Simpósio de Susceptibilidade Genética Aplicada à Saúde

GENETIC PROFILING AND THERAPEUTIC TARGET ANALYSIS OF BREAST CANCER GENES IN PATIENTS FROM PARANÁ, BRAZIL

MATEUS LUCAS FALCO* 1; RAFAELA DA ROSA-RIBEIRO 1;DAVID LIVINGSTONE ALVES FIGUEIREDO 1; EMERSON CARRARO 1; AMANDA RAZERA 1; GABRYELA PAULISTA SCHIMDT 2; JOÃO RICARDO FORNAZARI BINI 2; CAROLINA PANIS 3.

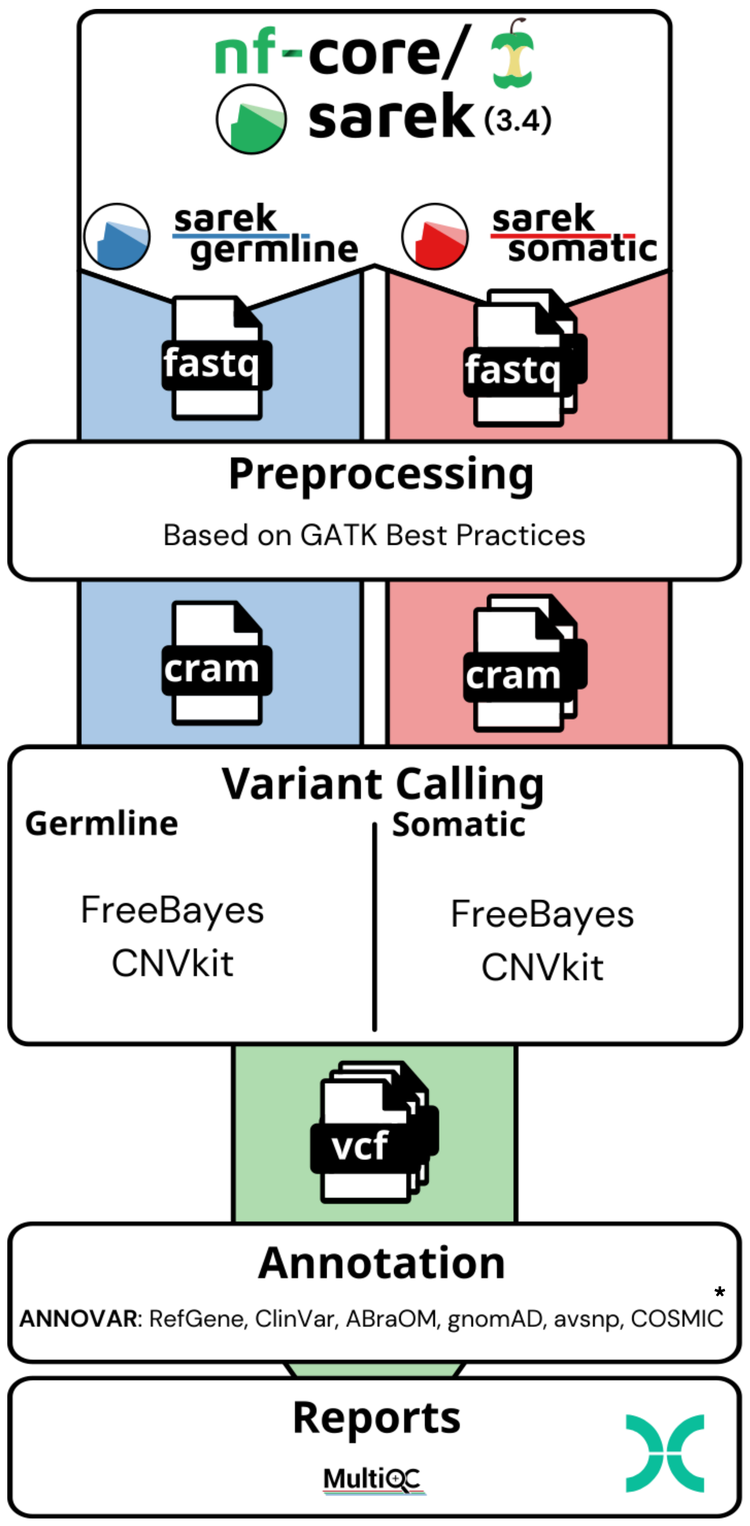
*matlucfalco@gmail.com

1 MIDWEST STATE UNIVERSITY
2 CAMPO REAL UNIVERSITY
3 THE WESTERN PARANÁ STATE UNIVERSITY

INTRODUCTION

This study investigates the genetic profile of breast cancer in patients from Paraná, Brazil, focusing on genes included in the MammaPrint panel, which is used to assess the risk of metastasis by analyzing the expression of genes linked to tumor aggressiveness. We ***aim*** *to gain insights into the molecular characteristics of breast cancer within this population, examining gene mutation frequencies and therapeutic targets to identify potential options for targeted treatments.*

METHODOLOGY



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

RESULTS

Our analysis identified several genes with high mutation frequencies, notably BLM (12.11%), DCK (10.42%), and CEP55 (9.99%), indicating their potential roles in breast cancer progression within this cohort. Genes such as BLM and BIRC5 are involved in essential pathways like DNA repair and apoptosis inhibition, which contribute to tumor survival and resistance to treatment. While some genes, such as BLM and CDKN2A, have existing therapeutic options (PARP and CDK4/6 inhibitors), others lack direct inhibitors, underscoring the need for new drug development. The observed mutation frequencies reflect a heterogeneous genetic profile in this population, which could impact individualized treatment approaches.

Gene	Mutation_Frequency	Known_Therapeutic_Targets	Pathway_Function	Therapeutic_Target_Compromise
BLM	12.11%	PARP inhibitors (e.g., Olaparib)	DNA repair (Homologous Recombination)	High; BLM mutations affect DNA repair pathways, critical in cancer treatments.
DCK	10.42%	Cytarabine, Gemcitabine	Pyrimidine metabolism	Moderate; DCK is involved in activating nucleoside analogs in chemotherapy.
CEP55	9.99%	No direct inhibitors; potential mitotic kinase targets	Cytokinesis, Cell Cycle	Moderate; critical for cytokinesis, elevated in cancers but lacking direct inhibitors.
ESPL1	9.96%	No direct inhibitors	Chromatid cohesion, separation	Moderate; influences cell division, with potential in targeting cohesion complexes.
BUB1B	9.39%	Mps1 inhibitors, Aurora kinase inhibitors	Mitotic checkpoint	Moderate; essential for spindle assembly checkpoint in mitosis.
CDCA7	6.43%	CDK inhibitors	Cell proliferation and differentiation	Moderate; implicated in cell cycle regulation. CDK inhibitors target cell cycle.
CCNB1	5.66%	CDK1 inhibitors (e.g., RO-3306)	G2/M phase of cell cycle	Moderate; Cyclin B1 overexpression linked to unchecked cell cycle progression.
GPR1	4.75%	No direct inhibitors	G-protein coupled receptor signaling	Low; limited evidence of direct therapeutic targeting.
BIRC5	4.34%	Survivin inhibitors (e.g., YM155)	Apoptosis inhibition, cell proliferation	High; anti-apoptotic role, often overexpressed in tumors. Targeted by survivin inhibitors.
FOXM1	3.33%	Thiostrepton, Proteasome inhibitors	Transcriptional regulation, cell cycle	High; FOXM1 overexpression leads to cell proliferation and survival in tumors.
AURKA	2.96%	Alisertib, MLN8237	Mitotic spindle assembly	High; AURKA is critical for mitosis and is frequently targeted in cancer therapies.
CTSD	2.85%	Pepstatin A, E64	Protease involved in cell survival	Low; therapeutic targeting limited but may be relevant in certain cancers.
GINS2	2.79%	No direct inhibitors	DNA replication, cell proliferation	Moderate; involved in DNA replication initiation.
CCNE1	2.61%	CDK2 inhibitors	G1/S phase transition of cell cycle	High; Cyclin E1 is a known driver of cell cycle in some cancers.
BUB1	2.53%	Mps1, Aurora kinase inhibitors	Mitotic checkpoint	Moderate; critical for cell cycle fidelity, important in cancerous cells.
CINP	2.30%	No direct inhibitors	DNA replication initiation	Low; limited therapeutic targeting, involved in replication.
CCNB2	2.17%	CDK1 inhibitors	G2/M transition in cell cycle	Moderate; essential in the cell cycle, but fewer direct therapies.
CDKN2A	2.07%	Palbociclib, Abemaciclib (CDK4/6 inhibitors)	Cell cycle control (Tumor suppressor)	High; CDKN2A mutations impair tumor suppression, targeted by CDK inhibitors.
BAG1	1.88%	Hsp70 inhibitors (e.g., VER-155008)	Apoptosis regulation	Moderate; involved in cell survival pathways.
CDC20	0.93%	APC/C inhibitors	Cell cycle regulation	Low; emerging therapeutic target in mitotic control.
CETN2	0.53%	No direct inhibitors	Centrosome function	Low; few therapeutic implications, involved in centrosome maintenance.

CONCLUSION

This study sheds light on the complex mutational landscape of breast cancer in a Brazilian cohort, identifying both actionable targets and areas where therapeutic options are limited. Genes with high mutation frequencies and known therapeutic options suggest pathways for personalized treatments, while the lack of inhibitors for key genes highlights areas for further research. These insights contribute to a broader understanding of breast cancer genetics in this regional population, supporting the potential for more personalized treatment strategies.

ACKNOWLEDGMENT

CNPq IPEC GUARAPUAVA UNICENTRO PARANÁ unioeste FUNDAÇÃO ARAUCÁRIA Apoio ao Desenvolvimento Científico e Tecnológico do Paraná PARANÁ SECRETARIA DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR GENOMAS PARANÁ