

Localization of Pedal Peptide 4-like Immunoreactivity in the Central Nervous System of *Biomphalaria* spp., Intermediate Hosts for Schistosomiasis

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Approximately 200 million people live at risk of contracting the parasitic disease schistosomiasis. The digenetic trematode worm species *Schistosoma mansoni*, which causes the most common form of intestinal schistosomiasis, requires freshwater snails from the genus *Biomphalaria* to serve as its primary intermediate host. Within the snail, *S. mansoni* larvae multiply and transform into cercariae that can infect humans. As infection by trematode parasites can alter neuropeptide expression in snail hosts, a neural transcriptomics approach was undertaken to explore the neuropeptidome of *Biomphalaria glabrata*, the major intermediate host in the Western Hemisphere, and *Biomphalaria alexandrina*, the principal intermediate host in Egypt. A *B. alexandrina* transcript (4,038 nucleotides) encoded a precursor prohormone (762 amino acids) from which 13 distinct pedal peptide 4-related neuropeptides could be liberated at dibasic cleavage sites. For this investigation, an antiserum (rabbit polyclonal) generated against C-FDSIGESGLSGIHQNYL-NH₂ was used to localize pedal peptide 4-like immunoreactivity (PP4li) in the central nervous system (CNS) of *B. alexandrina* and *B. glabrata*. In both species, a single symmetrical pair of large (30-40 μm) lateral cell bodies was present in the buccal ganglion. Small (5-15 μm) PP4li cells were scattered across the surface of the pedal and cerebral ganglia. In *B. glabrata* a cluster of 15 to 20 medium sized (20 – 30 μm) neurons was present in the anterolateral quadrant of the ventral surface of the left parietal ganglion. These cells appeared to give rise to fiber tracts projecting to the visceral ganglion and ultimately to the intestinal nerve. Additional clusters of heterogeneous (15 – 30 μm) cells were present in the anteromedial quadrant of the left parietal ganglion and in the most anterior part of the visceral ganglion. Clusters of small (5-10 μm) weakly labeled cells were present in the lateral half of each pleural ganglion. These results suggest that members of the pedal peptide 4 family could regulate feeding and reproduction, two classes of behavior that are altered during the course of infection in this host-parasite system.