Trypanosomatide (glyco)lipids membrane organization and their role in the infectivity

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Our group have been studying the organization and biological role of (glyco)(sphingo)lipids of *Leishmania* and *Trypanosoma cruzi*. *Leishmania* life cycle presents two forms: promastigotes, found in the midgut of sandflies, and amastigotes, the obligatory intracellular form that proliferate inside of mammalian macrophages. Recently it was demonstrated that Triton X-100 insoluble membranes present in amastigote forms are enriched in glycosphingolipids and sterols, whereas, in promastigote forms Triton X-100 insoluble membranes are enriched in GIPLs, inositol phosphorylceramide, and sterols. The disruption of these microdomains using methyl-beta-cyclodextrin, or incubation of parasites with monoclonal antibodies that recognize specifically parasite glycosphingolipids or GIPLs reduced significantly *Leishmania* (*Leishmania*) *amazonensis* and *Leishmania* (*Viannia*) *braziliensis* infectivity. These results indicate that the membrane organization as well as the glycolipids present in these microdomains are important for the parasite/host interaction. Effects of synthesis inhibitors of sphingolipids and their derivatives as Aureobasidin A (AbA), an inhibitor of inositolphosphorylceramide synthase, and myriocin, an inhibitor of serine palmitoyltransferase, were analyzed *in vitro* on parasite growth and infectivity. Parasites presented different susceptibilities to AbA and myriocin, thus, treatment of *T. cruzi* with AbA (10 to 20µM) caused a significant inhibition of axenic epimastigotes and amastigotes growth in VERO cells. Also AbA (10µM) inhibited significantly *L.* (*L.*) *amazonensis* promastigotes and amastigotes growth. For *L.* (*V.*) *braziliensis*, myriocin (20µM) inhibited promastigote cytokinesis. Effects of these inhibitors on sphingolipid pattern and parasite cell cycle are being analyzed in order to get additional information about the role of this lipid class in parasite biology. These studies may contribute for the establishment of drugs, more effective and less toxic, for the treatment of these parasitic diseases.

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