LIPIDOMICS APPLICATIONS IN THE CLINICAL RESEARCH

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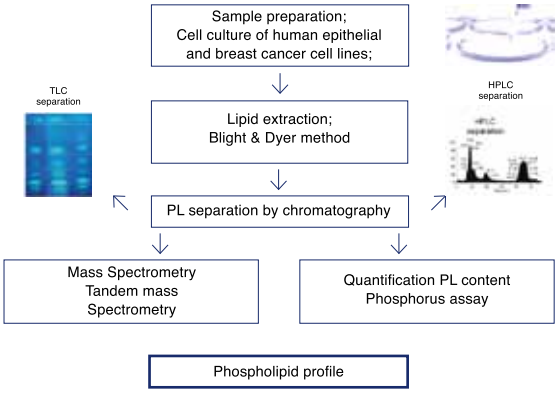

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Lipids are important cellular components and lipid signaling mediators and alteration in lipid metabolism have been found in different diseases. In our lab we used mass spectrometry approaches to identify changes in lipid profile in normal and pathological conditions, such as immunology, depression, diabetes, and cancer with the aim to provide new markers that will be used in clinical evaluation. Our lab is currently focused in the following lines of research:

1) The role of lipids in breast cancer has been largely understudied. Besides their contribution to the cell membrane mass, lipids regulate membrane fluidity, are an energy source and have roles in cellular signalling; all processes altered in malignant progression. We used a lipidomic approach in which phospholipids were separated by thin layer chromatography and analyzed by ESI-MS/MS. Differences in the spectra of sphingomyelins and phosphoinositides - two PLs with roles in regulation of cell survival and motility – were found between non malignant (MCF10A) and breast cancer cells with different degrees of aggressiveness (Fig. 2). Presently, we are extending these studies to breast tumours with the aim to identify prospective biomarkers of disease progression.

2) Prevalence of skin inflammatory disorders has increased in recent years being estimated that 15-20% of the general population suffers from allergic contact dermatitis (ACD). Currently, the sensitizing potential of chemicals is assessed through animal tests; however growing ethical concerns and actual legislative framework impose the development of new alternative tests. A growing body of data suggests that phospholipids (PLs) play important roles in the modulation of immune responses. Presently we were using lipidomic profiling to prospect lipid biomarkers of skin sensitization. We found that phosphatidylcholines and phosphatidylserines molecular species may discriminate immunogenic compounds form irritants. Analysis of such alterations may be therefore valuable in a future in vitro test platform for skin sensitization prediction.

3) Myocardial mitochondria dysfunction seems to represent an important pathogenetic factor underlying cardiomyopathy, a common complication of type 1 diabetes mellitus (T1DM). Despite significant progress in the understanding of the molecular mechanisms of mitochondrial function in the heart, the interplay between phospholipids and membrane proteins in mitochondria still poorly comprehended. Results from our lab showed that mitochondria from T1DM heart presented lower OXPHOS activity and lower transcription ability, related with phospholipid remodeling characterized by higher phosphatidylcholine levels, lower phosphatidylglycerol, phosphatidylinositol and sphingomyelin content, higher amounts of long fatty acyl side chains and increased peroxidation, particularly of cardiolipin (CL). These results suggest that phospholipid remodeling of heart mitochondria is an early event in T1DM pathogenesis and is related with OXPHOS dysfunction.

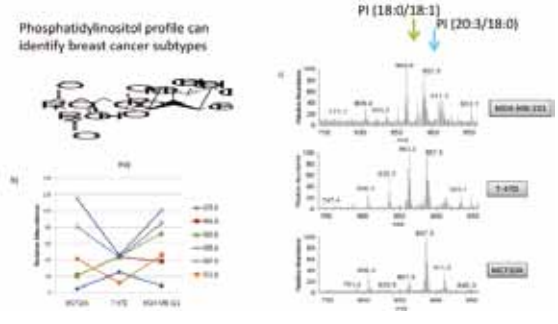

FIGURE 1
Workflow describing lipidomic analysis of cells, tissues and biofluids for disease biomarkers identification.

FIGURE 2
Different phoshatidylinositol (PI) profiling from breast cancer cells.