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Abstract

Breast cancer (BC) is not only the most frequently diagnosed cancer, but also the leading cause of cancer death among women worldwide. This study aimed to screen the potential salivary biomarkers for breast cancer diagnosis, staging, and biomarker discovery. For the first time, a UPLC-MS based method along with multivariate data analysis, was proposed for the global saliva metabonomics analysis and diagnosis of BC, which used both hydrophilic interaction chromatography (HILIC) and reversed-phase liquid chromatography (RPLC) separations and operated in both positive (ESI+) and negative (ESI-) ionization modes. On account of different polarities of endogenous metabolites, this method was established to overcome the boundedness of a single chromatographic approach. As a result, 18 potential metabolites for diagnosing BC were identified. A nonparametric Mann-Whitney U test, heat map, and the receiver operating characteristic (ROC) were exploited to analyze the data with the purpose of evaluating the predictive power of the 18 biomarkers. Significant differences ($P<0.05$) were disclosed in terms of the levels of the 18 potential biomarkers between BC patients and healthy controls (HC). Among the 18 biomarkers, three up-regulated metabolites, LysoPC (18:1), LysoPC (22:6) and MG (0:0/14:0/0:0) displayed the area under the curve (AUC) values of 0.920, 0.920 and 0.929, respectively, indicating the high accuracy of this method to predict BC. In this study, an integrated metabonomics analysis in human saliva for identifying potential biomarkers to diagnose and stage BC was successfully eastablished, which was non-invasive, reliable, low-cost, and simple. The HILIC was demonstrated to be essential for a comprehensive saliva metabonomics profiling as well as RPLC separation. This saliva metabonomics technique may provide new insight into the discovery and identification of diagnostic biomarkers for BC.