Inference of phenotypes for BCAA degradation in human gut microbiome using subsystems approach.

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Genome-scale reconstruction of metabolic pathways and regulatory networks for essential nutrients, such as amino acids and vitamins, in human microbiota is one of the critical tasks of modern genomics. The human gut community is composed of metabolically versatile anaerobic microorganisms from a large number of taxonomic orders that mostly belong to the Bacteria domain. The gut microbiota acts as an exquisitely tuned metabolic ldquo; organrdquo; within the host. Recent availability of complete genomes for thousands of microbial gut species and expansion of the human gut metagenomics and metatranscriptomic data sets open new opportunities to apply the comparative genomics approaches for identification of essential enzymes, transporters and regulators involved in key metabolic pathways, and provide the basis for genomic assignment of metabolic phenotypes to gut bacterial species. Amino acids are building blocks of proteins and peptides, and also serve as precursors for many essential metabolites including nucleotides, cofactors, etc. Amino acid degradation is an important metabolic process since host degradation of proteins releases significant amounts of oligopeptides and free amino acids that become partially available for gut microbiota. Previously we have reconstructed biosynthetic capabilities of gut bacteria for amino acids using the comparative genomics-based approach applied to 2228 genomes. The studied bacteria showed high level of conservation of amino acid biosynthesis phenotypes on the taxonomic level of species. We reported that amino acid auxotrophic phenotypes are rare in the human gut microbiota, whereas the larger number of studied bacteria is capable of de novo synthesis of all 20 amino acids. In current study, we investigated metabolic pathways of amino acid catabolism in the same set of reference gut bacteria. We found that some members of microbial community are not capable to degrade branched-chain amino acids (BCAA), while other members possess complete catabolic biosynthetic pathways for these nutrients. In addition, many gram-positive bacteria possess an alternative BCAA catabolic pathway that is merged with the branch chain fatty acid synthesis pathway. Also, there is another disjunctive pathway which is suggested to be an offshoot from another various metabolic routes. Metatranscriptomic data suggest that BCAA degradation genes are differentially expressed in gut microbial communities exposed to different diets.