



Microbiota against cancer
International research program

REVIEW #5

March 2021

First and bigger network and biobanking of cancer patients stools for building up gut oncomicrobiome signatures for a better diagnosis and treatment of malignancies in Europe.

New publication within the ONCOBIOME Consortium

Grajeda-Iglesias C, Durand S, *et al.* report that Akk, especially if it is pasteurized, causes significant changes in metabolism, elevating the concentrations of several metabolites that have been previously associated with positive effects on health, strongly suggesting that Akk impacts the gut microbiota by creating the conditions to produce “good metabolites” and “good bacteria”.

Aging *Grajeda-Iglesias C, Durand S, et al.*

[Claudia Grajeda-Iglesias, Sylvère Durand, Romain Dailière, Kristina Iribarren, Fabien Lemaitre, Lisa Derosa, Fanny Aprahamian, Noémie Bossut, Nitharsshini Nirmalathasan, Frank Madeo, Laurence Zitvogel, Guido Kroemer \(2021\). Oral administration of Akkermansia muciniphila elevates systemic antiaging and anticancer metabolites. Aging \(Albany NY\). 13, Advance.](#)

Gut microbiota alterations are observed in the transition from health to disease.

Over the past decades, scientific research strives to elucidate the mechanisms of interaction between the host and the gut flora inducing a shift in the abundance or in the variety within this complex ecosystem. For instance, through the transfer of the intestinal flora by fecal microbial transplantation (FMT) from humans to mice, the causal involvement of intestinal dysbiosis in some diseases, such as obesity, diabetes type 2, liver diseases, different types of cancer, and also with aging, has been established.

Efforts made on the isolation and characterization of individual bacterium or consortia of several microbes from human gut, have allowed the identification of species with a positive impact on health.

One prominent bacterium that has wide pro-health effects is Akkermansia muciniphila (Akk), epidemiologically associated with the consumption of health-related food items, leanness, exercise, fitness and healthy aging. Its anti-obesity and anti-diabetic effects have been validated at the clinical level. Interestingly, similar effects have been observed with the pasteurized form of this bacterium, posing the question whether Akk has to be alive to achieve these effects or whether it can be pasteurized.

In their current study, Grajeda-Iglesias C, Durand S, *et al.* investigated the impact of the transfer of live or pasteurized Akk on the ileum, colon, liver and plasma metabolome of FMT-treated mice, in an unbiased fashion, by means of mass spectrometric metabolomics. In addition, a defined sequence of interventions involving sham gavage (phosphate buffered saline, PBS), oral administration of broad-spectrum antibiotics (ATB), FMT from cancer patients, and gavage of a series of distinct bacterial species, selected for their positive effects on cancer immunotherapy response, were used for comparison. In total, 1.637.227 mass spectrometric measurements were performed in this study.

Gavage with different bacteria, including live Akk and FMT alone, gradually recovered the massive metabolite depletion caused by the ATB treatment, supporting the importance of the ileal microbiota for the breakdown of nutrients into small molecules. Liver and plasma metabolome ATB-mediated shifts were less pronounced than the changes in the ileal and colic metabolome, confirming that the internal milieu is protected against external perturbations.

Looking at the specific case of Akk, the authors demonstrated major effects on the metabolome of FMT-treated mice, with important differences between live Akk versus the pasteurized form.

- [Live Akk](#) provoked an increase in spermidine and other polyamines in the gut and in the liver.
- [Pasteurized Akk](#) was more efficient in elevating the intestinal concentrations of polyamines, short-chain fatty acids, 2-hydroxybutyrate, as well multiple bile acids, which also increased in the circulation.

All these metabolites have previously been associated with human health, providing a biochemical basis for the beneficial effects of Akk.



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KEY DATES

Meet - virtually - the ONCOBIOME team at the following events and learn more about the consortium:

- EACR / June 20th – 23th
- IHMC / June 27th – 29th

KEY FIGURES



18

teams across 9 European countries and Montréal



9000

cancer patients



25 000

stool biobanking



15

million euros

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