Metabolic exchange by essential vitamins in the human intestinal microbiota

Alexander Arzamasov[1], Matvei S. Khoroshkin[1], Semen A. Leyn[1], Dmitry A. Rodionov[1]

[1]*Institute for Information Transmission Problems, Moscow, Russian Federation*

e-mail: arzamasov.alexander@gmail.com, khorms@gmail.com, semen.leyn@gmail.com, rodionov@iitp.ru

Background: Metabolite exchange is an important process shaping the structure of microbial communities. However, very little is known about crossfeeding by specific nutrients between microbial community members. Among micronutrients, vitamins of B-group are of high significance as they are precursors of nearly all metabolic coenzymes that are universally essential in all forms of life. Many members of microbial communities are not capable to synthesize some or all B-vitamins (auxotrophs), while other members possess complete biosynthetic pathways for these nutrients (prototrophs). Therefore, vitamin exchange between auxotrophs and prototrophs can be an important factor shaping microbial community structure. Human microbiome is a set of all symbiotic, commensal and parasitic microorganisms that inhabit the human body.

Results: We used the metabolic subsystem approach implemented in SEED genomic platform to study potential metabolite exchange between bacteria that inhabit human gastrointestinal tract. Using publicly available information on the composition of the human gut microbiota and the PATRIC database of reference microbial genomes, we selected a set of ~2300 bacterial strains with available complete of draft genomic sequences and uploaded them into the SEED workspace. Then we analyzed these genomes and reconstructed metabolic pathways for synthesis of 8 B-vitamins and trheir respective cofactors (thiamine/TPP, riboflavin/FMN/FAD, niacin/NAD, folate/THF, pantothenate/CoA, pyridoxine/PLP, biotin, cobalamin/B12) and queuosine that is a modified nucleoside that is present in certain tRNAs in bacteria and eukaryotes. We also analyzed genomic distributions of known uptake transporters for vitamins and their metabolic precursors. The inferred vitamin proto-/auxotrophic phenotypes and predicted transporters allowed us to classify the studied organisms with respect to their biosynthetic and transport capabilities. The studied bacteria showed high level of conservation of proto-, auxotrophic phenotypes on the

taxonomic level of species. Incomplete biosynthesis pathways for some vitamins, such as biotin, thiamine and pantothenate, suggest certain vitamin deficiencies can be alternatively supplemented by their metabolic precursors (e.g. dethiobiotin, thiazole, pantoate). Overall, vitamin auxotrophic phenotypes are much more abundant in the human gut microbiota and only a small subset of microorganisms can synthesize all vitamins.

Conclusions: We performed genomic reconstruction of vitamin biosynthesis and salvage pathways in over 2300 members of human gut microbiota. Our results strongly suggest that crossfeeding by vitamins and their precursors is an important for gut community. We propose several types of transporters that could be involved in vitamin sharing by prototrophs. In summary, the obtained in silico reconstructions of vitamin metabolic and transport pathways contribute to our understanding of metabolic crossfeeding processes in human gut microbiome.

Acknowledgments: This research was supported by the Russian Science Foundation (grant #14-14-00289).