Akkermansia muciniphila Alone Increases Small Intestine Tuft Cell Population via Succinate Production

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Introduction: The gastrointestinal tract harbors millions of different bacteria. These bacteria interact with the intestinal epithelium both directly and via secreted products to stimulate and activate the intestinal mucosa. *Akkermansia muciniphila* has recently become a microbe of interest due to its reported impacts in both health and disease. *A. mucin* is a mucin-degrading microbe which has been extensively studied using *in vivo* models with a complete gut microbiome, but these models are limited in their ability to specifically elucidate the role of *A. muciniphila*. In this study, we utilized a germ-free model to evaluate the impact of *A. muciniphila* alone on gut epithelial cells. **Methods:** We inoculated adult germ-free mice with either Brain Heart Infusion (BHI) bacterial growth media (vehicle control) or 10^9 viable *A. muciniphila* in BHI. The intestines of germ-free control and *A. muciniphila* mono-associated mice were collected after 21 days. Bacterial Fluorescence in Situ Hybridization (FISH) staining was used to confirm the presence of bacteria in mono-associated mice and absence in control mice. Immunofluorescent (IF) staining was performed to examine changes in abundance and function of intestinal cell types. **Results:** In our germ-free model, *A. mucin* alone was not found to affect stem cell or paneth cell populations. Mice mono-associated with *A. mucin* were observed to have decreased numbers of Chromagranin A positive enteroendocrine cells in the small intestine compared to germ-free control mice. While populations of mucus-producing goblet cells were not affected by *A. mucin*, changes in mucus composition were observed. *A. mucin* mono-associated mice exhibited decreased sialic acid and fucose residues compared to germ-free controls. Most notably, we found a significant increase in tuft cell number in *A. mucin* mice compared to controls. Mass spectrometry of conditioned media identified succinate as a byproduct of *A. mucin*. Succinate has been shown to activate small intestinal tuft cells and to expand tuft cell numbers. Analysis of the *A. mucin* genome further confirmed its capability to produce succinate. **Conclusions:** Our data elucidates the impact of *A. mucin* alone on the mammalian small intestine, specifically its ability to increase tuft cell population via succinate production. These findings could help inform human conditions, such as Parkinson's Disease and Multiple Sclerosis, that are associated with an over-abundance of *A. mucin*.