

Giardia Secretome Highlights Secreted Tenascins as a Key Component of Pathogenesis

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Abstract

Giardia is a protozoan parasite of public health relevance that causes gastroenteritis in a wide range of hosts. Two genetically distinct lineages (assemblages A and B) are responsible for the human disease. Although it is clear that differences in virulence occur, pathogenesis and virulence of *Giardia* remains poorly understood. The genome of *Giardia* is believed to contain ORFs which could encode as many as 6,000 proteins. By successfully applying quantitative proteomic analyses to the whole parasite and to the supernatants derived from parasite culture of assemblages A and B, we confirm expression of ~1,600 proteins from each assemblage, the vast majority of which being common to both lineages. To look for signature enrichment of secreted proteins, we considered the ratio of proteins in the supernatant compared with the pellet which defined a small group of enriched proteins, putatively secreted at a steady state by cultured growing trophozoites of both assemblages. This secretome is enriched with proteins annotated to have N-terminal signal peptide. The most abundant secreted proteins include known virulence factors such as cathepsin B cysteine proteases and members of a *Giardia* superfamily of cysteine rich proteins which comprises VSPs, HCMPs and a new class of virulence factors, the *Giardia* tenascins. We demonstrate that physiological function of human enteric epithelial cells is disrupted by such soluble factors even in the absence of the trophozoites. We are able to propose a straightforward model of *Giardia* pathogenesis incorporating key roles for the major *Giardia* derived soluble mediators.

Citation: Audrey Dubourg, Dong Xia, John P Winpenny, Suha Al Naimi, Maha Bouzid, Darren W Sexton, Jonathan M Wastling, Paul R Hunter, Kevin M Tyler *Giardia Secretome Highlights Secreted Tenascins as a Key Component of Pathogenesis*. protocols.io

dx.doi.org/10.17504/protocols.io.k97cz9n

Published: 04 Jan 2018

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✓ PROTOCOLS

1. [Giardia supernatant cleansing protocol](#)

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2. [Concentration of Giardia supernatant proteins](#)

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3. Sodium Dodecyl Sulfate PolyAcrylamide Gel Electrophoresis (SDS-PAGE) with Sypro staining

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4. Proteomics Analysis

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5. Giardia Electrophysiological Assays

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