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Opinion

COVID-19 and Our Gut Microbiome: Evidence of Close Association[1] and Intestinal Virulence in COVID-19[2]

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It's not yet clear how that signal in the gut reaches the brain, but one likely conduit is the vagus nerve. The vagus connects the brain-stem to many organs, including the colon, making it the longest of the twelve cranial nerves that carry signals between the brain and the rest of the body. "It's a highway". And research in humans and animals suggests that it has a crucial role in ferrying at least some messages between the gut and the brain [1,2].

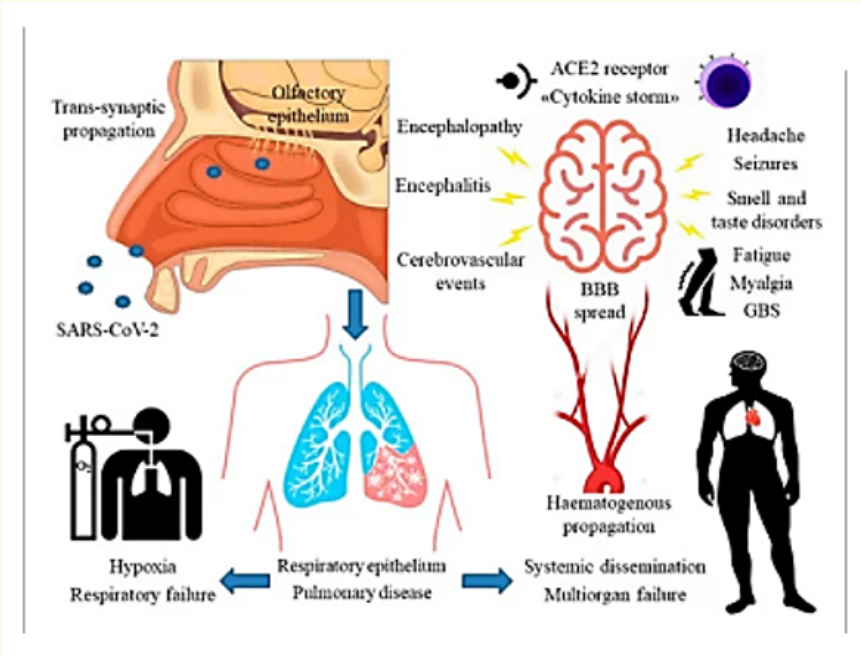

Figure 1: *Main neurological manifestations of COVID-19 and proposed mechanisms of SARS-CoV-2 neuroinvasion. ACE2: Angiotensin II Converting Enzyme Receptor-2; BBB: Blood-Brain Barrier; GBS: Guillain-Barré Syndrome (Credit ref. [3]).*

[1]https://ec.europa.eu/jrc/en/news/covid-19-and-our-gut-microbiome-evidence-close-relationship

[2]https://www.sciencedirect.com/science/article/pii/S1672022921002060

In addition to bacteria and fungi, the human gut also contains a huge variety of viruses known together as the gut virus [4,5]. Virome consists of RNA and DNA viruses that chronically infect their eukaryotic hosts (humans, animals, plants) and prokaryotic (bacteria). The intestinal virus is used to regulate the microbiota ecology of the intestinal bacteria living together and the immunity of the mammalian host.

By RNA sequence of fecal RNA virus shotgun, an active presence of SARS-CoV-2 was found in 47% of patients with COVID-19, even in the absence of gastrointestinal symptoms and after respiratory clearance of SARS-CoV-2 [6]. Meanwhile, COVID-19 patients also underrepresented the mild pepper spot virus (RNA virus), which originated in the diet [7]. By DNA sequence of a fecal DNA virus shotgun, 19 viruses were identified as enriched in COVID-19 patients, while 26 viruses were enriched in non-COVID-19 controllers. Among them, the majority in the fecal-enriched DNA viruses of non-Cubid-19 controls were prokaryotic viruses, particularly bacteriophages. In contrast, more eukaryotic viruses were enriched in the feces of COVID-19 patients, which may be the result of infection with SARS-CoV-2. The eukaryotic viruses may harness the host's immune dysfunction after SARS-CoV-2 infection to expand. Intestinal virulence in COVIID-19 showed more gene coding abilities associated with stress, inflammation, and varicose veins. At the patient's baseline, the abundance of feces of the RNA virus, the chlorotic pepper virus, and multiple bacteriophage species found to be inversely correlated with the severity of COVID-19. Abundance of these viruses has also been linked to inverse blood levels of pro-inflammatory proteins, white blood cell counts, and neutrophil counts, indicating that intestinal viruses may target the host's immune response to SARS-CoV-2 infection. These data highlight that intestinal virulence may contribute to immunological and physiological changes in the host during COVID-19. The use of the antiviral drug lopinavir-ritonavir [8] was associated with a decrease in the abundance of listeria in COVID-19. This suggests that antiviral drugs may direct the ecology of the bacteriophage-host bacterium in the gut. It is probably also due to its role in regulating the defensiveness of the host against SARS-CoV-2.

Among the viruses enriched in COVID-19, the *Escherichia* and *Enterobacter* phage were prominent. The expansion of these phages involved intestinal inflammation and the host interferon response in mice and humans. In addition, an abundance of their host bacteria also increased in the gut after SARS-CoV-2 infection Joint expansion of *Escherichia* phage and *Escherichia* has also been reported in intestinal inflammation and rash of *Escherichia* phage is triggered by lysis of the *Escherichia* bacterial host under inflammatory conditions. Intestinal inflammation in itself can increase the transmission of bacteriophages between bacteria [9]. Therefore, changes in the ecology of the intestinal virus (focusing on the bacteriophage community) are caused. This at least in part, by changes in the bacterial microbiome under the influence of SARS-CoV-2 infection followed by immune dysfunction. Similarly, the dysbiosis of the intestinal virus continued along with the dysbiosis of the microbiome of the intestinal bacteria. This even after the breakdown of COVID-19 disease. A strong correlation was observed between the composition of the virus and the bacterial microbiome in COVID-19 patients. An integrated ecological network analysis of the bacterial and microbial virus in COVID-19 revealed three bacterial species, *Faecalibacterium prausnitzii*, *Bacteroides vulgatus* and *Ruminococcus gnavus* (multiplicity of these bacterial species was also associated with the severity of COVID-19 and/or its severity [10-13], and Microviridae bacteria form nodes of a central network. These viral bacterial species may be keystone species that play prominent roles in mediating microbial-microbial interactions in the gut's microbial ecology.

Concluding Remarks and Perspectives

SARS-CoV-2 infection leads to complicated immunological and pathophysiological responses in the host. This, along with the phenotypic changes in the host. The gut microbiome varies widely in COVID-19, including the bacterial, bacterial, and viral microbiome. Moreover, subsequent bacterial, fungal, and opportunistic virus rashes under the circumstances of SARS-CoV-2 infection and silent/overt colitis in COVID-19 pose additional threats to host health and intestinal microbiome recovery. As a result, the ecology of the gut microbiome has changed.

Research activities highlighted how the microorganisms present in the human digestive tract can affect the severity of COVID-19 and show for the first time that the virus replicates in gut bacteria [14].

Often referred to as the second brain of the human body [15-17], the gut microbiome is a group of bacteria, fungi, viruses and small parasites that reside in our gut. There is growing evidence of a strong link between the gut and the brain. For example, it causes people to develop emotional eating or a stomach ulcer under pressure or to "feel" anxiety, happiness or "gut" intuition.

Coronavirus replicates in human and animal cells. However, a new study by JRC shows that SARS-CoV-2 may replicate in our gut bacteria. This suggests the hypothesis of a close relationship between our gut and COVID-19. In addition, this recently observed viral replication mechanism opens up new scenarios in understanding the biology of SARS-CoV-2.

The microbiome of the gut communicates with other organs in the body. It plays a role in digestion, the division of the gut and digestive waste from other organs, our inflammatory and immune responses to disease, and the communication between our various organs.

Therefore, it is easy to understand that if SARS-CoV-2 mainly affects the respiratory system, a growing number of studies show that the virus can also interact with our gut microbiome, making the disease more severe.

By reviewing more than 70 scientific papers, this JRC study summarizes the putative interactions between gut microbiome and COVID-19. Many studies suggest a link between SARS-CoV-2 infection and an intestinal microbial imbalance, also known as intestinal dysbiosis. However, the understanding of whether the severity of COVID-19 is a primary cause, a secondary reason, a concurrent cause, or the result of an intestinal imbalance is still debatable. Several studies also show that SARS-CoV-2 may endanger our intestinal barrier.

This permeability allows bacterial endotoxins to escape from the gut and reach the bloodstream-intestinal bacteria, found in the lungs of patients suffering from COVID-19. In order words, this permeability can lead to multi-organ complications, affecting patients' lungs, heart, liver, kidneys.

How to treat our intestines?

Each person's gut microbiome is unique. Its composition varies according to its age, genes, diet and environmental factors.

In any case, scientists recommend adopting a healthy diet, rich in grains, fruits and vegetables, to help the gut microbiome fulfill its functions.

In addition to a diet, the application of pre-pro biotics to rehabilitate the gut microbiome, before during, and after SARS-CoV-2 infection is highlighted in the scientific literature. By stimulating the growth of specific bacteria in the gut, both can limit gastrointestinal symptoms due to COVID-19 and ultimately limit secondary infections.

However, a healthy diet and consuming probiotics will never replace the official vaccine and medical treatments, which remain the best way to protect ourselves from severe forms of COVID-19.

Bibliography

1. https://medcraveonline.com/JMEN/the-microbiome-and-incurable-diseases-discussion-review.html

2. http://www.rawvl.be/index_htm_files/How%20does%20coronavirus%20kill.pdf

3. https://www.mdpi.com/1422-0067/21/15/5475/htm

4. Kumamoto CA. "Inflammation and gastrointestinal Candida colonization". *Current Opinion in Microbiology* 14 (2011): 386-391.

5. Virgin HW. "The virome in mammalian physiology and disease". *Cell* 157 (2014): 142-150.

6. Cao J., *et al*. "Integrated gut virome and bacteriome dynamics in COVID-19 patients". *Gut Microbes* 13 (2021): 1-21.

7. Zuo T., *et al.* "Temporal landscape of human gut RNA and DNA virome in SARS-CoV-2 infection and severity". M*icrobiome* 9 (2021): 91.

8. https://www.ecronicon.com/ecpt/pdf/ECPT-08-00475.pdf

9. Norman JM., *et al*. "Disease-specific alterations in the enteric virome in inflammatory bowel disease". *Cell* 160 (2015): 447-460.

10. Yeoh YK., *et al*. "Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19". *Gut* 70 (2021): 698-706.

11. Zuo T., *et al.* "Alterations in gut microbiota of patients with COVID-19 during time of hospitalization". *Gastroenterology* 159 (2020): 944-955.

12. Tang L., *et al*. "Clinical significance of the correlation between changes in the major intestinal bacteria species and COVID-19 severity". *Engineering* 6 (2020): 1178-1184.

13. Sokol H., *et al*. "SARS-CoV-2 infection in nonhuman primates alters the composition and functional activity of the gut microbiota". *Gut Microbes* 13 (2021): 1-19.

14. https://ec.europa.eu/jrc/en/news/covid-19-and-our-gut-microbiome-evidence-close-relationship

15. https://www.actascientific.com/ASNE/pdf/ASNE-02-0078.pdf

16. https://www.nature.com/articles/d41586-021-00260-3

17. https://medcraveonline.com/JMEN/the-microbiome-and-incurable-diseases-discussion-review.html

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