How to build a host-parasite interactome: a proof of concept for *Schistosoma mansoni* and *Leishmania spp.*

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Eukaryotic vector-borne parasites represent a huge burden for human health worldwide.
Malaria, Schistosomiasis and Leishmaniasis are the first causes of morbidity and death worldwide, affecting about 1 billion people living between the tropics.
Each parasite has evolved strategies to evade the host immune response, while finding its final destination, independently of the entry point.
It is therefore important for both diagnostics and therapeutics to know which are the molecular players in this survival game. Under this respect we have undertaken a high throughput screening of the interactions between the secreted proteins from the human parasite *Schistosoma mansoni* and the components of the human extracellular matrix.
S. mansoni is an extracellular parasitic trematode, which lives attached to the veins of the portal system around the liver. Before attaining this final site, the infectious larval form cercaria travels from the epidermis to the derma, then reaches one capillary and heads to the lungs, where it matures into the juvenile form, which then travels to the final tropism and reaches the sexual adult stage.
Previous studies of the secretomes of these three stages evidenced the presence of a handful proteins always expressed and secreted, and a number specific for each stage [1,2].
In order to set up a proof of concept we have selected three of these proteins, which also display a moonlighting behaviour: enolase, protein disulfide isomerase and thioredoxin glutathione reductase.
Then we used surface plasmon resonance imaging to screen such proteins for their human partners among 78 proteins, glycoproteins, and glycosaminoglycans (GAG) known to be the major components of the Extracellular Matrix (ECM). Those positive hits were subsequently tested for complex formation by small angle X-ray scattering, in order to reveal both the stoichiometry and the structure of the complexes.
Here we present the results on SmEnolase, whose major interacting protein partners are plasminogen, tropoelastin, tumor endothelial marker 8 (TEM8), while the major interacting GAGs are dermatan sulfate and chondroitin sulfate.
In *Leishmania* the first stage of infective parasite life cycle, corresponding to the cercaria of *Schistosoma*, is promastigote. The promastigotes of 24 different strains of 6 species of *Leishmania*, divided by tropism (visceral, cutaneous and mucocutaneous), have been screened against the same subset of human ECM components assayed for *Schistosoma* [3]. Very interestingly, common partners of interaction have been found between *S. mansoni* and *L. donovani* and *L. infantum*, which share a common visceral tropism.
As a counterpart, the enolase from *L. major* has also been assayed. Some partners of LmEnolase are in common with SmEnolase (fig. 1) while some others are tropism-specific, being *L. major* cutaneous. Therefore a small number of different parasite proteins could be used as markers for tropism, thus restraining the diagnosis to a more specific infectious agent.

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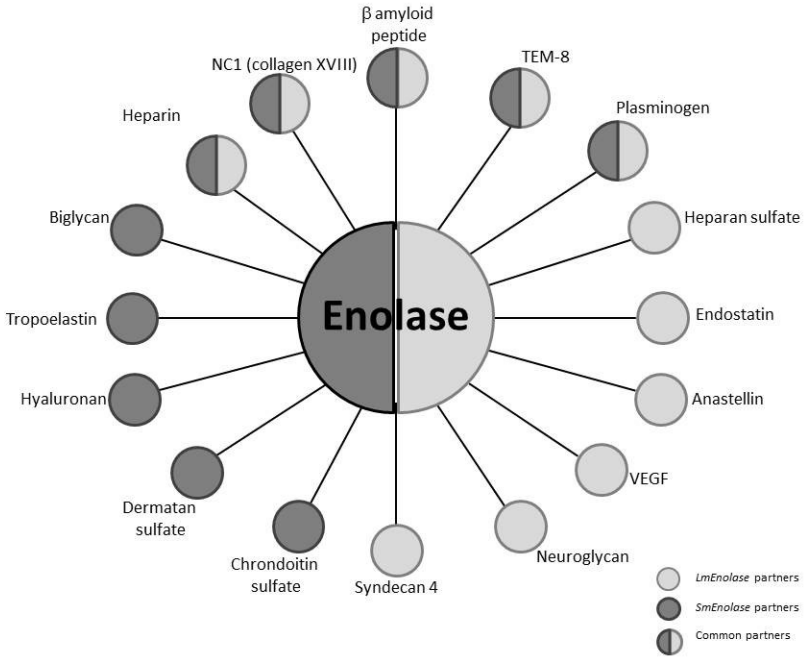

Figure 1. Human Extracellular Matrix components interacting with either or both SmEnolase and LmEnolase.