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TITLE

ZINC-BINDING PROPERTIES OF SCHISTOSOMA MANSONI MEG 3 ISOFORMS

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ABSTRACT

Schistosomiasis is a neglected tropical disease responsible for a significant number of deaths, particularly in low and middle income countries. The primary causative agent of schistosomiasis in the Americas, Schistosoma mansoni, demonstrates a remarkable ability to persist within its definitive host, often surviving for decades without being cleared by the human immune system. The precise mechanisms behind this immune evasion remain poorly understood. A group of proteins, referred to as MEGs (micro-exon genes), has attracted considerable attention due to their unique structural features, which may contribute to the parasite's survival strategies. This study aims to investigate specific MEG-encoded proteins, with a focus on the isoforms of MEG 3, which are abundant in egg secretions and have been associated with liver fibrosis. Through recombinant expression in E. coli BL21 (DE3) strain, we have successfully expressed the MEG 3.1, 3.2, and 3.3 isoforms, although all isoforms were found to be insoluble and required purification under denaturing conditions. The presence of 16 conserved cysteine residues in these proteins complicates the refolding process, which was accomplished through dialysis. However, the high cysteine content suggests a potential role in metal binding, such as zinc, similar to metallothioneins. We assessed the zinc binding capacity through isothermal titration calorimetry (ITC) and found that MEG 3.1 is able to bind Zn2+ and Cu2+, although with lower affinity for the latter. The presence of both Zn^2 and Cu^2 also promoted the oligomerization of MEG 3.1, 3.2, and 3.3. Since MEG 3 isoforms are secreted by both lung-stage schistosomula and eggs, they come into direct contact with the host immune system. The involvement of the MEG 3 protein family in zinc homeostasis and immune regulation suggests their potential as novel therapeutic targets for schistosomiasis, offering new avenues for disease intervention strategies.

KEYWORDS

MEG's; Schistosoma; Zinc

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