European Commission

SCIENCE BEHIND THE DEBATE

Relationship between the gut microbiome and diseases, including COVID-19

Human microbiome

All the microorganisms living in association in and on the human body.

- in mouth
- in lungs
- in intestine
- on skin

An average 70 kg man has 200 g bacteria, ($3.8x10^{13}$ bacteria).

Gut microbiome

has a high diversity of microbes.
(mainly bacteria, but also fungi, viruses, small opportunistic parasites)

1000–1500
different species of bacteria

+/- 160 species
in average per person based on environmental and genetic factors

+/- 95% of the body's entire microbiome is located in the intestine.

The composition of the gut microbiome varies according to

- age
- environmental factors
- genetics
- diet

Therefore, there is up to now no standard profile for a healthy microbiome.

Gut microbiome functions

- immune response
- digestion
- gut permeability
- inter-organ communication
- inflammatory response

Keeping the gut microbiome in equilibrium

- healthy diet
- bacteriotherapy
- SYN BIOTICS
- PRO BIOTICS
- PRE BIOTICS

A dysbiosis

occurs when the usual bacteria species presence and quantities in the gastrointestinal tract are altered, which might have an impact on the gut microbiome functions.

Dysbiosis could favour the appearance and severity of diseases states.

- infections
- immune-mediated diseases
- inflammation
- worsening of chronic diseases

SARS-CoV-2

microbiota changes persisted up to 30 days after disease resolution

Perspective

The effects of diet on microbiome and on human diseases should be considered, in particular in the context of the COVID-19 pandemic, to provide more precise information on the benefits of nutrients to disfavour dysbiosis. Given the increasing number of scientific publications about pre- and probiotics benefits and about immunity-related microbiome, new clinical studies are expected to shed light on how to improve individuals health & well-being by better understanding those mechanisms.

Joint Research Centre

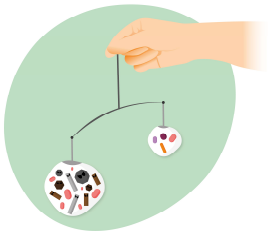
Gut microbiome functions

95% of the human microbiome resides in the guts[1]. The gut microbiome is not only fundamental for the **digestion**. It also supports:

- the **gut barrier** that regulates absorption of nutrients but also prevents viruses and toxins to pass into the blood and lymph systems.
- the **immune response**: several common gut bacteria help regulate the immunosystem.
- the **inflammatory response**: some of the metabolic subproducts produced by the gut bacteria have anti-inflammatory properties.
- the **inter-organ communication**: the gut communitcate via molecular signals with the liver, the central nervous system, the lungs and the heart.

Therefore, the human gut microbiota is important for the preservation of health.

Equilibrium and diseases



Exposure to environmental factors, including diet, toxins, drugs, and pathogens can cause **dysbiosis** (unbalance between harmless and opportunistic bacteria that can potentially cause gastrointestinal symtoms). Ageing and diseases also impact the gut microbiome diversity. As a result, the gut microbiome is a very dynamic organ that is constantly changing.

Dysbiosis could favour the appearance or evolution of diseases, such as infections, immune-mediated diseases (e.g. allergy and auto-immune disorders). **Dysbiosis could also worsen underlying disease** (e.g. rheumatoid arthritis, different types of cancer, diabetes mellitus, obesity, cardiovascular diseases, asthma, and metabolic, autoimmune and neurodegenerative disorders, such as Parkinson's disease).

In the case of **SARS-CoV-2 infection**, dysbiosis has been observed in the majority hospitalized patients, whose clinical state deteriorates significantly more in presence of gastrointestinal symptoms. The disruption of the gut barrier integrity, linked to dysbiosis, could let SARS-CoV-2 to pass between lungs and intestines, via the circulatory and lymphatic systems, and potentially to reach other organs.

One study suggests that the gut microbiota may underlie the predisposition of normal individuals to severe COVID-19.

Besides, some evidences suggest that viral replication could occur in the microbiome, and that **SARS-CoV-2 can exist and replicate in the guts** even after disappearance of the respiratory symptoms or in the absence of gastrointestinal symptoms.

As **there is no standard composition of a healthy microbiome**, relative comparisons from faecal analysis can help defining sets of bacteria and of their metabolites commonly and abundantly present in healthy or sick individuals.

In the case of the COVID-19, a few pilot studies report that the faecal microbiota of infected patients was significantly modified compared with controls, with an enrichment of opportunistic pathogens and a depletion of beneficial bacteria, at all times of hospitalization.

The increased use of antibiotics in handling the different complications of COVID-19 might also be involved in microbiome perturbation of COVID-19 patients.

Scientists hypothesise that the gut micobiome could be involved in the degree of COVID-19 severity and in the persistence of the symptoms. However, they highlight the need for further research on the mechanisms of action of the gut microorganisms on the inflammatory and imune response and with the virus.

Bacteriotherapy and healthy diet

Scientists suggest the use of pre- and pro-biotics (the term bacteriotherapy is sometimes used) to help maintaining or restoring a healthy gut microbiome, not in the aim to cure COVID-19 but to help the microbiome to play its usual regulation role and reduce gastrointestinal symptoms and, eventually, to prevent secondary infections.

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. **Prebiotics** are non-digestible food ingredients stimulating the activity and growth of probiotics after colon fermentation and feed the gut microbiome.

Synbiotics are mixtures of pre- and pro-biotics.

Pre- and pro-biotics would enhance the intestinal epithelial barrier, compete with pathogens for nutrients, produce antimicrobial substances and modulate the imune system.

A healthy diet contributes to a healthy microbiome. It includes sufficient intake of essential nutrientes, such as vitamin A, C, D and E, B_6, B_{12}, folate, zinc, copper, selenium, iron, omega-3 fatty acids and aminoacids. Sufficient protein intake is also crucial for optimal antibody production. Moreover, phytochemicals (such as carotenoids and polyphenols), dietary fibres and omega 3 fatty acids interact positively with the microbiome. **A healthy diet is rich in cereals, whole grains, legumes, fruits and vegetables and it helps the gut microbiome to fulfil its functions.**

Unhealthy diet has often been correlated with chronic inflammation.

Since, the microbiome is affected by genetic and environmental variations, some experts propose personalized food or personalised supplements consisting of bacteria or bacteria metabolites in parallel to other current treatments.

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[1] The full list of references is reported in: Toussaint B., Raffael B. (co-authors), Petrillo M., Puertas Gallardo A., Munoz Pineiro A., Patak A., Querci M., Relationship between the gut microbiome and diseases, including COVID-19, EUR 30810, Luxembourg: Publications Office of the European Union, 2021, ISBN 978-92-76-41080-5, doi:10.2760/54454, JRC125924.

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