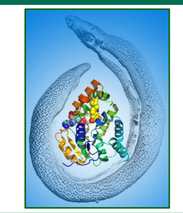
Using Molecular Structure to Design a Pan-specific Schistosomiasis Drug

Alexander B. Taylor[1], Xiaohang Cao[1], Stacey R. Stahl[1], Stephen P. Holloway[1], Timothy J.C. Anderson[2], Stanton F. McHardy[3], Philip T. LoVerde[1] and P. John Hart[1]

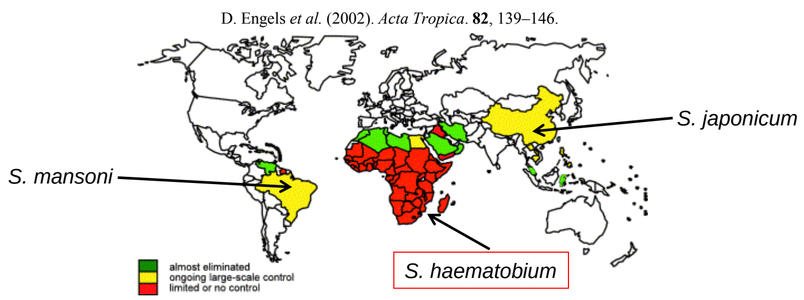
[1]The University of Texas Health Science Center at San Antonio, [2]Texas Biomedical Research Institute and [3]The University of Texas at San Antonio

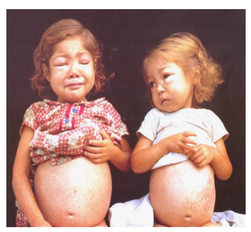


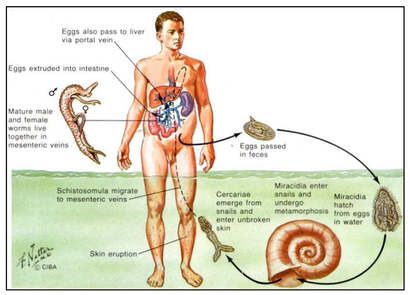
The Problem: Schistosomiasis

Schistosomes, commonly known as the blood fluke, infect an estimated 200 million people worldwide in 76 countries. The parasite is acquired from an intermediate freshwater snail host found mainly in Asia, Africa, and South America. Schistosomiasis, the chronic illness resulting from schistosome infection, is classified by the World Health Organization as a neglected tropical disease. Of the three main human blood fluke species, *Schistosoma mansoni* and *S. haematobium* together account for >99% of schistosomiasis cases worldwide with *S. japonicum* causing the remainder. Only one drug, praziquantel, is used to treat schistosomiasis worldwide and emerging resistance underscores the need for an alternative drug. Oxamniquine (OXA) is an earlier generation drug used until the 1990s that was effective against *S. mansoni* only. Our goal is to develop an oxamniquine derivative drug that is effective against all three human schistosome parasites.

D. Engels *et al.* (2002). *Acta Tropica*. **82**, 139–146.



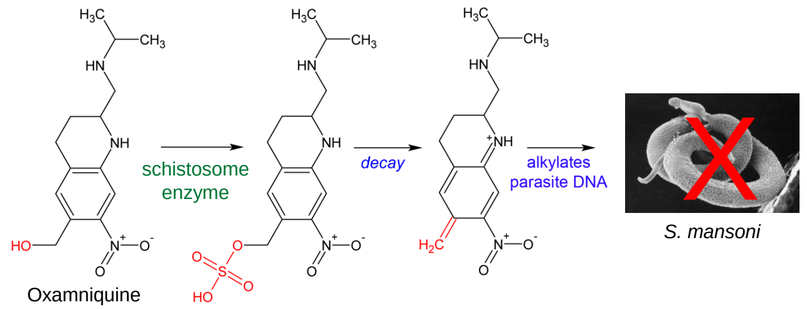




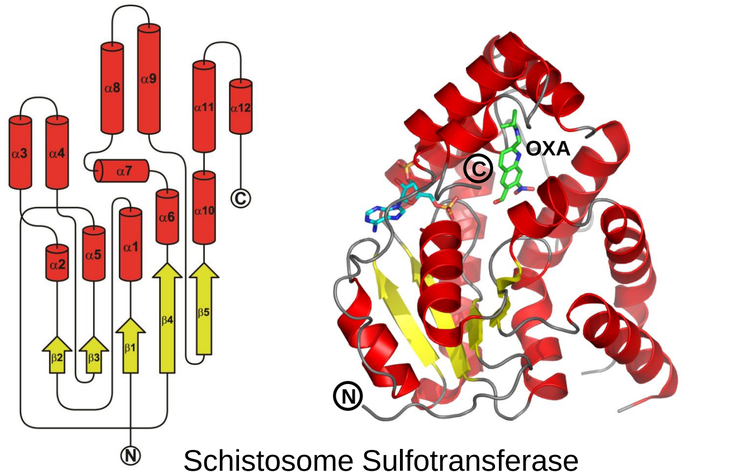
Collaborators:

- Phil LoVerde, Parasitology, University of Texas Health Science Center
- Tim Anderson, Genetics, Texas Biomedical Research Institute
- Stan McHardy, Medicinal Chemistry, University of Texas at San Antonio Center for Innovation in Drug Discovery
- John Hart, Structural Biology, University of Texas Health Science Center X-ray Crystallography Core Laboratory

Drug Mechanism



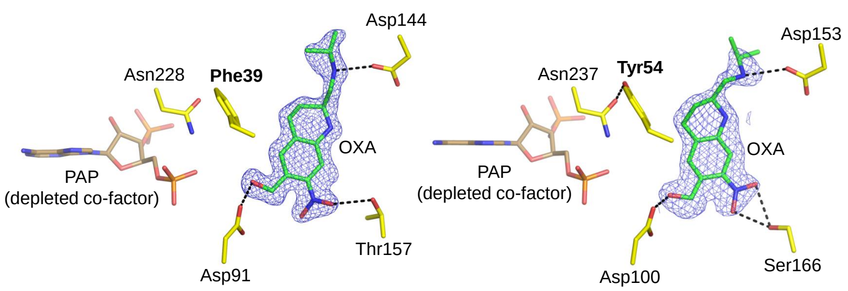
Drug Target



Schistosome Sulfotransferase

Valentim *et al*. (2013). *Science*. **342**, 1385-1389.

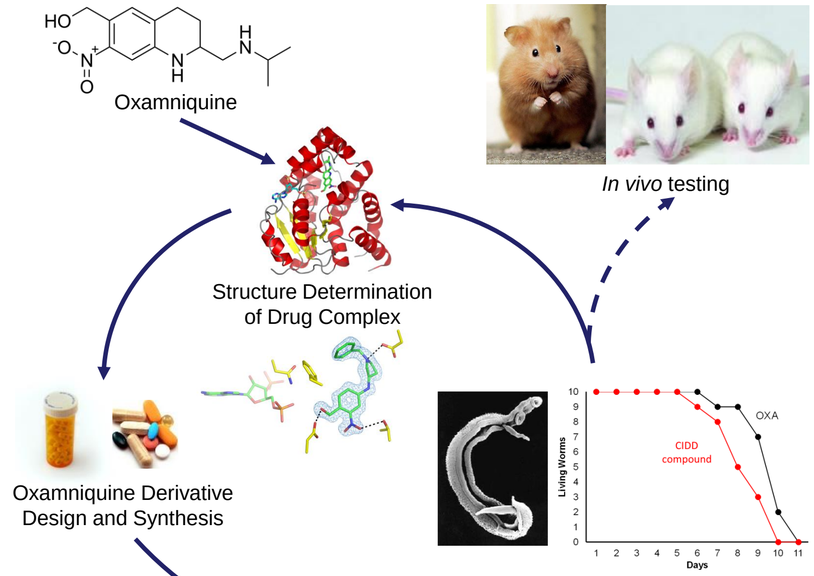
Drug Binding



S. mansoni OXA complex

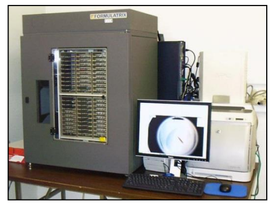
S. haematobium OXA complex

Iterative Process for Drug Optimization



Macromolecular Structure Technology

High-throughput Crystallization Robotics



Automated Crystal Imaging System

X-ray Diffractometer

X-ray Crystallography Core Laboratory, Med. Bldg. Room 436C
Director: John Hart, Ph.D.
Senior Research Scientist: Alex Taylor, Ph.D.

NIH National Institutes of Health Turning Discovery Into Health

UT Medicine CTRC Health Science Center San Antonio

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