Секция «Биоинформатика»

Inference of phenotypes for amino acid 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, vitamins and polysaccharides, 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 interrelated taxonomic orders that mostly belong to the Bacteria domain. The gut microbiota acts as an exquisitely tuned metabolic "organ", thus delimiting the well-being of host, Recent availability of complete genomes for thousands of microbial gut species and expansion of the human gut metagenomics and metatranscripto data sets open new opportunities to develop and 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 elementary units of proteins and peptides, and also serve as precursors for many essential metabolites including hormones, 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 2,856 genomes representative of the human gut microbiome. 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 are capable of de novo synthesis of all 20 amino acids. In current study, we investigated metabolic pathways of amino acid degradation in the same set of bacterial genomes representing the human gut microbiome. As result, we reconstructed various metabolic pathways for degradation of six amino acids (lysine, histidine, tryptophan, threonine, methionine and proline) and report that some members of microbial community are not capable to degrade certain or all studied amino acids, while other members possess complete catabolic pathways. Several alternative pathways for utilization tryptophan were analyzed; these pathways are characterized by different products including histamine, indole, indoleacetate, indolelactate and indolepropionate that have important influence on human health.