Akkermansia muciniphila sialidases' roles in growth on mucin and nutrition sharing in the human gut

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Akkermansia muciniphila is a core human gut microbiome member, strongly associated with host metabolic health[1]. Despite being a mucolytic specialist, *A. muciniphila* contributes to a balanced mucin turnover in healthy humans. In the lower gut, mucin *O*-glycans are heavily capped with fucose, sialic acid and sulphate units. The capping confers resistance to microbial attack and provides nutrients and adhesion site for distinct bacteria adapted to the mucus biogeography. Despite the relevance of mucin glycosylation in host-microbe symbiosis/pathogenesis, the initial steps of mucin glycan breakdown by *A. muciniphila* remain unexplored. Here, we described the molecular preferences of *A. muciniphila* sialidases on mucin-conjugated and free *O*-glycans including those from colonic mucins. While GH33 sialidases displayed broad, albeit variable, preferences to different sialyl-motifs, we discovered the defining member of a novel inverting sialidase family with strict *O*-glycan specificity to the sialyl-T antigen. This enzyme exhibited unique structural features consistent with its strict specificity. Finally, we showed that the sialic acid released by *A. muciniphila* sialidases was not utilized, but shared with other health-beneficial mucus-associated bacteria *in vitro*. These findings bring novel insights into the initiation of mucin *O*-glycan degradation by *A. muciniphila* and the contribution of sialidases to syntrophy with the mucus-associated microbial community.

Bibliographic references:

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