Glycomics & Lipidomics

Extended Abstract

# Lipid uptake and intracellular transport in a parasitic platyhelminth

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## Abstract

Fatty acid binding proteins (FABPs) are intracellular proteins that bind long chain fatty acids and other hydrophobic ligands. They differ in their tissue distribution, the specificity and affinity for its ligands. The specific function of FABPs is still under investigation; however, recently promising findings have been obtained. Some members could be involved in cell proliferation and growth modulation, in gene expression regulation and could collaborate with membrane transporters for fatty acid uptake from the extracellular medium. We have studied FABPs´ roles in the uptake and intracellular transport of BODIPY FL C-16 fatty acid in the parasitic platyhelminth Mesocestoides vogae. It is worth mentioning that these parasites are unable to synthesize their own fatty acids by de novo. For this reason they should capture these molecules from the host, which would make FABPs essential molecules for their survival. Parasite larvae were submitted to immunomicroscopic analysis in toto and in cryosections, showing a diffuse cytosolic distribution of FABPs with some expression in nuclei and mitochondria. FABPs distribution was confirmed by mass spectrometry identification from 2D-electrophoresis of larvae subcellular fractions. Furthermore, the ability of these proteins to bind the fluorescent ligand was analyzed in vitro. Our results indicated that FABPs are strong candidates for the intracellular transport of fatty acids, carrying them to different cell compartments including the nucleus. In this sense, M. vogae FABPs could participate in several cellular processes fulfilling most of the functions attributed to vertebrate's counterparts.

Two main families of lipid binding proteins have been identified in parasitic Platyhelminthes: hydrophobic ligand binding proteins (HLBPs) and fatty acid binding proteins (FABPs). Members of the former family of proteins are specific to the Cestoda class, while FABPs are conserved across a wide range of animal species. Because Platyhelminthes are unable to synthesize their own lipids, these lipid-binding proteins are important molecules in these organisms. HLBPs are a high molecular mass complex of proteins and lipids. They are composed of subunits of low molecular mass proteins and a wide array of lipid molecules ranging from CoA esters to cholesterol. These proteins are excretory-secretory molecules and are key serological tools for diagnosis of diseases caused by cestodes. FABPs are mainly intracellular proteins of low molecular weight. They are also vaccine candidates. Despite that the knowledge of their function is scarce, the differences in their molecular organization, ligand preferences, intra/extracellular localization, evolution, and phylogenetic distribution, suggest that platyhelminths HLBPs and FABPs should play different functions. FABPs might be involved in the removal of fatty acids from the inner surface of the cell membrane and in their subsequent targeting to specific cellular destinations. In contrast, HLBPs might be involved in fatty acid uptake from the host environment.

Long chain fatty acids (LCFA) are involved in various cellular processes, including membrane synthesis, control of energy supply, and protein modification. LCFA and some of their active metabolites also function as signaling and regulatory molecules; they facilitate a dynamic interplay between the extracellular media, cellular membranes, cytoplasmic stores, and nuclei to control multiple biological activities. The hydrophobic nature of LCFA renders them poorly soluble in aqueous solution, so their intracellular transport to sites of metabolism and action is believed to be mediated by lipid binding proteins.

Parasitic helminths express high levels of lipid binding proteins and are incapable of de novo synthesis of fatty acids and cholesterol (Smyth and McManus, 1989 and references therein). They depend largely on the sequestration and utilization of host lipids during infection to survive. It is therefore essential that these parasites have an efficient binding system for the uptake and transport of key hydrophobic molecules. In this metabolic context, lipid-binding proteins might play an important role in the exchange of lipids between parasite and host organism. These proteins might also be involved in the uptake, transfer, and storage of hydrophobic ligands, in the targeting of ligands to specific organelles or pathways, in the sequestration of toxic compounds, and in the regulation of gene expression.

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