Identification of Metabolite Variations Among Luminal B Breast Cancer Using Serum NMR-Metabolomics

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INTRODUCTION

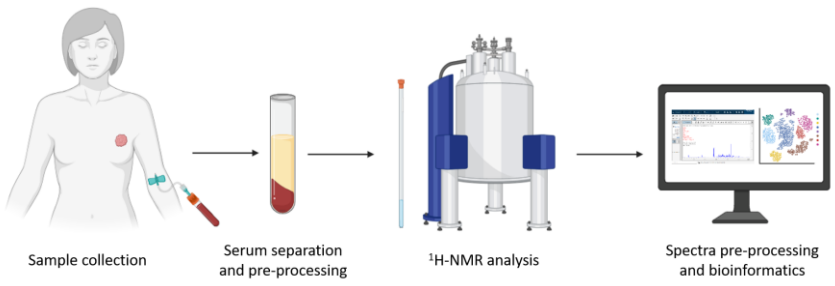
Breast cancer is a heterogeneous disease with four major molecular subtypes: luminal A, luminal B, HER2+, and basal-like. Luminal B, although hormone receptor–positive like luminal A, shows more aggressive behavior and lower response to hormonal therapy. This heterogeneity impacts treatment and clinical management, underscoring the need for better stratification strategies. NMR-based metabolomics is a valuable tool to detect metabolic alterations and potential biomarkers, which, in turn, may support luminal B stratification and improve diagnosis, prognosis, and personalized therapy.

AIMS

This study aimed to investigate the serum metabolome of luminal B breast cancer patients to find potential alterations on metabolite composition that allow its sub-stratification.

METHODS

Serum samples were obtained from 103 luminal B breast cancer patients and stored at -80 °C. For metabolomics analysis, serum samples were treated with methanol and analyzed in a Bruker Ascend 600 MHz spectrometer (D_2O, 25 °C). Spectra were pre-processed using Topspin 4.4.1 software. Metabolite pre-identification and quantification were performed using COLMAR 1D with global spectral deconvolution. Statistical analyses were performed with RStudio Desktop (version 2025.05.0+496).



CONCLUSIONS

These findings suggest the presence of metabolically distinct subgroups within luminal B breast cancer and highlight the potential of NMR-based metabolomics for luminal B patient sub-stratification.

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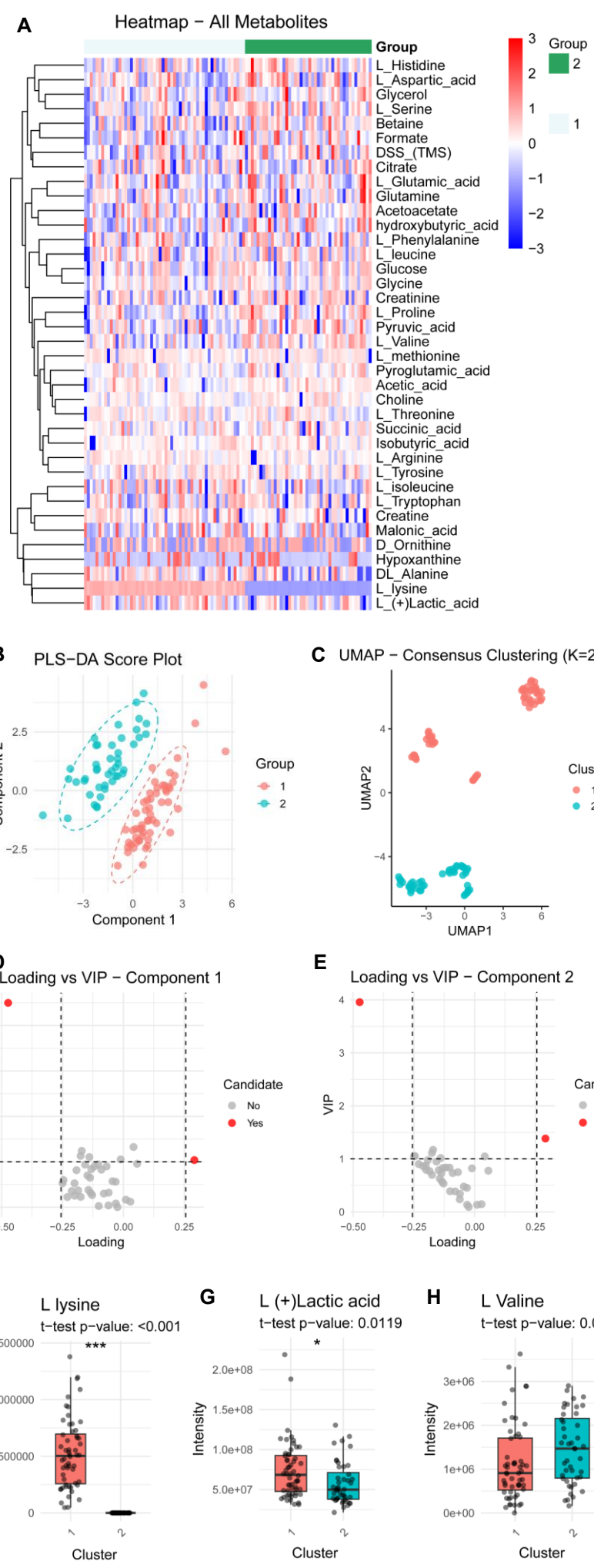
RESULTS



Figures: A. Heat Map of metabolite levels across the analyzed samples. The color scale indicates relative differences between groups (x-axis: groups; y-axis: metabolites). **B.** PLS-DA (Partial Least Squares Discriminant Analysis) score plot (accuracy = 99.16%). **C**. Unsupervised UMAP (Uniform Manifold Approximation and Projection) analysis. **D, E**. Loading vs VIP (variable importance in projection) plots of component 1 (D) and 2 (E) derived from PLS-DA analysis, showing the contribution and importance of each metabolite in group discrimination. **F-H.** Boxplots of lysine (F), lactate (G) and valine (H) relative levels across experimental groups. Statistical significance was assessed using one-way ANOVA. Asterisks indicate significant differences.

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