Simpósio de Susceptibilidade Genética Aplicada à Saúde

INVESTIGATION OF GENETIC VARIANTS IN THE 21 GENES OF THE ONCOTYPE DX PANEL IN PATIENTS WITH LUMINAL B BREAST CANCER

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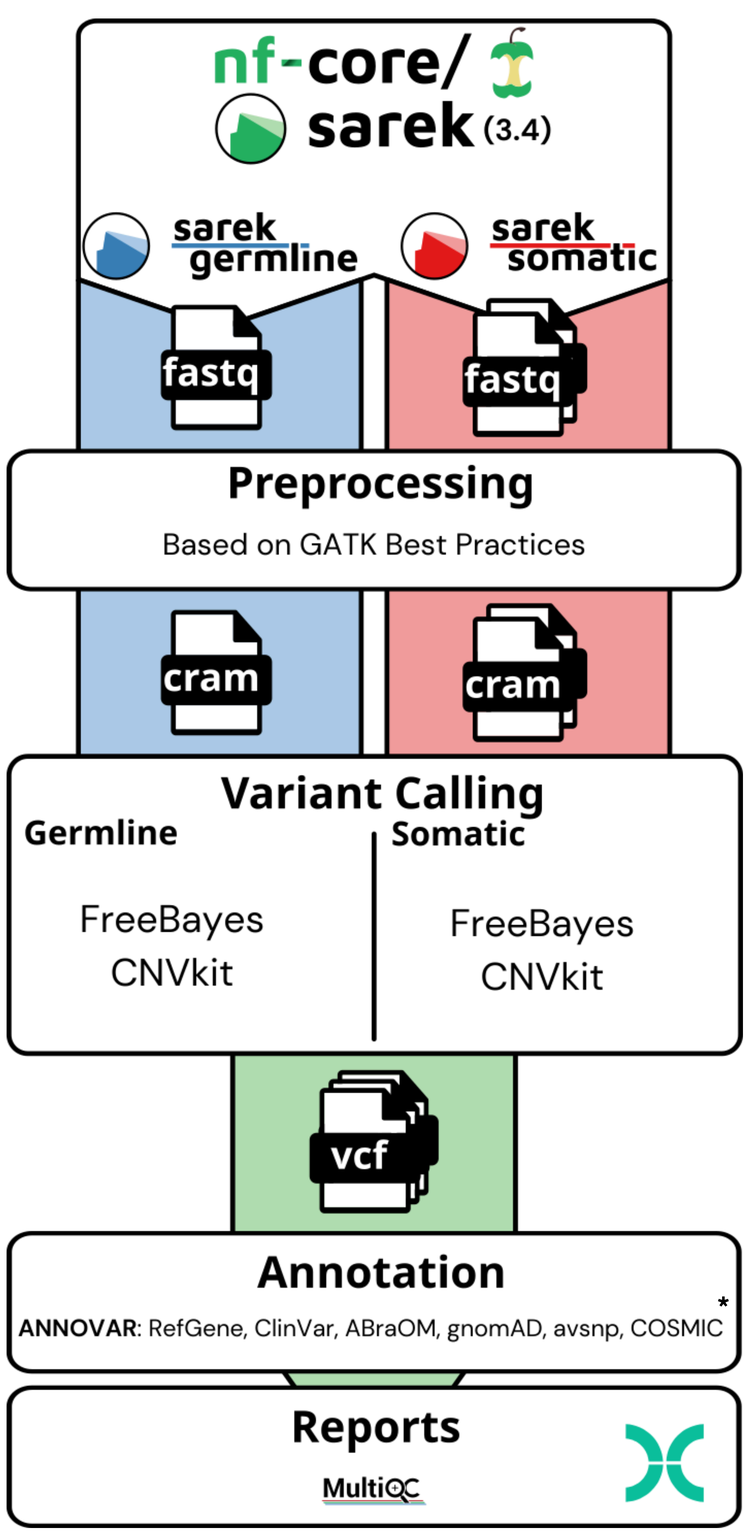
INTRODUCTION

Breast cancer is a major public health concern, especially the Luminal B subtype, known for its unique clinical outcomes. The Oncotype DX panel, consisting of 21 genes, offers insights into tumor biology and aids in treatment planning. This study ***aims*** *to identify the frequency and nature of genetic variants in the genes comprising the Oncotype DX panel in biopsy samples from Luminal B breast cancer patients from Paraná, Brazil.*

METHODOLOGY



*GRCh 38; RefGene (20211019); ClinVar (20240924); gnomAD 41 exome; ABraOM (20181204); avsnp150; COSMIC 100

RESULTS

The investigation identified significant genetic variants associated with breast carcinogenesis in Luminal B breast cancer. In the MKI67 gene, a 44.44% alteration frequency was observed, with multiple missense variants correlating to increased tumor aggressiveness and cellular proliferation. The ERBB2 gene exhibited an 18.52% alteration frequency, indicating its link to resistance in HER2-positive tumors, often unresponsive to standard therapies. The SCUBE2 gene showed a 14.81% frequency, suggesting its role in cell adhesion and signaling within tumor microenvironments. TFRC has an 11.11% alteration frequency and is crucial for iron homeostasis, influencing cell survival and tumor growth. Variants in GSTM1, MMP11, and MYBL2 (3.70% each) indicate a genetic predisposition affecting tumor development and invasiveness, implicating these genes in extracellular matrix degradation and inflammatory responses.

Oncotype DX Analysis

Gene	Percent	Variants	Remarks	Pathways	Therapeutic Targets
MKI67	44.44	rs142585399, rs970309070, rs41306648	High expression linked to aggressive tumor proliferation (SCHROEDER et al., 2023)	PI3K/AKT, mTOR, Cell Cycle	Not a direct target but helps in monitoring proliferation for therapy decisions
ERBB2	18.52	rs200455249, rs2059694956	Significant in HER2-positive tumors and therapy resistance (SMITH et al., 2023)	HER2/ERBB Signaling	HER2 inhibitors (Trastuzum)
SCUBE2	14.81	rs1235516723, rs141220103	Implicated in cell adhesion and signaling within tumor microenvironments	TGF-β, Notch	Investigational target for tumor microenvironment modulation
TFRC	11.11	rs41301359, rs143381225	Role in iron homeostasis, crucial for cell survival and tumor growth	Iron Metabolism, Apoptosis	Anti-TFRC therapies in early stages for targeting iron dependency
GSTM1	3.70	-	Linked to somatic modifications and breast cancer predisposition (LEE et al., 2021)	Detoxification, Redox Balance	Potential antioxidant adjunct therapies
MMP11	3.70	-	Involved in extracellular matrix degradation and tumor invasiveness	ECM Remodeling, MAPK	MMP inhibitors under exploration in cancer treatments
MYBL2	3.70	-	Genetic predisposition for tumor progression	Cell Cycle, Transcription Regulation	Investigational pathway-specific inhibitors targeti

CONCLUSION

This study underscores the importance of genetic variants in the Oncotype DX panel for understanding Luminal B breast cancer and guiding therapy. Key findings include high alteration frequencies in MKI67, ERBB2, SCUBE2, and TFRC, which influence tumor aggressiveness, therapy resistance, and cellular survival. MKI67 variants mark increased proliferation, while ERBB2 variants highlight challenges in HER2-positive therapy response. Alterations in SCUBE2 and TFRC affect cell adhesion, signaling, and metabolic demands, offering potential therapeutic targets. These insights provide a foundation for more personalized treatment strategies tailored to the genetic profile of Luminal B breast cancer patients.

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