Consiglio Nazionale delle Ricerche

Istituto di Biologia Cellulare e Neurobiologia
Institute of Cell Biology and Neurobiology
CNR-IBCN

SEMINAR ANNOUNCEMENT

Schistosoma mansoni: Genetic basis of oxamniquine drug resistance, drug mode of action and drug redesign

Philip LoVerde
University of Texas Health Science Center, San Antonio, Texas

Thursday, 1 March 2018
11:00 - 12:00

Monterotondo CNR Seminar Room

Highlights

Human schistosomiasis is a disease caused by species of the genus *Schistosoma,* which globally affects over 250 million people. The major species affecting humans are *S. mansoni, S. haematobium,* and *S. japonicum.* There is currently only one method of treatment (monotherapy), the drug Praziquantel. Constant selection pressure through mass chemotherapy - this year alone will see the administration of over 250 million doses - has yielded evidence of resistance to PZQ. This has been observed in both the laboratory and field. The goal of this research is to develop a second drug for use in conjunction with PZQ**.** Previous treatment of *S. mansoni* included, among others, the use of oxamniquine (OXA), a prodrug that is enzymatically activated in *S. mansoni* but is ineffective against *S. haematobium* and *S. japonicum.* The OXA activating enzyme was identified, described, and crystallized by our laboratories as being a sulfotransferase (SmSULT). The focus of this research is to reengineer OXA to be effective against *S. haematobium* and *S. japonicum*. An iterative process of using structural data to inform chemical synthesis of derivatives, which are then tested *in vitro*, provides us with novel compounds with improved anti-schistosomal activity. This process and the results will be presented.

Host: Donato Cioli