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WNT SIGNALING PATHWAY ANALYSIS IN SEARCH OF POTENTIAL BIOMARKERS AND THERAPEUTIC TARGETS FOR CANCER PATIENTS

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Introduction

In recent years, an increase in the number of new cases of diagnosed hormone-dependent neoplasms has been observed. According to the currently available data, one of the signaling pathways involved in the development and progression of these tumors is the WNT pathway, which is particularly important for the regulation of the cell cycle and embryonic development.

Aim of the study

The aim of the study was to evaluate the influence of WNT pathway effectors on patients struggling with breast and endometrial cancers in two independent studies incorporating different bioinformatical tools. The research was focused on identification of novel biomerkers and/or therapeutic targets for this group of patients. The analyses could also contribute to the better understanding of WNT regulation mechanisms and the biological processes associated with the genes of interest.

Materials & Methods

FOR BREAST CANCER ANALYSIS

1. Weighted Gene Correlation Network Analysis (WGCNA) on expression data from The Cancer Genome Atlas (TCGA) regarding 2573 WNT target genes selected on the basis of data deposited in the Gene Transcription Regulation Database (GTRD)
2. Differentially Expressed Genes (DEGs) extraction using EdgeR from comparisons between tumor samples and normal samples, as well as ER positive and ER negative patients
3. Kaplan-Meier survival estimation curves for each gene (DEG) regarding patients with breast cancer, which were further grouped into specific signatures in each comparison
4. Diagnostic potential evaluation of the signatures with ROC curves

FOR ENDOMETRIAL CANCER ANALYSIS

1. Seurat (Single Cell RNA-Seq Analysis) on Gene Expression Omnibus datasets regarding WNT-associated potential biomarkers
2. Cell clusters distribution on UMAP (Uniform Manifold Approximation and Projection) charts and cell type classification
3. Gene expression analysis for each cluster

Results

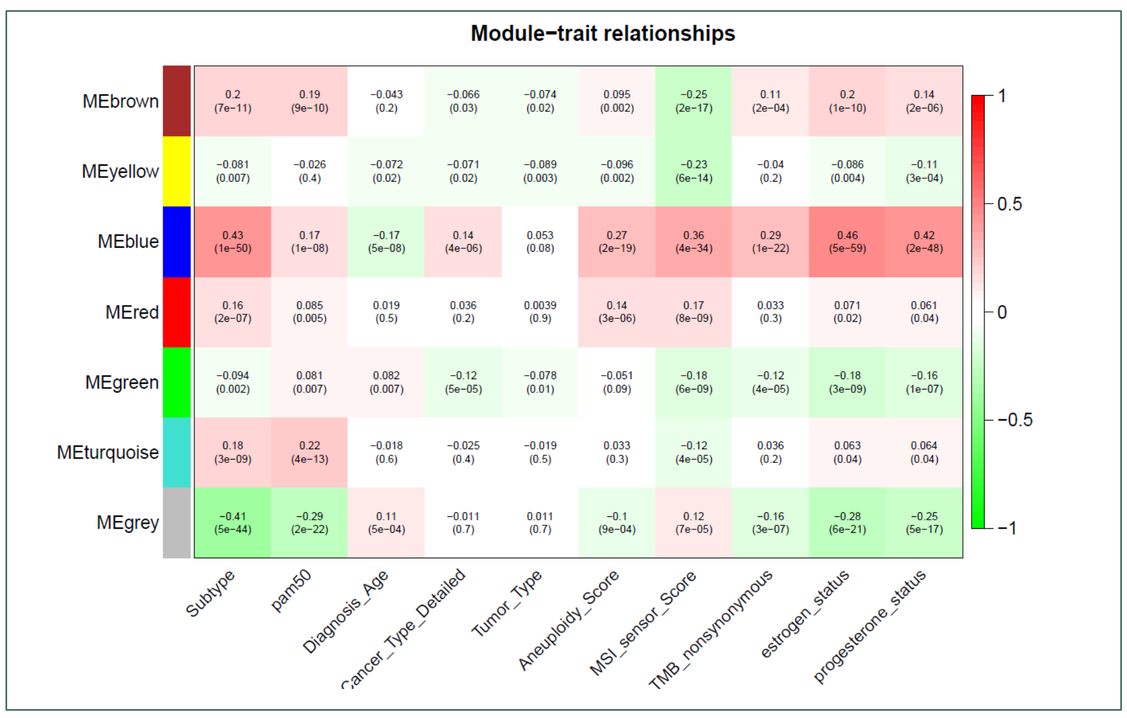

Fig. 1. WGCNA heatmap presenting the correlation of each module with specific clinical traits in the breast cancer study.

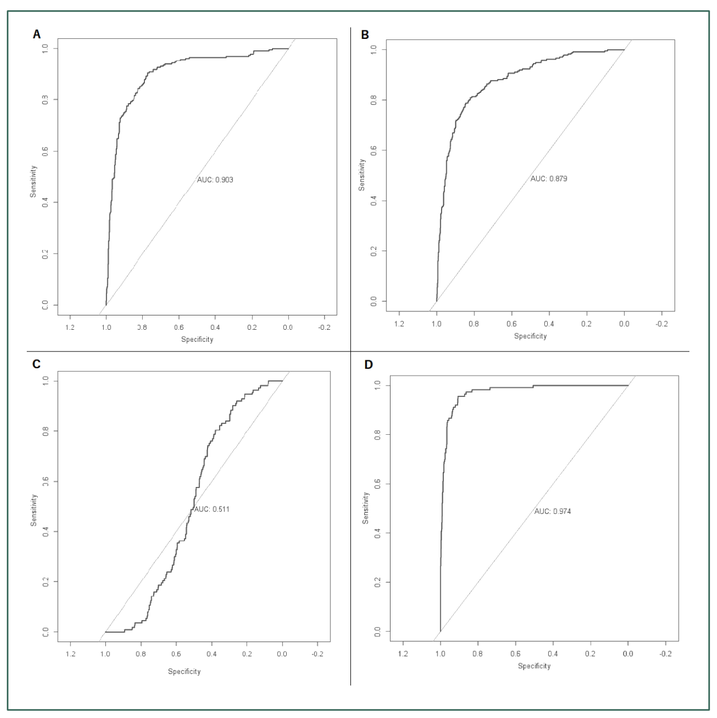

Fig. 4. ROC curves showing the predictive value of individual signatures (Fig. 3.) from ER+ vs ER-OS comparisons, AUC=0.903 (A); ER+ vs ER-DFS, AUC=0.879 (B); normal vs. tumor OS, AUC=0.511 (C); normal vs tumor DFS, AUC=0.974 (D) in the breast cancer study.

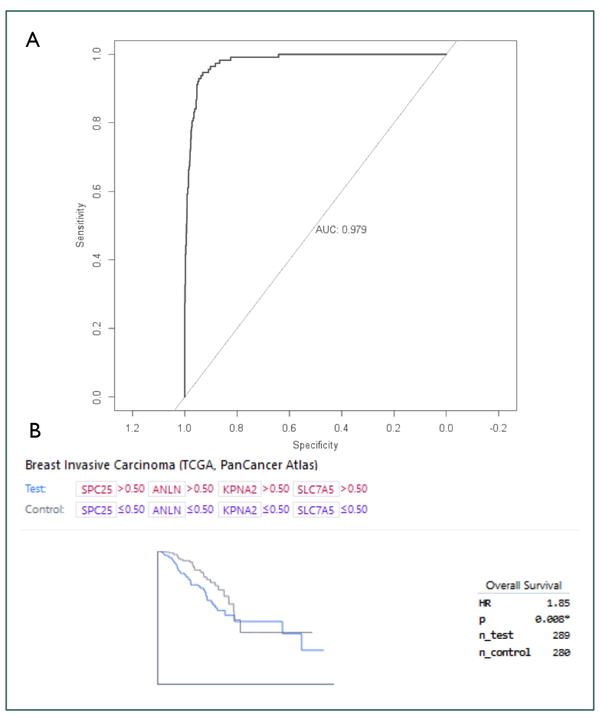

Fig. 5. Panel of *SPC25*, *ANLN*, *KPNA2* and *SLC7A5* genes in ROC analysis (AUC 0.979) (A), and Kaplan-Meier survival analysis (p=0.008) (B) in the breast cancer study.

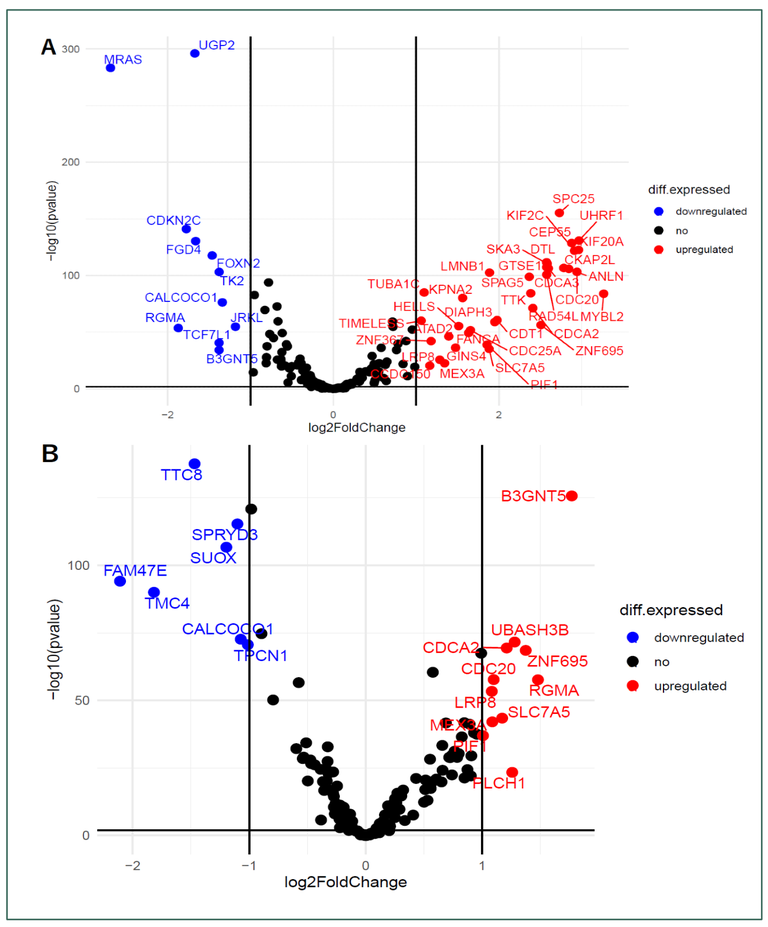

Fig. 2. DEGs extracted from tumor and normal samples comparison (A) as well as ER+ and ER- comparison (B) in the breast cancer study.

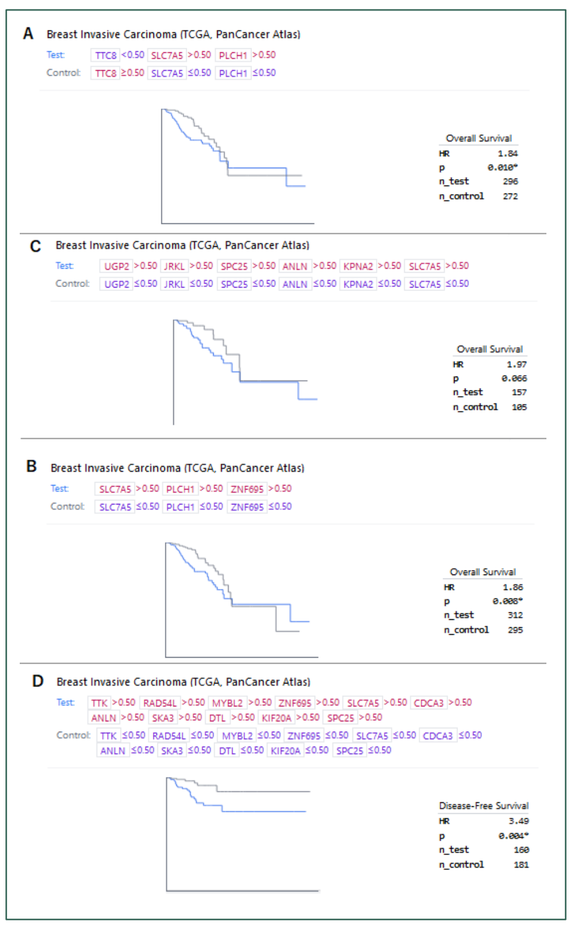

Fig. 3. Kaplan-Meier curves of breast cancer patients survival for individual signatures from ER+ vs ER-OS comparisons (A); ER+ vs ER- DFS (B); normal vs tumor OS (C); normal vs tumor DFS (D).

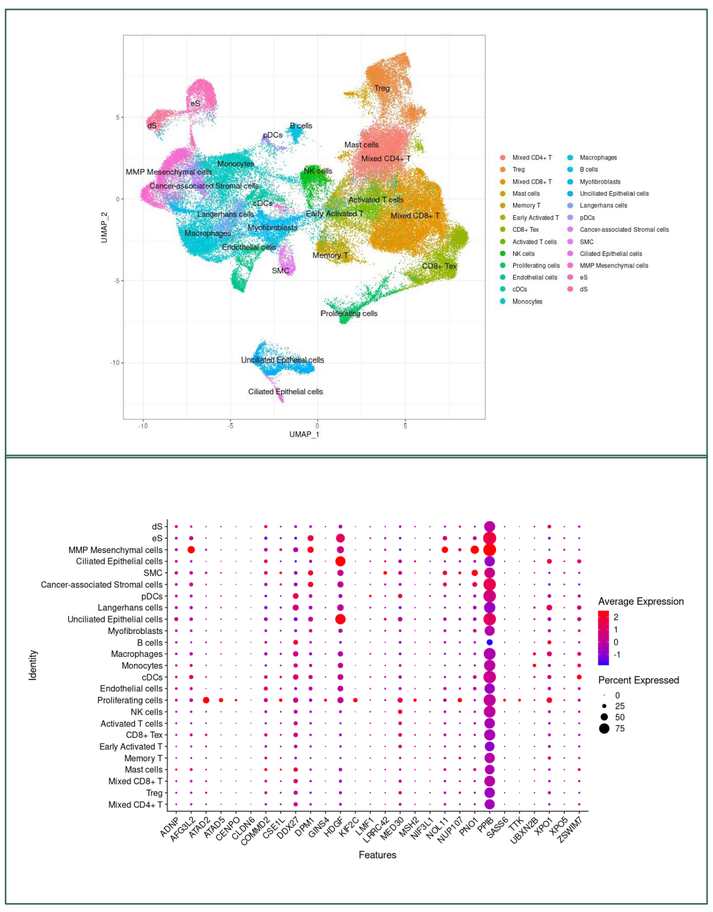

Fig. 6. UMAP chart distinguishing cells into individual clusters in the ongoing endometrial cancer study. The clusters were obtained for resolution 0.5 using seurat findclusters function.

Fig. 7. Gene expression patterns in distinguished cells.

Conclusion

The preliminary results obtained in the analyses suggest a high prognostic and diagnostic potential of the extracted genes in both breast cancer and endometrial cancer patients. Further research will be conducted to validate these results.