Principal Investigator: Douwe van Sinderen
Grant Title: Fucosylated human milk oligosaccharides and the infant microbiome

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Abstract

This objectives of this project were to (i) assess the ability of human-derived bifidobacteria to metabolize fucose-containing human milk oligosaccharides (HMOs), (ii) determine the genes and associated metabolic pathway by which bifidobacteria utilize such fucosylated HMOs, and (iii) to investigate possible syntrophic interactions when bifidobacteria utilize fucosylated HMOs. The methods that were used to fulfill these objectives were quite varied and included a range of molecular biological, microbiological and biochemical techniques, such as comparative genome analysis, transcriptomics, metabolomics, gene cloning, protein overexpression, enzymatic assays, mutational analysis and *in vitro* bacterial cultivations. Our results show that only specific human-derived bifidobacterial species or strains are able to utilize fucosylated HMOs, and that such strains employ a particular gene set and associated pathway to achieve this (See Figure for a schematic view). Interestingly, fucose metabolism itself is also differentially present among bifidobacterial species, where certain species engage in syntrophic interactions with other bifidobacteria that can degrade fucosylated HMOs, yet do not utilize the fucose moiety. Our results also demonstrate that the fucose metabolic pathway is separate from the 'bifid shunt', through which all other carbohydrates are being metabolized by members of the genus *Bifidobacterium*, and that fucose metabolism leads to the production of 1,2-propanediol. Finally, the genes that allow fucose metabolism are mainly present in bifidobacteria that are typically associated with breast-fed infants, highlighting the specific co-evolutionary adaptation of such bifidobacteria to allow colonization of and interaction with their new-born human host.