Cryptococcus neoformans Capsule: Structural Biology Study by Molecular and Meta Dynamics Simulations

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INTRODUCTION. Cryptococcus neoformans is a widely distributed fungus responsible for cryptococcosis, criptococcal meningitis and meningoencephalitis. The fungus produces a characteristic polysaccharide capsule that protects the fungus by decreasing host immune responses, depleting complement components and inhibiting the antigen-presenting capacity of monocytes. The major capsule components are glucuronoxylomannan (GXM) polymers. These polymers are elongated with participation of divalent ions, mostly calcium. GXM is formed by three mannoses, a glucuronic acid and a variable number of xyloses. The form and number of xyloses determine the C. neoformans serotype. B and C serotypes are able to infect immunocompetent individuals, being a major concern for public health. Based on these data our work aims to understand the molecular basis of GXM different serotypes and their interactions with calcium ion.

MATERIAL AND METHODS: The GXM of different serotypes (A to D) were constructed starting by the disaccharides that compose them. They were simulated by metadynamics, a method that screening all conformational space in the search of free energy minima, in order to use these geometries to construct the GXM units. These units were simulated by molecular dynamics and compared with the disaccharides’ glycosydic linkages. The position of calcium ions in relation to one or two GXM chains was calculated by metadynamics. All simulations were performed with GROMACS suite and GROMOS43a1 force field. RESULTS AND DISCUSSION: All serotypes have a similar behavior in the mannose-mannose and mannose-glucuronic acid bonds. The mannose-xylose bonds however, present increased flexibility in B and largely increased in C serotypes. The calcium ion interacts with the carbonyl of glucuronic acid in all serotypes. CONCLUSION: This work presents a new insight in the structural biology of C. neoformans capsule, but further studies are necessary to deepen the characterization of such differences among serotipes.

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