## GENAPP: A WEB APPLICATION FOR PREDICTING PLASMODIUM FALCIPARUM RESISTANCE TO SELECTED ANTIMALARIA DRUGS

AKINWALE, MERCY OJOCHENWUMI (22PBF02392) B.Sc Physiology, University of Ibadan, Ibadan

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BY

## AKINWALE, MERCY OJOCHENWUMI (22PBF02392) B.Sc Physiology, University of Ibadan, Ibadan

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) DEGREE IN BIOINFORMATICS IN THE DEPARTMENT OF COMPUTER AND INFORMATION SCIENCES, 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 fulfilment of the requirements for the award of the degree of Master of Sciences in Bioinformatics in the Department of Computer and Information Sciences, College of Science and Technology, Covenant University, Ota, Nigeria.

Miss Adefunke F. Oyinloye (Secretary, School of Postgraduate Studies)

**Signature and Date** 

Prof. Akan B. Williams (Dean, School of Postgraduate Studies)

Signature and Date

#### DECLARATION

I, AKINWALE MERCY OJOCHENWUMI (22PBF02392), declare conducted this research entitled "GENAPP: A WEB APPLICATION FOR PREDICTING *PLASMODIUM FACLIPARUM* RESISTANCE TO SELECTED ANTIMALARIA

**DRUGS".** It was carried out under the supervision of Prof. Jelili O. Oyelade. Concepts of this research project are the results of the research carried out by Akinwale Mercy Ojochenwumi, and other researchers' ideas have been fully recognized.

#### AKINWALE, MERCY OJOCHENWUMI

**Signature and Date** 

## **DEDICATION**

I dedicate this project to God Almighty for His grace, wisdom and knowledge given to me throughout my Master's Degree Programme. Also, I thank my family and friends for their unending love and support.

#### CERTIFICATION

This is to certify that this dissertation titled "A WEB APPLICATION FOR PREDICTING PLASMODIUM FACLIPARUM RESISTANCE TO SELECTED ANTIMALARIA DRUGS" is original research carried out by AKINWALE, MERCY OJOCHENWUMI (2PBF02392) in the Department of Computer and Information Sciences, College of Science and Technology, Covenant University, Ota, Ogun State, Nigeria under the supervision of Prof. Jelili O. Oyelade. We have examined and found this work acceptable as part of the requirements for the award of Master of Science (M.Sc.) in Computer Science.

Prof. Jelili O. Oyelade (Supervisor)

Signature and Date

Prof. Olufunke Oladipupo (Head of Department)

Prof. Zacchaeus O. Omogbadegun (External Examiner)

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

Signature and Date

**Signature and Date** 

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# **ABBREVIATIONS**

#### ABBREVIATION

### MEANING

ACT	Artemisinin-based Combination Therapy
AMR	Antimalaria Resistance
CNV	Copy-Number Variation
CQ	Chloroquine
DHA	Dihydroartemisinin
LUM	Lumefantrine
PIQ	Piperaquine
HLF	Halofantrine
IC50	50% Inhibitory Concentration
GWAS	Genome- Wide Association Study
ENA	European Nucleotides Archive
DNA	Deoxyribonucleic Acid
ML	Machine Learning
NCBI	National Center for Biotechnology
	Information
EMBL-EBI	European Molecular Biology
	Laboratory-
	European Bioinformatics Institute
PFCRT	Plasmodium falciparum Chloroquine
	Resistance
WHO	World Health Organization
PFK13	Plasmodium falciparum K13-propeller
	domain.

#### ABSTRACT

Antimalarial drug resistance poses a significant challenge to global malaria control efforts, particularly in regions burdened by Plasmodium falciparum, the deadliest malaria parasite. The development and spread of resistance to widely used antimalarial drugs, such as chloroquine, Lumefantrine, Halofantrine, Quinine, Piperaquine and Dihydroartemisinin, have greatly impacted treatment efficacy and disease outcomes. This resistance is driven by various genetic mutations in *P. falciparum*, which confer the ability to survive drug exposure. This study explores the prediction of antimalarial drug resistance using machine learning algorithms Random Forest, Gradient Boosting Machine (GBM), and Support Vector Machine (SVM). Focusing on six key antimalarial drugs Chloroquine, Dihydroartemisinin, Lumefantrine, Quinine, Halofantrine, and Piperaquine the research aims to identify genetic markers that contribute to resistance and develop predictive models to enhance treatment strategies. To avoid model overfitting, 5-fold cross-validation was conducted on the training set to choose the optimal hyperparameter values. Regardless of the resistance mechanism, whether acquired resistance or point mutations in the chromosome, the accuracy (mean crossvalidation score) of Random Forest had an average of 83% across all drugs. The model significantly classified the resistant isolates from the sensitive isolates of the parasite and could be used as potential tools in antimalarial resistance surveillance and clinical studies. A number of genes associated with antimalaria drug resistance were identified. Novel genes and loci were also discovered, of interest are genes on chromosomes 1, 4, 7, 8, 9, 10, 11, 17 and 19.

Keywords: Machine learning, Antimalarial drug resistance, Plasmodium falciparum, genomic studies, phenotype prediction, malaria eradication