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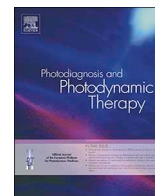
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Letter to the editor

The role of primary and secondary bio-molecules in optical diagnosis of pandemic COVID-19 outbreak



This letter to the editor aims to introduce primary and secondary biomarkers whose reflectance, transmittance and fluorescence signals can be used for optical diagnosis of COVID-19 to the scientific community and persuade to build portable, cost effective, label free and real time optical devices for its detection.

Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) belong to the family of coronaviruses which were considered to be mutated from bats through penguin's camels and civets respectively to humans. SARS-CoV-2 is responsible for COVID-19. WHO on March 2020 declared COVID-19 a pandemic, as it has effected approximately 7.4 million people till 11th of June 2020. Still no one can say when this epidemic will be over because in some developing countries of Southeast Asia, like Pakistan and India, still its peak has not yet appeared. It can transmit through direct routes including cough, sneeze, and droplet inhalation after touching with nose, mouth and eye mucous membranes. Secondary interaction with surfaces like plastic, hospital benches and air droplets for hours. SARS-CoV-2 reaches the lungs through respiratory track and angiotensin converting enzymes-2 (ACE-2) receptors existing inside the nose, mouth, tongue and lungs [1–3]. The patients on ACE inhibitors (ACE-Is) and angiotensin receptor blockers (ARBs) who are on long term immunotherapy are its soft target but the exact relationship between ACE-2 levels, severity of infection and viral infectivity are still unclear. Once its spikes (S) make a bond with ACE-2 receptor, biological mechanisms triggered, results change in the biological activities of specific molecules that can be used directly or indirectly for the early diagnosis of COVID-19. The real-time reverse transcription polymerase chain reaction (rRT-PCR) is the gold standard method of diagnosis using nasopharyngeal swab but simultaneously it is time consuming, costly, susceptible to error and especially diagnosis devices are not easily portable. Second diagnostic technique is computed tomography (CT) that relies on symptom's like consolidation or ground glass opacities [4,5]. Keeping in view the epidemic nature of COVID-19, we need early stage, cost effective, real time diagnosis and portable devices to detect this disease so that treatment can be started to save the vulnerable population.

ACE-2 receptor exists on top of pneumocytes lung cells in the alveoli and have significant role in forming alveoli surfactant and maintaining enough surface tension to keep the sacs open for the exchange of oxygen and carbon dioxide [6]. The SARS-CoV-2 produces millions of copies during replication. It damages to the pneumocytes that activate specific inflammatory mediator to stimulate the macrophages to release specific Interleukin-6 (IL-6), tumor necrosis factor TNF- α and cytokine Interleukin-1 (IL-1). As some of the new proteins comes into play, immune response activates first defense IgG-type antibodies and specific neutralizing antibodies (IgM type). This whole cycle of biological activities ending in vasodilation of alveoli by increasing capillary permeability and goes towards alveoli's edema and finally alveolar

collapse. So, consolidation (damaged pneumocytes type-1, 2 neutrophils, proteins and Reactive Oxygen Species (ROS)) and ground glass opacities that causes cough, hypoxia and increases breathing rate. Due to inflammatory response, patient becomes hypotensive and all of its multi-organ system like kidneys and liver start malfunctioning so Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and creatinine values are also rehabilitated. All the biomolecular level changes occurred during SARS-CoV-2 incubation period (4–14 days), alter the concentration of neutrophils, nucleic acids, cytokines (such as IL-1, IL-6) [6], blood components, proteins, Nucleic acids, lipids, carbohydrates, hormones, phosphate, carotenoids, electrolytes, IgG, IgM, Nicotinamide Adenine Dinucleotide (NADH), sputum components and Flavin Adenine Dinucleotide (FAD). So the above mentioned biomolecules containing biomarkers, vary their molar concentration during incubation period and can become a rich source of COVID-19 diagnosis. Some of them rely on optical method based detection system while the other depends on specific signatures. For example, IgG and IgM show very strong Raman signatures for dengue and COVID-19 detection [7,8]. Nucleic acid based tests are most sensitive for early detection of COVID-19 [9] Cytokines such as IL-1 and IL-6 have specific antibody receptors that can be diagnosed using Enzyme-Linked Immunosorbent Assay (ELISA) [10] and calorimetric assays such as LAMP and RT-LAMP assay based techniques [11]. Some of the electrolytes also change their concentration level during this infection so bio fluid samples can be used in Micro-Electromechanical System (MEMS) that is the base of miniature portable diagnosis devices [12] to scan the mass on airports or even during flying. Similarly, nucleic acid and protein bound coenzymes molecules like NADH, FAD have their own specific fluorescence biomarkers when excited with UV-A light [13] and can be used for label free detection of COVID-19 on early stages employing portable optical detection systems. We would like to reinforce the potential of COVID-19 studies using the fluorescence, Raman signature and conductivity based techniques described in this letter for its diagnosis as current as well as futuristic in order to speed up the diagnostic process and contribute to the cure of this pandemic outbreak.

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