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# The cellular distribution and stage-specific expression of two dynein light chains from the human blood fluke *Schistosoma japonicum*

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**Abstract**

Schistosomes are pathogenic helminth parasites of human portal veins. Their body wall is a highly active syncytial tegument involved in an array of host interactions. The cytoskeletal organization and dynamics of this syncytium are poorly understood, but predominant motor components are the LC8 class of cytoplasmic dynein light chains (DLC). Four LC8 members occur in schistosomes, two of which are expressed in the tegument. Here, we describe the cytoplasmic distribution, stage-specific expression and cellular location of two diverse LC8 molecules of *Schistosoma japonicum*. SjDLC1 was detected in surface-membrane specific extracts of adult worms and was shown by quantitative immuno-electron microscopy to predominate along heptalaminate membranes of the worm surface. SjDLC3 also occurs in the tegument, but was shown to be present in basal layers of the tegument and did not preferentially co-localize with particular membrane components. SjDLC3 was also detected in the gastrodermis. SjDLC1 is expressed only in mammalian–parasitic stages, whereas SjDLC3 is expressed throughout the life-cycle. The data suggest that SjDLC1 is preferentially located to the host-interactive distal parasite membrane, and plays a role in surface membrane dynamics, while SjDLC3 is a ubiquitous motor component of schistosome epithelia of all stages.


*Keywords:* Dynein light chains; Cytoskeleton; Membrane transport; Syncytium; *Schistosoma*; Parasitology

## 1. Introduction

Schistosomes are platyhelminth parasites of humans, responsible for significant human morbidity and mortality in many tropical countries. Adult schistosomes live as paired adults in mesenteric portal veins

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of their hosts, where they feed on blood and excrete eggs that must traverse gut or bladder tissues to escape to the external environment. Three species of schistosomes namely, *Schistosoma mansoni*, *S. japonicum* and *S. haematobium*, are responsible for the majority of human infections. Both *S. japonicum* and *S. mansoni* cause intestinal schistosomiasis, major complications of which are hepatosplenic enlargement and hepatic fibrosis brought about by immune responses to entrapped parasite eggs in the liver (Ross et al., 2002). *S. haematobium* causes urinary schistosomiasis.

The tegument of all species of adult schistosomes is formed by a single polarized syncytium that lines the entire body surface (Gobert, Stenzel, McManus, & Jones, 2003; Hockley, 1973; Tyler & Hooge, 2004). With the exception of the miracidium, all life-cycle stages of schistosomes are bound by a syncytial tegument that has the same general features, but which reaches the greatest size and complexity in the mammalian–parasitic stages (Threadgold, 1984). This syncytial structure is highly polarized, displays evidence of extensive cytoplasmic trafficking (Gobert et al., 2003; Hockley & McLaren, 1973), and is a major nutritional surface. The tegument derives dissolved serum metabolites and ions by direct absorption coupled with either passive diffusion or directed transport mediated by surface receptors and transporters (Dalton, Skelly, & Halton, 2004; Smyth & Halton, 1983). The heptalaminate surface membrane also appears to bind host molecules to evade host immune recognition (Loukas, Jones, King, Brindley, & McManus, 2001; Pearce & MacDonald, 2002; Torpier, Capron, & Ouaissi, 1979). The molecular adaptations driving the extensive cytoplasmic transport have not been elucidated to any extent, and knowledge of the dynamic organization of the tegument, its cytoskeletal arrangement and interactions of molecular motors with cargo is poorly understood (Jones, Gobert, Zhang, Sunderland, & McManus, 2004; MacGregor & Shore, 1990).

The conventional molecular motors in cells consist of the myosin, kinesin and dyneins. Of these, only the LC8 family of cytoplasmic dynein light chains (DLCs), regulatory components of dyneins among other complexes, has been demonstrated unequivocally to occur in the tegument (Hoffmann & Strand, 1996; Kohlstadt et al., 1997; Yang, Jones, Fan, Hughes-Stamm, & McManus, 1999). Two schistosome DLCs have been described for *S. mansoni* and four for *S. japonicum* (Argiro et al., 2000; Hoffmann & Strand, 1996, 1997; Kohlstadt et al., 1997; Yang et al., 1999) and a summary of known schistosome DLCs is presented in Jones et al. (2004). Schistosome DLC1 is present in the tegument of schistosomula and adult worms and in schistosomiasis mansoni is a potent stimulator of human T-cells (Kohlstadt et al., 1997; Yang et al., 1999). Schistosome DLC5 is also expressed in the tegument in both *S. mansoni* and *S. japonicum* and has been shown to be recognized by hosts vaccinated with radiation-attenuated cercariae (Hoffmann & Strand, 1996; Zhou, Yi, Zeng, & Zhou, 2000). Knowledge of the other schistosome DLCs, SjDLC2, 3 and 4, is poor. It is known that DLC3 is more highly expressed in male worms than females (Fitzpatrick, Johansen, Johnston, Dunne, & Hoffmann, 2004; Hoffmann, Johnston, & Dunne, 2002). The genes for SjDLC2 and 4 encode an identical peptide that, in addition to substantial sequence identity with other DLCs, carries a phosphopantetheine binding motif (Yang et al., 1999).

The occurrence of multiple members of divergent LC8 molecules (Wilson, Salata, Susalka, & Pfister, 2001) in the distinctive parasitism-adapted syncytium of schistosomes raises many interesting questions relative to their function in maintaining this important surface layer. In view of the importance of the schistosome tegument in host interaction and parasite surface maintenance, we are investigating the functional biology of the DLCs of *S. japonicum*. Here, we report on the membrane affinities, molecular characterization and sub-cellular distribution of two schistosome DLCs, SjDLC1 and 3. SjDLC1 has an open reading frame of 587 nucleotides and its predicted molecular mass is 10.5 kDa. SjDLC3 has an open reading frame of 667 nucleotides and its predicted molecular mass is 12.3 kDa. These two molecules share only 55% amino acid sequence identity (Yang et al., 1999).

## 2. Materials and methods

### 2.1. Parasites and antigen preparations

*S. japonicum* is maintained in *Oncomelania hupensis hupensis* snails and laboratory mice and rabbits from natural parasite populations collected in the snails in