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Schistosomiasis under scrutiny

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Schistosomiasis a major public health problem in the southern hemisphere, with an estimated 75 million people at risk of infection and 2.4 million individuals infected in China alone. The platyhelminth schistosomes are the causative agent, with *Schistosoma japonicum* endemic in Asia and China and *S. mansoni* in Africa and South America. In the September 14 Nature Genetics, two groups report the transcriptome analysis of the species native to their countries: Sergio Verjovski-Almeida and colleagues at the University of San Paolo on *S. mansoni* and Wei Hu and colleagues of the Chinese National Human Genome Center on *S. japonicum*. Both teams report the identification of both novel genes and genes not previously reported in schistosomes, as well as the identification of the molecular mechanisms for host-dependent maturation, immune evasion, development, signaling, and sexual dimorphism. The analyses also identify potential vaccine candidates and drug targets.

Hu *et al.* generated expressed sequence tags (ESTs) from egg stage and male and female adult *S. japonicum* and sequenced 48,251 clones selected at random. These were clustered into 13,131 gene sets - chistosomes have an estimated 15,000 genes - and BLASTX analysis showed that 35.1% had no similarity to known genes, while 6.3% of genes were present in humans, mice, fruitflies, nematodes, yeast, and *Arabidopsis*. Phylogenetic analysis showed that the schistosomes are closer to *Drosophila melanogaster* than to *Caenorhabditis elegans*; they share with fruitflies genes associated with schistosome blood-feeding activities, but they do not share genes such as insulin-like growth factor binding - proteins and tumor necrosis factor family proteins that are involved in acquired immunity in vertebrates. The transcriptome contained genes with similar roles to mammalian sequences involved with endocrine and immunological processes such as insulin receptor and insulin-like growth factor receptor 1. Three hundred ninety seven genes were differentially expressed between adult and egg stages, with only 52 homologous to known genes (*Nature Genetics* 2003, DOI:10.1038/ng1236).

Verjovski-Almeida *et al.* used low-stringency reverse transcriptase polymerase chain reaction on adult and six stage-specific cDNA libraries, resulting in 163,586 EST reads that generated 30,988 assembled EST sequences, estimated to be 92% of the *S. mansoni* transcriptome. Of these, 77% represent novel paralogs, new orthologs, or genes with unknown function. About 14,000 genes were predicted, of which 7200 are expressed in the adult stage, and Gene Ontology classifications were assigned to 8001 ESTs, concerned with protein metabolism, intercellular communication, and transcriptional regulation. Proteins conserved among the eukarya or the metazoa were used to build base sets, and 645 genes were identified that may be essential to more complex metazoan cell functions, while 1443 genes were present in humans, fruitflies, nematodes, yeast, and *Plasmodium*. Identification of insulin and fetal growth factor receptors supported the concept of host molecules acting on parasitic receptors to control development (*Nature Genetics* 2003, DOI:10.1038/ng1237).

"One main benefit from our project should be the identification of novel proteins amenable to rational drug design... By analogy with other systems, we have singled out a number of chemotherapeutic possibilities from a potentially long list," conclude Verjovski-Almeida *et al*.

"The new *S. japonicum* ESTs provide numerous leads for further investigation of molecular mimicry, antigen presentation, immune modification and immune inhibitors in [the] host-parasite relationship...

This report increases substantially the available sequence information for *S. japonicum* in particular and for the genus *Schistosoma* at large," Hu *et al*. conclude.

References

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