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## NATURAL NEUROIMUNOMODULATION IN CORONAVIRUS INFECTION

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### Current state of knowledge

During these months of 2020, all the attention of doctors and researchers is directed towards discovering the extremely efficient methods of treating Covid-19 infected patients.

As soon as it appeared at the end of 2019, SARS-CoV-2, renamed Covid-19 a few weeks later by the Health Organization (WHO), looked like a flu, but the virus actually produced a much more complex disease.

Covid-19 infection is a very complex respiratory, renal, neurological disease. Covid-19 infection causes symptoms such as dry cough, respiratory problems, fever, but there are lesser known symptoms that may indicate the presence of Covid-19 in some patients. Among these less well-known signs of illness are digestive problems, chills, confusion, headaches. About 8% of patients infected with Covid-19 have frequent headaches, according to a medical study published in the Lancet. Also, dizziness is quite common, if it is intense, it is most likely a patient with a more severe form of Covid-19 infection. Disease and confusion may be the only symptoms that prove Covid-19 presence in the body. A report from a health care center in Washington showed that of 35% of people who were Covid-19 positive, half had no symptoms.

Lymph node follicles are the most important tissue reservoir for Covid-19. In asymptomatic patients, Covid-19 is present only in the lymph, where the contact with the immune system begins where the virus infects the follicular CD4+ T cells (Th cells) present there and the existing bacteria, and if the virus does not circulate further the disease does not appear. If the virus reaches the bloodstream (1-2% of cases), complications, inflammatory cytokine storm and hypercoagulability occur. Dysbiosis of the nasopharyngeal microbiome attracts dysbiosis of the intestinal microbiome and activation of the intestinal microbiome-brain axis. If you intervene quickly at the first sign of disease with the modulation of the activity of the microbiome, the implication of the immune system (neuroimmunomodulation) is suppressed the appearance of the disease.

There is the microbiome: buccal, nasal, intestinal, cardiac, dermal, even the microbiome in the brain with which Covid-19 interacts. When the evolution is complicated, it is necessary to intervene with drug treatment to support the affected organs. Although there is renal impairment, coronaviruses and their traces were not found in the urine of patients. Knowing that the infection also causes digestive symptoms, coronaviruses have been shown in faeces.

It is said that in 1-2% of cases Covid-19 reaches the bloodstream.

Some patients have symptoms such as confusion, restlessness, anxiety, malaise. These manifestations raise questions about the impact of Covid-19 on the brain and nervous system. Neurological symptoms are manifested by loss of smell, taste, neurological pain, even thrombotic strokes. In patients with confusion or agitation, brain scans revealed inflammatory processes. Virulent and deadly, Covid-19 even spreads to the brain in some patients.

The microbiome is essential for promoting immune function for disease prevention and control. Specifically, with regard to viral infections, there must be an adequate immune response to protect the body. The intestinal microbiota with low diversity will consequently lead to a deficient immune function.

Eighty percent of immune cells reside in the gastrointestinal tract. Strokes and cases of encephalitis have been reported. To a lesser extent, the impairment of the olfactory nerve has been described, which causes difficulties in the perception of smell, taste.

Any process that disrupts bowel-brain communication can lead to neurological complications. It seems that some of the patients have serious problems of mental disorder, confusion that even generates forgetting where they are. This state of disorder of spatio-temporal orientation due to lack of oxygen in the blood, many patients end up having the brain (with microthrombosis) more affected than the lungs.

Dysbiosis of the intestinal microbiota may lead to impaired brain function. The microbiota, the intestine and the brain communicate through the microbiota-intestine-brain axis in a bidirectional way.

With the help of natural remedies the brand Deniplant the authors have made several products for autoimmune, metabolic and neurological disorders that act as immunomodulators of the human microbiome.

We assume that the Covid-19 virus creates a dysbiosis of the intestinal microbiome. Virologists have reported that Covid-19 can affect the brain and nervous system (this link has been seen with other viruses).

Viruses can affect the brain in two main ways. The first pathway is triggered by an abnormal immune response, called a "cytokine storm", which causes inflammation of the brain: this process is called autoimmune encephalitis. The second pathway consists of a direct infection of the brain and is called viral encephalitis. The brain is protected by the blood-brain barrier to block invasive substances, but it can sometimes be crossed. Some researchers have hypothesized that the nose may be a pathway to the brain, as odor loss is a common symptom for many patients with Covid-19, but the theory is not verified and many patients who lose their odor have no neurological problems. serious. The intestinal microbiota may influence the permeability of the blood-brain barrier.

## **Project motivation**

The reason why the discovery could be important is to continue learning how the gut microbiome can influence brain function and behavior, and the fact that it may have its own population of bacteria could be a real benchmark.

A healthy gut microbiome is crucial in creating an adequate response to coronavirus. A diverse microbiome is a healthy microbiome, which contains many different species that each play a role in immunity and health. Specialists from all over the world are trying to unravel the mysteries around the coronavirus, trying to understand how it works in the body. These neurological manifestations are thought to raise questions about the impact of Covid-19 on the brain and nervous system.

The motivation of the project is the study of the influence of the intestinal microbiota in terms of health and the appearance of symptoms in Covid-19 infection. In all the conditions

that are determined by Covid-19 there is a close link between the microbiome and these conditions. The diversity of the microbiome decreases as we age, it could help to explain some of the symptoms related to age, changes in immune responses, so it is necessary to maintain a healthy microbiome throughout life. If the patient feels confused, if he has trouble thinking, there are reasons to analyze the bidirectional bowel-brain relationship.

### **The main objective**

Increased immunity is the best barrier to viruses, including Covid-19. The most important barrier in its pathway is a competent immune system. A varied diet is essential for immunity. Natural therapies (neuroimmunomodulation) targeting the microbiome may play a role in the fight with Covid-19. The research focuses on the topic of maintaining the balance of the normal intestinal microbiota and its interaction with Covid-19.

### **Specific objectives**

The diagnosis of Covid-19 infection is currently based on the detection of viral nucleic acid by real-time PCR in nasopharyngeal exudate, brohoalveolar lavage or tracheobronchial aspiration. In this project, we will discuss the biological interaction on the intestinal-brain microbiome axis and explore how this communication may be involved in neurological complications in Covid-19 infection. We aim to highlight new ideas in changing the composition of the intestinal microbiota, which may occur as a result of Covid-19 infection, and to try a promising therapeutic approach to treat CNS disorders by neuroimmunomodulation using natural remedies (bacteriophage Deniplant). The goal is to build and use halimeters equipped with special sensors that can measure the state of the oral, nasal, esophageal, pulmonary, intestinal microbiome, making an EGO software (digital Altrego) equipped with artificial intelligence, as an extension of its own memory for storing and processing all habits related to human health and the microbiome.

### **Expected results**

Currently the treatment is symptomatic and supportive, there is no etiological treatment. The new findings will help us better understand how to care for the patient infected with Covid-19 and the nerve complications that occur.

It was surprisingly concluded that probiotics could be useful in therapy against Covid-19. The composition of the human gut microbiota changes over time, when the diet changes and with the change of health.

The authors are convinced that in the near future natural remedies that act as neuroimmunomodulators of the intestinal microbiome will be effective in the infection with Covid-19, thus achieving the desire to create those foods with a dual role of function, nutrition and health.

### **Project evaluation**

The present studies refer to the immunomodulation of the intestinal microbiota that influences the immune system to prevent the storm of inflammatory cytokines in the brain.

The brain and gastrointestinal tract are tightly connected to form a two-way neuro-neural communication system. The communication between the intestine and the brain is based on the intestine-brain axis, which is so well established that the functional state of the intestine is always linked to the functional state of the brain.

These findings suggest the role of the intestinal microbiome in modulating Covid-19 infection.

The results of the studies are promising, but so far there are no certainties. Too many people talk about Covid-19 without relying on scientific data and without proper knowledge.