Structural and functional diversity of the *N*-acetyl hexosaminidases from *Akkermansia muciniphila*

Mathias JENSEN [1], Jens Preben MORTH [1], Maher Abou HACHEM [1]

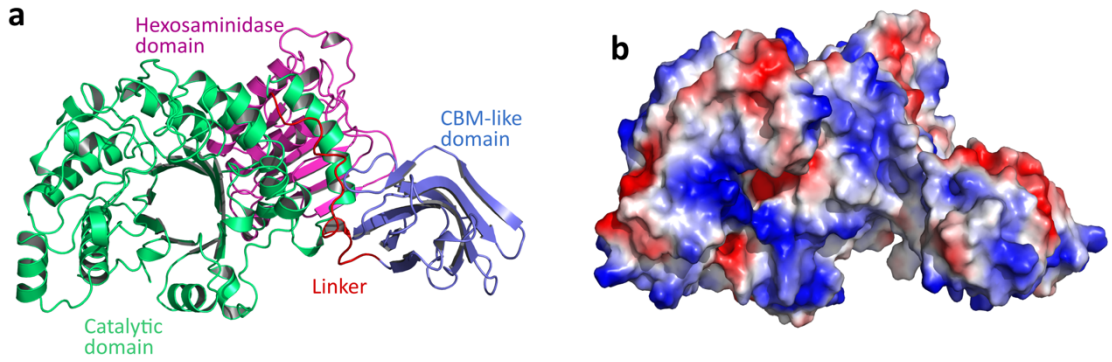
[1] Section of Protein Chemistry & Enzyme Technology, Department of Biotechnology & Biomedicine, DTU, DENMARK

matjen@dtu.dk

Akkermansia muciniphila is an atypical metabolic specialist of the human Gut Microbiota (HGM), which colonizes the outer layer of gastrointestinal mucus [1]. *A. muciniphila* specializes in the degradation of mucin, a heavily *O*-glycosylated glycoprotein that form the major component of mucus [2].

The most represented family of glycoside hydrolases (GHs) in the genome of *A. muciniphila* is family 20, comprising 11 enzymes. Here, we screen the specificity of the aglycone (-1) subsites of the aforementioned enzymes, using *para*-nitrophenyl β-d-*N*-acetylglucosamine/galactosamine (*p*NP-β-GlcNAc/*p*NP-β-GalNAc) to shed light on their functional diversity. The GH20 enzymes displayed mostly dual HexNAc activity, but some displayed a strong preference for one of these two HexNAc components of mucin.

We also report the structure of a previously uncharacterized GH20 from *A. muciniphila*. Comparison of the new structure to previously characterized counterparts from the same bacterium, revealed commonalities and differences, most notably, the presence of a C-terminal uncharacterized and structurally unique domain, which may resemble a new binding domain, and unique loop conformations around the active site. These findings that promote our understanding of the exoglycosidases machinery that *A. muciniphila* deploys to harness mucin *O*-glycans for growth will be presented.



(A) Overview of GH20 domains (B) Electrostatic surface potential

Bibliographic references:

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