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Extended Abstract

The cellular location of endo-acting galactanases confers keystone or recipient status to arabinogalactan degrading organisms of the human gut microbiota

Jose Munoz

Northumbria University, UK, E-mail: jlmunoz@um.es

Abstract

Glycans, the major source of energy for the human gut microbiota (HGM), are metabolized primarily by the Bacteroides genus. Arabinogalactan proteins (AGPs) are a higher heterogenous group of plant glycans in which the ?1, 3-galactan backbone and ?1, 6-galactan side chains are conserved features. Diversity is provided by the extensive and highly variable nature of the sugars that decorate both the backbone and side chain galactans. The mechanisms by which nutritionally relevant AGPs are degraded at a cellular and biochemical level are poorly understood, as is the impact of this process on the ecology of the HGM. To address these issues we have explored how the HGM organism Bacteroides thetaiotaomicron metabolizes highly complex AGPs. The work provides a degradative model that reveals a repertoire of exo-acting family GH43 ?1, 3-galactanases that release backbone galactose units that are attached at O6 to the side chains. The oligosaccharide side chains are depolymerized by the synergistic action of exo-acting enzymes in which catalytic interactions is dependent on whether degradation is initiated by a lyase or glycoside hydrolase. Growth studies of the 20 HGM Bacteroides species on a complex AGP revealed three keystone organisms that facilitated utilization of fragments of the glycan by the 17 other bacteria, which thus acted as recipients. The ability to function as a keystone organism was conferred by a surface endo-?1, 3-galactanase, which, when engineered into a recipient enabled the bacterium to also utilize complex AGPs and facilitate the growth of the other Bacteroides species. This study underpins future pre- and pro-biotic strategies to exploit AGPs to manipulate the structure of the HGM. Glycans are major nutrients for the human gut microbiota (HGM). Arabinogalactan proteins (AGPs) comprise a heterogenous group of plant glycans in which a β1,3-galactan backbone and β1,6-galactan side chains are conserved. Diversity is provided by the variable nature of the sugars that decorate the galactans. The mechanisms by which nutritionally relevant AGPs are degraded in the HGM are poorly understood. Here we explore how the HGM organism Bacteroides thetaiotaomicron metabolises AGPs. We propose a sequential degradative model in which exo-acting glycoside hydrolase (GH) family 43 β1,3-galactanases release the side chains. These oligosaccharide side chains are depolymerized by the synergistic action of exo-acting enzymes in which catalytic interactions are dependent on whether degradation is initiated by a lyase or GH. We

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identified two GHs that establish two previously undiscovered GH families. The crystal structures of the exo- β1,3-galactanases identified a key specificity determinant and departure from the canonical catalytic apparatus of GH43 enzymes. Growth studies of Bacteroidetes spp. on complex AGP revealed three keystone organisms that facilitated utilisation of the glycan by 17 recipient bacteria, which included B. thetaiotaomicron. A surface endo-β1,3- galactanase, when engineered into B. thetaiotaomicron, enabled the bacterium to utilise complex AGPs and act as a keystone organism.

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