Multiplatform plasma metabolic and lipid fingerprinting of breast cancer: A pilot control-case study in Colombian Hispanic women

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Abstract

Breast cancer (BC) is a highly heterogeneous disease associated with metabolic reprogramming. The shifts in the metabolome caused by BC still lack data from Latin populations of Hispanic origin. In this pilot study, metabolomic and lipidomic approaches were performed to establish a plasma metabolic fingerprint of Colombian Hispanic women with BC. Data from ^{1}H-NMR, GC-MS and LC-MS were combined and compared. Statistics showed discrimination between breast cancer and healthy subjects on all analytical platforms. The differentiating metabolites were involved in glycerolipid, glycerophospholipid, amino acid and fatty acid metabolism. This study demonstrates the usefulness of multiplatform approaches in metabolic/lipid fingerprinting studies to broaden the outlook of possible shifts in metabolism. Our findings propose relevant plasma metabolites that could contribute to a better understanding of underlying metabolic shifts driven by BC in women of Colombian Hispanic origin. Particularly, the understanding of the up-regulation of long chain fatty acyl carnitines and the down-regulation of cyclic phosphatidic acid (cPA). In addition, the mapped metabolic signatures in breast cancer were similar but not identical to those reported for non-Hispanic women, despite racial differences.

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Introduction

Breast cancer (BC) remains the most frequent type of cancer and the main cause of cancer deaths among women worldwide [1]. According to GLOBOCAN, breast cancer mortality rates in developed countries have declined in the last years, but the incidence rates continues to rise, especially in Latin America and other developing regions [1, 2]. Mortality reduction has been associated with the advances in medical diagnostic methods and the development of new therapies; however, the high heterogeneity of breast cancer still poses challenges to the understanding of its characteristic phenotype. Reported findings of breast cancer have suggested prognosis and predictive biomarkers based on alterations in genes (e.g. BRCA1 and BRCA2) [3, 4] and protein expression (e.g. mTOR, ras, PKC) [5–7]. In the past few years, metabolites have been proposed as BC markers, along with genes and proteins.

Metabolomics is a consolidated field that has enabled to observe differences in metabolic signatures generated by a pathological state such as cancer. These differences allow to postulate molecular mechanisms involved in cancer, proposing and evaluating promissory treatment targets and diagnosis tools [8–10]. Although the identification of breast cancer biomarkers by metabolomics is still at an early stage, exploratory studies have allowed highlighting alterations in aerobic glycolysis, *de novo* lipogenesis, glutaminolysis, glycerolipid, glycerophospholipid and amino acid metabolism [11–15]. These alterations have been used to identify metabolic changes associated with advanced metastatic breast cancer in cell lines [16, 17] and serum [18], as well as breast cancer subtypes in plasma [13, 19] and tissue [13, 19–21]. Moreover, the identification of suitable targets for drug development in cell lines [22–24] and therapy selection in cell lines [25] and serum [26] have also been achieved.

High-throughput analytical chemical techniques such as chromatography coupled to mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy [27, 28] have been used in metabolomics, along with univariate and multivariate statistics [29, 30], in order to provide information on a large number of metabolites, in particular those with altered levels between healthy subjects