

**Título: Influence of sialidase during *Histoplasma capsulatum* and macrophage interaction**

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**Resumo:**

Histoplasmosis is a worldwide systemic mycosis caused by the pathogen *Histoplasma capsulatum* (Hc). Infection begins when microconidia or hyphal fragments are inhaled and reach the lung. Histoplasmosis symptoms are frequently mild and the infection usually controlled by the host. However, in immunocompromised patients a disseminated process can occur and different organs and tissues are infected. Within the host, infectious propagules differentiate to the yeast form, which are internalized by resident alveolar macrophages in a mechanism that involves complement receptor 3 at macrophage surface and HSP60 at Hc cell wall. Hc can inhibit phagolysosomal fusion or control the pH of this environment, being able to replicate within these phagocytes.. Recent data from our laboratory suggest that accumulation of the glycosphingolipid (GSL) monosialotetrahexosylganglioside (GM1), a lipid raft marker, increases Hc association with macrophages. Also, the absence of GM1 and other complex GSL at macrophage membrane causes a decrease of adhesion and internalization of Hc. It is believed that GM1 presence at the contact area of Hc and macrophages might occur due to recruitment of this GSL from other areas of the cell membrane to the adhesion sites. Another hypothesis is that sialidases from macrophages can convert other GSL to GM1. To investigate the participation of sialoglycoconjugates during Hc infection in macrophages we performed experiments using the sialidase inhibitors Zanamivir and DANA (2,3-dideidro-2-deoxy-N-acetylneuraminic acid). Bone marrow derived macrophages were treated with these drugs and then challenged with Hc yeasts. Inhibitory effect was accompanied by GM1 increase at host cell surface. Data shows that both drugs reduced the ability of macrophages to engulf Hc. The higher inhibitory effect was found when 15µM of DANA was used. Our results suggest that the sialidase inhibitors reduced conversion of more complex GSL to GM1 and this effect was associated with a substantial decrease in the adhesion rate and phagocytosis. The role of sialylated glycoproteins during this process is under investigation.

**Palavras-chave:** *Histoplasma capsulatum*, pathogen-host interaction, GM1, sialidase, sialidase inhibitors.

**Agencias de Fomento:** CAPES, CNPq, FAPERJ e Fogarty.