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GOOD HEALTH AND WELL- BEING IN THE DIFFERENT CURRENT TREATMENT STRATEGIES FOR CORONAVIRUS DISEASE 2019 (COVID-19): A MINI REVIEW

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ABSTRACT

People of all ages must lead healthy lives and advance wellbeing in order for sustainable development to occur. The global economy is being weakened by COVID-19, which is also disrupting the lives of billions of people worldwide. By the end of 2019, the novel coronavirus that causes severe acute respiratory syndrome (SARS-CoV2) abruptly began to spread, giving rise to the term coronavirus disease 2019 (COVID19). There is currently no proven treatment for COVID-19. Finding efficient therapies is urgently needed to care for patients and control the spread of SARS-CoV2 among humans. The treatment medicines that may be employed to fight the SARS-CoV2 infection were emphasized for the current review. Numerous medications have been repurposed for COVID19 therapy since the disease's emergence. Regarding the treatment of COVID-19, existing medications such as chloroquine (CQ), Along with chloroquine, we also investigated monoclonal antibodies, restorative plasma, Chinese herbal treatment, and natural compounds, including remdesivir, hydroxychloroquine (HCQ), and nucleoside analogues. Although initial clinical trials demonstrated that CQ/HCQ had antiviral activities, further investigations revealed significant debate over its suitability for treating COVID-19. Preventing the virus from interacting with human cell receptors for angiotensin converting enzyme 2 is one of these medicinal medicines' biological defenses against SARS-CoV2. Many of studies about the role of nanomaterials in treating Covid-19,

based on their unique physical, chemical and biological properties, which depend on shape and size, as the use of nanomaterials is considered a promising future to eliminate viruses, including Covid-19.

KEYWORDS: COVID-19, antiviral treatment, vaccine treatment, plasma treatment.

INTRODUCTION

Since countries declared public emergencies due to the entry of an intruder virus coming from China during the period from February to March 2020, the economic, social and health sectors have begun to be affected one by one, and the state of panic is rising little by little as a result of the outbreak of a new disease, Covid-19, which the World Health Organization classified as a worldwide pandemic. which led to human losses. And, as a result of its economic and social implications, its wreaked havoc on society, with particularly severe ramifications in the sports business. Many communities experienced periods of isolation and reduced economic activity as a result of the lockdown. Sports activities have been halted due to the shutdown. Acute respiratory symptoms, which point to a respiratory tract infection, are the main clinical indicators of COVID-19. Acute respiratory distress of notable magnitude the coronavirus-2 (SARS-CoV-2) is the source of this sickness. In December 2019, the virus was initially discovered in Wuhan, China's Hubei Province. It quickly expanded to other regions of the world and turned into a pandemic. The US government has not designated a particular treatment target for the coronavirus that causes severe acute respiratory syndrome (SARS-CoV-2). Administration of Food and Drugs (FDA). Covid-19. Various medications are being used in clinical trials and compassionate use procedures due to their limited clinical experience and in vitro activity (against SARS-CoV-2 or kindred viruses). There is currently no recognized effective medication [1].

For COVID-19, there is no proven therapy. The most crucial strategy is to stop viral transmission through quick isolation and disease control measures. Due to the fact that COVID-19 spreads primarily through respiratory droplet infection, extreme caution is required when using personal protective equipment, assessment, notification of the true picture and masks, as well as prevention of spread through travel restriction, isolation, and screening of individuals. Acute lung damage and pneumonia are mostly treated empirically. [2]

Current therapies:

The People's Republic of China's National Health Commission released Diagnosis and Treatment of Pneumonia Caused by COVID-19(updated to version 6) [3], states that current treatments primarily concentrate on symptomatic and respiratory support due to the absence of COVID-19 effective antiviral treatment. WHO advised extracorporeal membrane

oxygenation (ECMO) for patients with persistent hypoxemia, and almost all patients accepted oxygen treatment [4]. According to their circumstances, some serious patients receive rescue therapy contains immunoglobulin G and recuperating plasma [5].

A vaccination, novel pharmacological compounds, or the repurposing of certain current medications are just a few of the therapy methods that urgently need to be designed and developed. On account of humanitarian considerations, the medical community and the biotech sector must act immediately.

Antiviral treatments:

Based on our past battles with the MERS-CoV and SARS-CoV outbreaks, we may be able to make some inferences for possible remedies for the coronavirus [6]. Antiviral medications and systemic corticosteroid therapy include methylprednisolone, ganciclovir, ribavirin and acyclovir. Neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, etc.) are another kind of medication [7,8], are ineffective and not recommended for COVID-19 for influenza viruses. Adenosine nucleotide analog prodrug Remdesivir (GS-5734), containing 1′-cyano substitutions and having broad-spectrum antiviral activity against different RNA viruses. Remdesivir may inhibit the NSP12 polymerase even in cases when ExoN proofreading activity remains unaltered, according to data from in vitro cell lines and mice models [9]. Remdesivir was reportedly used to treat the first COVID-19 infection to happen in the US [10]. A repurposed medication with considerable promise to treat COVID-19 is chloroquine. Chloroquine has been used to treat malaria for a long time [11], while its mechanism of action against some viral infections is unclear. Several potential processes are looked into: Chloroquine has a strong impact on the infection and dissemination of the SARS-CoV and can impede numerous viruses' pH-dependent replication processes [12, 13]. Additionally, TNF- and IL-6 synthesis and release are suppressed by chloroquine's immunomodulatory actions. Furthermore, it functions as a brand-new family of autophagy inhibitors [14], which may prevent viral infection and replication. Numerous studies have shown that chloroquine prevents SARS-CoV cellular receptors from being glycosylated [13] and to continue to function in Vero E6 cells during the COVID-19 infection's both the entrance and post-entry phases [15]. The recently discovered SARS-CoV-2 was successfully inhibited in vitro by remdesivir and chloroquine together.

MERS-prognosis CoV's may be improved by the HIV treatment drugs lopinavir and ritonavir, which are protease inhibitors [16,17] and SARS-CoV [18] patients, according to earlier research. After receiving lopinavir/ritonavir (Kaletra®, AbbVie, North Chicago, IL, USA) medication, the coronavirus viral levels of a COVID-19 patient in Korea dramatically reduced, according to a report [19]. Physicians treating patients with symptoms associated with pneumonia at the Shanghai Public Health Clinical Center in China also combined Western and Chinese medicine.

Arbidol, Shufeng Jiedu Capsule, and lopinavir/ritonavir (Kaletra®) were all used together in this treatment (SFJDC, a traditional Chinese medicine) [20]. The other antiviral medications include favipiravir, nafamostat and nitazoxanide. Antiviral medication has been the subject of several emergency clinical studies. While no antiviral medication has been proven to be effective by rigorous "randomized, double-blind, placebo-controlled studies", Certain therapeutic effects of various medications have been demonstrated in clinical studies. According to the current agreement, It is recommended to focus on patients who are extremely sick and have high-risk features when administering drugs with potential antiviral effects early in the course of the illness. Lopivir/ritonavir and ribavirin should not be used separately. It is not advised to take azithromycin alone or in combination with hydroxychloroquine. The following medications may still be used and further tested in clinical

Drugs applied or suggested	Status	Action mode	Target diseases	Anti-infective mechanism	Study
Chloroquine	Approved, Investigational, Vet approved	9-aminoquinolin	Malaria, autoimmune disease	Increasing endosomal pH, immunomodulating, autophagy inhibitors	[21-24]
Lopinavir/Ritonavir	Approved	Protease inhibitors	HIV/AIDS, SARS, MERS	Inhibiting HIV-1 protease for protein cleavage, resulting in non-infectious, immature viral particles	[25-27]
Ribavirin	Approved	Synthetic guanosine nucleoside	HCV, SARS, MERS	Interfering with the synthesis of viral mRNA (a broad-spectrum activity against several RNA and DNA viruses)	[28-30]
Oseltamivir	Approved	Neuraminidase inhibitor	Influenza viruses A	Inhibiting the activity of the viral neuraminidase enzyme, preventing budding from the host cell, viral replication, and infectivity	[31,32]
Remdesivir (GS5734)	Experimental	Nucleotide analogue prodrug	Ebola, SARS, MERS	Interfering with virus post-entry	[33-35]
Nafamostat	Investigational	Synthetic serine protease inhibitor	Influenza, MERS, Ebola	Prevents membrane fusion by reducing the release of cathepsin B; anticoagulant activities	[36,37]
Ganciclovir	Approved, Investigational	Nucleoside analog	AIDS-associated cytomegalovirus Infections	Potent inhibitor of the Herpesvirus family including cytomegalovirus	[38]
Penciclovir/ Acyclovir	Approved	Nucleoside analog	HSV, VZV	A synthetic acyclic guanine derivative, resulting in chain termination	[39]
Favipiravir (T-705)	Investigational	Nucleoside analog: Viral RNA polymerase inhibitor	Ebola, influenza A(H1N1)	Acting on viral genetic copying to prevent its reproduction, without affecting host cellular RNA or DNA synthesis	[40-42]
Nitazoxanide	Approved, Investigational, Vet approved	Antiprotozoal agent	A wide range of viruses including human/animal coronaviruses	Modulating the survival, growth, and proliferation of a range of extracellular and intracellular protozoa, helminths, anaerobic and microaerophilic bacteria, viruses	[43-45]

Table 1: *(widely used antiviral medications with high potency)*

may now be combined with an Fc fragment and utilized to combat the virus on the cell surface. There may be hope for the human immunoglobulin G, Fc domain linked to the extracellular domain of the ACE2 protein [46]. The COVID-ACE2 Fc fusion protein may be able to neutralize the virus and stop lung damage. Additionally, it can be utilized to provide healthcare professionals with passive immunity. They are all still quite experimental. A medicine named CAMOSTAT that affects the TMPRSS 2 protein is mentioned in an intriguing research [47] as a potential way to block viral entrance since the protein is used by the virus.

Nutritional Supplements treatments:

Unknown is the function of dietary supplements in the management or prevention of COVID-19. For both therapy and prevention, a number of supplements are being studied in conjunction with other therapeutic methods (such as zinc, vit. D, and vit. C) [48–57]. Adverse reactions from high dosages and the possibility of medication interactions are safety issues [58-60].

Utilizing a zinc supplement may be beneficial for phagocytosis and intracellular killing as well as immune function modulation. At order to inhibit viral replication, ARB (losartan and telmisartan) should be administered in therapeutic levels combined with zinc. The epithelial cells of alveoli and trancheobronchial spaces are highly expressed with ACE2 receptors, which may facilitate viral entrance [61]. So, it is possible to experiment with using ARBs in nebulization.

Traditional Chinese Medicine Therapy (TCMT) or Herbal treatments:

In China, traditional Chinese medicine is still widely used today, having been heavily utilized during the last SARS-COV outbreak. These were the five plants that were used the most frequently: Astragali Radix (Huangqi), Lonicerae Japonicae Flo, Atractylodis Macrocephalae Rhizoma (Baizhu), Saposhnikoviae Radix (Fangfeng), Glycyrrhizae Radix Et Rhizoma (Gancao), and Astragali Radix (Huangqi) [62].

oxygen therapy and monitoring:

Target SpO2 > 94 percent and administer supplementary oxygen treatment right away to patients who have SARI, respiratory distress, hypoxemia, or shock. Adults experiencing emergency symptoms, such as difficulty breathing or no breathing at all, severe respiratory distress, coma, convulsions shock, central cyanosis need to have their airways managed and

given oxygen treatment in order to achieve SpO2 levels of 94 percent or above during resuscitation. During resuscitation, start oxygen treatment at 5 L/min and adjust flow rates until the goal SpO2 is 93 percent; Use a reservoir bagged face mask if the patient's condition is really bad (at 10-15 L/min). The goal is > 90% SpO2 in non-pregnant individuals after the patient is stabilized, and 92-95 percent in pregnant patients [63-72].

During resuscitation, children should get oxygen treatment and airway control with a target of getting their SpO2 to 94 percent or higher; if not, the target is 90 percent. Emergency symptoms in children include difficulty breathing or no breathing at all, severe breathing difficulties, convulsions, shock, coma, or central cyanosis [72]. In order to ensure that small children would endure the procedure, nasal prongs or a nasal cannula should be used.

Convalescent Plasma Therapy (CPT):

The creation of a system with a suitable infrastructure is necessary to undertake convalescent plasma treatment for COVID-19. The necessity for convalescent serum donation necessitates the recruitment of a group of donors who have fully recovered from their disease. Apheresis processing requires blood banking facilities. It is necessary to undertake certain tests, such as virological assays to quantify viral neutralization and serological assays to identify SARS-CoV-2 antibodies in serum. The required laboratory assistance should be implemented in order to carry out the testing for neutralizing antibodies. It is necessary to create protocols for the secure collection and application of convalescent plasma. It is recommended to combine clinical usage with clinical studies to evaluate the effectiveness, safety, and immunologic responses. It is important to expedite regulatory assessment and clearance. Pharmaceutical firms should strive to provide very pure preparations with a high titer of SARS-CoV-2 neutralizing antibodies as opposed to convalescent plasma. Although It takes months to prepare hyper-immunoglobulin, it may be safer and have a greater level of neutralizing action [73].

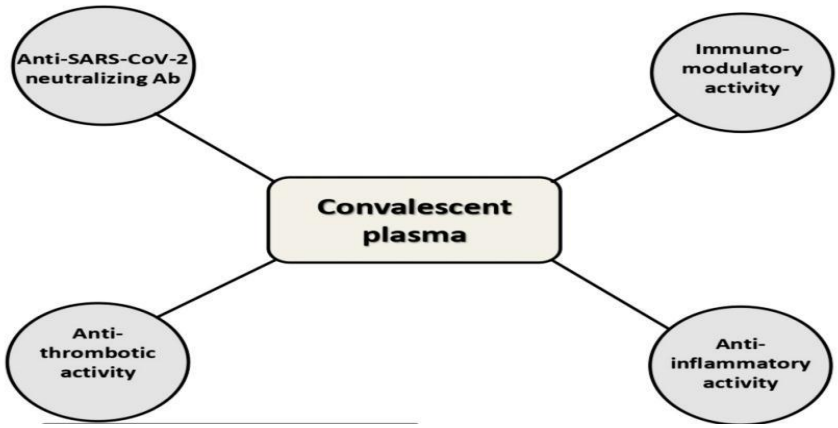


Figure (1): *(Mechanisms of action of anti COVID-19 convalescent plasma [73].)*

Blood plasma is taken from a patient who has recovered and given to a patient who is exhibiting symptoms called convalescent plasma (CP) therapy. Since more than a century ago, several infectious illnesses have been prevented and treated by CP treatment, a traditional kind of adaptive immunotherapy [74]. Testing grounds for the efficiency of CP included the Spanish flu in 1915–1917, SARS (in 2003), influenza A (H1N1) (in 2009), Ebola (in 2013) and avian flu A (H5N1) (in 2014) [78]. According to a number of short observational research projects conducted throughout the course of the COVID-19 epidemic, CP may be an important component of a successful treatment plan for individuals with severe illness [79]. Wuhan's COVID-19 pandemic saw the first use of CP treatment on five patients who had advanced illness [80]. According to computed tomography (CT) scan results, the inflammatory biomarkers of four out of the five patients had improved, and the pulmonary lesions in all of the patients had as well. In the study by Duan et al., it was reported that clinical results in 10 patients who underwent a just one infusion of CP improved and that no negative consequences were observed [16]. Two short case studies with five and six patients later revealed similar outcomes, respectively [81,82]. In their investigation, Salazar et al. [83] treated 25 patients with CP therapy and shown that it was a secure therapeutic alternative. The Food and Drug Administration (FDA) of the United States states that CP administration may have a therapeutic effect on the treatment of COVID-19 [84]. Even more emphasis has been placed on the fact that the therapeutic impact of CP treatment is also protective [85]. The simplest and most practical method of acquiring passive immunity use of plasma with high-titer antibodies obtained from COVID-19 disease survivors in this instance [86,87]. Virus neutralization supplied by the produced antibodies serves as the primary definition of protection in CP therapy [88].

Nanotechnology treatment:

The FDA has not yet authorized any vaccinations or medications for the treatment of COVID-19 patients, as was previously noted. Therefore, quick COVID-19 point-of-care nano-diagnosis is essential for identifying COVID-19 patients and stopping the spread of the SARS-CoV-2 virus [89–92]. Nanomaterials can be used to diagnose COVID-19 because of their adjustable physicochemical characteristics, which include size, shape, charge, and chemical functionalities [93–95]. To effectively destroy various viral diseases, including coronaviruses causing SARS or MERS, nanomaterials offered a strong foundation. Therefore, the use of nanomaterials shows tremendous promise in the development of innovative therapeutic approaches for the treatment of COVID-19 [96-101].

Similar to MERS-CoV, SARS infection the function of CoV-2 depends on the S protein, as was indicated in the introduction. Current antiviral nanoparticles are appropriate for treating

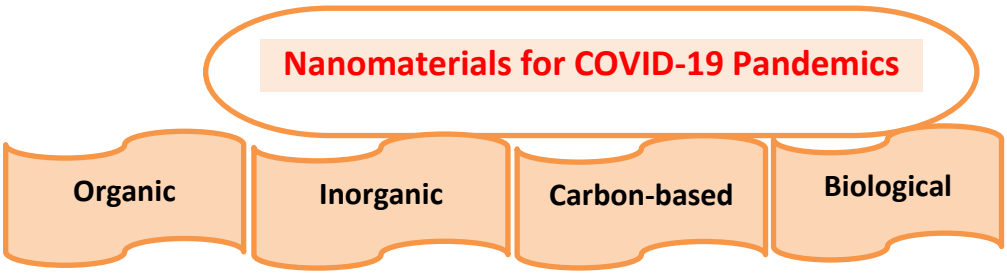
COVID-19 because of the way that S protein and ACE2 interact on the host cell membrane. MERS-CoV and host cell membrane fusion, which is mediated by HR1/HR2, can be stopped by pregnancy-induced hypertension (PIH), an effective heptad repeat 1 (HR1) peptide inhibitor. The S protein is essential in the process of SARS-infection CoV-2, as was mentioned in the introduction, which is comparable to MERS-CoV. Based on the interaction between S protein and ACE2 on the host cell membrane, existing antiviral nanoparticles can treat COVID-19. An effective heptad repeat 1 (HR1) peptide inhibitor that can stop MERS-CoV and host cell membrane fusion is pregnancy-induced hypertension (PIH). Furthermore, Oczechin et al., developed boronic acid ligands in conjunction with carbon quantum dots (CQDs) to obstruct the protein S-receptor's interaction with the host cell membrane, so blocking the virus from entering the host cells [103]. In order to stop the COVID-19 virus from spreading, inhaling silver nanoparticles (Ag NPs) has been used as a first-line treatment [104,105]. Ag NPs' antiviral effect could stem from their ability to cling to RNA virus surface glycoproteins, preventing the virus from infecting host cells. Copper's antibacterial and antiviral qualities have been known since the beginning of time. More recently, evidence has emerged that copper may be helpful against the SARS-CoV-2 virus due to its capacity to destroy coronaviruses. Viral lipids and proteins are harmed, which starts the deactivation process [106].

An increasing corpus of studies has also demonstrated that nanomaterials might be employed as tools for immune control, therefore inducing an immune response in the fight against illness. For example, adding amino groups to graphene oxide altered the STAT1/IRF1 interferon's signaling pathway in T cells, causing them to produce more chemoattractants [107].

<table>
<tr><td>Polymeric NP</td><td>Metallic NP</td><td>Fullerenes</td><td>Nano fibrous</td></tr>
<tr><td>Lipid NP</td><td>Metalic oxide</td><td>Graphene</td><td>Nanosponges</td></tr>
<tr><td>Dendrimers</td><td>Ceramics</td><td>Carbon Nanotubes</td><td>Nano bodies</td></tr>
<tr><td>Micelles</td><td rowspan="2">Semiconductor Nanomaterials</td><td>Quantum Dots</td><td rowspan="2">VLNPs</td></tr>
<tr><td>Liposomes</td><td>Carbon Nanofiber</td></tr>
</table>

SARS-CoV-2 is thought to be 125 nm in size and is regarded as a natural nanomaterial [108]. Next-generation vaccines can be made possible by nanomaterials that imitate the inherent immunostimulatory properties of viruses. A lipid nanoparticle and messenger RNA (mRNA) vaccination against SARS-CoV and MERS has been investigated [109, 110]. In order to generate

high neutralizing antibody titers in mice, McKay et al. created a lipid nanoparticle-encased, self-amplifying RNA that expresses the SARS-CoV-2 S protein selectively. Their research offers fresh perspectives on vaccine development and immunogenicity assessment, which will hasten the transition of nanomaterial-based vaccinations from the laboratory to the clinic [111-113].



CONCLUSIONS

Despite the fact that clinical and experimental research revealed that some medicinal substances might be used to treat or prevent SARS-CoV-2 infection, before effective treatments and vaccinations for SARS-CoV-2 infection, several challenges must yet be addressed.

Though clinical and experimental studies indicated that some medicinal substances might be used to treat or prevent SARS-CoV-2 infection, significant problems still need to be resolved in order to create efficient medications and vaccines for SARS-CoV-2 infection. The solution to this problem is to modify the nucleosides of NAs such that active NAs can pass through the cell's membrane [89,90]. SARS-CoV-2 is prevented from entering the body and packaging itself by a number of natural ingredients and Chinese herbs, however in order to boost the potency of their antiviral effects, it is necessary to fully identify the molecular targets of the chemicals found in Chinese herbs. Additionally, several TCMs and natural plant components have potent antiviral effects and little toxicity, making them candidates for use as first-aid medications for SARS-CoV-2 infection [91,92]. SARS-genomic CoV-2's RNA, structural proteins, and non-structural proteins have been discovered, and as a consequence, efficient DNA or mRNA, or inactivated-viral vaccines, have been produced for immunizing healthy people in order to stop the virus from spreading. Certain mRNA vaccines or inactivated viral vaccines have been authorized for use in the immunization of healthy people against SARS-CoV2 in a number of nations, including the USA, Canada, China, Japan, and the UK. As a result, the likelihood of SARS-CoV2 infection in various populations throughout the world will likely fall considerably in the near future due to the rapid advancement of medicine discovery and vaccine development.

REFRENCES

- World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. https://www.who.int/publicationsdetail/clinicalmanagement-of-severe-acute-respiratory infection-when-novel-coronavirus-(ncov)-infection-issuspected.
- Phadke, M. and Saunik, S. (2020). COVID-19 treatment by repurposing drugs until the vaccine is in sight. Drug Development Research, PP: 1-3. https://doi.org/10.1002/ddr.21666,wileyonlinelibrary.com/journal/ddr.
- National Health Commission of the People's Republic of China. (2020). Diagnosis and Treatment of Pneumonia Caused by 2019-nCoV (version 6). [Google Scholar]
- WHO.(2020). Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. https://www.who.int/publications-detail/clinical-management-of severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected. Accessed 28 Jan 2020.
- Chen L, Xiong J, Bao L, Shi Y. (2020). Convalescent plasma as a potential therapy for COVID-19. Lancet Infect Dis. 2020. 10.1016/s1473-3099(20)30141-9.
- Zumla A, Chan JF, Azhar EI, Hui DS, Yuen KY. (2016). Coronaviruses - drug discovery and therapeutic options. Nat Rev Drug Discov. 15(5):327–347. doi: 10.1038/nrd.2015.37.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. (2020). Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020. 10.1001/jama. 1585 [Epub ahead of print].
- Li H, Wang YM, Xu JY, Cao B. (2020). Potential antiviral therapeutics for 2019 Novel Coronavirus. Chin J Tuberc Respir Dis. 43(0): E002.
- Agostini ML, Andres EL, Sims AC, Graham RL, Sheahan TP, Lu X, et al. (2018). Coronavirus susceptibility to the antiviral remdesivir (gs-5734) is mediated by the viral polymerase and the proofreading exoribonuclease. mBio. 9(2): e00221–e00218. doi: 10.1128/mBio.00221-18.
- Holshue Michelle L., DeBolt Chas, Lindquist Scott, Lofy Kathy H., Wiesman John, Bruce Hollianne, Spitters Christopher, Ericson Keith, Wilkerson Sara, Tural Ahmet, Diaz George, Cohn Amanda, Fox LeAnne, Patel Anita, Gerber Susan I., Kim Lindsay, Tong Suxiang, Lu Xiaoyan, Lindstrom Steve, Pallansch Mark A., Weldon William C., Biggs Holly M., Uyeki Timothy M., Pillai Satish K. (2020). First Case of 2019 Novel Coronavirus in the United States. New England Journal of Medicine. 382(10):929–936. doi: 10.1056/NEJMoa2001191.
- Aguiar ACC, Murce E, Cortopassi WA, Pimentel AS, Almeida M, Barros DCS, et al. (2018). Chloroquine analogs as antimalarial candidates with potent in vitro and in vivo activity. Int J Parasitol Drugs Drug Resist. 8(3):459–464. doi: 10.1016/j.ijpddr.2018.10.002.

- Savarino A, Boelaert JR, Cassone A, Majori G, Cauda R. (2003). Effects of chloroquine on viral infections: an old drug against today's diseases? Lancet Infect Dis. 3(11):722–727. doi: 10.1016/S1473-3099(03)00806-5.
- Vincent MJ, Bergeron E, Benjannet S, Erickson BR, Rollin PE, Ksiazek TG, et al. (2005). Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2:69. doi: 10.1186/1743-422X-2-69.
- Golden EB, Cho HY, Hofman FM, Louie SG, Schonthal AH, Chen TC. (2015). Quinoline-based antimalarial drugs: a novel class of autophagy inhibitors. Neurosurg Focus. 38(3): E12. doi: 10.3171/2014.12. FOCUS14748.
- Wang Manli, Cao Ruiyuan, Zhang Leike, Yang Xinglou, Liu Jia, Xu Mingyue, Shi Zhengli, Hu Zhihong, Zhong Wu, Xiao Gengfu.(2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Research. 30(3):269–271. doi: 10.1038/s41422-020-0282-0.
- Cvetkovic RS, Goa KL. (2003). Lopinavir/ritonavir: a review of its use in the management of HIV infection. Drugs. 63(8):769–802. doi: 10.2165/00003495-200363080-00004.
- Arabi YM, Asiri AY, Assiri AM, Aziz Jokhdar HA, Alothman A, Balkhy HH, et al. (2020). Treatment of Middle East respiratory syndrome with a combination of lopinavir/ritonavir and interferon-β1b (MIRACLE trial): statistical analysis plan for a recursive two-stage group sequential randomized controlled trial. Trials. 21(1):8. doi: 10.1186/s13063-019-3846-x.
- Chu CM, Cheng VC, Hung IF, Wong MM, Chan KH, Chan KS, et al. (2004). Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax. 59(3):252–256. doi: 10.1136/thorax.2003.012658.
- Lim J, Jeon S, Shin HY, Kim MJ, Seong YM, Lee WJ, et al. (2020). Case of the index patient who caused tertiary transmission of COVID-19 infection in Korea: the application of lopinavir/ritonavir for the treatment of COVID-19 infected pneumonia monitored by quantitative RT-PCR. J Korean Med Sci. 35(6): e79. doi: 10.3346/jkms.2020.35. e79.
- Wang Z, Chen X, Lu Y, Chen F, Zhang W. (2020). Clinical characteristics and therapeutic procedure for four cases with 2019 novel coronavirus pneumonia receiving combined Chinese and Western medicine treatment. Biosci Trends. 10.5582/bst.2020.01030.

- Savarino A, Boelaert JR, Cassone A, Majori G, Cauda R. (2003). Effects of chloroquine on viral infections: an old drug against today's diseases? Lancet Infect Dis. 3(11):722–727. doi: 10.1016/S1473-3099(03)00806-5.

- Vincent MJ, Bergeron E, Benjannet S, Erickson BR, Rollin PE, Ksiazek TG, et al. (2005). Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2:69. doi: 10.1186/1743-422X-2-69.
- Golden EB, Cho HY, Hofman FM, Louie SG, Schonthal AH, Chen TC. (2015). Quinoline-based antimalarial drugs: a novel class of autophagy inhibitors. Neurosurg Focus. 38(3): E12. doi: 10.3171/2014.12. FOCUS14748.
- Wang Manli, Cao Ruiyuan, Zhang Leike, Yang Xinglou, Liu Jia, Xu Mingyue, Shi Zhengli, Hu Zhihong, Zhong Wu, Xiao Gengfu. (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Research. 30(3):269–271. doi: 10.1038/s41422-020-0282-0.
- Cvetkovic RS, Goa KL. (2003). Lopinavir/ritonavir: a review of its use in the management of HIV infection. Drugs. 63(8):769–802. doi: 10.2165/00003495-200363080-00004.
- Arabi YM, Asiri AY, Assiri AM, Aziz Jokhdar HA, Alothman A, Balkhy HH, et al. (2020). Treatment of Middle East respiratory syndrome with a combination of lopinavir/ritonavir and interferon-β1b (MIRACLE trial): statistical analysis plan for a recursive two-stage group sequential randomized controlled trial. Trials. 21(1):8. doi: 10.1186/s13063-019-3846-x.
- Chu CM, Cheng VC, Hung IF, Wong MM, Chan KH, Chan KS, et al. (2004). Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax. 59(3):252–256. doi: 10.1136/thorax.2003.012658.
- PAAASLD-IDSA H Guidance & Panel Hepatitis C guidance 2018 update: AASLD-IDSA recommendations for testing, managing, and treating hepatitis C virus infection. Clin Infect Dis. 2018;67(10):1477–1492. doi: 10.1093/cid/ciy585.
- Tsang K, Zhong NS. (2003). SARS: pharmacotherapy. Respirology. 2003;8(Suppl 1): S25–S30. doi: 10.1046/j.1440-1843.2003.00525. x.
- Arabi YM, Shalhoub S, Mandourah Y, Al-Hameed F, Al-Omari A, Al Qasim E, et al. (2019). Ribavirin and interferon therapy for critically ill patients with middle east respiratory syndrome: a multicenter observational study. Clin Infect Dis. 10.1093/cid/ciz544.
- McQuade B, Blair M. (2015). Influenza treatment with oseltamivir outside of labeled recommendations. Am J Health. 72(2):112–116.
- Jefferson T, Jones M, Doshi P, Spencer EA, Onakpoya I, Heneghan CJ. (2014). Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. BMJ. 348: g2545. doi: 10.1136/bmj. g2545.
- Agostini ML, Andres EL, Sims AC, Graham RL, Sheahan TP, Lu X, et al. (2018). Coronavirus susceptibility to the antiviral remdesivir (gs-5734) is mediated by the viral

polymerase and the proofreading exoribonuclease. mBio. 9(2): e00221–e00218. doi: 10.1128/mBio.00221-18.

- Tchesnokov EP, Feng JY, Porter DP, Gotte M. (2019). Mechanism of inhibition of ebola virus rna-dependent rna polymerase by remdesivir. Viruses. 11(4): E326. doi: 10.3390/v11040326.
- Lo MK, Feldmann F, Gary JM, Jordan R, Bannister R, Cronin J, et al.(2019). Remdesivir (GS-5734) protects African green monkeys from Nipah virus challenge. Sci Transl Med. 11(494): eaau9242. doi: 10.1126/scitranslmed. aau9242.
- Hsieh HP, Hsu JT. (2007). Strategies of development of antiviral agents directed against influenza virus replication. Curr Pharm Des. 13(34): 3531–3542. doi: 10.2174/138161207782794248.
- 37- Nishimura H, Yamaya M. A. (2015). synthetic serine protease inhibitor, Nafamostat Mesilate, is a drug potentially applicable to the treatment of ebola virus disease. Tohoku J Exp Med. 237(1):45–50. doi: 10.1620/tjem.237.45.
- Al-Badr AA, Ajarim TDS. (2018). Ganciclovir. Profiles Drug Subst Excip Relat Methodol. 43:1–208. doi: 10.1016/bs.podrm.2017.12.001.
- Shiraki K. (2018). Antiviral drugs against alphaherpesvirus. Adv Exp Med Biol. 1045:103–122. doi: 10.1007/978-981-10-7230-7_6.
- Furuta Y, Gowen BB, Takahashi K, Shiraki K, Smee DF, Barnard DL. (2013). Favipiravir (T-705), a novel viral RNA polymerase inhibitor. Antivir Res. 100(2):446–454. doi: 10.1016/j.antiviral.2013.09.015.
- Goldhill DH, Te Velthuis AJW, Fletcher RA, Langat P, Zambon M, Lackenby A, et al. (2018). The mechanism of resistance to favipiravir in influenza. P Natl Acad Sci USA. 115(45):11613–11618. doi: 10.1073/pnas.1811345115.
- Cardile AP, Warren TK, Martins KA, Reisler RB, Bavari S. (2017). Will there be a cure for Ebola? Annu Rev Pharmacol. 57:329–348. doi: 10.1146/annurev-pharmtox-010716-105055.
- Rossignol JF. (2014). Nitazoxanide: a first-in-class broad-spectrum antiviral agent. Antivir Res. 110:94–103. doi: 10.1016/j.antiviral.2014.07.014.
- Cao J, Forrest JC, Zhang X. (2015). A screen of the NIH clinical collection small molecule library identifies potential anti-coronavirus drugs. Antivir Res. 114:1–10. doi: 10.1016/j.antiviral.2014.11.010.
- Rossignol JF. (2016). Nitazoxanide, a new drug candidate for the treatment of Middle East respiratory syndrome coronavirus. J Infect Public Health. 9 (3):227–230. doi: 10.1016/j.jiph.2016.04.001.
- Fedson, D. (2016). Treating the host response to emerging virus disease. Annals of Translational Medicine, 4(21), 421.

- Hoffmann, M., Kleine-Weber, H., Schroeder, S., Krüger, N., Herrler, T., Erichsen, S., … Pöhlmann, S. (2020). SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically-Proven Protease Inhibitor. Cell. https://doi.org/10.1016/j-cell2020.02.052.
- ProgenaBiome. (2020). A study of hydroxychloroquine, vitamin C, vitamin D, and zinc for the prevention of COVID-19 infection (HELPCOVID-19). Retrieved April 9, 2020. Available on the World Wide Web at: https://clinicaltrials.gov/ct2/show/NCT04335084?cond=COVID&intr=zinc&draw=2&rank=2
- 49- Istinye University. (2020). Proflaxis using hydroxychloroquine plus vitamins-zinc during COVID-19 pandemia. Retrieved April 9, 2020. Available on the World Wide Web at: https://clinicaltrials.gov/ct2/show/NCT04326725?cond=COVID&intr=zinc&draw=2&rank=3
- Progena Bione.(2020). A study of quintuple therapy to treat COVID-19 infection (HAZCpaC). Retrieved April 9, 2020. Available on the World Wide Web at: https://clinicaltrials.gov/ct2/show/NCT04334512?cond=COVID&intr=zinc&draw=2&rank=4
- University of Melbourne. (2020). World-first trial to test benefit of intravenous zinc in COVID-19 fight. Retrieved April 9, 2020. Available on the World Wide Web at: https://medicalxpress.com/news/2020-04-world-first-trial-benefit-intravenous-zinc.html
- University of Palermo. (2020). Use of ascorbic acid in patients With COVID 19. Retrieved April 9, 2020. Available on the World Wide Web at: https://clinicaltrials.gov/ct2/show/NCT04323514?cond=COVID&intr=vitamin+C&draw=2&rank =1
- Providence Health and Services. (2020). Hydroxychloroquine in patients with newly diagnosed COVID-compared to standard of care. Retrieved April 9, 2020. Available on the World Wide Web at: https://clinicaltrials.gov/ct2/show/NCT04334967?cond=COVID&intr=vitamin+C&draw=2&rank= 4
- Washington University. (2020). Hydroxychloroquine for COVID-19 PEP. Retrieved April 9, 2020.Available on the World Wide Web at: https://clinicaltrials.gov/ct2/show/NCT04328961?cond=COVID&intr=vitamin+C&draw=2&rank= 5
- ZhiYong Peng. (2020). Vitamin C infusion for the treatment of severe 2019-nCoV infected pneumonia. Retrieved April 9, 2020. Available on the World Wide Web at:

https://clinicaltrials.gov/ct2/show/NCT04264533?cond=COVID&intr=vitamin+C&draw=2&rank= 6

- Universite de Sherbrooke. (2020). Lessening organ dysfunction with vitamin C (LOVIT). Retrieved April 9,2020. Available on the World Wide Web at: https://clinicaltrials.gov/ct2/show/NCT03680274?cond=COVID&intr=vitamin+C&draw=2&rank= 8
- Universidad de Granada. (2020). Vitamin D on Prevention and Treatment of COVID-19 (COVITD-19). Retrieved April 9, 2020. Available on the World Wide Web at: https://clinicaltrials.gov/ct2/show/NCT04334005?cond=COVID&intr=Vitamin+D&draw=2&rank= 1
- National Institutes of Health (NIH). (2020). Zinc: fact sheet for health professionals. Retrieved April 9, 2020. Available on the World Wide Web at: https://ods.od.nih.gov/factsheets/ZincHealthProfessional/
- National Institutes of Health (NIH). (2020). Vitamin C: fact sheet for health professionals. Retrieved April 9, 2020.Available on the World Wide Web at: https://ods.od.nih.gov/factsheets/VitaminCHealthProfessional/
- National Institutes of Health (NIH). (2020). Vitamin D: fact sheet for health professionals. Retrieved April 9, 2020.Available on the World Wide Web at: https://ods.od.nih.gov/factsheets/VitaminDHealthProfessional/
- Song, Z., Xu, Y., Bao, L., Zhang, L., Yu, P., Qu, Y., … Qin, C. (2019). From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses, 11(1), 59.
- Luo H, Tang Q-L, Shang Y-X, Liang S-B, Yang M, Robinson N, et al. (2020). Can Chinese medicine be used for prevention of corona virus disease 2019 (COVID-19)? A review of historical classics, research evidence and current prevention programs. Chin J Integr Med. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32065348.
- WHO. (2020). Pocket book of hospital care for children: guidelines for the management of common childhood illnesses. Geneva: World Health Organization; 2013
  http://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/, accessed 4 March 2020.
- Force ADT, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E et al. (2012). Acute respiratory distress syndrome: The Berlin Definition. JAMA. 2012;307(23):2526-33. Epub 2012/07/17. Doi:10.1001/jama.2012.5669.
- Khemani RG, Smith LS, Zimmerman JJ, Erickson S, (2015). Pediatric Acute Lung Injury Consensus Conference G Pediatric acute respiratory distress syndrome: definition, incidence, and epidemiology: proceedings from the Pediatric Acute Lung Injury

Consensus Conference. Pediatr Crit Care Med. 2015;16(5 Suppl 1): S23-40. Epub 2015/06/04. Doi 10.1097:

- Riviello ED, Kiviri W, Twagirumugabe T, Mueller A, Banner-Goodspeed VM, Officer L et al. (2016). Hospital incidence and outcomes of the acute respiratory distress syndrome using the Kigali modification of the Berlin Definition. Am J Respir Crit Care Med. 2016;193(1):52-9. Epub 2015/09/10. doi: 10.1164/rccm.201503-0584OC.
- Goldstein B, Giroir B, Randolph A, (2005). International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med 2005;6(1): 2-8. Epub 2005/01/08. doi: 10.1097/01.PCC.0000149131. 72248.E6.
- Davis AL, Carcillo JA, Aneja RK, Deymann AJ, Lin JC et al. (2017). American College of Critical Care Medicine clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock. Crit Care Med 2017;45(6):1061-93. Epub 2017/05/17. doi: 10.1097/CCM.0000000000002425.
- Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H et al. (1996). The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med. 1996;22(7):707-10. Epub 1996/07/01. doi: 10.1007/bf01709751
- Park WB, Poon LLM, Choi SJ, Choe PG, Song KH, Bang JH et al. (2018). Replicative virus shedding in the respiratory tract of patients with Middle East respiratory syndrome coronavirus infection. Int J Infect Dis. 2018; 72:8-10. Epub 2018/05/13. doi: 10.1016/j.ijid.2018.05.003.
- Yan G, Lee CK, Lam LTM, Yan B, Chua YX, Lim AYN et al. (2020). Covert COVID-19 and false-positive dengue serology in Singapore. Lancet Infect Dis. 2020. Epub 2020/03/08. doi: 10.1016/S1473-3099(20)30158-4.
- WHO. (2020). Oxygen therapy for children: a manual for health workers. Geneva: World Health Organization; 2013 http://www.who.int/maternal_child_adolescent/documents/child-oxygen-therapy/en/, accessed 10 March 2020.
- Choi, J.Y. (2020). Convalescent Plasma Therapy for Coronavirus Disease 2019.Infect Chemother. 2020 Sep;52(3):307-316 https://doi.org/10.3947/ic.2020.52.3.307. PP: 307-316.
- Casadevall A, Pirofski LA. (2020). The convalescent sera option for containing COVID-19. J Clin Invest 2020;130(4):1545–8.

- Luke TC, Kilbane EM, Jackson JL, Hoffman SL.(2006). Meta-analysis: convalescent blood products for Spanish influenza pneumonia: a future H5N1 treatment? Ann Intern Med 2006;145(8):599–609.
- Soo YO, Cheng Y, Wong R, Hui DS, Lee CK, Tsang KK, et al. (2004). Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients. Clin Microbiol Infect 2004;10(7):676–8.
- Hung IF, To KK, Lee CK, Lee KL, Chan K, Yan WW, et al. (2011). Convalescent plasma treatment reduced mortality in patients with severe pandemic influenza A (H1N1).2019 virus infection. Clin Infect Dis 2011;52(4):447–56.
- Zhou B, Zhong N, Guan Y. (2007). Treatment with convalescent plasma for influenza A (H5N1) infection. N Engl J Med 2007;357(14):1450–1.
- Use of convalescent whole blood or plasma collected from patients recovered from Ebola virus disease for transfusion, as an empirical treatment during out breaks. Geneva: World Health Organization; 2014. Available: www.who.int/csr/resource s/publications/ebola/convalescent-treatment/en (Accessed 16 July 2020).
- Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, et al. (2020). Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci U S A 2020;117(17):6-9490.
- Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al. (2020). Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA 2020;323(16):1582–9.
- Ye M, Fu D, Ren Y, Wang F, Wang D, Zhang F, et al. (2020). Treatment with convalescent plasma for COVID-19 patients in Wuhan, China. J Med Virol 2020;92(10):901-1890. Zhang B, Liu S, Tan T, Huang W, Dong Y, Chen L, et al. (2020). Treatment with convalescent plasma for critically ill patients with severe acute respiratory syndrome coronavirus 2 2 infection. Chest 2020;158(1): e9–13.
- Salazar E, Perez KK, Ashraf M, Chen J, Castillo B, Christensen PA, et al. (2020). Treatment of COVID-19 patients with convalescent plasma in Houston, Texas. medRxiv; 2020.
- FDA. Investigational covid-19 convalescent plasma-emergency INDs. https://www. fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device- exemption ideprocess-cber/investigational-covid-19-convalescent-plasma-emergency-inds.
- Seghatchian J, Lanza F. Convalescent plasma, an apheresis research project targeting and motivating the fully recovered COVID 19 patients: a rousing message of clinical benefit to both donors and recipients alike. Transfus Apher Sci 2020;59. June (3):102794.
- Lanza F, Seghatchian J. (2020). Reflection on passive immunotherapy in those who need most: some novel strategic arguments for obtaining safer therapeutic plasma or

autologous antibodies from recovered COVID-19 infected patients. Br J Haematol. 2020;190(July (1)): e27–9.

- Casadevall A, Pirofski LA.(2020). The convalescent sera option for containing COVID-19. J Clin Invest 2020;130(April (4)):1545–8.nfection. Chest 2020;158(1):e9–13.
- Nguyen, T., Bang, D. D., and Wolff, A. (2019). Novel coronavirus disease (COVID- 19): Paving the road for rapid detection and point-of-care diagnostics. Micromachines 11, 1–7. doi:10.3390/MI110303062020
- Chan, W. C. W. (2020). Nano Research for COVID-19. ACS Nano 14 (4), 3719–3720. doi:10.1021/acsnano.0c02540
- Chauhan, G., Madou, M. J., Kalra, S., Chopra, V., Ghosh, D., and Martinez-Chapa, S. O. (2020). Nanotechnology for COVID-19: Therapeutics and Vaccine Research. ACS Nano 14 (7), 7760–7782. doi:10.1021/acsnano.0c04006
- Sharma, A., Kontodimas, K., and Bosmann, M. (2021). Nanomedicine: A Diagnostic and Therapeutic Approach to COVID-19. Front. Med., 8. doi:10.3389/fmed.2021.648005
- Cheng, L.-C., Jiang, X., Wang, J., Chen, C., and Liu, R.-S. (2013). Nano–bio effects: interaction of nanomaterials with cells. Nanoscale 5, 3547–3569. doi:10.1039/ C3NR34276J
- Zhu, M., Nie, G., Meng, H., Xia, T., Nel, A., and Zhao, Y. (2013). Physicochemical Properties Determine Nanomaterial Cellular Uptake, Transport, and Fate. Acc. Chem. Res. 46, 622–631. doi:10.1021/ar300031y
- Liu, Y., Workalemahu, B., and Jiang, X. (2017). The Effects of Physicochemical Properties of Nanomaterials on Their Cellular Uptake In Vitro and In Vivo. Small 13, 1701815. doi:10.1002/smll.201701815
- Abd Ellah, N. H., Gad, S. F., Muhammad, K., E Batiha, G., and Hetta, H. F. (2020). Nanomedicine as a promising approach for diagnosis, treatment and prophylaxis against COVID-19. Nanomedicine 15, 2085–2102. doi:10.2217/ nnm-2020-0247
- Barar, J. (2020). COVID-19 clinical implications: the significance of nanomedicine. BioImpacts BI 10, 137. doi:10.34172/bi.2020.16
- Bonam, S. R., Kotla, N. G., Bohara, R. A., Rochev, Y., Webster, T. J., and Bayry, J. (2020). Potential immuno-nanomedicine strategies to fight COVID-19 like pulmonary infections. Nano Today, 101051. doi:10.1016/j.nantod.2020.101051
- hapiro, R. S. (2021). COVID-19 vaccines and nanomedicine. Int. J. Dermatol. doi:10.1111/ijd.15673
- Varahachalam, S. P., Lahooti, B., Chamaneh, M., Bagchi, S., Chhibber, T., Morris, K., et al. (2021). Nanomedicine for the SARS-CoV-2: state-of-the-art and future prospects. Int. J. Nanomedicine 16, 539. doi:10.2147/ijn.s283686

- Itani, R., Tobaiqy, M., and Al Faraj, A. (2020). Optimizing use of theranostic nanoparticles as a life-saving strategy for treating COVID-19 patients. Theranostics 10, 5932–5942. doi:10.7150/thno.46691
- Łoczechin, A., Séron, K., Barras, A., Giovanelli, E., Belouzard, S., Chen, Y. T., et al. (2019). Functional Carbon Quantum Dots as Medical Countermeasures to Human Coronavirus. ACS Appl. Mater. Inter. 11, 42964–42974. doi:10.1021/acsami.9b15032
- 104- Sarkar, S. (2020). Silver nanoparticles with bronchodilators through nebulisation to treat COVID 19 patients. Curr. Med. Res. 3, 449–450. doi:10.15520/ jcmro.v3i04.276
- Zachar, O. (2020). Formulations for COVID-19 Early Stage Treatment via Silver Nanoparticles Inhalation Delivery at Home and Hospital. Sci. Prepr. Doremalen, V. (2020). c or r e sp ondence Aerosol and Surface Stability of SARS- CoV-2 as Compared with SARS-CoV-1. Nejm, 0–2.
- 107- Orecchioni, M., Bedognetti, D., Newman, L., Fuoco, C., Spada, F., Hendrickx, W., et al. (2017). Single-cell mass cytometry and transcriptome profiling reveal the impact of graphene on human immune cells. Nat. Commun., 1109. doi:10.1038/ s41467-017-01015-3
- 108- Kostarelos, K. (2020). Nanoscale nights of COVID-19. Nat. Nanotechnol. 15, 343–344. doi:10.1038/s41565-020-0687-4
- 109- Garber, K. (2018). Alnylam launches era of RNAi drugs. Nat. Biotechnol. 36, 777–778. doi:10.1038/nbt0918-777
- 110- Jackson, L. A., Anderson, E. J., Rouphael, N. G., Roberts, P. C., Makhene, M., Coler, R. N., et al. (2020). An mRNA Vaccine against SARS-CoV-2 — Preliminary Report. N. Engl. J. Med. 383 (20), 1920–1931. doi:10.1056/NEJMoa2022483
- 111- McKay, P. F., Hu, K., Blakney, A. K., Samnuan, K., Brown, J. C., Penn, R., et al.(2020). Self-amplifying RNA SARS-CoV-2 lipid nanoparticle vaccine candidate induces high neutralizing antibody titers in mice. Nat. Commun. 11, 3523. doi:10.1038/s41467-020-17409-9
- 112- Al-Jandeel TJ, Al-Karawi AS, Abdulrazzaq OI, Tareq S. An Evaluation of Laboratory Tests for COVID-19 Infection in Patients Residing in the Baghdad-Iraq. International Journal of Chemical and Biochemical Sciences, 2023; 23(1).
- 113- T.J. Al-Jindeel, A.S. Al-Karawi, H.O. Kready, M. Mohammed. (2021). Prevalence of COVID-19 virus infection in asymptomatic volunteers in Baghdad city/Iraq during 2021. International Journal of Health Sciences. 6(S2): 5524-5530.