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INTESTINAL AND LIVER FATTY ACID BINDING PROTEINS (FABP): STRUCTURAL AND FUNCTIONAL ANALYSIS

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Introducción:

The evolution of different families of intracellular soluble lipid binding proteins (SLBP) may be connected to the wide range of functions attributed to lipids as well as their low solubility in the cellular media. Among these SLBP, the mammalian fatty acid binding proteins (FABPs) are ubiquitously produced. The large number of FABP types and the distinct expression pattern of each of them suggest overlapping as well as distinct functions in specific tissues; based on specific structural elements. Structure-function studies indicate that subtle conformational changes that occur upon ligand binding may promote distinct FABP-protein or FABP-membrane interactions that could define their specificity.

Objetivos:

We used a combination of in vitro and in cell studies to assess the differential functionality of abundantly coexpressed FABP in the enterocyte, liver and intestinal fatty acid binding proteins.

Materiales y Métodos:

FABP Purification. Brominated Lipid Quenching. Sucrose loaded vesicle binding assay. Photo-Crosslinking Analysis of Membrane Interacting Proteins. Membrane structure destabilization: Terbium Leakage Assay. Cell culture of Caco-2 cells. Knock-Down of LFABP. Doubling time. Assimilation and Metabolism of Fatty Acids. Cytokines determination by Real Time PCR.

Resultados:

The analysis of the intestinal FABP interaction with membranes shows that both proteins are able to interact with phospholipid bilayers. It is worth to notice that different techniques allowed to evidence modulation by several factors and the results do not exclude each other. The brominated lipids quenching assay shows that the portal region seems to be the protein-membrane interactive subdomain. Moreover, the results could be indicating that a conformational modification could take place when the protein interacts with negative charged vesicles, compared to zwitterionic vesicles. On the other hand, the photocrosslinking assays show that apo-IFABP interacts with membranes to a greater extent than holo-IFABP. In contrast, apo-LFABP appears to interact in a greater extent with membranes than holo-LFABP. Considering the information brought of several experiments, we propose that IFABP could be delivering FA to membranes, whereas LFABP may be interacting to remove FA from membranes.

We have recently obtained a Caco-2 LFABP knock down cell line and we have observed a marked decrease in the duplication time. Fatty acid uptake assays showed a decrease in oleid acid (OA) incorporation while palmitic acid assimilation increased. In addition 14C-OA metabolism analysis has shown differential distribution of radioactitivy among lipid components.

Conclusiones:

The use of several structural variants of IFABP highlighted the importance of the helical region and specific residues have been identified in the portal domain, crucial for ligand transport and membrane binding properties of FABPs. On the other hand, modification of intestinal FABPs expression in culture cells has an impact on several cellular processes, mainly lipid metabolism but also cell proliferation and differentiation. FABPs' participation in regulating fatty acid metabolism, may ultimately impact on systemic metabolism.