Comparative proteomics of *Giardia duodenalis* from humans and cattle

Robert Francis Lascelles Steuart
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I declare that this thesis is my own account of my research and contains as its main content work which has not previously been submitted for a degree at any tertiary education institution.

Robert Francis Lascelles Steuart

Abstract

Giardia duodenalis is a gastrointestinal parasite capable of infecting humans as well domesticated animals, for example cattle. There are seven distinct genetic groups, termed assemblages A-G, with assemblages A and B able to infect humans and assemblage E specific to livestock, including cattle. The level of genetic variation between the assemblages has been studied over multiple loci and the phylogenetic relationship between these assemblages is well known. There is however, little information available on the protein differences between the assemblages. Proteins of the human infective assemblages A and B were compared using SDS-PAGE and 2D-PAGE to determine proteins of difference. Proteins determined to be assemblage-specific were then identified using mass spectrometry. In total, eleven proteins of difference were identified between assemblages A and B. Four proteins; alpha 2 giardin, GASP-180, UPL-1 and GLORF-C4, were chosen for further characterisation. Genetic analysis confirmed that alpha 2 giardin is absent from assemblage B and that the size variation seen in the GASP-180 protein is mirrored by a series of indels in a portion of the gene sequence. The UPL-1 gene did not show any variation indicating the protein variation seen is likely due to post translational modification. The GLORF-C4 protein, which is involved in the formation of cysts, was only identified in assemblage B. Therefore, the ability of assemblages A and B to undergo the encystment process was also studied. The assemblage B isolates produced fully formed cysts 24 hrs faster than assemblage A isolates. Analysis of levels of GLORF-C4 mRNA indicated that the gene is constitutively expressed in assemblage B and induced in assemblage A. The proteins of the human infective assemblages were then compared to those of the livestock infective assemblage E, with thirteen protein variants identified, the majority of which are the same as those

identified between assemblages A and B. The proteins identified in this study are the first protein variants documented between assemblages of *G. duodenalis*.

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