

Study on gut microbiome of Mongolian associated with diet and health

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論 文 内 容 の 要 旨

The gut microbiota plays an important role in host health homeostasis. People in Mongolia maintain a lifestyle centered on dairy products and animal-based foods, which are believed to shape their unique gut microbiota. It is further noted that Mongolians have a low prevalence of type 2 diabetes (T2D) (10.6%, WHO, 2016) and a high rate of obesity (20.6%, WHO, 2016), which is known to be a co-occurrence risk of T2D. To elucidate the relationship between the gut microbiota, diet, and health status, the following studies were conducted in this thesis study.

To characterize the gut microbiome of Mongolian individuals, a comparative study was conducted using fecal samples from Mongolia (n=98) and five Asian countries: Korea (n=6), China (n=28), Japan (n=79), Thailand (n=27), and Indonesia (n=29). The abundance of *Prevotella*, known to be associated with carbohydrate-based diets, was higher in the Mongolian samples. This finding seems contradictory to the fact that Mongolian diets are primarily animal-based. The high consumption of grains such as wheat and millet as carbon sources in their daily diet may contribute to high *Prevotella* colonization in the gut. Additionally, *Lactobacillus* was remarkably higher in Mongolian samples, which may reflect the habitual consumption of fermented dairy products and contribute to their health homeostasis.

Second, to unravel the paradox of the lower prevalence of T2D than expected from the obesity rate, a comparative analysis of the gut microbiome was conducted in two groups: individuals with obesity and T2D (DO: n = 31) and those without T2D (NDO: n = 35). The NDO group was more highly colonized by short-chain fatty acid (SCFA)-producing bacteria, such as *Faecalibacterium* and *Anaerostipes*. Notably, the acetate concentration was significantly higher in the NDO samples ($p = 0.007$, after adjusting for sex and body mass index). The NDO samples exhibited a higher abundance of genes related to SCFA biosynthesis, which are primarily encoded by lactic acid bacteria and *Anaerostipes hadrus*, according to whole-shotgun metagenomic analysis. These results suggest that the SCFA produced by the gut microbial community plays a role in preventing the onset of T2D co-occurring with obesity in Mongolians.

Third, to investigate the impact of airag, a traditional Mongolian fermented mare's milk, on the gut microbiome of Mongolians, a comparative analysis was conducted on samples of herders collected in summer (high airag consumption, n=40) and winter (low airag consumption, n=24). The results indicated that the gut microbiome exhibited higher levels of *Lactobacillus* and SCFA-producing bacteria in the summer. An amplicon sequence variant corresponding to *Lactobacillus helveticus* was consistently detected in the airag samples (n=16), as well as in the fecal samples from herders. These findings suggest that airag has the potential to support Mongolian health by modulating the gut microbiota.

Finally, the effect of modern fermentation containers on the microbial composition of airag was investigated. A comparative analysis was conducted to assess the microbiome differences between airags produced in plastic containers (modern-type container, n=77) and khohuur (traditional-type container, n=79). Airag in khokhuur demonstrated significantly higher alpha diversity than in plastic containers. In khokhuur, a greater variety of bacteria encompassing lactic acid bacterial species and environmental bacteria were observed with lower levels of lactic acid fermentation, suggesting an increase in the microbiological value and food functionality of the airag.

In conclusion, the presence of SCFA-producing and lactic acid-producing bacteria is crucial for the health of Mongolians under animal dietary habits. The formation of gut microbiota appears to be supported by the high consumption of fermented dairy products, represented by airag.