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### Fructophilic Lactic Acid Bacteria: Their Niche-Specific Adaptation and Practical Importance

#### Introduction

Fructophilic lactic acid bacteria (FLAB) are a special group of lactic acid bacteria (LAB), which prefer fructose over glucose as a growth substrate. They can metabolize glucose only when external electron acceptors are present. Fructose, oxygen, and pyruvate are used as the electron acceptors<sup>1</sup>. Such unique microbes are only found in fructose-rich niches, including flowers, fruit surfaces, fermented fruits, and guts of honey bees. They taxonomically belong to two phylogenetically distant microbial groups, which are the genera *Apilactobacillus* and *Fructobacillus*. Here, I introduce their adaptation manner to their habitats and practical importance in the unique microbes.

#### Methods

FLAB were phenotypically and genomically characterized to study adaptation to their habitats. Consumption history of FLAB was evaluated by studying a presence of viable FLAB cells in fresh honeys.

#### Results

FLAB were poor sugar fermenters and metabolized only limited number of carbohydrates. Indeed, several genes involved in carbohydrate metabolism, including phosphotransferase system, were missing in genomes of FLAB. Moreover, complete bifunctional alcohol/acetaldehyde dehydrogenase gene (*adhE*), which is essential to convert acetyl-CoA to ethanol and to maintain NAD/NADH balance in the phosphoketolase pathway, was missing in the microbes. The absence of the gene induced inability of glucose metabolism in FLAB. Pan-genome analysis of genes involved in metabolism revealed that the phylogenetically distant two FLAB genera shared similar gene reduction profiles during adaptation to their habitats, indicating that the adaptation to new habitats, as observed for FLAB, is convergent evolution<sup>2</sup>. FLAB have several potential beneficial properties, including strong fructose metabolic properties and production of valuable compounds (nicotinamide mononucleotide, novel bacteriocin, exopolysaccharides, etc.). Postbiotic properties were studied in healthy adults, while no studies reported probiotic properties of FLAB in humans. One of the reasons for this lack would be an absence of FLAB species in the QPS list. Viable FLAB cells were present in fresh honey samples tested (harvested within a week), and 29% of the fresh honey samples contained FLAB with levels of over 10<sup>5</sup> CFU/g<sup>3</sup>. FLAB species found in the tested fresh honeys were mostly *Apilactobacillus kunkeei* and *Fructobacillus fructosus*, which are the inhabitants of honey bee guts. On the other hand, they are absent in aged honey samples (aged over 2 weeks after harvest).

#### Discussion

FLAB adapted to their habitats at the genome level and lost number of genes involved in metabolism during adaptation to fructose-rich habitats. Several beneficial properties were reported in FLAB. Humans have long consumption history of honeys, suggesting that humans have a long history of the safe consumption of viable FLAB through fresh honey without specific health concerns.

#### References

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3. Takatani N and Endo A. Viable fructophilic lactic acid bacteria present in honeybee-based food products. FEMS Microbiol. Lett. 2021, 368(21-24):fnab150.