Title : Glycomic analysis of the filarial nematode *Brugia malayi* and characterization of anti-glycan antibody responses during infection

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Abstract:
Around 75 million people worldwide are infected with filarial nematodes, responsible for lymphatic filariasis (LF) and other diseases causing chronic disablement. Elimination programs have resulted in a substantial reduction of the rate of infection in certain areas creating a need for sensitive and reliable diagnostic tools in order to establish a proper population surveillance, avoid LF resurgence and meet the World Health Organization 2030 NTD roadmap objectives.

Glycans from parasitic helminths are emerging as potential antigens for use in diagnostic serological assays. Thus, we investigated the glycan repertoire of the filarial nematode *Brugia malayi* aiming to identify species-specific elements. Glycosphingolipid (GSL), N-linked and O-linked glycans were extracted from several *Brugia malayi* life-stages using enzymatic and chemical release. Glycans were purified and characterized using a combination of ultra-high performance liquid chromatography, mass spectrometry (MALDI-TOF-MS) and glycan sequencing techniques. Parasite GSL and N-glycans were printed onto microarrays so that the anti-glycan antibody response of the host during infection could be assessed. The comprehensive glycomic analysis of *Brugia malayi* revealed the presence of several antigenic motifs such as phosphorylcholine, widespread in filarial nematodes, and interestingly, some more specific components such as terminal glucuronic acid-containing glycans. In parallel, glycan microarray screening showed a preferential recognition of most glycan structures by immunoglobulin (Ig) G from *Brugia malayi* infected individuals, relative to uninfected donors. To evaluate the potential of glycans as diagnostic antigens, cross-reactivity with other filarial parasites, as well as differences in recognition for current and past infections were addressed. Finally, a longitudinal set of rhesus macaque plasma allowed us to study the dynamics of anti-glycan IgG and IgM responses during establishment of brugian filariasis. Altogether, our work highlights a specific antibody response from the host to *Brugia malayi* N-linked and GSL-glycans that could be exploited as potential diagnostic markers to detect LF.