Etudes structurales et fonctionnelles des biomarqueurs du parasite *Schistosoma mansoni*

Understanding immune evasion of parasite *Schistosoma mansoni*: Structural and functional investigation of secreted biomarkers

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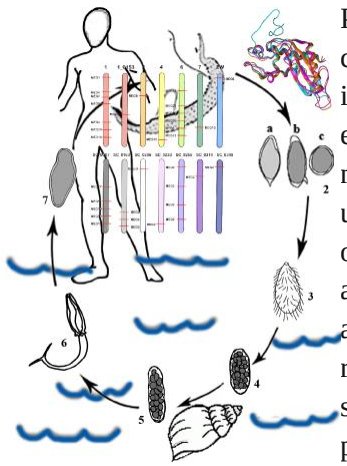

Parasitic trematodes of the genus Schistosoma are digenean with a complex life cycle, involving 2 free living stages and 2 hosts, a mollusk as intermediate and a mammal definitive one. Each life stage is adapted to its environment and modulates it in turn. We are interested in the macromolecules excreted and secreted by the stages infecting humans to understand their role in immune system modulation. In particular we focus on two families of highly variable proteins: Micro-exons genes (MEGs) and Venom antigen-like proteins (VALs). Both families have no enzymatic activities, are differently expressed during the lifetime and are particularly rich in Cys. On top of being transcribed by several genes, alternative splicing increases the variability and the number of isoforms per each gene product. We are producing in heterologous systems candidates of both families and characterising their structure by means of macromolecular crystallography (MX), SAXS, NMR and also their interactions with circulating host partners and receptors by means of molecular-scale biophysics (DLS, SPR, fluorescence spectroscopy). Moreover, given their abundance in blood circulation, VALs have been validated as biomarkers and are going to be exploited in a point-of-care (POC) diagnostic test, following the WHO NTD-Roadmap 2030.

The project will be hosted by the analytical science institute located in Lyon/Villeurbanne (France). This new institute comprise around 200 researchers and is among the largest analytical science center in Europe. The lab is fuly equipped for heterologous expression and purification of proteins (http://nmrbiolchem.univ-lyon1.fr/equipment.html). Cutting edge instruments are available like High field NMR spectrometers (From 600 to 1000MHz). The thesis project will be developed inside the Biosys group and will benefit from the expertise of the group members. The successful candidate should have completed (or in stage of completion) M.Sc. degree either in biochemistry, structural biology, biology, physical chemistry or related fields.[1-3]

References

1: Miele AE. Schistosomiasis: Epidemiology, Diagnosis and Treatment. NovaScience Publisher. ISBN: ISBN: 978-1-63117-186-4

2: Miele AE, et al. Comparative analysis of secreted protein disulfide isomerases from the tropical co-endemic parasites *Schistosoma mansoni* and *Leishmania major*. Sci Rep. 2019 Jul 2;9(1):9568. doi: 10.1038/s41598-019-45709-8.

3: Silvestri et al. Fragment-Based Discovery of a Regulatory Site in Thioredoxin Glutathione Reductase Acting as "Doorstop" for NADPH Entry. ACS Chem Biol. 2018 Aug 17;13(8):2190-2202. doi: 10.1021/acschembio.8b00349.