



Metabolomic analysis of breast cancer in Colombian patients: Exploring molecular signature in different subtypes and stages

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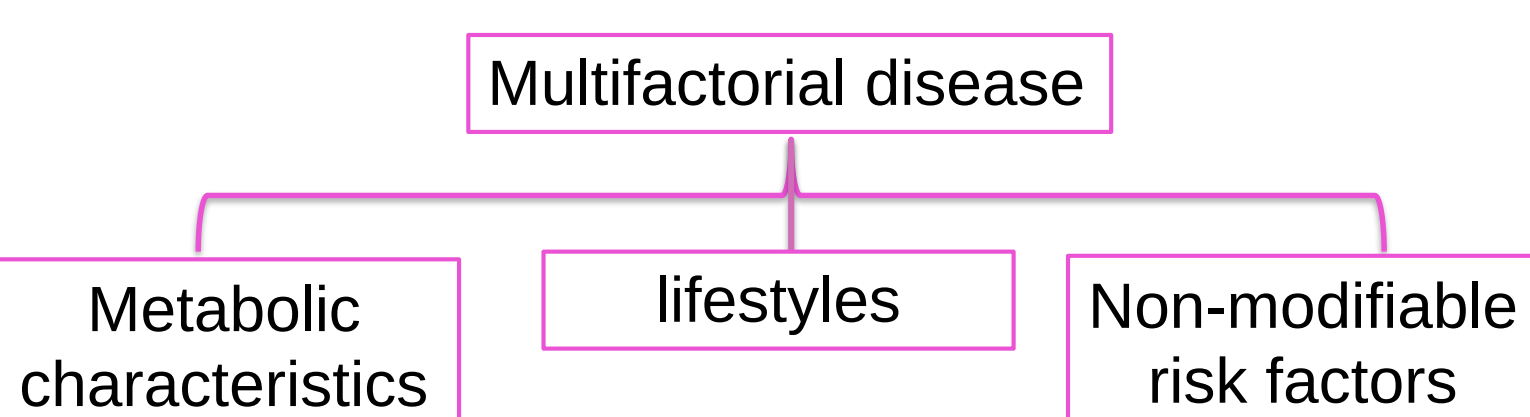
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INTRODUCTION

Breast cancer (BC)

is a neoplasm characterized by high heterogeneity and is influenced by intrinsic molecular subtypes and clinical stage, aspects that remain underexplored in the Colombian population.



In Colombia, BC is the most prevalent malignancy among women and the leading cause of cancer-related mortality, with 17,018 cases and 4752 deaths in 2022.

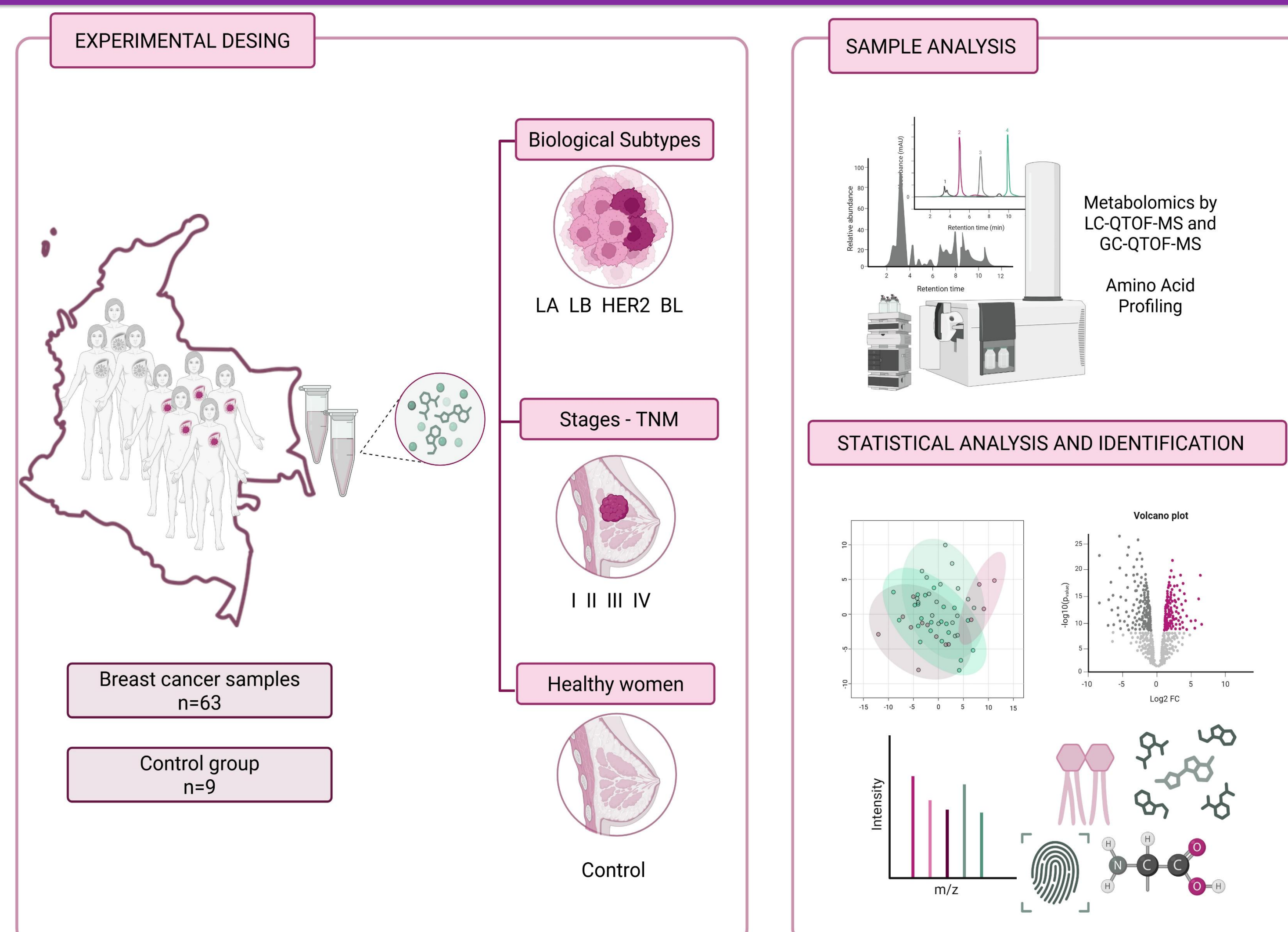
Based on these molecular insights, hormone receptor status and gene expression profiles significantly impact key metabolic pathways and physiological mechanisms, particularly those involved in energy generation and biosynthesis. These alterations generate specific metabolic fingerprints that can serve as biomarkers for different disease phenotypes.

According to the American Joint Committee on Cancer (AJCC) of 2018, this disease is classified according to the anatomical information of the tumor, as well as the expression of estrogen receptors (ER), progesterone (PR), and human epidermal growth receptor-2 (HER2).

OBJETIVE

This study aimed to characterize metabolic alterations associated with subtypes and disease progression in a group of newly diagnosed, treatment-naïve Colombian women using an untargeted metabolomics approach, from May 2021 to August 2023.

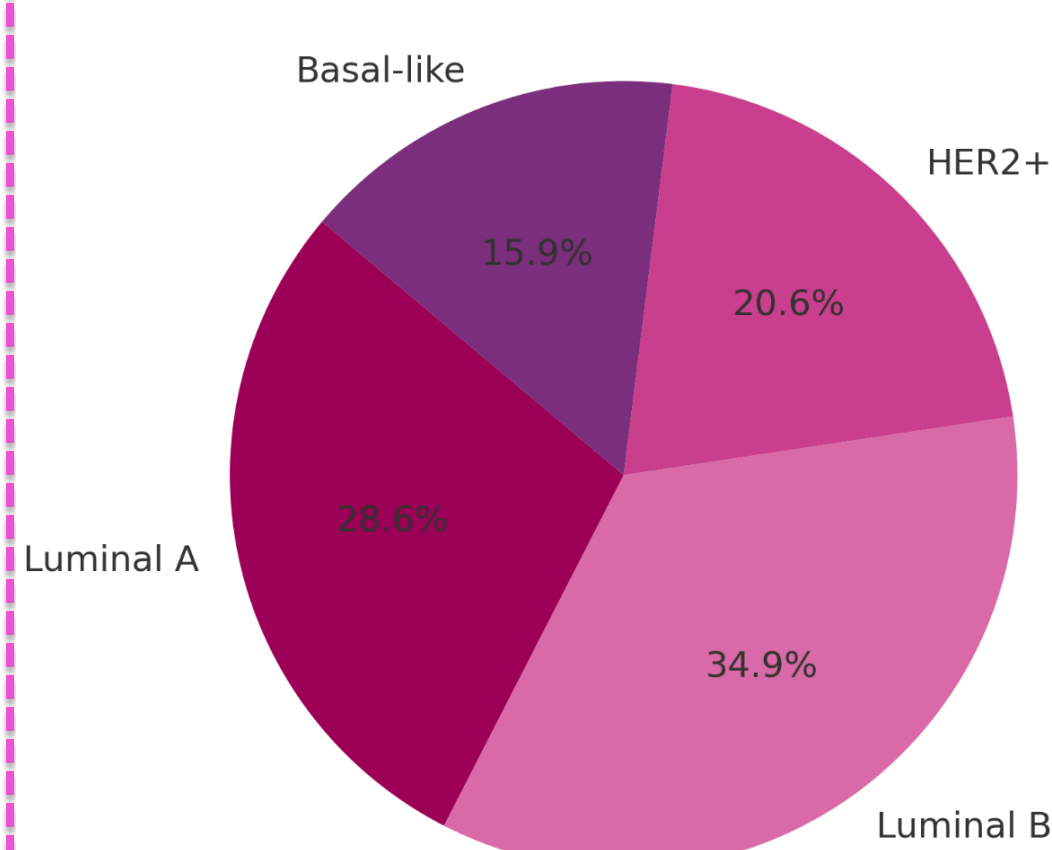
METODOLOGY



RESULTS AND DISCUSSION

Tumor types and stages according to TNM

A. Distribution by Breast Cancer Subtypes (n=63)



B. Distribution by TNM Stages (n=63)

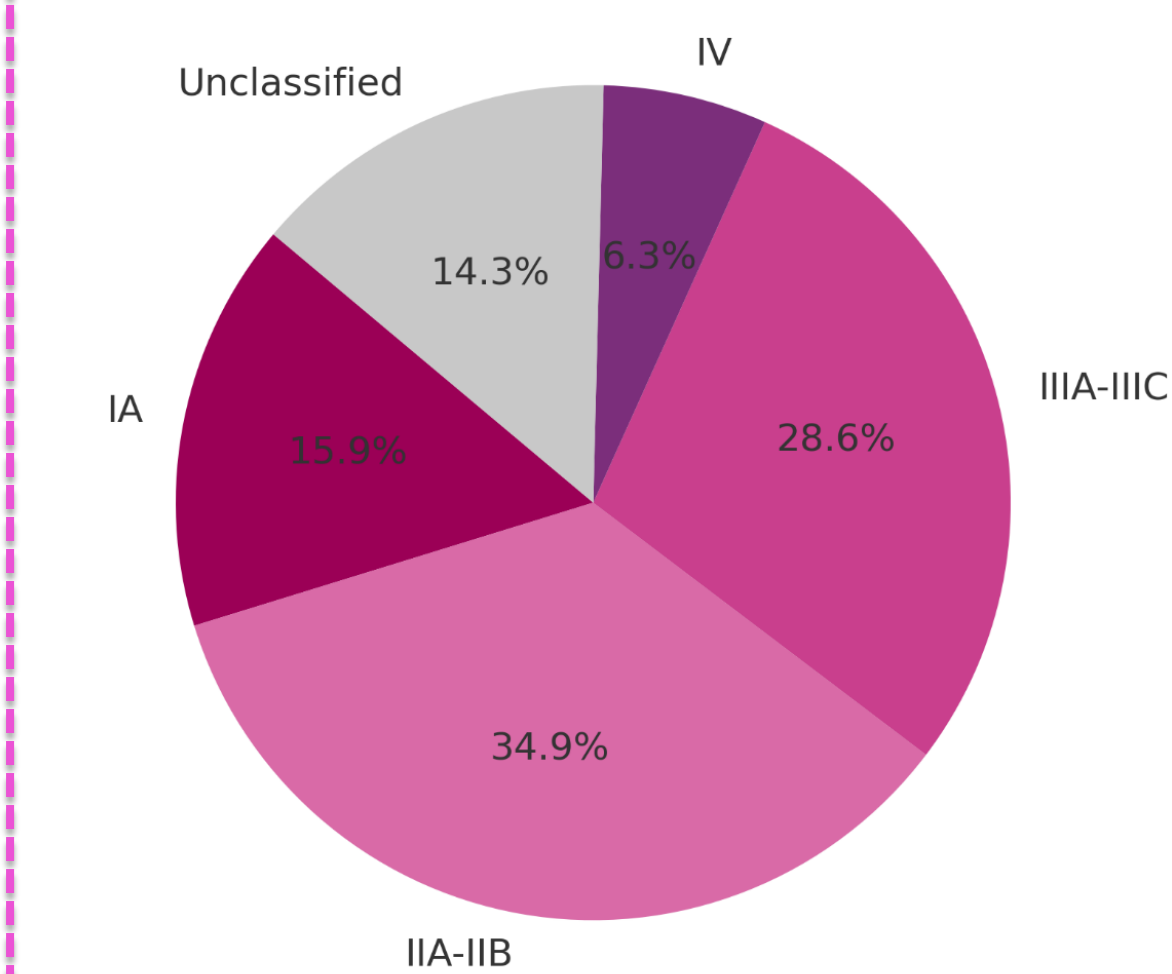


Figure 1. A. TNM classification of tumor stages in ductal carcinomas B. Sample distribution in the different types of CS B tumors.

Global metabolic alterations:

A total of **64 significantly altered metabolites** were identified across molecular subtypes and TNM stages using LC-QTOF-MS, GC-QTOF-MS, and amino acid profiling.

Hierarchical clustering revealed two main metabolic hubs:

- Lipid metabolism:** characterized by increased phosphatidylcholines and decreased lysophosphatidylcholines.
- Carbohydrate and energy pathways:** involving glycolysis intermediates and TCA-related metabolites.

Key finding: Luminal B tumors exhibited a hybrid metabolic phenotype combining enhanced glycolysis and intense lipid remodeling, distinguishing them from Luminal A, HER2+, and Basal-like tumors.

Biomarkers associated with TNM stages:

Metabolomic profiling revealed **distinct metabolic signatures** between early and advanced stages:

- Early stages (I-II):** Higher levels of **ribose**, **glutamic acid**, and **glycerol** suggest an upregulation of carbohydrate and energy metabolism.
- Advanced stages (III-IV):** Marked alterations in lipid pathways, including increased **phosphatidylcholines (PC 38:6, PC 36:5)** and depletion of **lysophosphatidylcholines (LPC 16:0, LPC 16:1)**.
- Diagnostic performance:** ROC curve analysis highlighted **ribose** (AUC = 0.978), **PC 38:6** (AUC = 0.91), and **glucuronic acid** (AUC = 0.86) as potential **biomarkers** for early detection and disease progression.

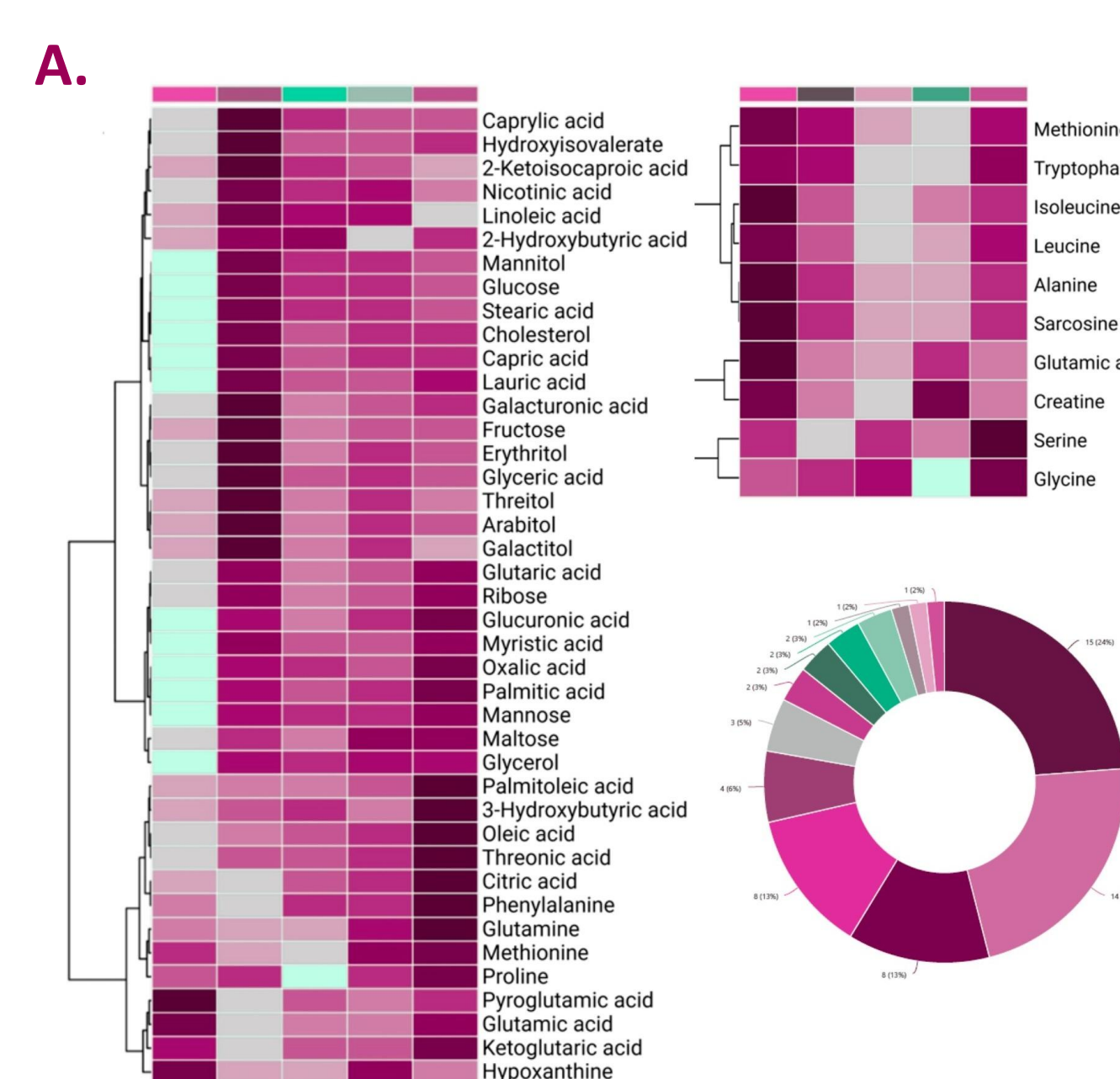
Subtypes and metabolic heterogeneity

Distinct metabolic profiles were observed among breast cancer subtypes:

- Luminal B:** Enrichment of long-chain fatty acids and glycolytic intermediates, reflecting **dual energy dependence**.
- HER2+ and Basal-like:** Increased amino acid turnover and oxidative stress metabolites.
- Luminal A:** Closer to control-like patterns, with fewer alterations in lipid metabolism.

These findings suggest that **molecular subtype-specific metabolic reprogramming** may underpin tumor behavior and treatment response.

METABOLIC ALTERATION



POTENTIAL DIAGNOSTIC BIOMARKERS

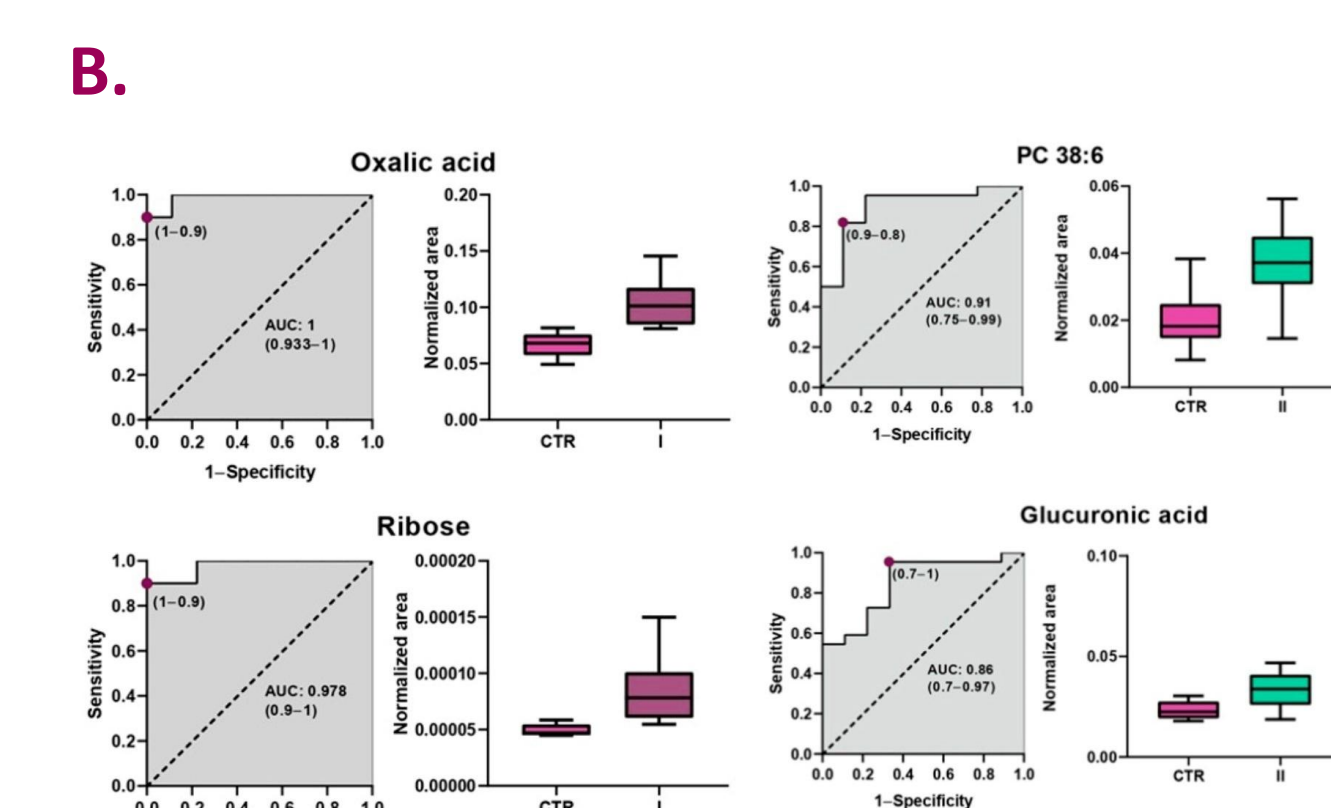


Figure 2. A. Hierarchical clustering heatmap of metabolite variations among breast cancer subtypes. B. Analysis of the Receiver Operating Characteristic curves (ROC) of potential plasma biomarkers.

Key points of the research

Distinct metabolic signatures:

Breast cancer subtypes exhibit heterogeneous metabolic profiles, with Luminal B showing a hybrid phenotype of enhanced glycolysis and lipid remodeling.

Stage-specific biomarkers:

- Early stages (I-II): ↑ Ribose, glutamic acid, glycerol → early detection potential (AUC > 0.95).

- Advanced stages (III-IV): ↑ PC 38:6, PC 36:5 + ↓ LPC 16:0 → progression indicators (AUC ≈ 0.90).

Clinical relevance: Metabolomic profiling supports **patient stratification** and could guide **personalized treatment strategies**.

Population-specific insights: First metabolomic study of breast cancer in Colombian patients, providing locally relevant biomarkers.

CONCLUSIONS

This is the **first metabolomic study of breast cancer in Colombian patients**, providing novel insights into population-specific metabolic alterations. Given the impact of **genetic background, lifestyle, and environmental factors** on metabolism, these results highlight the importance of developing **locally validated biomarkers** for breast cancer management. Our findings highlight a **progressive metabolic reprogramming** along tumor development. Early-stage tumors exhibited alterations in **carbohydrate and energy metabolism**, while advanced stages were dominated by **lipid remodeling**. This metabolic transition suggests that tumor aggressiveness is associated with a shift from energy generation through glycolysis to complex lipid biosynthesis and membrane remodeling.

REFERENCE

León-Carreño L, et al. (2025) Metabolomic Analysis of Breast Cancer in Colombian Patients. *Int. J. Mol. Sci.* 26(15):7230. DOI: 10.3390/ijms26157230

This poster summarizes findings from our published article (IJMS, 2025).