Cross feeding of *Akkermansia muciniphila* and *Anaerostipes caccae.* By L.W.Chia[1], S.Aalvink[1], H.Wopereis[1,2], J.Knol[1,2], W.M.deVos[1,3], and C.Belzer[1], [1]*Laboratory of Microbiology, Wageningen University, Wageningen, The Netherlands;* [2]*Nutricia Research, Utrecht, The Netherlands; and* [3]*Department of Veterinary Biosciences Department of Bacteriology & Immunology, University of Helsinki, Finland.*

Background

Despite the dynamic conditions along and within the human gastrointestinal tract [1], the microbial population is found to be a stable ecosystem resilient to stressors [2]. Apart from incoming food and host derived components [3], species within the microbiota can also obtain energy from synthrophic relationships and microbial cross feeding. As an example, bio-active molecules, such as short chain fatty acid (SCFA) [4], produced by microbial fermentation can be used as an energy source among microbial entities (Fig 1). This study aims to elucidate a syntrophy relationship between key species at gut mucosal layer. The specific objective is to study the dependency of the butyrate-producing *Anaerostipes caccae* [5] on the mucin-degrading *Akkermansia muciniphila* [6].

Results

Mucin-derived sugars utilization by A. caccae

A. caccae is not able to consume mucin as a source of energy. However, the mucin-derived sugars; GlucNac, galactose, and mannose can be utilized by the micro-organism. Fermentation of these mucin sugars resulted in lactate and butyrate as the main metabolites. In the presence of GlucNac there was also production of acetate as a result of the N-acetyl group. When adding acetate to the growth media as a source of energy, that could potentially come from *A. muciniphila* as an result of mucin degradation, an increase of butyrate production and growth were measured (Fig 2).

Cross feeding between A. caccae and A. muciniphila

In cross feeding experiment, a co-culture was made of *A. muciniphila* and *A. caccae.* Both organisms were able to grow on basal media with mucin as sole carbon and nitrogen source together. Succinate, acetate, 1,2-propanediol, propionate, and butyrate were the main metabolites. At 6 days, sufficient acetate was present in the media for *A. caccae* to increase its butyrate production. Furthermore, in accordance with the sugar test result, acetate uptake by *A. caccae* was observed (Fig 3a). qPCR (not shown) and FISH results from the co-culture experiments confirmed the presence and viability of both *A. muciniphila* and *A. caccae* (Fig 3b).

Conclusions

We demonstrated a cross-feeding between *A. caccae and A. muciniphila*, in which *A. muciniphila* degrades mucin into simple sugars and acetate, that provide enough energy for *A. caccae* to support growth and butyrate production. Within the microbiota we hypothesize that many of these cross feedings are taking place especially at the mucosal surface. Unravelling these can give insight into the mucus associated microbiota and its potential health benefits for the human host.

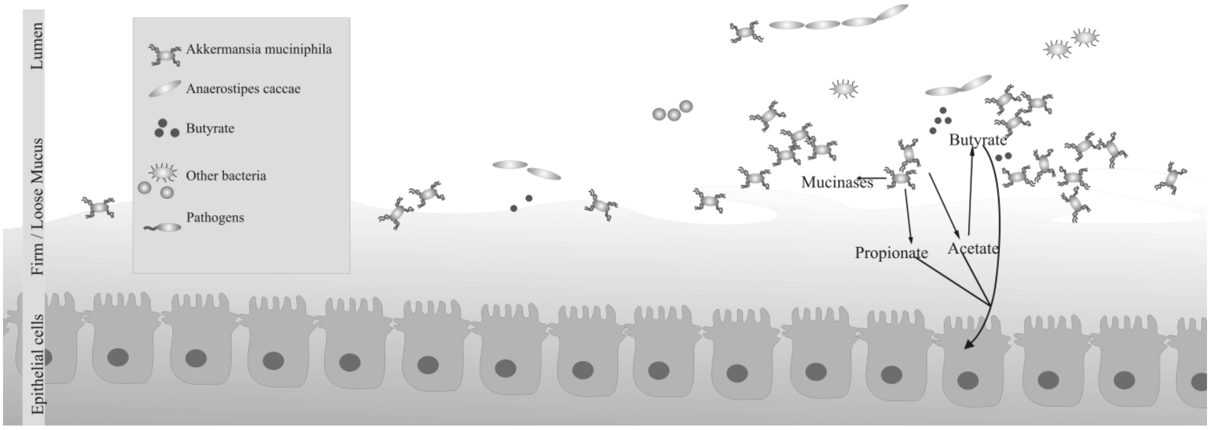

Figure 1. Illustration of mucosal syntrophy between *A. muciniphila* and *A. caccae*.

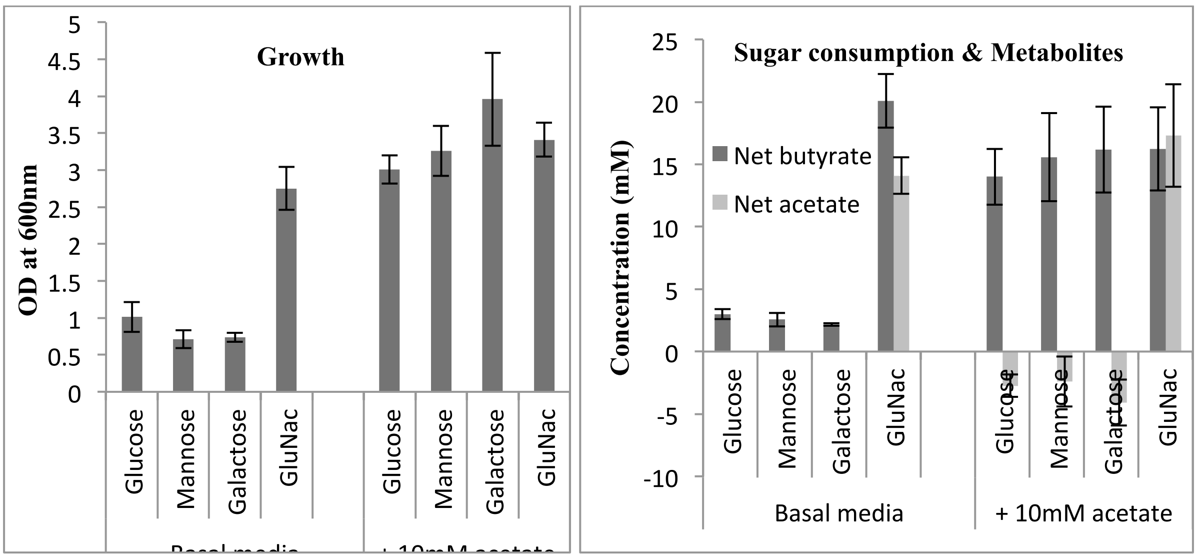

Figure 2: Microbial mass and butyrate production of *A. caccae* in mucin-derived sugars.

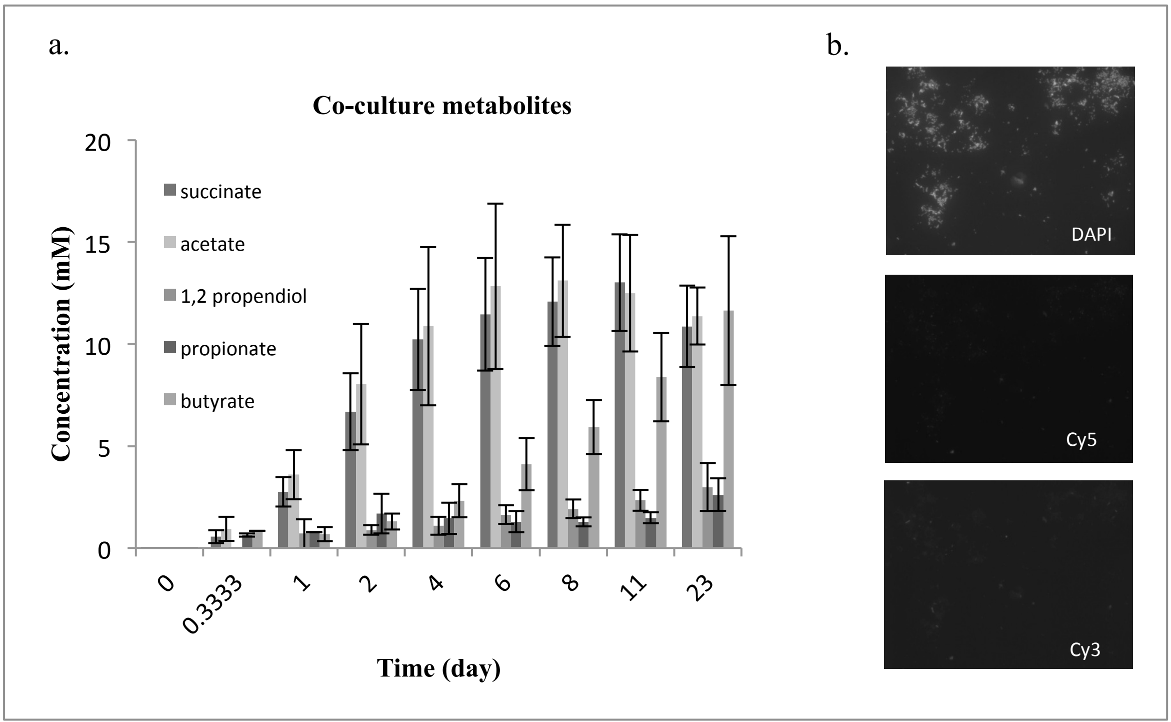

Figure 3: a. Co-culture metabolites and, b. FISH diagram (pictures from the same view with DAPI: total count, Cy5-labelled: *A. muciniphila*, Cy3-labelled: *A. caccae*).

References

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