STUDY OF THE CONTRIBUTIONS OF GENETIC POLYMORPHISMS IN VITAMIN D BINDING PROTEIN AND RECEPTOR TO PROSTATE CANCER AMONG YORUBA MEN

By

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11CP011795

A DISSERTATION SUBMITTED TO THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF SCIENCE AND TECHNOLOGY, COVENANT UNIVERSITY OTA, NIGERIA

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M.Sc. RESEARCH PROJECT

Submitted to

DEPARTMENT OF BIOCHEMISTRY,
COLLEGE OF SCIENCE AND TECHNOLOGY,
COVENANT UNIVERSITY
OTA, NIGERIA.

SUPERVISOR: DR S.O. ROTIMI

MAY, 2018.

ACCEPTANCE

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

DECLARATION

I, PETER OLAMIDE ADEYEMI (11CP011795), declare that this M.Sc. dissertation titled: "Study of the contributions of genetic polymorphisms in vitamin d binding protein and receptor to prostate cancer among yoruba men" was undertaken by me under the supervision of Dr. S.O. ROTIMI. The work presented in this dissertation has not been presented, either wholly or partly for the award of any degree elsewhere. All sources of scholarly information used in this dissertation were duly acknowledged.

Peter, Olamide Adeyemi ……

(Student) Signature and Date

CERTIFICATION

We certify that the dissertation titled: “Study of the contributions of genetic polymorphisms in vitamin d binding protein and receptor to prostate cancer among yoruba men” is an original work carried out by PETER, Olamide Adeyemi with Matriculation Number: 11CP011795, of Biochemistry Programme in the Department of Biochemistry and Molecular Biology, College of Science and Technology, Covenant University Ota, Ogun State, Nigeria. We have examined the work and found it acceptable for the award of Master of Science (M.Sc.) degree in Biochemistry.

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DEDICATION

This dissertation is dedicated to God Almighty, the Omnipotent and Omniscient, the giver of life and the ingenious architect of my destiny for His faithfulness, tender-mercies and graciousness towards me.

I also dedicate this dissertation to my dear parents, Engr. and Mrs. Kolawole Peter, whom God, my source has used as the resources for the pursuit of my academics in Covenant university.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Figure **Description** **Page**

ABBREVIATIONS

3D-CRT	Three Dimensional Conformal Radiation Therapy
AR	Androgen receptor
ARMS	Amplification Refractory Mutation System
BMI	Body mass index
Bp	Base pairs
BRCA1	Breast cancer 1, early onset
BRCA2	Breast cancer 2, early onset
CDK	Cyclin-dependent kinase
CDKI	Cyclin-dependent kinase inhibitor
CI	Confidence interval
CRPC	Castrate Resistant Prostate Cancer
CYP	Cytochrome P450 Mixed Function oxidases
DNA	Deoxyribonucleic Acid
DRE	Digital rectal examination
EBRT	External Beam Radiation Therapy
EDTA	Ethylenediaminetetraacetic Acid
ERG	ETS Related Gene
GWAS	Genome Wide Association Studies
HPC	Hereditary Prostate Cancer gene
HRPC	Hormone Refractory Prostate Cancer
IMRT	Intensity Modulated Radiation Therapy
LOH	Loss of Heterozygosity
OR	Odds ratio
PCR	Polymerase chain reaction
PIN	Prostate intraepithelial neoplasia
PSA	Prostate specific antigen

PTEN	Phosphatase and Tensin Homolog
RAF	Raf Proto-oncogene Serine
Rb	Retinoblastoma
RFLP	Restriction Fragment Length Polymorphism
SBRT	Stereotactic Body Radiation Therapy
SCNA	Somatic Copy Number Alteration
SNP	Single Nucleotide Polymorphisms
TMPRSS2	Transmembrane Protease Serine 2
TRUS	Trans rectal ultrasound
UK	United Kingdom
UN	United Nations
US	United States
USA	United States of America
UV	Ultra Violet Light
VDBP	Vitamin D Binding Protein
VDR	Vitamin D Receptor

ABSTRACT

Incidence of prostate cancer is rising and it is the most common cancer in men. Multiple factors have been suggested for the etiology of prostate cancer including ethnic, genetic and diet. Vitamin D (calcitriol) has been shown to have role in cell growth and differentiation. Vitamin D binding protein (VDBP), is the main transporter of vitamin D in the bloodstream and also different cells express vitamin D receptor (VDR) that is required for calcitriol action. Genetic variants of the VDBP and the VDR gene have been shown to account for a significant variability in the levels and systemic effects of vitamin D. Polymorphism in VDR gene has been associated with prostate cancer in some epidemiological studies; but, there is rarity of information in the Nigerian context. Specifically, we genotyped population-based samples of 100 diagnosed prostate cancer cases and 96 age matched controls using restriction fragment length polymorphism to determine single nucleotide polymorphisms rs7041 and rs4588 in VDBP and amplification refractory mutation system PCR for Single nucleotide polymorphisms in VDR rs2228570, rs731236, rs7975232 and rs1544410 that are reportedly associated with the prevalence and risk of prostate cancer. Statistical analysis was done using MEDCALC® statistical software and Microsoft Excel to determine p-value, odds ratio and confidence intervals. Our analysis showed that VDR rs731236 heterozygote **t** and rs1544410 were significantly associated with PCa risk (p=0.02), Odds ratio for rs731236 heterozygote **t** is (1.8) and rs1544410 is (0.04) respectively. On the other hand, the mutated G allele for VDBP rs7041 was found in 13% of the cases and none in the controls as well as the mutated A allele for rs4588 which was found in 12% of the cases and none in the control. The polymorphisms in the VDR and VDBP genes appeared to be responsible for susceptibility to prostate cancer in the Yoruba population.