

Review Article

Impact of Research on Mankind Welfare against COVID-19

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Abstract: The Corona virus disease 2019 is an infectious viral disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2). It is characterized by cough, fever, breathlessness, sore throat and sometimes fatigueness. Research has played a vital and efficient role in discovering the etiopathogenesis of the diseases. The various pharmaceutical and biomedical approaches of research investment along with its overall growth have been increased efficiently over the past decades. The various research approaches against COVID-19 have been taken into consideration. The spike protein feature of the Virus is utilized by the Researchers to predict the risk of infection and to monitor the phylogenetic and evolutionary dynamic related to corona virus. In order to view the mechanism of attachment of corona virus at molecular level to various oligosaccharide, researchers have revealed that the cryo-EM entities of coronavirus known as OC43 S (a type of trimer of glycoprotein) in isolated and in associated form 9-O-acetylated sialic acid. In the relay of development of the effective therapeutics that possess the power to block viral entry, Mr. Genwei from the Pentelute's lab had executed the computational novel simulations involving the associations amongst the ACE2 receptor and the receptor binding domain of the corona virus which was having the spike like protein. Many efficient drugs and vaccines are in development phase like Fusogenix DNA vaccine, AdCOVID and various others have surpassed the clinical trial such as Moderna's RNA Vaccine, Chinese Can Sino Biologics Inc Vaccine etc. COVID-19 has also a challenging issue for scientist and researchers. Its mutational rate, gene specificity and adaptability towards host is unique features through which its existence is highly potential, Medical sciences, Biotechnology, Bioinformatics, Social sciences etc. all are doing golden handshake to bring more and more research opportunities to serve in the benefit of human kind. High throughput data generated by Next Generation Sequencing is opening a new door to find out the novel targets, miRNA identification and effective therapeutics against COVID-19. Therefore the article summarizes the significant contribution of research in this pandemic and how this is benefiting the mankind.

Keywords: SARS-CoV-2, Research, Computational, Phylogenetic, Simulations, NGS.

INTRODUCTION

Commencement of 2020 has experienced the origination of type of deleterious malady known as COVID-19 which is most commonly caused due to the infection of a corona virus Severe Acute Respiratory Syndrome Corona virus 2 (SARS-CoV-2). There is a necessity to understand the physiology of this virus and should start working efficiently to develop ways to control its spread. Research has played a vital and efficient role in discovering the etiopathogenesis of the diseases. The various pharmaceutical and biomedical approaches of research investment along with its overall growth has been increased efficiently over the past decades, and its approval is done by the Department of Food and Drug Administration (FDA), United States.. A recent literature study revealed that in 2015 the pharmaceutical companies spend about \$2.6 billion, further upgraded from \$802 million in 2003. The reutilization along with repurposing of the Drugs represented as one of the most operative drug based discovery strategy from the existing slot of drugs. This can gradually results into the shortening of the time period and thus reduce the cost of the drugs. The de novo drug discovery and other randomized clinical trials are not such cost effective and are time taking too[1].

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Still many experimental outlooks against reutilising of the drugs are costly and it is time-consuming. The various Computational and Algorithm approaches present the testable hypotheses for the systematic repositioning of the drugs. The structure-based methods are not applied for the 3D structures of proteins hence are not available in most of the human and different viral based target. When the single viral proteins are targeted they often experience the high risk of resistance against a particular drug. This happens because of the viral genomes evolution [2].

Coronavirus Genome and Its Causal Agents

The Corona viruses are mostly enveloped viruses having the positive sense RNA. Their size ranges from 60 nm to 140 nm in diameter. Presence of spike like projections surrounding its surface and gives it an appearance like a crown. This crown like appearance was viewed through the electron microscope so for named as "corona virus". There are Four corona viruses which have been reported in circulation of humans. They are as follows - HKU1, NL63, 229E and OC43. They generally causes mild respiratory diseases [3].

Corona viruses are classified to the family of viruses that can cause various types of infirmities and infections such as the common cold, severe acute respiratory syndrome (SARS) and also the Middle East respiratory syndrome; this is often known as (MERS). In the year 2019, the progression of a new corona virus was identified [4]. It causes the disease outbreak which was started in China, such virus is now popularly known as the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). This disease is also known as "corona virus"2019 (COVID-19). The World Health Organization (WHO) proclaimed the COVID-19 outbreak as a pandemic on March 2020 as it was causing deleterious effects on human body [5].

Mode of transmission and its manifestations

The transmission of this virus takes place by inhalation and contact .The various symptoms include cough fever, breathlessness, sore throat and sometimes fatigueness. The etiology of this virus is thus not detected in most of the cases. In case of elderly people with concomitant immunity, this disease may progress and can lead to viral pneumonia, the acute respiratory distress syndrome (ARDS) and multi organ dysfunction like Lung and Kidney failure. Still many people are asymptomatic at initial stage but they can show the above symptoms later on.

Incredible role of research against covid-19 are

VARIOUS APPROACHES AGAINST COVID-19	RESEARCH INITIATIVE TAKEN
<p>A) The spike protein feature of the Virus is utilized by the Researchers to predict the risk of infection and to monitor the phylogenetic and evolutionary dynamic related to corona virus.</p>	<ul style="list-style-type: none"> ▪ The spike protein of corona virus is having the different sequence length along with their identities. They were having little similarities among remote relatives, which cause the problem in the alignment [6]. ▪ In order to make the analysis and modelling a simple and fast task, they applied the usage of three different features which encodes the algorithms from many dimensions [7]. It includes Composition, Position and Properties. ▪ Many features are incorporated to master the different models of prediction. Amongst them, the most prominent predictive model had received the rate of maximum 98.18%ACC which is coupled with the MCC of approximately 0.96 only when the GGAP (g = 3) has been considered. This indicates that GGAP with value of 3 showed the medium rate of representation [8].
<p>B) On the basis of Structure of human corona virus and its attachment to sialic acid receptor</p>	<ul style="list-style-type: none"> ▪ The infectious cycle of Corona virus is initially started by the glycoprotein based transmembrane spike (S) protein. (9) It attaches itself to the host receptors resulting into the fusion of the upper coat of the virus and cell membranes. ▪ In order to view the mechanism of attachment of corona virus at molecular level to various oligosaccharide , researchers have revealed that the cryo-EM entities of coronavirus known as OC43 S(a type of trimer of glycoprotein) in isolated and in associated form 9-O-acetylated sialic acid[10]. ▪ The Results revealed that the ligand binding is associated with fast kinetics to that surface which is actually the exposed groove and such type of interactions which are identified at a particular place [11]. They are very crucial for S-mediated entry of the virus into the cells of the host. ▪ The carbohydrate mainly the monosaccharides which are free did not result in the activation of these conformational fusogenic changes. The site of interaction of receptor is conserved in all the glycoproteins of the Corona viruses that is involved in the 9-O-acetyl-sialoglycans[12]. ▪ They are having the same type of architecture as those with the special binding pockets of ligands. They are related to esterases of hemagglutinin of corona viruses and Rhino virus.

<p>C)The Various Molecular Based Targeting Strategy against ACE-2 Receptor:</p>	<ul style="list-style-type: none"> ▪ In the relay of development of different effective therapeutics against Corona virus, a team of chemists from MIT has taken an initiative to develop the drug which they believe is capable of blocking the entry of corona viruses into the human cells [13] ▪ This potent drug is actually short fragment of protein which is reported on human cells surface. According to the latest clinical study by the biochemist, they estimated that their novel molecule of peptide is capable of binding to the viral protein that is used by corona viruses to enter the human cells.(14) ▪ The physiological study of SARS-CoV-2 revealed that there is a specific part of the spike protein which is known as the "receptor binding domain", is capable of binding to a receptor known as Angiotensin-converting enzyme 2 (ACE2). This is specifically present on human cell and lung surface [15]. ▪ In the relay of development of the effective therapeutics that possess the power to block viral entry, Mr. Genwei from the Pentelute's lab had executed the computational novel simulations involving the associations amongst the ACE2 receptor and the receptor binding domain of the corona virus which was having the spike like protein [16]. ▪ The above results estimated that the position where the receptor binding domain fixes itself to the ACE2 receptor is found to be a stretch of the ACE2 protein that results in the formation of a structure known as an Alpha Helix [17].
<p>D)Preference of using peptide drugs:</p>	<ul style="list-style-type: none"> ▪ The Peptide drugs are very necessary and essential for this purpose. The advantage and utility of these drugs involves relatively easy manufacturing in the enormous quantities. ▪ These peptide drugs also have a larger surface area as compared to the small surface-molecule drugs [18]. ▪ Having large surface area, they can really grip onto the corona virus resulting into the inhibition of the arrival of the cells. ▪ The use of a small surface molecule, will be difficult for blocking the entire area which the virus is using [19].

The major contribution of research in pharmaceutical companies towards development of vaccines and drugs against covid-19:

S. No	DRUG/ VACCINE	COMPANY/ UNIVERSITY	LOCATIO N	POSSIBLE FUNCTIONS
1.	Fusogenix DNA vaccine	Entos Pharmaceuticals	Edmonton, Alberta	<ul style="list-style-type: none"> ➤ Its delivery is based on proteolipid vehicle that connect the genetic burden into the cell directly. ➤ It's function is based on the development of the novel Corona virus protein derived multiple epitope that out turn in stimulation of an immune response in the body of an infected person to prevent further infection against COVID -19 [20].
2.	ChAdOx1 nCoV-19	University of Oxford , Jenner Institute	England	<ul style="list-style-type: none"> ➤ It is an adenovirus vaccine vector. They are capable of inducing the Humoral and Cell- Mediated Immunity [21]. They are being tested under clinical trial by Thames Valley region.
3.	AdCOVID	Altimune unite with University of Alabama, Birmingham (UAB)	Clopper Road, Gaithersburg	<ul style="list-style-type: none"> ➤ Altimune worked jointly with the University of Alabama, Birmingham (UAB)to undertake this initiative[22]. ➤ The main aim of this collaboration is to develop an international vaccine for the treatment of SARS CoV-2, namely AdCOVID [23]. ➤ They are currently engaged in the testing the immunogenicity [24].
4.	Coronavirus vaccine	Medicago	USA	<ul style="list-style-type: none"> ➤ Medicago is currently undertaken various therapeutic approaches to develop drug candidate for novel coronavirus targeting Virus-Like Particles (VLP) released [25]. ➤ Further it is jointly working with Infectious Disease Research Centre, Laval University to develop antibodies in oppose to coronavirus [26].
5.	NP-120 (Ifenprodil)	Algernon Pharmaceuticals	Vancouver, Canada	<ul style="list-style-type: none"> ➤ The Algernon has revealed that they are exploring this drug as a possible therapeutics against corona virus [27]. ➤ It is antagonist receptor of N-methyl-d-aspartate (NDMA) glutamate receptor [28]. ➤ This drug is being sold under the brand name of Cerocal [29]. ➤ Research studies suggested the efficacy of NP-120 in enhancing the survival rate of mice infected with influenza virus [30].

6.	Moderna's RNA Vaccine	Moderna Inc	Cambridge, Massachusetts	<ul style="list-style-type: none"> ➤ They utilized the concept of novel sequences of mRNA against the infectious proteins, thereby increasing the immunity of the body via the production of antibodies. ➤ They efficiently worked with their team and completed their first stage of clinical trial
7.	Chinese Can Sino Biologics Inc Vaccine	Can Sino Biologics Inc	China	<ul style="list-style-type: none"> ➤ These vaccines work by attenuating the power of a virus by checking their further progression and multiplication. ➤ This vaccine helps in increasing the T-Cell production and thereby enhancing the overall immunity of the human body.

The various website links which are available to attain the information regarding coronavirus are as follows:

S.No	Website Link	Information
1	https://www.who.int/	<ul style="list-style-type: none"> ▪ Latest advices on the basis of biomedical research against on Corona virus.
2	https://www.nih.gov/	<ul style="list-style-type: none"> ▪ Clinical trial on Corona virus
3	https://www.coronavirus.gov/	<ul style="list-style-type: none"> ▪ Disease information
4	http://www.nih.gov/news-events/	<ul style="list-style-type: none"> ▪ About Corona virus treatment and vaccines development
5	https://www.who.int/emergencies/diseases/	<ul style="list-style-type: none"> ▪ Medical research initiative against covid-19
6	https://www.springernature.com/gp/researchers/	<ul style="list-style-type: none"> ▪ Monitoring the evolutionary dynamic of Coronavirus.
7	https://bigd.big.ac.cn/ncov	<ul style="list-style-type: none"> ▪ Protein Sequences study of corona virus
8	https://www.biomedcentral.com/	<ul style="list-style-type: none"> ▪ Latest drugs and vaccines against corona virus.
9	https://www.thelancet.com/	<ul style="list-style-type: none"> ▪ About Epidemiology of Corona virus
10	Aarogya Setu App (https://www.mygov.in/aarogya-setu-app/)	<ul style="list-style-type: none"> ▪ This app works by forming a user data base in order to create a network of information .This can even alert citizens and government of infectious victims of the COVID-19.

CONCLUSION

This is very true that every problem leads us to open doors of its solutions. Some just take longer to figure out .COVID- 19 has also a challenging issue for scientist and researchers. Its mutational rate, gene specificity and adaptability towards host is unique features through which its existence is highly potential. In future many focussed researches will be taken care in order to fight against it. From UV sensitization system to drug repurposing or vaccine development has given a lot of scope for researchers for keeping the survival of human races. Information Technology, Medical sciences biological sciences, Biotechnology, bioinformatics, Social sciences etc all are doing golden handshake to bring more and more research opportunities to serve in the benefit of human kind. High throughput data generated by Next Generation Sequencing is opening a new door to find out the novel targets, miRNA identification and effective therapeutics against COVID-19.

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