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Review Article

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General effects of virus variants on COVID-19 vaccines reports from Israel

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Indroduction

The coronavirus changes, perceiving genetic changes as the world rushes to vaccinate people as quickly as possible. It is normal for viruses, including SARS-CoV-2, to mutate. But is there a limit to how much the virus can change and still make people sick or can the virus simply develop indefinitely?

It turns out there is a limit, but we do not precisely know what it is; And we can't start predicting all the possible mutations the virus could go through, virologists told Live Science. The number of possible genetic mutations is more significant than all the atoms in the apparent universe. k. "Much of the genome can be replaced" (figure 1).

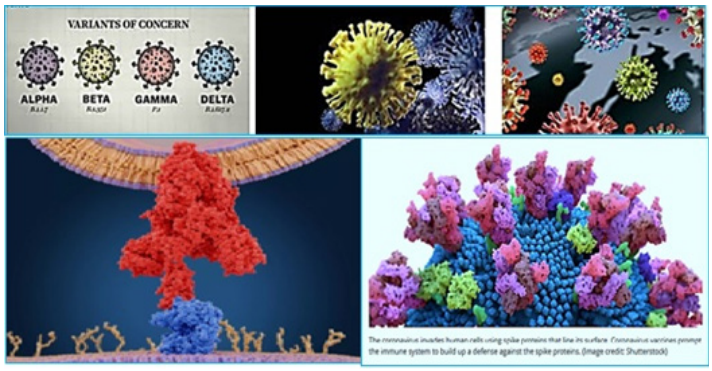

Figure 1: Is there a limit to how much the coronavirus can mutate? The possibilities are seemingly endles [1].

Tracking SARS-CoV-2 Version

All viruses, including SARS-CoV-2, the virus that causes COVID-19, change over time. Most of the changes have little to no effect on the properties of the virus. However, certain changes may affect the characteristics of the virus, such as its ease of spread, the severity of the associated disease or vaccine performance, therapeutic drugs, diagnostic tools, or other public and social health measures.

In collaboration with partners, expert networks, national authorities, institutions and researchers, the World Health Organization has been monitoring and evaluating the evolution of SARS-CoV-2 since January 2020. During the end of 2020, the emergence of increased public health risks led to the characterization of specific variants of interest (VOIs) and variants of concern (VOCs) to prioritize global Monitoring and research, and ultimately to inform the ongoing response to the COVID-19 epidemic.

The World Health Organization and its international networks of experts monitor changes in the virus, so that if significant amino acid substitutes are identified, we can inform countries and the public of any changes needed to respond to the version and prevent it from spreading. Globally, systems have been established and strengthened to identify "signals" of potential VOIs or VOCs and evaluate them based on the risk posed to global public health. In addition, national authorities may choose to designate other versions of local interest/concern.

Reducing transmission through established and proven disease control methods/measures and avoiding enclosures to animal populations are crucial aspects of the global strategy to reduce the occurrence of mutations that have negative consequences for public health.

The current strategies and measures recommended by the World Health Organization continue to work against variants of viruses identified since the onset of the epidemic. Evidence from many countries with the widespread transmission of VOCs has indicated that public and social health (PHSM) measures, including pollution prevention and control (IPC) measures, have been effective in reducing COVID-19 cases, hospitalizations, and deaths. National and local authorities are encouraged to continue to strengthen existing PHSM and IPC means. Leaders also encourage strengthening tracking and sequencing capabilities and implementing a systematic approach to provide a representative indication of the extent of SARS-CoV-2 versions based on the local context and identify exceptional epidemiological events [2] (table 1).

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Additional amino acid changes monitored*	Earliest documente samples
Alpha	B.1.1.7 #	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa May-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020
Delta	B.1.617.2§	G/478K.V1	21A	+S:417N	India, Oct-2020

WHO label§	Pango lineage*	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021
Mu	B.1.621	GH	21H	Colombia, Jan-2021	30-Aug-2021

Table 1: Tracking SARS-CoV-2 variants (credit ref [3]).

Foreword

COVID-19 vaccines are currently under development or approved and expected to provide at least Some protection against new virus versions. Because these vaccines elicit a broad-training response that includes a variety of immune proteins, antibodies, and cells, genetic changes or mutations in the virus should not make the vaccines completely effective. In case each of these vaccines is less effective the vaccines to protect against these versions [4]. In new versions of the COVID-19 virus [5]. The World Health Organization is working with researchers, health [6] professionals and scientists to understand how these versions affect the virus's behavior, including their impact on Vaccine efficacy, if any. See WHO Disease News For up-to-date information on the effects of COVID-19 Virus versions on the effectiveness of the various vaccines. This is an area where evidence remains preliminary and evolving rapidly.

We hear about versions of the SARS-CoV-2 virus that cause COVID-19. How much should we worry about? And do vaccines protect against these versions? Most viral mutations have little effect on the ability of the virus to cause infections and diseases. But depending on where the changes are in the virus's genetic material, they may affect the properties of the virus, such as transmission (e.g., it may spread more or less easily) or severity (e.g., it may cause more or less severe disease).

The Virus Invasion

A SARS-CoV-2 particle penetrates a person's nose or mouth and floats through the airways until it brushes a lung cell that has an ACE2 receptor on the surface. The virus binds to this cell, slips in and uses the cell machines to help make copies of itself. They break out, leave the immune system to try to neutralize or destroy the pathogens, but viruses can prevent or intercept the signals, and buy time for extensive replication before a person shows symptoms [7] (figure 2 and 3).

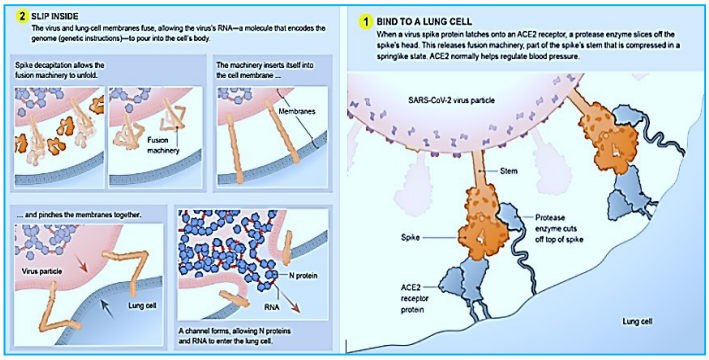

Figure 2: Virus Invasion

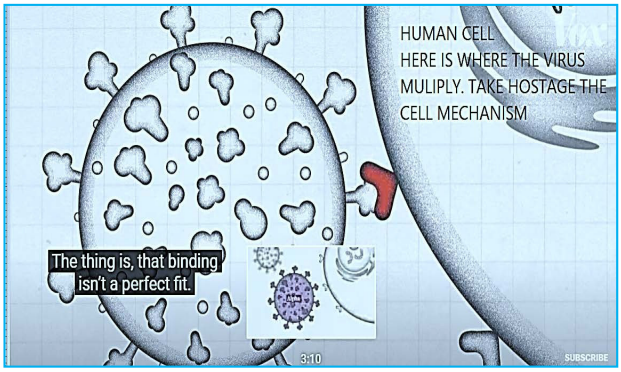

Figure 3: The symbiosis virus human cell. Pike ace2 receptor (red) build a channel for virus genetic molecules to enter the human cell (ref. [8]).

Since the beginning of the last year, we have been following this virus. We know it has undergone many changes, and there have been versions in the past. Now this time, there were a few specific versions reported to the WHO. One identified in the UK, and another effect in South Africa. Delta in Inia and the currently disturbing Omega originates in Peru. They have one thing in common; we call it the N501Y mutation. But otherwise, the two are different. The concern is that these multi-versions were related to an increase in cases in these two countries. And scientists have now researched this and found that these versions tend to spread faster, are more transferable or more infectious. So that's the worrying part. However, it seems that so far, they do not appear to cause more severe diseases or higher mortality rates or different clinical manifestations.

They appear to behave more or less like the previous viruses and cause a similar type of disease.

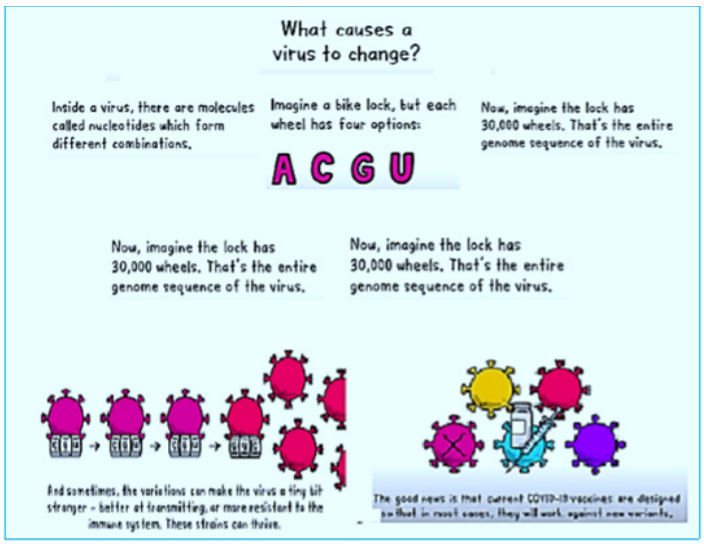

Figure 4: Viruse mutation and vaccines effect (credit ref. [9]).

Although most of the mutations in severe respiratory syndrome corona 2 The genome (SARS-CoV-2) is expected to be harmful or purified quickly or relatively Neutral, a small part will affect the functional properties and may change the infection, diseases Hardware or interactions with host immunity. The emergence of SARS-CoV-2 at the end of 2019 was Followed by a period of relatively evolutionary stagnation lasting about 11 months. Since the end of 2020, However, the evolution of SARS-CoV-2 was characterized by the emergence of groups of mutations, In the context of 'variants of concern', which affect the characteristics of the virus, including transmission And antigenicity, probably in response to the changing immune profile of the human population [10] (Figure 4). There is increasing evidence for reduced neutralization of some SARSCoV-2 versions by Serum after vaccination; However, a greater understanding of defense adapters is It is necessary to assess how this may affect the effectiveness of the vaccine. Despite this, manufacturers Platforms are being prepared for a possible update of vaccine sequences, and this is essential for this Monitoring of genetic and antigenic changes in the global virus population is done on the side Experiments to elucidate the phenotypic effects of mutations. In this review, we summarize the Literature on SARS-CoV-2 spike protein [11] mutations, the major antigen, focusing on their substances (figure 5).

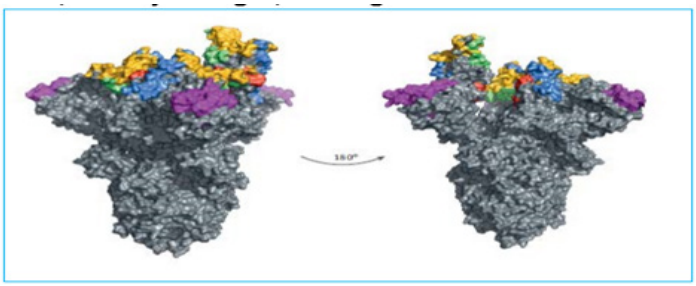

Figure 5: Spike of coronaviruses. The colored are various linear epitopes for different mutations.

The members of the corona family have sharp protrusions that protrude above the surface of their outer shell. These bumps are known as spike proteins. They are basically glycoproteins. This means that they contain carbohydrate (such as a sugar molecule). Pop-up proteins are the ones that give viruses their name. Under the microscope, these spikes can look like a fringe or a crown (and a corona is a Latin crown).

Spike proteins play an important role in the way these viruses infect their hosts. Examples of Corona include those that cause Severe Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS). Their barbed proteins work a bit like shape-locking choices. They can change shape to interact with protein across human cells. These prickly proteins capture the virus in the cell. This allows them to enter these cells. On February 19, 2020, researchers described the three-dimensional structure of the spike protein on the coronavirus behind the 2020 global epidemic. This confirmed that the prickly protein of the new virus is also changing shape. Moreover, it adheres to its target on human cells 10 to 20 times as strong as the SARS spike protein does for the same target. Researchers now say that such a tight grip could help the COVID-19 virus spread more easily from person to person [12]. Affects antigenicity and their binding in protein structure, and discusses them. The context of the mutation frequencies observed in global sequence data systems [13].

The SARS-CoV-2 protein (S) protein is exposed on the viral surface and is the first point of contact between the virus and the host. For these reasons, it represents the main thing. This interaction is the target for Covid Vaccines 19. In recent months, versions of this protein have begun to emerge. Their ability to reduce or evade recognition by S-directed antibodies is a threat Immunological therapies and raises concerns about their implications for vaccine efficacy. To Develop a model capable of predicting the potential effect of S protein mutations on an antibody. The binding sites, a multi-microsecond molecular dynamics, without bias, of a few S-glycosylated versions, glycosylated. It applied a simple structuredynamics-energy-based Strategy to predict potential changes in immunogenic regions in each version. We are recovering Epitopes as known in the D614G reference sequence. By comparing our results, obtained in Isolated S proteins in solution, for recently published data on antibody binding and reactivity in new S versions, we show directly that Changes in protein S, consistently translated into the loss of potentially immune regions. Our findings may be so. Reconnect qualitatively to the decrease characterized by experiments of some of the Abs induced against the dominant result to identify variants. While it is based on the study of spike versions of SARS-CoV-2, our computational epitope prediction The strategy is mobile and feasible to study the immune system in mutants of interested proteins [14] (figure 6).

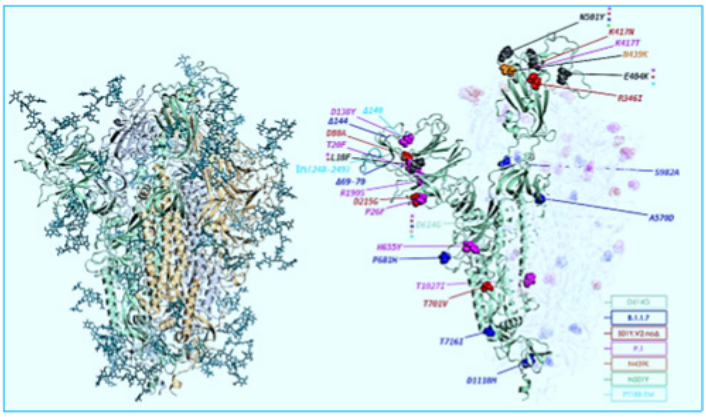

Figure 6: Spike and surrounding epitopes, there is a difference in different mutations (credit ref. [13]).

Israel Faces Corona Pandemic

Corona morbidity in Israel continues with the welcome collapse. In the past week, an average of only about 1,000 new patients per day were counted. There were only 433 patients in the hospitals this morning, about 300 in critical condition. The number of respirators, however, is still high 157. However, there is room for optimism in this sector as well [15]. Every day less than 20 people are defined in critical condition for the first time, compared to over 100 at the height of the morbidity wave, so the number of respirators is expected to continue to decline although some will not recover.

The total number of deaths from the plague reached 8,046 over the weekend. Of these, 1,614 have died since the Variant Delta arrived in Israel. In the field of the deceased, too, the numbers are declining. In the last week, an average of less than 10 people per day, died in Israel, when at the height of the disease wave we stood at about 30. Worldwide, the number of people diagnosed is about 244.2 million and the known number of deaths is 4.96 million.

On a global average, a slight alarming trend has begun in the past week of an overall increase in morbidity from about 405,000 cases per day a week ago to about 412,000 cases today. The mortality graph does not yet show an increase in it, but we do see a halt to the decline that has taken place so far. However, it is important to remember that the mortality graph usually lags behind the morbidity graph by about three weeks, so the trend may well be reversed here as well.

At the top of the daily morbidity table yesterday was the UK with about 45,000 cases, as in their previous record set in July, shortly before they allowed all the restrictions there. Many experts have warned the British that a return policy to their routine could come at a high price, which seems to materialize on the ground. The concern in the UK is that, as in Israel, the effects of the protective decay of the first two doses of the vaccine are also beginning to be seen. Although they started giving a third dose there, the operation is running lazily and many have not yet received a first dose, let alone all the children who cannot yet be vaccinated. The number of people hospitalized in the UK is also rising, albeit slowly due to the vaccines, but the British health system fears that the illness in Corona combined with the flu that is expected to return could collapse the system again. Others argue that the dream of herd immunity through disease is nothing more than a baseless myth, and fear that if morbidity continues to climb there will be no escape from reversing restrictions or any closure during the Christmas period.

In Eastern Europe, too, the situation continues to deteriorate. In Russia, more than 1,000 deaths were recorded yesterday as a result of Corona, the most since the outbreak. The number is particularly disturbing when one remembers that the Russians report very selectively and the real mortality there is at least 3 times greater than the reporter, and some believe that much more than that. About 230,000 have so far officially died in Russia from Corona. Given that the excess mortality rate in Russia between April 2020 and last June was more than double that number. Without counting the dead since June about whom there is still not enough information, it is clear that there is not much connection between the reported number and reality. Although there are suspicions about the vaccines made in Russia in the West, doctors in Russia also see there that the number of unvaccinated patients is increasing relative to their number in the population. Unfortunately, so far in Russia we have vaccinated only about 35 percent of the population, and there are not enough vaccinated to block the spread of the virus.

While the effectiveness of corona vaccines is becoming clearer day by day there are still many who fear the vaccine because of exposure to intimidation and lies. For them, the American CDC published a study that followed vaccines between December and June and found that no serious problems were recorded among vaccinated. On the contrary, vaccines against Corona died less fully vaccinated for all non-corona reasons. This may be because those who rushed to get vaccinated are inherently more cautious than complacent people, but the study clearly shows that the vaccine itself is very safe.

This coming Tuesday, there will be a meeting of the FDA Advisory Committee of Experts. Regarding childhood vaccines between the ages of 5 and 11 on whether to approve the vaccine or not. Data from clinical trials that have already been published indicate that the vaccine is safe and effective for children as well. More about this source textSource text required for additional translation [16] information [17].

Experts in Israel: "The fourth wave is in decline, but, likely, it will not be the last"

"The fourth wave in decline. The fifth wave is certainly possible," says Prof. Hershko: You see the end of the wave, but there are a lot of young people in a difficult situation. I do not understand those who are delayed from getting vaccinated. So a fifth wave is undoubtedly possible. Prof. Alon Hershko, Head of the Internal Medicine and Corona Department at Hadassah Ein Kerem, carefully identifies the beginning of the end of the fourth wave of the Corona. "It seems that the fourth wave is fading. Fortunately, there is a decrease in the number of active patients and the number of infections," says Prof. Hershko, who says that the intensive care unit is still busy with the severe patients of the disease and younger patients than initially expected. "Most of them, like everyone else, are not vaccinated. We also have critically ill patients with acne and because the disease is severe we expect the decline in numbers to take longer" Hershko further notes that the decrease

in the number of critically ill patients is due in some cases to the death of the patients, so the figure is not necessarily encouraging. On the effectiveness of the third vaccine campaign, Hershko says that those who refuse the third vaccine are an incomprehensible phenomenon in his eyes. "It's a short and simple action that is served on a tray of money, and it's an action that protects us and its effectiveness has been proven beyond any doubt and yet people linger. I do not understand." Is the fifth wave on the way? Prof. Hershko recommends being modest when talking about the surprising epidemic that has not been seen before in the near or distant past since epidemic waves arrive at unexpected times as happens with other respiratory viruses that come mainly in winter. "There is a likelihood of a fifth wave, if we do not act in the right way, ie immunization and observance of all the rules." Referring to the interns' protest, Prof. Hershko says that there is agreement on the need to take measures to prevent the interns' burnout, but that a reduction in the interns' working hours necessitates additional manpower and no such increase has been prepared so far. In addition, he says, when such a significant decision is made it is necessary to listen to the field factors, but the relevant factors were not in the discussion on shortening shift hours, "decisions were made here that do not match the needs on the ground." "The most disturbing thing is that the plan needs to be precise. If we hospitals need to get organized for such a fundamental change, we need to get a goal and expectation to get ranked, which is not possible. We do not know what the schedules are. So what do you need to do to get organized? [18].

The Alpha and Omega of COVID-19: Yes, the Pandemic Will End (but Not Soon) [19].

The following is an opinion piece. The views and opinions expressed in this article are those of the author and do not necessarily reflect the official position of Technology Networks.

The news about COVID-19 seems to be flooded with Greek letters. We hear about viral versions like Delta and Lambda, a terminology used when scientists understood the unintentional bias (and sometimes the persecution) associated with the geographical labeling of versions. A century later, considerable frustration remained in some circles, given that the "Spanish influence" apparently began in Kansas. However, Spain took the blame because it did not participate in the First World War and not censored. In addition, the Spanish press reported infections of their royal family (although the British royalty suffered at the time), thus creating a label that continues to this day. To avoid repeating this mistake, the classification of new versions is similar to the hurricane terminology, with alphabetical names of significant new versions.

Like all previous ones, this epidemic and others yet to come begins when a virus infects a person. This "patient zero" is the first victim of an elaborate series of microscopic kidnapping incidents. SARS-CoV-2, like all viruses, is looking for hosts, which it can subdue and maneuver to promote its spread and thus ensure its survival.

But this kidnapping of the body is pretty imperfect. Instead, the production of new viruses by an infected person tends to be rather sloppy, well below the error rate of those trained in Six Sigma. For example, on average, the mechanism that produces SARS-CoV-2 makes about one error per 300,000 nucleotides. Given that the viral genome (all complementary to its RNA) is made up of 30,000 base pairs, this means that about one in ten virus particles released by an infected cell will be a mutation.

Most mutants have no effect or they may even create a defective virus. Indeed, it is understandable to think that a mutation is a good thing since it necessarily limits the number of infectious viruses. The problem is that each infected cell produces something on the order of a thousand offspring. These viruses in turn infect other cells and result in a dramatic expansion in active viral particles.

A closer look reveals that mutations in SARS-CoV02 tend not to be random but focus on a specific viral protein, known as "spike", or "S" protein. If a change in S would allow the virus to become even more skilled at harvesting its prey, then the evolutionary mechanisms of "strong survival" would allow this mutant to become more common. As this new immigrant expands within the population, he eventually earns the nickname of the "variant". The best way to protect yourself and those around you is to get vaccinated.

Even more promising is that those technologies that have proven so effective and easy in generating safe and effective vaccines (i.e., mRNA and adenvirus-based vectors) can be easily modified to address new versions. Similar to influenza vaccines, we may require reinforcements with COVID-19 vaccines updated every few years. Even more promising is that some research suggests that a limited number of mutations can facilitate enhanced function of S. If this is true, it means that once we are all protected from these variations, today's tragedies will become a distant memory.

Achieving this goal may take a year or may take a decade. Either way, the omega of the plague is in sight. To achieve this, we must all work together to develop these new technologies and ensure that the public widely and appropriately accepts them. Antibodies against Corona Viruses are a group of viruses originally from a number of recent outbreaks, including SARS (Severe Acute Respiratory Syndrome) in 2003, MERS (Middle East Respiratory Syndrome) in 2012 and most recently an outbreak of COVID-19, the disease caused by the SARS virus CoV-2. Our collection of antibodies against Corona was obtained mostly from a B-cell sequence of human patients. In addition to the original human IgG1 antibodies, recombinant antibody technology has enabled the production of various engineered formats designed to open up new experimental options for in vitro and in vivo use. This year, the anti-SARS CR3022 tribe has been shown to have a high affinity for the so-called 2019 nCoV. Cloning is now available in our catalog in formats such as IgM, IgA, antibody fragments and IgG in various species and isotopes. You can learn more about the CR3022 clone in our blog post here. The Absolute Antibodies team works hard to support the research and development of coronavirus therapies by supplying related reagents to customers worldwide and providing engineering services and antibody production. We continue to add new reagents to our catalog, including recombinant anti-human immunoglobulin antibodies for COVID-19 diagnosis and ACE2 Fc fusion proteins. Please read about the corona work in our company here, and download our recombinant corona antibody booklet here [20].

Please view our collection of antibodies against our Corona Below

(figure 7).

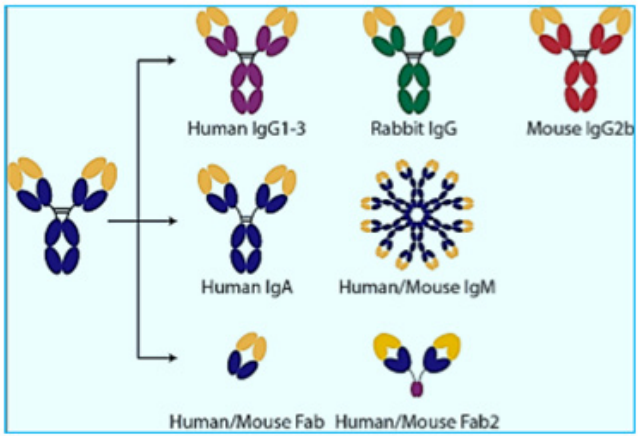

Figure 7: Antibodies (credit ref [21]). The ACE2-targeting monoclonal antibody as potent and broadspectrum coronavirus blocker.

The evolution of viruses, such as SARS-CoV-2, makes coronavirus prevention or treatment strategies highly sought after. Here we report a monoclonal antibody targeting human angiotensin to enzyme 2 (ACE2), 3E8, blocking the S1 subunits and pseudo-virus structures from several coronary arrays, including mutant variants of SARS-CoV-2, SARS-CoV-2 (SARS - CoV-2-D614G, B.1.1.7, B.1.351, B.1.617.1 and P.1), SARS-CoV and HCoV-NL63, without significantly affecting the physiological activities of ACE2 or causing severe toxicity In ACE2 "knock-in" mice. 3E8 also blocked live SARS-CoV-2 infection in the in vitro and preventive mouse model of COVID-19. Cryo-EM and alanine walk studies have revealed the major linking residues in ACE2 interacting with the CDR3 domain of the 3E8 heavy chain. Although a full assessment of safety in non-human primates is necessary prior to clinical development of 3E8, we provided a potent and "broadspectrum" management strategy against all corona viruses that use ACE2 as entry receptors and uncovered an anti-corona epitope in human ACE2 [22].

Previous research has found that the ACE2 RBD linking site does not overlap with its catalytic site [23]. Therefore, it is assumed that targeting the ACE2 RBD linking site with antibodies can block the entry of all ACE2-dependent viruses while saving In the physiological activities of ACE2. Thus, in theory, such antibodies can be utilized to manage current and future coronavirus outbreaks and tolerate viral mutations. By targeting ACE2, in addition, the antibody could be evaluated in HCoV-NL63 people, when COVID-19 patients are no longer available for clinical trials.

To examine the hypothesis, we created a monoclonal antibody, i.e. 3E8, to target the RBD linker site in ACE2. The curing potentials and safety profiles of 3E8 are investigated and the major 3E8 linker sites on the human ACE2 molecule have been revealed by cryo-EM and mutation studies to assist in the search for future drugs [24].

ACE2 as Drug Target of Coronavirus Treatment, Simplified Updated Review

Since its first appearance in December 2019, ongoing updates around the world show that the number of new cases of Corona 2019 (COVID19) is growing rapidly, indicating that not only is COVID-19 showing a rapid spread pattern, but human intervention is necessary to solve it. To date (27-5-2020) and according to the World Health Organization (WHO), the number of approved cases of COVID-19 has crossed 4.5 million with more than 307,500 deaths. Almost all countries were affected by COVID-19, and as a result, various drug trials were conducted, however, targeted treatment remained accessible to the public. Recently, Angiotensin-Converting Enzyme-2 (ACE2) has received some attention for its discovery as a potential COVID-19 binding target.

Blockade of the ACE2 (RBD) receptor domain by a specific ligand can prevent COVID-19 binding, resulting in cellular entry and damage. Comparatively, soluble ACE2, which has a higher affinity for COVID-19 [25], can neutralize COVID-19 without affecting the naturally occurring homeostatic function of ACE2. Finally, ACE2 mutations and their possible effect on COVID-19 binding activity may allow researchers to CE2 represents a promising target to weaken or prevent COVID-19 related cellular vulnerability [26]. Hypertension, kidney failure, thrombosis and diabetes: Mother COVID-1 identify high-risk groups before exposing them to COVID-19.9 endothelial disease? A Diabetes: Is COVID Comprehensive evaluation of clinical and basic findings [27]. How 2-COV-SARS affects the body (Ref. [26]). The CDC has identified elderly and older people suffering Severe chronic medical conditions such as heart, lungs or kidneys Disease at higher risk for COVID-19 [28]. Stated by CDC, early data suggest that older patients are twice as likely COVID19. This is because as people progress in age, theirs changes in the immune system, making it difficult for their bodies to fight diseases and infection, and because many adults are older It is likely to suffer from basic health conditions that cause it It is difficult for them to cope and recover. Age increases the risk of this the respiratory system or lungs will close when he is an adult suffers from COVID-19. The CDC says that the best way to do this To prevent disease is to avoid exposure [29,30] (figure 8).

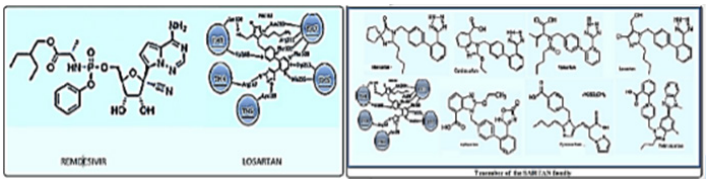

Figure 8: Ace2 Blockers, Losartan family.

The "SARTAN" family consists of a fairly new group of drugs (Losartan, Valsartan, Candsartan, Irbsartan, Telemisartan, eprosartan, azilsartan), all of which act as antagonists in Angiotensin 1 receptor (AT1). AT1 receptor antagonists are Specific Renin-Angiotensin-Aldosterone System (RAAS) Specific. B1 Selective receptor works independently on the ANG II Synthesis pathway, allowing for more selective blocking of Effects mediated by AN1-ANG-II compared to ACE inhibitors.However, by inhibiting the negative feedback mediated by ANG The AT1 receptor of II on the release of renin in the kidneys, these drugs may cause Over-stimulation of the AT2 receptor by enhancing ANG II plasma Levels. Increased mediation of AT2 receptors in Production of blood relays (nitrogen oxide, cGMP, prostaglandins) as well as the antigrowth

properties of this receptor may contribute To further reduction in blood pressure and prevention of Hypertension and remodeling. AT1 receptor antagonists no Inhibiting the breakdown of quinine and cough is not a common side effect. AT1 receptor antagonists are widely used as antihypertensives Medications, especially in patients with type 2 diabetes or intolerance ACE inhibitors. Researchers from the University of Minnesota The medical school has recently started enrolling patients Launched clinical trials with antihypertensive drugs, Losartan, As a potential treatment for those recently diagnosed COVID-19 [12]. Both studies are multi-site trials, one for patients Needs hospitalization and the other for diagnosed patients who Do not need hospitalization [31-36].

The person should isolate and contact a healthcare provider estimate the other causes of their symptoms and possibly re-examine. Until we know more, the CDC advises all patients, whether or not they do They passed COVID-19, to continue to maintain safety Precautions to prevent COVID-19 infection [38]. Cumulative evidence supports the cessation of isolation and Precautions for people with COVID-19 who use established symptoms strategy. This update incorporates recent testimonials from Duration of insulation and recommended precautions for prevention Transferring SARS-CoV-2 to others, without limitation Prolonged isolation and unnecessary use of laboratory testing a means. The ability to recover a virus with the potent of replication Decreases even after the start of symptoms. For patients with mild To moderate COVID-19, a virus did not recover for 10 days after signs [39]. Therefore, recovery of the virus is appropriate Replicate between 10-20 days after the onset of symptoms Documented in people with severe COVID-19, which b Some cases have been complicated by an immune condition [33-37].

However, in a series of patients, it was estimated that 88% and 95% From their samples, they no longer created the same competent virus. After 10 and 15 days, respectively, after the onset of symptoms. Recovery with SARS-CoV-2, not yet been finally confirmed in Every person is replaced so far. If, and if so when, people Maybe re-affected with SARS-CoV-2 remains unknown and is The subject of the investigation. People infected with a person Betacoronavirm virus appears to be associated with susceptibility Again about 90 days after the infection occurs. Hence, for For people who have recovered from SARS-CoV-2 disease, PCR is Cheerful during the 90 days after the start of the infection, probably 22 Represents continued shedding of viral RNA instead of re-infection. Sharp rise in morbidity over the weekend: the number of severe patients reached 324.

Chronicle of failure: This is what the outbreak of the Delta strain in Israel looked like, and this is how the government reacted.

The corona virus returned to our lives long before we could forget it, somewhere in mid-June. From mid-June, the corona began to spread again in Israel. The first local outbreak was in Binyamina, and verified vertebrae began to be discovered elsewhere in the country as well. Since then the government has made only a few individual decisions that have not prevented the further spread of the Delta strain. From 20 patients in June, to more than 200 today: this is what the outbreak in Israel looked like and this is how the government reacted day after day.

According to the decision, starting on August 8, ie starting today, the green label will apply to any number of participants - in halls and event gardens, conferences, cultural and sports events, sitting in restaurants, gyms and studios, hotels, cinemas. The character will also apply in prayer houses with over 50 worshipers. And so we have come this far. Although the spread of the disease will be inevitable, even today Health Minister Horowitz said he will try to avoid as much as possible a locksmith. “This is a very difficult step - I do not accept the arguments that need to be decided now and paralyze the 23 country in advance,” he said. “Closure is a last resort, and as long as there is a chance to avoid it - we will do everything possible.”

According to the Ministry of Health, 3,849 Israelis were diagnosed as positive for Corona in the day between Friday and Saturday. The number of seriously ill patients has jumped by 67 since Friday morning. 16 patients who contracted the virus have died.

Significant increase in patients is difficult over the weekend: just hours before the “green mark” expands in the shadow of the high morbidity and in the background the discourse on additional restrictions being considered in case the third vaccine does not affect morbidity, the Ministry of Health last night (Saturday) Friday to sit. The number of serious patients also rose to 324 and 16 patients died.

Meanwhile, the percentage of positive tests remains the same and stands at 3.79% out of 102,760 tests conducted yesterday. Of the seriously ill patients hospitalized in corona wards across the country, 71 are critical and 49 are respiratory.

Race against time to Avoid Closure

In the Ministry of Health, there have been discussions in recent days about the issue of the number of patients who, if we reach it, will have to “press the brakes,” as Prime Minister Naftali Bennett defined it. This number stands at 700-600 seriously ill patients - this is what we published for the first time on Tuesday in “Ulpan Shishi”. If the doubling rate remains the same and the vaccines do not give their signals as expected, reaching the target number will actually cut the reach to 1,400-1,200 patients difficult - so this is the stopping point set by the Ministry of Health. What, after all, are the caveats to this number? First, if it seems that the effect of the third vaccine will cause a severe decrease in patients - they may not need the quarantine at all because the horizon will look more favorable. Also, if a reduction of the coefficient of infection is seen, i.e. the rate of condition will be lower, it will also severely affect the addition of patients. A week ago, officials and TV commentary played it kooler, “no panic, we are vaccinated, only moderate symptoms, continue with your business as usual”.

Now we hear different music; all that was said and discussed was premature. So now it starts to hit us.

Some years ago, two majour publication regarding the future microbial pasndemic were delibvered: President Obama warned the United States to prepare for a return to schedule in 2014, Bill Gates, and many others warned the world of the impending global pandemic caused by microbes. They demanded that the scientific, industrial, and economic should prepare, some research is done but in low gear, too slowly as we experience today. [40] and more against the outbreak of a virus epidemic. But did not devote the

full energy and means to its preparation. And here it happens. Starting today the green character is expanding: the obligation to wear masks will also apply to gatherings outside Restrictions on places of recreation and leisure are repeated - only the vaccinated, recovering and those who received a negative result will be able to enter. In accordance with the decisions of the Corona Cabinet, the green label will be expanded starting today (Sunday) and will be applied to all entertainment centers to any number of participants. The significant innovation is that unvaccinated people will be required to pay out of pocket for a corona test, which they will have to perform just 24 hours before each entry into public places. In addition, last night we published for the first time data that indicate the vaccine's effectiveness also in the Delta variant: people who have not been vaccinated infect and infect 6.5 times more than those who are vaccinated.

The vaccine is the only thing that mankind has developed to stop the coronary epidemic and also this vaccine is only partially effective. However, there is currently no effective cure for the disease. And it is spread by a person-to-person transition. There is no cure yet for Covid19. Only one treatment, a drug called Remdesivir, has been approved by the F.D.A. for the disease, and researchs suggests it may provide only a modest benefit to patients.i Vaccine refusers are currently the most dangerous component that spreads the disease. And should be vaccinated by coercion. The current law allows them to evade the law. Therefore, the existing law must be improved and these refusers must be brought to the right path in order to maintain public health. If not in persuasion then in coercion that objects of life we are.

It seems to me that those who refuse the vaccine are treated equally: Well: There is currently no cure for corona disease. Only the drug Ramadsibir gives a partial solution. The only way to slow down the spread of the virus today is solely with a vaccine. Whoever does not accept this may be his right when it comes to himself but because his refusal causes harm to other citizens. These elements must be fought in the ways of crime prevention. Either vaccinate them or deprive them of the benefits that vaccinators have. There is no other way but to force if objects of life we are. The virus does not understand democracy, law and other vegetables. It just strives to reproduce and change. It's that simple. And those who refuse do not have hope. And the prophet Isaiah has already said: Come, my people, come in your chambers and close your door for you, my dear, almost for a moment until you pass by.

Coronavirus Drug and Treatment Tracker [41]

Remdesivir,Favipiravir (also known as Avigan), Molnupiravir, Recombinant ACE-2, Ivermectin. Oleandrin, Lopinavir and ritonavir, Hydroxychloroquine and chloroquine.

Mimicking the Immune System [42]

Convalescent plasma, Monoclonal antibodies, Bamlanivimab and etesevimab, REGEN-COV, Sotrovimab,Interferons (table 2).

New additions and recent updates

July 30	The F.D.A. approves **REGEN-COV** for the prevention of Covid-19 in people exposed to the virus.
June 29	The F.D.A. authorizes **Baricitinib** for emergency use in hospitalized patients who need supplemental oxygen.
June 26	The F.D.A. pauses the use of **bamlanivimab and etesevimab** because of the rise of Beta and Gamma coronavirus variants.
June 25	The F.D.A. authorizes **tocilizumab** for emergency use in hospitalized patients.
May 26	The U.S. warns that some coronavirus variants are proving resistant to the combination of **bamlanivimab and etesevimab**.
May 18	The F.D.A. pushes back against claims that **leronlimab** is effective against Covid-19.

This list provides a snapshot of the latest research on the coronavirus, but does not constitute medical endorsements. Always consult your doctor about treatments for Covid-19.

Table 2: Remdsivir, Chloroquine, Lopinavir, Ribavirin, Favipiravir Experimental Agents or a Cure for COIVD 19? [43].

EXO-CD24

Researchers in Israel conducted a small pilot study on a drug called EXO-CD24 to see if it could inhibit cytokine storms. In February 2021 they announced that 31 of the 35 hospitalized patients had been discharged after three to five days of drug treatment. But it was impossible to know if the drug helped them, because the experiment was not large, blind or placebo-controlled. These preliminary results were also not published in a journal or published online.

However, Israeli Prime Minister Benjamin Netanyahu called EXO-CD24 a "miracle cure." In March, Brazilian President Jair Bolsonaro announced that his administration intended to sign a memorandum of understanding for a nasal spray version of EXO-CD24, which he said could appear as "the real solution to Cubid treatment."

The Quest for Remedy

The quest for remedy is on highest volume. However, until today no real remedy is allocated. The only effective drug compound, Remdesivir, is considered only as a palliative drug.

Recent spread of SARS-CoV-2 has sparked significant health concerns of emerging infectious viruses [44]. Drug reuse is a tangible strategy for developing antiviral drugs in a short period of time. In general, drug reuse begins with a virtual scan of approved drugs using mooring simulations. However, the actual damage rate is low, and most of the predicted compounds are false positives. To address the challenges, an advanced virtual screening report with pharmacopoeial screening before and after anchoring 6,218 drugs to COVID-19. It should be noted that 7 of 38 compounds showed efficacy in inhibiting SARS-CoV-2 in Vero cells. Three of them were also found to inhibit SARS-CoV-2 in human Calu-3 cells. Furthermore, three drug combinations showed strong synergistic effects in inhibiting SARS-CoV-2 at their clinically achievable concentrations.

Following the Science Isn't Curing Covid Confusion [45]

Mixed messages about the delta variant show (again) that experts can measure risk, but can't tell people how much danger to accept.

908/5000 Translation results The Delta version is the new scare story of the plague. Its spread to the U.S. did not lead to an increase in the number of deaths or overcrowded wards in hospitals, but the news of its rainfall in the July 4th parade. Public health experts responded with an awkward spray of conflicting recommendations, conflicting information and seemingly inconsistent scientific facts. The result, as in the earlier stages of the Covid-19 blow, was unnecessary confusion and rage. Should vaccinated people wear masks? Depends on who you ask. Can economic life return to normal? Experts' opinions change. Some say it depends on local conditions. Dr. Anthony Pauchi, the White House medical adviser, says everyone should rub shoulders with Alabama, which has a low vaccination rate and typhoid fever. The Delta version emerged as a threat around the same time that U.S. public health authorities encouraged people to make their own decisions about corona virus safety instead of pushing for uniform standards of behavior. "That they stopped doing because of the plague.

Delta Variant and Vaccines

There are two very resonable reasons to get vaccinated. The first is to protect yourself from a serious illness if you catch the infection. We know that there is a certain percentage of people from all age groups who suffer from a serious illness and you may have a chance of dying from this disease. And we want to protect that. So, that's why you want to get vaccinated, in the first place. But second, if you get vaccinated and yes, you may still get the infection because we know these vaccines will not protect you 100% from the infection. So there is a small risk of getting infected and you can pass it on to others.

Why do one wants to take the risk of doing it? Why do one want to be one person in the transfer chain? We need to do today, to break the transmission chains and gain control of this pandemic. So that's why we say get vaccinated as soon as you can access your vaccine when it's your turn and continue to take all precautions so that you completely protect yourself as well as protect others around you.

The Airport Factor: *Assessing the Impact of International and National Aviation Mobility on the Spread of Covid-19.*

This project is designed to evaluate the impact of air travel on the rate of Covid-19 infection. We ask: To what extent does the prevalence of the virus depend on the volume, origin and range of passengers entering the airport areas in the months leading up to the outbreak, once we examine the compositional factors of the areas and their policy against epidemics? We address both flight data and local demographic, socio-economic and policy characteristics, focusing on sub-national areas hosting major national and international airports. We will focus on the three most affected global regions from Covid-19 in early 2020: Europe, North America and China. By assessing the impact of air travel connectivity relative to other factors, our research can help design travel restrictions that meet the spread of future epidemics while minimizing the socio-economic implications of reduced mobility [46].

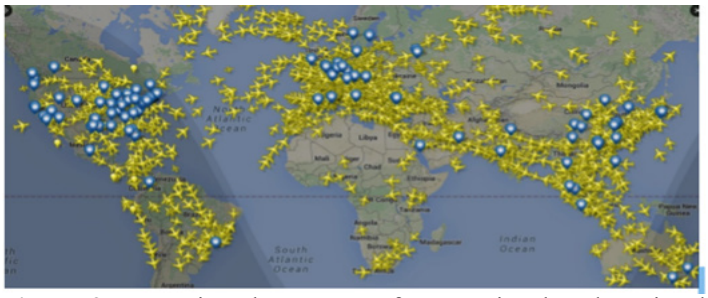

Figure 9: Assessing the Impact of International and National Aviation Mobility.

We estimate [47] the on earth spread of COVID-19 by international air travelers ahead of the World Health Organization (WHO) declaration on March 11, 2020 that the world is officially experiencing an epidemic - defined as the "global spread of a new disease". Our estimates suggest that the "global spread" of the disease occurred weeks before the World Health Organization declaration. In particular, we estimate that global exports of COVID-19 cases began to rise at an accelerated rate on February 19, 2020, three weeks before the World Health Organization declaration. By the end of month February, about two weeks before the World Health Organization declaration, more than five cases of COVID 31 19 per day or almost 40 per week had been issued worldwide by air travel.

10 Million passengers expected to pass through Tel Aviv's [48] airport in the next four months.

August 22 is predicted to be Ben Gurion Airport's busiest day, with 110,000 passengers expected to board or disembark from 600 flights Some 10 million passengers are to pass through Israel's Ben Gurion Airport this summer, the Israel Airports Authority (IAA) announced monday (figure 10).

Figure 10: Passengers at Ben Gurion Airport.

The airport will see 2.6 million travelers in July, according to IAA, and another 2.8 million in August. In September, just before the Jewish New Year (Rosh Hashanah), 2.3 million passengers will pass through the country's largest airport. Another 2.28 million passengers are expected to travel through its gates in October.

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