Characterizing the Mucin-Degrading Capacity of the Human Gut Microbiota

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Abstract:

Introduction: Mucus provides a critical barrier for the colonic epithelium by excluding microbes and luminal antigens from direct interaction with epithelial cells, providing a lubricant for stool, and limiting the diffusion of harmful compounds. This barrier function is due in part to the extensive glycan structures found in mucus. Mucin protein is heavily O-glycosylated with core structures containing α- and β- linked N-acetyl-galactosamine, N-acetyl-glucosamine, and galactose. These core structures are elongated and commonly modified by α-linked fucose, sialic acid and sulfate residues. The sialic acid and sulfate residues protect the underlying mucin glycans from degradation. However, some gut microbes harbor glycosyl hydrolases (GHs) that enzymatically degrade mucin glycans. The released oligosaccharides can then be used as a primary carbohydrate source for the mucus-associated microbiota. Despite the growing number of bacterial genome sequences available, our knowledge of the mucin-degrading capacity of human gut commensal microbes remains fragmented. The aim of the present study was to systematically examine the CAZyme mucin-degrading profiles of the human gut microbiota. **Methods & Results**: Using the CAZy database, we identified 13,156 genomes harboring at least one gene copy of GH families involved in mucin degradation. Commensal microbes were identified using the Human Microbiome Project consortium in the Joint Genomes Institute Integrated Microbial Genomes database, resulting in 4,385 genomes for downstream analysis. Within the Verrucomicrobia phlyum, all *Akkermansia glycaniphila* and *muciniphila* genomes harbored gene copies of sialidases (GH33), fucosidases (GH29, GH95), endo-β-1,4-galactosidases (GH2, 35), mucin core GHs (GH84 and GH89), endo-acting O-glycanases (GH16), and sulfatases (GH20, GH2, GH42); consistent with their known ability to degrade mucus. Interestingly, the only representative of the Lentisphaerae phylum, *Victivallales*, harbored a GH profile that closely mirrored *Akkermanisa*. In the Actinobacteria phlyum, we found that several *Actinomadura, Actinomyces, Bifidobacteria, Streptacidiphilus* and *Streptomyces* species contained gene copies of mucin-degrading GHs. Within the Bacteroidetes phylum, we identified mucin degrading GHs in *Alistipes, Alloprevotella, Bacteroides, Fermenitomonas Parabacteroides, Prevotella* and *Phocaeicola* species. Firmicutes contained *Abiotrophia, Blautia, Enterococcus, Paenibacillus, Ruminococcus, Streptococcus,* and *Viridibacillus* species with mucin-degrading GHs. Far fewer mucin-degrading GHs were observed in the Proteobacteria phylum, with only 3-4 GHs families found in *Klebsiella, Mixta* and *Enterobacter*. We confirmed the mucin-degrading capability of 26 representative gut microbes by growing these bacteria in a chemically defined media lacking glucose supplemented with porcine intestinal mucus. **Conclusions**: These data greatly expand our knowledge of mucin degradation within the human gut microbiota.