

**CHARACTERISATION OF MED-12 MUTATIONS IN UTERINE
LEIOMYOMAS OF NIGERIAN WOMEN**

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OCTOBER, 2021

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BY

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**A DISSERTATION SUBMITTED TO THE SCHOOL OF
POSTGRADUATE STUDIES IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE AWARD OF MASTER OF SCIENCE (M.Sc.)
DEGREE IN BIOCHEMISTRY IN THE DEPARTMENT OF
BIOCHEMISTRY, COLLEGE OF SCIENCE AND TECHNOLOGY,
COVENANT UNIVERSITY.**

OCTOBER, 2021.

ACCEPTANCE

This is to attest that this dissertation is accepted in partial fulfilment of the requirement for the award of the degree of Master of Science in Biochemistry in the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Nigeria

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DECLARATION

I, KOYEJO, OLUWATOSIN DEBORAH (19PCP02018) declare that this research was carried out by me under the supervision of Dr. O. A. Rotimi of the Department of Biochemistry, Covenant University. I attest that this dissertation has not been presented either wholly or partly for the award of any degree elsewhere. All the sources of data and scholarly information used in this dissertation are duly acknowledged.

KOYEJO, OLUWATOSIN DEBORAH

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Signature & Date

CERTIFICATION

We certify that this dissertation titled “**CHARACTERISATION OF MED-12 MUTATIONS IN UTERINE LEIOMYOMAS OF NIGERIAN WOMEN**” is an original research carried out by **KOYEJO, OLUWATOSIN DEBORAH (19PCPO2018)** in the Department of Biochemistry, College of Science and Technology, Covenant University, Ota, Ogun State, Nigeria under the supervision of Dr. O. A. Rotimi. We have examined and found the work acceptable as part of the requirements for the award of a degree of Master of Science in Biochemistry.

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DEDICATION

I dedicate this report to God Almighty, my rock, my strength, my light and my saviour for the unlimited grace, knowledge and insight given to me to successfully complete this work. I also dedicate this report to my ever-caring parents, Engineer and Mrs. Oladimeji Koyejo for their support and constant encouragement.

ACKNOWLEDGEMENTS

I return all glory, honour and adoration to God the creator, the beginning and the end of everything, for His grace, love and guidance and for the knowledge He bestowed me to complete this program. I acknowledge the Chancellor of Covenant University Dr. David Oyedepo for the vision that birthed this great institution from which I have greatly benefited. I also appreciate the Vice Chancellor Prof. Abiodun Adebayo and the entire Management team of Covenant University for their commitment towards raising a new generation of leaders. To the current Dean of the School of Postgraduate Studies, Prof. Akan Williams, and the Postgraduate School staff, I appreciate you for the diverse training and programs organized towards capacity building for successful postgraduate research.

My sincere gratitude goes to the supervisor allocated to me for this project, Dr. O. A. Rotimi for her persistent, unrelenting and detailed supervision despite her busy schedule to ensure that this write-up was well put together to duly represent the main aims and goals of Biochemistry. I also appreciate her for every sacrifice in time and effort to put me through the necessary steps during this research. Additionally, I appreciate all the faculty members of the Department of Biochemistry for their comments, remarks, corrections and helpful tips during the presentation of this work. I would also like to appreciate the Head of Department (HOD), College of Science and Technology (Biochemistry department), Professor S. Afolabi for the opportunity to participate in this course, thus enabling me to improve on my research skills and be moulded to represent the science field boldly in future. Finally, I appreciate the faculty and staff of Biochemistry department for every time and relentless effort invested towards bringing out the best in me both as a student and a researcher.

THANK YOU ALL AND GOD BLESS!!!

TABLE OF CONTENTS

CONTENTS	PAGE
COVER PAGE	I
TITLE PAGE	II
ACCEPTANCE	III
DECLARATION	IV
CERTIFICATION	V
DEDICATION	VI
ACKNOWLEDGMENTS	VII
TABLE OF CONTENTS	VIII
LIST OF FIGURES	XIV
LIST OF TABLES	XV
LIST OF TABLES	XVI
ABSTRACT	XVII
CHAPTER ONE: INTRODUCTION	1
1.1. Background to the Study	1
1.2. Statement of the Problem	3
1.3. Research Questions	3
1.4. Rationale/Justification	4
1.5. Aim	5
1.6. Specific Objectives	5

CHAPTER TWO: LITERATURE REVIEW	6
2.1. PATHOGENESIS AND BASIS FOR THE SPREAD OF FIBROID CELLS	8
2.1.1. Cellular Basis for Fibroid Progression	8
2.1.2. Genetics Role in Fibroid Development	9
2.1.2.1. Cytogenetic irregularities in fibroids	13
2.1.3. Ethnic/Tribal Disparities in Fibroid Tumour Biology	13
2.1.3.1. Catechol-O-methyltransferase expression	14
2.1.3.2. Vitamin D	14
2.1.4. Growth Factors (GFs)	15
2.1.4.1. Growth factor receptors and signalling pathways in uterine leiomyoma	20
2.1.5. The Extracellular Matrix	20
2.1.6. Hormonal relationship with fibroids: Progesterone and oestrogen	21
2.1.6.1. Oestrogens	21
2.1.6.2. Progesterone	21
2.1.6.3. Progesterone receptors	22
2.2. SYMPTOMS OF FIBROIDS	22
2.2.1. Infertility and Uterine Leiomyomas	22
2.2.2. Uterine Fibroid Associated with Dysmenorrhea and Substantial Menstrual Bleeding	23
2.3. DIAGNOSIS OF FIBROIDS	23
2.3.1. Ultrasonography	24
2.3.2. Saline Infusion Sonohysterography	24
2.3.3. Magnetic Resonance Imaging (MRI)	

2.4. AVAILABLE TREATMENT OPTIONS FOR UTERINE FIBROIDS	25
2.5. INDEGINEOUS DIETARY PHYTOCHEMICALS THAT HAVE PROVEN TO BE EFFECTIVE IN TREATING/MANAGING UTERINE FIBROIDS	26
2.5.1. Epigallocatechin Gallate	27
2.5.2. Curcumin	28
2.5.3. Isoliquiritigenin	29
2.5.4. Genistein	30
2.5.5. Resveratrol	31
2.5.6. Fisetin	32
2.6. BIOINFORMATICS AND DRUG DEVELOPMENT	32
2.6.1. <i>In-silico</i> (Computer Aided) Drug Discovery and Development	32
2.6.2. Types of <i>In-silico</i> (Computer Aided) Drug Discovery and Development	33
2.6.3. The Systematic Process of Computer-Aided Tumour Drug Design	35
2.7. DNA SEQUENCING	43
2.7.1. Sanger's sequencing	44
2.7.1.1. Challenges using Sequencing Technique	44
CHAPTER THREE: MATERIALS AND METHOD	45
3.1. Chemicals and Reagents	45
3.2. Study Design	45
3.3. Study Sites	45
3.4. Study Population	46

3.5. Sampling Technique	46
3.6. Data Collection	46
3.7. Sample Collection	46
3.7.1. Sample size	46
3.7.2. Myometrial and uterine myoma tissue collection and preparation	47
3.8. Laboratory Procedures	47
3.8.1. Nucleic acid extraction	47
3.8.2. MED-12 Mutation Detection (Amplification and Sequencing)	48
3.9. <i>In Silico</i> Procedures	49
3.9.1. Molecular docking analysis	49
3.10. Statistical data analysis	49
CHAPTER FOUR: RESULTS	50
4.1. Patient Information	50
4.2. MED-12 Mutation Analysis	51
4.3. Computational Analysis on Mutated Sequences	52
4.4. Protein Modelling Using Pepfold-3 To Determine Effect on Protein Phenotype	53
4.5. Molecular Docking Analysis	55
CHAPTER FIVE: DISCUSSION	60
CHAPTER SIX: CONCLUSION AND RECOMMENDATION	60
6.0. Conclusions	60
6.1. Contribution to Knowledge	60
6.2. Recommendations	60

LIST OF FIGURES

Figure 1: Schematic universal map showing the typical UL-MED-12 mutational occurrence reported (in %) for investigated countries	4
Figure 2: Schematic, showing the fibroid origin stem-cell dysregulation hypothesis and continued proliferation of uterine fibroids.	7
Figure 3: Diagram showing the Mammalian Mediator Complex	10
Figure 4: The mediator complex and its function in regulating transcription	11
Figure 5: Diagram showing factors engaged with leiomyoma development and advancement.	13
Figure 6: Ethnic/Racial Differences in Fibroid Biology	13
Figure 7: Signalling Pathways in Uterine Leiomyoma	15
Figure 8: Interplay of events between oestrogen and progesterone with growth factors, in addition to signalling pathways in leiomyoma growth	22
Figure 9: Molecular and cellular pathways underlying fibrosis in fibroid development that are targeted by dietary phytochemicals	27
Figure 10: Structure of EGCG	28
Figure 11: Curcumin's Structure	29
Figure 12: Structure of Isoliquiritigenin	29
Figure 13: Structure of Genistein	30
Figure 14: Structure of Resveratrol	30
Figure 15: Diagram of Fisetin showing its antitumor pharmacological effects	31
Figure 16: CADD's role in the drug discovery and development process.	33
Figure 17: The lead discovery process	46

Figure 18: Lead discovery and the computational process	36
Figure 19: Workflow from Bioinformatics tools to drug development	38
Figure 20: Structure based virtual screening in drug development	40
Figure 21: A typical DNA sequencing result	40
Figure 22: Summary of the Sanger's (chain-termination) method for DNA sequencing	43
Figure 23: View of the bad starting peaks of a dye-terminator read sequence	44
Figure 24: PCR amplification of DNA extracted from tissue specimens of fibroid patients.	44
Figure 25: Protein sequence alignment results obtained from mutated DNA sequences	51
Figure 26: Disordered exon-2 proteins due to sequence mutations	51
Figure 27: Docking pose of Amentoflavone, and its interacting amino acids	53
Figure 28: Gingetin as the phytochemical with the second highest binding affinity of 10.0	54
Figure 29: Sciadopitysin as the phytochemical with the third highest binding affinity of 9.8	55

LIST OF TABLES

Table 1: Summary of clinical and pathological information of cases analysed	50
Table 2: Pathogenicity prediction of MED-12 exon 2 mutations by various <i>in silico</i> algorithms	52
Table 3: Top 5 highest binding phytochemicals with their binding affinities	54

ABSTRACT

Uterine fibroids (leiomyomas) are typical benign smooth muscle pelvic tumours in women of reproductive years. Its occurrence depends on race, age at menarche and has been found to arise in about 17.9%-26% of Nigerian women. MED-12, a transcriptional regulator, is known to harbour genetic mutations causal to the pathogenesis of leiomyomas in roughly 70% of women worldwide. However, the precise relationship between genetic mutations and protein/disease phenotype is not well-explained. The mutation frequency in Nigerian women is also unknown. The aim of this study was to characterize MED-12 mutations in leiomyomas of Nigerian women and apply the molecular docking methodology in understanding the binding of target-directed phytochemicals to this gene. The study was a multi-centre cross-sectional study conducted in Ogun and Abuja, Nigeria. DNA was extracted from the fibroid tissue collected, and MED-12 gene amplified followed by sequencing to identify the corresponding mutations. For Bioinformatics analysis phytochemicals were docked unto the active site of the MED-12 gene to quantify their binding affinities, thus identifying lead compounds from indigenous sources for the possible treatment and management of fibroid tumours. Among the included patients, 24% (6/24) of their leiomyomas had MED-12 missense, nonsense, frameshift, insertion and deletion mutations in a least one of their sequences. Amentoflavone, a biflavonoid, had the highest binding affinity of 10.2 to the MED-12 gene. This study is the first to characterise MED-12 mutations from Nigeria and agrees with previous findings that somatic MED-12 mutations are critical to the development and progression of uterine leiomyomas irrespective of ethnic background. Therefore, we recommend that mutation screening can assist in molecular diagnostics of uterine leiomyomas. Furthermore, *in vivo* studies and clinical trials should be promoted to aid the development of these high binding phytochemicals as treatment options.