The localization, differential expression, and potential immunological role of thioredoxin peroxidase -2 (TPX-2) in the filarial parasite Brugia malayi

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Abstract

The nematode parasite *Brugia malayi* is one of the two major causative agents of human lymphatic filariasis and elephantiasis. The parasite is transmitted by biting mosquitoes, mostly of the *Mansonia* genus and this disease affects more than 100 million people in tropical and subtropical regions around the world. Global eradication of the disease using current chemotherapeutic regimes and mosquito control has proven unsuccessful. Production of a vaccine that provides immunity or more effective drug treatments are prospects for the future but will be difficult tasks. A better understanding of differential gene expression during the *Brugia* life cycle is crucial. One of the critical life cycle stages for establishment of infection in the human host are the L3 infective stage (the first stage to enter the human host and exposed to the host immune system). Identification of L3 stage-specific genes and /or up-regulated genes will contribute to increased understanding of the infective capabilities and survival strategies of *Brugia.* ^ The gene that encodes thioredoxin peroxidase-2 (*Bm-tpx-2*) was found to be highly expressed in the L3 stage of the parasite. Thioredoxin peroxidase-2 is an antioxidant enzyme important in the detoxification of H_2O_2 produced as a result of aerobic metabolism and by host immune cells as an assault against the invading parasite. RT-PCR shows *Bm-tpx-2* to be up-regulated in the vector derived L3, the L4 and the adult female stages. The protein was localized within the protective cuticle of the vector derived L3 stage and the L4 stage, as well as within the uterus of the adult female. These expression and localization patterns suggest a protective role for TPX-2 against the host immune system. ^ ELISA studies using sera from individuals living in an endemic area for *B. malayi* showed total IgG production against *Bm*-TPX-2 in both symptomatic and asymptomatic patients. These ELISA data indicate that TPX-2 is exposed to the host immune system sometime during development and this protein is immunogenic. A vaccine trial using an animal model (jird) showed production of IgG against TPX-2 in the immunized animals, although these animals did not exhibit significant protection against subsequent challenge with L3 larvae. ^

Subject Area

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