Comparative genomics analysis of human gut microbiome demonstrated broad distribution of metabolic pathways for mucin glycans foraging

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Mucins are heavily glycosylated proteins with high molecular weight and they are produced by epithelium in most animals. In the human intestine, mucins are responsible for forming of the mucus layer [1-2]. Recent finding demonstrated that alterations in mucin glycoconjugates (MGC) impact on the composition of human gut microbiota (HGM) [3-5]. Here, we present a systematic analysis of HGM encoded systems for degradation of MGC.

We applied genomic analysis to 397 HGM genomes microorganisms found in the human gut belonging to the phyla of Actinobacteria, Bacteroidetes, Euryarchaeota, Firmicutes, Fusobacteria, Proteobacteria, Synergistetes, Tenericutes, and Verrucomicrobia. For the annotation of gene functions, the PubSEED platform (http://pubseed.theseed.org) was used. The gene function annotation was done using available literature data, protein sequence similarity, protein domain structure, and genome-context based approaches, including gene chromosomal clustering and phyletic patterns.

We analyzed genes required for the degradation of MGC to monosaccharides as well as genes for the utilization of these monosaccharides (fucose, galactose, N-acetylgalactosamine, N-acetylglucosamine, and N-acetylneuraminic acid) as carbon and energy sources. Genes for utilization of one or more monosaccharides were found in 369 (93%) studied genomes. In addition to previously known genes involved in MGC degradation, we predict four non-orthologous replacements for enzymes and four novel transport systems for MGC-derived monosaccharides.

The analysis of genes for utilization of multiple monosaccharides in large number of co-

inhabiting organisms revealed the following roles of the gut microbial community in MGC foraging. First, different monosaccharides demonstrated distinct distribution patterns across the analyzed genomes, which correlated with distribution of these monosaccharides in nature and particularly within the human intestine. Second, 339 genomes encoded only partial pathways, i.e., the presence of either the glycosyl hydrolases (GHs) for cleavage of a monosaccharide from MGC or the catabolic pathway for the utilization of a monosaccharide. Based on these pathways, we propose that there exist exchange pathways for MGC-derived monosaccharides within HGM. Consistently, we show that 338 (85%) of the analyzed genomes may be involved in such exchange pathways. Third, the analysis of MGC-degrading GHs allows us to predict the ability of each analyzed microorganism to degrade specific types of MGC. Finally, we predict so-called beneficial pairs of organism, i.e., pairs of organisms that can utilize specific MGCs, which cannot be degraded by any microbe alone. The 325 (82%) of the analyzed genomes are capable to form such pairs.

We demonstrate that the HGM community is highly adapted to utilization of MGCs as sources of carbon and energy and suggest that this adaptation may be a consequence of co-evolution.

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