Gut microbes love lactose

Gut microbes ferment lactose to the metabolite butyrate, which interacts with host cells.

When we eat, there are two parties that celebrate: the human body that receives nutrients from the diet, and the microbes living in the gastrointestinal tract and feeding on all the food leftovers. There are millions of bacteria in the intestine, and it becomes increasingly recognized that they are important for human health. Depending on the composition, food can change the microbes that live in the gut, and their activity. In the Nordic countries, fermented dairy is very popular, and it contains a mixture of the milk sugar lactose, lactic acid which is produced during fermentation, and many peptides and amino acids. Many people feel good after eating fermented dairy even though it is not completely clear why. Therefore, we initiated BioDairy, to investigate the response of gut microbes and cells from the intestine to lactose.

The special role of lactose

There is an ongoing debate whether lactose really reaches the lower gastrointestinal tract. This probably depends on whether the person who consumes fermented dairy still possesses the enzyme lactase. Lactase is a very active enzyme in babies in the upper gastrointestinal tract, but in older people, it is produced much less. In Denmark, the majority of adults still have the lactase enzyme, but in other parts of the world, it is lacking for most of the population. The digestion of lactose also depends on how fast lactose is consumed, for example whether lactose is drunk as milk or eaten as yogurt, and how much lactose there is to start with. Indeed, we do not know completely what happens to lactose on the way through the gut.

When lactose meets the gut microbiota

No matter what, it is difficult to find out how lactose impacts the intestinal microbiota in humans. To be able to test how the microbes respond to lactose without the problem of lactase or no lactase, we used model systems that mimic the demanding conditions such bacteria need to grow, for example the complete absence of oxygen and a diverse mixture of nutrients. We also collected fresh fecal samples, which contain microbes that only recently lived in the colon, to start our model system. Our results show that the microbes that live in the colon are ready to use any lactose that arrives. There was indication that some microbes worked together: one group expressed enzymes to split the lactose molecule to release simple sugars, which others used to ferment to a number of different fermentation metabolites. But we also identified some bacteria that could utilize lactose all by themselves. Very importantly, we observed that there was higher production of butyric acid with lactose. Butyric acid is a fermentation metabolite that is often related to human health.

ABSTRACT

It was the overall objective of BioDairy to determine the impact of lactose on microbial interactions and host immune response. We provide mechanistic understanding and identify microbial and metabolic biomarkers that respond to lactose. We also show that degradation of lactose to lactic acid and further transformation to butyric acid is required for a strong effect on the immune system. This underlines the important interaction between gut microbes and milk for a healthy gut.

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Photo: Colourbox

Butyric acid affected intestinal immune cells more than lactic acid

Indeed, butyric acid tightly interacts with the host cells in the gut and is therefore a very important metabolite. Bacteria often use lactic acid, which is also present in fermented dairy, to produce butyric acid. When we compared the impact of the direct action of lactic and butyric acid on key immune cells, we found a much stronger effect of butyric acid compared to lactic acid pointing at the importance of bacteria that utilize lactic acid to produce butyric acid in the gut. In parallel, we observed that antigen presenting cells were affected by butyric acid and became more efficient in taking up and present dietary antigens in a way that probably prevents the development of autoimmune and allergic reactions. These results further established the important interaction between gut microbes and fermented dairy.

PROJECT OVERVIEW

Title: Health biomarkers of dairy intake (BioDairy), Sundhedsbiomarkører for mælkeindtag (BioDairy)

Project manager: Clarissa Schwab, professor, Dept. Biol & Chem Eng, Aarhus University

Participants: Hanne Frøkiær, professor, Dept. Vet & Animal Sci, University of Copenhagen

Project period: 01.01. 2023-31.12. 2024

Objective: BioDairy aims to generate a platform of tools that will aid in identifying microbial and immunological biomarkers in response to fermented dairy consumption.

PROJECTS RELATED TO THE DANISH DAIRY RESEARCH FOUNDATION

How can the industry benefit from this research?

In BioDairy, we identified gut bacterial and metabolite biomarkers that responded to the presence of lactose. Taken together, BioDairy provided an experimental platform to decipher the individual roles of dairy fermentation products on the complex interplay of host and intestinal microbiota. The mechanistic understanding on the role of lactose on intestinal immunological health gained by BioDairy will allow to sustain the market position of dairy producers.