BIO.09 - Purification and evaluation of antifungal properties of lectin-Fc proteins against *Aspergillus fumigatus*

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Introduction: Fungal diseases have emerged as significant cause of human morbidity and mortality, particularly in the setting of immunocompromised individuals. Currently, the number of cases of severe and usually fatal mycosis, such as aspergillosis caused by A*spergillus fumigatus*, has increased exponentially, along with fungal resistance to antifungals. Therefore, it is necessary to investigate and develop new therapeutic options. Passive immunization, which historically is not correlated to resistance, is an excellent alternative to eliminate fungal infections, mainly targeting surface structures common to all fungi; for example, chitin and β–glucan, which are essential components of fungal cell walls. However, these polysaccharides are poorly immunogenic. To overcome this drawback, our group has developed and characterized lectin-Fc chimeras (WGA-Fc (IgG2a) and dectin-Fc (IgG2a and IgG2b)), based on the recognized affinity of WGA (wheat germ agglutinin) and dectin-1 against chitin and β–glucan, respectively. The chimeric proteins were expressed, characterized and evaluated *in vitro* and *in vivo* against *Candida albicans, Cryptococcus neoformans* and *Histoplasma capsulatum*.

Objective: The aim of this work is the purification and multifactorial evaluation of the antifungal properties of these lectin-Fc-proteins against *A. fumigatus*.

Methodology: Immunogenic assays analyzes were performed to analyze the binding of the chimeras to the surface of the conidia. Next, the effect of the lectin-Fc proteins on fungal growth and complement activation was evaluated. Phagocytosis and intracellular viability assays were also performed using bone marrow-derived macrophages.

Results: First, the binding of the chimeras to the surface of the conidia was confirmed; and dectin-Fc (IgG2b) displayed the highest binding. Incubation of the chimeras with the conidia during 7 and 9 hours resulted in inhibition of fungal growth, related to controls. A higher binding of complement proteins to the surface of opsonized conidia with lectin-Fc proteins was also observed when pre-treated fungal cells were incubated with mouse serum. The increase of the deposition of the complement proteins on the surface of the fungus also resulted in the fungus death. Phagocytosis and fungal cell viability assays showed augmentation in effector functions of macrophages in the presence of the chimeras. Pre-treatment of the conidia with the fusion proteins increased the phagocytosis by the macrophages when compared to the control; whereas only dectin-Fc (IgG2a) showed higher percentages of adhesion and association. In addition, there was a reduction of intracellular fungal viability when the conidia were previously treated with the lectin-Fcs, in comparison to the controls.

Conclusion: WGA-Fc and dectin-Fc proteins could display excellent broad *spectrum* antifungal activity, damaging directly cell walls structures or making conidia more susceptible to the clinically used antifungal drugs. Their evaluation in the defense against *A. fumigatus* will allow the development of new therapeutic products for individuals belonging to risk groups.

Keywords: lectin-Fc; *Aspergillus*; mycosis