UNESCO/UNITWIN COVID-19

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Under UNESCO Chair -Life Sciences (Biophysics, Biotechnology and Environmental Health)

Title: The mechanism of COVID-19 virus protein spikes interaction with host cell membrane and its age-dependency.

Mechanism of action of SARS-COV2 in host cell

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Introduction: While severe acute respiratory syndrome coronavirus (SARS-CoV) was initially thought to enter cells through direct fusion with the plasma membrane, more recent evidence suggests that virus entry may also involve endocytosis (1). Cell entry of severe acute respiratory syndrome coronavirus (SARS-CoV) is mediated by the viral spike (S) protein. Using the isolated SARS-CoV-2 virus, scientists subsequently identified a critical host susceptibility factor (2). When cultured cells overexpressed the transmembrane protein angiotensin converting enzyme 2 (ACE2) protein from humans, bats, pigs, or civet cats, they became hypersensitized to infection, showing that ACE2 is a SARS-CoV-2 receptor (2). These findings harken back to the earlier SARS-CoV, which also utilizes both human and animal ACE2 proteins as receptors and exhibits a zoonotic distribution that matches its binding to the ACE2 receptor orthologs (3).

Pathophysiology: The findings by Zhou and colleagues highlight interactions of the entering SARS-CoV-2 virus with host factors; specifically those interactions with the 'corona' of spike (S) proteins projecting from virus membranes. The most threatening bat-derived CoVs are those with distinctively human-tropic S proteins. Once inside human lungs, S proteins interact with host susceptibility factors, including receptors and proteases, which causes massive protein conformational changes triggering virus–cell membrane fusion and infection. S-specific neutralizing antibodies and antiviral agents interfere with these susceptibility factors

and protect from infection (1). The receptor-binding domains on the SARS-CoV-2 S proteins bind with high affinity to human ACE2 (4), A coronavirus contains four structural proteins, including spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins (5). Among them, S protein plays the most important roles in viral attachment, fusion and entry, and it serves as a target for development of antibodies, entry inhibitors and vaccines (6). Zhou *et al.* noted unique features on a separate (N-terminal) domain of the SARS-CoV-2 S proteins that may confer binding to alternative host-cell receptors (1).

Histopathology: Post-mortem samples from a 50-year old male patient from Wuhan were taken from the lung, liver, and heart. Histological examination showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates. The lung showed evident desquamation of pneumocytes and hyaline membrane formation, indicating acute respiratory distress syndrome (ARDS). Lung tissue also displayed cellular and fibromyxoid exudation, desquamation of pneumocytes and pulmonary oedema. Interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes, were seen in both lungs. Multinucleated syncytial cells with atypical enlarged pneumocytes characterized by large nuclei, amphophilic granular cytoplasm, and prominent nucleoli were identified in the intraalveolar spaces, showing viral cytopathic-like changes. No obvious intranuclear or intracytoplasmic viral inclusions were identified(7)

Septic shock: The clinical pictures of patients with COVID-19 and with sepsis are particularly serious, characterized by a wide range of signs and symptoms of multiorgan involvement. These signs and symptoms include respiratory manifestations such as severe dyspnea and hypoxemia, renal impairment with reduced urine output, tachycardia, altered mental status, and functional alterations of organs expressed as laboratory data of hyperbilirubinemia, acidosis, high lactate, coagulopathy, and thrombocytopenia. The reference for the evaluation of multiorgan damage and the related prognostic significance is the Sequential Organ Failure Assessment (SOFA) score, which predicts ICU mortality based on lab results and clinical data (8).

Possible protection:

UV Radiation - There is some idea behind UV radiation on COVID-19. WHO does not recommend direct UV radiation on body as it may harm skin and induce other side effects. One of the most promising and neglected ideas for combating the spread of covid-19 is the use of ubiquitous ultraviolet light in our built environment (trains, offices, hospitals, etc). Ultraviolet light is already being used as a disinfecting agent across the world; it goes by the acronym UVGI - “Ultraviolet germicidal irradiation”. The energetic photons of UVC light break chemical bonds in DNA and kill/inactivate both viruses and bacteria. One of the explanations

of the flu and other infections seasonality is that the Sun's UV kills viruses. However, people spend a lot of time indoors even during summer, and especially during self-isolation. Most of our infections are happening indoors: at home, in transport and in working places. UV from Sun could be part of the explanation of the lower instances of coronavirus in southern hemisphere (9).

Dietary supplementation - Role of balanced diet and nutritional supplement to increase immunity to fight COVID-19. Increase milk or diery products are recommended. Role of spices are also need to be evaluated.

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