

**W0023**

**Structural Basis of Human Hookworm-Host Interactions and Vaccine Development.** Oluwatoyin Asojo., Pathology and Microbiology Dept., Univ. of Nebraska Medical Center, 4033 Wittson Hall, Omaha, NE 68198.

Human hookworm infection is a major cause of anemia and malnutrition of adults and children in the developing world. As part of on-going efforts to control hookworm infection, The Human Hookworm Vaccine Initiative has identified candidate vaccine antigens from the infective L3 larval stages and adult stages of the parasite. The L3 larval stages including a family of pathogenesis related-1 (PR-1) proteins known as the ancylostoma secreted proteins (ASPs). A novel crystal structure of *Na*-ASP-2, a PR-1 protein secreted by L3 infective larvae of the human hookworm, *Necator americanus*, has been solved to resolution limits of 1.68 Å and to R factor 17% using the recombinant protein expressed in and secreted by *Pichia pastoris*. The overall fold of *Na*-ASP-2 is a 3 layer alpha-beta-alpha sandwich flanked by an N-terminal loop and a short cysteine rich C-terminus.

Adult stage antigens include the cytosolic glutathione-S-transferases (GSTs). Nematode GSTs facilitate the inactivation and degradation of a variety of electrophilic substrates (drugs) via the nucleophilic addition of reduced glutathione. Parasite GSTs also play significant roles in multi-drug resistance and the modulation of host-immune defense mechanisms. In an effort to clarify the structural basis of the failure of hookworm chemotherapy, we have recently solved the structures of two major GSTs, *Na*GST-1 and *Na*GST-2 from *Necator americanus*, to the resolution limits of 2.2 Å and 1.8 Å (respectively) using recombinant protein expressed in and secreted by *Pichia pastoris*. The structures are complexes with glutathione usurped during the fermentation process. *Na*-GST-1 has typical GST fold and dimer. The *Na*-GST-1 structure reveals a novel binding cavity for glutathione. This mode of binding is unique and different from all previously observed structures as typified by *Na*-GST-2.