

Title: The role of mucin glycoproteins in *Giardia* pathogenesis

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Back ground and Aims

Giardia duodenalis (syn *G. lamblia*, *G. intestinalis*) is the third most common cause of infectious gastrointestinal disease in Australia and is the most common intestinal parasite in the developed world. Although the current prevalence of giardiasis in the developing world is not known, previous estimates by the WHO indicate over 200 million people have symptomatic diseases, termed giardiasis, with 500,000 new cases occurring annually (WHO, 1996). Children are most commonly infected by *Giardia* and those living in poor and disadvantaged communities both in the developed and developing world are most at risk of chronic nutritional disorders and failure to thrive associated with the infection (Savioli, 2006). It is due mainly to the impacts of the parasite on child health that the WHO included *Giardia* in the neglected diseases initiative in 2004.

Although a common cause of disease in the developed and developing world, the pathogenesis of giardiasis is only just being resolved. The main pathologic changes following infection lead to a malabsorptive syndrome which may culminate in diarrhoea. However, it is not understood how *Giardia* is able to circumvent or interact with the innate barrier mechanisms in the small intestine and gain access to the epithelial surface.

An area that is receiving much attention of late is the role of the mucus layer in innate barrier function. The first line of defense micro-organisms encounter when trying to traverse the intestinal mucosa is the overlying mucus-gel layer. Increasing interest has been directed toward the protective properties of mucin as a barrier against epithelial attachment, and the mechanisms by which pathogens can utilise these mucin glycoproteins to facilitate adhesion and colonisation.

Giardia has previously been observed to bind to intestinal mucus which facilitated growth and adhesion to glass slides *in vitro*. It has also been reported that infection of the jejunum with *Giardia* resulted in greater goblet cell number and mucin secretion compared to controls. However these findings are based on small sample size studies with little attention directed at determining the mechanisms of attachment and utilisation of the mucus layer and intestinal epithelium in initiating infection. Thus the aim of this study is to investigate the interaction between the intestinal mucus layer and *Giardia* and the possible involvement of mucin glycoprotein in the pathogenesis of *Giardia* infection.

Methods

A mouse infection model of giardiasis will be utilised for this study. Intestinal samples will be collected from infected and control mice. 1-2cm tissue samples from each intestinal region will be collected for histological analysis. Another 10-15 cm of each intestinal region will also be utilised, cut open and mucus collected by scraping mucosa with a glass slide. These samples will be frozen in liquid nitrogen in preparation for mucin purification and characterisation. Histological comparisons and comparisons in mucin composition between infected and control mice will be used to determine the role of mucins in the pathogenesis of giardiasis.