

# Remdsevir, Chloroquine, Lopinavir, Ribavirin, Favipiravir Experimental Agents or a Cure for COIVD 19? Report

#### Shimon Shatzmiller\*

Department of Biological Chemistry, Ariel University, Ariel, Israel

\*Corresponding Author: Shimon Shatzmiller, Department of Biological Chemistry, Ariel University, Ariel, Israel.

Received: March 20, 2020; Published: May 29, 2020

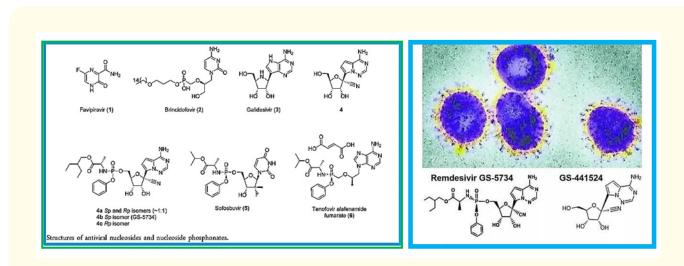


Figure 1

Coronaviruses (Co Vs) affecting upper respiratory tract were first identified in humans in mid-1960 [1]. In late 2002, there was emergence of a life threatening CoV of atypical pneumonia, named severe acute respiratory syndrome CoV (SARSCoV).

FDA approves first rapid COVID-19 Test [2] March 21, 20206:38 PM ET.

The Food and Drug Administration has approved the first rapid point- of-care COVID-19 test, that can deliver results in less than an hour.

Cepheid, a Silicon Valley diagnostics company, made the announcement on Saturday, saying it has received emergency authorization from the government to use the test.

The number of corona patients in Israel rose to 945, 20 of them in serious condition, 3,030 medical staff in isolation.

More than 167,000 have fallen in Corona in the world.

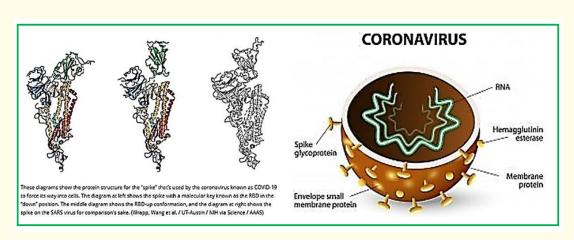


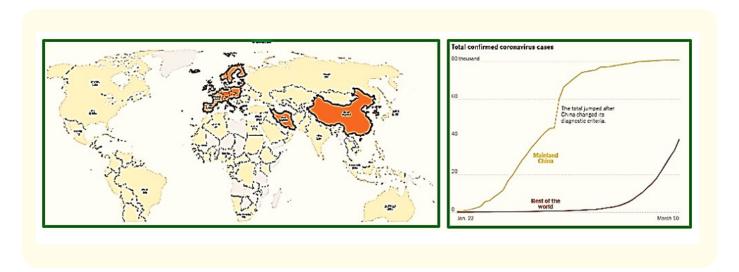
Figure 2: Scientists create atomic-scale map of coronavirus' deadly weapon, pointing out a path to fighting it [3].

## The complete data

While China and South Korea are trying to recover, the focus of the spread of the Corona virus has shifted to Italy, Spain and Iran, where the infectious records are breaking. The highest mortality rate (7.3%) was recorded in Italy - the largest of the countries with thousands of patients.

## 16.03.20, 00:44

The Coronavirus continues to spread around the world at an alarming rate, and as of Sunday evening, more than 167,000 people were infected in 156 countries. The death toll worldwide is more than 6,450 people. In Israel, too, there was an increase, and the number of patients last night was 213, compared with exactly 39 a week ago.



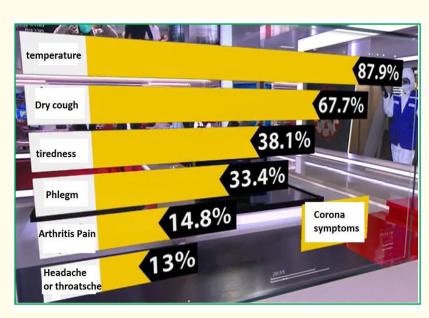


Figure 3: The main spread of COIVD worldwide 17 March 2020 [4].

## A cure for the Chinese corona virus? [5,6]

The drug prepared in California's Gilead Laboratories to fight your EBOLA virus and failed to do so turned out to be effective against the current Chinese corona virus. The Chinese health authorities have applied for this material. The substance blocks the synthesis of RNA in the cells of the cells. Already rescued one patient in the US from death and brought him to recovery. The material was one of hundreds of stonemasons that failed to reach their original purpose [7].

Remdesivir (6) [8] Discovered by Gilead (California) is a nucleotide surrogate [9,10].

Remdesivir blocks RNA synthesis in the cell.

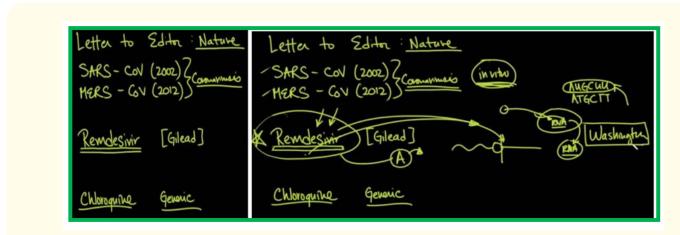


Figure 4

#### The agents remdesivir and chloroquine effectively inhibit the recently emerged coronavirus (2019-nCoV) in vitro [11]

Findings indicate that the agents remdesivir and chloroquine are biologically effective in the control of 2019-nCoV infection *in vitro*. Since these compounds have been used in human patients with a safety track record and shown to be effective against various ailments, we suggest that they should be assessed in human patients suffering from the novel coronavirus disease.

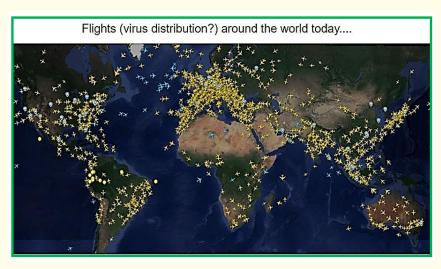


Figure 5

## Remdesivir

Health officials from WHO have noted that Gilead's remdesivir has demonstrated efficacy in treating the coronavirus infection.

Health officials from WHO have noted that Gilead's remdesivir has demonstrated efficacy in treating the coronavirus infection.

Remdesivir is a broad-spectrum antiviral drug originally designed to target Ebola. Researchers have found that remdesivir is highly effective at fighting the novel coronavirus. This treatment is not yet approved in humans, but two clinical trials for this drug have been implemented in China. One clinical trial was recently also approved by the FDA in the United States.

#### Chloroquine

WASHINGTON - The US is fast-tracking the anti-malarial drug chloroquine for use as a treatment against the new coronavirus, US President Donald Trump said Thursday.

"We're going to be able to make that drug available almost immediately, and that's where the FDA [Food and Drug Administration] has been so great," Trump told reporters [12].

Doctors can also use a number of different therapies to limit the immune system's response to viruses, like fever and inflammation, which can sometimes cause more damage to a patient than the virus itself. Anti-inflammatory drugs like corticosteroids and chloroquine are often used to lessen these symptoms. Chloroquine, a widely-used anti-malarial and autoimmune disease drug, has recently been reported as a potential broad spectrum antiviral drug [8-10]. Chloroquine is known to block virus infection by increasing endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-CoV [13-16].

"Chloroquine, a relatively safe, effective and cheap drug used for treating many human diseases including malaria, amoebiasis and human immunodeficiency virus is effective in inhibiting the infection and spread of SARS CoV in cell culture. The fact that the drug has significant inhibitory antiviral effect when the susceptible cells were treated either prior to or after infection suggests a possible prophylactic and therapeutic use".

Chloroquine is a drug that's used to fight malaria and autoimmune diseases. It's been in use for more than 70 years Trusted Source and is considered safe. Researchers have discovered that this drug is effective at fighting the SARS-CoV-2 virus in studies done in test tubes. At least 10 clinical trials Trusted Source are currently looking at the potential use of chloroquine as an option for combating the novel coronavirus.

Gilead Sciences has partnered with Chinese health authorities to conduct a randomized Phase III clinical trial to evaluate the use of the antiviral drug candidate study (GS-5734) for the potential treatment of corona virus.

According to a publication published in the New England Journal of Medicine (NEJM), the drug was found to show encouraging results when given to the first U.S. patient infected with the Wuhan virus.

The US patient was re-treated for compassion on the seventh day of illness and his clinical condition was confirmed to improve on day eight.

In Beijing, China, the new placebo-controlled third phase trial of Gilad's drug will be performed at Friendship Hospital. The study should enroll 270 patients with mild to moderate pneumonia caused by the coronoid virus.

#### Lopinavir

The severe acute respiratory syndrome (SARS, COIVD 19) is a life-threatening viral infection caused by a positive, single stranded RNA virus from the enveloped coronavirus family. Associated with fever, cough, and respiratory complications, the illness causes more than 15% mortality worldwide. So far, there is no remedy for the illness except supportive treatments. However, the main viral proteinase has recently been regarded as a suitable target for drug design against SARS infection due to its vital role in polyproteins processing necessary for coronavirus reproduction.

Figure 7

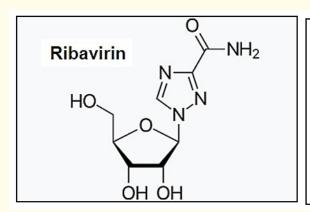
#### Lopinavir; A potent drug against coronavirus infection: insight from molecular docking study

**Background:** The severe acute respiratory syndrome (SARS) is a life threatening viral infection caused by a positive, single stranded RNA virus from the enveloped coronaviruse family. Associated with fever, cough, and respiratory complications, the illness causes more than 15% mortality worldwide. So far, there is no remedy for the illness except supportive treatments. However, the main viral proteinase has recently been regarded as a suitable target for drug design against SARS infection due to its vital role in polyproteins processing necessary for coronavirus reproduction [17].

#### Ribavirin

**Objectives:** The present in silico study was designed to evaluate the effects of anti-HIV-1 proteases inhibitors, approved for clinical applications by US FDA, on SARS proteinase inhibition.

The potential for CoVs to cause significant human disease is well demonstrated, with six known HCoVs-HKU1, OC43, NL63, 229E, SARS- CoV and MERS-CoV-causing colds, pneumonia, systemic infection, and severe or lethal disease [18]. Four of these viruses have been identified in just the last 10 years, with two, SARS-CoV and MERS-CoV, causing lethal respiratory and systemic infection [1,3-6]. Studies over the past decade have expanded the known phylogenetic, geographic, and species diversity of CoVs, and support multiple emergence events of CoVs into humans from bats and other zoonotic pools. The most recent evidence for CoV trans-species movement comes from the emergence of the novel MERS-CoV. From April 2012 to June 2013 MERS-CoV has caused 72 laboratory-confirmed cases and up to 50% mortality from severe respiratory and systemic disease in at least 8 countries, with evidence for human-to-human transmission. MERS-CoV is most closely related to the bat CoVs HKU4 and HKU5, and the recently identified receptor dipeptidyl peptidase 4 (DPP4) is present on both human and bat cells, providing a compelling argument that zoonotic CoV infections resulting in severe human disease may be more frequent events than previously thought. Because of the lack of epidemiological data, it remains unknown whether multiple introductions from a zoonotic source or human transmission of a mild or asymptomatic disease is responsible for these continuing cases of sporadic severe infections. However, based on the high mortality rates associated with SARS-CoV and those reported for MERS-CoV, this novel virus potentially represents a serious threat to global health for which no vaccines or therapeutics currently exist.



Ribavirin, also known as tribavirin, is an antiviral medication used to treat RSV infection, hepatitis C and some viral hemorrhagic fevers. [1] For hepatitis C, it is used in combination with other medications such as simeprevir, sofosbuvir, peqinterfero n alfa-2b or peqinterferon alfa-2a. [1] Among the viral hemorrhagic fevers it is used for Lassa fever, Crimean—Congo hemorrhagic fever, and Hantavirus infection but should not be used

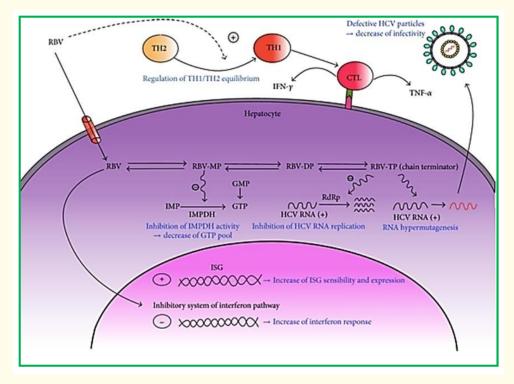


Figure 8

The ribavirin carboxamide group can cause the natural nucleoside drug to resemble adenosine or guanosine, depending on its rotation. For this reason, when ribavirin is incorporated into RNA, as a base analogue of adenine or guanine, it aligns equally with either uracil or cytosine, resulting in mutations in RNA-dependent RNA replication in viral RNA. Such hyper-emotion can be fatal to RNA viruses. Ribabirin (1-  $\beta$ -D-ribofuranosyl-1,2,4-triazole-3-carboxamide) is a guanosine nucleotide analogue and a broad spectrum direct antiviral agent (DAA). Ribabirin was discovered 30 years ago and is effective *in vitro* and/or *in vivo* against some RNA or DNA viruses [1-3]. This DAA is most commonly used to treat hepatitis C virus (HCV), severe human respiratory virus (RSV) infection, some blood fever, and more

recently for immunosuppressed patients infected with hepatitis E virus (HEV) [4]. Based in part on the authors' work [5-16], this article focuses on the context of HCV infection in the ribavirin mechanism of action, its efficacy according to different therapeutic schedules, and its side effects and toxicity. Because clinical and pharmacological data indicate that adequate and early exposure to ribavirin improves the virologic response, the relevance of ribavirin drug monitoring in different patient populations and different therapeutic situations, including new promising treatment strategies, is also discussed.

While initial antiviral activity of RBV against CoVs was not mutagenic, ExoN2 CoVs treated with 5-FU demonstrated both enhanced susceptibility during multiplication, as well as decreased specific infection, consistent with 5-fluorouracil (5-FU); Functions as a mutagen. Comparison of next-generation and next-generation sequences of 5 FU-treated SARS-CoV populations revealed a 16-fold increase in ExoN2 population mutations compared to ExoN +. Ninety percent of these mutations represented transitions A: G and U: C, which correspond to the 5-FU combination during RNA synthesis.

Together our results provide direct evidence that CoV ExoN activity provides a critical proofing function during virus replication.

Furthermore, these studies identify ExoN as the first viral protein that differs from the RdRp that determines the susceptibility of RNA viruses to mutagens. Finally, our results show the importance of ExoN as a target for inhibition, suggesting that small molecule inhibitors of ExoN activity could potentially be Co-CoV therapy in combination with RBV or RNA polynomials [19-21].

Lethal mutagenesis is beyond the direction of virus extinction mediated by enhanced mutation rates during viral genome replication and is currently being investigated as a new antiviral potential strategy. Viral load and virus capacity are known to affect the extinction of the virus. Here we examine the effect or multiplicity of infection (MOI) on the progeny production of some RNA viruses under enhanced mutagenesis. The effect of basal mutant 5-fluorouracil (FU) mutation on the replication of the rhinovirus chorionitis virus (LCMV) can also delay progeny production and extinction of the virus in infections with high multiplicity of infection (MOI) or moderate titration without extinction in MOI. The effect of MOI is similar to the LCMV and vascular vesicular (VSV) virus, but minimal or absent to the oral and abdominal disease (FMDV) and encephalitis virus (EMCV). The increase in Shannon mutation frequency and entropy (mutant spectrum complexity) as a result of virus transfer in the presence of FU, was more pronounced in low MOI for LCMV and VSV, and high MOI for FMDV and EMCV. We present an extension of the deadly defection model that agrees with the experimental results.

#### Scientists demonstrate how COVID-19 infects human cells [22]

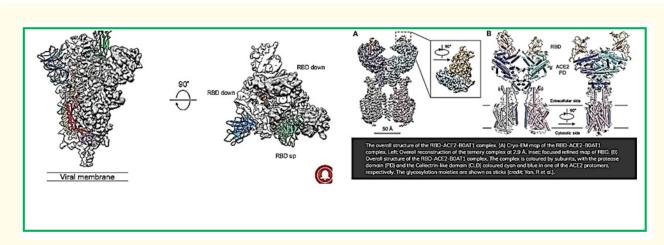


Figure 9

123

Researchers have used cryogenic electron microscopy to show that coronaviruses enter human cells through an interaction with angiotensin-converting enzyme 2 (ACE2).

Scientists demonstrate how COVID-19 infects human cells.

Researchers have used cryogenic electron microscopy to show that coronaviruses enter human cells through an interaction with angiotensin-converting enzyme 2 (ACE2).

Scientists exploring how coronaviruses like COVID-19 infect human cells have shown that the SARS-CoV-2 spike (S) glycoprotein binds to the cell membrane protein angiotensin-converting enzyme 2 (ACE2) to enter human cells.

COVID-19 has been shown to bind to ACE2 via the S protein on its surface. During infection, the S protein is cleaved into subunits, S1 and S2. S1 contains the receptor binding domain (RBD) which allows coronaviruses to directly bind to the peptidase domain (PD) of ACE2. S2 then likely plays a role in membrane fusion.

#### The hope?

Gilad is said to expedite Remdesivir's laboratory tests against 2019-nCoV samples and is working with Chinese authorities.

The company said in a statement: "Gilad is working closely with World Health Authorities to respond to the outbreak of the novel Coronavirus (2019-nCoV) through the appropriate experimental use of the compound design for our investigations. "While there is no antiviral data for remdesivir showing anti-2019- nCoV activity at this time, data available in other coronaviruses gives us hope." Remdesivir is not yet licensed or approved. *In vitro* and *in vivo* analysis in animal models demonstrated drug activity against Middle Eastern Respiratory Syndrome (MERS) and Severe Respiratory Syndrome (SARS), which are viral pathogens with structural similarity to the 2019-nCoV. The Hawahan virus currently lacks specific drugs or treatments. Gilad's drug is among the first to enter clinical trials [23].

Gilead Sciences has partnered with Chinese health authorities to conduct a randomized Phase III clinical trial to evaluate the use of the antiviral drug candidate study (GS-5734) for the potential treatment of corona virus. The company originally developed the drug to treat the Ebola virus, but it was found to be ineffective.

Preclinical tests have revealed that the drug may help treat the new 2019-nCoV virus. According to a publication published in the New England Journal of Medicine (NEJM), the drug was found to show encouraging results when given to the first U.S. patient infected with the Wuhan virus. The US patient was re-treated for compassion on the seventh day of illness and his clinical condition was observed to improve on day eight. In Beijing, China, the new placebo-controlled third phase trial of Gilad's drug will be performed at Friendship Hospital. The study should enroll 270 patients with mild to moderate pneumonia caused by the coronoid virus. Gilad is said to expedite Remdesivir's laboratory tests against 2019-nCoV samples and is working with Chinese authorities. The company said in a statement: "Gilad is working closely with World Health Authorities to respond to the outbreak of the novel Coronavirus (2019-nCoV) through the appropriate experimental use of the compound design for our investigations. "While there is no antiviral data for remdesivir showing anti-2019-nCoV activity at this time, data available in other coronaviruses gives us hope." Remdesivir is not yet licensed or approved. *In vitro* and *in vivo* analysis in animal models demonstrated drug activity against Middle Eastern Respiratory Syndrome (MERS) and Severe Respiratory Syndrome (SARS), which are viral pathogens with structural similarity to the 2019-nCoV. The Hawahan virus currently lacks drugs or treatments.

#### **Favipiravir**

Favilavir, the first approved coronavirus drug in China [24].

Figure 10

The National Medical Products Administration of China has approved the use of Favilavir, an anti-viral drug, as a treatment for coronavirus. The drug has reportedly shown efficacy in treating the disease with minimal side effects in a clinical trial involving 70 patients. The clinical trial is being conducted in Shenzhen, Guangdong province.

Phiabiravir, also known as T-705, Avigan, or favilavir is an antiviral drug developed by Toyama Chemical (Fujifilm Group) from Japan with activity against many RNA viruses. Like other experimental antivirals (T-1105 and T-1106), it is a pyrazine carboxamide derivative. Experiments in animal fever virus have shown activity against influenza viruses, the West Nile virus, yellow fever virus, oral and oral disease as well as other flaviruses, rabbits, virus builders and alphaviruses. Activity against enteroviruses and fracture fever virus was demonstrated. Favipiravir showed limited efficacy against virus affinity in animal studies, but was less effective than other antiviruses such as MK-608. The agent also showed some effectiveness against rabies, and it has been used experimentally in some people infected with the virus.

In February 2020, Pipiravir was investigated in China for experimental treatment of COVID-19 disease (new coronavirus virus). On March 17, officials suggested bin Wuhan and Shenzhen.

#### Mechanism of action revealed for remdesivir, potential coronavirus drug

Researchers have demonstrated how the drug known as remdesivir works, presenting the viral RNA polymerase of coronaviruses as a target for these conditions [25].

Gilead Sciences has partnered with Chinese health authorities to conduct a randomized Phase III clinical trial to evaluate the use of the antiviral drug candidate study (GS-5734) for potential treatment of corona virus.

The company originally developed the drug to treat the Ebola virus, but it was found to be ineffective. Preclinical tests have revealed that the drug may help treat the new 2019-nCoV virus.

According to a publication published in the New England Journal of Medicine (NEJM), the drug was found to show encouraging results when given to the first U.S. patient to contract the Vaughan virus.

The American patient was re-treated with compassion on the seventh day of the illness and his clinical condition was found to improve on the eighth day.

In Beijing, China, the new third-phase placebo-controlled trial of Gilad's drug will be performed at Friendship Hospital. The study should enroll 270 patients with mild to moderate pneumonia caused by the coronoid virus.

Gilad is scheduled to expedite Remedizier's laboratory tests against 2019-nCoV samples and is working with Chinese authorities.

The company said in a statement: "Gilad is working closely with World Health Authorities to respond to the outbreak of the novel Coronavirus (2019-nCoV) through appropriate experimental use of the compound design for our investigations.

"While there is no antiviral data for remdesivir showing anti-2019 nCoV activity at this time, data available in other coronaviruses gives us hope".

Remdesivir is not yet licensed or approved. *In vitro* and *in vivo* analysis in animal models demonstrated drug activity against Middle Eastern Respiratory Syndrome (MERS) and Severe Respiratory Syndrome (SARS), which are viral pathogens with structural similarity to the 2019- nCoV.

The Hawaiian virus currently lacks medication or treatments.

Using the polymerase enzymes from the coronus virus that cause MERS, scientists at Gut's lab have discovered that the enzymes can incorporate remdesivir, similar to an RNA building block, into new RNA strands. Shortly after adding remdesivir, the enzyme stops being able to add more subunits of RNA. This stops the genome duplication.

Scientists speculate that this may happen because remdesivir- containing RNA takes on an odd form that does not fit the enzyme. To make sure, they will need to collect structural data on the recently synthesized enzyme and RNA. Such data can also help researchers plan future drugs for even more activity against polymerase. They offer the coronavirus viral RNA polymerase as a target.

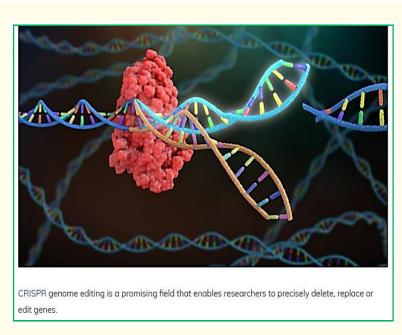


Figure 11

Editing CRISPR Genome is a promising field that allows researchers to delete, replace, or edit genes accurately.

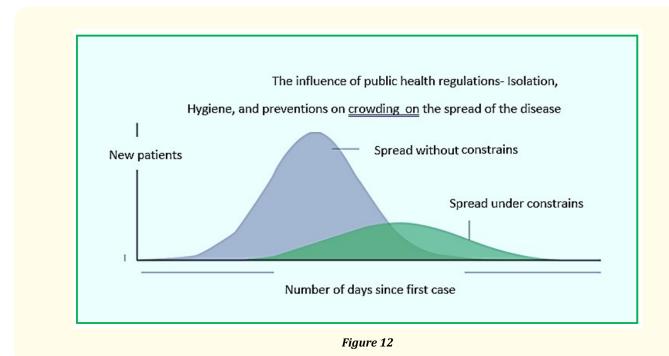
CRISPR-Cas is a prokaryotic defense system whereby bacteria use RNA molecules and proteins related to CRISPR (Cas) to target and destroy the DNA of invading viruses. These molecular machines have been redirected by researchers to target and edit specific sections of any DNA, whether bacterial or human.

#### **CRISPR technology challenges**

Despite the success of CRISPR, the technique is far from refined. In some situations, the editing process can cause a change in off-target DNA and cause unwanted effects. Also, CRISPR-Cas9 is a large molecular complex, with both a Cas9 nucleus and a single transgenic RNA (sgRNA) guide that helps the nucleus locate its target. This can make it difficult to deliver to the cell nucleus, where CRISPR needs access to DNA, which is difficult.

## Why are we trying to delay the Corona instead of letting it "hit" us and pass quickly?

The number of corona patients in Israel is rising, but government steps are in the meantime preventing uncontrolled expansion. If we manage to moderate the rate of infection, we may find that the health system can cope with its climax.



## And what will happen after the isolation is exhausted and infectious cases begin to emerge that are unclear as to their origin?

Then the next phase of "social remoteness" will take effect. Blitzer explains: "The first stage in social distancing is the prevention of mass gathering, such as games and music performances, because one such event can dramatically change the situation. They have already begun to do so (ban on gathering of more than 5,000 people; RL) and I estimate That the numbers will decrease.

"The next step will include a recommendation to close smaller gatherings, to theaters and small events. More advanced stages of social remoteness are more profoundly violating daily life - changes in school, workplace and public transport - and these will come.

#### **Final Remarks**

You can assume that as the plague deepens. More sticking. More patients. More victims. The separation between humans will increase as this is the only way to fight the virus reproduction. I hear that there is a complete closure on Israel. It's just a matter of time. Because the virus, with all the hardships we make it so that it does not migrate from person to person, can escape and wander to its victims. There is no administrative pithrow for the plague but a microbial affliction.

Facing the virus with various failures in its reproductive path or bringing in the "virus-eaters" arena in the form of macrophages or dendrites or chemicals and drugs that stand in the way of the virus within the human body. Does that sound like a fiction movie? This will be the reality. Something new was happening. Infection with children. The children pass the virus easily because their immune system is stable and properly functioning. But in the elderly the situation is already different. In addition to all those "childhood diseases" that have been incarcerated in the body and employ, all the lives of the elderly, their immune systems in containing those measles, mumps, chickenpox and herpes viruses, they already have chronic illnesses and are weak and living with assistive medicine. They are the ones infected with the viruses that the children spread in the space we exist in. And they can cause the death of the elderly and so the children should be prevented from getting infected. And that justifies the quarantine on the children. And postponing schooling until the rage passes.

The cry on the Corona is one: it is neither a smartphone nor a car navigation program. It's biotechnology and biology and medicine and it's just neglected because there's no quick profits in it. Simple and for that matter.

That is why we stand and are now all over the world before a broken trough. It will take years to close the gap.

But from reading the scientific articles I am optimistic. Scientists have come up with some solutions to eradicate the Corona family's cruel virus. Let them work and don't tell them "bring money from home," as you have for years. Shame and shame. There is a "big dock" that is a nice virus, kills only 5% and mostly elderly people. But unfortunately, biotechnology and medicine mostly require a lot of time.

The virus can only be curbed by drugs and vaccines. All administrative steps may slow down the spread but not stop it completely.

And, as in other cases, it is the salvation of God that will bring the virus to rest, like those in AIDS and Ebola. And he said in the pomp, "And the salvation of God comes in a blink of an eye....."

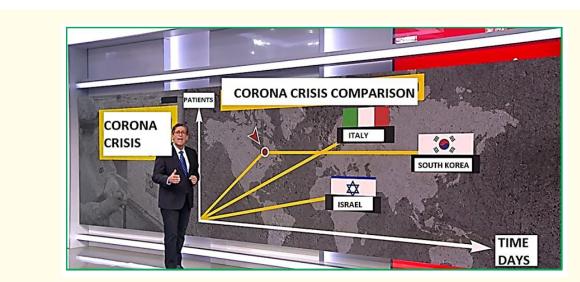
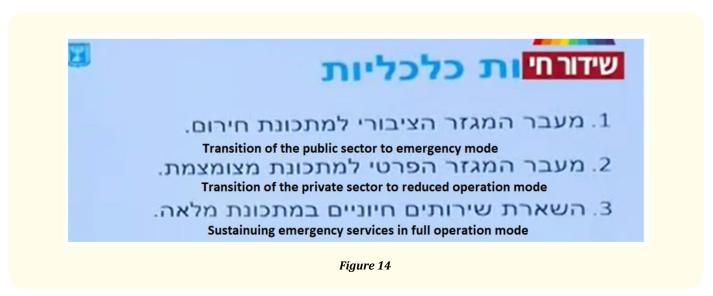


Figure 13

How does Israel deal with the Corona compared to other countries? In terms of the growth curve in the number of patients in the country compared with the growth in Italy and South Korea, one can learn about the desired action to stop the spread of the virus. To compare the steps taken or not taken, the number of patients in the different countries over the days must be examined - and see how the different modes of action have affected the situation.



The prime minister today again faced the cameras with a series of dramatic directives to the public and made it clear that this is just the beginning. We heard a detailed explanation of keeping each other apart, crowds, and the virus passing through the air. Along the way, a political message about the time has also come to an emergency government. But what did we not hear from the Prime Minister tonight? We did not hear what would happen to the fate of small businesses, the self-employed and the tens of thousands of people who have already lost or will soon lose their jobs. At one point, the prime minister announced the closure of restaurants, cafes and gyms until a new announcement, without providing any explanation of what the fate of these industries would be. We have not heard how the state intends to assist them, what solutions will be offered, and how they - such a critical part of the economy - are supposed to overcome the crisis that hit them. 100000 laid off workers for help only 15000 received a reply.

The Ebola epidemic was the mouthpiece that warned the world of the worse and demanded the next epidemic. But the politicians did not think it was serious and continued the usual corruption and stealing of bribes and salutes.

And now, the day of the command has come and today those who run away are trying to tell us night and night stories. They were not preparing for hit. Now they will pay dearly and in many lives. Especially the elderly. In the meantime, the situation is not so bad, but it should be expected in the coming days. What is left to do? Only the closure is full. This is the wrath of the prophet Isaiah. And he had invented the method already. Enter the room to close the doors and wait for rage to pass.

## The first human trial of a vaccine to protect against pandemic coronavirus has started in the US

Four patients received the job at the Kaiser Permanente research facility in Seattle, Washington, reports the Associated Press news agency. The vaccine cannot cause Covid-19 but contains a harmless genetic code copied from the virus that causes the disease. Experts say it will still take many months to know if this vaccine, or others also in research, will work. The first person to get the jab on Monday was a 43-year-old mother-of-two from Seattle [26].

Closure of Israel 324 patients in Israel 5 patients in serious condition.

10 patients, 3,000 in isolation: "Closing a neighborhood in Modi 'in".

Against the backdrop of Netanyahu's remarks, the outbreak of the outbreak may be closed: About a quarter of the "Gems" neighborhood has become isolated after ten have fallen in Corona. All students in 3 schools in isolation, having celebrated Purimon together. In assessing a situation in which the mayor has decided that in the meantime no closure will be imposed, but the possibility is still at hand.

90 more patients: The number of corona patients in Israel rose to 427.

During the night, the Ministry of Health will diagnose 90 additional corona patients in Israel. Five in hard mode, ten in middle mode.

Among the patients diagnosed yesterday: two IDF permanent staff.

GILT (gamma-interferon-inducible lysosomal thiol reductase) restricts cellular entry mediated by the SARS-CoV glycoprotein envelope, the Ebola virus and the Lassa fever virus.

Interferons (IFNs) control viral infections by generating expression of IFN-stimulating genes (ISGs) that limit clear viral replication steps.

The report here deals with GAMT (GILT), an ISG (IFN-stimulated genes) associated with lysosomal cells, limits the infectious entry of selected RNA viruses. Specifically, we demonstrated that GILT was constitutively expressed in lung epithelial cells and fibroblasts and could be further expressed by type II interferon. While GILT overexpression inhibited the entry mediated by the SARS coronavirus glycoprotein envelope (SARS-CoV), the Ebola virus (EBOV) and the LASV virus, the GILT depletion enhanced the entry mediated by these enveloped glycoproteins. Furthermore, mutations that impaired the reductase-thiol activity or disrupted N-linked glycosylation, a post-operative change essential for lysosomal location, have greatly impaired the GILT restriction of viral entry. We found that induction of GILT expression reduced the level of cathepsin L activity required for these RNA viruses to enter lysosomes. Our data suggest that GILT is an innovative antiviral ISG that specifically inhibits the entry of enveloped RNA viruses into lysosomes through disruption of the metabolism and function of cathepsin L and may play a role in immune control and pathogenesis of these viruses [27].

## Minister Arden to police: "Prepare for the possibility of full closure -inevitable decision"

During the consultation of all the heads of the internal security bodies, the Minister of Public Security instructed them to prepare to implement a decision on a full closure, which may be adopted in the coming days. "In the situation created, this is an inevitable decision that will save many lives," he said, and urged that he be urgently presented with a detailed plan to implement a decision.

Minister of Internal Security Gilad Arden instructed the police and internal security bodies to prepare for the implementation of a full closure decision, during a telephone call by all the heads of the internal security bodies, which took place last Tuesday. In Arden's estimation, such a decision may well be made in the coming days. "I believe that in the created situation it is an inevitable decision that will save many lives," he told them [28].

#### Having background diseases? This is how you protect yourself from the Corona virus

Many people with background illness are at risk, due to the outbreak of the corona virus. Experts explain what the risks are, who needs to worry and look after his health, and how to do it. In addition, they also recommend how to spend time at home without compromising health, physical and mental all the details.

With the spread of the Corona virus in Israel and around the world, a great deal of concern has begun, especially among many Israelis who are suffering from other chronic diseases that could pose a risk due to the outbreak of the virus. In addition, the fact that the isolation

and the general atmosphere even in those who are not in isolation can aggravate the illnesses they regularly face. Five Expert Advisers for Patients: Here's how to work properly in dealing with the virus and maintaining your health [29].

#### FDA-approved home and lab tests

You can find information about each home or lab test that FDA has approved or cleared by searching FDA's Database of *In Vitro* Diagnostic (IVD) Tests [30].

#### To use this database:

- 1. Enter a search term (for example the type of test, name, company, or other key word) in the blank space
- 2. Click on "search"
- 3. Review the listing of products that match your search term
- 4. Select any products for additional information (including decision summaries).

#### 21 March 2020, 1071 corona identified in Israel



Figure 15

## **Bibliography**

- 1. DAJ Tyrrell., et al. "Cultivation of a Novel Type of Common-cold Virus in Organ Cultures". British Medical Journal (1965): 1467-1470.
- 2. "FDA Approves First Rapid COVID-19 Test" (2020).
- 3. "Scientists create atomic-scale map of coronavirus' deadly weapon, pointing out a path to fighting it" (2020).
- 4. "Coronavirus Map: Tracking the Global Outbreak" (2020).
- $5. \quad http://www.ecns.cn/z/2020-01-23/detail\text{-}ifzsyram6090121.shtml}$
- 6. Researchers work to create a COVID-19 viral epitope map.
- 7. "Wuhan Institute of Virology and Chinese Army Submit Patent for Gilead Anti-Ebola Drug To Fight Coronavirus" (2020).

- 8. Dustin Siegel., et al. "Adenine C-Nucleoside (GS-5734) for the Treatment of Ebola and Emerging Viruses". Journal of Medicinal Chemistry 60 (2017): 1648-1661.
- 9. Coronavirus Epidemic Update 11: Antiviral Drugs, Treatment Trials for nCoV (Remdesivir, Chloroquine).
- 10. Wang M., et al. "Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) *In vitro*". *Cell Res* (2020).
- 11. Manli Wang., et al. "Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) *In vitro*". *Cell Research* 30 (2020): 269–271.
- 12. https://www.timesofisrael.com/us-to-fast-track-anti-malaria-drug-to-treat-coronavirus/
- 13. Savarino A., et al. "New insights into the antiviral effects of chloroquine". Lancet Infectious Diseases 6.2 (2006): 67-69.
- 14. Yan Y., et al. "Anti-malaria Drug Chloroquine Is Highly Effective in Treating Avian Influenza A H5N1 Virus Infection in an Animal Model". Cell Research 23.2 (2013): 300-302.
- 15. Vincent MJ., et al. "Chloroquine is a potent inhibitor of SARS coronavirus infection and spread". Virology Journal 2 (2005): 69.
- 16. Mackenzie AH. The American Journal of Medicine 75 (2005): 40-45.
- 17. Mohammad Reza Dayer, et al. "Lopinavir; A Potent Drug against Coronavirus Infection: Insight from Molecular Docking Study". Archives of Clinical Infectious Diseases 12.4 (2017): e13823.
- 18. Everett Clinton Smith., *et al.* "Coronaviruses Lacking Exoribonuclease Activity Are Susceptible to Lethal Mutagenesis: Evidence for Proofreading and Potential Therapeutics". *PLOS Pathogens* 9.8 (2013): e1003565.
- 19. De la Torre JC. "Arenavirus extinction through lethal mutagenesis". Virus Research 107 (2005): 207-214.
- 20. Agudo R., *et al.* "Molecular characterization of a dual inhibitory and mutagenic activity of 5-fluorouridine triphosphate on viral RNA synthesis. Implications for lethal mutagenesis". *Journal of Molecular Biology* 382 (2008): 652-666.
- 21. Moreno H., *et al.* "Mutagenesis-mediated virus extinction: virus-dependent effect of viral load on sensitivity to lethal defection". *Plos ONE* 7 (2012): e32550.
- 22. Scientists demonstrate how COVID-19 infects human cells.
- 23. "Gilead's remdesivir to enter trials for coronavirus treatment".
- 24. Coronavirus treatment: Vaccines/drugs in the pipeline for COVID-19.
- 25. Mechanism of action revealed for remdesivir, potential coronavirus drug.
- 26. Coronavirus: US volunteers test first vaccine.
- 27. Danying Chen., *et al.* "GILT restricts the cellular entry mediated by the envelope glycoproteins of SARS-CoV, Ebola virus and Lassa fever virus". *Emerging Microbes and Infections* 8 (2019): 1 1511-1523.
- 28. https://www.mako.co.il/news-israel/2020\_q1/Article-5a2a1b385dce071026.htm?sCh=31750a2610f26110&pId=173113802

Remdsevir	Chloroguine	Loninavir R	lihavirin	Faviniravir	<b>Experimental A</b>	gents or a	Cure for	COIVD 192	Report
Kemusevii,	Cilioi oquille,	LUUIIIavii, i	MDavii III.	ravibilavii	Ladel Illielital A	gents of a	Cureior		Kenoit

าด	https://www.malzo.co	$\frac{1}{1}$	a1 / Articla 2/E02622/0c	ა∩71∩26 h+m2cCh=217⊑∩	a2610f26110&pId=17311380
<b>ム</b> フ.	. HULDS://www.w.mako.co.	.11/11ews-151aet/2020	U 1 / AI ULIE-3430303340U	20/1040.114111:5611-51/30	a2010120110&DIU-1/31130U

132

30. https://www.fda.gov/medical-devices/tests-used-clinical-care/find-all-fda-approved-home-and-lab-tests

Volume 8 Issue 6 June 2020 ©All rights reserved by Shimon Shatzmiller.