EVALUATION OF SINGLE NUCLEOTIDE POLYMORPHISMS OF MESENCHYMAL EPITHELIAL TRANSITION GENE IN NIGERIAN BREAST CANCER PATIENTS

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A DISSERTATION SUBMITTED TO THE SCHOOL OF POSTGRADUATE STUDIES IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE MASTER OF SCIENCE, (M.Sc) IN BIOCHEMISTRY IN THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF SCIENCE AND TECHNOLOGY, COVENANT UNIVERSITY, OTA, OGUN STATE, NIGERIA

AUGUST, 2024

ACCEPTANCE

This is to attest that this dissertation is accepted in partial fulfillment of the requirements for the award of a Master of Science (M.Sc.) in Biochemistry in the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Nigeria.

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DECLARATION

I, **AMUJI, DORIS NNENNA (22PCP02378),** hereby declare that this research work was carried out by me under the supervision of Prof. Emeka E.J. Iweala of the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Ogun State. I attest that the dissertation has not been presented either wholly or partially for the award of any degree elsewhere. All sources of data and scholarly information used in this dissertation were duly acknowledged

AMUJI, DORIS NNENNA

Signature and Date

CERTIFICATION

We certify that the dissertation titled "**EVALUATION OF SINGLE NUCLEOTIDE POLYMORPHISMS OF MESENCHYMAL EPITHELIAL TRANSITION GENE IN NIGERIAN BREAST CANCER PATIENTS**" is an original work carried out by **AMUJI, DORIS NNENNA (22PCP02378)** in the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Ogun State, Nigeria under the supervision of Prof. Emeka E.J. Iweala. We have examined and found this work acceptable as part of the requirement for the award of a Master of Science (M. Sc.) degree in Biochemistry.

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(External Examiner) **Signature and Date**

Prof. Akan B. Williams
(Dean, School of Postgraduate Studies) **Signature and Date**

DEDICATION

This dissertation is dedicated to EL ROI, who, in his infinite mercies, granted me the intellectual and physical strength to complete this work.

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LIST OF ABBREVIATIONS

HCC	Hepatocellular carcinoma
PTC	Papillary thyroid cancer
LS-SCLC	Limited-stage small-cell lung cancer
NPC	Nasopharyngeal carcinoma
EGFR	Epidermal growth factor gene
TKD	Tyrosine kinase domain
lncRNAs	Long non-coding RNAs
SNPs	Single-nucleotide polymorphisms
ER	Estrogen receptor
TNBC	Triple-negative breast cancer
IARC	International Agency for Research on Cancer
PAHO	Pan American Health Organization
uPA	Urokinase-type plasminogen activator
TMPRSS13	Transmembrane protease serine 13
c-MET	Mesenchymal-epithelial transition factor
SH2	Src homology-2 domains
GRB2	Growth factor receptor-bound protein-2
STAT3	Signal transducer and activator of transcription 3
PI3K	Phosphatidylinositol-3 kinase
VEGF	Vascular endothelial growth factor
HGF	Hepatocyte growth factor
NSCLC	Non-small cell lung cancer

ABSTRACT

Breast cancer (BC) is a nationwide health issue, and understanding genetic risk factors is crucial for early detection and personalized treatment strategies. The Mesenchymal Epithelial Transition (MET) proto-oncogene, encoding the c-MET receptor tyrosine kinase (RTK), is key in BC progression and metastasis. This study identified single nucleotide polymorphisms (SNPs) of the MET gene, namely rs40239, rs1621, and rs41736, in Nigerian BC patients and their association with BC risk. The research involved 150 participants, including 75 BC patients and 75 healthy controls. DNA was extracted from participants' blood using the QIAamp DNA Mini Kit. The target SNPs (rs40239, rs1621, and rs41736) were genotyped on the DNA using the TaqMan SNP genotyping assay, and the allele frequencies were compared. An X^2 test was employed to examine the association between the SNPs and BC risk. The results showed the presence of the SNPs with varying distributions in the participants. For MET rs40239, the AA genotype was more common in controls (60%) compared to patients (17%), though the association with BC risk was not statistically significant (OR=4.706, 95% CI: 0.959 – 23.096, p=0.062). For MET rs1621, no significant association with BC risk was found, with an odds ratio of 1.188 (95% CI: 0.516-2.733, p=0.426), and the genotype distribution showed minimal differences between controls and patients. Similarly, MET rs41736 also showed no significant association with BC risk (OR=0.954, 95% CI: 0.904 - 1.006, p=0.262), with genotype distributions showing minimal differences between groups. These findings suggest that while there were some differences in genotype distributions, none of the SNPs showed a statistically significant association with BC risk in this study. The results are crucial for understanding the genetic and functional implications of these *MET* gene variants of BC in the underrepresented African population. This would pave the way for future investigations that could influence strategies for early detection, diagnosis, and precision treatment of BC.

KEYWORDS: Breast cancer, Single nucleotide polymorphism, Genotype, Prognosis