# 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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## List of Acronyms

| | |
|---|---|
| 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.