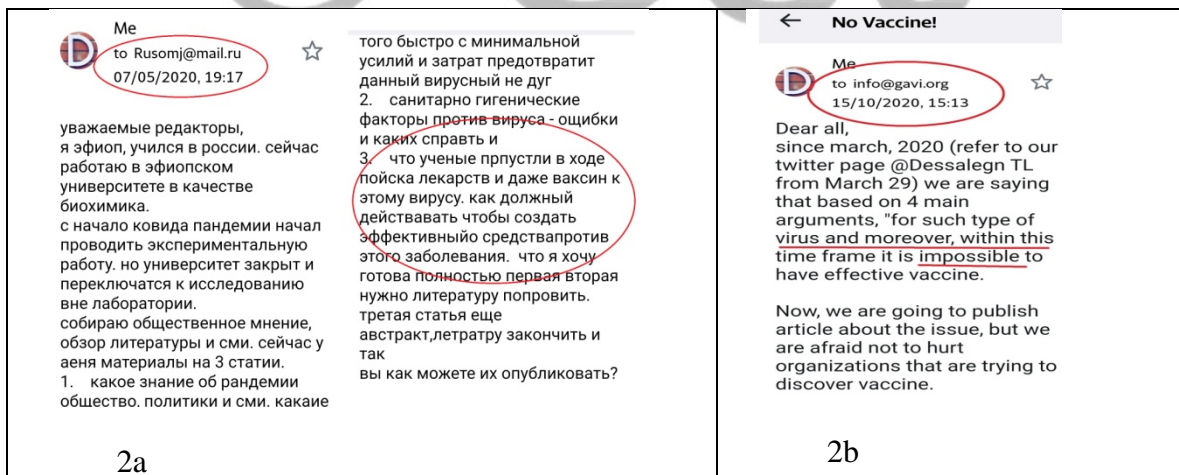
1.1.3 Since March 29, 2020, we tried to forward our thoughts (refere to picture 1a-c) that to anatomy-physiology and biochemistry contexts, for antibody (if any at all) the lower human respiratory organs system (HROS) may not give adequate response. Based on this in our earlier two works, we tried to address to the globe through publication [12} that “For such type of virus and moreover within this short of time frame, it is impossible to have effective vaccine against SARS-CoV-2”.

Picture 1: Email from March 29, and April 27, 2020 to publisher, and WHO in which we expressed that others prevention options are better than vaccination



picture 1a: On March 29, 2020 (see the circled in red) we sent email to a publisher. In it, we expressed “vaccines are not the effective solution” (enlarge it to see the underlined in red)
 picture 1b: a Letter to WHO on April 27, 2020. In it we claimed that if world want to stop the pandemic, instead of vaccination: “proper public awareness”; “establishing (liberated from governmental-political influence), a task force members which are relevant specialists)” must take a responsibility; and “religious leaders should influence on their believers”, etc are the first effective steps

Picture 2: letters to a vaccine developer (May and October 15, 2020), in which we inform that vaccination against SARS-CoV-2 is not feasible



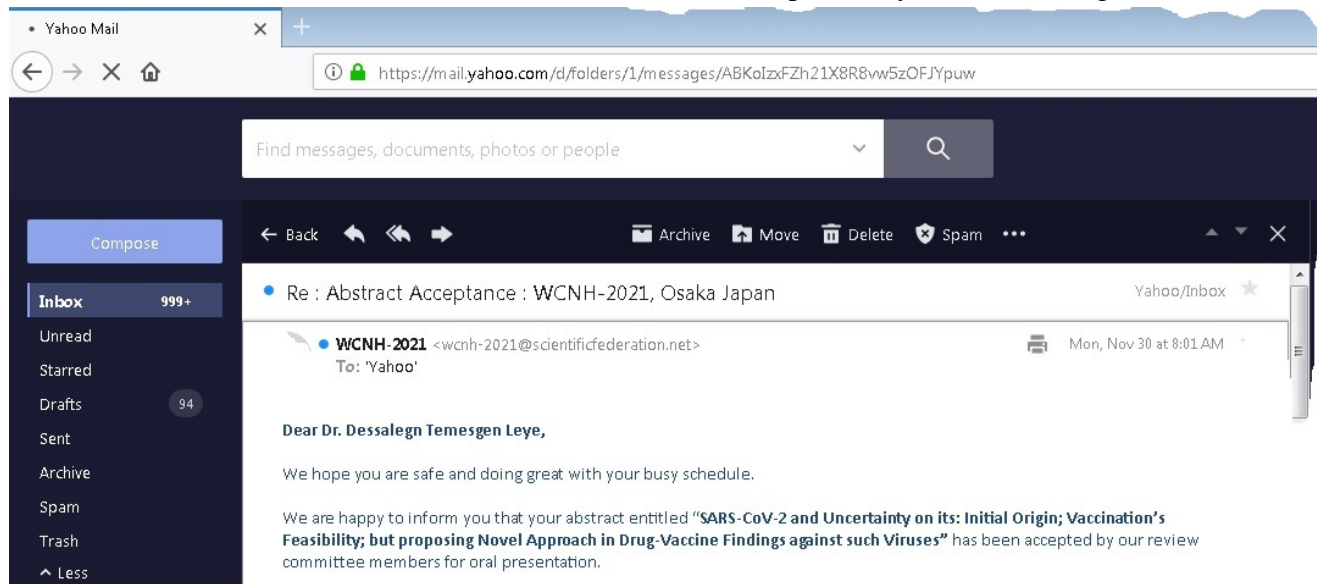
Picture 2a: letter in Russian language, sent on May 7, 2020 (see the circled). In it, we expressed that before starting vaccine development project, there must be issues, which should be solved (enlarge the picture and look into the underlined)

Picture 2b: letter to one of vaccine developer. Sent on October 15, 2020. In it we informed that there are at least 4 reasons why it is impossible to have not a feasible but even effective vaccine against such type of virus.

Instead, two months ago 5 vaccine developers appeared as finalist of the battling with ready products. Well, what make us worry is that they do not want to illustrate what, how they produce and test their product. Certainly, sometimes biopharmaceutical companies and business oriented scientists for us are seemed like a bakery, who do not bother whether there is a good climate to grow the wheat!. Through, not mainly as a biochemist, but since, we are pedagogic, we couldn't neglect all what we think: today's youth do not want to think over, just take from the internet the same principle for different purposes - during our biochemistry course delivery for different types of students, we gave the same assignments-questions with the following common instructional phrase: "based on your future specialty". However, most of them give similar response: they just copy down similar data from internet. In the same way, we are afraid that developers just only focus on how to develop vaccine through instructions of a text book like in [13] or as instruction in the [14,15,16]. The issue more concern us, when we listen that vaccine developers are going to have special permission (without passing through essential testing procedures) to implement their products - a tendency, which is dangerous not only for this pandemic, but also for the whole scientific principle.

1.1.4 Although, we have had skeptical relation with its effectiveness, not to destruct the vaccine development processes, we decided to wait at least for a while, until there comes vaccination result. Because, as we have cautioned in our earlier work [11] that a hope from vaccination will make public ignorant from following the self isolation - following the prevention based proper prophylaxis measures (PPPM), no matter to have one or two shot, if it has no side effect. Therefore, instead of publishing the work, we applied and accepted to present it in a conference (refer below to picture 3b), but tried to contact manufacturers to forward them our thoughts-concerns (refer to picture 2a-b). However there is no response till now. Additionally, we were waiting any transparency as expressed a mRNA design in [18] on how vaccines are acting on the body, in particular how its antibody interact with the lower respiratory organs (we were expect information that can convince us). To the contrary, still there are no even full tasting phases.

Picture 3: one of the three email about the article's acceptance by conference organizers



Picture 3: A confirmation letter that our abstract accepted to present on the conference

1.1.5 at the end of the day, it is sad that in this 21st century, where human is trying to explore the universe, this by implementing the PPPM easily preventable virus, is crumbling million lives as an autumn leaf! Hence,

1.2 Aim of this research is to:

1.2.1 Remind vaccine developers our doubts that vaccination is not feasible than others prevention based proper prophylaxis measures (PPPM), about which we have had published [11].

1.2.2 Broadly elaborate our concerns on vaccination's drawbacks: Yes, we have had prepared this article earlier on May, 2020 (refer to picture 2a). However, although, based on our biochemistry background, we were not agreed on the vaccine development race even among countries, we have hadn't confidence - not to be one of non-logical anti-vaccination (there were anti-vaccination against measles [19]) to give this study for publishing. But, today, when many are openly opposing/suspiciously or at minimum skeptically or directly expressing [20,21,22] against vaccination, and even Dr. Fauci, although he is a part of authorities, tries to balance the issue by giving scientific arguments; when known journalists like Mr. Tucker Carlson of Tonight openly show his skeptic about the efficacy of vaccination). Certainly, there were baseless anti-vaccine movements like expressed in [19] during measles epidemic. Anyhow, we decided to publish it, but almost reformed the content, in particular the bibliography part fully changed, since many research articles on the issue are appearing these days.

1.2.3 Give a clue that this work is advantageous (at least on raised issue in) not only for the current pandemic, but also for the future concerns on disease based disasters [11].

2. Objectives

To achieve the above mentioned aims, we constructed the followings 4 objectives (each of them can withstand a criteria of separate article) to the global scientists, not only, due to ethnical pressure on us here in Ethiopia, we ourselves have no possibility to perform experimental proofing our hypothesizes and postulations, but also the urgent pandemic's issues do not give time to publish them separately!

2.1 Analyzing and postulating the possible initial sources/origin of SARS-CoV-2

2.2 Sorting out the international criteria for appraise the effectiveness of vaccines

2.3 Elaborating why it is impossible to have feasible vaccine for SARS-CoV-2

2.4 Suggesting novel approaches in drug-vaccine discovery for: COVID-19 and similar diseases

3. Methodologies

As this work is relying more on analyzing with a literature review, to achieve our objectives, we will have:

3.1 structure of the analysis-review design: can be classified into materials, tools and procedures

3.1.1 Materials: Gathered literature data, individuals' opinion, and Medias' information. Data collecting policy:

Since the pandemic is relatively new, on May, 2020, at the time, when the first variety of this work was ready for publication, there were no enough research works about SARS-CoV-2. Therefore, we were more relied on Media information. However, today, we used at least half of literature from research articles, but most of the data are going to be retrieve from internet sources.

3.1.2 Tools: biochemistry concepts and epidemiological principles

Instead of comparing literature given among themselves (Principle of literature review based research works [23,24]), this work is a theory-analysis based with constructing several hypothesizes but, due to economical and ethnical pressing in Ethiopia, impossible to handle experiment based research) to be implemented as individual research objects. Hence, the tools are consisting the biochemistry and anatomy-physiology principles.

3.1.3 Procedure:

Analyzing the gathered data (materials) Vs to the biochemistry-anatomy-physiology contexts and epidemiological principles, filtering (leading) them to the reality/facts, and looking for (selecting-sorting) - what to include in the conclusion-recommendation part of the work.

3.1.4 Exceptionality of terminologies to be used within this article

Must be list out and mark their meanings, which must serve within the boundary of this work

3.1.5 After raw data collection (Result – section 4)

Aiming to find solutions for the mentioned problems (refer to the statement of the problem (1.2)) through the objectives (point 2.1-2.4), we should organize the rest 3 sections as follows: the discussion parts are orienting at least on the 4 objectives, whereas, the conclusion and the recommendation parts may be shorten up to three parts (the second and the third objectives may be combined together into a single) or expanded into 5 subsections (points) in each of them.

3.2 Types of data on which this work is going to be focused will be structured as follows:

This article will have the followings 5-8 sections: introduction, objective, methodology, results, discussion, conclusion, and bibliography or although for a literature review, it is not advisable, some of them can be paired like introduction-objectives, methodology, result-discussion, conclusion-recommendation, to make the in-text body easily understandable and to make easy to cite any issue within the in-text body, we subdivided topologically as for example 3.2.1.1, 3.2.1.2

3.2.1 SARS-CoV-2: nature, as a pathogen in particular

We will collect data about: the biology (nature) of SARS-CoV-2; its initial source/origin; COVID-19's symptoms; statistical data of infected, cured and death within a year (in table or bar graph form); and SARS-CoV-2 as a pathogen, etc.

3.2.2 Measures that are taken and taking against COVID-19

collecting data on how battled and battling against viruses, in particular how are the PPPM for respiratory based infectious virus pathogens: PPPM; treatment; and control measures to combat the COVID-19's pandemic

3.2.3 vaccination to combat SARS-CoV-2's pandemic

what is vaccine; international criteria to recognize a vaccine as an effective, efficacy and feasible; etc.

3.2.4 is vaccination against SARS-CoV-2 feasible for such type of virus

what kind vaccines, how they are acting, sites that they should impact on and are these sites easily available for the vaccine's antibody, the exceptionality of the anatomy-physiology of HROS); etc.

3.2.5 are there alternative novel approaches to combat COVID-19

4. Results of collected data:

4.1 Exceptional terms' meanings within this article

Some terms (scientific words), whose definitions must be the same throughout the in text-body at least within this work should be highlighted: This day, if you have a pal Pay card, you can publish any content in a known journal that has Scopus indexation [25] and others. Because, of the “any content” we encounter even at the language-terminology level (no control-peer review on how to use scientific words), as a result, which we even confused on known scientific terminology meanings.

Therefore, here under listed some important but with temporary meanings that we are using inside the text-body:

pathogen – microbe (bacteria or virus) that can destruct the normal human metabolism;

antigen–part of pathogen or result of its biochemical reaction's product, which may induce metabolism disorder in the host organism

antibody – protein based specific organic molecules (Ig – immunoglobulin) that are produced by the victim organism (host) to the response of antigen/pathogen's biological actions

alveolar sac is a sac like end (base) part structure of a lungin which the two types of alveolar cells – the pneumocyte I (type I) and pneumocyte II (type II) together with the macrophage cells are included

alveoli/alveolar or alveolus is the specific epithelial cells (pneumocyte I and II) within the alveolar/alveolus sac

effective– a positive desired result at least within in *vitro*

efficacy– a positive desired result both within *vitro* and *vivo*

feasibility – Additional to the efficacy, should contain positive impact on the socio-economy beneficiary

origin – the start place or biological source of a living thing, for instance the initial of a pathogen

picture – an image, which is prepared with a help of camera or scanner

figure – formula or scheme on a paper or screen which is drawn by hand or with a device, for instance mathematical, physical and or chemical, formulas.

chart – a figure like scheme which can be in circle form (pie chart), line (with arrows, others shapes connected each other and lines) or graph form that represent a quantity-quality with a ratio/scale

4.2 SARS-CoV-2: nature, as a pathogen in particular

4.2.1 Biology: nature of SARS-CoV-2

Well, although as a contagious of the virus study of its nature was not enough at the beginning, for today there appeared works like [25,26,27], in which one can retrieve more or less some data.

Additionally:

SARS-CoV-2, causing severe disease in about 15% and death in approximately 0.4%, due to diffuse alveolar damage featuring intra-alveolar edema and lymphoplasmacytic infiltrate. SARS-CoV-2 enter into the body through nasal and oral cavity. The virus invade the epithelial cells of HROS. It mostly spikes with epithelial cells through their membrane, in particular spike to angiotensin-converting enzyme 2 (ACE2) [28,29] Then its capsid endocytosis into the cytoplasm of the host cell []. There the RNA of the virus will attach to the host cell's ribosome as the mRNA of the host cell doing [29,30,] for further processing to produce several virions.

After, bursting the host cell (because of the pressure that caused by additional viruses the volume of the host cell increases as a result it bursts (torn apart and the virions released and invading others normal host cells. SARS-CoV-2 is a single-stranded, positive-sense RNA, enveloped, helical virus that synthesizes 4 structural proteins: Its S1 subunit mediates cell entry by binding to ACE after “priming” by transmembrane protease serine S2. Given its size, location, and essential function, spike is predicted to be a key target of antibodies [25,28,31,32]. However, there are information that as if not only the epithelial cells of the HROS, but also mouse models revealed that intranasal administered SARS-CoV enters the brain primarily *via* the olfactory bulb, followed by rapid transneuronal spread to connected areas, including the thalamus and the brainstem [33] or in [34] informed that the virus can invade endothelial cells!

4.2.2 Initial source/origin of SARS-CoV-2

Ways that are applied in identifying the origin of a pathogen, in particular of SARS-CoV-2

deeply understanding the reason from where emerged not only infectious diseases, but also even chronic - is the half way of solving a disease related problem! Yes, not only for infection (communicable) diseases, but even for non-communicable diseases, identifying the source of the pathogen is the third if not half of the way to stop a disease. Therefore, identifying the exact origin of the SARS-CoV-2 is necessary even for the future

Data on the origin of SARS-CoV of 2003 and MERS-CoV serves as a basement to assume about the origin of novo corona virus SARS-CoV-2. However, there are also thoughts as if the SARS-CoV-2 is a result of laboratory manipulation. Certainly, it is not new that many countries are armed with a biological weapon, or when to the sake of science – during experimental study may appeared a pathogen, which because out of control can became pathogenic. On this probability, the USA and China have had a dispute. Except relying on SARS-CoV of 2003 and MERS-CoV of 2012/3, yet no one show the exact origin from where this pathogen appeared. Nevertheless, the research data and Media information on its source are collected:

We have assess literature given, where there are information about possible source (from where begin) of the pathogen SARS-CoV-2. The collected literatures lead us to generalize – suggest its source as: bat, pangolin, seafood etc, however most of the researchers tends to zoonotic character [3,31,32,33,34,35]. There are even Media information [34,39,40] as if the virus developed within experimental laboratory!

4.2.3 SARS-CoV-2 as a pathogen and the disease COVID-19

SARS-CoV-2, causing severe disease in about 15% and death in approximately 0.4%, due to diffuse alveolar damage featuring intra-alveolar edema and lymphoplasmacytic infiltrate [25,28]

Cause: The COVID-19 is causing by a contagious pathogen β -coronavirus – sever acute respiratory syndrome β -coronavirus 2 (SARS-CoV-2) [25,34,41]

4.2.3.2 SARS-CoV-2 infectious symptoms

Under the “symptoms” its definition: asymptomatic, mild, moderate, severe and critical are help full to identify the type of infection and its impact. Therefore, the exact identification of these symptoms is the second decisive factor (after the origin identification task) to combat both communicable or non-communicable diseases. However, regarding to SARS-CoV-2 yet little effort has done to characterize its symptoms and destructive roles, because impossible to have universal symptoms as the: virus has no constant nature; victims are different in age, health, location-environment, and genetic, social interaction-cultural factors, with its hidden (Ebola is better to be discovered since it is visualize), etc.

If symptoms were universal for all patients, then its spreading rate was able to be minimized (if not abolished at all). Anyway, Symptoms: sneezing, mucosing, coughing, headache, fever, short breathing, weakness, etc. are indicated in many literatures, among which [25,34,41,42,43] can be taken as references.

If fever; short breathiness; and weakness, then may lead to lethal end [25,44]

4.2.3.2 Role of proper symptoms' establishment

Anyhow, if we properly understand the symptoms, we can take appropriate measures for treatment. For this, it is better to have a medical test, whether there are symptoms or not. Therefore, recently there are two types (swab (PCR test) and blood samples) of technology based detecting [45,46,47]. However, we again hypothesize that both techniques have drawbacks: during swab sample taking, there may not be found the virus and or its debris on the nasal or oral cavity; we are witnessed when a nurse is taking swab sample from the lower part of oral cavity, where there is enough temperature and enzymes that do not let the virus to reproduce itself (can kill) or terminate its growth [12]; even we have passed through a webpage, in which there is an instruction how and from where to take swab - only from nostrils. The other issue is that, as we have informed in our earlier work [30], mucus may not let the virus to spike with the upper HROS's epithelia on the nasal or throat part may not give the virus a chance to spike with epithelia of upper HROS, but by directing to the alveolus sac it infect the pneumocytes cells [25, 43,44,45], a situation that cannot give a chance for swab sampling to reveal the infection.. Just may pass and enter to the alveolus sac for further replication through invading the pneumocytes (the issue that was the main reason why we studied this work). The same faults can be to the blood testing issue, because, not everyone can produce antibody (adopted) against the antigen, as a result, which may achieve false negative result.

What next after: Elaborating SARS-CoV-2's biology; investigating its origin; and identifying its main symptoms? We suggested and suggesting since March 29, 2020 (picture 1 and 2) and with published works in [11,12,30] to stop (if not abolish) this pandemic is implementing properly the easiest, fastest, and cheap, but feasible way of stopping this pandemic

Scale up the appropriate awareness on how not to be infected, train on the PPPM issues; isolate the infected not to infect others; and of course treat them [11]!

Rather, what world now engaging in a fascinated manner is vaccination!, the reason that forced us to prepare this work. Therefore, let us look through the vaccination issue

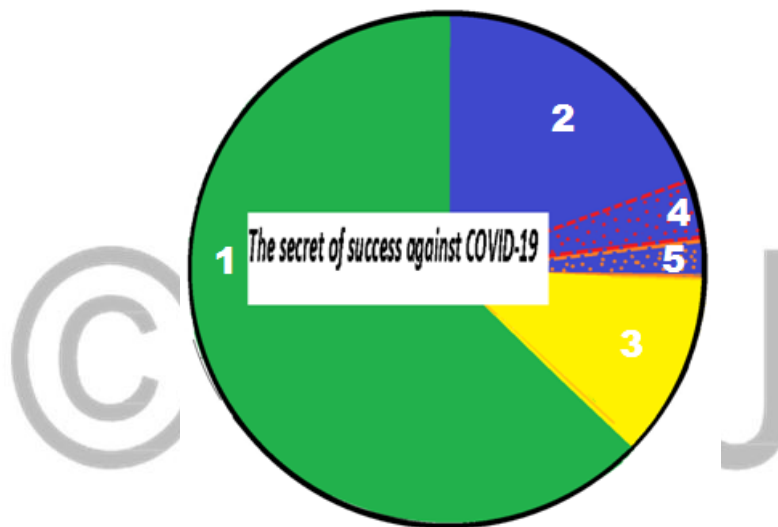
4.3 Role of Vaccination

In our earlier work, we too didn't neglect the vaccination prophylaxis measure, even although it relates to PPPM, we separately indicate it. However, due to the natures of both of the SARS-CoV-2 and its host, as seen in our pie chart (refer below), for vaccination measure we gave it the least portion (5th place) in battling activities):

4.3.1 Prevention options against a disease depends on its nature, whom and how it infect, etc. However, all measures can be grouped into: PPPM and drug based treatments etc. As we continuously trying to address [disclosing], for such virus, the easiest, cheapest and with fastest outcome is - the accurate usage of the prevention based prophylaxis measures.

4.3.2 Proportion (activities load) of measures against the pandemic

As we tried to show in the pie chart form, we can group the whole process of combating the pandemic into 5 sections: PPPM, studying the nature of the pathogen, treatment (drug) and vaccine developments. Yes, as seen in the pie chart the vast portion is



the PPPM (1 green color painted), where, 2 represent the portion for studying the biology of SARS-CoV-2, treatment take the 3rd (yellow colored), 4 stands for drug discovery's portion and the smallest volume goes to the vaccine (5th in the pie) discovery.

PPPM:

If we properly take into account the four groups (neglect vaccination) of PPPM: “stay at home”; for those who couldn't stay at home – “safe masking” covering the mouth and the nose (only through which the virus can enter into the body), until we return back to home; the “safe distance” keeping; and “perform proper hygiene-sanitation measures” like hand washing, disinfecting outer garments, including shoes etc. However, world now is engaged in vaccination part of combat's PPPM.

Well, yes, one of these PPPM is vaccination, as seen in the pie chart the 5th, we gave it the least portion. However, as 6 months ago, when we were roaring [11] that if we want to cut the COVID-19's prevalence stay at home or face masking should be prioritized, world was focusing on hand washing (although in [37] inform us as if endothelial cells too can be targeted for the SARS-CoV-2; the authors of [36,45] too propose the nerve cells as a possible victims; and the article [48] offer us as if the virus can survive the body's temperature, mechanical and enzymatic (catabolic) digestives to be infectious through faeces!!), if

we carry a kilogram SARS-CoV-2 with our hands, it couldn't infect us, unless we transfer even one virus into nasal or oral cavity) and today also world shifted into vaccination style! Thus, is vaccination feasible?

4.3.3 Vaccination and SARS-CoV-2's pandemic

4.3.3.1 History and results of vaccine development

The known start time to a vaccination type of healing dated to the 18th century, since then vaccination grows and till now hundreds tried, but around 20-30 types of vaccine have satisfaction (table 4) [2,10,21,31,3749,50},

4.3.3.2 World's success in vaccine development in table form

Table 3a: samples of vaccines, most of which are transmitted through air and direct contact

Disease	Spread through	vaccine
Chickenpox	Air, direct contact	varicella
Diphtheria	Air, direct contact	DTaP
Hib	Air, direct contact	Hib from haemophylus
Hepatitis A	Direct contact, contaminated food or water	HepA
Hepatitis B	Contact with blood or body flood	HepB
Influenza (flu)	Air, direct contact	Flu vaccine
Measles	Air, direct contact	MMR
Mumps	Air, direct contact	MMR
Pertussis	Air, direct contact	DTaP
Polio	Air, direct contact, mouth	IPV
Pneumococcal	Air, direct contact	PCV13
Rotavirus	mouth	RV
Rubella	Air, direct contact	MMR against rubella
Tetanus	Through cuts	DTaP

Adopted from CDC document: Immunization schedules / <https://www.cdc.gov/vaccine>

Current antiviral vaccine designs can be described as falling into 2 camps: protein based or gene based [51}. Protein-based vaccines deliver the immune system-stimulating antigen to the body. This category includes whole-inactivated (killed) antigen, as in the polio and flu shots, and subunit vaccines and virus-like particles, like in the hepatitis B and human papillomavirus vaccines (table 3b).

Table 3b: samples of vaccines list, based on their design technology

Types of vaccines	Name	Types of vaccine	Against which disease
Live, attenuated	Measles, mumps, rubella, varicella, influenza, rotavirus, zoster, yellow fever	Subunit/conjugate	Human papillomavirus, hepatitis B, influenza, type b, pertussis, pneumococcal, meningococcal
Inactivated/killed	Polio, hepatitis A, rabis	Toxoid	Diphtheria, tetanus

Adopted from [34]

“...currently no vaccine or antiviral therapy against HRVS [51]
the work [52] indicate us that in 2019, no effective vaccine for HRV.

4.3.3.3 Is vaccination impossible? Yes, for some infection!

What a negative attitude of human being is that he do not want to reveal his negative side. Scientists too are not exceptional. Since the history of vaccine implementation, there are numerous failures, but most of them are not registered. Even, within this year according to [] there were 115 design claims. However, we are not sure about their detail processes of design.

Anti tuberculosis effective vaccine yet not established, because of many reasons, let us see what some others authors suggest:

“...its efficacy is suboptimal [37]”; “...We do not have effective vaccine against tuberculosis [38]”; If we examine the table 3a, the CDC couldn't included any vaccine for this old HROS's disease”; “...less likely have effect vaccine for this the tuberculosis that grows together with human being [39]” have no effective vaccine, because the Mycobacterium tuberculosis has co-evolved with humans for thousands of years; around 15 vaccines on trial, using aerosol vaccination, only one licensed vaccine for today. It more works for infants; moreover, in [40], believes that it is impossible to treat tuberculosis; and in the work [42] too, remind and cautioned us how it is not easy to develop vaccine for strained viruses like influenza.

The same researchers' conclusion can be listed out for HRV.

Why we do not have still effective vaccine against HRV?

Yes, all these authors yet have no elaborated answer.

4.4 How to prove at least vaccine's efficacy

Yes, we tried to get answers, however, because of that in our mind we were searching an answer, which we already want to have (poor pedagogy), although they may satisfy others, but we couldn't trust on them. We need answer in which should raised issues like: is the design fulfill the criteria for vaccination development? Is blind experimenting policies were implemented? Is internal and external evaluators were involved? Is the international relevant organizers are certified it for testing, are all three testing phases' results performed with at least double blind design? And of course, the main our concern as a biochemist is the question - how far the created antibody can reach to its real targets?

Let us start to see the mentioned above each questions independently:

4.4. criteria (preconditions) to be recognized as an effective vaccine are:

4.4.1 According to WHO [WHO/IVB/13.07 / 10.2017 / Vaccination in acute humanitarian Today's vaccination issues to combat COVID-19

4.4.2 Recently, the only companies that are still on the race are: Pfizer [], Moderna [], Novavok [], Arstemi [], Sinovac of China, etc. In this month, ... however, none of them certified by international organizations like WHO

Table 4: infected and death tolls in each 3 months of 2020 (WHO sources)

March		June		September		December		March 2021
positive	dead	positive	dead	positive	dead	positive	dead	
750890	36405	10021401	499913	3273000	991224	79231893	1754574	??????????

4.5.5 The anatomy-physiology of HROS

4.4 are there alternative novel approaches to combat COVID-19

5. Discussion

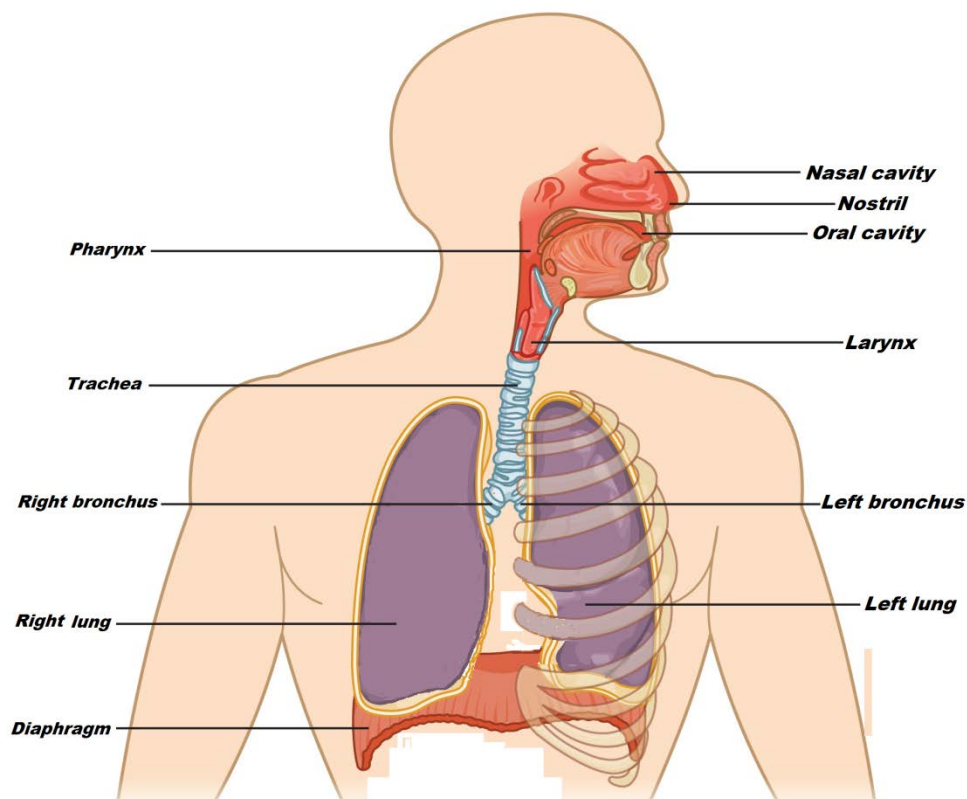


Figure 2 HROS in detail

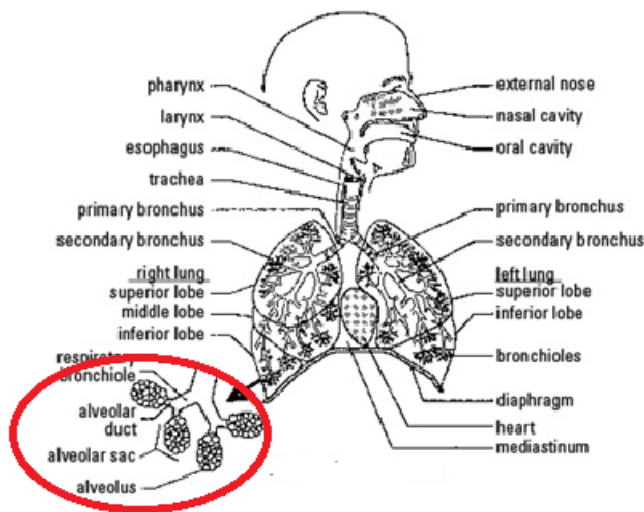


figure 2 adopted from [organs and structures of respiratory system – anatomy and physiology}

As seen in figure 2 we circled its part with a sphere red circle to show the important part of the figure for the given work: What is that circle contain?

The part (site) is the place where gas exchange between atmosphere and the body takes place. This location can be considered as the second, next to our skin that directly contact with the atmosphere. It shows alveolar sacs [}. A sac in which two main types of cells are located: pneumocyte I and II epithelial cells and macrophage cells[}. However, literatures on the issue (in them we can get not the same answer for the questions: what kind cells and their roles?) are contradicting each others:

Additionally, let us see different expression of different authors (almost all derived from Google search engine without authors identification), which can help us to have better understanding about this main site of gas exchange and the main part of HROS, which is more severely affects by SARS-CoV-2:

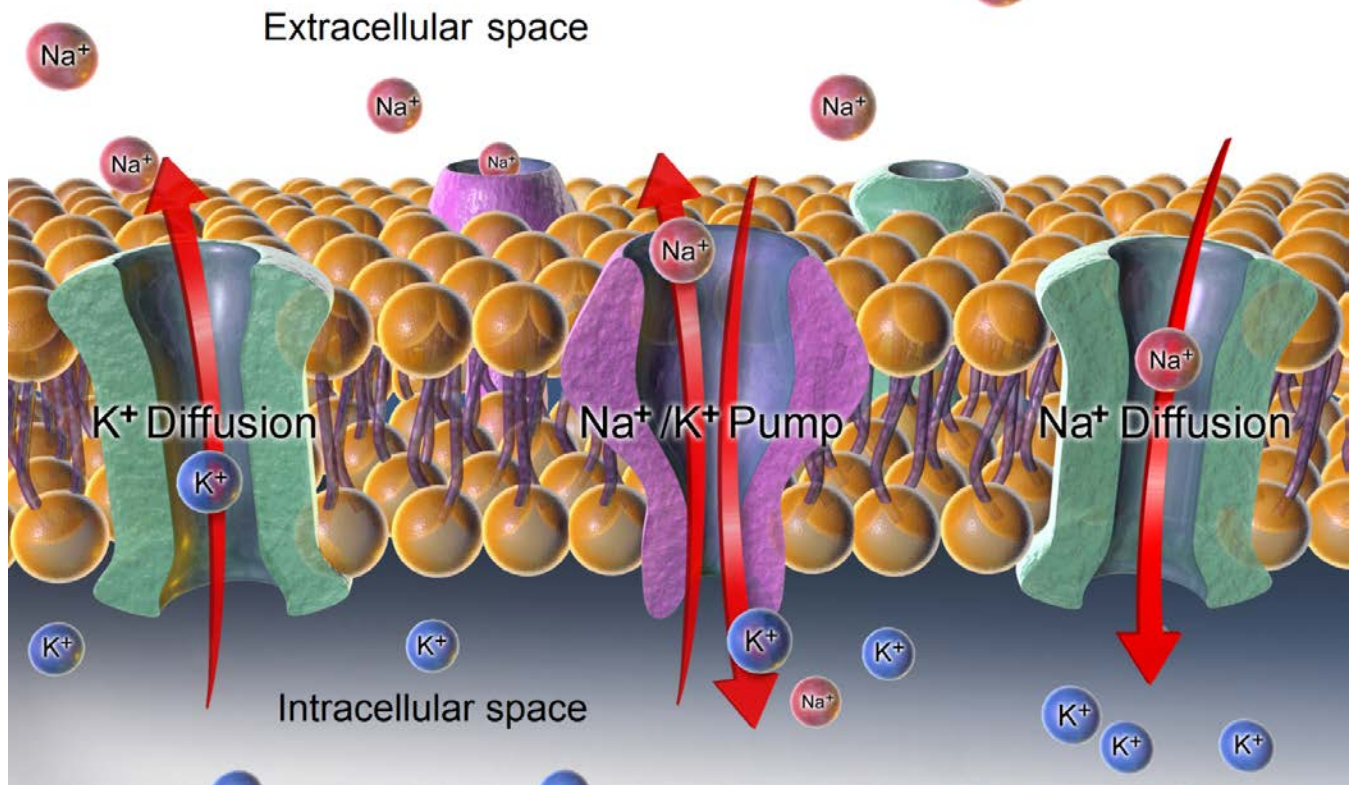
figure 3 LROS

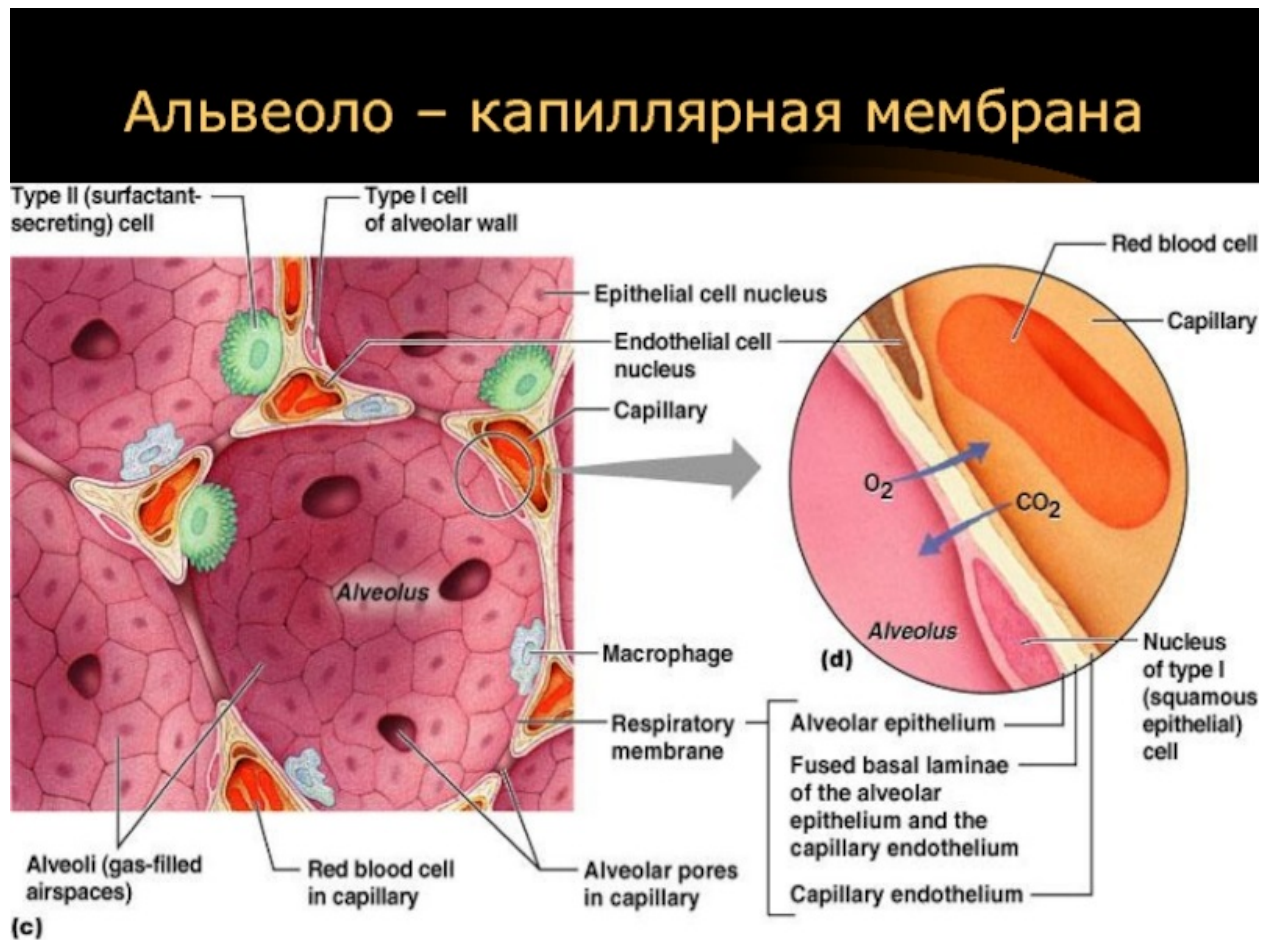
figure 4 alveolus (a sac that contain three types of one layer epithelial cells – pneumocytes) and their capillary-alveolus relation

These epithelial cells are particular to mammalian lungs are involved in gas exchange [}. The respiratory bronchiole extends 2-11 ducts, and each duct opens into 5-6 alveolar sacs, which clusters of alveoli open (refer to figure 2 and 3a, b, and c). Alveoli is forming only up to age 8. Each alveoli has a size of 25nm and 200-500µm [}. Totally in both lungs contain 300 million alveoli. They produce around 70m² [}.

Figure 3: different expressions on the structure and function of cells within the alveolar [] or alveolus {} sac (even the name of the sac is differs, based on authors.

Figure 3a ()





In the figure 3a. More or less this figure is a detail illustration that we have got from internet sources: the author/s divided it into two: “c” (general structure and content of analveolarsac) and “d” (the last site, where CO_2 and O_2 (refer to the scheme of chemical reactions of respiration process) are exchanging through diffusion (refer to figure 3 c. Figure 3b ()

conclusion

- 6.1 Understanding the origin of a pathogen is a half way to combat not only an infection, but also the non-
- 6.2 COVID-19’s pandemic situation
- 6.3 Yes, the mentioned above (6.1 and 6.2) - the prevention based prophylaxis measures that are proportionally
- 6.4 Elaborating why it is impossible to have feasible vaccine for SARS-CoV-2.
 - 6.4.1-6.4.6 (5+1 groups of ours justifications),the forwarded our suggestions - since March 29, 2020 (refer to
 - 6.4.1 before starting a vaccine developing project, which of the followings must have positive answers: is the
 - 6.4.1.1 Certainly, we know that there are two dozen efficacy vaccines (refer to table 3 in point 4.2 and?

6.4.1.2 Are we sure that the unusual large size of the coronavirus do not negatively influence on the

6.4.1.3 Is a vaccinated person can able to produce Ig's types sufficiently and continuously (that can long 6.4.1.4 Within a year, many of those who are exposed to be infected are already infected (around 70

6.4.1.6 Incase, if the virus causes severe symptoms on children and adults, rather with elderly people.

6.4.2. Is it not

6.4.2.2 If we n?

6.4.2.3 It was

6.4.3. Is vaccination issue

6.4.3.1 Almost the

6.4.3.2 There 6.4.3.3 How far the vaccination (shooting) procedures are convenient for the recieipient?

6.4.3.4 How vaccination's

6.4.4 Exceptionality of SARS-CoV-2

(epithelial cells – alveolar cells)?

6.4.4.1 to the: nature of SARS-CoV-2; biochemistry (metabolism processes) concept; and anatomy-physiology exceptionality of the respiratory organs (refer to figure 2-3) that the virus attacking; can a vaccine be effective?

6.4.4.2 We need possible

6.4.4.3 Moreover,

6.4.4.5 Children.

6.4.5 Suggesting

6.4.6 May be better

6.4.7 6.4.5.2 Comparatively

6.4.8 safety;effectively; and

6.4.9

6.4.5.3 Theoretically 6.4.6 Evaluations of: the

6.4.6.1 Is the vaccine ?

6.4.6.2 Are independent 6.4.6.3 Are not included: adverting, political battling, competition, etc. in this vaccination race? If yes, couldn't be lead to bias?

6.4.6.4 If developers

“6.4.4”? biochemistry

6.4.6.5 Did

6.4.6.6 Does the

6.4.6.7 Did

6.4.6.8 Did?

7. Recommendation

We are afraid that: biopharmaceutical products' producers, business oriented scientists; politicians and even countries, which are just oriented not for

7.1 have a tolerance, instead of vaccination, better to implement the following steps for any HROS' infection:

7.5 let us 7.6 Neutrally from: business; political ambitions; and battling countries among each other on the vaccination issues: please let us work together

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