Stromal-Fibroblastic remodelling and involution signatures in non-tumoral tissue of postpartum breast cancer patients: implications for breast cancer risk

J. de la Haba-Rodríguez[1,2], R. Peña-Enríquez[2], D. Ponferrada[1], R. Bautista[3], S. Romero-Martín[4], E. Contreras[4], A. Díaz-Chacón[2], C. Morales[1], B. Rodríguez[1], P. Sanchez[1], A. Martinez[5], C. León[6], J. Cejas-Arjona[6], P. Notario[6], P. Rioja-Torres[6], J. Raya-Povedano[4], M. Álvarez[4], S. Guil-Luna[2]

[1]Medical Oncology Department, Reina Sofía University Hospital, Córdoba, Spain, [2]New therapies in cancer group (CG06), Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), University of Córdoba, Córdoba, Spain, [3]Bioinformatics Unit, Supercomputing and Bioinformatics Centre (SCBI), Malaga, Spain, [4]Radiodiagnosis Department, Reina Sofía University Hospital, Córdoba, Spain, [5]Anatomical Pathology Department, Reina Sofía University Hospital, Córdoba, Spain, [6]Breast Surgery Department, Reina Sofía University Hospital, Córdoba, Spain.

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Abstract #1418

INTRODUCTION AND OBJECTIVE

Breast cancer in young women under 45 is a **growing public health concern**, with around 50% of cases occurring in **mothers within 5-10 years after childbirth**.

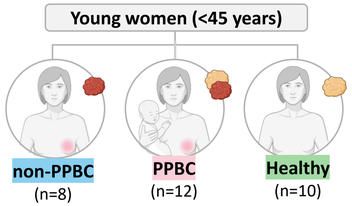
This entity, **postpartum breast cancer (PPBC),** is characterized by **aggressive clinical behaviour** and **higher metastasis and mortality rates** compared to age-matched BC patients. Despite its recognized poor prognosis, the **molecular mechanisms driving PPBC remain poorly understood**, and this knowledge gap limits the ability to identify women at higher risk and develop prevention strategies.



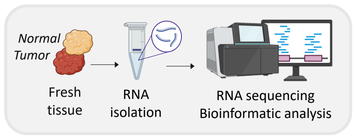
This study aimed to **characterize the transcriptomic alterations in both tumoral and histologically normal adjacent breast tissue from PPBC patients**, compared to non-PPBC and healthy controls, with a focus on identifying early risk signatures.

MATERIALS AND METHODS

RNA-seq analysis was performed on fresh breast tissue samples collected from 30 young women (≤ 45 years) at the Reina Sofia Hospital of Córdoba:



- Paired tumor and histologically normal adjacent tissue (NAT) from PPBC patients
- Tumor tissue from non-PPBC patients
- Normal breast tissue from healthy women



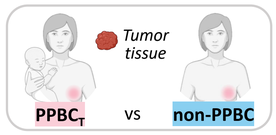
	non-PPBC	PPBC	Healthy
Age, years Median (min-max)	42.6 (40-45)	38.5 (32-45)	35.6 (24-45)
Parity status, n (%)			
Parous	5 (63)	12 (100)	5 (50)
Nulliparous	3 (38)	0 (0)	5 (50)
IHC subtype, n (%)			
Luminal A	4 (50)	3 (25)	N/A
Luminal B	1 (13)	3 (25)	
HER2+	1 (13)	4 (33)	
Triple negative	2 (25)	2 (17)	

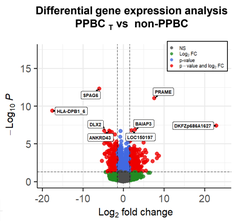
Differential expression (DESeq2) and pathway enrichment analyses (GSEA) were performed to identify key altered genes and pathways in PPBC. Differentially expressed genes (DEGs) were defined by |Fold change|>1.5 and adj p <0.05. Shared overexpressed DEGs in PPBC tumor/normal tissues were evaluated as biomarker candidates by multivariate ROC analysis.

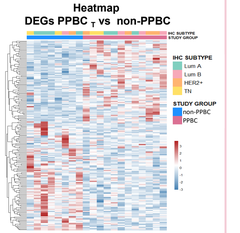
Acknowledgments We thank all the patients who participated in this study, as well as the researchers and clinical staff involved in the project from the Medical Oncology, Radiodiagnostics, Breast Surgery, and Pathological Anatomy Units at the Reina Sofía University Hospital (HURS) in Córdoba for their collaboration. Study funded by the Carlos III Health Institute (PI22/00969).

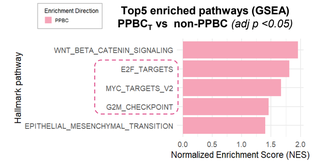
RESULTS

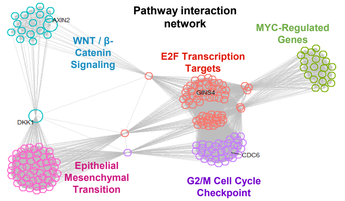
1 Aggressive proliferative and WNT/β-catenin–driven profile in PPBC tumors





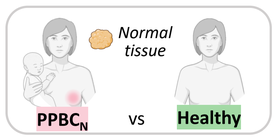


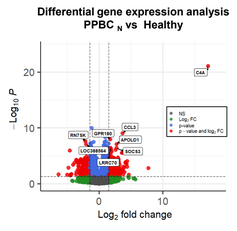


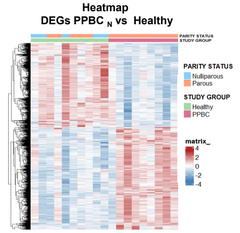


Enrichment of **cell cycle activation pathways** (E2F, MYC and G2M checkpoint) indicates high proliferative activity, alongside **WNT/β-catenin and EMT dysregulation** driving invasiveness

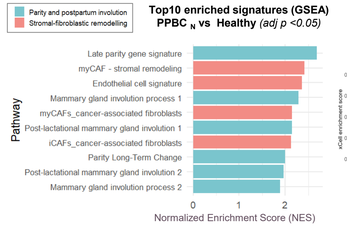
2 Stromal and involution-like remodeling in PPBC normal adjacent tissue

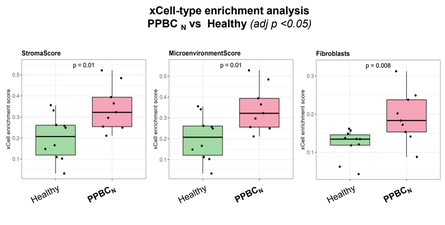


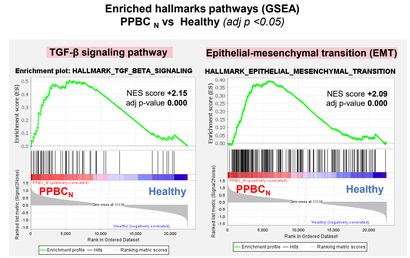




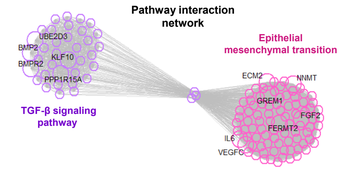
Non-tumoral breast tissue of PPBC patients showed a **unique molecular imprint** absent in healthy women



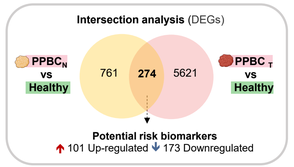


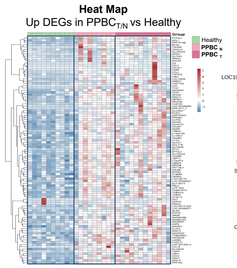


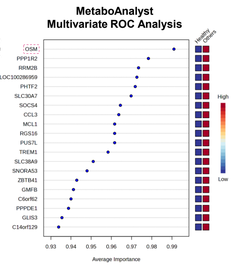
Enrichment of **stromal-fibroblastic remodeling** (TGF-β, EMT, CAFs) and **post-lactational signatures** (late parity, breast involution process)



3 Shared PPBC tumor/normal gene signature reveals potential biomarkers







Upregulated genes shared by **PPBC tumor and normal tissue** (AUC > 0.9) are mainly linked to **profibrotic and cytokine signaling**

CONCLUSIONS



Molecular alterations in PPBC extend beyond the tumor itself, involving **adjacent normal tissue**



Stromal-fibroblastic remodelling postpartum microenvironment that may favour **malignancy**



Potential for risk assessment and early prevention strategies in postpartum women

Juan de la Haba Rodríguez
juahaba@gmail.com

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