CLASSIFICATION ANALYSIS REVEALS THE MOLECULAR HETEROGENEITY OF BREAST CANCER THROUGH THE EXPRESSION OF VIMENTIN AND ALPHA-SMOOTH MUSCLE ACTIN

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Introduction

Breast cancer (BC) is the most common and deadly cancer in women, with its aggressiveness influenced by molecular subtypes. A critical driver of disease progression is the epithelial-mesenchymal transition (EMT) (Figure 1), a biological process that facilitates metastasis and contributes to resistance against conventional therapies. This study focuses on two key EMT markers, vimentin and α-smooth muscle actin (α-SMA), whose elevated expression indicates greater invasiveness and poor prognosis, making them potential prognostic indicators and therapeutic targets in BC management.

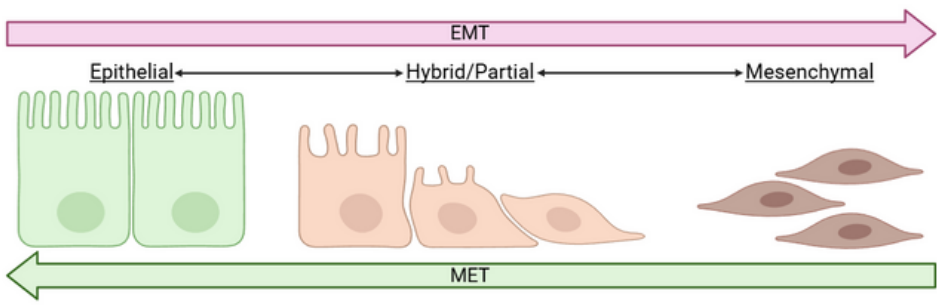

Figure 1: Schematic representation of the immunohistochemistry technique.

Objective

This study aims to evalute the input image, the expression levels of vimentin and α-SMA in a cohort of BC patients treated at Luxemburgo Hospital, employing classification algorithms to identify patterns associated with disease.

Methodology

FFPE tumor tissue samples from 19 BC patients were analyzed by immunohistochemistry (IHC) for vimentin and α-SMA (Figure 2).

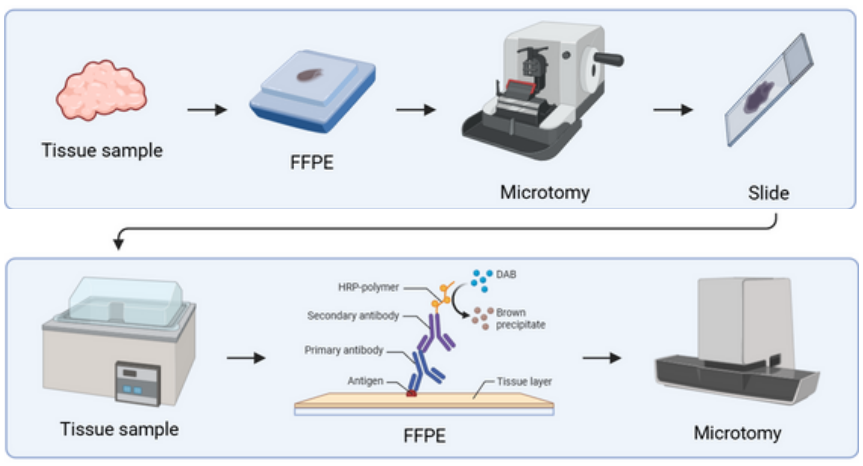

Figure 2: Schematic representation of the immunohistochemistry technique.

The digital images were processed in Aperio ImageScope using a positive pixel counting algorithm to quantify expression (Figure 3), and the data was then classified into clusters using the K-means algorithm based on the expression levels of both markers.

Results and Discussion

The K-means analysis identified four distinct clusters based on the levels of expression of vimentin and α-SMA in the BC subtypes (Figure 4).

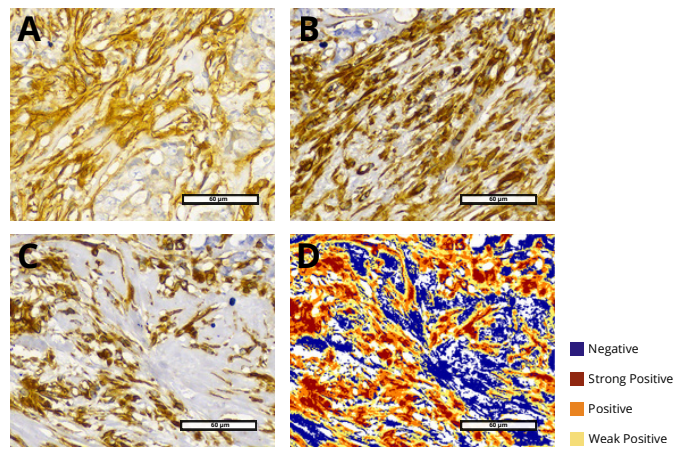

Figure 3: Histological section of breast tumor tissue showing epithelial–mesenchymal transition markers. (A) Vimentin immunostaining (clone J144). (B) α-SMA immunostaining (clone 1A4). (C) Vimentin-stained sample before software analysis. (D) Quantitative assessment of immunopositive staining intensity using ImageScope (Leica).

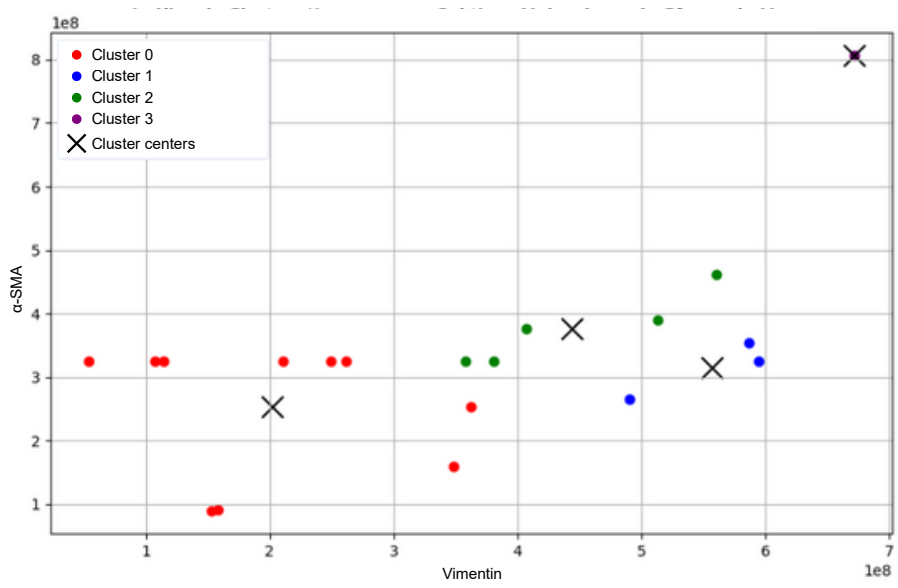

Figure 4: K-means clusters of breast cancer samples based on Vimentin and α-actin expression.

Cluster 0, composed of samples from Luminal A and B, exhibited discrete levels of the markers. Cluster 1, which includes Luminal B and Triple Positive, showed higher levels of expression of vimentin and α-SMA. Cluster 2, primarily composed of Luminal A and B patients, displayed moderate expression levels, especially for vimentin. Finally, Cluster 3, consisting solely of Triple Negative patients, exhibited intense levels of expression of vimentin and α-SMA.

Conclusion

The K-means analysis revealed distinct patterns in the expression of vimentin and α-SMA among BC subtypes, reflecting distinct tumor biology across different molecular subgroups. The clusters 0, 1, and 2 erre predominantly composed of Luminal A, B, and Triple Positive BC patients, respectively. The clusters showed an increase expression of these markers, ranging from discrete to moderate, which could be associated with lower invasiveness and better treatment prospects in luminal A and B. In contrast, the cluster 3, made up of Triple Negative patients, had the highest expression levels, reflecting high invasiveness and potential resistance to treatment. These results underscore the importance of these markers as valuable prognostic indicators and suggest their potential as therapeutic targets.

References

AGRADECIMENTOS