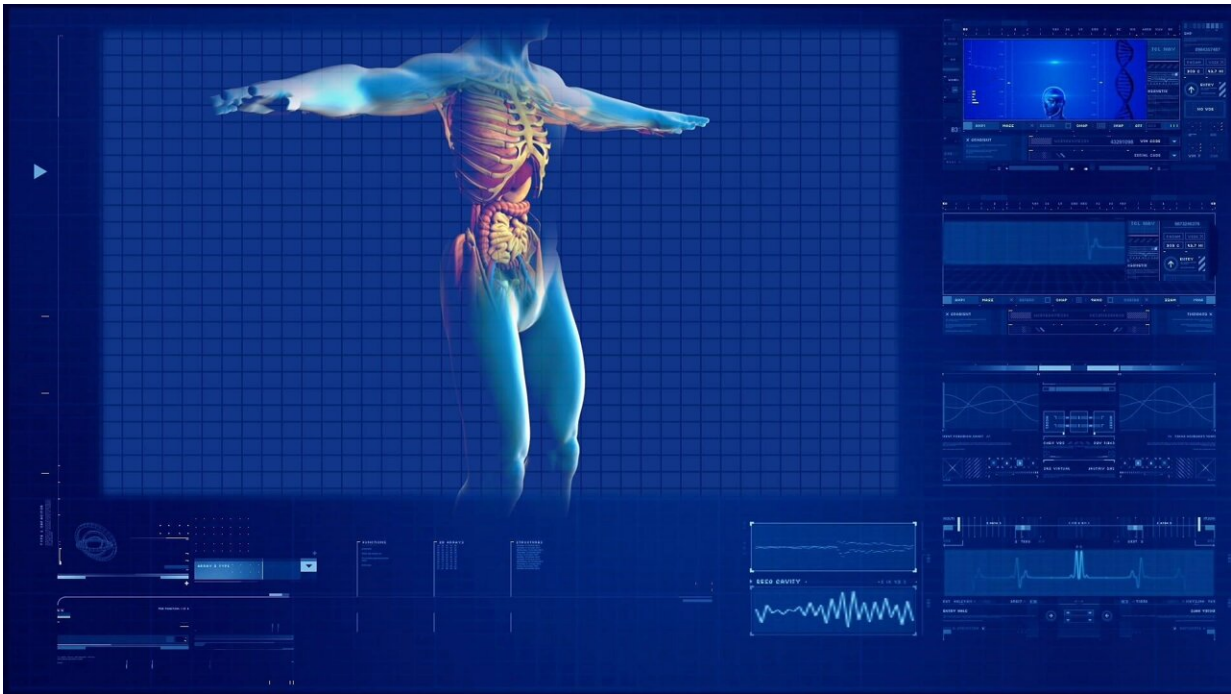


# Another secret of fibromyalgia discovered in microbiome

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Affecting up to four percent of the population and mostly women, fibromyalgia is a syndrome that causes pain, fatigue and cognitive issues. Poorly understood, the condition has no cure and is difficult to diagnose. Now, thanks to the work of a team of scientists from the Research Institute of the McGill University Health Centre (RI-MUHC), McGill University, Université de Montréal and the Institute for Pain Medicine at

Rambam Health Care Campus in Haifa, Israel, there is hope on the horizon.

After showing for the first time, in 2019, that fibromyalgia was linked to alterations in the gut microbiome, this team of researchers has taken a major step towards better understanding the association between [gut bacteria](#) and the syndrome. In a new study, they present the first evidence that patients with fibromyalgia show different amounts and species of bile-metabolizing gut bacteria, as well as different concentrations of [bile acids](#) in the blood, compared to healthy people. They also show that some of these differences are correlated with the severity of the symptoms. Published in the scientific journal *Pain*, these findings could pave the way for the development of diagnostic and therapeutic tools for those suffering from fibromyalgia.

## **A signature characterized by a unique composition of bile acids**

Secreted by the liver, human bile acids help the body digest oils and fats but also carry out many biological activities in other body systems. Once metabolized in the gut, they are recirculated to the liver and blood and become secondary bile acids.

In this study, comparing 42 healthy women with 42 women with fibromyalgia, the researchers observed that bile-metabolizing bacteria that were more abundant in the gut were not identical in both groups, and that women with fibromyalgia had significant alterations in their serum concentration of secondary bile acids.

"The change in bile acids that we observed in patients with fibromyalgia in our study is distinct enough to be used as an effective biological signature to detect individuals with fibromyalgia. That's an important step forward, considering that diagnosing fibromyalgia is often a long

process that requires eliminating other conditions that can cause similar symptoms," says Dr. Amir Minerbi, joint first author of the study, who has transitioned from the Alan Edwards Pain Management Unit at the McGill University Health Centre (MUHC) to Rambam's Institute for Pain Medicine during the time of the study.

Using [artificial intelligence](#), the team also found that the presence of six specific secondary bile acids was sufficient to predict by over 90 percent accuracy if an individual within the study had fibromyalgia.

"Machine and statistical learning have helped us to characterize which gut bacteria change in abundance and which human bile acids are important makers of the disease," says study joint-first author Emmanuel Gonzalez, Ph.D., from the Canadian Center for Computational Genomics and the Department of Human Genetics at McGill University. "These approaches provided an accurate biological signature of fibromyalgia and, although our study cohort was relatively small, these findings are a promising sign that artificial intelligence might be able to considerably enhance accurate diagnosis of the disease."

## **Alterations associated with symptoms severity**

The researchers collected stool samples from all participants for microbiome bacteria analysis as well as blood samples for bile acids analysis. To see if there were associations between the observed biochemical alterations and the severity of symptoms, they asked participants with fibromyalgia to fill out questionnaires assessing their pain, fatigue, sleep quality and cognitive and somatic problems. The patients also described their physical functioning, work difficulties, morning tiredness, muscular stiffness, anxiety and depression symptoms.

The researchers identified a secondary bile acid called alpha-muricholic

acid (aMCA) that was on average five times less present in fibromyalgia patients than in healthy participants. They found that its presence was negatively correlated with most of the syndrome symptoms, including pain, fatigue, unrefreshing sleep and cognitive complaints.

"If this is corroborated in future studies, we may be exploring a potential new mechanism involving one specific secondary bile acid that influences chronic pain," says the senior author of the study, Dr. Yoram Shir, from the MUHC Alan Edwards Pain Management Unit.

Using DNA sequencing technologies and artificial intelligence, the team searched for correlations between serum bile acid concentrations and various clinical variables. The analyses confirmed that at least some of the observed differences in the patients' microbiome composition and bile metabolizing bacteria were likely to be attributed to fibromyalgia, rather than to other individual or [environmental factors](#).

"For example, irritable bowel syndrome and depressive disorder are common among individuals with fibromyalgia, but we were able to demonstrate that alterations to specific bile acids associated with fibromyalgia were not correlated with these conditions," says bioinformatics expert Emmanuel Gonzalez.

Because diet is a factor that influences the composition of the gut microbiome, the scientists also conducted analyses looking at the dietary intake of each participant and found no correlation between the consumed nutrients and symptoms.

## **The first report implicating bile acid alterations in chronic pain**

Like the team's previous study linking fibromyalgia to the [gut microbiome](#) (published in *Pain* in 2019), this new study emanated from

the Fibromyalgia Microbiome Project, that was conducted between 2017 and 2018 at the MUHC Alan Edwards Pain Management Unit and at the West Island Rheumatology Clinic, in Montreal, Canada. Despite the challenges of the COVID-19 pandemics, the team of researchers specializing in clinical research, human nutrition, environmental biology and bioinformatics continued their collaboration and, in less than three years, were able to publish this new study establishing the first significant association of blood bile acid concentrations with chronic pain.

"Our findings show a strong relationship between patient microbiome composition, bile acids and the severity of fibromyalgia symptoms. Understanding the biological mechanism of [fibromyalgia](#) is critical, because it shows that this condition is real, and because it brings us closer to developing an effective treatment to these women and men in [pain](#)," says Dr. Shir.

**More information:** Amir Minerbi et al, Altered serum bile acid profile in fibromyalgia is associated with specific gut microbiome changes and symptom severity, *Pain* (2022). [DOI: 10.1097/j.pain.0000000000002694](#)

Amir Minerbi et al, Altered microbiome composition in individuals with fibromyalgia, *Pain* (2019). [DOI: 10.1097/j.pain.0000000000001640](#)

Provided by McGill University Health Centre

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