POLYSACCHARIDES FROM *CRYPTOCOCCUS NEOFORMANS* INDUCE CELL DEATH IN MURINE MACROPHAGE

Villena, SN[1]; Pinheiro RO[1]; Souza IM[1] Pinheiro, CS[1]; Luna, TGS[1]; Nunes MP[1]; Takiya, CM[2]; Previato, JO[1]; Mendonça-Previato L[1]; DosReis GA[1]; Freire de Lima, CG[1]

[1]Institutos de Biofisica Carlos Chagas Filho [2] and Ciências Biomédicas, UFRJ

C. neoformans is an opportunistic fungus covered with polysaccharides which are the most prominent virulence factors. The capsule is constituted by glucuronoxylomannans (GXM), galactoxylomannans (GalXM) and manoproteins. In this work, we investigated the effects of purified soluble GXM and GalXM from mating types a and alpha. The GalXM from both mating types induced secretion of the proinflammatory cytokine TNF-a in RAW 264.7 murine macrophage cell line. By contrast, GXM induced secretion of TGF-β, suggesting that GalXM and GXM may have different modulatory activities on macrophages. Following addition of both GXM and GalXM to macrophages, we observed reduction in cellular viability through of incorporation ^{3}H thymidine and an increase in expression of inducible nitric oxide synthase (iNOS) and nitric oxide (NO) production. However, these effects were more pronounced in cells treated with GalXM. In addition, GalXM or GXM induced an extensive vacuolization in RAW 264.7 cells. Vacuoles were characterized as autophagosomes by electron-microscopy. The reduction in cell viability was independent from either autophagy or NO production, since treatment with inhibitors Wortmannin or L-NIL failed to restore cellular viability. Reduction of macrophage viability was due to cell apoptosis, as measured by the TUNEL technique, and was restored by treatment with anti-FasL antibody. These results suggest an involvement of the Fas-FasL pathway in the modulatory effects of *C. neoformans* capsular polysaccharides on macrophages.

FAPERJ, CNPq, CAPES, HFSPO/CGFL, HHMI/GADR