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COVID-19 War, Human Microbiota Function

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Keywords

Coronavirus disease; Human corona viruses (HCovs); Covid-19; Unfolded proteins response.

Editorial

Worldwide all countries are frightening and suffering from the COVID-19 attack with extraordinary death rate, which the exact mechanism is not elucidated yet [1]. The pathogenesis of the COVID-19 virus can be separated in 4 ways: 1) Communication with organs microbiota, 2) Expression of immune-stimulating compounds, 3) Mutations in hosts cells or microbiota genes and 4) Possible dynamic reaction of COVID-19 virus, post treatment action. Human microbiota is internal and external bacteria, fungi (including yeasts), protozoa and viruses, in different anatomical parts of the body. Some of the microbiota produced remains persistent and others are not- persistent that could be produced and/or cleared physiologically. COVID-19 can be entered subjects' body via two pathways directly, and indirectly. In a direct pathway it passes through eyes, respiratory system, mucosal membranes using aerosolized particles or droplets. In an indirect pathway it contaminates subjects' biggest organ namely skin, inconspicuously. Moreover, COVID-19 might find the opportunity to be present and colonize at subjects' tissues and cells, however [1-3]. Normally, the presence of oral, respiratory, and gut commensal bacteria is largely establishing a barrier against different antigens and pathogens. Several human respiratory viruses are neuroinvasive and neurotropic, with potential neuropathological consequences in vulnerable populations. Understanding the supporting mechanisms of neuroinvasion and communication of respiratory viruses including COVID-19 and Human Corona Viruses (HCovs) with the nervous system is also essential to estimate theoretically pathological short- and long-term consequences [4]. Besides, subject's Brain-Gut-Heart axis regulates immunological responses, which also determines microbial hemostasis, and vice versa. Furthermore, microbial combination changes might also affect hormonal and immunological reaction

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1

against pathogens like COVID19 and HCovs. After the COVID-19 enters the body, it might change the balance of the microbiota combination, eventually. Changes in microbiota's count and combination could be beneficial or detrimental to subject's Brain-Gut-Heart axis that regulates immune reactions. For example, in one hand, the presence of some Gram-positive bacterial microbiota i.e. staphylococcus aureus has been shown to prevent influenza virus infections [5], and the presence of some Gram-negative bacteria in the lung microbiota, such as Bacteroides fragilis, which plays an important role in reducing lung inflammation, signify beneficial effects. In the other hand, some Gram-negative lung bacterial microbiota i.e. Prevotella and Veillonella spp. are associated with elevation of Th-17 cell-mediated lung inflammation [6], signify detrimental effects. Furthermore, Bacteroides fragilis found the most prevalence Gram-negative microbiota in oral cavity and lung. This typic Gram-negative genus of bacteria presents a huge amount of lipopolysaccharide (LPS), which could be considered as a "clock-bomb" in order to its endotoxin carriage capacity [7]. Unspecific and irrelevant prescriptions against COVID-19 have shown that bactericidal antibiotics such as vancomycin, tavanex (levofloxacin), azithromycin, cefazolin, etc., and Calcium (Ca⁺²) level enhancers are used in patients in the case of serum Ca^{+2} levels was decreased. Consequently random shut down of organs is inevitable due to cytokines storms. After clinical symptoms of the COVID-19 patients were (applicably) assessed, One might speculate that (a-)specific antibiotics prescription in one hand, might challenge subject's systemic blood circulation with severe endotoxemia, LPS release, and cytokine storm. Subsequent of bactericidal antibiotics usage to kill Gram-negative microbiota of either oral cavity, lung or gut axial increased explosion of side effects i.e. release of different endotoxins i.e. LPS, LOS. On the other hand, different COVID-19 patient's responses indicated that most of the patients had "negative bacterial cultures" of blood and lung aspirate, whereby the yeast and fungal culture's test were positive. One might speculate that microbiota population changes definitely after a regiment of unspecific bactericidal antibiotic-therapy, which might increase simultaneously antibiotic-resistant condition, and/or an initiation of random shutdown of organs, eventually [7]. Moreover, different laboratories' results are showing that bacterial cultures of patients are not completely negative, even after COVID-19 positive ICU's patients, receiving antibiotics in Hospitals, routinely (unpublished data). One might wonder whether bacterial flora of subjects could becoming suppressed after COVID-19 infection and colonization; or prescribed bactericidal antibiotics has direct relationship (cause-effect), which aggravate cytokine storm, and sudden septic onset that in association with calciumhypertonic auxiliary therapy, is resulting in patient death, via premature apoptotic processes, eventually. In the other hand, might (unsuccessful) cure/cares clearly show a significant negative change in the liver enzyme profile, as well. Besides, when Medici are planning to prevent severe endotoxemia in COVID-19 patients by prescribing (general) (a-)specific antibiotics to manage Gram-negative microbiota, One might recommend to use at least that categories of bacteriostatic antibiotics, where less endotoxins being released, instead of using bactericides administration. Additionally, the use of probiotics to stablish normal balance in

2

lung and gut microflora could be considered in the case of antibiotic sensitivity and resistance susceptibility of subjects [8]. To reduce the risk of mix-infection, One might recommend better to prevent either possible contamination of yeast and fungi; or medicate suitable (multi-)therapeutic administrations against yeast and fungi; or (re-)consider other nosocomial bacteria, as well. Unfortunately, no investigation was published yet to evaluate the probability of viral infection, which investigate fungi or yeast proliferations aiming all changes in human- or environmental microbiota and microflora combination, simultaneously. Another speculative conspiracy theory might consider the possibilities, where the COVID-19 might undergo self-unknown-(epi-)genetic mutations in different subjects, after colonization. In one hand, COVID-19 might trigger different microbiomes to also undergo (un-)known mutations. In the other hand, (un-)known entry pathways can provide a good platform to escape immune system and make (un-)predictable mutations. It is noteworthy that some kind of disruption of the body's natural microbial defense barrier, especially via the lungs, can lead to wrong decisions in the body's vital and defense biosensors, unusually. Action and dynamic reactions of microbiota and their intervention/collaboration with the COVID-19 actions, might provide completely new diagnostic and therapeutic strategies for Medici. How cellular and molecular protein response systems, such as the unfolded proteins response (UPR) system, play a key role in maintaining the life of the body's cells in the face of deadly inflammation caused by released LPS or Ca⁺² overload during deadly endotoxemia and cell apoptosis is not elucidated completely [9]. So, One might suggest that Covid19 might change cells' fate by altering the body's natural microbial balance and UPR machinery, whereby toxic substances spread from different cells to each other, which might induce random shut down (un-)intentionally. Further in-details studies needed to confirm how microbiota combination is changing post-Covid19 infection, inter- and intra-personally.

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