MS02-1-5 Schistolysin 2, a new parasporin-related protein from Schistosoma mansoni: structural and functional studies
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Abstract
Schistolysin 2 is a member of one of the two aerolysin-related families recently discovered by David Duval and colleagues [1, 2]: the Schistolysins and the Biomphalysins. They identified 2 genes in *Schistosoma mansoni* and 23 in *Biomphalaria glabrata*, respectively. The snail *Biomphalaria glabrata* is the intermediary host of the worm *Schistosoma mansoni,* the causative agent of intestinal schistosomiasis [3]. This neglected tropical disease affected 236 million people worldwide in 2019, 90% in sub-Saharan Africa. In 2020, the WHO called for new therapies to support the action of Praziquantel, the recommended treatment against all forms of schistosomiasis, and eliminate the disease [4].
Our goal is to determine the biochemical and structural properties, as well as the biological role and activity, of proteins from both families, in order to characterise their structure-function relationships. To date, the structural study of Schistolysin 2 is the most advanced. It is produced as a stable octamer, the crystal structure of which has been determined at 2.6 Å resolution. SAXS experiments brought complementary data.
Two questions arise: does the observed octamer correspond to a (pre)pore state and does it possess cytotoxic activity? According to the comparison carried out using the DALI server, the most structurally similar protein is a non-toxic crystal protein from *Bacillus thuringiensis* (PDB: 2D42) [5]. Interestingly, this protein and Schistolysin 2 display a very similar structure to the *Clostridium perfringens* epsilon toxin (PDB: 1UYJ), an aerolysin-like β-pore-forming toxin [6]. To determine the role and activity of Schistolysin 2, its gene expression is studied by in situ hybridization and its production by immunofluorescence assays in the adult worm. In addition, cellular toxicity tests with the purified form are being carried out. The combination of structural and functional data should allow us to understand the role of this protein in *Schistosoma mansoni*, and possibly help in the development of new therapies against schistosomiasis or for other applications.

References
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Orthogonal views of the octameric Schistolysin 2.