Predicting changes in microbial metabolite productions using whole metagenomic sequencing data based on the microbial gene-metabolite network model

Jungyong Ji[1], Sungwon Jung[1,2,3*]

[1]Department of Health Sciences and Technology, GAIHST, Gachon University, Incheon 21999, Republic of Korea

[2]Department of Genome Medicine and Science, Gachon University College of Medicine, Incheon 21565, Republic of Korea

[3]Gachon Institute of Genome Medicine and Science, Gachon University Gil Medical Center, Incheon 21565, Republic of Korea

: Corresponding author

Abstract

Studies on crosstalk of microbiome-metabolome have been conducted to infer microbial or metabolic features that have importance on human health, mainly, through functional, mass spectrometry profiling and integrative analysis. However, there have been few researches identifying change in the individual metabolite level based solely on microbial genome. In this study, we propose the method that predicts individual metabolite's change using the network built by utilizing known gene-metabolite interaction information. Specifically, by predicting the change of individual metabolites level rather than pathway level, we can directly estimate each metabolic potential of a given microbial genomic content. The network algorithm used here is reporter metabolite which identifies metabolites around which most significant microbial gene family abundance's changes occur, where it is constructed with individual interactions and gene families with differential abundances. For benchmark evaluation of the proposed method, we used a publicly available paired dataset of shotgun metagenomics and metabolomics from an inflammatory bowel diseases (IBDs) cohort with controls, and evaluated the concordance between our predicted changes and the previously reported changes. The overlap between the predicted and the measured metabolic class was statistically significant, especially for the metabolites with large changes. This method of predicting individual metabolites based on microbial genomes will help narrow a number of metabolites down to their target range before performing costly and incomplete mass spectrometry, and is expected to contribute to developing strategies for disease treatment and prevention by investigating candidate metabolites directly associated with disease pathogenesis.