Massive Crisis On Coronavirus Disease (Covid-19) – An Outbreak
Situation Stay Aware & Be Protective

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ABSTRACT

Corona viruses are a large group of viruses which are found in avian and mammalian species. It has been reported that, the identification and characterization of a novel corona virus (2019-nCoV) which caused a pandemic of acute respiratory syndrome in humans in Wuhan, China. By 26 January 2020 it has caused 2,050 laboratory-confirmed infections with 56 fatal cases. Furthermore, it was found that 2019-nCoV is 96% identical at the whole-genome level to a bat corona virus. The new corona virus SARS-CoV-2 binds with human respiratory cells in order to hijack them to produce more viruses. The new virus attaches to a receptor on respiratory cells called angiotensin-converting ACE2. The most abundant protein in corona virus is the nucleocapsid protein.
INTRODUCTION:

Corona viruses are a group of viruses which are found in avian and mammalian species. In morphology and chemical structure they resemble each other. The difference is, in humans they are only proved to cause mild upper respiratory infections but in animals various corona viruses invade many different tissues and cause a variety of diseases \[1-2\]. In 1960 Corona viruses were first, which have an infectious bronchitis virus in chickens and two in human patients with the common cold. (774 deaths), MERS-CoV in 2012 (over 400 deaths), MERS-CoV outbreak in South Korea in 2015 (36 deaths) and SARS-CoV-2 pandemic (formerly known as 2019-nCoV) in 2019 (Over 7154 deaths). All most all of these have serious respiratory tract infections\[3-6\].

![Figure 1 showing the Structure of SARS Associated Corona Virus](image1)

It has been reported that, the identification and characterization of a novel corona virus (2019-nCoV) which caused a pandemic of acute respiratory syndrome in humans in Wuhan, China. By 26 January 2020 it has caused 2,050 laboratory-confirmed infections with 56 fatal cases. At the early stage of the outbreak full-length genome sequences were obtained from five patients. Covid-19 and SARS-CoV are almost identical to each other and share 79.5% sequence identify to SARS-CoV. Furthermore, it was found that 2019-nCoV is 96% identical at the whole-genome level to a bat corona virus. The pair wise protein sequence analysis of seven conserved non-structural proteins shows that this virus belongs to the species of SARS-CoV. From the broncho-alveolar lavage fluid of a critically ill patient 2019-nCoV virus was isolated. It has been confirmed that the novel CoV uses the same cell entry receptor, ACE2, as SARS-CoV. Bat is the natural reservoir host of corona viruses \[7-10\]. Metagenomic RNA sequencing\[11\] of a sample of bronchoalveolar lavage fluid from the patient identified a new RNA virus strain from the family Coronaviridae and was designated as ‘WH-Human 1’ corona virus (and has also been mentioned to as ‘2019-nCoV’). Phylogenetic analysis of the entire viral genome (29,903 nucleotides) revealed that the virus was most closely related (89.1% nucleotide similarity) to a gaggle of SARS-like coronaviruses (genus Betacoronavirus, subgenus Sarbecovirus) that had previously been found in bats in China\[12\].

Form various studies it has been found that warm and wet air lowers both the influenza virus survival times and the virus to human transmission efficiency. Above 30°C (86°F) airborne influenza virus survival may be less at air temperatures where the humidity is above 50%.\[13\] At higher temperatures i.e. 38°C and higher relative humidity i.e. more than 95% Virus survival times were much lower.\[14\]

![Figure 2 Showing the Number of Corona Virus Cases Confirmed](image2)

Virus-laden droplet nuclei are more efficiently produced at lower relative humidity because of increased evaporation of expelled droplet particles, such that more viruses remain airborne longer. In do survive and infectious in air with a low absolute humidity such as <0.007 kg water/kg air\[15\]. When airborne droplets evaporate, then very light airborne
droplet nuclei are formed. Virus in airborne droplet nuclei may remain in the air for many hours.

**Figure 3 showing the Schematic diagram of the SARS coronavirus structure**

The most abundant protein in coronavirus is the nucleocapsid protein. The N-protein is a highly immunogenic phosphoprotein, and it is normally much conserved. The N protein of coronavirus is often used as a marker in diagnostic assays. To aid the efforts of developing vaccines and neutralizing antibodies against this virus, Sino Biological Inc. has developed a panel of research reagents for SARS-CoV-2, including recombinant antigens (the N protein, S protein, the S1 and S2 subunits of the S protein, and the RBD domain of the S proteins), antibodies, antigen detection kits and genes. It is important to understand how the virus enters cells, which can contribute to research on drugs or even a vaccine for the virus.

**MECHANISM OF ACTON**

To infect a human host, viruses must be able to gain entry into individual human cells. They use these cells' machinery to produce copies of themselves, which then spill out and spread to new cells. The exact mechanism of cell entry is not known. Possibly the virus binds with human cell's membrane, releasing its content to cytoplasm. Alternatively the human cell ingest the virus in a process known as endocytosis. Then inside the cytoplasm the endosome opens to release its genetic material (a single stranded RNA). The virus hijakes the cell’s machinery to replicate the RNA and N-proteins and uses the endoplasmic reticulum to form its M-protein and the important S-protein. After replication the virus is carried out by golgi bodies out of the cell in a process called exocytosis, so that it can infect other cells. Mean while the excessive bio production in endoplasmic reticulum leads to apoptosis.

**Figure 4 showing the Replication of Corona Virus Infection**

On Feb. 19 in the journal Science, a research team led by scientists at the University of Texas at Austin described the tiny molecular key on SARS-CoV-2 that gives the virus entry into the cell. This key is called a spike protein, or S-protein. Last week, Zhou and his team described the rest of the puzzle: the structure of the ACE2 receptor protein (which is on the surfaces of respiratory cells) and how it and the spike protein interact. The researchers published their findings in the journal Science on March 4.

"If we think of the human body as a house and 2019-nCoV [another name for SARS-CoV-2] as a robber, then ACE2 would be the doorknob of the house's door. Once the S-protein grabs it, the virus can enter the house," Liang Tao, a researcher at Westlake University who was not involved in the new study, said in a statement.
Zhou and his team used a tool called cryo-electron microscopy, which employs deeply frozen samples and electron beams to image the tiniest structures of biological molecules. The researchers found that the molecular bond between SARS-CoV-2's spike protein and ACE2 looks fairly similar to the binding pattern of the coronavirus that caused the outbreak of SARS in 2003. There are some differences, however, in the precise amino acids used to bind SARS-CoV-2 to that ACE2 receptor compared with the virus that causes SARS (severe acute respiratory syndrome), the researchers said.

"While some might consider the differences subtle," Gallagher said, "they might be meaningful with respect to the strength with which each of those viruses stick." That "stickiness" could affect how easily a virus transmits from one person to another. If any given viral particle is more likely to enter a cell once it enters the human body, transmission of disease is more likely. There are other corona viruses that circulate regularly, causing upper respiratory infections that most people think of as the common cold. Those corona viruses don't interact with the ACE2 receptor, Gallagher said, but rather, they get into the body using other receptors on human cells.

**TREATMENT**

The structure of SARS-CoV-2's "key" and the body's "lock" could theoretically provide a target for antiviral drugs that would stop the new coronavirus from getting into new cells. Most antiviral drugs already on the market focus on halting viral replication within the cell, so a drug that targeted viral entry would be new territory.

The viral spike protein is also a promising target for vaccines, because it's the part of the virus that interacts with its environment and so could be easily recognized by the immune system. Even so, developing either drugs or a vaccine will be a challenging task. Treatments and vaccines not only have to prove effective against the virus, but must also be safe for people. U.S. Centers for Disease Control and Prevention officials have said that the earliest a coronavirus vaccine could be available is in a year to a year and a half. Yadi Zhou et al in 2020 had studied the Network-based drug repurposing for novel coronavirus 2019-nCoV/SARS-CoV-2. They presented a network-based methodology for systematic identification of putative repurposable drugs and drug combinations for potential treatment of 2019-nCoV/SARS-CoV-2. Integration of drug–target networks, HCoV–host interactions, HCoV-induced transcriptome in human cell lines, and human protein–protein interactome network are essential for such identification. Based on comprehensive evaluation, they have prioritized 16 candidate repurposable drugs and 3 potential drug combinations for targeting 2019-nCoV/SARS-CoV-2. However, although the majority of predictions have been validated by various literature data, all network-predicted repurposable drugs and drug combinations must be validated in various 2019-nCoV/SARS-CoV-2 experimental assays[16] and randomized clinical trials before being used in patients.

Although 2019-nCoV/SARS-CoV-2 shared high nucleotide sequence identity with other HCoVs, their predictions are not 2019-nCoV/SARS-CoV-2 specific due lack of the known host proteins on 2019-nCoV/SARS-CoV-2. They have used a low binding affinity value of 10 μM as a threshold to define a physical drug–target interaction. However, a stronger binding affinity threshold 1 μM may be a more suitable cut-off in drug discovery, although it will generate a smaller drug–target network. Although sizeable efforts were made for assembling large scale, experimentally reported drug–target networks from publicly available databases, the network data may be incomplete and some drug–target interactions may be functional associations, instead of physical bindings. For example, Silvestrol, a natural product from the flavagline, was found to have antiviral activity against Ebola[17] and Corona viruses[18]. After adding its target, an RNA helices enzyme EIF4A76, silvestrol was predicted to be significantly associated with HCoVs (Z = −1.24, P = 0.041) by network proximity analysis. To increase coverage of drug–target networks, we may use computational approaches to systematically predict the drug-target interactions further[19-20]. In addition, the collected virus–host
interactions are far from completeness and the quality can be influenced by multiple factors, including different experimental assays and human cell line models. We may computationally predict a new virus–host interactome for 2019-nCoV/SARS-CoV-2 using sequence-based and structure-based approaches[21]. Drug targets representing nodes within cellular networks are often intrinsically coupled with both therapeutic and adverse profiles[22], as drugs can inhibit or activate protein functions (including antagonists vs. agonists). The current systems pharmacology model cannot separate antiviral effects from those predictions due to lack of detailed pharmacological effects of drug targets and unknown functional consequences of virus–host interactions. Comprehensive identification of the virus–host interactome for 2019-nCoV/SARS-CoV-2, with specific biological effects using functional genomics assays[23-24], will significantly improve the accuracy of the proposed network-based methodologies further.

The dose–response and dose–toxicity effects for both repurposable drugs and drug combinations cannot be identified in the current network models due to a lack of the complete drug-target information. For example, Mesalazine, an approved drug for inflammatory bowel disease, is a top network-predicted repurposable drug associated with HCoVs. Yet, several clinical studies showed the potential pulmonary toxicities including pneumonia associated with mesalazine usage[25-26]. Integration of lung-specific gene expression[27] of 2019-nCoV/SARS-CoV-2 host proteins and physiologically based pharmacokinetic modeling[28] may reduce side effects of repurposable drugs or drug combinations. Preclinical studies are warranted to evaluate in vivo efficiency and side effects before clinical trials. Furthermore, we only limited to predict pairwise drug combinations based on our previous network-based framework[29]. However, we expect that our methodology remain to be a useful network-based tool for prediction of combining multiple drugs toward exploring network relationships of multiple drugs’ targets with the HCoV–host subnetwork in the human interactome. Finally, we aimed to systematically identify repurposable drugs by specifically targeting nCoV host proteins only. Thus, our current network models cannot predict repurposable drugs from the existing anti-virus drugs that target virus proteins only. Thus, combination of the existing anti-virus drugs with the network-predicted repurposable drugs or drug combinations may improve coverage of current network-based methodologies by utilizing multi-layer network framework.

The study offers a powerful, integrative network-based systems pharmacology methodology for rapid identification of repurposable drugs and drug combinations for the potential treatment of 2019-nCoV/SARS-CoV-2. Their approach can minimize the translational gap between preclinical testing results and clinical outcomes, which is a significant problem in the rapid development of efficient treatment strategies for the emerging 2019-nCoV/SARS-CoV-2 outbreak. From a translational perspective, if broadly applied, the network tools developed here could help develop effective treatment strategies for other emerging viral infections and other human complex diseases[30].

The Covid-19 vaccine was tested on 1st human by U.S. government on 16th March 2020. As covid-19 is spreading rapidly worldwide The Research Councils under the Ministry of AYUSH, Government of India have issued advisory based on the Indian traditional medicine practices Ayurveda, Homeopathy and Unani. As per the Ayurvedic Practices we need to have some preventive steps like all need to maintain personal hygiene, have to wash hands often with soap and water for at least 20 seconds. We have to avoid touching eyes, nose, and mouth with unwashed hands, close contact with people who are sick. Sick persons need to stay at home. Face should be covered during cough or sneeze and after coughing or sneezing hands should be washed properly. Touched objects and surfaces should be cleaned and disinfected frequently. N95 mask should be used during traveling or working in public places to avoid droplet transmission. If someone suspects Corona Viral infection, he should wear a mask and need to immediately contact your nearest hospital.
CONCLUSION:
A cluster of cases of pneumonia of unknown cause was detected in Wuhan City, Hubei Province of China on 31 December 2019 was informed by WHO. Chinese authorities identified the causative virus of corona virus disease (COVID-2019) on 7th January 2020. During the first 2 months of the current outbreak, Covid-19 an epidemic disease spread rapidly throughout China and caused varying degrees of illness. It was observed that 2019-nCoV is 96% identical at the whole-genome level to a bat corona virus. The common symptoms are respiratory problems. Patients often presented without fever and many did not have abnormal radiologic findings. It causes lymphocytopenia and in some cases it’s also showing kidney problems. It causes as it is spreading worldwide very fast prevention and treatment is very necessary. It’s most important to maintain hygiene. Standard recommendations to prevent infection spread include regular hand washing, covering mouth and nose when coughing and sneezing, thoroughly cooking meat and eggs. Avoid close contact with anyone showing symptoms of respiratory illness such as coughing and sneezing. The Covid-19 patients should be identified and isolated for treatment as well as to prevent the spread among public. Ayurvedic and homeopathic medicines should be used for prevention.

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REFERENCES
9. Yang, L. Li Yang,1 Zhiqiang Wu,1 Xianwen Ren,1 Fan Yang,1 Guimei He, Junpeng Zhang, Jie Dong, Lilian Sun, Yafang Zhu, Jiang Du, Shuyi Zhang, and Qi Jin corresponding author. Novel SARS-like Betacoronaviruses in Bats,
10. Hu B. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus


suppository. Asia Pac. Allergy, 2013;3(2),136–139.


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