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| **Platform Area** Structural Nutrition |
| **Topic Area** Digestive Health |
| The gut microbiota is intimately linked with overall health and wellness. Research has shown that food and nutrients may directly affect the composition and function of gut microbiota. This project will examine the mechanisms of how structured dairy lipids interact with the gut microbiota, which has implications for support of immunity and mental health. |
| **Project Title** Tailoring the Milk Fat Globule-Bacterial Interaction to Improve Gut Health |
| **Background** In recent years, infant formula companies have begun to include milk fat globule membrane (MFGM) ingredients in formulations for the beneficial effects on cognitive development and gut maturation. Furthermore, the focus on understanding how the MFGM affects the gut microbiome of developing infants is gaining momentum. Current evidence shows that MFGM supplementation increases the abundance of beneficial bacteria, such as bifidobacteria and some species of lactic acid bacteria (LAB), which are associated with a reduced risk of several metabolic diseases, and an effect on the gut-brain axis through the production of bacterial neuromodulatory molecules. LAB and bifidobacteria interact with MFGM glycoconjugates affecting bacterial gene expression and improving adhesion to epithelial cells and growth rate. Lipid components of the MFGM, especially the sphingolipids, are shown to have a protective role against gastrointestinal tract (GIT) bacterial infections. Importantly, the MFGM can compete for bacterial surface adhesion sites in both pathogenic and beneficial bacteria, decreasing the ability for attachment to intestinal epithelial cells.  In a previous study, Dr. Caroline Thum (co-advisor on this PhD project) demonstrated the interaction of milk fat globules (MFGs) with two strains of *Lactobacillus fermentum*, AGR1485 and AGR1487, using optical tweezers and a flow cytometer. The two bacterial strains used in this research were previously isolated from saliva swabs of adult human volunteers. AGR1485 was isolated from a healthy individual and AGR1487 was isolated from a healthy individual who was later diagnosed with inflammatory bowel disease. Earlier *in vitro* studies reported that AGR1487 has a detrimental effect on intestinal barrier integrity whereas AGR1485 maintains intestinal integrity. Preliminary results show that AGR1487 strongly interacts with MFG surfaces compared to AGR1485, increasing the number of MFG-AGR1487 complexes. Interaction with MFG surfaces also increases gene expression of AGR1487.  So far, it is still unclear why for some bacteria, MFGM interaction impairs binding to the target site of action, and for others, MFGM improves attachment to the GIT and alters metabolism, which may ultimately influence the effects on GIT health.  Our hypothesis is:   * MFGM and MFGM ingredients tailors GIT microbiota metabolism that affects the adhesive properties of bacterial cells. |
| **Aim** This project will explore the fundamental aspects of the interaction between MFGM components and the gut bacteria, investigating both MFGM and bacterial structural properties and bacterial metabolism that ultimately may affect the gut microbiota and host health. |
| **Specific Objectives**   1. Identify probiotic strains that benefit from MFGM-bacterial interaction by improving attachment and/or bacterial metabolites profile. 2. Test the effects of MFGM, commercially available MFGM ingredients, purified MFGM lipids and proteins on the overall GIT microbiota composition, gene expression and production of proteins that modulate cell adhesion to structured lipids. |
| **Experimental Approach**   1. Test the effects of MFGM and MFGM ingredients on the overall GIT microbiota composition, gene expression and binding properties.   Fecal inoculum from young children, adults and the elderly will be collected and used to test the effects of MFGM ingredients on the overall GIT microbiota composition using 16S rRNA gene sequencing. Gene expression of the fecal community exposed to MFGM ingredients will be investigated using metatranscriptome analysis. Specific strains identified as correlated to the utilization of MFGM components or expression of genes linked to the interaction with MFGM will be selected for further studies.   1. Identify probiotic strains that benefit from MFG-bacterial interaction by improving attachment and/or bacterial metabolites profile.   MFG-bacterial interaction will be explored with the knowledge of bacterial strains that have beneficial effects on gut health. The effects of MFGM and MFGM ingredients on bacterial growth, gene expression and metabolism will be determined, as above. Bacterial adhesion will be measured using a cell culture model, flow cytometer, and optical tweezers. |
| **Contribution of This Research to the Dairy Industry** |
| This knowledge will help to tailor MFGM ingredients and MFGM ingredient-probiotic combinations to improve the GIT microbiota for different human age groups. |

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Applications close October 31, 2022.