Giardia Duodenalis Alters Biochemical Properties of Intestinal Mucus During Infection

Elena Fekete, Thibault Allain, Andre Buret

Introduction

The intestinal secretory mucin MUC2 is a highly glycosylated protein that is critical for intestinal barrier function and homeostasis. Mucin glycans are synthesized by glycosyltransferase enzymes via progressive addition of various sugar residues to form a polysaccharide chain. The composition of glycan chains and their terminal modifications dramatically influences physical and chemical properties of a mucin and overall mucus barrier function (Arike et al, 2017). Disruptions to mucin glycosylation patterns have been demonstrated during intestinal diseases including gastrointestinal cancers, inflammatory bowel disease, and enteric infections (Bergstrom et al, 2013). During *Giardia duodenalis* infections, intestinal barrier function is disrupted, resulting in an increase in intestinal permeability that may facilitate translocation of microbes and microbial antigens to trigger disease (Allain et al, 2020). To date, interactions between *Giardia* and mucin glycans have not been studied, and it is unknown if disruptions to mucosal glycosylation patterns may contribute to *Giardia* pathogenesis.

Methods

3-4 week old C57BL/6 mice were infected with *Giardia duodenalis* strain GS/M for 7 days. Tissue sections from the jejunum and colon were collected and stained with various fluorescein-coupled lectins (CONA, DBA, PNA, WGA, SNA, UEA-1) and fluorescence was quantified and normalized to tissue area. Quantitative PCR (qPCR) was performed for glycosyltransferase genes in the jejunum and colon.

Results

The abundance of mucin-associated glycans was altered in the small and large intestines of *Giardia*-infected mice in comparison to controls at day 7 PI. In the jejunum, N-acetylglucosamine abundance was increased upon infection, while sialic acid and fucose abundance decreased. Conversely, mannose and sialic acid abundance increased in the distal colon. Although N-acetylglucosamine abundance was similar between infected and control mice, upon infection the distribution was altered, and abundance decreased in the epithelium but increased in the lumen. Expression of mucin-associated glycosyltransferase genes was also altered in the small and large intestines of *Giardia* infected mice. Gene expression of the Core 2 synthase C2GnT2 increased in both the jejunum and distal colon upon infection, expression of

the sulfotransferase Chst4 decreased, and expression of both the fucosyltransferase Fut2 and the sialyltransferase St6GalNAc1 increased.

Conclusions

Glycosylation patterns and the expression of glycosyltransferase genes are altered in the small and large intestines of *Giardia*-infected mice. These alterations represent a novel mechanism of pathogenesis and may contribute to *Giardia*-induced intestinal barrier dysfunction and dysbiosis. Additionally, disruption of intestinal mucus glycosylation may contribute to the pathogenesis of many intestinal parasites.