ACTA SCIENTIFIC CANCER BIOLOGY (ISSN: 2582-4473)

Volume 4 Issue 6 June 2020

Short Communication

2019-nCoV: Strategy to Combat the Ongoing Outbreak and Future Perspectives

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Received: March 31, 2020

Published: May 13, 2020

Outbreak of COVID-19 is caused by the novel coronavirus designated as 2019-nCoV or SARS-CoV-2. This super-spreader has proven to be devastating for health care systems. The trajectory of this outbreak is impossible to predict in any nation so far; effective response requires prompt action from the public and private health strategies for immediate development and implementation of effective treatment to counterattack the infective 2019-nCoV particles.

In mid-1960s, similar novel viruses were first identified that infected variety of animals (viz. birds, mammals). In 2003, SARS-CoV (Severe Acute Respiratory Syndrome coronavirus) caused severe atypical pneumonia in numerous people of southern China, and then in 2012 MERS-CoV (Middle East Respiratory Syndrome coronavirus) in Saudi Arabia were identified that emerged from animal reservoirs to cause global epidemics. These viruses have evolved and have caused severe outbreaks in humans, resulting in dangerous epidemics and pandemics together. Like many common flu viruses, SARS-CoV-2 virus spreads due to close contact between people, and probably contracts through eyes, nose and mouth as droplets that cause an illness characterized by fever, runny nose, cough, headache, diarrhoea, nausea, vomitting, and shortness of breath. Prevention of this spread through isolation and quarantining methods is the best strategy to control the pandemic activity of this devastating virus.

Coronavirus 2019-nCoV is an enveloped, positive (+) single-stranded RNA virus of beta type that can be divided into 4 genera viz. alpha, beta, gamma, and delta. Alpha and beta CoVs sub-classes are known to infect humans and cause upper respiratory tract infections with higher fatality rates especially in older patients. Human-to-human transmission of 2019-nCoV is the cause of spread of the virus, which is not air-borne yet, as confirmed by the WHO. As health care practitioners who attend the patients are in close contact of the victims, they are most prone to contract the viral infection. It is therefore of utmost importance to control the disease before the community spread stage is reached.

Human angiotensin-converting enzyme 2 (ACE2), is found primarily in cells of the lower respiratory tract, rather than in the upper airway, acts as the receptor for 2019-nCoV. The full spectrum of Covid-19 ranges from severe progressive pneumonia, respiratory tract illness to multiorgan failure, and death. Most patients require mechanical ventilation almost within 24 - 48 hours of admission for critical care. Elder people are more prone to this infection and require intensive care. Males are a little more susceptible than females. Covid-19 appears to be having different impacts on different populations across the world when we compare countries like China, Italy, Iran, Spain, UK, Germany, USA and India. The median length of stay in critical care with ventilation is usually three - five days for both survivors and non-survivors. Most critical care patients require advanced cardiovascular and renal support.

COVID-19 is one of the greatest threats in past 100 years to humanity through the emergence of a pandemic virus. In the city of Wuhan in China, a novel strain of coronavirus (2019-nCoV) was detected first in December 2019, which rapidly spread throughout the World in early 2020 with alarming morbidity and mortality that has resulted in more than 7.5 Lakhs active cases and more than 0.57 Lakhs deaths till March 31st 2020 since its appearance. The death toll will continue to raise day-to-day during respective log phases in several countries and it is difficult to estimate the accurate number statistically. Thus, rapid identification and development of effective interventions against 2019-nCoV is a major challenge and of utmost priority.

Strategy for prevention and therapy

Unfortunately, no direct therapeutics have yet been proven effective for the treatment of 2019-nCoV infected patients with severe illness. Thus, development of therapeutics in response to this outbreak is urgently required. After the emergence of SARS in 2003, lopinavir, a human immunodeficiency virus (HIV) type 1 aspartate protease inhibitor was identified through screening of approved drugs against the virus that caused SARS in humans. Ritonavir, another protease inhibitor is combined with lopinavir to increase its efficiency through the inhibition of cytochrome P450 circuit. During this pandemic emergency the only hope for treatment is repurposing of the existing therapeutics against RNA viruses in a combinatorial approach available from previous incidences, observations, results and experiences.

Several options can be envisaged to control 2019-nCoV infection, including small-molecule drugs, peptides/oligonucleotide-based therapies, specific monoclonal antibodies and vaccines. Development of new strategies require several months to few years to advance or prosper successfully and obviously need preclinical testing, development and finally FDA approved clinical trials. Because of the current emergency of the 2019-nCoV outbreak, many research laboratories should focus on repurposing of the potential existing antiviral agents based on therapeutic experience against the previous outbreaks by other similar viruses. Throughout the Globe, biomedical research laboratories are trying to initiate countermeasure development for 2019-nCoV using prototypes viz, SARS-CoV and MERS-CoV.

Figure

As no effective antiviral treatments or vaccines are presently available against 2019-nCoV, it is important to understand the host response to this virus, unique transcriptional signature genes and surface proteins, which may guide us for the development of novel therapeutics and treatment strategy. Thus, urgent and efficient biomedical research has become critical for the development of antibody-based immunoassay or nucleic acid-based kit for detection of SARS-CoV-2 infection to combat the ongoing outbreak and immediate focus to develop target-based medicine. The potential approaches to develop additional products and techniques for early diagnosis, followed by proper treatment of 2019-nCoV is now crucial. Globally Biomedical Scientists have already initiated their brainstorming activities to identify and validate the drug targets against which therapeutics will be developed that should pass the pre-clinical and clinical trials. The spike glycoprotein will be a promising therapeutic target. The delivery systems of therapeutics against spike glycoprotein should be another crucial issue for the treatment and prevention of 2019-nCoV. In the current context, Nanotechnology may help us to encapsulate the probable and potential anti-CoV-2 drug candidates in combination as nanoformulations coated with peptide against spike glycoprotein of 2019-nCoV for targeting and loading specifically the infecting particles in patient's body to destroy them at low doses.

Future perspectives

Characterization of the transcriptome and proteome of 2019-nCoV using direct RNA sequencing and protein profiling of infected cells may tell us the direction of research and development against this pandemic disease. Biomedical Scientists should consider the following due to outbreak of Coronavirus 2019-nCoV: (i) "Short-term (3 - 6 months)" and "mid-term (6 - 12 months)" goals regardless of immediate outcome. This is important as 2019-nCoV spread may reduce with time throughout the year-2020 but certainly can regain the power again through mutations during propagation in host or even through 'Epigentic Switching' in the Host cell genome by a newly appeared or mutated viral factor of 2019-nCoV. (ii) Scientists should think about all types of approaches during next couple of years including long term like 1 - 2 years because of speculative and much more severe attack by possible "Next Generation 2019-nCoV" with enhanced empowerment through mutation. Hence, they should think about parallel alternative plans or approach with progression of planned research as and when required, if any. (iii) 2019-nCoV may change the status of patients of other diseases like COPD/Asthma, Cardiac, Cancer, etc. for example it can change the grades of cancers and enhance the potential of cancer cells to be metastasized, may even think about the brain cancer patients, as they are extremely difficult to cure.