METABOLIC NETWORK ANALYSIS OF MYCO-BACTERIUM TUBERCULOSIS (MTB)

BY

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AN MSc RESEARCH PROJECT REPORT SUBMITTED TO THE DEPARTMENT OF COMPUTER AND INFORMATION SCIENCE, SCHOOL OF POST GRADUATE STUDIES, COVENANT UNIVERSITY, OTA, OGUN STATE.

IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF MASTER OF SCIENCE (M.Sc.) DEGREE IN COMPUTER SCIENCE.

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CERTIFICATION

We, the undersigned certify that this project work was carried out by **ACHAS MOSES JOY** in partial fulfilment of the requirement for the award of Master of Science (Honours) Degree in Computer Science, Covenant University, Ota, Nigeria

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DECLARATION

It is hereby declared that this research was undertaken by ACHAS MOSES JOY which is based on the original study in the department of Computer and Information Science, College of Science and Technology, Covenant University, Ota. Under the supervision of Dr O.J. Oyelade. Ideas and views in this research work are products of the original research undertaken by ACHAS Moses Joy and the views of other researchers used in this research has been referenced and acknowledged.

Dr. O.J Oyelade

Supervisor

Signature…… Date: ……

DEDICATION

This work is dedicated to the Almighty God, the very purpose of my existence, the one who was, who is and is to come for the privilege to begin and finish this phase of my life.

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TB	Tuberculosis
FBA	Flux Balance Analysis
Ac1PIM1	acyl phosphatidylinositol mannoside
Ac1PIM2	acyl phosphatidylinositol mannoside di-mannose
Ac1PIM3	acyl phosphatidylinositol mannoside tri-mannose
Ac1PIM4	acyl phosphatidylinositol mannoside tetra-mannose
Ac2PIM2	di-acyl phosphatidylinositol mannoside di-mannose
PIM1	phosphatidylinositol mannoside
PIM2	phosphatidylinositol mannoside di-mannose
PIM3	phosphatidylinositol mannoside tri-mannose
PIM4	phosphatidylinositol mannoside tetra-mannose
PIM5	phosphatidylinositol mannoside penta-mannose
PIM6	phosphatidylinositol mannoside hexa-mannose
arabinanagalfragund	arabinan-arabinofuranose-galactofuranosyl(30)-rhamanosyl-N-acetylglucosamyl-undecaprenyl diphosphate
arach	Arachidic acid
clpn160190	cardiolipin (dihexadecanoyl, dimethylstearoyl)
peptido_TB1	peptidoglycan subunit
peptido_TB2	peptidoglycan subunit

fcmcbtt	iron(III) chelated carboxymycobactin T
hdca	Hexadecanoate
hdcea	Hexadecenoate
hexc	hexacosanoate
kmycolate	kmycolate(c) keto mycolate (2 cyclopropanated rings)
mbhn	methyl behenic acid
mcbts	mycobactin S
mfrrppdima	phenolic glycolipid
mmmycolate	methoxy mycolate (1 cyclopropanated ring)
mycolate	mycolate (2 cyclopropanated rings)
mocdca	10-methylstearic acid
mkmycolate	keto mycolate (1 cyclopropanated rings)
ocdca	octadecanoate
ocdcea	octadecenoate
pa160	1,2-dihexadecanoyl-sn-glycerol 3-phosphate
pa160190	1,2-sn-glycerol 3-phosphate
pa190190	1,2-sn-glycerol 3-phosphate
pdima	phthiocerol dimycocerosate A (Mtb)
pe160	phosphatidylethanolamine (dihexadecanoyl,)
pg160	Phosphatidylglycerol (dihexadecanoyl,)

pg160190	Phosphatidylglycerol (hexadecanoyl, methylstearoyl)
pg190	Phosphatidylglycerol (dimethylstearoyl,)
ppdima	phenol phthiocerol dimycocerosate (Mtb)
tmha1	tetramycolyl hexaarabinoside (tdm1 + tdm2 +tre)
tmha2	tetramycolyl hexaarabinoside (tdm1 + tdm3 + tre)
tmha3	tetramycolyl hexaarabinoside (tdm1 + tdm4 + tre)
tmha4	tetramycolyl hexaarabinoside (tdm2 + tdm3 + tre)
ttdca	tetradecanoate
phdca	phenol palmitic acid

ABSTRACT

Tuberculosis is a multisystem disorder that is characterized by the formation of hematomas, a type of swelling that is filled with blood that is caused due to breakage in the wall of a blood vessel. This hematomas occurs in different organ of the infected victim has claimed the life of most of its victims. This disease is caused by a bacterium known as *Mycobacterium Tuberculosis (MTB)* which can be represented as a metabolic system. Every biological system is made up a metabolites which include genes, proteins and enzymes that are inter-connected which define the function, features and characteristics of the biological system. These biological systems can be analysed using different computational techniques among which is flux balance analysis. Flux balance analysis is a constraint based approach to metabolic network analysis. It's based on the steady state assumption of $S.v = 0$. A more grounded understanding of this features, characteristics and nature of this bacterium will lead to better approaches to reduce the damage of the disease.

The flux balance analysis of *MTB* involves the conversion of the metabolic network into a matrix format known as a stoichiometric matrix. This matrix is formed by using the metabolites in the metabolic network as rows and the reactions as the columns. The stoichiometric matrix used in this research is an 828 by 1027 matrix. The analysis of the stoichiometric matrix resulted into a linear problem where the number of unknown is greater than the number of equations. This linear problem was solved using "extreme pathways" and "simplex method" algorithms which makes up a Flux Balance Analysis approach to metabolic network analysis. The extreme pathways algorithm help extract the independent paths in the network while the simplex method is used to optimize the metabolic network to extract metabolites peculiar to an objective function.

At applying the constraint of the steady state assumption, the result showed 1022 distinct pathways instead of the initial 1027 eliminating 5 other reactions. The output from the extreme pathways was used in the optimization process using biomass as the target flux to get metabolites peculiar to biomass production. After the optimization, the result shows 32 new metabolites that become activated when a value of 1 is used to represent the biomass components. The optimization result also shows two categories of metabolites: those that are part of the biomass that become inactive after optimization, those that remain active after the optimization test. The output of this research only focus on the analysis of the metabolic network using biomass as the optimization target.