CHARACTERIZATION OF CD14 AS THE GLUCURONOXYLOMANNAN RECEPTOR IN HUMAN EPITHELIAL ALVEOLAR CELLS

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Cryptococcus neoformans is an encapsulated fungal pathogen infecting mainly immunosuppressed patients. Host invasion is followed by inhalation of infectious propagules, which first interact with alveolar components. Glucuronoxylomannan (GXM) is the major capsular polysaccharide of *Cryptococcus neoformans*. Receptors for GXM in macrophages, neutrophils, and endothelial cells include CD14, CD18 and Toll-like receptors 2 and 4. The receptors for GXM in epithelial cells, however, remain to be characterized. The present work aimed to characterize the GXM receptor in A549 cells, a human type 2 alveolar epithelial cell line. A GXM-binding protein was purified from polysaccharide-treated cells. The purified molecule, which presented a molecular mass corresponding to CD14 , retained its ability to bind GXM, as demonstrated by enzyme-linked immunosorbent assays (ELISA). The interaction of cryptococci with A549 cells was inhibited by CD14 ligands, supporting the hypothesis that this molecule is the epithelial receptor for surface antigens expressed by *C. neoformans*. GXM-CD14 complexes were identified in lysates obtained from polysaccharide-treated A549 cells, confirming that CD14 is a receptor for GXM in these cells. Polysaccharide-treated cells secreted increased levels of interleukin-8 (IL-8). Accordingly, GXM-mediated IL-8 production was inhibited by anti-CD14 antibodies. In summary, our study indicates that GXM can activate a local immune response in the alveolus through binding to CD14 in epithelial cells.