

Niche-Specific Genome Evolution in Gastrointestinal Probiotics

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Introduction

Probiotics are defined as health-promoting microbes which confer health benefits upon the host. *Lactobacillus* is regarded as the most diverse probiotic genus which harbors over 200 species among which are many strains with proved functional probiotic characteristics [1-3]. The economic significance of probiotics have courage scientists to study the biochemistry, genomics, phylogeny and physiology of *lactobacilli*, exhaustively. The genomic data highlighted the probiotic capabilities as strain specific traits which may be a result of the niche-specialization of the genomes of these bacteria to certain ecological niches (in this case the gastrointestinal tract of various animals). Another interesting feature of this genus may be the association between the genome size and the environmental distribution of its species [4,5]. The proposal of a co-evolutionary relationship between these bacteria with their hosts originates from the fact that certain *Lactobacillus* species have the capability to colonize the gastrointestinal tract (GIT) of animals and even some *lactobacilli* show degrees of host-specificity in this regard. This evolutionary trend has resulted in a considerable rate of reductive evolution which is mirrored in their small genomes [4-6].

The main trend in the evolution of the genomes of *lactobacilli* is genome decay which resulted in the general metabolic simplification although there are also accumulative evidences on gene duplications and acquisition events. Such evolutionary event have been detected in habitat specialist *lactobacilli*. For examples *L. helveticus* (cheese inhabitant), *L. sakei* (meat inhabitant), and *L. gasseri* (GIT inhabitant). High inter and intra-species variability observed in *lactobacilli* is also attributed to the evolutionary events and these traits are considered as lifestyle adaption regions in the genome of *Lactobacilli* species [7-8]. Accumulation of pseudo genes and insertion sequence (IS) elements and decreasing rate of G+C content are known as characteristic features of a reductive genome minimization. Such evolutionary events are shown to be linked to a passage through a development bottleneck. The host-specificity

and eco-physiological adaptations of pathogenic or non-pathogenic microbial species to anew habitats are the result of a reductive evolution. This is a development field which is associated to lack of selection pressure during evolutionary conversion from free-living to a host-associated lifestyle [9].

Genome minimization is a critical evolutionary approach which can drive the environmental adaptation of species. The cellular adaptation to the environmental parameters may not just depend on gene absence or presence, but is also dependent on the accumulation of specific adaptive variations of genes. Phylogenetic analyses can be highly helpful to study the potential role of such genome variations in niche-specialization [8]. Recent phylogenomic studies delineated two major lineages of *Lactobacillus* species: 1) habitat generalist *lactobacilli* with large genomes (*L. plantarum*; ~ 3.3 Mb, *L. paracasei*; ~ 3.1 Mb, *L. casei*; ~ 2.9 Mb, and *L. brevis*; 2.3-2.7 Mb), and 2) habitat specialist *lactobacilli* with smaller genomes (average genome size of 1.3-2.0 Mb) (*L. helveticus*, *L. sakei*, *L. gasseri*, and *L.johnsonii*) [7].

Niche-specificity in the genus *Lactobacillus*

A considerable number of *lactobacilli* have adapted a defined environments through niche-specific genome specialization. The genomes of *L. crispatus*, *L. gasseri*, *L. iners*, and *L. johnsonii*, are small and show very high niche-specificity to the GIT environment. Similarly, strains of *L. helveticus* show adaption to dairy environments. Similarly, *L. sakei* (meat inhabitant) has a small genome and its genome is indicative of some selective specializations to the meat environment. Thus, various evolutionary trends may have led to the strain-specific features and niche-specificity of such species [7].

Niche-specificity of GIT-Specialized *lactobacilli*

Certain species of *Lactobacillus* have the capability for colonization of the GIT in animals. Among such *lactobacilli* are various members of the *L. acidophilus* phylogenetic group (previously

known as *L. delbueckii* group). *L. acidophilus* is the most diverse phylogenetic group of the genus. However, members of this group have small genomes and the type strains harbored in this group have been mostly isolated from samples associated to vagina and GIT of animals. Another group of the genus *Lactobacillus* which tend to have a selective affinity to the GIT environment fall into the *L. salivarius* phylogenetic group. *Lactobacillus gasseri* and many other members of *L. acidophilus* phylogenetic group, are amongst the GIT-associated species which shows a selective adaptation to the GIT environment. Niche-specialization of such species for survival and growth in GIT is linked to various characters which are mandatory for probiotics (acid tolerance, resistance to bile salts, adhesion to the host epithelial cells, bacteriocin production, modulation of the innate and adaptive immune systems). Also, this bacterium is a true autochthonous member of the “probiome” of the human GIT. Survival of such GIT-specialized *lactobacilli* in the extreme environment of GIT is thought to be associated to bile salt hydrolase enzymes and a unique set of bile transporters. Interestingly, homologs of bile salt associated transporters have only been found in strains of *L. gasseri* and *L. acidophilus*. These findings indicate the importance of such genes for *L. gasseri* and *L. johnsonii* in colonization of the GIT environment [8,9].

Conclusion

Genome minimization is the main trend in the evolution of *Lactobacillus*. Based on the genomics and ecology data, the genus niche-specialized *Lactobacillus* species seems to have smaller genomes and a very narrow distribution. These species have had a higher rate of reductive evolution. *L. helveticus* (in dairy products), *L. sakei* (in meat), *L. crispatus*, *L. gasseri*, *L. iners*, and *L. johnsonii* (in GIT and vagina) are niche-specialized *lactobacilli*. GIT-specialized species have evolved to resist the harsh environment of the GIT.

Such particular adaptations can also be observed in the other microbial inhabitants which show a selective affinity to the GIT environment.

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