Comparative genomics of cytochrome P450 monooxygenase redox systems in mycobacteria

By

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DECLARATION

I, **SEISO CAIPHUS RASELEMANE** (SOUTH AFRICAN ID NUMBER: [redacted]), hereby certify that the dissertation submitted by me for the degree MASTER OF HEALTH SCIENCES IN BIOMEDICAL TECHNOLOGY, is my own independent work; and complies with the Code of Academic Integrity, as well as other relevant policies, procedures, rules and regulations of the Central University of Technology (Free State). I hereby declare, that this research project has not been previously submitted before to any university or faculty for the attainment of any qualification. I further waive copyright of the dissertation in favour of the Central University of Technology (Free State).

SEISO CAIPHUS RASELEMANE **DATE**

Dedication

This thesis is dedicated to my

Grandfather

Tshepiso Isaac Raselemane

And

Grandmother Nthabiseng Evodia Raselemane

And late Grandmother Manotshi Ella Mareka

ACKNOWLEDGEMENTS

Foremost, I would like to extend my sincere and heartfelt gratitude to the following people and organizations, who have been my pillar of strength throughout the completion and success of my masters study.

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But by the grace of God I am what I am, and His grace to me was not in vain. No, I worked harder than all of them — yet not I but the grace of God that was with me.

CONTENTS

LIST OF ABBREVIATIONS AND ACRONYMS

%	Percentage
2Fe	Two-iron
2S	Two-sulfur
3Fe	Three-sulfur
4Fe	Four-sulfur
7Fe	Seven-sulfur
Adx	Adrenodoxin
ADR	Adrenodoxin reductase
b-type heme	Iron protoporphyrin IX
C	Carbon
C-C	Carbon-carbon bond
CoA	Co-enzyme A
CPR	Cytochrome P450 reductase
C-terminal	Carbon terminal end
CYP	Cytochrome P450
DNA	Deoxyribonucleic acid
ER	Reticulum Endoplasmic
et al.	*Et alia* (and others)
FAD	Flavin adenine dinucleotide
FDR	Ferredoxin reductase

Fdx	Ferredoxin
Fe^{II}	Ferrous iron
Fe^{III}	Ferric iron
Fe-S	Iron-sulphur
Fig	Figure
FAD	Flavodoxin-flavin mononucleotide
FMN	Flavin mononucleotide
GR	Glutathione reductase
H+	Hydrogen ion
HEM	Heme group
ID	Identity
Kd	Equilibrium dissociation constant
kDa	Kilodalton
KEGG	Kyto Encylopedia of genes and genomes
MAFFT	Multiple sequence alignment program
MAV	*Mycobacteria avium* complex
MCL	Mycobacteria causing leprosy
MTC	*Mycobacterial tuberculosis* complex
M. tuberculosis	*Mycobacterium tuberculosis*
mV	Millivolts
N-	Substitution of Nitrogen atom

NADP	Nicotinamide adenine dinucleotide phosphate
NAD (P) H	Reduced nicotinamide adenine dinucleotide phosphate
N-terminal	Amino terminal end
NO	Nitric Oxide
NTM	Nontuberculosis mycobacteria
N_2O	Nitrous Oxide
nm	Nanometre
O	Oxygen
OFOR	2-oxo-acid-ferredoxin oxidoreductase
ONFR	Oxygenase-coupled NADH:ferredoxin reductases
O-O	Oxygen - oxygen bond
P450	Cytochrome P450 monoxgyenase
P	Pigment
PDR	Phthalate dioxygenase reductase
PHyML	Maximum likelihood phylogenies
PFOR	Phthalate family oxygenase reductase
RH	Substrate
ROH	Product
S	Sulphur
Sp	Species
TB	Tuberculosis

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CHAPTER 1

ABSTRACT

Cytochrome P450 monooxygenases (CYPs/P450s) are heme-thiolate proteins found in species belong to different biological kingdoms. P450s found to play key role in organism's physiology due to their regio- and stereo-specific catalytic activity. All P450s need electrons to perform their enzymatic reactions. Except self-sufficient P450s, most P450s receive electron form different P450 redox proteins. It is logical that if one can inhibit P450 redox protein that eventually result not only in loss of all P450s functions but also led to the death of an organism.

Mycobacterium tuberculosis, the deadliest pathogen of human, was found to have 20 P450s in its genome. Studies revealed that *M. tuberculosis* P450s can serve as novel drug targets. This suggests P450 redox proteins are very important in keeping *M. tuberculosis* P450s physiological function. With the exception of few studies on *M. tuberculosis* P450 redox proteins nothing is known about the P450 redox content in species of *Mycobacterium*. Therefore, the aim of this study is to perform comparative genomics of P450 redox partners in 81 mycobacterial species genomes.

Genome data-mining of 81 mycobacterial species revealed presence of 1063 P450 redox proteins grouped into ferredoxins (662) and ferredoxin reductases (401). Phylogenetic anlaysis of ferredoxins revealed presence of two major clades of ferredoxins with characteristic Pfam/InterPro protein domains. The clade with domains Fer4 (PF00037), Fer4_7 (PF12838) and Fer4_9 (PF13187) was associated with the same InterPro entry (IPR17896) and it was classified under group 2 and the clade supported with 83% boostrap proportion with domains Fer4_13 (PF13370), Fer4_15 (PF13459) and Fer4_19 (PF06902) shared similar HMM-motifs which was classified under as group 1.

Comparative analysis of ferredoxins across mycobacterial species revealed interesting patterns. *Mycobacterial tuberculosis* complex species showed 1-6 ferredoxins in their genomes. Mycobacteria causing leprosy (MCL) included two species namely mycobacterium leprae TN and mycobacterium leprae Br4923 which both contained a single ferredoxin. The other group which is known to be Nontuberculosis mycobacteria (NTM) showcased a range of 7-18 for ferredoxins. *Mycobacterium avium* complex species showed a range from 4 -19 ferredoxins in their genomes. Saprophytes showed a high number of ferredoxins with the range of 8-26.

Phylogenetic analyses indicated presence of two major divergent clades of ferredoxin reductases (FdRs) in mycobacteria; the Bacterial-type, which belong to the Plant-type FdRs, and the Gluthatione Reductase (GR)-type. Within the GR-type FdRs, two different clades were identified: the adrenodoxin (Adr)-like clade and the oxygenase-copuled NADH-ferredoxin reductase (ONFR)-like clade. Mycobacterial tuberculosis complex species showed 0-8 FdRs in their genomes. MCL species contained two FdRs. NTM species contained 2-7 FdRs in their genome. Saprophytes showed a high number of FdRs with the range of 0-12. Mycobacterium avium complex species showed 3-7 FdRs in their genomes. *Mycobacterium chelonae-abscessus* complex ranged from 1-6 FdRs.

Results generated in this study on genome data-mining, annotation and phylogenetic analysis of P450 redox proteins will be submitted to high impact factor journal.

Apart from my Masters study, I supervised one B. Tech student project and also worked on a few other bioinformatics projects and earned co-authorship. Most of my research articles are published in high impact factor journals. The following is a list of my research articles:

1. SC Raselemane (co-author) (2016) Molecular evolutionary dynamics of cytochrome P450 monooxygenases across kingdoms: Special focus on mycobacterial P450s. Scientific Reports 6, Article number: 33099.

2. SC Raselemane (co-author) (2015). Diversity and evolution of cytochrome P450 monooxygenases in Oomycetes. Scientific Reports 5, Article number: 11572.

In addition to the above credits, I was featured on national TV and in newspapers for discovering a novel drug target. I also presented work at both national and international (Canada) conferences.

CHAPTER 2

INTRODUCTION AND LITERATURE REVIEW

2.1. Introduction to Cytochrome P450 monooxygenases

Cytochrome P450 monooxygenases (CYPs/P450s) represent one of the largest and oldest gene superfamilies (Degtyarenko and Archakov, 1993) present in species of all biological kingdoms. P450s are intracellular heme-proteins that activate molecular oxygen for the oxidative metabolism of a great variety of organic molecules. P450s are believed to have been discovered about 55 years ago. P450, a cellular chromophore, was named due to the fact that pigment (P) has 450-nm spectral peak when reduced and bound to carbon monoxide (see Figure 2.1) (Nebert and Russel, 2002). P450 proteins are arranged into families and subfamilies on the basis of percentage amino acid sequence identity (Nelson *et al*., 1993; Nelson, 1998 and 2006). All P450 are believed to share a common fold, have a molecular weight of 45–60 kDa and contain a single *b*-type heme (iron protoporphyrin IX). This prosthetic group is deeply resided inside the protein globule, whereby there is formation of the fifth ligand of the heme-iron, that is why the name heme-thiolate proteins or hemo-proteins is given to P450 enzymes (Omura and Sato, 1964).

P450 catalysis contributes to vital processes such as carbon source assimilation, biosynthesis of hormones, structural components of cells, and also carcinogenesis and degradation of xenobiotics in an organism (Werck-Reichhart and Feyereisen. 2000). The reactions catalysed can be extremely diverse as e.g. hydroxylations, N-, O- and S-dealkylations, sulphoxidations, epoxidations, deaminations, desulphurations, dehalogenations, peroxidations, and N-oxide reductions (Sono *et al*., 1996; Guengerich, 2001; Bernhardt *et al*., 2006). P450s are represented by the abbreviation CYP followed by a number denoting the family (proteins with more than 40% sequence identity), a letter

designating a subfamily (more than 55% identity) and a number representing the individual protein within the subfamily, for example, CYP106A2.

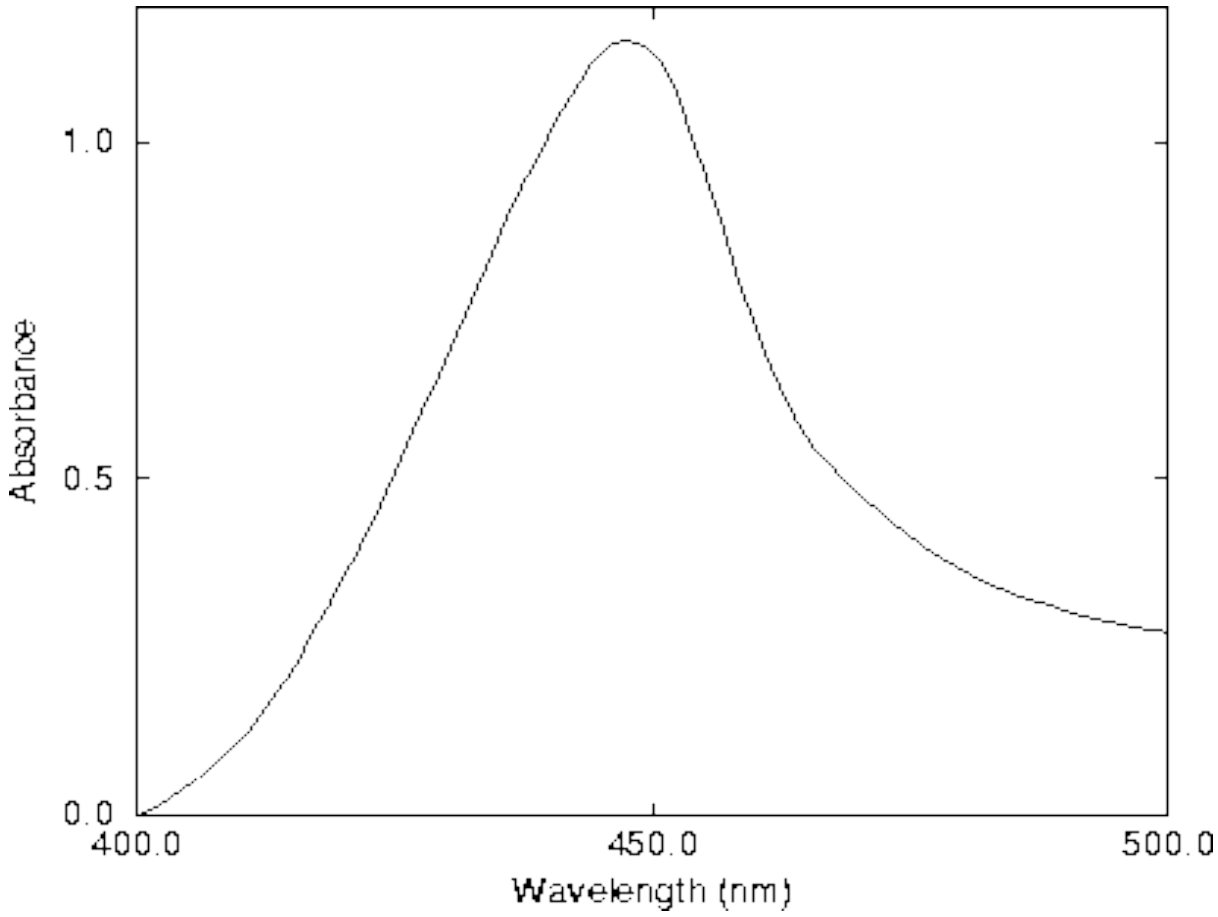

Figure 2.1. The absorption spectrum of cytochrome P450-CO complex showing the characteristic Soret peak at approximately 450 nm (Taken from Estabrook *et al*., 1963)

The P450s have a major impact on human physiology. Their capacity to perform regio- and stereo-selective oxygenations of numerous organic substrates has attracted interest in the biotechnology sector, since the P450s provide a cleaner and "greener" route to synthesis of several high value chemicals (Bell *et al*., 2003; Urlacher *et al*., 2004; Kubo *et al*., 2006;). The most extensively studied bacterial P450s are CYP101 and CYP102 from *Pseudomonas putida* and *Bacillus megaterium*, respectively. P450cam (CYP101) represents

the first P450 to have been structurally characterized using X-ray crystallography (Poulos *et al*., 1987) and its active site indicates that the substrate camphor is positioned relative to the heme moiety by a combination of hydrogen bonding and hydrophobic contacts with complementary amino acid residues, such that the 5-exo hydrogen of camphor is orientated for oxidative metabolism (Poulos *et al*., 1987).

2.1.1. P450 and chemistry of oxygen activation: the catalytic cycle

The monooxygenases are divided into two classes, the internal and the external monooxygenases (Ruckpaul *et al*., 1989). Internal monooxygenases extract two reducing equivalents from the substrate to reduce one atom of dioxygen to water, whereas external monooxygenases utilize an external reductant (Ruckpaul *et al*., 1989). P450s are external monooxygenases. The classical P450 reaction is the introduction of an atom of oxygen which is derived from molecular oxygen to facilitate hydroxylation at an un-activated carbon centre on a molecule.

Cytochrome P450 systems catalyse the following reaction:

$$RH + O2 + NAD(P)H + H^{+} \rightarrow ROH + H2O + NAD(P)^{+}$$

In this equation, RH can be one of a large number of possible substrates, and protons are delivered to the catalytic centre of the P450 through active-site amino acid side chains.

However, this process is achieved when oxygen is bound to ferrous heme at the centre of a *b*-type heme bound to the P450. The present model of P450 activity involves the further reductive activation and protonation of the oxyferrous species, ultimately leading to formation of a highly reactive ferryl-oxo intermediate and the production of a molecule of water.

The substrate binding to a P450 lowers redox potential by approximately 100mV (Ruckpaul *et al*., 1989), and that makes electron transfer favourable from its redox partners, which is NADH or NADPH. Subsequently, change in the spin state of the heme iron at the active site takes places. The next stage in the is called reduction of the Fe^{3+} ion by an electron transferred from NAD(P)H *via* an electron transfer chain (http://www.tcm.phy.cam.ac.uk/~mds21/thesis/node49.html). The next stage is oxygen binding where an O_2 molecule binds rapidly to the Fe^{2+} ion making Fe^{2+} - O_2. It is believed that there is evidence that support this complex regarding that it undergoes a slow conversion to a more stable complex Fe^{3+} - O_2^- (Archakov and Buchmanova, 1990).

Stoichiometry of the reaction requires second reduction and this has been found to the rate-determining step of the reaction (Yoshio *et al*., 1977). When the bond energies of O_2, O_2^- and O_2^{2-} are compared it clearly shows that the Fe^{3+} - O_2^{2-} complex is the most favourable starting point for the next stage of the reaction to occur (Levis, 1996). Raman spectroscopy also proved that the presence of a superoxide (O_2^-) is complex (Egawa *et al*., 1991). The O_2^{2-} reacts with two protons from the surrounding solvent, breaking the O-O bond, forming water and leaving an $(Fe - O)^{3+}$ complex. Production takes place where the Fe-ligated O atom is transferred to the substrate forming a hydroxylated form of the substrate. Then lastly release of a production, the product is released from the active site of the enzyme which returns to its initial state (see Figure 2.2). In the 'classical' P450 catalytic cycle, hydroxylation of the substrate is shown. However, P450s lend themselves to more diverse chemical transformations such as reductive dehalogenation, sulphoxidation, epoxidation, acyl bond cleavage and N-oxidation (Walsh *et al*., 2000; Hyland *et al*., 2003; Jin *et al*., 2003; Sharma *et al*., 2003; Lawson *et al*., 2004; De Voss *et al*., 2004)

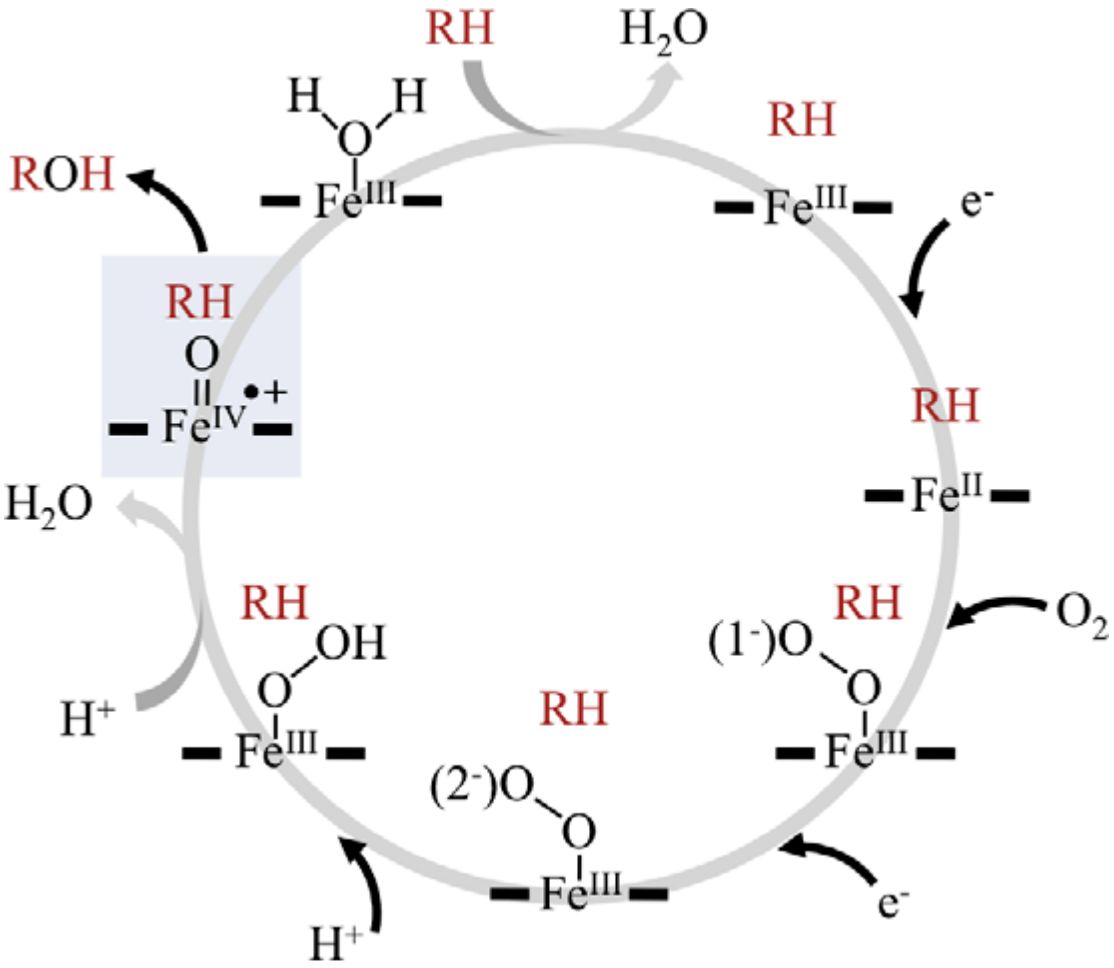

Figure 2.2. General P450 catalytic cycle depicting oxygen activation and subsequent hydroxylation of substrate (RH) into product (ROH) (taken from Ouellet *et al*., 2010).

2.2. Redox partners

Redox partner systems are required for P450 function. Mammalian liver P450 enzymes were classified under integral membrane proteins and to interact with a similarly membrane-anchored NADPH-dependent reductase containing both FAD and FMN cofactors (NADPH-cytochrome P450 monooxygenase reductase (CPR) (Smith *et al*., 1994). NADH-specific FAD-containing reductase, putidaredoxin reductase, and the 2Fe-2S cluster-containing ferredoxin, putidaredoxin were identified as P450cam redox partners. Small redox proteins such as bacterial flavodoxins and ferredoxins participates in several key metabolic pathways. Ferredoxins are obligate one-electron carriers, and typically bind iron–sulphur cofactors with 2Fe-2S, 3Fe-4S or 4Fe-4S clusters. Iron atoms are generally co-ordinated to sulphur atoms from cysteine residues in the protein. Flavodoxins bind an FMN cofactor non-covalently, are able to carry one or two electrons and are frequently isolated in their single-electron reduced semiquinone form (McLean *et al*., 2005).

Redox partners have different classes that perform different functions (Figure 2.3 and Table 2.1). Class I is a P450 system that contains most bacterial cytochrome P450 systems and mitochondrial P450 systems from eukaryotes (Hannemann *et al*., 2007). Bacterial cytochrome system and mitochondrial system are not phylogenetically related but both have separate proteins in common which are: FAD-containing reductase which is known to transfer reduction equivalent from a pyridine nucleotide (that is NADH or NADPH) to the ferredoxin, which is the second component of the system, which in turn reduces the cytochrome P450 itself (Hannemann *et al*., 2007). The three proteins are soluble in bacteria while in eukaryotes only the ferredoxin is soluble protein to mitochondrial matrix, whereas the other two components which are the reductase and cytochrome P450 are associated to membrane to the inner mitochondrial membrane (Gunsalus and Sligar, 1978; Lambeth, 1990; Bernhardt, 2006). The electrons that vital for the P450 catalysed reactions are normally

provided by NADH and transferred through a NADH- dependent FAD-containing reductase and a type of ferredoxin that has [3Fe-2S] (Bernhaldt, 2006).

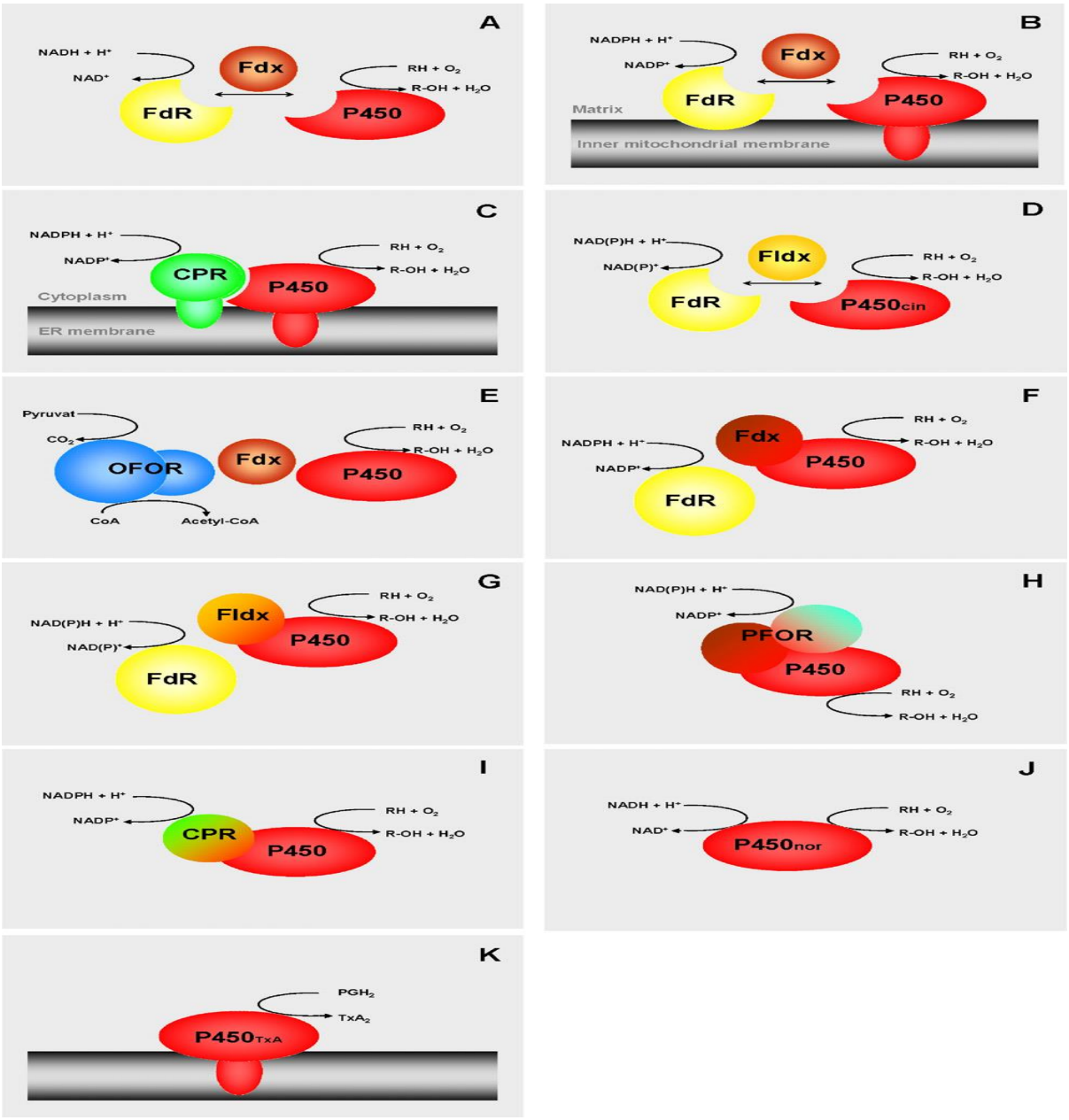

Figure 2.3. Schematic representations of different types of P450 redox systems (taken from Hannemann *et al*., 2007). (A) Class I, bacterial system., (B) Class I, mitochondrial system., (C) Class II microsomal system.,(D) Class III, bacterial system., example P450cin., (E) Class IV, bacterial thermophilic system., (F) Class V, bacterial [Fdx]–[P450] fusion system., (G) Class VI, bacterial [Fldx]–[P450] fusion system., (H) Class VII, bacterial [PFOR]–[P450]

fusion system., (I) Class VIII, bacterial [CPR]–[P450] fusion system., (J) Class IX, soluble eukaryotic P450nor., (K) Independent eukaryotic system, example P450TxA.

Table 2.1. Classes of P450 systems classified depending on the topology of the protein components involved in the electron transfer to the P450 enzyme (Taken from Hannemann *et al*., 2007).

Class/source	Electron transport chain	Localization/remarks
Class I Bacterial Mitochondrial	 NAD(P)H ▸ [FdR] ▸[Fdx] a ▸ [P450] NADPH ▸[FdR] ▸[Fdx] ▸[P450]	Cytosolic, soluble P450: inner mitochondrial membrane, FdR: membrane associated, Fdx: mitochondrial matrix, soluble
Class II Bacterial Microsomal A Microsomal B Microsomal C	 NADH ▸[CPR] ▸[P450] NADPH ▸[CPR] ▸[P450] NADH ▸[cytb5Red] ▸[cytb5] ▸[P450]DPH ▸[CPR] ▸[cytb5] ▸ [P450]	Cytosolic, soluble; *Streptomyces carbophilus* Membrane anchored, ER Membrane anchored, ER Membrane anchored, ER

Class III Bacterial	NAD(P)H ▸ [FdR] ▸ [Fldx] ▸ [P450]	Cytosolic, soluble, *Citrobacter braakii*
Class IV Bacterial	Pyruvat, CoA ▸ [OFOR] ▸ [Fdx] ▸ [P450]	Cytosolic, soluble, *Sulfolobus tokadaii*
Class V Bacterial	NADH ▸ [FdR] ▸ [Fdx–P450]	Cytosolic, soluble, *Methylococcus capsulatus*
Class VI Bacterial	NAD(P)H ▸ [FdR] ▸ [Fldx–P450]	Cytosolic, soluble, *Rhodococcus rhodochrous* strain 11Y
Class VII Bacterial	NADH ▸ [PFOR–P450]	Cytosolic, soluble, *Rhodococcus* sp strain NCIMB 9784, *Burkholderia* sp.,

		Ralstonia metallidurans
Class VIII Bacteria, fungi	NADPH ▸ [CPR–P450]	Cytosolic, soluble, *Bacillus megaterium*, *Fusarium oxysporum*
Class IX Only NADH dependent, fungi	NADH ▸ [P450]	Cytosolic, soluble, *F. oxysporum*
Class X Independent in plants/mammals	[P450]	Membrane bound, ER

Abbreviated protein components contain the following redox centers:

Fdx, Ferredoxin (iron–sulphur-cluster)

aFdx, Ferredoxin containing iron–sulphur-cluster of [2Fe–2S], [3Fe–4S], [4Fe–4S], [3Fe–4S]/ [4Fe–4S] type.

FdR, Ferredoxin reductase (FAD)

CPR, Cytochrome P450 reductase (FAD, FMN)

Fldx, Flavodoxin (FMN)

OFOR, 2-Oxoacid ferredoxin oxidoreductase (thiamin pyrophosphate, [4Fe–4S] cluster)

PFOR, Phthatate-family oxygenase reductase (FMN, [2Fe–2S] cluster).

Eukaryote has the most common P450s which is Class II and this class perform extremely diverse catalytic reactions (Hasler *et al*., 1999). Class II system are responsible for the oxidative metabolism of endogenous compounds, including fatty acids, steroids, prostaglandins, as well as exogenous compounds ranging from therapeutic drugs and environmental toxicants to carcinogens (Hasler *et al*., 1999). The class II system is normally situated in the endoplasmic reticulum of the eukaryotes which contains two integral membrane proteins namely: the P450 and the CPR which are compact with prosthetic groups FAD and FMN that transfers electrons that are provided from NADPH to one of the many P450 isozymes (Hasler *et al*., 1999).

The reductase has grown as a synthesis of two proteins where FMN-binding domain of CPR is homologous with bacterial flavodoxins, whereas the FAD-binding domain shows a high degree of similarity to two FAD-containing ferredoxin $NADP^+$ reductase and NADH-cytochrome b_5 reductase (Porter *et al*., 1986). Pair of electrons from NADPH is transferred to CPR through FAD and these electrons are transferred one at a time to P450 through FMN. P450, in turn, use these reducing equivalents for the hydroxylation of a variety of substrates (Wang *et al*., 1997). Cytochrome b_5 is a 17 kDa heme protein that is connected with the microsomal and mitochondrial portions of eukaryotic cells (Lederer *et al*., 1983) alongside with its electron donor protein NADH-cytochrome b_5 reductase.

Class III has the main composition of a three-component P450 system characteristic for bacterial (and mitochondrial) systems: electrons are transferred from the primary electron donor – i.e. NAD(P)H – via a NAD(P)H-dependent FAD-containing ferredoxin reductase and a second auxiliary redox protein to the cytochrome P450. The second mediator protein is an iron–sulfur protein in case of the class I systems, whereas with the novel CYP176A1 (P450cin) from *Citrobacter braakii* the natural immediate electron donor of the P450 is suggested to be a flavodoxin (Hannemann *et al*., 2007). The class VI cytochrome P450

system consist of a putative NAD(P)H-dependent flavoprotein reductase and a flavodoxin-P450-fusion protein and thus situated between P450BM3 and P450cin systems which also uses same redox centres namely, FAD, FMN and heme which happen to differ in numbers and trait of different proteins (Hannemann *et al*., 2007).

Class V P450 systems consists of two separate protein constituents which is putative NAD (P)H-dependent reductase which is unfamiliar and a P450-ferredoxin-fusion protein. The perfect example of the Class V is believed to be sterol 14α- demethylase CYP51 from *Methylococcus capsulatus* which is the only P450 existent in *M*. *capsulatus* and the primary structural organisation is different and unique (Jackson *et al*., 2002). The bacterial fusion system of class VII comprises a completely original class of P450 systems. Structurally class VII is organized in such a way that a P450 is C-terminally fused to a reductase domain, which is usually not connected with P450 systems, the domain reductase is thought to be phthalate dioxygenase reductase domain. CYP116B2 (P450RhF) from *Rhodococcus* sp. strain NCIMB 9784 is the first class VII cytochrome P450 to be reported (Hannemann *et al*., 2007).

P450s which are fused to CPR in a single polypeptide chain are found in Class VIII and therefore are catalytically self-sufficient as monooxygenases. P450 of this type have been discovered in various prokaryotes and lower eukaryotes (Warman *et al*., 2005). The cytosolic fatty acid hydroxylase flavocytochrome CYP102A1 of the soil bacterium *B*. *megaterium* is the most studied member of this class, however, P450BM3 functions as a model of the mammalian hepatic P450 enzymes because of it structure which uses different membrane-embedded and reductase enzymes to operate a similar electron transfer system (Warman *et al*., 2005). CYP102A1 has a molecular weight of 119 kDa (Narhi *et al*., 1986) and is a fully soluble single polypeptide (Ruettinger *et al*., 1989; Munro *et al*., 2002). CYP102A1 is composed of a heme-containing P450 oxygenase domain, associated *via* a short protein linker to a diflavin reductase domain containing 1 equivalent each of the cofactors FAD and FMN

(Narhi *et al*., 1986) which is related to mammalian CPR by sequence, structure, and function (Narhi *et al*., 1987).

Class IX is the only system that uses the nitric oxide reductase as a special case of a P450. Denitrification reaction took a place when CYP55 play a significant physiological role and that results in the protection of the fungus from nitric oxide (NO) inhibition of mitochondria, especially when dioxygen becomes limiting (Daiber *et al*., 2005). NO reductase activity employed NADH to form nitrous oxide (N_2O) but not NADPH as the sole effective electron donor, this was showcased in P450 (Nakahara *et al*., 1993). It is a common thing that most P450s function as monooxygenases and require a consecutive delivery of two electrons through different types of redox proteins, while independent intramolecular transfer system is used by some P450s to catalyse substrate conversion. In this case it is class X that uses independent system and this class of P450 systems also distances the independent P450 allene oxide synthase, fatty acid hydroperoxide lyase, divinyl ether synthase, prostacyclin synthase, and thromboxane synthase (Hannemann *et al*., 2007). The catalytic features of the first three members of class X are shared by prostacyclin synthase and thromboxane synthase, two other P450s that catalyze the rearrangement of C20 acyl peroxides in the arachidonic acid cascade of mammals (Hannemann *et al*., 2007).

In a study Munro and co-workers (2007) presented a little different classification. Figure 2.4 represents various types of different redox partner systems proposed by these authors.

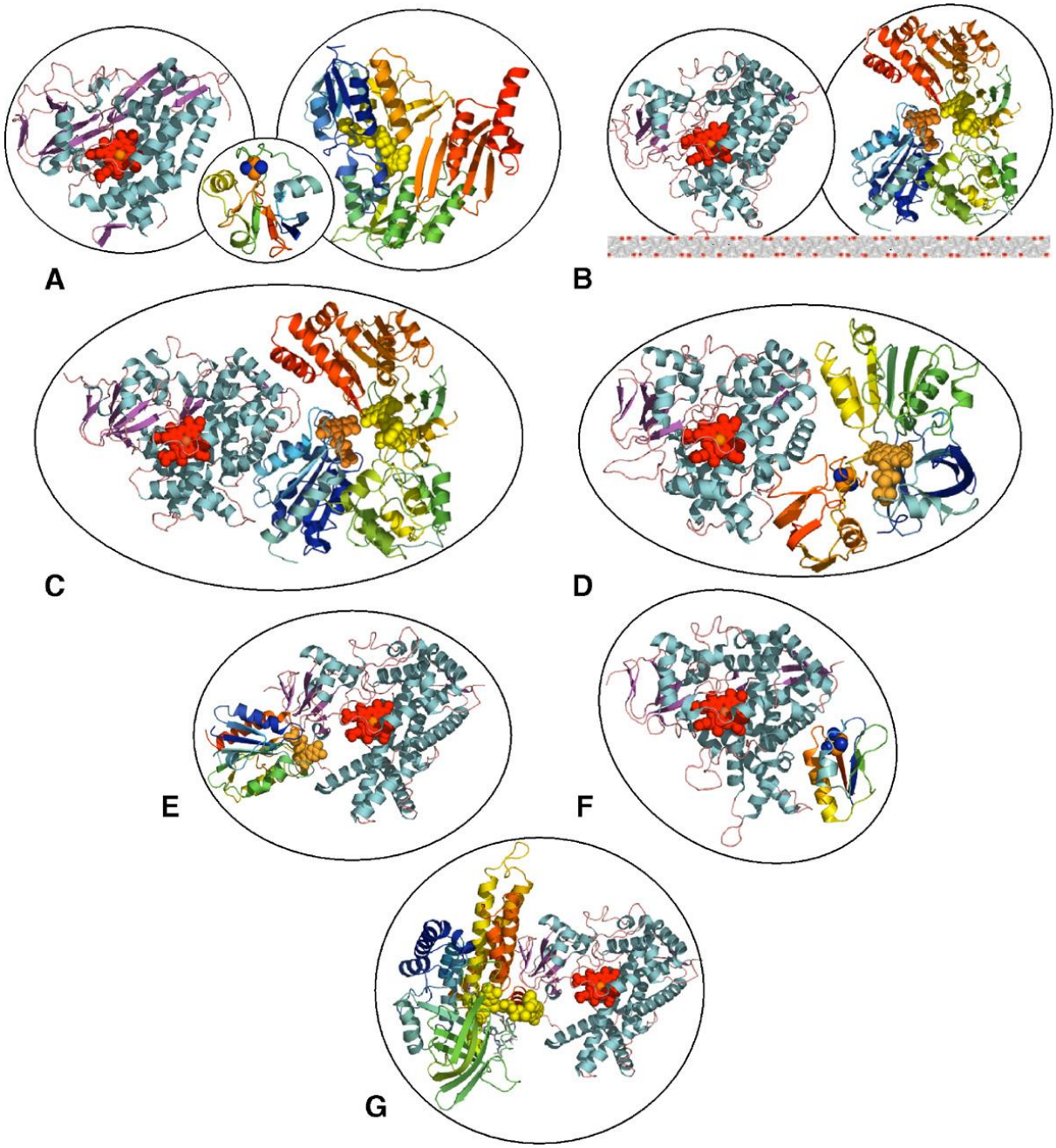

Fig 2.4. Biodiversity of P450 redox partner systems (taken from Munro *et al*., 2007). Biodiversity of P450 redox partner systems. Several distinctive types of cytochrome P450 redox partner systems have been discovered in recent years, and the original classification of P450 systems into class I and II is now seen to be outdated. The figures show atomic

structures for either the true components of the various types of different redox partner systems, or else for structurally resolved homologues. Discrete polypeptides are enclosed in circles. Panel A shows a classical class I system, comprised of P450cam (PDB code 2CPP), the 2Fe–2S ferredoxin putidaredoxin (1PDX) and the FAD-binding putidaredoxin reductase (1QIR). Panel B shows a membranous class II system comprising rabbit CYP2C5 (1DT6) and rat cytochrome P450 reductase (CPR, 1AMO). Panel C illustrates the P450 BM3-type P450–CPR fusion with the BM3 heme domain (1FAG) shown with rat CPR. Panel D shows the P450–PFOR type system illustrated as a P450 (P450 eryF, PDB code 1OXA) linked to phthalate dioxygenase reductase from *Pseudomonas cepacia* (2PIA). Panel E illustrates the XplA P450–flavodoxin type fusion shown as human CYP2D6 (2F9Q) linked to *E. coli* flavodoxin (1AG9). Panel F shows the McCYP51FX P450–ferredoxin type fusion system illustrated as the *Mycobacterium tuberculosis* CYP51 (1EAI) with a 3Fe–4S ferredoxin from *Pyrococcus furiosus* (1SJI). Panel G shows a putative P450-acyl CoA dehydrogenase (ACAD) fusion enzyme from Pseudomonas fluorescens, illustrated as P450 epoK from *Sorangium cellulosum* (1Q5E) linked to a FAD-binding medium chain acyl CoA dehydrogenase from pig liver (3MDE). Cofactors are illustrated in spacefill. Hemes are in red, flavins (FAD and FMN) are in yellow or orange, respectively. Iron–sulfur clusters are in orange/blue.

2.3. *Mycobacterium Tuberculosis*

Tuberculosis (TB), once referred to as the ‘‘white death’’ is a debilitating human disease caused by the bacterial pathogen *M. tuberculosis*. *M. tuberculosis* was discovered by Robert Koch in a world known lecture on March 24, 1882 (Koch, 1882). It is now estimated that one third of the world’s population is infected with *M. tuberculosis* and that an infected individual has approximately 10% chance of developing TB in their lifetime (Kizza *et al.*, 2015). *M. tuberculosis* has the potential to synthesise all the essential amino acids, vitamins, and

enzyme co-factors, involving some unusual metabolic pathways that differ from those in other bacteria. The tubercle bacillus can metabolise a variety of carbohydrates, hydrocarbons, alcohols, ketones and carboxylic acids. It can also assimilate not only a range of carbohydrates but also a number of other compounds such as lipids and proteins. *M. tuberculosis* is a gram-positive bacterium with a guanine and cytosine rich genome (average 65.6% G + C). The proteome of *M. tuberculosis* consists of approximately 4,000 polypeptides, many of which are potential new drug targets.

Due to the global epidemic of TB and to identify drug targets the genome of *M. tuberculosis* has been sequenced (Cole *et al.*, 1998). The genome sequence of *M. tuberculosis* revealed that the pathogen encoded surprisingly hefty number of P450s (20 in all) in comparison with other genomes of similar size (McLean *et al.*, 2005). At the time, this was an unprecedented number of P450s in a prokaryotic genome. The large number of these oxidase enzymes was consistent with the obligate aerobe nature of *M. tuberculosis*, and also understandable both in light of the known specificity of many other eukaryotic and prokaryotic P450s for lipid substrates, and in view of the complex lipid biochemistry in *M. tuberculosis* (Daffé and Etienne, 1999; Munro *et al.*, 2002; Hsu *et al.*, 2007). The genome of *M. tuberculosis* encodes several ferredoxin and ferredoxin- NAD (P) H reductase-like proteins, a combination of which, in principle, should support the catalytic activity of each of the (Table 2.2) 20 putative P450 enzymes.

Table 2.2. Key facts about *M. tuberculosis* P450 enzymes (taken from Ouellet *et al.*, 2010).

CYP/gene	**Microarray/Proteomics and other key facts**
CYP121A1	Induced in isoniazid- and thiolactomycin treated cells. Partially or completely deleted in many clinical H37Rv isolates. Inactivation by transposon-insertion

CYP/gene	Microarray/Proteomics and other key facts
(*Rv2276*)	mutagenesis confers resistance to beta-lactams. Possible role in virulence.
CY123A1 (*Rv0766c*)	Up-regulated by high temperatures and mRNA levels are higher in the phoP mutant. Part of a putative operon with CYP51 and a ferredoxin. Protein detected in the membrane fraction. Potential candidates for drug targeting.
CYP124A1 (*Rv2266*)	Gene located near *cyp128* and a sulfotransferase *sft3*. Expression repressed in infected mouse lungs.
CYP125A1 (*Rv3545c*)	Induced in macrophage. Essential for infection in mice. Predicted to be in the *kstR* regulon. Part of an operon with *fadE28, fadE29, Rv3542c, Rv3541c* and *ltp2*. Up-regulated during infection of dendritic cells. Potential candidates for drug targeting.
CYP126A1 (*Rv0778*)	Part of a putative operon with *purB*, a probable adenylosuccinate lyase PurB. Located near essential genes encoding enzymes involved in the *de novo* biosynthesis of purine.
CYP128A1 (*Rv2268c*)	Up-regulated after starvation. Part of a putative operon with *sft3*, a sulfotransferase involved in biosynthesis of a sulfolipid S881.
CYP130A1 (*Rv1256c*)	Absent from *M. bovis* and *M. bovis* BCG strains (deletion RD10).
CYP132A1 (*Rv1394c*)	Possible role in virulence. Transcription controlled by adjacent AraC transcription factor. Induced after 30 min of post-diamide stress. Up-regulated during infection of dendritic cells.
CYP135A1	Conserved only in *M. tuberculosis* complex strains and distantly related

CYP/gene	Microarray/Proteomics and other key facts
(*Rv0327c*)	*Nocardioides sp*. Induced after 30 min of post-diamide stress.
CYP135B1 (*Rv0568*)	Protein detected in the cytosol fraction
CYP136A1 (*Rv3059*)	Distantly related to CYP51. Possibly involved in lipid degradation. Located near a gene (*fadE22*) encoding for an acyl-CoA dehydrogenase.
CYP137A1 (*Rv3685c*)	Protein detected in the membrane fraction
CYP138A1 (*Rv0136*)	Up-regulated by high temperatures. Up-regulated after 2h incubation in the presence of lung surfactant .Up-regulated under iron-limitation conditions.
CYP139A1 (*Rv1666c*)	Adjacent to *pks17*, *pks9* and *pks11* and a putative macrolide transporter.
CYP140A1 (*Rv1880c*)	Closest relative to the only P450 enzyme in *M. leprae*.
CYP141A1 (*Rv3121*)	Absent from *M. bovis* and *M. bovis* BCG strains (RD5). Up-regulated after 2h incubation in the presence of lung surfactant.
CYP142A1 (*Rv3518c*)	Predicted to be in the *kstR* regulon. Pseudogene in *M. bovis* and *M. bovis* BCG due to a 2-bp deletion causing a frame-shift. Protein detected in the cell wall fraction.

CYP/gene	Microarray/Proteomics and other key facts
CYP143A1 (*Rv1785c*)	Adjacent to a probable ferredoxin (*Rv1786*).
CYP144A1 (*Rv1777*)	Up-regulated during infection of dendritic cells. Potential candidate for drug targeting.
CYP51B1 (*Rv0764c*)	Shows sterol 14α-demethylase activity. Possible role in host sterol/steroid metabolism.

Recent studies from our laboratory showed that Mycobacteria possess the highest P450 diversity percentage compared to other microbes and have a high coverage of P450s (≥1%) in their genomes, as found in fungi and plants (Parvez *et al*., 2016). This indicates P450s are playing a role in *M. tuberculosis* physiology.

2.4. Rational, aims and objectives of the study

P450s are widespread in species belong to different kingdoms of life and their catalytic functions and the composition of their electron transfer chains are manifold. New genome sequencing projects will certainly lead to even more potential redox partners of P450s. Recent progress in the biochemical and structural characterization of *M. tuberculosis* P450 enzymes and their accessory redox partners provides key insights on their function(s), but much remains to be done. Use of P450 monooxygenases as novel drug target against *M. tuberculosis* is gaining momentum (Hudson *et al*., 2012; Parvez *et al*., 2016). P450s need redox partners to perform their reactions. If one can target redox partners it will result inhibition of all P450s and eventual inhibition of *M. tuberculosis* growth. Hence,

M. tuberculosis P450 redox proteins are excellent drug targets. However, to date, study on P450 redox protein analysis across Mycobacteria are not reported. In the current study, I aim to perform comparative genomics of redox partners in Mycobacteria (81 species) *via* by genome data-mining and phylogenetic analysis.

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CHAPTER 3

GENOME DATA-MINING OF P450 REDOX PARTNERS IN MYCOBACTERIA

3.1. Introduction

P450s, with the exception of self-sufficient P450s, interact with their corresponding redox protein partners to perform enzymatic reaction (Hannemann *et al*., 2007). Class I P450 systems has the most bacterial P450s along with the mitochondrial P450s from eukaryotes but they have no relation in terms of phylogenetic (Werck-Reichhart and Feyereisen, 2000). Both groups consist of composition of three separate proteins in common: a FAD-containing reductase, which its main function is to transfer reduction equivalents from a pyridine nucleotide nicotinamide adenine dinucleotide (i.e. NADH or NADPH) to the next component of the system which will be ferredoxin, which functions by reducing the cytochrome P450 itself (Werck-Reichhart and Feyereisen, 2000).

P450s are categorized into different classes and sub-classes based on their auxiliary external redox partner proteins (Hannemann *et al*., 2007; Munro *et al*., 2007). Electron transfer from a redox partner to the P450 is a crucial step in the P450 catalytic cycle. Bacterial and mitochondrial P450s receive electrons from a small soluble iron-sulfur protein, whereas the redox partner for mammalian microsomal enzymes is a FAD FMN-dependent NADPH-cytochrome P450 oxidoreductase (CPR).

In CPR, FAD serves as an electron acceptor from NADPH, whereas the FMN moiety interacts with and reduces the P450. The problem of redox partner recognition and mechanism of electron transfer has been one of the most important and intriguing in the area of P450 research, in particular, and in biological electron-transfer reactions, in general. The involvement of both electrostatic and hydrophobic forces in protein–protein interactions between P450s and their redox partners has been demonstrated (Hintz and Peterson 1981,

Bernhard *et al*., 1984; Nadler *et al*., 1988; Stayton *et al*., 1988; Voznesensky *et al*., 1992; Shen *et al*., 1993; Hannemann *et al*., 2007).

3.1.1. *Mycobacterium tuberculosis* P450 redox partners

M. *tuberculosis* genome holds numerous candidate redox systems to maintain P450 function (Table 3.1). There are several ferredoxins with obvious redox partner systems being those that are chromosomally adjacent to P450s, for instance two examples exist in *M*. *tuberculosis*; 3Fe–4S ferredoxin Fdx (adjacent to CYP51) which was shown to support the sterol demethylase activity of CYP51 and 3Fe–4S ferredoxin encoded by Rv1786 which is adjacent to CYP143 (Bellamine *et al*., 1999).

Table 3.1. *M*. *tuberculosis* cytochrome P450 redox partners (taken from Ouellet *et al*., 2010)

Protein (Rv #)	**gene**	**Comments**
FdX	(Rv0763c)	3Fe-4S ferredoxin; supports catalysis with CYP51; mediates electron transfer from FprA; part of putative operon containing cyp123 and cyp51 (Bellamine *et al*., 1999; Zanno *et al*., 2005).
Rv1786	(Rv1786)	Putative ferredoxin; located near CYP143 (Rv1785c) (McLean *et al*., 2007).
FdxA	(Rv2007c)	Putative ferredoxin, predicted 3Fe-4S or 4Fe-4S; cluster, induced by hypoxia and low pH in vitro; structure available of related (87% identical) *M*. *smegmatis* FdxA (Fukuyama *et al*., 1989; Sherman *et al*., 2001; Ricagno *et al*., 2007)
FdxB	(Rv3554)	Putative fusion of ferredoxin and ferredoxin reductase domains
FdxC	(Rv1177)	predicted to have both 3Fe-4S and 4Fe-4S clusters; required for optimal growth in vitro, structure available of related *M*. *smegmatis* FdxA (87% identical) (Sassetti *et al*., 2003; Ricagno *et al*., 2007)

FdxD	(Rv3503c)	Putative ferredoxin.
FprA	(Rv3106)	Ferredoxin reductase, reduces Rv0763c to support CYP51 activity, homology to mammalian ADR, structure available (McLean *et al*., 2003; Sabri *et al*., 2009)
FprB	(Rv0886)	Putative fusion of a ferredoxin and FprA-like domains
FdrA	(Rv0688)	Flavoprotein reductase reduces FdX to support CYP51 activity (Zanno *et al*., 2005).

FdxA (Rv2007c), a ferredoxin that might bind both 4Fe–4S and 3Fe–4S cofactors is another potential P450 redox partner. The structure of *M. smegmatis* FdxA proved that it belongs to the class of 7Fe-ferredoxins (Ricagno *et al*., 2007). FdxA transcription is induced by hypoxia and low pH *in vitro* (Fisher, *et al*., 2002; Sherman *et al*., 2001). Such acidic conditions might mimic the environment that is encountered by *M. tuberculosis* cells phagocytosed by host immune cells. FdX ferredoxins are iron-sulfur proteins that transfer electrons in a wide variety of metabolic reactions and most probably involved in electron transport for P450 system, it is also similar to putative ferredoxins FdxD and Rv1786 from *M. tuberculosis* and could belong to the bacterial type ferredoxin family and is differentially expressed during *M. tuberculosis* infection in mice (Etienne *et al*., 2002). Rv1177 is required for optimal growth *in vitro* and it encodes the ferredoxin FdxC, which has similar cofactor content to FdxA. Rv3503c encodes putative ferredoxin FdxD. RV3106 generates oxidized ferredoxin from ferredoxin (catalytic activity: reduced ferredoxin + $NADP^{(+)}$ = oxidized ferredoxin + NADPH), its essentiality is unknown, however, homologues are shown to be essential in other organisms (Li *et al*., 2001; Rückert *et al*., 2005). RV3106 adrenodoxin reductase homologue and supports P450 activity and it is also structurally resolved. The best characterized *M. tuberculosis* P450-related redox protein is FprA, an NADPH-ferredoxin

reductase, which is structurally and functionally related to the mammalian adrenodoxin reductase (ADR) family by approximately 40% sequence identity. Flavoprotein reductase FdrA (Rv0688) is another enzyme shown to drive *M. tuberculosis* CYP51 sterol demethylation (Zanno *et al*., 2005).

In eukaryotic mitochondrial P450 systems, a P450 system that is like prokaryotic class I redox system exists, which includes enzymes like the FAD-containing ADR and the 2Fe–2S adrenodoxin (Müller *et al*., 2001). FprA is an ADR homologue in *M. tuberculosis*, which is evident from both its amino acid sequence and from its atomic structure (Bossi *et al*., 2002). It is reduced by both NADPH and NADH, although NADPH binding is much tighter. NADPH reduces the FprA FAD cofactor to its semiquinone (single electron reduced) form, whereas NADH reduces it fully to hydroquinone. FprA is a soluble enzyme that transfers electrons to *M. tuberculosis* Fdx and thus is a viable *M. tuberculosis* P450 partner enzyme. FdxB is another putative ferredoxin reductase–ferredoxin fusion in which the ferredoxin is likely to bind to a 2Fe–2S cluster. Other potential FAD-containing ferredoxin reductase redox partners are encoded by Rv0688 and Rv1869c genes (see Table 3.1). In the case of Rv0688, some similarities with the primary structure of *Rhodococcus* phthalate dioxygenase reductase (PDR) strike resonance given the recent characterization of natural P450–PDR fusion proteins (with potential detoxification roles) in this genus and in other bacteria (McLean, *et al*., 2005).

3.1.2. Structural and functional analysis of *M. tuberculosis* P450 redox partners

A class I P450 electron transfer system comprising FprA, Fdx, and CYP121 P450s was reconstituted and their ability to transfer electrons to CYP121 is shown (McLean *et al*., 2008). The enzymatic properties of the *M. tuberculosis* CYP51-like protein have been characterized. Both a 3Fe-4S MT ferredoxin (Fdx) and *E. coli* flavodoxin (Fld) are found to

support the 14α-demethylase activity (Bellamine *et al*., 1999). The adrenodoxin reductase-like FprA has been structurally and catalytically characterized and shown to support CYP51 catalysis (Bossi *et al*., 2002; McLean *et al*., 2003).

3.1.3. *In vivo* expression analysis of *M. tuberculosis* P450 redox partners

The genome of *M. tuberculosis* encodes two 7Fe and three 3Fe ferredoxins (Fds), respectively. The two 7Fe Fds are thought to be crucial: in particular FdxC was shown to be essential for optimal growth of *M. tuberculosis* (Sassetti, 2003). Whereas FdxA was reported to be induced under conditions of hypoxia and low pH. Hypoxia (which is associated with *M. tuberculosis* persistence in the latent state) and acidity (which mimics the environment of phagocytosed cells) induce FdxA expression which is controlled by the transcriptional regulator DevR (or DosR) (Sherman *et al*., 2001). The DosR regulon contains several genes that respond to signals including oxygen levels and nitric oxide (Park *et al*., 2003). However, because acidity does not upregulate DosR, a different mechanism must operate to induce FdxA at low pH. Thus, FdxA seems to be a key protein in general *M. tuberculosis* stress responses. FdxA is also induced by heat shock and by treatment with thiolactomycin and isoniazid drugs that inhibit mycolic acid synthesis in *M. tuberculosis* and by other antibacterials (McLean *et al*., 2006).

3.2. Materials and Methods

3.2.1. Species and their genome database information

Mycobacterial species genomes that are publicly available at KEGG website were used for genome data mining of P450 redox partners. To date, 81 mycobacterial species genomes were public available. Table 3.2 shows the mycobacterial species selected in this study and their respective genome database at KEGG website.

Table 3.2. Mycobacterial species and their genome database links.

KEGG CODE	Species code	*Species Name*	Database link
T00015	mtu	*Mycobacterium tuberculosis* H37Rv	http://www.genome.jp/kegg-bin/show_organism?org=mtu
T02178	mtv	*Mycobacterium tuberculosis* H37Rv	http://www.genome.jp/kegg-bin/show_organism?org=mtv
T00053	mtc	*Mycobacterium tuberculosis* CDC1551	http://www.genome.jp/kegg-bin/show_organism?org=mtc
T00540	mra	*Mycobacterium tuberculosis* H37Ra	http://www.genome.jp/kegg-bin/show_organism?org=mra
T00545	mtf	*Mycobacterium tuberculosis* F11	http://www.genome.jp/kegg-bin/show_organism?org=mtf
T00940	mtb	*Mycobacterium tuberculosis* KZN 1435	http://www.genome.jp/kegg-bin/show_organism?org=mtb
T01690	mtk	*Mycobacterium tuberculosis* KZN 4207	http://www.genome.jp/kegg-bin/show_organism?org=mtk
T02141	mtz	*Mycobacterium tuberculosis* KZN 605	http://www.genome.jp/kegg-bin/show_organism?org=mtz
T01775	mtg	*Mycobacterium tuberculosis* RGTB327	http://www.genome.jp/kegg-bin/show_organism?org=mtg
T01994	mti	*Mycobacterium tuberculosis* RGTB423	http://www.genome.jp/kegg-bin/show_organism?org=mti
T01991	mte	*Mycobacterium tuberculosis* CCDC5079	http://www.genome.jp/kegg-bin/show_organism?org=mte
T02679	mtur	*Mycobacterium tuberculosis* CCDC5079	http://www.genome.jp/kegg-bin/show_organism?org=mtur

T01992	mtl	*Mycobacterium tuberculosis* CCDC5180	http://www.genome.jp/kegg-bin/show_organism?org=mtl
T01993	mto	*Mycobacterium tuberculosis* CTRI-2	http://www.genome.jp/kegg-bin/show_organism?org=mto
T02142	mtd	*Mycobacterium tuberculosis* UT205	http://www.genome.jp/kegg-bin/show_organism?org=mtd
T02526	mtn	*Mycobacterium tuberculosis* Erdman = ATCC 35801	http://www.genome.jp/kegg-bin/show_organism?org=mtn
T02616	mtj	*Mycobacterium tuberculosis* Beijing/NITR203	http://www.genome.jp/kegg-bin/show_organism?org=mtj
T02617	mtub	*Mycobacterium tuberculosis* 7199-99	http://www.genome.jp/kegg-bin/show_organism?org=mtub
T02652	mtuc	*Mycobacterium tuberculosis* CAS/NITR204	http://www.genome.jp/kegg-bin/show_organism?org=mtuc
T02653	mtue	*Mycobacterium tuberculosis* EAI5/NITR206	http://www.genome.jp/kegg-bin/show_organism?org=mtue
T02749	mtx	*Mycobacterium tuberculosis* EAI5	http://www.genome.jp/kegg-bin/show_organism?org=mtx
T02654	mtuh	*Mycobacterium tuberculosis* Haarlem/NITR202	http://www.genome.jp/kegg-bin/show_organism?org=mtuh
T02845	mtul	*Mycobacterium tuberculosis* Haarlem	http://www.genome.jp/kegg-bin/show_organism?org=mtul
T03152	mtut	*Mycobacterium tuberculosis* BT1	http://www.genome.jp/kegg-bin/show_organism?org=mtut

T03153	mtuu	*Mycobacterium tuberculosis* BT2	http://www.genome.jp/kegg-bin/show_organism?org=mtuu
T03154	mtq	*Mycobacterium tuberculosis* HKBS1	http://www.genome.jp/kegg-bin/show_organism?org=mtq
T00132	mbo	*Mycobacterium bovis* AF2122/97	http://www.genome.jp/kegg-bin/show_organism?org=mbo
T00463	mbb	*Mycobacterium bovis* BCG Pasteur 1173P2	http://www.genome.jp/kegg-bin/show_organism?org=mbb
T00864	mbt	*Mycobacterium bovis* BCG Tokyo 172	http://www.genome.jp/kegg-bin/show_organism?org=mbt
T01727	mbm	*Mycobacterium bovis* BCG Mexico	http://www.genome.jp/kegg-bin/show_organism?org=mbm
T02451	mbk	*Mycobacterium bovis* BCG Korea 1168P	http://www.genome.jp/kegg-bin/show_organism?org=mbk
T03363	mbz	*Mycobacterium bovis* ATCC BAA-935	http://www.genome.jp/kegg-bin/show_organism?org=mbz
T01575	maf	*Mycobacterium africanum*	http://www.genome.jp/kegg-bin/show_organism?org=maf
T01585	mce	*Mycobacterium canettii* CIPT 140010059	http://www.genome.jp/kegg-bin/show_organism?org=mce
T02419	mcq	*Mycobacterium canettii* CIPT 140060008	http://www.genome.jp/kegg-bin/show_organism?org=mcq
T02420	mcv	*Mycobacterium canettii* CIPT 140070008	http://www.genome.jp/kegg-bin/show_organism?org=mcv
T02421	mcx	*Mycobacterium canettii* CIPT 140070010	http://www.genome.jp/kegg-bin/show_organism?org=mcx
T02422	mcz	*Mycobacterium canettii* CIPT 140070017	http://www.genome.jp/kegg-bin/show_organism?org=mcz

T00047	mle	*Mycobacterium leprae* TN	http://www.genome.jp/kegg-bin/show_organism?org=mle
T00842	mlb	*Mycobacterium leprae* Br4923	http://www.genome.jp/kegg-bin/show_organism?org=mlb
T00156	mpa	*Mycobacterium avium* subsp. paratuberculosis K-10	http://www.genome.jp/kegg-bin/show_organism?org=mpa
T02662	mao	*Mycobacterium avium* subsp. paratuberculosis MAP4	http://www.genome.jp/kegg-bin/show_organism?org=mao
T00433	mav	*Mycobacterium avium* 104	http://www.genome.jp/kegg-bin/show_organism?org=mav
T03342	mavr	*Mycobacterium avium* 2285 (R)	http://www.genome.jp/kegg-bin/show_organism?org=mavr
T03430	mavd	*Mycobacterium avium* subsp. avium DJO-44271	http://www.genome.jp/kegg-bin/show_organism?org=mavd
T01754	mit	*Mycobacterium intracellulare* MOTT-02	http://www.genome.jp/kegg-bin/show_organism?org=mit
T01755	mir	*Mycobacterium intracellulare* MOTT-64	http://www.genome.jp/kegg-bin/show_organism?org=mir
T02158	mia	*Mycobacterium intracellulare* ATCC 13950	http://www.genome.jp/kegg-bin/show_organism?org=mia
T03407	mie	*Mycobacterium intracellulare* 1956	http://www.genome.jp/kegg-bin/show_organism?org=mie
T02325	mid	*Mycobacterium indicus pranii*	http://www.genome.jp/kegg-bin/show_organism?org=mid

T02732	myo	*Mycobacterium yongonense*	http://www.genome.jp/kegg-bin/show_organism?org=myo
T00434	msm	*Mycobacterium smegmatis* MC2 155	http://www.genome.jp/kegg-bin/show_organism?org=msm
T02191	msg	*Mycobacterium smegmatis* MC2 155	http://www.genome.jp/kegg-bin/show_organism?org=msg
T03433	msb	*Mycobacterium smegmatis* MC2 155	http://www.genome.jp/kegg-bin/show_organism?org=msb
T02423	msa	*Mycobacterium smegmatis* JS623	http://www.genome.jp/kegg-bin/show_organism?org=msa
T03409	msn	*Mycobacterium smegmatis* INHR1	http://www.genome.jp/kegg-bin/show_organism?org=msn
T03432	msh	*Mycobacterium smegmatis* INHR2	http://www.genome.jp/kegg-bin/show_organism?org=msh
T00435	mul	*Mycobacterium ulcerans*	http://www.genome.jp/kegg-bin/show_organism?org=mul
T00449	mva	*Mycobacterium vanbaalenii*	http://www.genome.jp/kegg-bin/show_organism?org=mva
T00498	mgi	*Mycobacterium gilvum* PYR-GCK	http://www.genome.jp/kegg-bin/show_organism?org=mgi
T01376	msp	*Mycobacterium gilvum* Spyr1	http://www.genome.jp/kegg-bin/show_organism?org=msp
T00657	mab	*Mycobacterium abscessus* ATCC 19977	http://www.genome.jp/kegg-bin/show_organism?org=mab
T02682	mabb	*Mycobacterium abscessus subsp. bolletii* 50594	http://www.genome.jp/kegg-bin/show_organism?org=mabb
T02177	mmv	*Mycobacterium abscessus subsp. bolletii*	http://www.genome.jp/kegg-bin/show_organism?org=mmv

		GO 06	
T03353	may	*Mycobacterium abscessus subsp. bolletii* MA 1948	http://www.genome.jp/kegg-bin/show_organism?org=may
T03499	mabo	*Mycobacterium abscessus subsp. bolletii* MC1518	http://www.genome.jp/kegg-bin/show_organism?org=mabo
T03329	maz	*Mycobacterium abscessus* 103	http://www.genome.jp/kegg-bin/show_organism?org=maz
T03341	mak	*Mycobacterium abscessus subsp. abcessus* MM1513	http://www.genome.jp/kegg-bin/show_organism?org=mak
T03534	mys	*Mycobacterium abscessus* DJO-44274	http://www.genome.jp/kegg-bin/show_organism?org=mys
T03535	myc	*Mycobacterium abscessus* 4529	http://www.genome.jp/kegg-bin/show_organism?org=myc
T00367	mmc	*Mycobacterium* sp. MCS	http://www.genome.jp/kegg-bin/show_organism?org=mmc
T00442	mkm	*Mycobacterium* sp. KMS	http://www.genome.jp/kegg-bin/show_organism?org=mkm
T00482	mjl	*Mycobacterium* sp. JLS	http://www.genome.jp/kegg-bin/show_organism?org=mjl
T01512	mjd	*Mycobacterium* sp. JDM601	http://www.genome.jp/kegg-bin/show_organism?org=mjd
T00694	mmi	*Mycobacterium marinum*	http://www.genome.jp/kegg-bin/show_organism?org=mmi
T01685	mrh	*Mycobacterium rhodesiae*	http://www.genome.jp/kegg-bin/show_organism?org=mrh

T02113	mmm	*Mycobacterium* sp. MOTT36Y	http://www.genome.jp/kegg-bin/show_organism?org=mmm
T02150	mcb	*Mycobacterium chubuense*	http://www.genome.jp/kegg-bin/show_organism?org=mcb
T02444	mli	*Mycobacterium liflandii*	http://www.genome.jp/kegg-bin/show_organism?org=mli
T02887	mkn	*Mycobacterium kansasii* ATCC 12478	http://www.genome.jp/kegg-bin/show_organism?org=mkn
T03652	mks	*Mycobacterium* kansasii 662	http://www.genome.jp/kegg-bin/show_organism?org=mks
T03653	mki	*Mycobacterium* kansasii 824	http://www.genome.jp/kegg-bin/show_organism?org=mki
T02959	mne	*Mycobacterium neoaurum*	http://www.genome.jp/kegg-bin/show_organism?org=mne
T03634	myv	*Mycobacterium sp*. VKM Ac-1817D	http://www.genome.jp/kegg-bin/show_organism?org=myv

3.2.2. Genome data mining of redox partners

Eighty one mycobacterial species genomes available for public use were data-mined for redox proteins (Table 3.2). Two methods were used to identify redox proteins. First, proteins were collected using the term “redox protein”. Second *M. tuberculosis* redox protein (total 9) were individually blasted against eighty one species and hit proteins were collected.

3.3. Results and Discussion

A total of 2190 redox proteins were identified in eighty one mycobacterial species (Table 3.3). Redox proteins number ranged from 8-57 in mycobacteria. Preliminary analysis suggested presence of ferredoxin, oxidoreductase and NADPH:adrenodoxin oxidoreductase etc. *M. abscessus subsp. bolletii* CCUG 48898 contained lower number of redox proteins (8) and *M. smegmatis* MC2 155 contained highest number of redox proteins (57).

Table 3.3. Genome data-mining of redox protein in mycobacterial species. Below table, each mycobacterial species code, full-name, number of redox protein hits identified and their protein IDs as per KEGG were shown.

Species code	Species name	No	Protein ID
mtc	*Mycobacterium tuberculosis* CDC1551	32	MT0787.1, MT1366, MT1643, MT2298, MT2597, MT3139, MT3290 1, MT3292, MT3315, MT3358, MT3525, ,MT3774, MT3783 ,MT3976, MT3607, MT1835, MT2063, MT1214, MT0909, mt3658, MT3676, mt3327, MT2846, MT1987, MT0352, MT0511, MT3189, MT1918, MT0716, MT0266, MT3402, MT1860
mtf	*Mycobacterium tuberculosis* F11	30	TBFG_10022, TBFG_12456, TBFG_12542, TBFG_13069, TBFG_13219, TBFG_13221, TBFG_13245, TBFG_13289, TBFG_13450, TBFG_13704, TBFG_13712, TBFG_13897, TBFG_10778, TBFG_13537, TBFG_11816, TBFG_12039, TBFG_11202, TBFG_13587, TBFG_13259, TBFG_12789, TBFG_10500, TBFG_13123, TBFG_10903, TBFG_11897, TBFG_10343, TBFG_13162, TBFG_10702, TBFG_10810, TBFG_10571
mtb	*Mycobacterium tuberculosis* KZN 1435	21	TBMG_00915, TBMG_01451, TBMG_00778, TBMG_03548, TBMG_02211, TBMG_01979, TBMG_02804, TBMG_03104, TBMG_03593, TBMG_03278, TBMG_01198, TBMG_00342, TBMG_00496, TBMG_00860, TBMG_03104, TBMG_02125, TBMG_03184, TBMG_00701, TBMG_00810, TBMG_00566, TBMG_00496
mtk	*Mycobacterium tuberculosis* KZN 4207	22	TBSG_00920, TBSG_01462, TBSG_01554, TBSG_03263, TBSG_00782, TBSG_03570, TBSG_02223, TBSG_01990, TBSG_02818, TBSG_03124, TBSG_03620, TBSG_03301, TBSG_00345, TBSG_00501, TBSG_00866, TBSG_03124, TBSG_02136, TBSG_02256, TBSG_03206, TBSG_00705, TBSG_00572, TBSG_00501
mtz	*Mycobacterium tuberculosis* KZN 605	23	TBXG_000906, TBXG_001438,TBXG_001530, TBXG_003221, TBXG_000771, TBXG_003519, TBXG_002192, TBXG_001963, TBXG_002784, TBXG_003083, TBXG_003569, TBXG_003259, TBXG_001187 ,TBXG_000340, TBXG_000493 ,TBXG_000852, ,TBXG_002107, TBXG_002225, TBXG_003165, TBXG_000694, TBXG_000803, TBXG_000563
mtg	*Mycobacterium tuberculosis* RGTB327	23	MRGA327_00160, MRGA327_04750, MRGA327_14985, MRGA327_15540, MRGA327_18760, MRGA327_19665, MRGA327_19800, MRGA327_21070, MRGA327_22675, MRGA327_23785, MRGA327_04750 , MRGA327_21565(4Fe-4S), MRGA327_11075, MRGA327_12375 ,MRGA327_07415 , MRGA327_21950, MRGA327_05550,MRGA327_19880, MRGA327_17010,MRGA327_19110,MRGA327_11545, MRGA327_04305, MRGA327_02135
mti	*Mycobacterium tuberculosis* RGTB423	25	MRGA423_00155, MRGA423_15140 ,MRGA423_15775 ,MRGA423_19000 ,MRGA423_19995, MRGA423_20010, MRGA423_20170, MRGA423_21510, MRGA423_23205, MRGA423_24370, , MRGA423_22055, MRGA423_11205, MRGA423_12495, MRGA423_22465, MRGA423_20255, MRGA423_17210, MRGA423_07345, MRGA423_02125, MRGA423_03085, MRGA423_19385, MRGA423_19380, MRGA423_11670, MRGA423_19585, MRGA423_04295, MRGA423_03510
mte	*Mycobacterium tuberculosis* CCDC5079	19	CCDC5079_2323 CCDC5079_3008 CCDC5079_3162 CCDC5079_3403 CCDC5079_3412 CCDC5079_1854 CDC5079_1089 CCDC5079_0817 CCDC5079_3295 CCDC5079_2546 CCDC5079_0315 CCDC5079_0461 CCDC5079_2863 CCDC5079_2896 CCDC5079_0640 CCDC5079_0735 CCDC5079_0461 CCDC5079_0527 CCDC5079_2981
mtur	*Mycobacterium tuberculosis* CCDC5079	32	CFBS_0027 CFBS_1409 CFBS_2371 CFBS_2671 CFBS_3221 CFBS_3381 CFBS_3383 CFBS_3406 CFBS_3449 CFBS_3620 CFBS_3892 CFBS_3902 CFBS_4094 CFBS_0802 CFBS_3719 CFBS_1875 CFBS_2117 CFBS_1256 CFBS_0929 CFBS_3770 CFBS_3420 CFBS_2933 CFBS_1256 CFBS_2427 CFBS_0512 CFBS_3276 CFBS_1961 CFBS_3318 CFBS_0723 CFBS_0835 CFBS_0585 CFBS_0512
mtl	*Mycobacterium tuberculosis*	18	CCDC5180_0487 CCDC5180_2295 CCDC5180_2971 CCDC5180_3114 CCDC5180_3362 CCDC5180_1829 CCDC5180_0810 CCDC5180_3247 CCDC5180_2943 CCDC5180_0312 CCDC5180_0454 CCDC5180_2826

	CCDC5180		CCDC5180_1704 CCDC5180_2857 CCDC5180_0631 CCDC5180_0727 CCDC5180_0519 CCDC5180_0454
mto	*Mycobacterium tuberculosis* CTRI-2	29	MTCTRI2_0025 MTCTRI2_0534 MTCTRI2_2569 MTCTRI2_3116 MTCTRI2_3259 MTCTRI2_3261 MTCTRI2_3283 MTCTRI2_3327 MTCTRI2_3488 MTCTRI2_3741 MTCTRI2_3750 MTCTRI2_3941 MTCTRI2_0782 MTCTRI2_3569 MTCTRI2_1817 MTCTRI2_2041 MTCTRI2_1209 MTCTRI2_0909 MTCTRI2_3618 MTCTRI2_3297 MTCTRI2_2829 MTCTRI2_0345 MTCTRI2_0497 MTCTRI2_3169 MTCTRI2_1901 MTCTRI2_3204 MTCTRI2_0704 MTCTRI2_0813 MTCTRI2_0569
mtd	*Mycobacterium tuberculosis* UT205	25	UDA_0022c UDA_0886 UDA_1324 UDA_1471 UDA_1608c UDA_1932 UDA_2391 UDA_2428 UDA_2454c UDA_2455c UDA_2238c UDA_2521 UDA_3053c UDA_3106 UDA_3197A UDA_3198A UDA_3219 UDA_3260c UDA_3416 UDA_3681c UDA_3862c UDA_3913 UDA_3914 UDA_3503c UDA_3106
mtn	*Mycobacterium tuberculosis* Erdman = ATCC 35801	23	ERDMAN_0028 ERDMAN_0577 ERDMAN_2774 ERDMAN_3342 ERDMAN_3508 ERDMAN_4021 ERDMAN_0845 ERDMAN_3844 ERDMAN_1975 ERDMAN_2211 ERDMAN_1320 ERDMAN_0979 ERDMAN_3899 ERDMAN_3543 ERDMAN_3042 ERDMAN_0374 ERDMAN_0538 ERDMAN_2061 ERDMAN_3441 ERDMAN_0759 ERDMAN_0879 ERDMAN_0538 ERDMAN_0614
mtj	*Mycobacterium tuberculosis* Beijing/NITR203	26	J112_00125 J112_02815 J112_04105 J112_13525 J112_16355 J112_17165 J112_19740 J112_20755 J112_04105 J112_18830 J112_09550 J112_10735 J112_04765 J112_06365 J112_19130 J112_17365 J112_14865 J112_01820 J112_02620 J112_16650 J112_04765 J112_09960 J112_16845 J112_03680 J112_04265 J112_03005
mtub	*Mycobacterium tuberculosis* 7199-99	29	MT7199_0022 MT7199_0540 MT7199_2460 MT7199_2552 MT7199_3087 MT7199_3234 MT7199_3236 MT7199_3258 MT7199_3294 MT7199_3302 MT7199_3463 MT7199_3736 MT7199_3745 MT7199_3931 MT7199_3564 MT7199_1812 MT7199_2038 MT7199_0905 MT7199_3616 MT7199_3272 MT7199_2809 MT7199_1207 MT7199_0344 MT7199_0502 MT7199_3139 MT7199_1895 MT7199_3179 MT7199_0706 MT7199_0815
mtuc	*Mycobacterium tuberculosis* CAS/NITR204	18	J113_00155 J113_03725 J113_17540 J113_21265 J113_22265 J113_22285 J113_25655 J113_26995 J113_05385 J113_24450 J113_12425 J113_13860 J113_08245 J113_24860 J113_02425 J113_12960 J113_05590 J113_04870
mtue	*Mycobacterium tuberculosis* EAI5/NITR206	26	J114_00135 J114_02810 J114_04075 J114_13485 J114_16325 J114_17120 J114_19620 J114_20635 J114_04075 J114_18730 J114_09545 J114_10740 J114_06365 J114_04715 J114_19010 J114_17320 J114_14805 J114_01820 J114_02620 J114_16620 J114_09960 J114_16810 J114_03670 J114_04240 J114_03000 J114_02620
mtx	*Mycobacterium tuberculosis* EAI5	18	M943_06945 M943_15755 M943_03995 M943_18015 M943_09300 M943_08070 M943_10425 M943_06175 M943_04625 M943_14340 M943_02555 M943_11865 M943_16035 M943_07495 M943_03575 M943_09710 M943_04160 M943_02905
mtuh	*Mycobacterium tuberculosis* Haarlem/NITR202	17	I917_00160 I917_03790 I917_05410 I917_17785 I917_21435 I917_22450 I917_22585 I917_24010 I917_25725 I917_27140 I917_24570 I917_12705 I917_14190 I917_08355 I917_24940 I917_19450 I917_04905
mtul	*Mycobacterium tuberculosis* Haarlem	28	TBHG_02457 TBHG_02982 TBHG_03129 TBHG_03608 TBHG_00755 TBHG_03447 TBHG_01744 TBHG_01965 TBHG_01161 TBHG_00874 TBHG_03494 TBHG_03166 TBHG_02708 TBHG_01894 TBHG_00380 TBHG_00333 TBHG_00490 TBHG_03037 TBHG_00874 TBHG_01824 TBHG_03013 TBHG_01708 TBHG_01411 TBHG_03072 TBHG_00683 TBHG_00326 TBHG_00558 TBHG_02978
mtut	*Mycobacterium tuberculosis* BT1	13	HKBT1_0027 HKBT1_1408 HKBT1_2362 HKBT1_2662 HKBT1_3208 HKBT1_3368 HKBT1_3370 HKBT1_3393 HKBT1_3436 HKBT1_3607 HKBT1_3876 HKBT1_3886 HKBT1_4076
mtuu	*Mycobacterium tuberculosis* BT2	31	HKBT2_0027 HKBT2_1414 HKBT2_2364 HKBT2_2665 HKBT2_3213 HKBT2_3375 HKBT2_3377 HKBT2_3400 HKBT2_3443 HKBT2_3614 HKBT2_3885 HKBT2_3895 HKBT2_4086 HKBT2_0803 HKBT2_3713 HKBT2_1882 HKBT2_2113 HKBT2_1260 HKBT2_0930 HKBT2_3764 HKBT2_3414 HKBT2_2924 HKBT2_0354 HKBT2_2420 HKBT2_0512 HKBT2_3713 HKBT2_3268 HKBT2_0930 HKBT2_1966 HKBT2_3310 HKBT2_0724
mtg	*Mycobacterium tuberculosis* HKBS1	31	HKBS1_0027 HKBS1_1412 HKBS1_2368 HKBS1_2669 HKBS1_3219 HKBS1_3378 HKBS1_3380 HKBS1_3403 HKBS1_3446 HKBS1_3617 HKBS1_3889 HKBS1_3899 HKBS1_4089 HKBS1_0802 HKBS1_3716 HKBS1_1878 HKBS1_0802 HKBS1_2118 HKBS1_1258 HKBS1_0929 HKBS1_3767 HKBS1_3417 HKBS1_2928 HKBS1_0354 HKBS1_2424 HKBS1_0512 HKBS1_3274 HKBS1_1962 HKBS1_3316 HKBS1_0723 HKBS1_0835

mbo	*Mycobacterium bovis* AF2122/97	22	Mb0539 Mb2550 Mb3079c Mb3223 Mb3697c Mb3706c Mb0786c Mb3533c Mb1814 Mb2030c Mb1210 Mb0910 Mb3584 Mb3259c Mb2798c Mb0345c Mb0502c Mb3133 Mb1900c Mb0707 Mb0819c Mb0576c
mbb	*Mycobacterium bovis* BCG Pasteur 1173P2	32	BCG_0052c BCG_0569 BCG_2542 BCG_3077c BCG_3221c BCG_3223 BCG_3246 BCG_3289c BCG_3339 BCG_3486 BCG_3731c BCG_3740c BCG_3925c BCG_0815c BCG_3567c BCG_1818 BCG_2024c BCG_1240 BCG_0938 BCG_3618 BCG_3353c BCG_3260c BCG_2793c BCG_0377c BCG_0533c BCG_3131 BCG_1905c BCG_3164 BCG_0737 BCG_0848c BCG_0606c BCG_0533c
mbt	*Mycobacterium bovis* BCG Tokyo 172	27	JTY_0539 JTY_2536 JTY_3072 JTY_3216 JTY_3218 JTY_3241 JTY_3285 JTY_3486 JTY_3732 JTY_3741 JTY_3927 JTY_0785 JTY_3567 JTY_1802 JTY_2019 JTY_1213 JTY_0908 JTY_3255 JTY_2787 JTY_0347 JTY_0503 JTY_3126 JTY_1889 JTY_3159 JTY_0707 JTY_0818 JTY_0576
mbm	*Mycobacterium bovis* BCG Mexico	28	BCGMEX_0022c BCGMEX_0540 BCGMEX_2437 BCGMEX_2534 BCGMEX_3074c BCGMEX_3218c BCGMEX_3220 BCGMEX_3244 BCGMEX_3287c BCGMEX_3337 BCGMEX_3484 BCGMEX_3731c BCGMEX_3740c BCGMEX_0786c BCGMEX_1799 BCGMEX_2006c BCGMEX_0909 BCGMEX_3351c BCGMEX_3258c BCGMEX_2786c BCGMEX_1212 BCGMEX_0347c BCGMEX_0504c BCGMEX_3128 BCGMEX_1886c BCGMEX_0708 BCGMEX_0819c BCGMEX_0577c
mbk	*Mycobacterium bovis* BCG Korea 1168P	29	K60_000250 K60_005570 K60_008160 K60_026200 K60_031660 K60_033240 K60_033470 K60_033890 K60_040790 K60_041130 K60_035540 K60_038100 K60_040120 K60_036380 K60_018710 K60_020800 K60_012700 K60_009450 K60_041260 K60_040920 K60_033600 K60_028720 K60_003580 K60_005190 K60_032230 K60_019560 K60_007330 K60_008500 K60_005950
mbz	*Mycobacterium bovis* ATCC BAA-935	20	LH58_07260 LH58_16245 LH58_04155 LH58_18975 LH58_09585 LH58_08380 LH58_10650 LH58_06490 LH58_04815 LH58_14740 LH58_02640 LH58_16535 LH58_07845 LH58_16710 LH58_03715 LH58_10020 LH58_14405 LH58_04330 LH58_03010 LH58_02640
MAF	*Mycobacterium africanum*	18	MAF_25360 MAF_30600 MAF_32060 MAF_35160 MAF_18080 MAF_20190 MAF_11960 MAF_08950 MAF_27810 MAF_03400 MAF_04960 MAF_31130 MAF_18910 MAF_17700 MAF_06970 MAF_05680 MAF_17760 MAF_04960
mce	*Mycobacterium canettii* CIPT 140010059	28	MCAN_00211 MCAN_24661 MCAN_25611 MCAN_30781 MCAN_32121 MCAN_32141 MCAN_32361 MCAN_32791 MCAN_34401 MCAN_36931 MCAN_37021 MCAN_38841 MCAN_07671 MCAN_35171 MCAN_18041 MCAN_20271 MCAN_11881 MCAN_08871 MCAN_28041 MCAN_03401 MCAN_04921 MCAN_31331 MCAN_18841 MCAN_17651 MCAN_31551 MCAN_06891 MCAN_07981 MCAN_05641
mcq	*Mycobacterium canettii* CIPT 140060008	28	BN44_10028 BN44_10584 BN44_60564 BN44_60564 BN44_60714 BN44_60739 BN44_70044 BN44_80075 BN44_120069 BN44_120078 BN44_120289 BN44_10833 BN44_80180 BN44_40043 BN44_40292 BN44_11316 BN44_10967 BN44_70011 BN44_60238 BN44_10378 BN44_10545 BN44_60625 BN44_40132 BN44_20330 BN44_10756 BN44_10869 BN44_10622 BN44_40006
mcv	*Mycobacterium canettii* CIPT 140070008	26	BN43_10028 BN43_10575 BN43_60036 BN43_60199 BN43_60225 BN43_60269 BN43_70069 BN43_90178 BN43_90187 BN43_90394 BN43_20198 BN43_70172 BN43_30924 BN43_31187 BN43_30245 BN43_60240 BN43_40463 BN43_10373 BN43_10534 BN43_60100 BN43_31010 BN43_30879 BN43_20118 BN43_20233 BN43_10613 BN43_30891
mcx	*Mycobacterium canettii* CIPT 140070010	27	BN42_10044 BN42_20263 BN42_41060 BN42_41239 BN42_41264 BN42_41310 BN42_50074 BN42_90185 BN42_90194 BN42_90396 BN42_20521 BN42_50183 BN42_30041 BN42_30305 BN42_21043 BN42_20670 BN42_41281 BN42_40756 BN42_20067 BN42_41139 BN42_21690 BN42_20441 BN42_30134 BN42_20558 BN42_20300 BN42_30006 BN42_20219
mcz	*Mycobacterium canettii* CIPT 140070017	27	BN45_10027 BN45_10590 BN45_60037 BN45_60215 BN45_60218 BN45_60245 BN45_60289 BN45_70061 BN45_110026 BN45_110035 BN45_110238 BN45_20032 BN45_70168 BN45_50042 BN45_50286 BN45_30238 BN45_20176 BN45_60260 BN45_51163 BN45_10372 BN45_60104 BN45_50134 BN45_40244 BN45_10786 BN45_20064 BN45_10628 BN45_10543
mle	*Mycobacterium leprae* TN	9	ML0424 ML1159 ML1736 ML2307 ML1489 ML2134 ML2501 ML0666 ML2276

mlb	*Mycobacterium leprae* Br4923	9	MLBr_00424 MLBr_01159 MLBr_01736 MLBr_02307 MLBr_01489 MLBr_02134 MLBr_02501 MLBr_00666 MLBr_02276
mpa	*Mycobacterium avium subsp. paratuberculosis* K-10	19	MAP0033c MAP1196 MAP1579c MAP1589c MAP2277c MAP2329 MAP2435c MAP3102c MAP3296c MAP3298 MAP4339 MAP0560 MAP2726c MAP2607c MAP2039 MAP0825 MAP3176 MAP0825 MAP3190
mao	*Mycobacterium avium subsp. paratuberculosis* MAP4	30	MAP4_0487 MAP4_0696 MAP4_1090 MAP4_1494 MAP4_3843 MAP4_0696 MAP4_1211 MAP4_2250 MAP4_3268 MAP4_3198 MAP4_3107 MAP4_3124 MAP4_1478 MAP4_3133 MAP4_1296 MAP4_3371 MAP4_0440 MAP4_0504 MAP4_0923 MAP4_3944 MAP4_0613 MAP4_0795 MAP4_0599 MAP4_2108 MAP4_4328 MAP4_4272 MAP4_4180 MAP4_2904 MAP4_3160 MAP4_3135(4Fe-4S),
mav	*Mycobacterium avium* 104	17	MAV_0040 MAV_0653 MAV_0915 MAV_1636 MAV_1949 MAV_3178 MAV_3921 MAV_4144 MAV_3963 MAV_4193 MAV_0862 MAV_1316 MAV_2150 MAV_3500 MAV_5072 MAV_1015 MAV_4007 MAV_4485
mavr	*Mycobacterium avium* 2285 (R)	33	LA63_06965 LA63_18080 LA63_03310 LA63_04010 LA63_03685 LA63_09145 LA63_04145 LA63_04060 LA63_07405 LA63_03030 LA63_08920 LA63_04020 LA63_06380 LA63_13250 LA63_11975 LA63_08555 LA63_16020 LA63_05975 LA63_09875 LA63_04500 LA63_15525 LA63_09915 LA63_19055 LA63_16845 LA63_23905 LA63_03885 LA63_18495 LA63_18560 LA63_15240 LA63_22380 LA63_20830 LA63_12860 LA63_16535
mavd	*Mycobacterium avium subsp. avium* DJO-44271	32	NF84_06830,NF84_17895,NF84_03215,NF84_03910,NF84_03595 ,NF84_04045,NF84_03960 NF84_07270,NF84_02960 NF84_08780,NF84_03920,NF84_06250,NF84_13100,NF84_11695,NF84_08415,NF84_03785, NF84_01950, NF84_14535, NF84_05845 ,NF84_09675 ,NF84_04400 ,NF84_15390 ,NF84_09715, NF84_18860, NF84_16680, NF84_15390, NF84_18305 NF84_18370, NF84_15105, NF84_22160, NF84_20635, NF84_12705,
mit	*Mycobacterium intracellulare*	26	OCO_00330 OCO_08380 OCO_16080 OCO_17020 OCO_37480 OCO_40040 OCO_40720 OCO_51410 OCO_10870 OCO_19540 OCO_07780 OCO_44570 OCO_12260 OCO_21220 OCO_08830 OCO_42200 OCO_37890 OCO_40550 OCO_39530 OCO_38590 OCO_28540 OCO_14710 OCO_23020 OCO_06350 OCO_22270 OCO_11870 OCO_44660
mir	*Mycobacterium intracellulare* MOTT-64	28	OCQ_00330 OCQ_07950 OCQ_08540 OCQ_13760 OCQ_14690 OCQ_38710 OCQ_41140 OCQ_41990 OCQ_44050 OCQ_52400 OCQ_18210 OCQ_45710 OCQ_34530 OCQ_12280 OCQ_20140 OCQ_166400 OCQ_08980 OCQ_41640 OCQ_40760 OCQ_32640 OCQ_39750 OCQ_27120 OCQ_28970 OCQ_28980 OCQ_06500 OCQ_21380 OCQ_45800 OCQ_11890
mia	*Mycobacterium intracellulare* ATCC 13950	34	OCU_00340 OCU_51350 OCU_07810 OCU_08460 OCU_16280 OCU_17220 OCU_17430 OCU_37570 OCU_39950 OCU_40630 OCU_05670 OCU_13400 OCU_07790 OCU_15300 OCU_44310 OCU_19690 OCU_19750 OCU_12220 OCU_33290 OCU_21470 OCU_08900 OCU_42130 OCU_37970 OCU_40460 OCU_39570 OCU_28180 OCU_28420 OCU_46960 OCU_38560 OCU_28410 OCU_15150 OCU_22470 OCU_11820 OCU_44400
mie	*Mycobacterium intracellulare* 1956	38	LG41_07635 LG41_17800 LG41_20295 LG41_03015 LG41_06455 LG41_03860 LG41_03470 LG41_04010 LG41_09270 LG41_08110 LG41_03925 LG41_02825 LG41_03870 LG41_130250 LG41_03725 LG41_06845 LG41_21115 LG41_14570 LG41_15760 LG41_09305 LG41_05925 LG41_10100 LG41_04370 LG41_15315 LG41_18775 LG41_16535 LG41_23695 LG41_00455 LG41_18315 LG41_18380 LG41_04965 LG41_20710 LG41_12640 LG41_16240 LG41_03190 LG41_04910 LG41_10575 LG41_21165
mid	*Mycobacterium indicus pranii*	35	MIP_00041 MIP_01026 MIP_01337 MIP_01339 MIP_01421 MIP_02218 MIP_02348 MIP_02748 MIP_02752 MIP_05679 MIP_01080 MIP_00228 MIP_010260 MIP_03857 MIP_04541 MIP_02763 MIP_01957 MIP_03002 MIP_05025 MIP_00230 MIP_01480 MIP_05882 MIP_03023 MIP_06111 MIP_03758 MIP_03722 MIP_07142 MIP_00235 MIP_05836 MIP_05856 MIP_03046 MIP_01666 MIP_01901 MIP_00219 MIP_04639
myo	*Mycobacterium yongonense*	38	OEM_00330 OEM_05700 OEM_07880 OEM_08150 OEM_14120 OEM_15020 OEM_38120 OEM_40320 OEM_40980 OEM_43160 OEM_52130 OEM_p100880 OEM_p101170 OEM_07860 OEM_17420 OEM_44760 OEM_33540 OEM_17520 OEM_12410 OEM_19090 OEM_08950 OEM_42560 OEM_38530 OEM_40800 OEM_07240 OEM_40050 OEM_31170 OEM_27010 OEM_47340 OEM_391000 OEM_08950 OEM_27000 OEM_43160 OEM_25480 OEM_20380 OEM_44850 OEM_12010 OEM_46940
msm	*Mycobacterium smegmatis* MC2 155	37	MSMEG_0051 MSMEG_0761 MSMEG_1017 MSMEG_1947 MSMEG_2297 MSMEG_2559 MSMEG_3568 MSMEG_4753 MSMEG_4819 MSMEG_4822 MSMEG_4917 MSMEG_5904 MSMEG_6597 MSMEG_5864 MSMEG_4423 MSMEG_1124 MSMEG_5122 MSMEG_5681 MSMEG_1604 MSMEG_1847

			MSMEG_0295 MSMEG_2893 MSMEG_6039 MSMEG_1742 MSMEG_4411 MSMEG_6836 MSMEG_5533 MSMEG_0637 MSMEG_5433 MSMEG_1416 MSMEG_1460 MSMEG_0670 MSMEG_4023 MSMEG_6264 MSMEG_4422 MSMEG_1132 MSMEG_3457
msg	*Mycobacterium smegmatis* MC2 155	57	MSMEI_0988 MSMEI_1558 MSMEI_1905 MSMEI_1910 MSMEI_2239 MSMEI_3485 MSMEI_4527 MSMEI_4528 MSMEI_4633 MSMEI_4695 MSMEI_6026 MSMEI_6039 MSMEI_6419 MSMEI_5705 MSMEI_4053 MSMEI_2499 MSMEI_6514 MSMEI_4698 MSMEI_4689 MSMEI_5744 MSMEI_0745 MSMEI_4732 MSMEI_1090 MSMEI_4993 MSMEI_5531 MSMEI_2010 MSMEI_1805 MSMEI_0288 MSMEI_2819 MSMEI_5878 MSMEI_1845 MSMEI_3589 MSMEI_1702 MSMEI_4267 MSMEI_4752 MSMEI_4054 MSMEI_4304 MSMEI_1945 MSMEI_0702 MSMEI_6654 MSMEI_5381 MSMEI_3841 MSMEI_5284 MSMEI_2039 MSMEI_5531 MSMEI_0621 MSMEI_19870 MSMEI_0652 MSMEI_1381 MSMEI_3512 MSMEI_6637 MSMEI_4080 MSMEI_5293 MSMEI_5252 MSMEI_6102 MSMEI_1100 MSMEI_3376
msb	*Mycobacterium smegmatis* MC2 155	56	LJ00_05040 LJ00_07575LJ00_11425 LJ00_17750 LJ00_24320 LJ00_32610 LJ00_29000 LJ00_20585 LJ00_12735 LJ00_33085 LJ00_23835 LJ00_23750 LJ00_23850 LJ00_23805 LJ00_29200 LJ00_03780 LJ00_24020 LJ00_21895 LJ00_05585 LJ00_25320 LJ00_28090 LJ00_03425 LJ00_09210 LJ00_18275 LJ00_08705 LJ00_20590 LJ00_09515 LJ00_22945 LJ00_21835 LJ00_19915 LJ00_33780 LJ00_03425 LJ00_27355 LJ00_19540 LJ00_10390 LJ00_16405 LJ00_24835 LJ00_10160 LJ00_03165 LJ00_11975 LJ00_10135 LJ00_14130 LJ00_03320 LJ00_07060 LJ00_07295 LJ00_17885 LJ00_13665 LJ00_33690 LJ00_03320 LJ00_19970 LJ00_26900 LJ00_26680 LJ00_30975 LJ00_21890 LJ00_05635 LJ00_09925
msa	*Mycobacterium smegmatis* JS623	40	Mycsm_01119 Mycsm_01449 Mycsm_01452 Mycsm_02167 Mycsm_02291 Mycsm_02551 Mycsm_04103 Mycsm_04630 Mycsm_05076 Mycsm_05225 Mycsm_06392 Mycsm_06728 Mycsm_06737 Mycsm_06739 Mycsm_05682 Mycsm_02382 Mycsm_04694 Mycsm_04480 Mycsm_04488 Mycsm_04467 Mycsm_04486 Mycsm_05549 Mycsm_05740 Mycsm_00403 Mycsm_06648 Mycsm_01930 Mycsm_04559 Mycsm_04590 Mycsm_05841 Mycsm_01404 Mycsm_04700 Mycsm_06610 Mycsm_04494 Mycsm_01297 Mycsm_05140 Mycsm_04917 Mycsm_00354 Mycsm_03759 Mycsm_06689 Mycsm_04920
msn	*Mycobacterium smegmatis* INHR1	42	LI99_29005(4Fe-4S), LI99_20590(3Fe-4S), LI99_12735(4Fe-4S), LI99_33090(4Fe-4S), LI99_23840(4Fe-4S), LI99_23755(4fe-4S), LI99_23855(4Fe-4S), LI99_29205(4Fe-4S), LI99_03780(4Fe-4S), LI99_24025(4Fe-4S), LI99_25325(4Fe-4S), LI99_20595(4Fe-4S), LI99_09925(4Fe-4S), LI99_27360(4Fe-4S), LI99_09210(4Fe-4S), LI99_05585(4Fe-4S), LI99_08705 LI99_21840 LI99_10390 LI99_05040 LI99_07575 LI99_11425 LI99_24325 LI99_32615 LI99_21900 LI99_09515 LI99_16410 LI99_24840 LI99_10160 LI99_03165 LI99_17755 LI99_28095 LI99_01480(4Fe-4S), LI99_18280(4Fe-4S) LI99_22950(4Fe-4S), LI99_19920(4Fe-4S), LI99_19545(4Fe-4S), LI99_23810 LI99_03425 LI99_33785LI99_21840LI99_33785 LI99_03425
msh	*Mycobacterium smegmatis* INHR2	38	LI98_29010(4Fe-4S), LI98_20595(3Fe-4S), LI98_12740(4e-4S), LI98_33095(4Fe-4S), LI98_23845(4Fe-4S), LI98_23760(4Fe-4S), LI98_23860(4Fe-4S), LI98_29210(4Fe-4S), LI98_03780(4Fe-4S), LI98_24030(4Fe-4S), LI98_05585(4Fe-4S), LI98_25330(4Fe-4S), LI98_27365(4Fe-4S), LI98_09925(4Fe-4S), LI98_28100 LI98_08705 LI98_10390 LI98_17895 LI98_05040 LI98_07575 LI98_11430 LI98_24330 LI98_32620 LI98_219 LI98_03425 LI98_24845 LI98_10160 LI98_07060 LI98_05635 LI98_09210(4Fe-4S), LI98_01480(4Fe-4S), LI98_18285(4Fe-4S), LI98_20600(4Fe-4S), LI98_22955(4Fe-4S), LI98_19550(4Fe-4S), LI98_28100 LI98_17760 LI98_03165
mul	*Mycobacterium ulcerans*	30	MUL_0040 MUL_0625 MUL_0895 MUL_1876 MUL_2511 MUL_2513 MUL_2541 MUL_2605 MUL_2912 MUL_2999 MUL_3811 MUL_4247 MUL_4256 MUP021 MUL_0472 MUL_2873 MUL_4066 MUL_0334 MUL_0316 MUL_3830 MUL_3090 MUL_3264 MUL_1025 MUL_2700 MUL_4142 MUL_4786 MUL_0264 MUL_0769 MUL_2358
mva	*Mycobacterium vanbaalenii*	47	Mvan_0866 Mvan_1329 Mvan_1743 Mvan_1744 Mvan_1806 Mvan_1862 Mvan_2040 Mvan_2813 Mvan_3045 Mvan_3240 Mvan_3710 Mvan_3749 Mvan_3965 Mvan_4109 Mvan_4120 Mvan_4176 Mvan_4303 Mvan_4712 Mvan_5099 Mvan_5315 Mvan_5432 Mvan_5849 Mvan_2235 Mvan_3976 Mvan_5849 Mvan_0549 Mvan_0681 Mvan_4235 Mvan_0399 Mvan_4179 Mvan_0299 Mvan_4529 Mvan_5031 Mvan_4186 Mvan_53090 Mvan_2893 Mvan_1767 Mvan_3180 Mvan_4257 Mvan_1910 Mvan_1290 Mvan_1327 Mvan_0467 Mvan_0400 Mvan_1216 Mvan_5348 Mvan_1519
mgi	*Mycobacterium gilvum* PYR-GCK	33	Mflv_0338 Mflv_0591 Mflv_0681 Mflv_1648 Mflv_2342 Mflv_2478 Mflv_2616 Mflv_3247 Mflv_4307 Mflv_4661 Mflv_4719 Mflv_4720 Mflv_4111 Mflv_2417 Mflv_1296 Mflv_2170 Mflv_1720 Mflv_3156 Mflv_2468 Mflv_1462 Mflv_3426 Mflv_2623 Mflv_0255 Mflv_2170 Mflv_0383 Mflv_1720 Mflv_4452 Mflv_4591 Mflv_5068 Mflv_4699(4fe-4S), Mflv_5247(4fe-4S), Mflv_2391(4fe-4S), Mflv_4547(4fe-4S), Mflv_0668(4fe-4S), Mflv_0570(4fe-4S),
msp	*Mycobacterium gilvum*	25	Mspyr1_00530 Mspyr1_17750 Mspyr1_21230 Mspyr1_25750 Mspyr1_35330 Mspyr1_36500 Mspyr1_39890 Mspyr1_39920 Mspyr1_45950 Mspyr1_55310

	Spyr1		Mspyr1_09810 Mspyr1_01440 Mspyr1_03730 Mspyr1_18940 Mspyr1_47050 Mspyr1_39020 Mspyr1_04970 Mspyr1_34540Mspyr1_19010,Mspyr1_09360, Mspyr1_05510,Mspyr1_19110,Mspyr1_18430,Mspyr1_19050, Mspyr1_19260 Mspyr1_16020
mab	*Mycobacterium abscessus* ATCC 19977	14	MAB_1465 MAB_1710c MAB_3415c MAB_3512 MAB_1213c MAB_4157c MAB_0930 MAB_0088c MAB_2240 MAB_3482 MAB_1043c MAB_4199 MAB_3838c MAB_2047c
mabb	*Mycobacterium abscessus subsp. bolletii* 50594	18	MASS_1457 MASS_1803 MASS_3219 MASS_3358 MASS_4808 MASS_4944 MASS_1p0060 MASS_2p0009 MASS_1211 MASS_4156 MASS_0913 MASS_0552 MASS_4335 MASS_4170 MASS_3512 MASS_3850 MASS_1327 MASS_2170
may	*Mycobacterium abscessus subsp. bolletii* MA 1948	14	LA62_07440 LA62_08705 LA62_08945 LA62_17355 LA62_25085 LA62_06160 LA62_21130 LA62_06720 LA62_08080 LA62_11400 LA62_17705 LA62_21205 LA62_22195 LA62_06160(4Fe-4S),
mabo	*Mycobacterium abscessus subsp. bolletii* MC1518	13	NF82_07400 NF82_08655 NF82_08805 NF82_17105 NF82_24745 NF82_06135 NF82_20825 NF82_06685 NF82_08040 NF82_11195 NF82_17440 NF82_21510 NF82_21885
mabl	*Mycobacterium abscessus subsp. bolletii* CCUG 48898 = JCM 15300 3	8	MMASJCM_1484 MMASJCM_3423 MMASJCM_3533 MMASJCM_1355 MMASJCM_1033 MMASJCM_1611 MMASJCM_4256 MMASJCM_4803
maz	*Mycobacterium abscessus* 103	13	LA61_07330 LA61_08600 LA61_08840 LA61_17260 LA61_24975 LA61_06065 LA61_21025 LA61_04605 LA61_07975 LA61_11290 LA61_17605 LA61_21100 LA61_22090
mak	*Mycobacterium abscessus subsp. abcessus* MM1513	15	LH56_00070 LH56_07030 LH56_07740 LH56_14535 LH56_17005 LH56_03400 LH56_16460 LH56_15135 LH56_12705 LH56_03190 LH56_06695 LH56_15775 LH56_04080 LH56_21915 LH56_18350
myc	*Mycobacterium abscessus* 4529	13	NF90_00070 NF90_07070 NF90_07865 NF90_15030 NF90_16270 NF90_17480 NF90_03455 NF90_16945 NF90_15630 NF90_13170 NF90_06730 NF90_03385 NF90_17930
mys	Mycobacterium abscessus DJO-44274	9	NF92_17475 NF92_03455 NF92_16940 NF92_04140 NF92_13170 NF92_18805NF90_07070 NF90_15030 NF90_16270
mmc	*Mycobacterium sp.* MCS	34	Mmcs_1334 Mmcs_1408 Mmcs_1815 Mmcs_3567 Mmcs_3697 Mmcs_3862 Mmcs_4527 Mmcs_4621 Mmcs_5251 Mmcs_2015 Mmcs_3705 Mmcs_4462 Mmcs_2259 Mmcs_3419 Mmcs_4865 Mmcs_0454 Mmcs_5186 Mmcs_5292 Mmcs_0618 Mmcs_2719 Mmcs_5289 Mmcs_4030 Mmcs_2580 Mmcs_3712 Mmcs_0319 Mmcs_4710 Mmcs_1358 Mmcs_2259 Mmcs_2875 Mmcs_1520 Mmcs_2269 Mmcs_4866 Mmcs_4256 Mmcs_3768
mkm	*Mycobacterium sp.* KMS	44	Mkms_0705 Mkms_1351 Mkms_1352 Mkms_1426 Mkms_1862 Mkms_3113 Mkms_3421 Mkms_3640 Mkms_3717 Mkms_3770 Mkms_3936 Mkms_4614 Mkms_4709 Mkms_4901 Mkms_4954 Mkms_5340 Mkms_5664 Mkms_5746 Mkms_2061 Mkms_5381 Mkms_3778 Mkms_2763 Mkms_1376 Mkms_3482 Mkms_0465 Mkms_1632 Mkms_4954 Mkms_2978 Mkms_0631 Mkms_0529 Mkms_3841 Mkms_5378 Mkms_4105 Mkms_4955 Mkms_2625 Mkms_3785 Mkms_0329 Mkms_4796 Mkms_2306 Mkms_2919 Mkms_3896 Mkms_1543 Mkms_2316 Mkms_4342
mjl	*Mycobacterium sp.* JLS	39	Mjls_1370 Mjls_1462 Mjls_1796 Mjls_2789 Mjls_3572 Mjls_3710 Mjls_3848 Mjls_4910 Mjls_5004 Mjls_5233 Mjls_5631 Mjls_1996 Mjls_0441 Mjls_4260 Mjls_4115 Mjls_4845 Mjls_3718 Mjls_1578 Mjls_4216 Mjls_0609 Mjls_0507 Mjls_5671 Mjls_4202 Mjls_4034 Mjls_4429 Mjls_3780 Mjls_2749 Mjls_5668 Mjls_4260 Mjls_5234 Mjls_2619 Mjls_3725 Mjls_5095 Mjls_1392 Mjls_2298 Mjls_2905 Mjls_3808 Mjls_3430 Mjls_4635 Mjls_4084
mjd	*Mycobacterium sp.* JDM601	22	JDM601_0524 JDM601_1387 JDM601_2789 JDM601_2913 JDM601_3423 JDM601_3951 JDM601_3492 JDM601_3498 JDM601_3439 JDM601_0812 JDM601_2873 JDM601_3855 JDM601_2406 JDM601_3492 JDM601_1956 JDM601_0700 JDM601_3605 JDM601_3499 JDM601_3634 JDM601_3735 JDM601_2324 JDM601_4002

mmi	*Mycobacterium marinum*	36	MMAR_0041 MMAR_0575 MMAR_0872 MMAR_1132 MMAR_1282 MMAR_1338 MMAR_1363 MMAR_1365 MMAR_1640 MMAR_2755 MMAR_3408 MMAR_3956 MMAR_4684 MMAR_5161 MMAR_5170 MMAR_5437 MMAR_2932 MMAR_4933 MMAR_4646 MMAR_0335 MMAR_3408 MMAR_3153 MMAR_4646 MMAR_1017 MMAR_4734 MMAR_4736 MMAR_2879 MMAR_3973 MMAR_4716 MMAR_4763 MMAR_4730 MMAR_2667 MMAR_4991 MMAR_2994 MMAR_2080 MMAR_4274 MMAR_3421 MMAR_2931
mrh	*Mycobacterium rhodesiae*	37	MycrhN_0177 MycrhN_0288 MycrhN_0336 MycrhN_0339 MycrhN_1105 MycrhN_3122 MycrhN_3524 MycrhN_3852 MycrhN_4314 MycrhN_5607 MycrhN_5866 MycrhN_6003 MycrhN_6317 MycrhN_3929 MycrhN_2409 MycrhN_0189 MycrhN_0469 MycrhN_1355 MycrhN_3206 MycrhN_0102 MycrhN_0030 MycrhN_5755 MycrhN_0118 MycrhN_3188 MycrhN_3146 MycrhN_4026 MycrhN_4000 MycrhN_4006 MycrhN_2333 MycrhN_1308 MycrhN_3995 MycrhN_4188 MycrhN_0199 MycrhN_0935 MycrhN_3649 MycrhN_3898 MycrhN_3989
mmm	*Mycobacterium sp.* MOTT36Y	32	W7S_00165 W7S_03425 W7S_04140 W7S_06735 W7S_08360 W7S_18770 W7S_19955 W7S_20330 W7S_21440 W7S_08340 W7S_07185 W7S_04360 W7S_21155 W7S_20245 W7S_08345 W7S_13830 W7S_05795 W7S_03810 W7S_09175 W7S_03995 W7S_02760 W7S_03820 W7S_03675 W7S_16725 W7S_09225 W7S_05985 W7S_09965 W7S_18975 W7S_13715 W7S_13835 W7S_07185 W7S_23690
mcb	*Mycobacterium chubuense*	32	Mycch_1421 Mycch_1780 Mycch_1899 Mycch_2113 Mycch_2203 Mycch_2912 Mycch_3366 Mycch_3748 Mycch_3965 Mycch_4077 Mycch_5481 Mycch_5499 Mycch_5863 Mycch_0448 Mycch_4564 Mycch_1660 Mycch_0257 Mycch_4523 Mycch_3622 Mycch_0396 Mycch_3591 Mycch_4429 Mycch_3612, Mycch_3606, Mycch_3616, Mycch_1683, Mycch_3679, Mycch_1678, Mycch_3933, Mycch_3701, Mycch_0360, Mycch_4406
mli	*Mycobacterium liflandii*	40	MULP_00035, MULP_00580, MULP_00894, MULP_00900, MULP_01029, MULP_01271, MULP_01443,MULP_01509,MULP_01534,MULP_01537,MULP_01793,MULP_02609,MULP_03672,MULP_04127,MULP_04239, MULP_05437, MULP_05446, MULP_05708, MULP_02900, MULP_02645, MULP_04861, MULP_05324, MULP_00312, MULP_03687, MULP_03686, ,MULP_03672, MULP_01143, MULP_03369 MULP_04956(FdxD_2), MULP_04958, MULP_01030(FdxD_3), MULP_04991, MULP_04938, MULP_04952, MULP_04147(FdxD_1), MULP_02412, MULP_05239(FdxD), MULP_03073(FdxA_1), MULP_05296(FdxB), MULP_03752,
mkn	*Mycobacterium kansasii* ATCC 12478	33	MKAN_04240(4Fe-4S) MKAN_09955, MKAN_23805, MKAN_11680, MKAN_09835, MKAN_01235, MKAN_09910, MKAN_01295, MKAN_00170, MKAN_10125, MKAN_13235, MKAN_07250, MKAN_03855, MKAN_11975, MKAN_12135, MKAN_01670, MKAN_15935, MKAN_22820,MKAN_24980 MKAN_22480 MKAN_19550 MKAN_00605 MKAN_01240 MKAN_01290 MKAN_09430 MKAN_03850 MKAN_04960 MKAN_04965MKAN_06260MKAN_23165 MKAN_03620 MKAN_29025 MKAN_11285 MKAN_09950
mks	*Mycobacterium kansasii* 662	18	LG40_09790 LG40_11130 LG40_09795 LG40_23565 LG40_11530 LG40_09670 LG40_01245 LG40_09745 LG40_01305 LG40_00175 LG40_09965 LG40_25730 LG40_07180 LG40_03870 LG40_13075 LG40_04235 LG40_09280 LG40_01300
mki	*Mycobacterium kansasii* 824	18	LH54_11255 LH54_09935 LH54_09940 LH54_11665 LH54_09815 LH54_01255 LH54_09890 LH54_01315 LH54_00175 LH54_10110 LH54_25860 LH54_07190 LH54_04235 LH54_03870 LH54_13215 LH54_09390 LH54_15880 LH54_01310
mne	*Mycobacterium neoaurum*	28	D174_23865(4Fe-4S), D174_16370(4Fe-4S),D174_12890(4fe-4S), D174_04625, D174_12405, D174_20885, D174_13840, D174_02960, D174_09705, D174_19220 D174_23865(4Fe-4S), D174_16370(4Fe-4S),D174_12890(4fe-4S), D174_04625, D174_12405, D174_20885, D174_13840, D174_02960, D174_09705, D174_19220 D174_09620 D174_03225 D174_16365 D174_23110, D174_08080, D174_13835 D174_01045 D174_07020 D174_07210 D174_10230 D174_20080 D174_25635 D174_04385 D174_01075 D174_15525 D174_13855 D174_06575
myy	*Mycobacterium sp.* VKM Ac-1817D	36	G155_05675, G155_07610 , G155_08110, G155_11010 ,G155_16260 ,G155_21205, G155_23550, G155_26450, G155_27135, G155_29555, G155_05095 ,G155_12035, G155_20605, G155_03130 ,G155_08940, G155_03435, G155_01205, G155_10200, G155_29565, G155_09940 , G155_23245, G155_27910 G155_20635, G155_03845, G155_20490, G155_20655, G155_04895, G155_20825, G155_22240, G155_22210, G155_01230, G155_16695, G155_07985, G155_07895, G155_13780(2Fe-2S), G155_24550(2Fe-2S),

3.4. Conclusion

In this advanced scientific era redox systems are very important in the sense that P450s needs redox partners to perform their reactions. P450s require sequential delivery of two electrons passed from one or more redox partner enzymes to facilitate their activity. Although the P450 enzymes themselves show remarkable similarity in overall structure, it is increasingly apparent that there is enormous diversity in the redox partner systems that drive the P450 enzymes. The present study showed that many redox partners hit proteins were identified in mycobacterial species. Future work involves annotation and phylogenetic analysis of identified redox proteins.

3.5. References

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CHAPTER 4

ANNOTATION AND PHYLOGENETIC ANALYSIS OF P450 REDOX PARTNERS IN MYCOBACTERIA

4.1. Introduction

P450s are commonly known to be catalytically versatile enzymes (Bernhardt, 2006; Syed *et al*., 2014; Durairaj *et al*., 2016), consisting of a heme group bound to a thiolate group hence the name heme-thiolate proteins was given and they activate resting molecular oxygen (Hamdane *et al*., 2008) in order to complete the monooxygenation of substrates. Some P450s needs redox partner proteins to perform oxidation reactions (Hannemann *et al*., 2007). These redox partners usually oxidize NAD(P)H/NADH and deliver the electrons to the heme domain (Hannemann *et al*., 2007). P450s consist of the same structural fold (Sirim *et al*., 2010) to maintain their functionality mostly as monooxygenases. However, the differences between all P450s exist within their electron transport chains when the insight of both eukaryotic and prokaryotic organisms is compared in terms of preference to redox proteins (Hannemann *et al*., 2007). Various classes of redox partners exists and they function differently from each other. Mitochondrial and bacterial belong to Class I system (Table 4.1) and their similarities led to discussion that they were evolutionary linked (Lewis and Hlavica, 1999). The only difference between mitochondrion and bacterial is the preference for the co-factor i.e. NADPH or NADH. The bacterial type prefers NADH and mitochondrial prefers NADPH (Lewis and Hlavica, 1999).

Class II system consist of microsomal type which contained NADPH, FAD and FMN-containing reductase within the electron transport chain. Microsomal P450s are known to receive electron another protein know as cytochrome b_5. Cytochrome b_5 receive electrons

from cytochrome b_5 reductase which prefers co-factor NADH (Table 4.1) (Archakov and Bachmanova, 1990). Class III is known for not utilizing redox partners and also not catalyzing monooxgenase reactions. Class III include allene oxide synthase (CYP74), thromboxane synthase (CYP5A1) and prostacylin synthase (CYP8) (Table 4.1).

Table 4.1. Types of P450 redox partners (Taken from Lewis and Hlavica, 2000).

Class[a]	Type	Electron transport chain
I	Bacterial[b]	NADH→FAD-containing reductase→iron-redoxin→P450
	Mitochondrial	NADPH→FAD-containing reductase→iron-sulfur redoxin P450
II	Microsomal[c]	NADPH→FAD- and FMN-containing reductase→P450
	Bacillus megaterium (BM3)[d]	NADPH→FAD- and FMN –containing reductase→P450
III		

[a]Class III P450s include allene oxide synthase (CYP74), thromboxane synthase (CYP5A1) and prostacyclin synthase (CYP8). These do not require auxillary redox partner and do not catalyse monooxygenase reactions. These unsual forms of P450 are involved the rearrangement of endoperoxides or hyroperoxides.

[b]Most bacterial P450s possess this form of electron transfer chain, with the notable exception of CYP102 which is an example of Class II P540 monooxygenase.

[c]The microsomal system in mammalia also involves the mediation of cyctochrome b5 (association with cytochrome b5 reductase for electron transfer from NADH) primarily for the second reduction step in the cycle.

[d]The redox system in *Bacillus megaterium* (CYP102) comprises directly-linked reductase and hemeprotein domains within a single polypeptide chain

Current chapter work includes annotation and phylogenetic analysis of P450 redox proteins in Mycobacterial species. The redox proteins identified in the Chapter 3 will be grouped into different redox proteins such as ferredoxins, ferredoxin reducatases and non P450 redox proteins. Furthermore, different groups will be created based on the prosthetic groups present in the P450 redox proteins.

4.2. Methods

Sequence from the previous chapter was used for the analysis. Conserved protein domains (matched to InterPro and Pfam database entries) were identified using the InterPro Scan plugin in Geneious. Sequence editing was perfomed using Geneious v.8.1.7. Conserved domains present in the sequences were selected and aligned using MAFFT v. 7.017 (Katoh,*et al*., 2002) for further analysis. Phylogenetic analysis was performed using Maximum likelihood method using PHYML (Guindo and Gascuel, 2003) as implemented in geneious, each with 1000 bootsrap replicates.

4.3. Results and discussion

The hypothetical redox proteins identified in previous chapter were subjected to annotation as described in the methods and classified all proteins into ferredoxins, ferredoxin reductases and non P450 redox proteins as shown in the below Table 4.2. Some reductases were found to be divergent hence they were named under iron-sulfur binding reductases.

Table 4.2. Annotation of P450 redox proteins in mycobacterial species. The species codes, their names and protein IDs were retrieved form KEGG website.

Species code	Species name	Number	Type	Protein ID
mtc	*Mycobacterium tuberculosis* CDC1551	6	Ferredoxin	MT3607(4Fe-4S), MT1835 (4Fe-4S), MT2063(fdxA; 4Fe-4S), MT1214(fdxC; 4Fe-4S); ; MT0787.1 (4Fe-4S)
		8	Ferredoxin reductase	MT0716 (ferredoxin reductase); MT1918 (NADP reductase), MT0909 (NADP); MT3658 (NAD), MT3327 (FAD & NAD), MT3676, MT2846, MT3189(fprA) MT1987
		17	Non P450 redox proteins	MT1366, MT3774 (thioredoxin-related protein); MT1643, Mt2298, MT2597 (Peroxiredoxin (PRX) family, Bacterioferritin comigratory protein (BCP) subfamily); MT3139 (glutaredoxin-like protein NrdH); MT3290.1, MT3292, MT3315, MT3358 , MT3525, MT3783 , MT3976, (conserved hypothetical protein); MT0266 (NAD(P)H-dependent nitrite reductase); MT3402 (alpha keto acid dehydrogenase complex, E3 component, lipoamide dehydrogenase) ; MT0511 (GMC family), MT1860
mtf	*Mycobacterium tuberculosis* F11	5	Ferredoxin	TBFG_10778, TBFG_13537(fdxD), TBFG_11816 , TBFG_12039(fdxA), TBFG_11202(fdxC),
		7	Ferredoxin reductase	TBFG_10903(fprB); TBFG_13259 (2Fe-2S, FAD, NADP), TBFG_12789 (2Fe- 2S); TBFG_13123 (fprA); ; TBFG_10702 (ferredoxin reductase) ; TBFG_11897 (ferredoxin reductase) TBFG_13587 (fdxB)
		1	Hypothetical iron-sulfur binding reductase	TBFG_10343 (4Fe-4S)
		16	Non P450 redox proteins	TBFG_10022, TBFG_13219, TBFG_13245 , TBFG_13289 , TBFG_13450, TBFG_13712, TBFG_13897, (transcriptional regulatory protein whib-like whiB5); TBFG_12456, TBFG_12542 (peroxiredoxin) ; TBFG_13069, TBFG_13221 (glutaredoxin-like protein NrdH), TBFG_13704 (thioredoxin-related protein), TBFG_10500 (GMC type) ; TBFG_13162 (NADPH quinone); TBFG_10571 (hypothetical oxidoreductases), TBFG_10810 (dihydrolipoamide dehydrogenase)
mtb	*Mycobacterium tuberculosis* KZN 1435	5	Ferredoxin	TBMG_00778, TBMG_03548(fdxD), TBMG_02211, TBMG_01979(fdxA), TBMG_02804(fdxC),
		7	Ferredoxin reductase	TBMG_03278,TBMG_00860(fprA) , TBMG_03104 (fprB), TBMG_02125 (3-phenylpropionate/trans-cinnamate dioxygenase ferredoxin reductase); TBMG_00701 (ferredoxin reductase), TBMG_03104(fprB), TBMG_01198 (2Fe-2S, NAD)
		1	Hypothetical iron-sulfur binding reductase	TBMG_00342 (4Fe-4S)
		8	Non P450 redox proteins	TBMG_00915 (glutaredoxin-like protein NrdH), TBMG_01451(peroxiredoxin); TBMG_00496(GMC-type), TBMG_00496 (GMC-type); TBMG_03184 (NADPH2:quinone reductase); TBMG_00810 (dihydrolipoamide dehydrogenase); TBMG_00566(oxidoreductases); TBMG_00496 (oxidoreductase gmc-type),
mtk	*Mycobacterium tuberculosis* KZN 4207	5	Ferredoxin	TBSG_00782(4Fe-4S), TBSG_03570(fdxD), TBSG_02223(4Fe-4S), TBSG_01990(fdxA) , TBSG_02818(fdxC)
		6	Ferredoxin reductase	TBSG_00705(ferredoxin reductase), TBSG_02136(ferredoxin reductase) TBSG_03124 (ferredoxin reductase), TBSG_00866 (ferredoxin reductase), TBSG_03301(oxidoreductases) TBSG_03620 (fdxB),
		1	Hypothetical iron-sulfur	TBSG_00345 (4Fe-4S)

			binding reductase	
		10	Non P450 redox proteins	TBSG_00501(oxireductase gmc-type)TBSG_00572(oxidoreductase), TBSG_03206 (quinone oxidoreducatase), TBSG_02256(oxidoreductase), TBSG_00501 (oxidoreductase gmc-type), TBSG_00920, TBSG_03263 (glutaredoxin-like protein NrdH); TBSG_01462, TBSG_01554 (peroxiredoxin), TBSG_00815(oxidoreductase)
mtz	*Mycobacterium tuberculosis* KZN 605	5	Ferredoxin	TBXG_000771(4Fe-4S), TBXG_003519 (fdxD), TBXG_002192(4Fe-4S), TBXG_001963(fdxA), TBXG_002784 (fdxC) ,
		6	Ferredoxin reductase	TBXG_003083(ferredoxin reductase), TBXG_003259(ferredoxin reductase), TBXG_001187(ferredoxin reductase) , TBXG_002107 (ferredoxin reductase), TBXG_000694(ferredoxin reductase), TBXG_003569(fdxB),
		1	Hypothetical iron-sulfur binding reductase	TBXG_000340(4Fe-4S)
		10	Non P450 redox proteins	TBXG_000563(oxidoreductase),TBXG_000803(oxidoreductase), TBXG_003165 (quinone), TBXG_002225 (oxireductase), TBXG_000852(oxidoreductase gmc-type) , TBXG_000493(oxireductase gmc-type) , TBXG_000906(glutaredoxin-like protein NrdH) TBXG_001438 ((peroxiredoxin) TBXG_001530 (peroxiredoxin), TBXG_003221 (glutaredoxin protein)
mtg	*Mycobacterium tuberculosis* RGTB327	5	Ferredoxin	MRGA327_04750 (4Fe-4S), MRGA327_21565(4Fe-4S), MRGA327_11075(4Fe-4S), MRGA327_12375(FDXA) ,MRGA327_07415 (fdxC),
		7	Ferredoxin reductase	MRGA327_21950(fdxb) MRGA327_05550(ferredoxin reductase), MRGA327_19880(ferredoxin reductase), MRGA327_17010(ferredoxin reductase), MRGA327_19110 (ferredoxin--NADP+ reductase) ,MRGA327_11545 (ferredoxin reductase), MRGA327_04305(ferredoxin reductase),
		1	Hypothetical iron-sulfur binding reductase	MRGA327_02135(4Fe-4S),
		10	Non P450 redox proteins	MRGA327_00160 (transcriptional regulatory protein whib-like whiB5), MRGA327_14985 (peroxiredoxin), MRGA327_15540(peroxiredoxin), MRGA327_18760 (glutaredoxin protein) ,MRGA327_19665 (glutaredoxin protein), MRGA327_19800 (transcriptional regulatory protein whib-like whiB5), MRGA327_21070 (transcriptional regulatory protein whib-like whiB5), MRGA327_22675 (transcriptional regulatory protein whib-like whiB5), MRGA327_23785(transcriptional regulatory protein whib-like whiB5)
mti	*Mycobacterium tuberculosis* RGTB423	3	Ferredoxin	MRGA423_22055(4Fe-4S), MRGA423_12495(FDxa), MRGA423_07345 (fdxC),
		7	Ferredoxin reductase	MRGA423_19385(ferredoxin reductase), MRGA423_04295(ferredoxin reductase), MRGA423_20255(ferredoxin reductase), MRGA423_11670 (Ferredoxin reductase), MRGA423_17210(ferredoxin reductase), MRGA423_19380(ferredoxin reductase) MRGA423_22465(FDXB),
		1	iron-sulfur-binding reductase	MRGA423_02125(4Fe-4S)
		14	Non P450 redox proteins	MRGA423_00155(transcriptional regulatory protein whib-like whiB5) ,MRGA423_15140(peroxiredoxin), MRGA423_15775((peroxiredoxin), MRGA423_19000 (glutaredoxin protein) ,MRGA423_19995 (transcriptional regulatory protein whib-like whiB5), MRGA423_20010 (glutaredoxin protein), MRGA423_20170 (transcriptional regulatory protein whib-like whiB5),MRGA423_21510(transcriptional regulatory protein whib-like whiB5), MRGA423_23205(transcriptional regulatory protein whib-like whiB5), MRGA423_24370 (transcriptional regulatory protein whib-like whiB5), MRGA423_19585(quinone oxidoreductase FADB4) MRGA327_04965, (oxidoreductase), MRGA327_03520(oxidoreductase), MRGA423_03085(oxidoreductase)
mte	*Mycobacterium tuberculosis* CCDC5079	2	Ferredoxin	CCDC5079_1854 (FDXA), CDC5079_1089 (fdxC),
		5	Ferredoxin reductase	CCDC5079_0817 (ferredoxin reductase), CCDC5079_3295 (fdxB), CCDC5079_0640(ferredoxin reductase),

				CCDC5079_2981 (ferredoxin reductase), CCDC5079_2546(ferredoxin reductase),
		1	Iron-sulfur binding reductase	CCDC5079_0315(4Fe-4S)
		11	Non P450 redox proteins	CCDC5079_2323 (peroxiredoxin), CCDC5079_3008 (K18955 WhiB family transcriptional regulator), CCDC5079_3162 (transcriptional regulatory protein WHIB-like WHIB3), CCDC5079_3403 (thioredoxin-like protein), CCDC5079_3412 (transcriptional regulatory protein WHIB-like WHIB3), CCDC5079_0461(Oxidoreductase gmc-type), CCDC5079_2863(ferredoxin reductase), CCDC5079_2896(quinone oxidorectase), CCDC5079_0461(Oxidoreductase gmc-type), CCDC5079_0735(oxidoreductase), CCDC5079_0527(oxidoreductase)
mtur	*Mycobacterium tuberculosis* CCDC5079	6	Ferredoxin	CFBS_0802(4Fe-4S), CFBS_3719(fdxD), CFBS_1875, (4Fe-4S), CFBS_2117(fdxA), CFBS_1256 (fdxC), CFBS_1256 (fdxC),
		7	Ferredoxin reductase	CFBS_0929(ferredoxin reductase), CFBS_3420 (ferredoxin reductase), CFBS_2933 (ferredoxin reductase), CFBS_3276 (ferredoxin reductase), CFBS_1961(ferredoxin reductase), CFBS_0723 (ferredoxin reductase) CFBS_3770 (fdxB),
		19	Non P450 redox proteins	CFBS_0027(whiB5; transcriptional regulator whib-like protein) ,CFBS_1409 (thioredoxin) ,CFBS_2371 (peroxiredoxin), CFBS_2671 (peroxiredoxin), CFBS_3221(putative glutaredoxin NrdH), CFBS_3381(whiB5; transcriptional regulator whib-like protein), CFBS_3383 (putative glutaredoxin protein), CFBS_3406 (whiB5; transcriptional regulator whib-like protein), CFBS_3449 (K18955 WhiB family transcriptional regulator), CFBS_3620(transcriptional regulatory protein whib-like WhiB3), CFBS_3892 (thioredoxin-related protein) CFBS_3902 (K18955 WhiB family transcriptional regulator), CFBS_4094(transcriptional regulatory protein WHIB-like WHIB6), CFBS_2427 (oxidoreductase), CFBS_2427 (oxidoreductase), CFBS_0512 (oxidoreductase gmc-type), CFBS_3318(quinone oxidoreductase FadB4), CFBS_0835(oxidoreductase) CFBS_0835 (oxidoreductase), CFBS_0585(oxidoreductase), CFBS_0512 (oxidoreductase gmc-type)
mtl	*Mycobacterium tuberculosis* CCDC5180	1	Ferredoxin	CCDC5180_1829(fdxa),
		6	Ferredoxin reductase	CCDC5180_0810(ferredoxin reductase), CCDC5180_2943(ferredoxin reductase), CCDC5180_2826(ferredoxin reductase), CCDC5180_1704(ferredoxin reductase), CCDC5180_0631(ferredoxin reductase), CCDC5180_3247(fdxB),
		1	iron-sulfur-binding reductas	CCDC5180_0312(4Fe-4S)
		10	Non P450 redox proteins	CCDC5180_0487(thioredoxin protein), CCDC5180_2295(peroxiredoxin), CCDC5180_2971(K18955 WhiB family transcriptional regulator), CCDC5180_3114(transcriptional regulatory protein WHIB-like WHIB3), CCDC5180_3362(K18955 WhiB family transcriptional regulator), CCDC5180_0454(oxidoreductase gmc-type), CCDC5180_2857(NADPH quinone oxidoreductase fadB4), CCDC5180_0727(oxidoreductase), CCDC5180_0519 (oxidoreductase), CCDC5180_0454 (oxidoreductase gmc-type)
mto	*Mycobacterium tuberculosis* CTRI-2	5	Ferredoxin	MTCTRI2_0782(4Fe-4S), MTCTRI2_3569(FdxD), MTCTRI2_1817(4Fe-4S), MTCTRI2_2041(fdxA), MTCTRI2_1209(fdxC),
		7	Ferrredoxin reductase	MTCTRI2_0909(ferredoxin reductase), MTCTRI2_3169(ferredoxin reductase), MTCTRI2_1901(ferredoxin reductase), MTCTRI2_0704(ferredoxin reductase), MTCTRI2_3297(ferredoxin reductase), MTCTRI2_2829(ferredoxin reductase) MTCTRI2_3618(fdxb),
		1	iron-sulfur-binding reductase	MTCTRI2_0345(4Fe-4S)
		16	Non P450 redox proteins	MTCTRI2_0025(transcriptional regulatory protein WHIB-like WHIB5), MTCTRI2_0534(thioredoxin protein), MTCTRI2_2569(peroxiredoxin), MTCTRI2_3116(K06191 glutaredoxin-like protein NrdH), MTCTRI2_3259(transcriptional regulatory protein WHIB-like WHIB7), MTCTRI2_3261(glutaredoxin protein), MTCTRI2_3283(transcriptional regulatory protein WHIB-like WHIB1), MTCTRI2_3327(transcriptional regulatory protein WHIB-like

				WHIB2), MTCTRI2_3488(transcriptional regulatory protein WHIB-like WHIB3), MTCTRI2_3741(membrane-anchored thioredoxin-like protein), MTCTRI2_3750(transcriptional regulatory protein WHIB-like WHIB4), MTCTRI2_3941(transcriptional regulatory protein WHIB-like WHIB6), MTCTRI2_0497(oxidoreductase GMC-type), MTCTRI2_3204(fadB4; NADPH quinone oxidoreductase), MTCTRI2_0813(oxidoreductase), MTCTRI2_0569
mtd	*Mycobacterium tuberculosis* UT205	1	ferredoxin	UDA_3503c(fdxD),
		2	Ferredoxin reductase	UDA_0886(ferredoxin reductase), UDA_3106(ferredoxin reductase),
		22	Non P450 redox proteins	UDA_0022c(K18956 WhiB family transcriptional regulator), UDA_1324(K05838 putative thioredoxin), UDA_1471 (K00384 thioredoxin reductase), UDA_1608c(peroxiredoxin), UDA_1932(atypical 2-Cys peroxiredoxin), UDA_2428(K03386 peroxiredoxin), UDA_2238c(K03386 peroxiredoxin), UDA_2521(K03564 peroxiredoxin), UDA_3053c(K06191 glutaredoxin-like protein NrdH), UDA_3197A(K18958 WhiB family transcriptional regulator), UDA_3198A(K18917 mycoredoxin), UDA_3219(K18955 WhiB family transcriptional regulator), UDA_3260c(K18955 WhiB family transcriptional regulator), UDA_3416(K18955 WhiB family transcriptional regulator), UDA_3681c(K18955 WhiB family transcriptional regulator), UDA_3862c(K18957 WhiB family transcriptional regulator), UDA_3913(K00384 thioredoxin reductase), UDA_3914 (K03671 thioredoxin 1), UDA_2391(sulfite reductase (ferredoxin), UDA_2454c (2-oxoglutarate/2-oxoacid ferredoxin oxidoreductase), UDA_2455c (ferredoxin), UDA_2454c (2-oxoglutarate/2-oxoacid ferredoxin oxidoreductase)
mtn	*Mycobacterium tuberculosis* Erdman = ATCC 35801	*5*	ferredoxin	ERDMAN_0845(4Fe-4S), ERDMAN_3844(fdxD), ERDMAN_2211(fdxA), ERDMAN_1320(fdxC),
		6	Ferredoxin reductase	ERDMAN_0979(ferredoxin reductase), ERDMAN_3543(oxidoreductase), ERDMAN_3042(oxidoreductase), ERDMAN_2061(ferredoxin reductase), ERDMAN_0759(ferredoxin reductase), ERDMAN_3899(fdxB)
		1	iron-sulfur-binding reductase	ERDMAN_0374(4Fe-4S)
		11	Non P450 redox proteins	ERDMAN_0028(WHIB-like transcriptional regulatory protein), ERDMAN_0577(thioredoxin protein), ERDMAN_2774(K03564 peroxiredoxin), ERDMAN_3342(K06191 glutaredoxin-like protein NrdH), ERDMAN_3508(glutaredoxin protein), ERDMAN_4021(thioredoxin-like protein), ERDMAN_0538(oxidoreductase), ERDMAN_3441(fadB4; NADPH quinone oxidoreductase), ERDMAN_0879(oxidoreductase) , ERDMAN_0538(oxidoreductase), ERDMAN_0614(oxidoreductase
mtj	*Mycobacterium tuberculosis* Beijing/NITR203	5	ferredoxin	J112_04105(4Fe-4S), J112_18830(fdxD), J112_09550(4Fe-4S), J112_10735(4Fe-4S), J112_06365(fdxC),
		8	Ferredoxin reductase	J112_04765(ferredoxin reductase), J112_17365(ferredoxin reductase), J112_14865(ferredoxin reductase), J112_16650(ferredoxin reductase), J112_04765(ferredoxin reductase), J112_09960(ferredoxin reductase), J112_03680(ferredoxin reductase), J112_19130(fdxB),
		1	iron-sulfur-binding reductase	J112_01820(4Fe-4S),
		12	Non P450 redox proteins	J112_00125(transcriptional regulatory protein WHIB-like WHIB5), J112_02815(thioredoxin protein), J112_13525(K03564 peroxiredoxin), J112_16355(glutaredoxin electron transport protein NrdH), J112_17165(glutaredoxin protein), J112_19740(thioredoxin-like protein), J112_20755(transcriptional regulatory protein WHIB-like WHIB6), J112_20755(transcriptional regulatory protein WHIB-like WHIB6), J112_02620(oxidoreductase gmc-type), J112_16845(NADPH quinone oxidoreductase), J112_04265(oxidoreductase), J112_03005(oxidoreductase)
mtub	*Mycobacterium tuberculosis* 7199-99	*3*	ferredoxin	MT7199_1812(4Fe-4s), MT7199_2038(FDXA), MT7199_1207(fdxc),

		7	Ferredoxin reductase	MT7199_3272(ferredoxin reductase), MT7199_2809(ferredoxin reductase), MT7199_3139(ferredoxin reductase), MT7199_1895(ferredoxin reductase), MT7199_0706(FERREDOXIN REDUCTASE) MT7199_0905(ferredoxin reductase) MT7199_3616(fdxb),
		1	Iron sulphur binding reductase	MT7199_0344(4Fe-4S)
		18	Non P450 redox proteins	MT7199_0022(PUTATIVE TRANSCRIPTIONAL REGULATORY protein), MT7199_0540(putative THIOREDOXIN protein), MT7199_2460(ALKYL HYDROPEROXIDE REDUCTASE C protein AHPC), MT7199_2552(K03564 peroxiredoxin), MT7199_3087(GLUTAREDOXIN-LIKE protein) NRDH), MT7199_3234(redox-sensing transcriptional regulator), MT7199_3236(K18917 mycoredoxin), MT7199_3258(redox-sensing transcriptional regulator), MT7199_3294(K00496 alkane 1-monooxygenase), MT7199_3302(K18955 WhiB family transcriptional regulator), MT7199_3463(K18955 WhiB family transcriptional regulator), MT7199_3736(THIOREDOXIN-LIKE protein), MT7199_3745(K18955 WhiB family transcriptional regulator) MT7199_3931(MT7199_3564), MT7199_0502(OXIDOREDUCTASE GMC-TYPE), MT7199_3179(NADPH QUINONE OXIDOREDUCTASE FADB4), MT7199_0815(oxidoreductase)
mtuc	*Mycobacterium tuberculosis* CAS/NITR204	5	ferredoxin	J113_05385(4Fe-4S), J113_24450(fdxD), J113_12425(Fe-4s), J113_13860(4Fe-4S), J113_08245(fdxc),
		3	Ferredoxin reductase	J113_12960(ferredoxin reductase), J113_04870(ferredoxin reductase) J113_24860(fdxb),
		1	iron-sulfur-binding reductase	J113_02425(4Fe-4S)
		9	Non P450 redox proteins	J113_00155(putative OXIDOREDUCTASE), J113_03725(thioredoxin protein), J113_17540(K03564 peroxiredoxin), J113_21265(K06191 glutaredoxin-like protein NrdH) J113_22265(K18958 WhiB family transcriptional regulator) ,J113_22285(glutaredoxin protein), J113_25655(thioredoxin-like protein), J113_26995(transcriptional regulatory protein WHIB-like WHIB6), J113_05590(oxidoreductase)
mtue	*Mycobacterium tuberculosis* EAI5/NITR206	5	ferredoxin	J114_04075(4Fe-4S), J114_18730(fdxD), J114_09545(4Fe-4S), J114_10740(4Fe-4S), J114_06365(fdxC),
		7	Ferredoxin reductase	J114_04715(ferredoxin reductase), J114_17320(ferredoxin reductase), J114_14805(ferredoxin reductase), J114_16620(ferredoxin reductase), J114_09960(ferredoxin reductase). J114_03670(ferredoxin reductase), J114_19010(fdxb),
		1	iron-sulfur-binding reductase	J114_01820(4Fe-4S)
		13	Non P450 redox proteins	J114_00135(transcriptional regulatory protein WHIB-like WHIB5), J114_02810(thioredoxin protein), J114_13485(K03564 peroxiredoxin), J114_16325(K06191 glutaredoxin-like protein NrdH), J114_17120(glutaredoxin protein), J114_19620(thioredoxin-like protein), J114_20635(transcriptional regulatory protein WHIB-like WHIB6), J114_04075(4Fe-4S), J114_02620(oxidoreductase), J114_16810(NADPH quinone oxidoreductase), J114_04240(oxidoreductase), J114_03000(oxidoreductase), J114_02620(oxidoreductase)
mtx	*Mycobacterium tuberculosis* EAI5	5	Ferredoxin	M943_03995(4Fe-4S), M943_18015(4Fe-4S), M943_09300(4Fe-4S), M943_10425(4Fe-4S), M943_06175(4Fe-4S)
		4	Ferredoxin reductase	M943_04625(ferredoxin reductase), M943_14340(ferredoxin reductase), M943_16035(ferredoxin reductase), M943_09710(ferredoxin reductase)
		9	Non P450 redox proteins	M943_06945(K05838 putative thioredoxin), M943_15755(glutaredoxin), M943_08070(oxidoreductase), M943_02555(oxidoreductase), M943_11865(oxidoreductase), M943_07495(oxidoreductase), M943_03575(oxidoreductase), M943_04160(oxidoreductase) M943_02905(oxidoreductase).
mtuh	*Mycobacterium tuberculosis*		Ferredoxin	I917_05410(4Fe-4S), I917_24570(fdx), I917_12705(4Fe-4S), I917_14190(4Fe-4S), I917_08355(fdxC),

	Haarlem/NITR202	5		
		2	Ferredoxin reductase	I917_04905(ferredoxin reductase) I917_24940(fdxb),
		10	Non P450 redox proteins	I917_00160(transcriptional regulatory protein WHIB-like WHIB5), I917_03790(thioredoxin protein), I917_17785(K03564 peroxiredoxin), I917_21435(K06191 glutaredoxin-like protein NrdH), I917_22450(glutaredoxin protein), I917_22585(transcriptional regulatory protein whiB-like whiB1), I917_24010(transcriptional regulatory protein WHIB-like WHIB3), I917_25725(thioredoxin-like protein), I917_27140(transcriptional regulatory protein WHIB-like WHIB6), I917_19450(oxidoreductase)
mtul	*Mycobacterium tuberculosis* Haarlem	5	Ferredoxin	TBHG_00755(4Fe-4S), TBHG_03447(FdxD), TBHG_01744(ferredoxin), TBHG_01965(FdxA), TBHG_01161(FdxC),
		7	Ferredoxin reductase	TBHG_00874(ferredoxin reductase), TBHG_03166(ferredoxin reductase), TBHG_02708(ferredoxin reductase), TBHG_03037(ferredoxin reductase), TBHG_00874(ferredoxin reductase), TBHG_01824(ferredoxin reductase), TBHG_03494(FdxB),
		16	Non P450 redox proteins	TBHG_02457(K03564 peroxiredoxin), TBHG_02982(K06191 glutaredoxin-like protein NrdH), TBHG_03129(glutaredoxin-like protein), TBHG_03608(thioredoxin-like protein), TBHG_01894(oxidoreductase), TBHG_00380(oxidoreductase), TBHG_00333(oxidoreductase), TBHG_00490(oxidoreductase), TBHG_03013(oxidoreductase), TBHG_01708(oxidoreductase), TBHG_01411(oxidoreductase), TBHG_03072(quinone oxidoreductase FadB4), TBHG_00683(oxidoreductase), TBHG_00326(quinone oxidoreductase), TBHG_00558(oxidoreductase), TBHG_02978(oxidoreductase)
mtut	*Mycobacterium tuberculosis* BT1	0	ferredoxin	
		0	Ferredoxin reductase	
		13	Non P450 redox proteins	HKBT1_0027(K18956 WhiB family transcriptional regulator), HKBT1_1408(K05838 putative thioredoxin), HKBT1_2362(K03386 peroxiredoxin), HKBT1_2662(K03564 peroxiredoxin), HKBT1_3208(K06191 glutaredoxin-like protein NrdH), HKBT1_3368(redox-sensing transcriptional regulator), HKBT1_3370(putative glutaredoxin protein), HKBT1_3393(K18955 WhiB family transcriptional regulator), HKBT1_3436(K18955 WhiB family transcriptional regulator), HKBT1_3607(K18955 WhiB family transcriptional regulator), HKBT1_3876(thioredoxin-related protein), HKBT1_3886(K18955 WhiB family transcriptional regulator), HKBT1_4076(transcriptional regulatory protein WHIB-like WHIB6).
mtuu	*Mycobacterium tuberculosis* BT2	6	ferredoxin	HKBT2_0803(4Fe-4S), HKBT2_3713(FdxD), HKBT2_1882(4Fe-4S), HKBT2_2113(fdxA), HKBT2_1260(FDxC), HKBT2_3713(FdxD),
		8	Ferredoxin reductase	HKBT2_0930(Ferredoxin reductase), HKBT2_3414(ferredoxin reductase), HKBT2_2924(ferredoxin reductase), HKBT2_3268(ferredoxin reductase), HKBT2_0930(ferredoxin reductase), HKBT2_1966(ferredoxin reductase), HKBT2_0724(ferredoxin reductase). HKBT2_3764(FdxB),
		1	iron-sulfur-binding reductase	HKBT2_0354(4Fe-4S),
		16	Non P450 redox proteins	HKBT2_0027(K18956 WhiB family transcriptional regulator), HKBT2_1414(K05838 putative thioredoxin), HKBT2_2364(K03386 peroxiredoxin), HKBT2_2665(K03564 peroxiredoxin), HKBT2_3213(K06191 glutaredoxin-like protein NrdH), HKBT2_3375(redox-sensing transcriptional regulator), HKBT2_3377(K18917 mycoredoxin), HKBT2_3400(redox-sensing transcriptional regulator), HKBT2_3443(K18955 WhiB family transcriptional regulator), HKBT2_3614(K18955 WhiB family transcriptional regulator), HKBT2_3885(thioredoxin-related protein), HKBT2_3895(K18955 WhiB family transcriptional regulator), HKBT2_4086(K18957 WhiB family transcriptional regulator), HKBT2_2420(oxidoreductase), HKBT2_0512(oxidoreductase gmc-type), HKBT2_3310(NADPH

				quinone oxidoreductase FadB4),
mtg	*Mycobacterium tuberculosis* HKBS1	5	ferredoxin	HKBS1_0802(4Fe-4S), HKBS1_3716(fdxD), HKBS1_1878(4fe-4S), HKBS1_2118(fdxA), HKBS1_1258(fdxC),
		7	Ferredoxin reductase	HKBS1_0929(ferredoxin reductase), HKBS1_3417(ferredoxin reductase), HKBS1_2928(ferredoxin reductase), HKBS1_3274(ferredoxin reductase), HKBS1_1962(ferredoxin reductase), HKBS1_0723(ferredoxin reductase). HKBS1_3767(fdxB),
		1	iron-sulfur-binding reductase	HKBS1_0354(4Fe-4S),
		17	Non P450 redox proteins	HKBS1_0027(K18956 WhiB family transcriptional regulator), HKBS1_1412(K05838 putative thioredoxin), HKBS1_2368(K03386 peroxiredoxin), HKBS1_2669(K03564 peroxiredoxin), HKBS1_3219(K06191 glutaredoxin-like protein NrdH), HKBS1_3378(K18958 WhiB family transcriptional regulator), HKBS1_3380(K18917 mycoredoxin), HKBS1_3403(; K18955 WhiB family transcriptional regulator), HKBS1_3446(redox-sensing transcriptional regulator), HKBS1_3617(K18955 WhiB family transcriptional regulator), HKBS1_3889(thioredoxin-related protein), HKBS1_3899(K18955 WhiB family transcriptional regulator), HKBS1_4089(K18957 WhiB family transcriptional regulator), HKBS1_2424(Oxidoreductase), HKBS1_0512(oxidoreductase gmc-type), HKBS1_3316(putative NADPH quinone oxidoreductase FadB4), HKBS1_0835(oxidoreductase).
mbo	*Mycobacterium bovis* AF2122/97	5	ferredoxin	Mb0786c(4Fe-4S), Mb3533c(FdxD), Mb1814(4Fe-4S), Mb2030c(fdxA), Mb1210(fdxC),
		7	Ferredoxin reductase	Mb0910(ferredoxin reductase), Mb3259c(ferredoxin reductase), Mb2798c(ferredoxin reductase), Mb3133(ferredoxin reductase), Mb1900c(ferredoxin reductase), Mb0707(ferredoxin reductase), Mb3584(fdxB),
		1	iron-sulfur-binding reductase	Mb0345c(4Fe-4S)
		9	Non P450 redox proteins	Mb0539(thioredoxin protein), Mb2550(K03564 peroxiredoxin), Mb3079c(K06191 glutaredoxin-like protein NrdH), Mb3223(K18917 mycoredoxin), Mb3697c(thioredoxin-like protein), Mb3706c(K18955 WhiB family transcriptional regulator), Mb0502c(oxidoreductase GMC-type), Mb0819c(oxidoreductase), Mb0576c(oxidoreductase).
mbb	*Mycobacterium bovis BCG* Pasteur 1173P2	5	ferredoxin	BCG_0815c(4Fe-4S), BCG_3567c(fdxD), BCG_1818(4Fe-4S), BCG_2024c(fdxA), BCG_1240(fdxC),
		8	Ferredoxin reductase	BCG_0938(ferredoxin reductase), BCG_3353c(ferredoxin reductase), BCG_3260c(ferredoxin reductase), BCG_2793c(ferredoxin reductase), BCG_3131(ferredoxin reductase), BCG_1905c(ferredoxin reductase), BCG_0737(ferredoxin reductase), BCG_3618(fdxB),
		1	iron-sulfur-binding reductase	BCG_0377c(4Fe-4S)
		18	Non P450 redox proteins	BCG_0052c(K18956 WhiB family transcriptional regulator), BCG_0569(thioredoxin protein), BCG_2542(K03564 peroxiredoxin), BCG_3077c(K06191 glutaredoxin-like protein NrdH), BCG_3221c(K18958 WhiB family transcriptional regulator), BCG_3223(K18917 mycoredoxin), BCG_3246(transcriptional regulatory protein whiB-like whiB1), BCG_3289c(K18955 WhiB family transcriptional regulator), BCG_3339(K18955 WhiB family transcriptional regulator), BCG_3486(K18955 WhiB family transcriptional regulator), BCG_3731c(membrane-anchored thioredoxin-like protein), BCG_3740c (K18955 WhiB family transcriptional regulator), BCG_3925c(K18957 WhiB family transcriptional regulator), BCG_0533c(oxidoreductase GMC-type), BCG_3164(NADPH quinone oxidoreductase fadB4), BCG_0848c(oxidoreductase), BCG_0606c(oxidoreductase), BCG_0533c(oxidoreductase GMC-type).
mbt	*Mycobacterium bovis BCG* Tokyo 172	5	ferredoxin	JTY_0785(4fe-4S), JTY_3567(fdxD), JTY_1802(4Fe-4S) JTY_2019(fdxA), JTY_1213(fdxC)
		5	Ferredoxin reductase	JTY_0908(ferredoxin reductase), JTY_3255(ferredoxin reductase), JTY_2787(ferredoxin reductase), JTY_ 1889(ferredoxin reductase), JTY_0707(ferredoxin reductase),

		1	iron-sulfur-binding reductase	JTY_0347(4fe-4S),
		16	Non P450 redox proteins	JTY_0539(putative thioredoxin protein), JTY_2536(K03564 peroxiredoxin), JTY_3072(K06191 glutaredoxin-like protein NrdH), JTY_3216(K18958 WhiB family transcriptional regulator), JTY_3218(putative glutaredoxin protein), JTY_3241(redox-sensing transcriptional regulator), JTY_3285(K18955 WhiB family transcriptional regulator), JTY_3486(K18955 WhiB family transcriptional regulator), JTY_3732(thioredoxin-like protein), JTY_3741(K18955 WhiB family transcriptional regulator), JTY_3927(K18957 WhiB family transcriptional regulator), JTY_0503(oxidoreductase GMC-type), JTY_3126(ferredoxin reductase), JTY_3159(K00344 NADPH2:quinone reductase), JTY_0818(oxidoreductase), JTY_0576(oxidoreductase).
mbm	*Mycobacterium bovis BCG* Mexico	4	ferredoxin	BCGMEX_0786c(4Fe-4S), BCGMEX_1799(4Fe-4S), BCGMEX_2006c(fdxA), BCGMEX_1212(fdxC),
		7	Ferredoxin reductase	BCGMEX_0909(ferredoxin reductase), BCGMEX_3351c(ferredoxin reductase), BCGMEX_3258c(ferredoxin reductase), BCGMEX_2786c(ferredoxin reductase), BCGMEX_3128(ferredoxin reductase), BCGMEX_1886c(ferredoxin reductase), BCGMEX_0708(ferredoxin reductase),
		1	iron-sulfur-binding reductase	BCGMEX_0347c(4Fe-4S)
		16	Non P450 redox proteins	BCGMEX_0022c(putative transcriptional regulatory protein whiB-like protein), BCGMEX_0540(putative thioredoxin protein), BCGMEX_2437(K03386 peroxiredoxin), BCGMEX_2534(K03564 peroxiredoxin), BCGMEX_3074c(K06191 glutaredoxin-like protein NrdH), BCGMEX_3218c(K18958 WhiB family transcriptional regulator), BCGMEX_3220(K18917 mycoredoxin), BCGMEX_3244(redox-sensing transcriptional regulator), BCGMEX_3287c(redox-sensing transcriptional regulator), BCGMEX_3337(redox-sensing transcriptional regulator), BCGMEX_3484(redox-sensing transcriptional regulator), BCGMEX_3731c(thioredoxin-like protein), BCGMEX_3740c(K18955 WhiB family transcriptional regulator), BCGMEX_0504c(oxidoreductase GMC-type), BCGMEX_0819c(oxidoreductase), BCGMEX_0577c(oxidoreductase)
mbk	*Mycobacterium bovis* BCG Korea 1168P	5	ferredoxin	K60_008160(4Fe-4S) K60_036380(FdxD), K60_018710(4Fe-4S), K60_020800(4Fe-4S), K60_012700(FdxC),
		8	Ferredoxin reductase	K60_009450(ferredoxin reductase), K60_032230(ferredoxin reductase), K60_019560(ferredoxin reductase), K60_007330(ferredoxin reductase), K60_041260(ferredoxin reductase), K60_040920(ferredoxin reductase), K60_033600(ferredoxin reductase), K60_028720(ferredoxin reductase)
		1	iron-sulfur-binding reductase	K60_003580(4Fe-4S)
		15	Non P450 redox proteins	K60_000250(K18956 WhiB family transcriptional regulator), K60_005570(thioredoxin protein), K60_026200(K03564 peroxiredoxin), K60_031660(K06191 glutaredoxin-like protein NrdH), K60_033240(K18917 mycoredoxin), K60_033470(K18955 WhiB family transcriptional regulator), K60_033890(K18955 WhiB family transcriptional regulator), K60_040790(K18955 WhiB family transcriptional regulator), K60_041130(K18955 WhiB family transcriptional regulator), K60_035540(K18955 WhiB family transcriptional regulator), K60_038100(thioredoxin-like protein), K60_040120(K18957 WhiB family transcriptional regulator), K60_005190(oxidoreductase GMC-type), K60_008500(oxidoreductase), K60_005950(oxidoreductase)
mbz	*Mycobacterium bovis* ATCC BAA-935	5	ferredoxin	LH58_04155(4Fe-4S), LH58_18975(4Fe-4S), LH58_09585(4Fe-4S), LH58_10650(4Fe-4S), LH58_06490(4Fe-4S),
		4	Ferredoxin reductase	LH58_04815(ferredoxin reductase), LH58_16535(ferredoxin reductase), LH58_10020(ferredoxin reductase), LH58_14740(ferredoxin reductase)
		11	Non P450 redox proteins	LH58_07260(K05838 putative thioredoxin), LH58_16245(K06191 glutaredoxin-like protein NrdH), LH58_16710(NADPH:quinone oxidoreductase), LH58_08380(oxidoreduxtase), LH58_02640(oxidoreductase), LH58_07845(FAD-dependent oxidoreductase), LH58_03715(Pyridine nucleotide-disulphide oxidoreductase), LH58_14405(pyridine nucleotide-disulfide oxidoreductase), LH58_04330(oxidoreductase), LH58_03010(oxidoreductase), LH58_02640(oxidoreductase)

maf	*Mycobacterium africanum*	4	ferredoxin	MAF_35160(fdxD), MAF_18080(4Fe-4S), MAF_20190(fdxA), MAF_11960(fdxC),
		5	Ferredoxin reductase	MAF_08950(ferredoxin reductase), MAF_31130(ferredoxin reductase), MAF_18910(ferredoxin reductase), MAF_06970(ferredoxin reductase), MAF_27810(ferredoxin reductase),
		1	iron-sulfur-binding reductase	MAF_03400(4Fe-4S)
		8	Non P450 redox proteins	MAF_25360(K03564 peroxiredoxin), MAF_30600(K06191 glutaredoxin-like protein NrdH), MAF_32060(K18917 mycoredoxin), MAF_04960(oxidoreductase), MAF_17700(oxidoreductase), MAF_05680(oxidoreductase), MAF_17760(oxidoreductase), MAF_04960(oxidoreductase)
mce	*Mycobacterium canettii CIPT* 140010059	4	ferredoxin	MCAN_07671(4Fe-4S), MCAN_35171(fdxD), MCAN_18041(4fe-4S), MCAN_20271(fdxA),
		5	Ferredoxin reductase	MCAN_08871(ferredoxin reductase), MCAN_31331(ferredoxin reductase), MCAN_18841(Ferredoxin reductase), MCAN_06891(ferredoxin reductase), MCAN_28041(ferredoxin reductase),
		1	iron-sulfur-binding reductase	MCAN_03401(4Fe-4S),
		18	Non P450 redox proteins	MCAN_00211(K18956 WhiB family transcriptional regulator), MCAN_24661(K03386 peroxiredoxin), MCAN_25611(K03564 peroxiredoxin), MCAN_30781(K06191 glutaredoxin-like protein NrdH), MCAN_32121(redox-sensing transcriptional regulator), MCAN_32141(K18917 mycoredoxin, MCAN_32361(redox-sensing transcriptional regulator), MCAN_32791(K18955 WhiB family transcriptional regulator), MCAN_34401(K18955 WhiB family transcriptional regulator), MCAN_36931(thioredoxin-like protein), MCAN_37021(K18955 WhiB family transcriptional regulator), MCAN_38841(K18957 WhiB family transcriptional regulator), MCAN_04921(oxidoreductase GMC-type), MCAN_31551(NADPH quinone oxidoreductase FADB4), MCAN_17651(oxidoreductase) MCAN_07981(oxidoreductase), MCAN_05641(oxidoreductase) MCAN_05641(oxidoreductase)
mcq	*Mycobacterium canettii CIPT* 140060008	5	ferredoxin	BN44_10833(4Fe-4S), BN44_80180(FdxD), BN44_40043(4Fe-4S), BN44_40292(fdxA), BN44_11316(fdxC),
		7	Ferredoxin reductase	BN44_10967(ferredoxin reductase), BN44_60625(ferredoxin reductase), BN44_40132(ferredoxin reductase), BN44_10756(ferredoxin reductase), BN44_70011(ferredoxin reductase), BN44_60238(ferredoxin reductase), BN44_10869(oxidoreductase)
		1	iron-sulfur-binding reductase	BN44_10378(4Fe-4S)
		15	Non P450 redox proteins	BN44_10028(redox-sensing transcriptional regulator), BN44_10584(thioredoxin protein), BN44_60564(K06191 glutaredoxin-like protein NrdH), BN44_60564 (K06191 glutaredoxin-like protein NrdH), BN44_60714(K18917 mycoredoxin), BN44_60739(K18955 WhiB family transcriptional regulator), BN44_70044(K18955 WhiB family transcriptional regulator), BN44_80075(K18955 WhiB family transcriptional regulator), BN44_120069(thioredoxin-like protein), BN44_120078(K18955 WhiB family transcriptional regulator), BN44_120289(K18957 WhiB family transcriptional regulator), BN44_10545(oxidoreductase GMC-type), BN44_20330(oxidoreductase), BN44_10622(oxidoreductase), BN44_40006(oxidoreductase)
mcv	*Mycobacterium canettii CIPT* 140070008	5	ferredoxin	BN43_20198(4Fe-4S), BN43_70172(fdxd), BN43_30924(4Fe-4S), BN43_31187(fdxa), BN43_30245
		5	Ferredoxin reductase	BN43_60100(ferredoxin reductase), BN43_31010(ferredoxin reductase), BN43_20118(ferredoxin reductase), BN43_60240(ferredoxin reductase), BN43_40463(ferredoxin reductase),
		1	iron-sulfur-binding reductase	BN43_10373(4Fe-4S)

		15	Non P450 redox proteins	BN43_10028(redox-sensing transcriptional regulator), BN43_10575(Putative thioredoxin protein), BN43_60036(K06191 glutaredoxin-like protein NrdH), BN43_60199(K18917 mycoredoxin), BN43_60225(K18955 WhiB family transcriptional regulator), BN43_60269(redox-sensing transcriptional regulator), BN43_70069(K18955 WhiB family transcriptional regulator), BN43_90178(thioredoxin-like protein), BN43_90187(K18955 WhiB family transcriptional regulator), BN43_90394(K18957 WhiB family transcriptional regulator), BN43_10534(oxidoreductase GMC-type), BN43_30891(oxidoreductase) BN43_30879(Oxidoreductase), BN43_20233(oxidoreductase), BN43_10613(oxidoreductase)
mcx	*Mycobacterium canettii* CIPT 140070010	5	Ferredoxin	BN42_20521)4Fe-4S), BN42_50183(FdxD), BN42_30041(4Fe-4S), BN42_30305(FdxA), BN42_21043(fdxC),
		1	iron-sulfur-binding reductase	BN42_20067(4Fe-4S),
		5	Ferredoxin reductase	BN42_41281(ferredoxin reductase), BN42_40756(ferredoxin reductase), BN42_41139(ferredoxin reductase), BN42_20441(ferredoxin reductase), BN42_30134(ferredoxin reductase),
		16	Non P450 redox proteins	BN42_10044(redox-sensing transcriptional regulator), BN42_20263(Putative thioredoxin protein), BN42_41060(K06191 glutaredoxin-like protein NrdH), BN42_41239(K18917 mycoredoxin), BN42_41239(K18917 mycoredoxin), BN42_41264(K18955 WhiB family transcriptional regulator), BN42_41310(K18955 WhiB family transcriptional regulator), BN42_50074(K18955 WhiB family transcriptional regulator), BN42_90185(K18955 WhiB family transcriptional regulator), BN42_90194(K18955 WhiB family transcriptional regulator), BN42_90396(K18957 WhiB family transcriptional regulator), BN42_21690(oxidoreductase), BN42_20558(oxidoreductase), BN42_20300(oxidoreductase), BN42_30006(oxidoreductase), BN42_20219(Putative oxidoreductase GMC-type)
mcz	*Mycobacterium canettii CIPT* 140070017	5	Ferredoxin	BN45_20032(4Fe-4S), BN45_70168(FdxD), BN45_50042(4Fe-4S), BN45_50286(fdxA), BN45_30238(fdxC),
		6	Ferredoxin reductase	BN45_20176(ferredoxin reductase), BN45_60260(ferredoxin reductase), BN45_51163(ferredoxin reductase), BN45_60104(ferredoxin reductase), BN45_50134(ferredoxin reductase), BN45_10786(ferredoxin reductase)
		1	iron-sulfur-binding reductase	BN45_10372(4Fe-4S)
		15	Non P450 redox proteins	BN45_10027(K18956 WhiB family transcriptional regulator), BN45_10590(thioredoxin protein), BN45_60037(K06191 glutaredoxin-like protein NrdH), BN45_60215(K18958 WhiB family transcriptional regulator), BN45_60218(K18917 mycoredoxin), BN45_60245(K18955 WhiB family transcriptional regulator), BN45_60289(K18955 WhiB family transcriptional regulator), BN45_70061(K18955 WhiB family transcriptional regulator), BN45_110026(K18955 WhiB family transcriptional regulator), BN45_110035(K18955 WhiB family transcriptional regulator), BN45_110238(K18957 WhiB family transcriptional regulator), BN45_40244(Putative oxidoreductase), BN45_20064(putative oxidoreductase), BN45_10628(oxidoreductase), BN45_10543(Putative oxidoreductase GMC-type)
mle	*Mycobacterium leprae* TN	1	Ferredoxin	ML1489(fdxA),
		2	Ferredoxin reductase	ML2134(ferredoxin reductase), ML0666(ferredoxin reductase)
		1	iron-sulfur-binding reductase	ML2501
		5	Non P450 redox proteins	ML0424(K03564 peroxiredoxin), ML1159(K05838 putative thioredoxin), ML1736(K06191 glutaredoxin-like protein NrdH), ML2307(K18955 WhiB family transcriptional regulator), ML2276(oxidoreductase)
mlb	*Mycobacterium leprae* Br4923	1	Ferredoxin	MLBr_01489(fdxA),
		2	Ferredoxin reductase	MLBr_02134(Ferredoxin reductase), MLBr_00666(ferredoxin reductase),
		1	iron-sulfur-binding reductase	MLBr_02501(4Fe-4S)
		5	Non P450 redox proteins	MLBr_00424(K03564 peroxiredoxin), MLBr_01159 (K05838 putative thioredoxin), MLBr_01736(K06191 glutaredoxin-like protein NrdH), MLBr_02307(K18955 WhiB family transcriptional regulator), MLBr_02276(FAD-

				linked oxidoreductase)
mpa	*Mycobacterium avium subsp. paratuberculosis* K-10	4	Ferredoxin	MAP_0560; MAP_2726c; MAP_2607c; MAP_2039;
		5	Ferredoxin reductase	MAP_1579c; MAP_2277c; MAP_0825; MAP_3176; MAP_0825
		10	Non P450 redox proteins	MAP_0033c; MAP_1196; MAP_1589c; MAP_2329; MAP_2435c; MAP_3102c; MAP_3296c; MAP3298; MAP_4339 ; MAP_3190
mao	*Mycobacterium avium subsp. paratuberculosis* MAP4	9	Ferredoxin	MAP4_1090(4Fe-4S), MAP4_1211(4Fe-4S), MAP4_3268(4Fe-4S), MAP4_3198(4Fe-4S), MAP4_3124(4Fe-4S), MAP4_1478(4Fe-4S), MAP4_3133(4Fe-4S), MAP4_1296(4Fe-4S), MAP4_3160(4Fe-4S),
		6	Ferredoxin reductase	MAP4_3035(Ferredoxin reductase), MAP4_0613(ferredoxin reductase), MAP4_4272(ferredoxin reductase), MAP4_0440(ferredoxin reductase), MAP4_0504(ferredoxin reductase), MAP4_0923(ferredoxin reductase)
		2	iron-sulfur protein	MAP4_0656(4Fe-4S), MAP4_3944(4Fe-4S),
		13	Non P450 redox proteins	MAP4_0487(K18917 mycoredoxin), MAP4_0696(K06191 glutaredoxin-like protein NrdH), MAP4_1494(K03564 peroxiredoxin), MAP4_2250(K03386 peroxiredoxin), MAP4_3843(K18956 WhiB family transcriptional regulator), MAP4_3107(4Fe-4S), MAP4_0599(quinone oxidoreductase FadB4), MAP4_3371(0xidoreductase), MAP4_0795(oxidoreductase) MAP4_2108(oxidoreductase), MAP4_4328(oxidoreductase), MAP4_4180(oxidoreductase), MAP4_2904(oxidoreductase)
mav	*Mycobacterium avium* 104	7	Ferredoxin	MAV_0653(4Fe-4S), MAV_0915(4Fe-4S), MAV_1636(4Fe-4S), MAV_1949(4Fe-4S, MAV_1316(4Fe-4S), MAV_2150(4Fe-4S), MAV_3500(FdxA),
		5	Ferredoxin reductase	MAV_5072(ferredoxin reductase), MAV_1015(ferredoxin reductase), MAV_4007(ferredoxin reductase), MAV_4485(ferredoxin reductase) MAV_0862(FdxB),
		1	iron-sulfur cluster	MAV_3963(2Fe-2S), MAV_4193(2Fe-2S)
		4	Non ferredoxin	MAV_0040(K18956 WhiB family transcriptional regulator), MAV_3178(K03564 peroxiredoxin), MAV_4144(K18917 mycoredoxin) MAV_3921(K06191 glutaredoxin-like protein NrdH)
mavr	*Mycobacterium avium* 2285 (R)	19	Ferredoxin	LA63_03310(4Fe-4S), LA63_04010(4Fe-4S), LA63_03685(4Fe-4S), LA63_09145(4Fe-4S), LA63_04145(4Fe-4S), LA63_04060(4Fe-4S), LA63_07405(4Fe-4S), LA63_03030(4Fe-4S), LA63_08920(4Fe-4S), LA63_04020(4Fe-4S), LA63_06380(4Fe-4S), LA63_13250(4Fe-4S), LA63_11975(4Fe-4S), LA63_08555(4Fe-4S), LA63_16020(4Fe-4S), LA63_05975(Fe-4S), LA63_09875(4Fe-4S), LA63_15525(4Fe-4S), LA63_03885(4Fe-4S)
		6	Ferredoxin reductase	LA63_04500(ferredoxin reductase), LA63_23905(ferredoxin reductase), LA63_18495(ferredoxin reductase), LA63_12860(ferredoxin reductase), LA63_19055(ferredoxin reductase), LA63_16845(ferredoxin reductase),
		7	Non P450 redox proteins	LA63_06965(K05838 putative thioredoxin), LA63_18080(glutaredoxin-like protein NrdH), LA63_18560(NADPH:quinone oxidoreductase), LA63_15240(FAD-dependent oxidoreductase), LA63_22380(oxidoreductase), LA63_20830(pyridine nucleotide-disulfide oxidoreductase), LA63_16535(pyridine nucleotide-disulfide oxidoreductase)
		1	cytochrome P450	LA63_09915(cytochrome P450)
mavd	*Mycobacterium avium subsp. avium* DJO-44271	18	Ferredoxin	,NF84_03215(4Fe-4S), ,NF84_03910(4Fe-4S), NF84_03595(4Fe-4S), ,NF84_04045(4Fe-4S), NF84_03960(4Fe-4S), NF84_07270(4Fe-4S), ,NF84_02960(4Fe-4S), NF84_08780(4fe-4S), NF84_03920(4Fe-4S), ,NF84_06250(4Fe-4S), ,NF84_13100(4Fe-4S),NF84_11695(4Fe-4S), NF84_08415(4Fe-4S), ,NF84_03785(4Fe-4S), NF84_01950(4Fe-4S), NF84_05845(4Fe-4S), NF84_09675(4Fe-4S), NF84_15390(4Fe-4S),
		5	Ferredoxin reductase	NF84_04400(ferredoxin reductase), NF84_18305(Ferredoxin reductase), NF84_18860(ferredoxin reductase), NF84_16680(ferredoxin reductase), NF84_12705(ferredoxin reductase),
		1	cytochrome P450	NF84_09715(cytochrome P450),
		8	Non P450 redox proteins	NF84_06830(K05838 putative thioredoxin), NF84_17895(K06191 glutaredoxin-like protein NrdH), NF84_18370(

				NADPH:quinone oxidoreductase), NF84_14535(oxidoreductase), NF84_15105(FAD-dependent oxidoreductase, NF84_22160(Oxidoreductase), NF84_20635(pyridine nucleotide-disulfide oxidoreductase), NF84_16385(pyridine nucleotide-disulfide oxidoreductase)
mit	*Mycobacterium intracellulare*	6	Ferredoxin	OCO_07800(4Fe-4S), OCO_17020(4Fe-4S), OCO_10870(4Fe-4S), OCO_19540(Fdx), OCO_12260(4Fe-4S), OCO_21220(fdxc),
		4	Ferredoxin reductase	OCO_08830(ferredoxin reductase), OCO_38590(Ferredoxin reductase), OCO_40550(ferredoxin reductase), OCO_39530(ferredoxin reductase),
		16	Non P450 redox proteins	OCO_00330(K18956 WhiB family transcriptional regulator), OCO_16080(K05838 putative thioredoxin), OCO_37480(K06191 glutaredoxin-like protein NrdH), OCO_40040(K18917 mycoredoxin), OCO_40720(rubredoxin-type Fe(Cys)4), OCO_51410(thioredoxin reductase), OCO_44570(molybdopterin oxidoreductase), OCO_42200(FAD dependent oxidoreductase), OCO_28540(FAD dependent oxidoreductase), OCO_14710(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), OCO_23020(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), OCO_06350(oxidoreductase), OCO_22270(FAD dependent oxidoreductase), OCO_11870(oxidoreductase),), OCO_44660(FAD dependent oxidoreductase) OCO_08380(bacterioferritin-associated ferredoxin),
mir	*Mycobacterium intracellulare* MOTT-64	6	Ferredoxin	OCQ_07950(4Fe-4S), OCQ_14690(4Fe-4S), OCQ_18210(fdxD), OCQ_34530(fdxa), OCQ_12280(4Fe-4S), OCQ_20140(fdxc),
		7	Ferredoxin reductase	OCQ_08980(ferredoxin reductase), OCQ_39750(ferredoxin reductase), OCQ_28970(ferredoxin reductase),), OCQ_41640(ferredoxin reductase), OCQ_40760(ferredoxin reductase), OCQ_32640(ferredoxin reductase), OCQ_16640(Ferredoxin)
		15	Non P450 redox proteins	OCQ_00330(K18956 WhiB family transcriptional regulator), OCQ_13760(K05838 putative thioredoxin), OCQ_41990(rubredoxin-type Fe(Cys)4 protein), OCQ_44050(K00384 thioredoxin reductase (NADPH), OCQ_52400(K00384 thioredoxin reductase), OCQ_45710(molybdopterin oxidoreductase), OCQ_27120(FAD dependent oxidoreductase), OCQ_06500(oxidoreductase), OCQ_21380(FAD dependent oxidoreductase) OCQ_38710(glutaredoxin-like protein NrdH), OCQ_41140(K18917 mycoredoxin), OCQ_48240(4fe-4S), OCQ_45800(FAD dependent oxidoreductase), OCQ_11890(oxidoreductase) OCQ_08540(bacterioferritin-associated ferredoxin),
mia	*Mycobacterium intracellulare* ATCC 13950	4	Ferredoxin	OCU_15300(4Fe-4S), OCU_12220(4Fe-4S), OCU_21470(fdxC) OCU_07170(FdxB)
		4	Ferredoxin reductase	OCU_08900(ferredoxin reductase), OCU_38560(ferredoxin reductase), OCU_40460(ferredoxin reductase), OCU_39570(ferredoxin reductase)
		26	Non P450 redox proteins	OCU_00340(K18956 WhiB family transcriptional regulator), OCU_51350(K00384 thioredoxin reductase (NADPH)), OCU_37570(glutaredoxin-like protein NrdH), OCU_39950(K18917 mycoredoxin), OCU_40630(rubredoxin-type Fe(Cys)4), OCU_44310(molybdopterin oxidoreductase), , OCU_42130(FAD dependent oxidoreductase), OCU_28410(FAD dependent oxidoreductase), OCU_15150(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), OCU_22470(FAD dependent oxidoreductase), OCU_11820(oxidoreductase), OCU_44400(FAD dependent oxidoreductase); OCU_07810(4Fe-4S), OCU_08460(bacterioferritin-associated ferredoxin), OCU_17220(4Fe-4S), OCU_17430(4Fe-4S), OCU_05670(4Fe-4S), OCU_13400(FdxD), OCU_07790(4Fe-4S), OCU_19690(fdxD), OCU_19750(FdxA), OCU_33290(FdxA), OCU_37970(4Fe-4S), OCU_28180(4Fe-4S), OCU_28420(4Fe-4S), OCU_46960(Fe-4S) OCU_16280(K05838 putative thioredoxin),
mie	*Mycobacterium intracellulare* 1956	18	Ferredoxin	LG41_03015(4Fe-4S) LG41_06455(4fe-4S), LG41_03860(4fe-4S), LG41_03470(4Fe-4S), LG41_04010(4Fe-4S), LG41_09270(4Fe-4S), LG41_08110(4Fe-4S), LG41_03925(4Fe-4S), LG41_02825(4Fe-4S), LG41_03870(4fe-4S), LG41_13025(4Fe-4S), LG41_03725(4Fe-4S), LG41_06845(4Fe-4S), LG41_15760(4Fe-4S), LG41_09305(4Fe-4S), LG41_05925(4Fe-4S), LG41_10100(4Fe-4S), LG41_15315(4fe-4S),

		6	Ferredoxin reductase	LG41_04370(Ferredoxin reductase), LG41_23695(ferredoxin reductase), LG41_18315(ferredoxin reductase), LG41_12640(Ferredoxin reductase) , LG41_18775(ferredoxin reductase), LG41_16535(ferredoxin reductase),
		1	CYP P450	LG41_00455(cytochrome P450)
		13	Non P450 redox proteins	LG41_07635(K05838 putative thioredoxin), LG41_17800(K06191 glutaredoxin-like protein NrdH), LG41_20295(K00384 thioredoxin reductase), LG41_21115(molybdopterin oxidoreductase), LG41_18380(NADPH:quinone oxidoreductase), LG41_14570(oxidoreductase), LG41_20710(oxidoreductase) LG41_16240(pyridine nucleotide-disulfide oxidoreductase) LG41_03190(pyridine nucleotide-disulfide oxidoreductase), LG41_04910(oxidoreductase) LG41_10575(FAD-dependent oxidoreductase) LG41_21165(FAD-linked oxidoreductase) LG41_04965(oxidoreductase)
mid	*Mycobacterium indicus pranii*	8	Ferredoxin	MIP_01026(FdXd), MIP_01339(4FS-4S), MIP_02348(4Fe-4S), MIP_00228(3fe-4S) MIP_01957(4Fe-4S), MIP_03002(4Fe-4S), MIP_04639 (putative electron transfer protein FdxB)
		5	Ferredoxin reductase	MIP_00230(ferredoxin reductase), MIP_01480(ferredoxin reductase), MIP_06111(Ferredoxin reductase), MIP_03758(ferredoxin reductase), MIP_05836(Ferredoxin reductase),
		3	Cytochrome P450	MIP_01080(Cytochrome P450), MIP_03857(Putative cytochrome P450), MIP_03023(Cytochrome P450 109)
		19	Non P450 redox proteins	MIP_00041(K18956 WhiB family transcriptional regulator), MIP_02218(K05838 putative thioredoxin), MIP_02752(Peroxiredoxin osmC), MIP_05679(K06191 glutaredoxin-like protein NrdH), MIP_05882(NADH-quinone oxidoreductase), MIP_04541(oxidoreductase), MIP_05856(Quinone oxidoreductase-like protein 2), MIP_03046(FAD dependent oxidoreductase), MIP_01666(oxidoreductase), MIP_01901(oxidoreductase), MIP_00219(oxidoreductase) MIP_05025(4Fe-4S), MIP_03722(4Fe-4S), MIP_07142(4Fe-4S), MIP_00235(4Fe-4S),MIP_01421(bacterioferritin-associated ferredoxin), MIP_02748(4Fe-4S), MIP_02763(4Fe-4S),
myo	*Mycobacterium yongonense*	8	Ferredoxin	OEM_05700(4Fe-4S), OEM_07880(4Fe-4S), OEM_15020(4fe-4S), OEM_07860(4Fe-4S), OEM_17420(fdxD), OEM_12410(4Fe-4S), OEM_19090(fdxC), OEM_26770 (ferredoxin),
		5	Ferredoxin reductase	OEM_08950(ferredoxin reductase), OEM_40800(ferredoxin reductase), OEM_40050(ferredoxin reductase), OEM_31170(ferredoxin reductase), OEM_39100(ferredoxin reductase)
		25	Non P450 redox proteins	OEM_00330(K18956 WhiB family transcriptional regulator), OEM_14120(K05838 putative thioredoxin), OEM_38120(K06191 glutaredoxin-like protein NrdH), OEM_40320(K18917 mycoredoxin), OEM_40980(rubredoxin-type Fe(Cys)4), OEM_43160(K00384 thioredoxin reductase), OEM_52130(K00384 thioredoxin reductase), OEM_p100880(K18958 WhiB family transcriptional regulator), OEM_p101170(K06191 glutaredoxin-like protein NrdH), OEM_44760(molybdopterin oxidoreductase), OEM_43160(K00384 thioredoxin reductase), OEM_42560(FAD dependent oxidoreductase), OEM_27000(FAD dependent oxidoreductase), OEM_25480(oxidoreductase), OEM_20380(FAD dependent oxidoreductase) OEM_44850(FAD dependent oxidoreductase), OEM_12010(oxidoreductase), OEM_46940(oxidoreductase)OEM_08150(4Fe-4S), OEM_33540(fdxa), OEM_17520(FdxA), OEM_38530(4Fe-4S), OEM_07240(FdxB), OEM_27010(4Fe-4S), OEM_47340(4Fe-4S),
msm	*Mycobacterium smegmatis* MC2 155	8	Ferredoxin	MSMEG_0761(4Fe-4S), MSMEG_2559(4Fe-4S), MSMEG_4819(4Fe-4S), MSMEG_4822(4Fe-4S), MSMEG_5904(4Fe-4S), MSMEG_1124(FdxA) MSMEG_5122(4Fe-4S), MSMEG_5533(4Fe-4S),
		1	iron-sulfur binding	MSMEG_0637(iron-sulfur binding oxidoreductase),
		7	Ferredoxin reductase	MSMEG_5681(ferredoxin reductase), MSMEG_0295(ferredoxin reductase), MSMEG_2893(ferredoxin reductase)

				MSMEG_6039(ferredoxin reductase), MSMEG_1742(ferredoxin reductase), MSMEG_4411(ferredoxin reductase), MSMEG_6836(ferredoxin reductase)
		1	Cytochrome P450	MSMEG_5864(cytochrome P450)
		20	Non P450 redox proteins	MSMEG_0051(K18957 WhiB family transcriptional regulator), MSMEG_1017 (K06191 glutaredoxin-like protein NrdH), MSMEG_1947(K18917 mycoredoxin), MSMEG_2297(K06191 glutaredoxin-like protein NrdH), MSMEG_4753(K03564 peroxiredoxin), MSMEG_4917(K05838 putative thioredoxin), MSMEG_6597(hydrolase of the alpha/beta superfamily protein), MSMEG_1604(oxidoreductase), MSMEG_4423(oxidoreductase), MSMEG_1416(oxidoreductase), MSMEG_0670(FAD dependent oxidoreductase), MSMEG_4023(oxidoreductase), MSMEG_6264(oxidoreductase), MSMEG_4422(oxidoreductase)MSMEG_3568(bacterioferritin-associated ferredoxin), MSMEG_1847(4Fe-4S) MSMEG_5433(4Fe-4S), MSMEG_1460(ferredoxin reductase), MSMEG_1132(FAD binding domain-containing protein), MSMEG_3457(oxidoreductase)
msg	*Mycobacterium smegmatis* MC2 155	14	Ferredoxin	MSMEI_4695(4Fe-4S), MSMEI_5705(4Fe-4S), MSMEI_4053(Fe3S4), MSMEI_2499(4Fe-4S), MSMEI_6514(Fe3S4), MSMEI_4698(4Fe-4S), MSMEI_4689(4Fe-4S), MSMEI_5744(fdxD), MSMEI_0745(4Fe-4S), MSMEI_4732(4Fe-4S), MSMEI_1090(fdxC), MSMEI_4993(fdxC), MSMEI_5381(4Fe-4S), MSMEI_3841(4Fe-4S),
		12	Ferredoxin reductase	MSMEI_2039(Ferredoxin reductase) MSMEI_5531(ferredoxin reductase), MSMEI_3512(ferredoxin reductase), MSMEI_0288(ferredoxin reductase), MSMEI_2819(ferredoxin reductase), MSMEI_5878(ferredoxin reductase), MSMEI_1845(ferredoxin reductase), MSMEI_3589(ferredoxin reductase), MSMEI_1702(ferredoxin reductase), MSMEI_4267(ferredoxin reductase), MSMEI_4054(ferredoxin reductase), MSMEI_4304(ferredoxin reductase), MSMEI_5531(ferredoxin reductase),
		31	Non P450 redox proteins	MSMEI_0988(K06191 glutaredoxin-like protein NrdH), MSMEI_1558(K18955 WhiB family transcriptional regulator), MSMEI_1905(K18917 mycoredoxin), MSMEI_1910(K18958 WhiB family transcriptional regulator), MSMEI_2239(K06191 glutaredoxin-like protein NrdH), MSMEI_4633(K03564 peroxiredoxin), MSMEI_6026(thioredoxin-like protein), MSMEI_6039(K18955 WhiB family transcriptional regulator), MSMEI_6419(OsmC-like family protein), MSMEI_4527(K00175 2-oxoglutarate/2-oxoacid ferredoxin oxidoreductase subunit beta), MSMEI_4528(K00174 2-oxoglutarate/2-oxoacid ferredoxin oxidoreductase subunit alpha), MSMEI_2010(K00338 NADH-quinone oxidoreductase subunit I), MSMEI_0702(oxidoreductase FAD-binding region), MSMEI_0621(FAD dependent oxidoreductase), MSMEI_0652(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), MSMEI_1381(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), MSMEI_6637(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), MSMEI_4080(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), MSMEI_5293(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), MSMEI_5252(FAD dependent oxidoreductase), MSMEI_1100(oxidoreductase), MSMEI_3376(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), MSMEI_1987 (NADPH quinone oxidoreductase FadB4)MSMEI_1845 (Oxidoreductase FAD-binding domain protein), MSMEI_6102(FAD dependent oxidoreductase), MSMEI_3589(Putative Iron-sulfur oxidoreductase), MSMEI_1702(Oxidoreductase FAD-binding region), MSMEI_4267(putative iron-sulfur oxidoreductase), MSMEI_4054(Putative Iron-sulfur oxidoreductase), MSMEI_4304(Oxidoreductase FAD-binding region), MSMEI_6654(Oxidoreductase FAD-binding domain protein)
msb	*Mycobacterium smegmatis* MC2 155	15	Ferredoxin	LJ00_29000(4Fe-4S), LJ00_20585(3Fe-4S), LJ00_12735(4Fe-4S), LJ00_33085 LJ00_23835(4Fe-4S), LJ00_23750(4Fe-4S), LJ00_23850(4Fe-4S), LJ00_29200(4Fe-4S), LJ00_03780(4Fe-4S), LJ00_24020(4Fe-4S), LJ00_05585(4fe-4S), LJ00_25320(4Fe-4S), LJ00_20590(4Fe-4S), LJ00_27355(4Fe-4S), LJ00_09925
		5	Ferredoxin reductase	LJ00_28090(Ferredoxin reductase), LJ00_08705(ferredoxin reductase), LJ00_10390(ferredoxin reductase), LJ00_17885(ferredoxin reductase), LJ00_21835(ferredoxin reductase),
		36	Non P450 redox proteins	LJ00_05040(K06191 glutaredoxin-like protein NrdH), LJ00_07575(K00384 thioredoxin reductase), LJ00_11425(

				K06191 glutaredoxin-like protein NrdH), LJ00_24320(K05838 putative thioredoxin), LJ00_32610(osmotically inducible protein OsmC), LJ00_10135(NADPH:quinone oxidoreductase), LJ00_13665(pyridine nucleotide-disulfide oxidoreductase), LJ00_33690(pyridine nucleotide-disulfide oxidoreductase), LJ00_03320(pyridine nucleotide-disulfide oxidoreductase), LJ00_19970(pyridine nucleotide-disulfide oxidoreductase), LJ00_26900(pyridine nucleotide-disulfide oxidoreductase), LJ00_21890(pyridine nucleotide-disulfide oxidoreductase), LJ00_21895(oxidoreductase), LJ00_03425(Fe-S oxidoreductase), LJ00_09515(oxidoreductase), LJ00_03425(Fe-S oxidoreductase), LJ00_16405(oxidoreductase), LJ00_24835(FAD-dependent oxidoreductase), LJ00_10160(FAD-dependent oxidoreductase), LJ00_03165(FAD-dependent oxidoreductase), LJ00_11975(oxidoreductase), LJ00_14130(oxidoreductase), LJ00_03320(oxidoreductase), LJ00_07060(pyridine nucleotide-disulfide oxidoreductase), LJ00_07295(pyridine nucleotide-disulfide oxidoreductase), LJ00_26680(FAD-dependent oxidoreductase), LJ00_30975(FAD-dependent oxidoreductase), LJ00_05635(FAD-linked oxidoreductase) LJ00_21835(oxidoreductase), LJ00_33780(oxidoreductase),LJ00_17750 LJ00_18275(4Fe-4S), LJ00_22945(4Fe-4S), LJ00_19915(4Fe-4S), LJ00_09210(4Fe-4S), LJ00_19540(4fe-4S)
msa	*Mycobacterium smegmatis* JS623	15	Ferredoxin	Mycsm_05682(4Fe-4S), Mycsm_02382(4Fe-4S), Mycsm_04694(4Fe-4S), Mycsm_04480(4Fe-4S), Mycsm_04488(4Fe-4S), Mycsm_04467(4Fe-4S), Mycsm_04486(4Fe-4S), Mycsm_05549(4Fe-4S), Mycsm_05740(4Fe-4S), Mycsm_00403(4Fe-4S), Mycsm_06648(4Fe-4S), Mycsm_01930(4Fe-4S), Mycsm_04559(4Fe-4S), Mycsm_04917(4Fe-4S), Mycsm_06689(4Fe-4S),
		2	Ferredoxin reductase	Mycsm_01570 (NADPH-dependent glutamate synthase beta chain-like oxidoreductase, K00528 ferredoxin--NADP+ reductase), Mycsm_05449 (NADPH-dependent glutamate synthase beta chain-like oxidoreductase, K00528 ferredoxin--NADP+ reductase)
		25	Non P450 redox proteins	Mycsm_01119 (regulator of disulfide bond formation), Mycsm_01449(K18917 mycoredoxin), Mycsm_01452(K18958 WhiB family transcriptional regulator), Mycsm_02167(K06191 glutaredoxin-like protein NrdH), Mycsm_02291(regulator of disulfide bond formation), Mycsm_02551(thioredoxin-like protein), Mycsm_04103(sulfite reductase), Mycsm_04630(K05838 putative thioredoxin), Mycsm_05076(thioredoxin domain protein), Mycsm_05225(K00384 thioredoxin reductase), Mycsm_06392(prolyl oligopeptidase family protein), Mycsm_06728(glutaredoxin-like protein NrdH), Mycsm_06737(K18957 WhiB family transcriptional regulator), Mycsm_06739(K18957 WhiB family transcriptional regulator), Mycsm_04590(flavodoxin reductase family protein), Mycsm_05841(flavodoxin reductase family protein), Mycsm_01404(flavodoxin reductase family protein), Mycsm_04700(flavodoxin reductase family protein), Mycsm_06610(flavodoxin reductase family protein), Mycsm_01297(flavodoxin reductase family protein), Mycsm_05140(flavodoxin reductase family protein), Mycsm_00354(Fe-S oxidoreductase), Mycsm_03759(NADH:flavin oxidoreductase), Mycsm_04920(NADH:flavin oxidoreductase) Mycsm_04494(4Fe-4S
msn	*Mycobacterium smegmatis* INHR1	16	Ferredoxin	LI99_29005(4Fe-4S), LI99_20590(3Fe-4S), LI99_12735(4Fe-4S), LI99_33090(4Fe-4S), LI99_23840(4Fe-4S), LI99_23755(4fe-4S), LI99_23855(4Fe-4S), LI99_29205(4Fe-4S), LI99_03780(4Fe-4S), LI99_24025(4Fe-4S), LI99_25325(4Fe-4S), LI99_20595(4Fe-4S), LI99_09925(4Fe-4S), LI99_27360(4Fe-4S), LI99_09210(4Fe-4S), LI99_05585(4Fe-4S),
		3	Ferredoxin reductase	LI99_08705(Ferredoxin reductase), LI99_21840(ferredoxin reductase), LI99_10390(ferredoxin reductase),
		23	Non P450 redox proteins	LI99_05040(K06191 glutaredoxin-like protein NrdH), LI99_07575(K00384 thioredoxin reductase), LI99_11425(K06191 glutaredoxin-like protein NrdH), LI99_24325(K05838 putative thioredoxin), LI99_32615(K06889 uncharacterized protein K07397 putative redox protein), LI99_21900(oxidoreductase), LI99_09515(oxidoreductase), LI99_16410(oxidoreductase), LI99_24840(FAD-dependent oxidoreductase), LI99_10160(FAD-dependent oxidoreductase), LI99_03165(FAD-dependent oxidoreductase)LI99_17755 LI99_28095(4Fe-4S), LI99_01480(4Fe-4S), LI99_18280(4Fe-4S) LI99_22950(4Fe-4S), LI99_19920(4Fe-4S), LI99_19545(4Fe-4S), LI99_23810 LI99_03425 LI99_33785LI99_21840(oxidoreductase), LI99_33785(oxidoreductase), LI99_03425(oxidoreductase)

msh	*Mycobacterium smegmatis* INHR2	14	Ferredoxin	LI98_29010(4Fe-4S), LI98_20595(3Fe-4S), LI98_12740(4e-4S), LI98_33095(4Fe-4S), LI98_23845(4Fe-4S), LI98_23760(4Fe-4S), LI98_23860(4Fe-4S), LI98_29210(4Fe-4S), LI98_03780(4Fe-4S), LI98_24030(4Fe-4S), LI98_05585(4Fe-4S), LI98_25330(4Fe-4S), LI98_27365(4Fe-4S), LI98_09925(4Fe-4S),
		4	Ferredoxin reductase	LI98_28100(ferredoxin reductase), LI98_08705(ferredoxin reductase), LI98_10390(Ferredoxin reductase), LI98_17895(ferredoxin reductase)
		20	Non P450 redox proteins	LI98_05040(K06191 glutaredoxin-like protein NrdH), LI98_07575(K00384 thioredoxin reductase), LI98_11430(glutaredoxin), LI98_24330(K05838 putative thioredoxin), LI98_32620(K07397 putative redox protein), LI98_219(oxidoreductase), LI98_03425(Fe-S oxidoreductase), LI98_24845(FAD-dependent oxidoreductase), LI98_10160 (FAD-dependent oxidoreductase), LI98_07060(pyridine nucleotide-disulfide oxidoreductase), LI98_05635(FAD-linked oxidoreductase), LI98_09210(4Fe-4S), LI98_01480(4Fe-4S), LI98_18285(4Fe-4S), LI98_20600(4Fe-4S), LI98_22955(4Fe-4S), LI98_19550(4Fe-4S), LI98_28100(ferredoxin reductase) LI98_17760 LI98_03165
mul	*Mycobacterium ulcerans*	7	Ferredoxin	MUL_0472(4Fe-4S), MUL_0334(4Fe-4S), MUL_0316(4Fe-4S), MUL_3090(4Fe-4S), MUL_3264(FdxA), MUL_1025(fdxC), MUL_2700(fdxC),
		2	Ferredoxin reductase	MUL_0264(ferredoxin reductase), MUL_0769(ferredoxin reductase)
		21	Non P450 redox proteins	MUL_0040(WhiB5; K18956 WhiB family transcriptional regulator), MUL_0625(thioredoxin protein), MUL_0895(K18955 WhiB family transcriptional regulator), MUL_1876(K06191 glutaredoxin-like protein NrdH), MUL_2511(K18958 WhiB family transcriptional regulator), MUL_2513(K18917 mycoredoxin), MUL_2541(K18955 WhiB family transcriptional regulator), MUL_2605(K18955 WhiB family transcriptional regulator), MUL_2912(K03386 peroxiredoxin), MUL_2999(K03386 peroxiredoxin), MUL_2999(K03386 peroxiredoxin), MUL_3811(K03564 peroxiredoxin), MUL_4247(membrane-anchored thioredoxin-like protein), MUL_4256(K18955 WhiB family transcriptional regulator), MUP021(K18958 WhiB family transcriptional regulator), MUL_4142(flavodoxin reductase Hmp), MUL_4786(flavodoxin oxidoreductase), MUL_2358(FAD-dependent oxidoreductase)MUL_2873(4Fe-4S), MUL_4066(FdxD), MUL_3830(Fe-4S),
mva	*Mycobacterium vanbaalenii*	12	Ferredoxin	Mvan_4176(4Fe-4S), Mvan_5849(FdxD), Mvan_2235(4Fe-4S), Mvan_3976(4Fe-4S), Mvan_5849(4Fe-4S), Mvan_0549(4Fe-4S), Mvan_0681(4Fe-4S), Mvan_4235(4Fe-4S), Mvan_0399(Fe-4S), Mvan_4179(Fe-4S), Mvan_0299(4fe-4S), Mvan_4529(4Fe-4S),
		4	Ferredoxin reductase	Mvan_5031(ferredoxin reductase), Mvan_1910 (ferredoxin reductase), Mvan_0467(ferredoxin reductase), Mvan_0400(ferredoxin reductase),
		31	Non P450 redox proteins	Mvan_0866(Redoxin domain protein), Mvan_1743(Rubredoxin-type Fe(Cys)4 protein), Mvan_1744(Rubredoxin-type Fe(Cys)4 protein), Mvan_1862(K00435 peroxiredoxin), Mvan_2040(K06191 glutaredoxin-like protein NrdH), Mvan_2813(K03564 peroxiredoxin), Mvan_3240(Redoxin domain protein), Mvan_1806(K18917 mycoredoxin), Mvan_3710(Redoxin domain protein), Mvan_3749(Redoxin domain protein), Mvan_4120(K03564 peroxiredoxin), Mvan_4303(K05838 putative thioredoxin), Mvan_4712(Glutaredoxin-like protein), Mvan_5099(Thioredoxin domain), Mvan_5315(redox-active disulfide protein 2), Mvan_5432(Redoxin domain protein), Mvan_1290(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), Mvan_1216(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), Mvan_5348(FAD-dependent pyridine nucleotide-disulfide oxidoreductase), Mvan_3045(bacterioferritin-associated ferredoxin), Mvan_3965(flavodoxin/ferredoxin), Mvan_4109(flavodoxin/ferredoxin), Mvan_4186(4Fe-4S), Mvan_5309(4Fe-4S) Mvan_2893(4Fe-4S), Mvan_1767(4Fe-4S), Mvan_3180(4Fe-4S), Mvan_4257(4fe-4S), Mvan_1329(ferredoxin reductase), Mvan_1327(ferredoxin reductase),Mvan_1519(FAD dependent oxidoreductase)
mgi	*Mycobacterium gilvum* PYR-	13	Ferredoxin	Mflv_0591(ferredoxin), Mflv_0681(ferredoxin), Mflv_2478(4Fe-4S), Mflv_4111(4Fe-4S), Mflv_2417(4Fe-4S) Mflv_2170(4Fe-4S), Mflv_3156(4Fe-4S), Mflv_4699(4fe-4S), Mflv_5247(4fe-4S), Mflv_2391(4fe-4S),

	GCK			Mflv_4547(4fe-4S), Mflv_0668(4fe-4S), Mflv_0570(4fe-4S),
		3	Ferredoxin reductase	Mflv 1720(ferredoxin reductase), Mflv 4452(ferredoxin reductase), Mflv 4591(ferredoxin reductase),
		17	Non P450 redox proteins	Mflv_1648(Thioredoxin domain), Mflv_2342(K05838 putative thioredoxin), Mflv_3247(K06889 uncharacterized protein K07397 putative redox protein), Mflv_4307(K06191 glutaredoxin-like protein NrdH), Mflv_4661(K18917 mycoredoxin), Mflv_4719(Rubredoxin-type Fe(Cys)4 protein), Mflv_4720(Rubredoxin-type Fe(Cys)4 protein), Mflv_1296(FAD dependent oxidoreductase), Mflv_0255(Oxidoreductase FAD-binding domain protein), Mflv_5068(FAD-dependent pyridine nucleotide-disulfide oxidoreductase)Mflv_0338(Sucraseferredoxin), Mflv_2616(pyruvate flavodoxin/ferredoxin oxidoreductase), Mflv_2468(4Fe-4S), Mflv_1462(4Fe-4S), Mflv_3426(4Fe-4S), Mflv_2623(4fe-4S), Mflv_0383(4Fe-4S),
msp	*Mycobacterium gilvum* Spyr1	11	Ferredoxin	Mspyr1_09810(4Fe-4S), Mspyr1_34540, Mspyr1_19010,Mspyr1_09360, Mspyr1_05510,Mspyr1_19110,Mspyr1_18430,Mspyr1_19050, Mspyr1_19260, Mspyr1_01440(ferredoxin), Mspyr1_03730(4Fe-4S), Mspyr1_16020, , Mspyr1_39470 , Mspyr1_34540 Mspyr1_01440
		0	Ferredoxin reductase	
		14	Non P450 redox proteins	Mspyr1_00530(K18957 WhiB family transcriptional regulator), Mspyr1_17750(K05838 putative thioredoxin), Mspyr1_21230(sulfite reductase), Mspyr1_25750(K06889 uncharacterized protein K07397 putative redox protein), Mspyr1_35330(predicted redox protein), Mspyr1_36500(K06191 glutaredoxin-like protein NrdH), Mspyr1_39890(K18958 WhiB family transcriptional regulator), Mspyr1_39920(Glutaredoxin-like protein), Mspyr1_45950(predicted redox protein), Mspyr1_55310(K06191 glutaredoxin-like protein NrdH), Mspyr1_18940(flavodoxin reductase family protein), Mspyr1_47050(flavodoxin reductase family protein), Mspyr1_39020(K00344 NADPH2:quinone reductase),), Mspyr1 04970(Fe-S oxidoreductase)
mab	*Mycobacterium abscessus* ATCC 19977	3	Ferredoxin	MAB_4157c(FdxD) MAB_2240(4Fe-4S) MAB_1327
		5	Ferredoxin reductase	MAB_0930(ferredoxin reductase), MAB_3482(ferredoxin reductase), MAB_0088c(ferredoxin reductase) MAB_3838c MAB_2047c
		6	Non P450 redox proteins	MAB_1465(K05838 putative thioredoxin), MAB_1710c(Conserved hypothetical protein (OsmC-like protein)), MAB_3415c(K06191 glutaredoxin-like protein NrdH), MAB_3512(K18917 mycoredoxin), MAB_1043c(Putative oxidoreductase), MAB_4199(Putative oxidoreductase)
mabb	*Mycobacterium abscessus subsp. bolletii* 50594	4	Ferredoxin	MASS_1211(4Fe-4S), MASS_4156(FdxD), MASS_1327 MASS_2170
		3	Ferredoxin reductase	MASS 0913(ferredoxin reductase), MASS 4170(ferredoxin reductase), MASS 3512(ferredoxin reductase),
		11	Non P450 redox proteins	MASS_1457(K05838 putative thioredoxin), MASS_1803(hydrolase of the alpha/beta superfamily protein), MASS_3358(K06191 glutaredoxin-like protein NrdH), MASS_4808(OsmC family protein), MASS_1p0060(K18958 WhiB family transcriptional regulator), MASS_2p0009(K18957 WhiB family transcriptional regulator), MASS_0552(putative oxidoreductase)MASS_3219(4Fe-4S), MASS_4944(4Fe-4S), MASS_4335(4Fe-4S), MASS_3850(ferredoxin reductase)
may	*Mycobacterium abscessus subsp. bolletii* MA	4	Ferredoxin	LA62_06160(4Fe-4S), LA62_21130(4Fe-4S), LA62_06720(4Fe-4S), LA62_11400(4Fe-4S),

	1948			
		6	Ferredoxin reductase	LA62_08080(ferredoxin reductase), LA62_17705(ferredoxin reductase), LA62_21205(Ferredoxin reductase), LA62_22195(ferredoxin reductase) LA62_20430 LA62_00445
		4	Non P450 redox proteins	LA62_07440(K05838 putative thioredoxin), LA62_08705(osmotically inducible protein OsmC), LA62_08945(K18955 WhiB family transcriptional regulator), LA62_17355(K06191 glutaredoxin-like protein NrdH),
mabo	*Mycobacterium abscessus subsp. bolletii* MC1518	4	Ferredoxin	NF82_06135(4Fe-4S), NF82_20825(4Fe-4S), NF82_06685(4Fe-4S), NF82_11195(4Fe-4S)
		3	Ferredoxin reductase	NF82_08040(Ferredoxin reductase), NF82_17440(Ferredoxin reductase), NF82_21885(ferredoxin reductase)
		6	Non P450 redox proteins	NF82_07400(K05838 putative thioredoxin), NF82_08655(K06889 uncharacterized protein K07397 putative redox protein), NF82_08805(K18955 WhiB family transcriptional regulator), NF82_17105(K06191 glutaredoxin-like protein NrdH), NF82_21510(Fe-S oxidoreductase). NF82_24745(4Fe-4S),
mabl	*Mycobacterium abscessus subsp. bolletii* CCUG 48898 = JCM 15300 3	1	Ferredoxin	MMASJCM_1355(4Fe-4S),
		3	Ferredoxin reductase	MMASJCM_1033(ferredoxin reductase), MMASJCM_4256(ferredoxin reductase), MMASJCM_1611(ferredoxin reductase)
		4	Non P450 redox proteins	MMASJCM_1484(K05838 putative thioredoxin), MMASJCM_3423(K06191 glutaredoxin-like protein NrdH), MMASJCM_3533(K18917 mycoredoxin), MMASJCM_4803(K17218 sulfide:quinone oxidoreductase)
maz	*Mycobacterium abscessus* 103	4	Ferredoxin	LA61_06065(4Fe-4S), LA61_21025(4Fe-4S), LA61_11290(4Fe-4S), LA61_00450 LA61_06615
		5	Ferredoxin reductase	LA61_04605(Ferredoxin reductase), LA61_07975(ferredoxin reductase), LA61_17605(Ferredoxin reductase), LA61_21100(ferredoxin reductase), LA61_22090(ferredoxin reductase)
		4	Non P450 redox proteins	LA61_07330(K05838 putative thioredoxin), LA61_08600(K06889 uncharacterized protein K07397 putative redox protein), LA61_08840(K18955 WhiB family transcriptional regulator), LA61_17260(K06191 glutaredoxin-like protein NrdH),
mak	*Mycobacterium abscessus subsp. abcessus* MM1513	6	Ferredoxin	LH56_17005(4Fe-4S), LH56_03400(4Fe-4S), LH56_16460(4Fe-4S), LH56_12705(4Fe-4S), LH56_04080 LH56_21915
		3	Ferredoxin reductase	LH56_15135(ferredoxin reductase), LH56_06695(ferredoxin reductase), LH56_18350
		6	Non P450 redox proteins	LH56_07030(K06191 glutaredoxin-like protein NrdH), LH56_14535(K06889 uncharacterized protein K07397 putative redox protein), LH56_15775(K05838 putative thioredoxin), LH56_03190(pyridine nucleotide-disulfide oxidoreductase) LH56_00070(4Fe-4S), LH56_07740(4Fe-4S),
myc	*Mycobacterium abscessus* 4529	4	Ferredoxin	NF90_17480(4Fe-4S), NF90_03455(4Fe-4S), NF90_16945(4Fe-4S), NF90_13170(4Fe-4S),
		3	Ferredoxin reductase	NF90_15630(ferredoxin reductase), NF90_06730(ferredoxin reductase), NF90_03385(ferredoxin reductase),
		6	Non P450 redox proteins	NF90_07070(K06191 glutaredoxin-like protein NrdH), NF90_15030(K06889 uncharacterized protein K07397 putative redox protein), NF90_16270(K05838 putative thioredoxin), NF90_00070(4Fe-4S), NF90_07865(4Fe-4S), NF90_17930
mys	*Mycobacterium abscessus* DJO-44274	5	Ferredoxin	NF92_17475 NF92_03455 NF92_16940 NF92_04140 NF92_13170
		1	Ferredoxin reductase	NF92_18805
		3	Non P450 redox proteins	NF90_07070(K06191 glutaredoxin-like protein NrdH), NF90_15030(K06889 uncharacterized protein K07397

				putative redox protein), NF90_16270(K05838 putative thioredoxin),
mmc	*Mycobacterium sp*. MCS	21	Ferredoxin	Mmcs_3697(4Fe-4S), Mmcs_4621(FdxD), Mmcs_2015(4fe-4S), Mmcs_3705(4Fe-4S), Mmcs_0454(3Fe-4S), Mmcs_5292 Mmcs_0618 Mmcs_2719 Mmcs_5289 Mmcs_4030 Mmcs_2580 Mmcs_3712 Mmcs_0319 Mmcs_4710 Mmcs_1358 Mmcs_2259 Mmcs_2875 Mmcs_1520 Mmcs_2269 Mmcs_4866 Mmcs_4256 Mmcs_3768
		1	Ferredoxin reductase	Mmcs_4462(ferredoxin reductase),
		12	Non P450 redox proteins	Mmcs_1334(Rubredoxin-type Fe(Cys)4 protein), Mmcs_1408(K18917 mycoredoxin), Mmcs_1815(K06191 glutaredoxin-like protein NrdH), Mmcs_3862(K05838 putative thioredoxin), Mmcs_4527(Thioredoxin domain protein), Mmcs_3697(4Fe-4S), Mmcs_5251(sucraseferredoxin), Mmcs_2259(4Fe-4S), Mmcs_3419(4Fe-4S), Mmcs_4865(ferredoxin (flavodoxin) oxidoreductase Mmcs_0454(3Fe-4S), Mmcs_5186(FAD-dependent pyridine nucleotide-disulfide oxidoreductase)
mkm	*Mycobacterium sp*. KMS	22	Ferredoxin	Mkms_4709(FdxD) Mkms_2061(4Fe-4S), Mkms_5381(FdxD), Mkms_3778(4Fe-4S), Mkms_2763(4Fe-4S), Mkms_0465(3Fe-4S) Mkms_0631 Mkms_0529 Mkms_3841 Mkms_5378 Mkms_4105 Mkms_4955 Mkms_2625 Mkms_3785 Mkms_0329 Mkms_4796 Mkms_2306 Mkms_2919 Mkms_3896 Mkms_1543 Mkms_2316 Mkms_4342
		1	Ferredoxin reductase	Mkms_1632(ferredoxin reductase),
		21	Non P450 redox proteins	Mkms_0705(redoxin domain-containing protein), Mkms_1351(rubredoxin-type Fe(Cys)4 protein), Mkms_1352(rubredoxin-type Fe(Cys)4 protein), Mkms_1426(K18917 mycoredoxin), Mkms_1862(K06191 glutaredoxin-like protein NrdH), Mkms_3113(K03564 peroxiredoxin), Mkms_3421(K03386 peroxiredoxin), Mkms_3717(K03564 peroxiredoxin), Mkms_3936(K05838 putative thioredoxin), Mkms_4614(thioredoxin domain-containing protein), Mkms_4901(redoxin domain-containing protein), Mkms_5664(redoxin domain-containing protein), Mkms_5746(redoxin domain-containing protein) Mkms_3640(4Fe-4S), Mkms_3770(4Fe-4S), Mkms_4954(flavodoxin/ferredoxin oxidoreductase), Mkms_5340(sucraseferredoxin), Mkms_1376(4Fe-4S) Mkms_3482(Fe-4S), Mkms_4954(flavodoxin/ferredoxin oxidoreductase), Mkms_2978(FAD dependent oxidoreductase)
mjl	*Mycobacterium sp*. JLS	26	Ferredoxin	Mjls_3710(4Fe-4S), Mjls_5004(FdXD), Mjls_1996(4Fe-4S), Mjls_0441(93Fe-4S), Mjls_4260(4fe-4S), Mjls_3718(4Fe-4S), Mjls_0609 Mjls_0507 Mjls_5671 Mjls_4202 Mjls_4034 Mjls_4429 Mjls_3780 Mjls_2749 Mjls_5668 Mjls_4260 Mjls_5234 Mjls_2619 Mjls_3725 Mjls_5095 Mjls_1392 Mjls_2298 Mjls_2905 Mjls_3808 Mjls_3430 Mjls_4635
		5	Ferredoxin reductase	Mjls_1578(Ferredoxin reductase), Mjls_4845(Ferredoxin reductase), Mjls_4216(Ferredoxin reductase), Mjls_4115(ferredoxin reductase) Mjls_4084
		9	Non P450 redox proteins	Mjls_1370(Rubredoxin-type Fe(Cys)4 protein), Mjls_1462(K18917 mycoredoxin), Mjls_1796(K06191 glutaredoxin-like protein NrdH) Mjls_3848(K05838 putative thioredoxin), Mjls_4910(Thioredoxin domain), Mjls_2789(K02192 bacterioferritin-associated ferredoxin), Mjls_3572(flavodoxin/ferredoxin), Mjls_5233(flavodoxin/ferredoxin), Mjls_5631(Sucraseferredoxin
mjd	*Mycobacterium sp*. JDM601	8	Ferredoxin	JDM601_3439(4Fe-4S), JDM601_3492(FdxD) JDM601_3498(FdxD), JDM601_3605 JDM601_3499 JDM601_3634 JDM601_3735 JDM601_2324
		6	Ferredoxin reductase	JDM601_0812(Ferredoxin reductase), JDM601_1956(Ferredoxin reductase), JDM601_0700(Ferredoxin reductase), JDM601_2873(ferredoxin reductase) ,JDM601_3855(Ferredoxin reductase) JDM601_4002

		8	Non P450 redox proteins	JDM601_0524(thioredoxin protein), JDM601_1387(K03564 peroxiredoxin), JDM601_2789(K06191 glutaredoxin-like protein NrdH), JDM601_2913(K18917 mycoredoxin)), JDM601_3951(membrane-anchored thioredoxin-like protein)JDM601_2406(FdxA) JDM601_3423(K02192 bacterioferritin-associated ferredoxin), JDM601_3951(membrane-anchored thioredoxin-like protein),
mmi	*Mycobacterium marinum*	14	Ferredoxin	MMAR_4933(4Fe-4S) MMAR_4734 MMAR_4736 MMAR_2879 MMAR_3973 MMAR_4716 MMAR_4763 MMAR_4730 MMAR_2667 MMAR_4991 MMAR_2994 MMAR_2080 MMAR_4274 MMAR_3421
		5	Ferredoxin reductase	MMAR_4646(Ferredoxin reductase), MMAR_3153(Ferredoxin reductase), MMAR_1017(ferredoxin reductase),MMAR_0335(Ferredoxin reductase) MMAR_2931
		17	Non P450 redox proteins	MMAR_0041(K18956 WhiB family transcriptional regulator), MMAR_0575(K06889 uncharacterized protein K07397 putative redox protein), MMAR_0872(K06889 uncharacterized protein K07397 putative redox protein), MMAR_1132(K18955 WhiB family transcriptional regulator), MMAR_1282(K18955 WhiB family transcriptional regulator), MMAR_1338(K18955 WhiB family transcriptional regulator), MMAR_1363(K18917 mycoredoxin), MMAR_1365(K18958 WhiB family transcriptional regulator), MMAR_1640(K06191 glutaredoxin-like protein NrdH), MMAR_2755(K03386 peroxiredoxin), MMAR_3408(ferredoxin/flavodoxin), MMAR_3956(K03564 peroxiredoxin), MMAR_5161(thioredoxin-like protein), MMAR_5170(K18955 WhiB family transcriptional regulator), MMAR_5437(K18957 WhiB family transcriptional regulator) MMAR_4684(bacterioferritin-associated ferredoxin), MMAR_3408(ferredoxin/flavodoxin)
mrh	*Mycobacterium rhodesiae*	20	Ferredoxin	MycrhN_3929(4Fe-4S), MycrhN_2409(4Fe-4S), MycrhN_0189(4Fe-4S), MycrhN_3206(4Fe-4S), MycrhN_5755 MycrhN_0118 MycrhN_3188 MycrhN_3146 MycrhN_4026 MycrhN_4000 MycrhN_4006 MycrhN_2333 MycrhN_1308 MycrhN_3995 MycrhN_4188 MycrhN_0199 MycrhN_0935 MycrhN_3649 MycrhN_3898 MycrhN_3989
		1	Ferredoxin reductase	MycrhN_0469(Ferredoxin reductase)
		1	cytochrome P450	MycrhN_0102(cytochrome P450)
		15	Non P450 redox proteins	MycrhN_0288(K06889 uncharacterized protein K07397 putative redox protein), MycrhN_0336(K18958 WhiB family transcriptional regulator), MycrhN_0339(K18917 mycoredoxin), MycrhN_1105(Glutaredoxin-like domain (DUF836), MycrhN_3524(thioredoxin domain-containing protein), MycrhN_3852(K05838 putative thioredoxin), MycrhN_5607(thioredoxin-like protein), MycrhN_5866(putative redox protein), MycrhN_6003(K06191 glutaredoxin-like protein NrdH) MycrhN_6317(putative redox protein), MycrhN_1355(Fe-S oxidoreductase)MycrhN_3122(4Fe-4S), MycrhN_4314(K00392 sulfite reductase (ferredoxin), MycrhN_0177(ferredoxin reductase MycrhN_0030(ferredoxin/flavodoxin)
mmm	*Mycobacterium sp*. MOTT36Y	17	Ferredoxin	W7S_03425(4Fe-4S), W7S_07185(4Fe-4S), W7S_03810 W7S_09175 W7S_03995 W7S_02760 W7S_03820 W7S_03675 W7S_16725 W7S_09225 W7S_05985 W7S_09965 W7S_18975 W7S_13715 W7S_13835 W7S_07185 W7S_23690
		3	Ferredoxin reductase	W7S_04360(Ferredoxin reductase), W7S_08345(ferredoxin reductase), W7S_20245(ferredoxin reductase)
		12	Non P450 redox proteins	W7S_00165(K18956 WhiB family transcriptional regulator), W7S_06735(K05838 putative thioredoxin), W7S_18770(glutaredoxin), W7S_19955(K18917 mycoredoxin), W7S_20330(rubredoxin-type Fe(Cys)4 protein), W7S_21440(K00384 thioredoxin reductase), W7S_21155(K03333 cholesterol oxidase), W7S_13830(FAD dependent oxidoreductase), W7S_05795(oxidoreductase) W7S_04140(bacterioferritin-associated ferredoxin), W7S_08360(4Fe-4S), W7S_08340(4Fe-4S),

mcb	*Mycobacterium chubuense*	15	Ferredoxin	Mycch_0448(4Fe-4S) Mycch_4564(4Fe-4S), Mycch_1660(4Fe-4S), Mycch_0257(4Fe-4S), Mycch_4523(4Fe-4S), Mycch_3591(4Fe-4S) Mycch_3612, Mycch_3606, Mycch_3616, Mycch_1683, Mycch_3679, Mycch_1678, Mycch_3933, Mycch_3701, Mycch_0360,
		2	Ferredoxin reductase	Mycch_1556(ferredoxin--NADP+ reductase), Mycch_4406
		15	Non P450 redox proteins	Mycch_1421(K18917 mycoredoxin), Mycch_1780(K06191 glutaredoxin-like protein NrdH), Mycch_1899(putative redox protein), Mycch_2113(thioredoxin-like protein), Mycch_2203(K18958 WhiB family transcriptional regulator), Mycch_2912(K07397 putative redox protein), Mycch_3748(K05838 putative thioredoxin), Mycch_3965(K00384 thioredoxin reductase), Mycch_4077(thioredoxin domain protein), Mycch_5481(K06191 glutaredoxin-like protein NrdH), Mycch_5499(K06191 glutaredoxin-like protein NrdH), Mycch_5863(K06191 glutaredoxin-like protein NrdH), Mycch_3622(flavodoxin reductase family protein), Mycch_4429(putative F420-dependent oxidoreductase, Rv1855c family), Mycch_0396(Fe-S oxidoreductase) Mycch_3366(ferredoxin),
mli	*Mycobacterium liflandii*	14	Ferredoxin	MULP_02645(4Fe-4S), MULP_03687(fdxc) MULP_04956(FdxD_2), MULP_04958, MULP_01030(FdxD_3), MULP_04991, MULP_04938, MULP_04952, MULP_04147(FdxD_1), MULP_02412, MULP_05239(FdxD), MULP_03073(FdxA_1), MULP_05296(FdxB), MULP_03752,
		6	Ferredoxin reductase	MULP_04861(ferredoxin reductase), MULP_05324(ferredoxin reductase), MULP_00312(ferredoxin reductase), MULP_03686(ferredoxin reductase), MULP_01646(ferredoxin reductase), MULP_01143(ferredoxin reductase)
		20	Non P450 redox proteins	MULP_00035(K18956 WhiB family transcriptional regulator), MULP_00580(K06889 uncharacterized protein K07397 putative redox protein), MULP_00894(glutaredoxin-like protein), MULP_00900(thioredoxin protein), MULP_01029(putative redox protein), MULP_01271(K18955 WhiB family transcriptional regulator), MULP_01443(K18955 WhiB family transcriptional regulator), MULP_01509(K18955 WhiB family transcriptional regulator), MULP_01534(glutaredoxin protein), MULP_01537(transcriptional regulatory protein Whib-like WhiB7), MULP_01793(K06191 glutaredoxin-like protein NrdH), MULP_02609(K03386 peroxiredoxin), MULP_03672(pyruvate ferredoxin/flavodoxin oxidoreductase), MULP_04127(K03564 peroxiredoxin), MULP_04239(K05838 putative thioredoxin)MULP_05437(membrane-anchored thioredoxin-like protein), MULP_05446(K18955 WhiB family transcriptional regulator), MULP_05708(K18957 WhiB family transcriptional regulator), MULP_03672(ferredoxin/flavodoxin oxidoreductase), MULP_03369(FAD-dependent oxidoreductase).
mks	*Mycobacterium kansasii* 662	16	Ferredoxin	LG40_09790 LG40_11130 LG40_09795 LG40_23565 LG40_11530 LG40_09670 LG40_01245 LG40_09745 LG40_01305 LG40_00175 LG40_09965 LG40_25730 LG40_07180 LG40_03870 LG40_13075 LG40_04235
		2	Ferredoxin reductase	LG40_09280 LG40_01300
mki	*Mycobacterium kansasii* 824	15	Ferredoxin	LH54_11255 LH54_09935 LH54_09940 LH54_11665 LH54_09815 LH54_01255 LH54_09890 LH54_01315 LH54_00175 LH54_10110 LH54_25860 LH54_07190 LH54_04235 LH54_03870 LH54_13215
		3	Ferredoxin reductase	LH54_09390 LH54_15880 LH54_01310
mkn	*Mycobacterium kansasii* ATCC 12478	18	Ferredoxin	MKAN_04240(4Fe-4S) MKAN_09955, MKAN_23805, MKAN_11680, MKAN_09835, MKAN_01235, MKAN_09910, MKAN_01295, MKAN_00170, MKAN_10125, MKAN_13235, MKAN_07250, MKAN_03855, MKAN_11975, MKAN_12135, MKAN_01670, MKAN_15935, MKAN_22820,
		7	Ferredoxin reductase	MKAN_24980(ferredoxin reductase), MKAN_22480(ferredoxin reductase), MKAN_19550(oxidoreductase) MKAN_00605(3-phenylpropionate/trans-cinnamate dioxygenase ferredoxin reductase component), MKAN_01240, MKAN_01290, MKAN_09430(ferredoxin--NADP+ reductase), MKAN_03850(ferredoxin--NADP+ reductase)
		8	Non P450 redox proteins	MKAN_04960(sulphite reductase), MKAN_04965(sulphite reductase), MKAN_06260(K05838 putative thioredoxin), MKAN_23165(K06191 glutaredoxin-like protein NrdH), MKAN_03620(oxidoreductase), MKAN_29025(4Fe-4S), MKAN_11285(4Fe-4S), MKAN_09950(4Fe-4S)
mne	*Mycobacterium neoaurum*	10	Ferredoxin	D174_23865(4Fe-4S), D174_16370(4Fe-4S),D174_12890(4fe-4S), D174_04625, D174_12405, D174_20885, D174_13840, D174_02960, D174_09705, D174_19220

		6	Ferredoxin reductase	D174_09620(ferredoxin reductase), D174_03225, D174_16365, D174_23110, D174_08080, D174_13835 (ferredoxin--NADP+ reductase)
		12	Non P450 redox proteins	D174_01045(K06889 uncharacterized protein K07397 putative redox protein), D174_07020(K00384 thioredoxin reductase), D174_07210(K04063 osmotically inducible protein OsmC), D174_10230(glutaredoxin), D174_20080(K05838 putative thioredoxin), D174_25635(OXIDOREDUCTASE), D174_04385(oxidoreductase), D174_01075(oxidoreductase), D174_15525 D174_13855 D174_06575(oxidoreductase)
myv	*Mycobacterium sp*. VKM Ac-1817D	16	ferredoxin	G155_05095(4Fe-4S), G155_12035(4Fe-4S) G155_20635, G155_03845, G155_20490, G155_20655, G155_04895, G155_20825, G155_22240, G155_22210, G155_01230, G155_16695, G155_07985, G155_07895, G155_13780(2Fe-2S), G155_24550(2Fe-2S),
		7	Ferredoxin reductase	G155_03130(ferredoxin reductase), G155_08940(ferredoxin reductase), G155_10200(ferredoxin reductase), G155_29565(ferredoxin reductase), G155_23245(ferredoxin reductase), G155_10535(ferredoxin NADP+ reductase), G155_05925(ferredoxin NADP+ reductase),
		13	Non P450 redox proteins	G155_05675(K18955 WhiB family transcriptional regulator), G155_07610(K00384 thioredoxin reductase), G155_08110(K06889 uncharacterized protein K07397 putative redox protein), G155_11010(glutaredoxin), G155_21205(K05838 putative thioredoxin), G155_27135(hypothetical protein), G155_29555(K06889 uncharacterized protein K07397 putative redox protein), G155_03435(oxidoreductase), G155_09940(oxidoreductase), G155_27910(oxidoreductase)G155_16260 G155_23550 G155_26450(4Fe-4S), G155_01205(4Fe-4S),

After successful classification of redox proteins into different classes i.e. ferredoxins and ferredoxin reductases further studies were conducted to identify different groups within these types of P450 redox protiens.

4.3.1. Ferredoxins (Fdx)

A total number of 662 ferredoxins were found in 81 mycobacterial species (Table 4.2) belong to six different categories. *Mycobacterial tuberculosis* complex species showed 1-6 ferredoxins in their genomes. Mycobacteria causing leprosy (MCL) included two species namely *Mycobacterium leprae* TN and *Mycobacterium leprae* Br4923 which both contained a single ferredoxin. The other group which is known to be Nontuberculosis mycobacteria (NTM) showcased a range of 7-18 for ferredoxins. Saprophytes showed a high number of ferredoxins with the range of 8-26. *Mycobacterium avium* complex species showed a range from 4 -19 ferredoxins in their genomes.

Phylogenetic anlaysis of ferredoxins revealed presence of two major clades of ferredoxins with characteristic Pfam/InterPro protein domains (Figure. 4.1 and Table 4.3). The clade with domains Fer4 (PF00037), Fer4_7 (PF12838) and Fer4_9 (PF13187) was associated with the same InterPro entry (IPR17896) and it was classified under group 2 of ferredoxins (Figure 4.1 and Table 4.3). The clade supported with 83% boostrap proportion with domains Fer4_13 (PF13370), Fer4_15 (PF13459) and Fer4_19 (PF06902) shared similar HMM-motifs which was classified under as group 1 (Figure 4.1 and Table 4.3). Some of the ferredoxin showed different Pfam/InterPro protein domains and their classification as P450 ferredoxins is difficult to assing. Hence these ferredoxins were classified under divergent ferredoxins. Based on Pfam/InterPro domain the divergent ferredoxins were classified into 12 groups (Table 4.3).

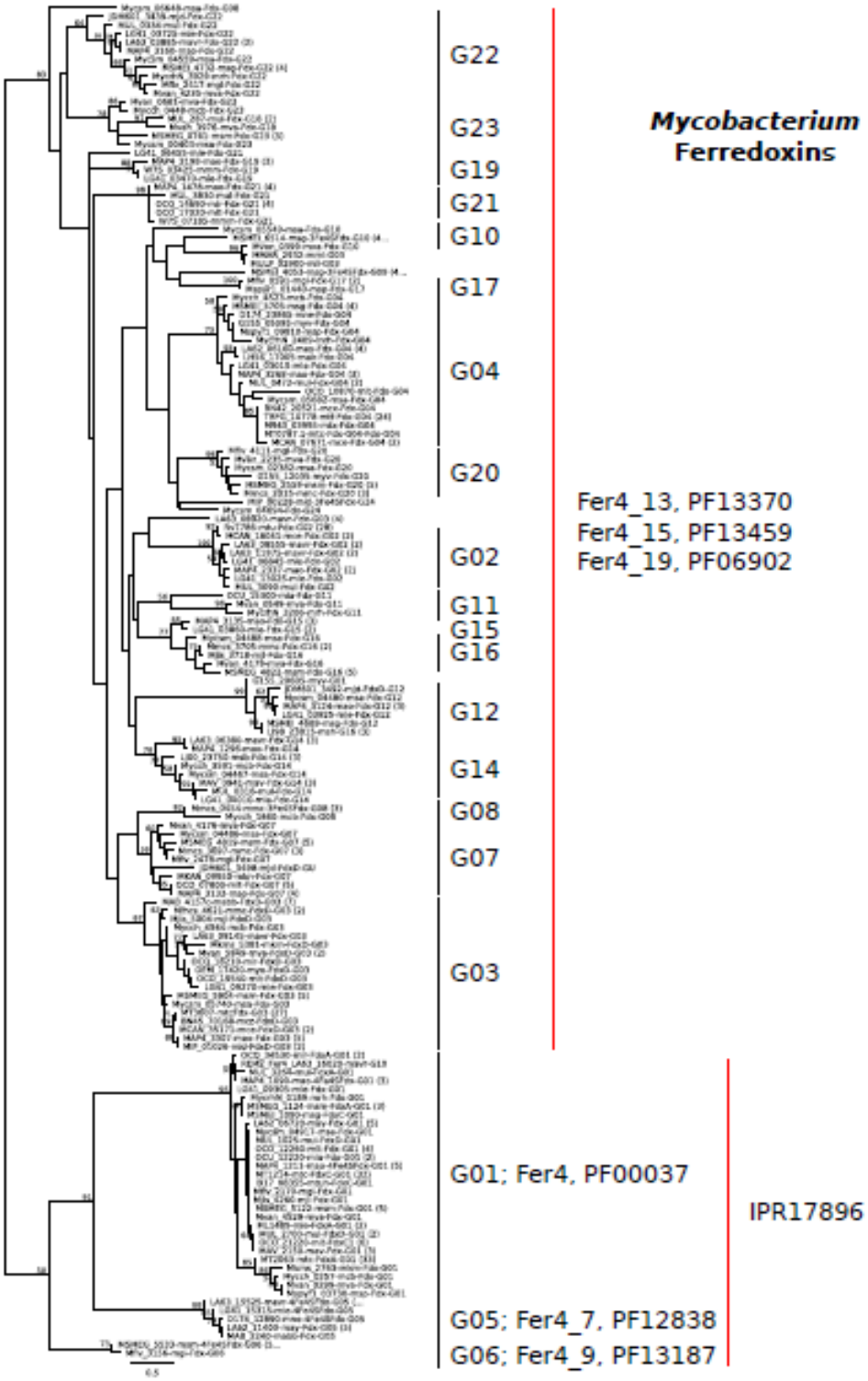

Figure 4.1. Maximul likelyhood phylogeny of *Mycobacterium* ferredoxins. Numbers on branches indicate bootstrap proportions (1000 replicates); supports below 50 are not shown. Assignment to groups and Pfam domain composition is given on the right. Terminal clades/groups are relatively well-supported.

Table 4.3. Classification of ferredoxin based on Pfam/InterPro protein domains.

Group 1	
Pfam/InterPro protein domains	Fer4_13, PF13370, Fer4_15, PF13459, Fer4_19, PF06902
Ferredoxins	
Mycsm_06648-msa-Fdx-G08, JDM601_3439-mjd-Fdx-G22, MUL_0334-mul-Fdx-G22, LG41_03725-mie-Fdx-G22, LA63_03885-mavr-Fdx-G22 (2), NF84_03785-mavd-Fdx-G22, MAP4_3160-mao-Fdx-G22, Mycsm_04559-msa-Fdx-G22, MSMEI_4732-msg-Fdx-G22 (4) LI98_24030-msh-Fdx-G22, LJ00_24020-msb-Fdx-G22, LI99_24025-msn-Fdx-G22 , MycrhN_3929-mrh-Fdx-G22, Mflv_2417-mgi-Fdx-G22, Mvan_4235-mva-Fdx-G22, Mvan_0681-mva-Fdx-G23, Mycch_0448-mcb-Fdx-G23, MUL_287-mul-Fdx-G18 (2) MULP_02645-mli-Fdx-G18,Mvan_3976-mva-Fdx-G18, MSMEG_0761-msm-Fdx-G23 (5) MSMEI_0745-msg-Fdx-G23, LJ00_03780-msb-Fdx-G23, LI99_03780-msn-Fdx-G23, LI98_03780-msh-Fdx-G23 , Mycsm_00403-msa-Fdx-G23, LG41_06455-mie-Fdx-G21, MAP4_3198-mao-Fdx-G19 (3) LA63_03685-mavr-Fdx-G19, NF84_03595-mavd-Fdx-G19 MT2063-mtc-FdxA-G01 , W7S_03425-mmm-Fdx-G19, LG41_03470-mie-Fdx-G19, MAP4_1478-mao-Fdx-G21 (4) MAV_1636-mav-Fdx-G21, LA63_07405-mavr-Fdx-G21, NF84_07270-mavd-Fdx-G21 , Mvan_5849-mva-FdxD-G03 , MUL_3830-mul-Fdx-G21, OCQ_14690-mir-Fdx-G21 (4) LG41_08110-mie-Fdx-G21, MIP_02348-mid, OEM_15020-myo-Fdx-G21 , OCO_17020-mit-Fdx-G21, W7S_07185-mmm-Fdx-G21, Mycsm_05549-msa-Fdx-G10, MSMEI_6514-msg-3Fe4SFdx-Fdx (4) LJ00_33085-msb-Fdx-G10, LI99_33090-msn-Fdx-G10, LI98_33095-msh-Fdx-G10 , Mvan_0399-mva-Fdx-G10, MSMEI_4053-msg-3Fe4SFdx-G09 (4) LJ00_20585-msb-3Fe4SFdx-G09, LI99_20590-msn-3Fe4SFdx-G09, LI98_20595-msh-3Fe4SFdx-G09 ,Mflv_0591-mgi-Fdx-G17(2), Mflv_0681-mgi-Fdx-G17 Mspyr1_01440-msp-Fdx-G17, Mycch_4523-mcb-Fdx-G04, MSMEI_5705-msg-Fdx-G04 (4) LJ00_29000-msb-Fdx-G04, LI99_29005-msn-Fdx-G04, LI98_29010-msh-Fdx-G04 , D174_23865-mneFdx-G04, G155_05095-myv-Fdx-G04, Mspyr1_09810-msp-Fdx-G04, MycrhN_2409-mrh-Fdx-G04, LA62_06160-may-Fdx-G04 (4) NF82_06135-mabo-Fdx-G04, LA61_06065-maz-Fdx-G04, NF90_17480-mys-Fdx-G04 , LH56_17005-mak-Fdx-G04, LG41_03015-mie-Fdx-G04, MAP4_3268-mao-Fdx-G04 (3) LA63_03310-mavr-Fdx-G04, NF84_03215-mavd-Fdx-G04 , MUL_0472-mul-Fdx-G04 (2) MMAR_4933-mmi-Fdx-G04, OCO_10870-mit-Fdx-G04, Mycsm_05682-msa-G04, BN42_20521-mcx-Fdx-G04, TBFG_10778-mtf-Fdx-G04 (24) TBMG_00778-mtb-Fdx-G04, TBSG_00782-mtk-Fdx-G04, TBXG_000771-mtz-Fdx-G04, MRGA327_04750-mtg-Fdx-G04, CFBS_0802-mtur-Fdx-G04, MTCTRI2_0782-mto-Fdx-G04, ERDMAN_0845-mtn-Fdx-G04, J112_04105-mtj-Fdx-G04, J113_05385-mtuc-Fdx-G04, J114_04075-mtue-Fdx-G04, I917_05410-mtuh-Fdx-G04, TBHG_00755-mtul-Fdx-G04, HKBT2_0803-mtu-Fdx-G04, HKBS1_0802-mtq-Fdx-G04, Mb0786c-mbo-Fdx-G04, BCG_0815c-mbb-Fdx-G04, JTY_0785-mtb-Fdx-G04, BCGMEX_0786c-mbm-Fdx-G04, K60_008160-mbk-Fdx-G04, LH58_04155-mbz-Fdx-G04, MAF_07750-maf-Fdx-G04, BN44_10833-mcq-Fdx-G04, BN43_20198-mcv-Fdx-G04 , M943_03995-mtx-Fdx-G04, MT0787.1-mtc-Fdx-G04, MCAN_07671-mce-Fdx-G04 (2) BN45_20032-mcz-Fdx-G04, Mflv_4111-mgi-Fdx-G20, Mvan_2235-mva-Fdx-G20, Mycsm_02382-msa-Fdx-G20, G155_12035-myv-Fdx-G20, MSMEG_2559-msm-Fdx-G20 (5), MSMEI_2499-msg-Fdx-G20, LI99_12735-msn-Fdx-G20, LJ00_12735-msb-Fdx-G20, LI98_12740-msh-Fdx-G20 , Mmcs_2015-mmc-Fdx-G20 (3) MAV_1949-mav-Fdx-G13, Mjls_1996-mjl-Fdx-G20 LA63_08920-mavr-Fdx-G13,MIP_00228-mid-3Fe4SFdx-G24, Mycsm_04694-msa-Fdx-G24, LA63_08920-mavr-Fdx-G03 (4), MAV_1949-mav-Fdx-G13, LA63_08920-mavr-Fdx-G13, NF84_08780-mavd-Fdx-G13, NF84_08780-mavd-Fdx-G13 , Rv1786-mtu-Fdx-G02 (28) MT1835-mtc-Fdx-G02, TBFG_11816-mtf-Fdx-	

G02, TBMG_02211-mtb-Fdx-G02, TBSG_02223-mtk-Fdx-G02, TBXG_002192-mtz-Fdx-G02, MRGA327_11075-mtg-Fdx-G02, CFBS_1875-mtur-Fdx-G02, MTCTRI2_1817-mto-Fdx-G02, J112_09550-mtj-Fdx-G02, MT7199_1812-mtub-Fdx-G02, J113_12425-mtuc-Fdx-G02, J114_09545-mtue-Fdx-G02, M943_09300-mtx-Fdx-G02, I917_12705-mtuh-Fdx-G02, TBHG_01744-mtul-Fdx-G02, HKBT2_1882-mtu-Fdx-G02, HKBS1_1878-mtq-Fdx-G02, Mb1814-mbo-Fdx-G02, BCG_1818-mbb-Fdx-G02, JTY_1802-mtb-Fdx-G02, BCGMEX_1799-mbm-Fdx-G02, K60_018710-mbk-Fdx-G02, LH58_09585-mbz-Fdx-G02, MAF_18080-maf-Fdx-G02, BN43_30924-mcv-Fdx-G02, BN42_30041-mcx-Fdx-G02, BN45_50042-mcz-Fdx-G02 , MCAN_18041-mce-Fdx-G02 (2) BN44_40043-mcq-Fdx-G02, LA63_08555-mavr-Fdx-G02 (2) NF84_08415-mavd-Fdx-G02, LA63_11975-mavr-Fdx-G02 (2) NF84_11695-mavd-Fdx-G02, LG41_06845-mie-Fdx-G02, MAP4_2337-mao-Fdx-G02 (2) >LA63_13250-mavr-Fdx-G02, LG41_13025-mie-Fdx-G02, MUL_3090-mul-Fdx-G02, OCU_15300-mia-Fdx-G11, Mvan_0549-mva-Fdx-G11, MycrhN_3206-mrh-Fdx-G11, MAP4_3135-mao-Fdx-G15 (3) LA63_04010-mavr-Fdx-G15, NF84_03910-mavd-Fdx-G15 , LG41_03860-mie-Fdx-G15 (2) OEM_07860-myo-Fdx-G15, Mmcs_3705-mmc-Fdx-G16 (2) Mkms_3778-mkm-Fdx-G16, Mjls_3718-mjl-Fdx-G16, Mvan_4179-mva-Fdx-G16, MSMEG_4822-msm-Fdx-G16 (5) MSMEI_4698-msg-4Fe4SFdx-G16, LJ00_23850-msb-Fdx-G16, LI99_23855-msn-Fdx-G16, LI98_23860-msh-Fdx-G16 ,JDM601_3492-mjd-G12, Mycsm_04480-msa-Fdx-G12, MAP4_3124-mao-Fdx-G12 (3) LA63_04060-mavr-Fdx-G12, NF84_03960-mavd-Fdx-G12 , LG41_03925-mie-Fdx-G12, MSMEI_4689-msg-Fdx-G12, LI98_23815-msh-G16 (3), LJ00_23805-msb, LI99_23810-msn, LA63_06380-mavr-Fdx-G14 (3) NF84_06250-mavd-Fdx-G14, NF84_13100-mavd-Fdx-G14 , MAP4_1296-mao-Fdx-G14, LJ00_23750-msb-Fdx-G14 (3) LI99_23755-msn-Fdx-G14, LI98_23760-msh-Fdx-G14 , Mycch_3591-mcb-Fdx-G14, Mycsm_04467-msa-Fdx-G14, MAV_0941-mav-Fdx-G14 (3) LA63_04145-mavr-Fdx-G14, NF84_04045-mavd-Fdx-G14, MUL_0316-mul-Fdx-G14, LG41_04010-mie-Fdx-G14, Mmcs_0454-mmc-3Fe4SFdx-G08 (3) Mkms_0465-mkm-Fdx-G08, Mjls_0441-mjl-3Fe4SFdx-G08 , Mycch_1660-mcb-Fdx-G08, Mvan_4176-mva-Fdx-G07, Mycsm_04486-msa-Fdx-G07, MSMEG_4819-msm-Fdx-G07 (5) >MSMEI_4695-msg-Fdx-G07,LJ00_23835-msb-Fdx-G07, LI99_23840-msn-Fdx-G07, LI98_23845-msh-Fdx-G07, Mmcs_3697-mmc-Fdx-G07 (3) Mkms_3770-mkm-Fdx-G07, Mjls_3710-mjl-Fdx-G07 , Mflv_2478-mgi-Fdx-G07, JDM601_3498-mjd-FdxD-GU, MKAN_09950-mkn-Fdx-G07, OCO_07800-mit-Fdx-G07 (5) OCQ_07950-mir4Fe-4S-G7, LG41_03870-mie-Fdx-G07, MIP_01339-mid-Fdx-G07, OEM_07880-myo-Fdx-G07, MAP4_3133-mao-Fdx-G07 (4) MAV_0915-mav -Fdx-G07, LA63_04020-mavr-Fdx-G07, NF84_03920-mavd-Fdx-G07 , MAB_4157c-mabb-FdxD-G03 (7) MASS_4156-mabb-FdxD-G03,LA62_21130-may-Fdx-G03, NF82_20825-mabo-Fdx-G03, LA61_21025-maz-Fdx-G03, LH56_03400-mak-Fdx-G03, NF90_03455-mys-Fdx-G03, Mmcs_4621-mmc-FdxD-G03 (2) Mkms_4709-mkm-FdxD-G03, Mjls_5004-mjl-FdxD-G03, Mycch_4564-mcb-Fdx-G03, LA63_09145-mavr-Fdx-G03, Mkms_5381-mkm-FdxD-G03, Mvan_5849-mva-FdxD-G03 (2) Mvan_5849-mva-Fdx-G03, OCQ_18210-mir-FdxD-G03, OEM_17420-myo-fdxD-G03, LG41_09270-mie-Fdx-G03, MSMEG_5904-msm-Fdx-G03 (5), MSMEI_5744-msg-FdxD-G03,LJ00_29200-msb-Fdx-G03, , LI99_29205-msn-Fdx-G03, LI98_29210-msh-Fdx-G03 , MT3607-mtc-Fdx-G03 (27) TBFG_13537-mtf-FdxD-G03, TBMG_03548-mtb-FdxD-G03, TBSG_03570-mtk-FdxD-G03, TBXG_003519-mtz-FdxD-G03, MRGA327_21565-mtg-FdxD-G03, MRGA423_22055-mti-FdxD-G03,CFBS_3719-mtur-FdxD-G03,MTCTRI2_3569-mto-FdxD-G03,Rv3503c-mtu-FdxD-G03,ERDMAN_3844-mtn-FdxD-G03,J112_18830-mtj-FdxD-G03,J113_24450-mtuc-FdxD-G03,J114_18730-mtue-FdxD-G03,M943_18015-mtx-FdxD-G03,I917_24570-mtuh-FdxD-G03,TBHG_03447-mtul-FdxD-G03,HKBT2_3713-mtu-FdxD-G03, HKBS1_3716-mtq-FdxD-G03,Mb3533c-mbo-FdxD-G03,BCG_3567c-mbb-FdxD-G03 ,JTY_3567-mtb-FdxD-G03, K60_036380-mbk-FdxD-G03, LH58_18975-mbz-FdxD-G03, MAF_35160-maf-FdxD-G03, BN44_80180-mcq-FdxD-G03, BN43_70172-mcv-FdxD-G03 , BN45_70168-mcz-FdxD-G03, MCAN_35171-mce-FdxD-G03 (2) BN42_50183-mcx-FdxD-G03, MAP4_3307-mao-Fdx-G03 (5) MAV_0653-mav-Fdx-G03, LA63_03030-mavr-Fdx-G03, NF84_02960-mavd-Fdx-G03, LG41_02825-mie-Fdx-G03 , MIP_01026-mid-FdxD-G03 (2) OEM_05700-myo-FdxD-G03, Mvan_0399-mva-Fdx-G10, MMAR_2932-mmi-G03,

MULP_02900-mli-G03, G155_20605-myv-Fdx-G12	
Group 2	
Pfam/InterPro protein domain	IPR17896 [Fer4 (PF00037), Fer4_7 (PF12838) and Fer4_9 (PF13187)]
Ferredoxins	
OCQ_34530-mir-FdxA-G01 (2) LG41_15760-mie-Fdx-G01, MUL_3264-mul-FdxA-G01, MAP4_1090-mao-4Fe4SFdx-G01 (3) MAV_3500-mav-Fdx-G01, NF84_15875-mavd-Fdx-G01 , LG41_09305-mie-Fdx-G01, MycrhN_0189-mrh-Fdx-G01, MSMEG_1124-msm-FdxA-G01 (3) LJ00_05585-msb-Fdx-G01, LI98_05585-msh-Fdx-G01 , MSMEI_1090-msg-fdxC-G01, LA62_06720-may-Fdx-G01 (5) NF82_06685-mabo-Fdx-G01, MMASJCM_1355-mabl-Fdx-G01, LH56_16460-mak-Fdx-G01, NF90_16945-mys-Fdx-G01 ,Mycsm_04917-msa-Fdx-G01, MUL_1025-mul-FdxD-G01, OCO_12260-mit-Fdx-G01 (4) OCQ_12280-mir-Fdx-G01, MIP_01957-mid-Fdx-G01, OEM_12410-myo-Fdx-G01 OCU_12220-mia-Fdx-G01 (2) OCU_12220-mia-Fdx-G01, MAP4_1211-mao-4Fe4SFdx-G01 (5) MAV_1316-mav-Fdx-G01 LA63_05975-mavr-Fdx-G01, NF84_05845-mavd-Fdx-G01, MAP4_1211-mao-4Fe4SFdx-G04 ,MT1214-mtc-FdxC-G01(32) TBMG_02804-mtb-FdxC-G01, TBSG_02818-mtk-FdxC-G01, TBXG_002784-mtz-FdxC-G01, MRGA327_07415-mtg-FdxC-G01, MRGA423_07345-mti-FdxC-G01, CCDC5079_1089-mte-FdxC-G01, CFBS_1256-mtur-FdxC-G01, CCDC5180_1082-mtl-FdxC-G01, MTCTRI2_1209-mto-FdxC-G01, ERDMAN_1320-mtn-FdxC-G01, J112_06365-mtj-FdxC-G01, MT7199_1207-mtub-FdxC-G01, J113_08245-mtuc-FdxC-G01, J114_06365-mtue-FdxC-G01, M943_06175-mtx-FdxA-G01, TBHG_01161-mtul-FdxC-G01, HKBT2_1260-mtu-FdxC-G01, HKBS1_1258-mtq-FdxC-G01, Mb1210-mbo-FdxC-G01, BCG_1240-FdxC-G01, JTY_1213-mtb-FdxC-G01, BCGMEX_1212-mbm-FdxC-G01, K60_012700-mbk-FdxC-G01, LH58_06490-mbz-FdxC-G01, MAF_11960-maf-FdxC-G01, MCAN_11881-mce-FdxC-G01, BN44_11316-mcq-FdxC-G01, BN43_30245-mcv-FdxC-G01, BN42_21043-mcx-FdxC-G01, BN45_30238-mcz-FdxC-G01, , I917_08355-mtuh-FdxC-G01, Mflv_2170-mgi-Fdx-G01, Mjls_4260-mjl-Fdx-G01, MSMEG_5122-msm-Fdx-G01 (5)MSMEI_4993-msg-FdxC-G01, , LJ00_25320-msb-Fdx-G01, LI99_25325-msn-Fdx-G01, LI98_25330-msh-Fdx-G01 Mvan_4529-mva-Fdx-G01, ML1489-mle-FdxA-G01 (2) MLBr_01489-mlb-FdxA-G01 , MUL_2700-mul-FdxD-G01 (2) MULP_03687-mli-FdxC-G01, OCO_21220-mit-fdxC1 (6) OCQ_20140-mir-FdxC1, OCU_21470-mia-FdxC1, LG41_10100-mie-Fdx-G01, MIP_03002-mid-Fdx-G01, OEM_19090-myo-FdxC1, MAV_2150-mav-Fdx-G01(3), MAV_2150-mav-Fdx-G01(3) LA63_09875-mavr-Fdx-G01, NF84_09675-mavd-Fdx-G01 , MT2063-mtc-FdxA-G01 (33) TBFG_12039-mtf-FdxA-G01, TBMG_01979-mtb-FdxA-G01, TBSG_01990-mtk-FdxA-G01, TBXG_001963-mtz-FdxA-G01, MRGA327_12375-mtg-FdxA-G01, MRGA423_12495-mti-FdxA-G01, CCDC5079_1854-mte-FdxA-G01, CFBS_2117-mtur-FdxA-G01, CCDC5180_1829-mtl-FdxA-G01, MTCTRI2_2041-mto-FdxA-G01, ERDMAN_2211-mtn-FdxA-G01, J112_10735-mtj-FdxA-G01, MT7199_2038-mtub-FdxA-G01, J113_13860-mtuc-FdxA-G01, J114_10740-mtue-FdxA-G01, M943_10425-mtx-FdxA-G01, I917_14190-mtuh-FdxA-G01, TBHG_01965-mtul-FdxA-G01, HKBT2_2113-mtu-FdxA-G01, HKBS1_2118-mtq-FdxA-G01, Mb2030c-mbo-FdxA-G01, BCG_2024c-mbb-FdxA-G01, JTY_2019-mtb-FdxA-G01, BCGMEX_2006c-mbm-FdxA-G01, K60_020800-mbk-FdxA-G01, LH58_10650-mbz-FdxA-G01,MAF_20190-maf-FdxA-G01, MCAN_20271-mce-FdxA-G01, BN44_40292-mcq-FdxA-G01, BN43_31187-mcv-FdxA-G01, BN42_30305-mcx-FdxA-G01, BN45_50286-mcz-FdxA-G01,CCDC5079_1854-mte-FdxA-G01, , Mkms_2763-mkm-Fdx-G01, Mvan_0299-mva-Fdx-G01, Mspyr1_03730-msp-Fdx-G01, LA63_15525-mavr-4Fe4SFdx-G05 (2) NF84_15390-mavd-Fdx-G05 , LG41_15315-mie-4Fe4SFdx-G05, D174_12890-mne-4Fe4SFdx-G05, LA62_11400-may-Fdx-G05 (5) NF82_11195-mabo-Fdx-G05, LA61_11290-maz-Fdx-G05, LH56_12705-mak-Fdx-G05,	

NF90_13170-mys-Fdx-G05 , MAB_2240-mabbFdx-G05, MSMEG_5533-msm-4Fe4SFdx-G06(5) MSMEI_5381-msg-4Fe4SFdx-G06, LJ00_27355-msb-Fdx-G06,LI99_27360-msn-Fdx-G06, LI98_27365-msh-Fdx-G06 ,Mflv_3156-mgi-Fdx-G06,REM2_Fer_LA63_16020-mavr-G10		
Divergent ferredoxins		
Groups	Pfam/InterPro protein domains	Protein IDs
Group 1		MAV_4796-mav-G03
Group 2	FAD_binding_3	MRGA423_03510-mti-G14, MT7199_1774-mtub-G05
Group 3	POR,POR_N,PFOR_II	Mmcs_3567-mmc-G05 (2) Mkms_3640-mkm-G05, Mflv_2616-mgi-G05, Mjls_3572-mjls-G05,
Group 4	AhpC-TSA	CCDC5079_0494-mte-G03
Group 5	NIR_SIR	MycrhN_4314-mrh-G06, Mycch_3366-mcb-G06
Group 6	Rieskie	Mvan_1329-mva-GU
Group 7	GFO_IDH_MocA,	LG41_04965-mie-

	GF0_IDH_MocA_C	G01
Group 8	Pyr-redox_3	Mvan_1519-mva-G05
Group 9	POR_N,PFOR_II, POR,EKR, Fer4, TPP enzyme	MycrhN_0030-mrh-G07, Mvan_4109-mva-G07, MMAR_3408-mmi-G07, Mkms_4954-mkm-G07 (2), Mmcs_4865-mmc-G07 Mjls_5233-mjl-G07
Group 10	OsmC	MycrhN_0177-mrh-G03
Group 11	Adh_short	LA63_14695-mavr-G02
Group 12	Pyr_redox_2, Pyr_redox_dim	MAF_08060-maf-G14, BN44_10869-mcq-G14

4.3.2 Ferredoxin reductase (FdR)

Ferredoxin reductase also proved to be part of redox proteins by showing that it is also capable of transferring electrons. Ferredoxin reductase were also divided into different groups for analyses of the phylogenetic tree. All total of 374 ferredoxin reductase were identified and were also eligible to transfer electrons to P450s. *Mycobacterium tuberculosis* complex ranged from 8-2 ferredoxins reductases, the species with highest number of ferredoxin reductases was *Mycobacterium tuberculosis* CDC1551, *Mycobacterium Beijing/NITR203*, *Mycobacterium bovis BCG Pasteur 1173P2* and *Mycobacterium bovis BCG korea 1168P*. Mycobacteria causing leprosy ranged from 2-2 with both species *Mycobacterium leprae TN* and *Mycobacterium leprae Br4923* having 2 numbers of ferredoxiin reductases. Nontuberculosis mycobacteria ranged from 7-2, *Mycobacterium kansasii ATCC 12478* had a highest number of ferredoxin reductases which is 7 and the lowest number of ferredoxins reductase was *Mycobacterium ulcerans* and *Mycobacterium kansassi* with both 2 reductases each. Saprophytes ranged from 0-6 with *Mycobacterium smegmatis MC2 155* and *Mycobacterium neoaurum* both obtaining highest number of ferredoxin reductases, and Mycobacterium vanaalenii showed no reductases. MAC ranged from 0-7 with *Mycobacterium intracellulare MOTT-64* with highest number of reductases 7 and *Mycobacterium avium subsp. paratubercoluis K-10* showed no number of reductases. MCAC ranged from 1-6 with *Mycobacterium abscessus subsp.bolletii MA 1948* showing highest number of ferredoxin reductases 6 and *Mycobacterium abscessus DJ0-44274* showed least number of ferredoxin reductase 1. Preliminary phylogenetic analyses (Figure 4.2) indicated two major divergent clades of ferredoxin reductase proteins; the bacterial-type, which belong to the Plant-type FdRs, and the gluthatione reductase (GR)- type (Aliverti *et al*., 2008). Within the GR-type FdRs, the adrenodoxin (Adr)-like clade and the oxgynase-coupled NADH-ferredoxin reductase (ONRF) - like clade were identified. Due to the sequence

divergence, separate phylogenies were generated for the bacterial-type and the GR-type FdRs.

4.3.2.1 Bacterial-type FdRs

Conserved Pfam domains characteristics of bacterial-type FdRs were the FAD_binding_6 (PF00970, IPR08333), The NAD_binding_1 (PF00175, IPR01433), and the Fer2 (PF00111, IPR001041) domains. The Group (G04) subclade also included the FA_desaturase domain (PF00487, IPR005804). FAD and NAD-binding domains were aligned and used in the phygenetic analysis. The best model of amino acid substitution according was the WAG+I+G+F.

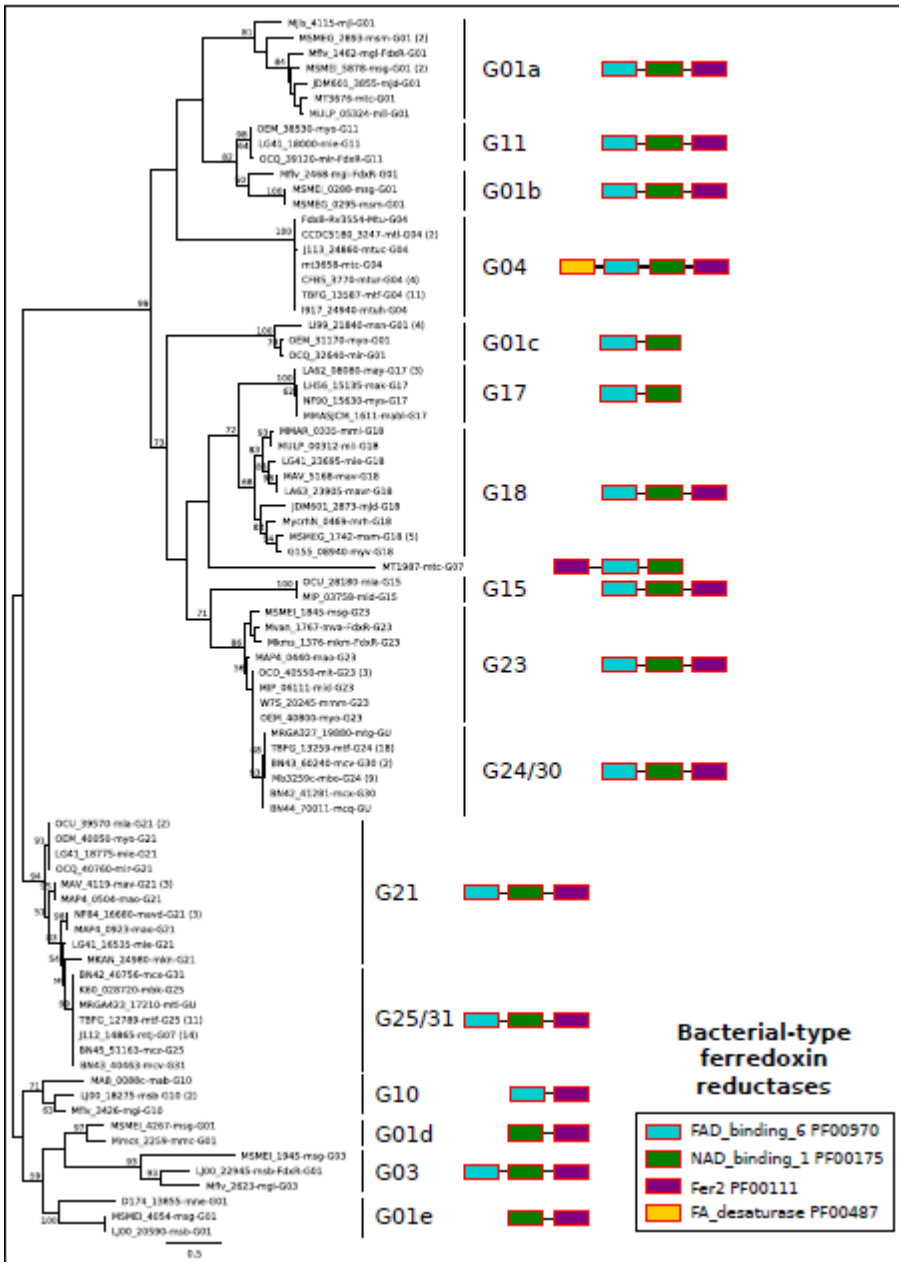

Figure 4.2. Maximum likelihood phylogeny of Bacterial-type FdRs based on alignment of FAD and NAD-binding domains. Numbers on branches indicate bootstrap proportions (1000 replicates); supports below 50 are not shown. Assignment to groups and Pfam domain composition is given on the right. Terminal clades/groups are relatively well-supported.

4.3.2.1 Glutathione reductase-type FdRs

There were two major clades of GR-type reductases; the AdR-like FdR clade and the ONFR-like FdR clade (Figure 4.3). The conserved domain found in all GR-type reductases was the Pyr_redox_2 (PF07992, IPR023753) domain. A subclade of AdR-like FdRs also contained the Fer4 domain (PF00037, IPR01879).In addition to the Pyr_redox_2 domain, all ONFR-like FdRs contained a C-terminal Reductase_C domain (PF07992, IPR023753).

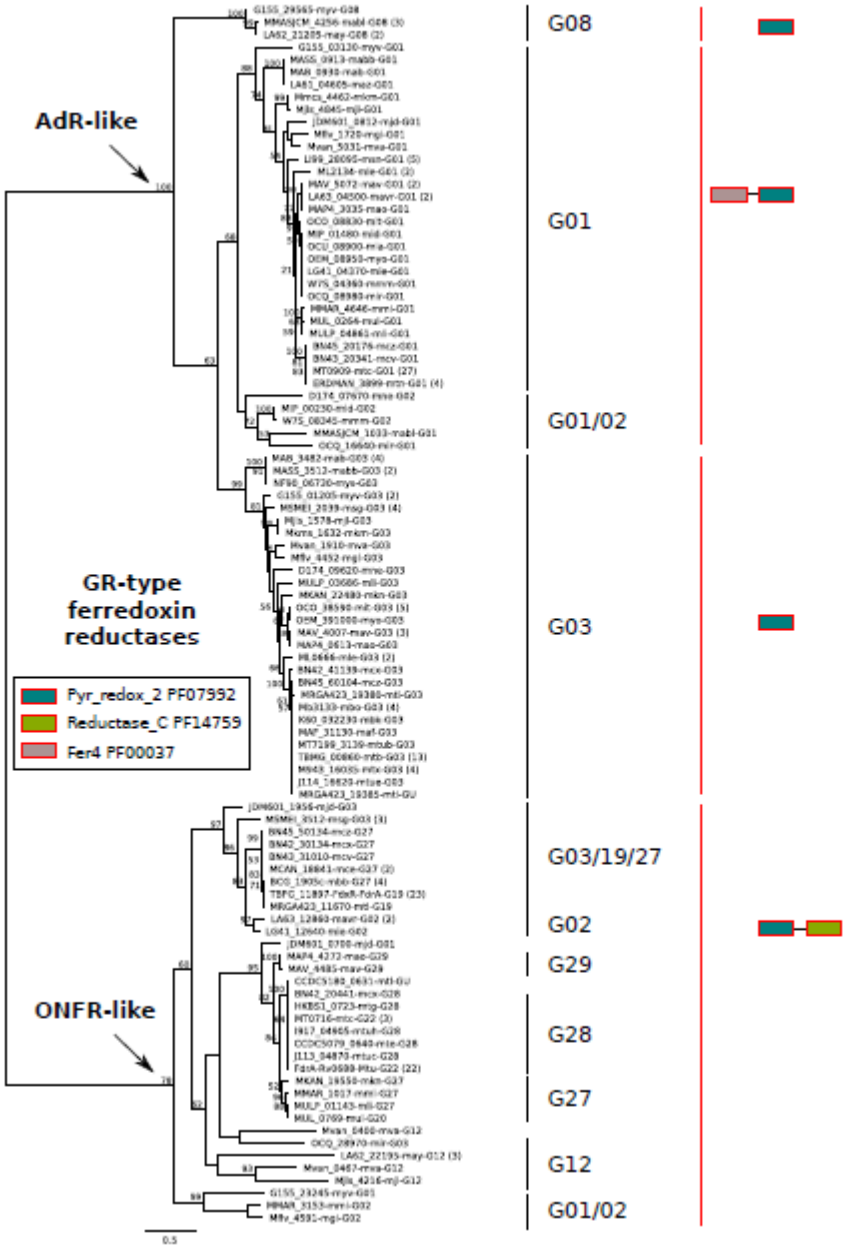

Figure 4.3. Maximum likelihood phylogeny of GR-type FdRs based on alignment of the the Pyr_redox_2. Numbers on branches indicate bootstrap proportions (1000 replicates); supports below 50 are not shown. Assignment to groups and Pfam domain composition is given on the right. The AdR-like and ONFR-like clades, as well as terminal clades/groups are relatively well-supported.

Table 4.4. Bacterial type ferredoxin reductase.

Group 1	FAD_binding_6 PF00970, NAD_binding_1 PF00175, Fer2 PF00111	Mjls_4115-mjl-G01, MSMEG_2893-msm-G01, MSMEI_2819-msg-G01 (2), Mflv_1462-mgi-fDXr-G01, MSMEI_5878-msg-G01, MSMEG_6039-msm-G01 (02), JDM601_3855-mjd-G01, MT3676-mtc-G01, MULP_05324-mli-G01, OEM_38530-myo-G11, LG41_18000-mie-G11, OCQ_39120-mir-FxdR-G11, Mflv_2468-mgi-FdxR-G01, MSMEI_0288-msg-G01, MSMEG_0295-msm-G01, MMAR_0335-mmi-G18, MULP_00312-mli-G18, LG41_23695-mie-G18, MAV_5168-mav-G18, LA63_23905-mavr –G18, JDM601_2873-mjd-G18, MycrhN_0469-mrh-G18, MSMEG_1742-msm-G18

		MSMEI_1702-msg-G18, LJ00_08705-msb-G18 LI99_08705-msn-G18 LI98_08705-msh-G18 (5), G155_08940-myv-G18, OCU_28180-mia-G15, MIP_03758-mid-G15, MSMEI_1845-msg-G23, Mvan_1767-mva-FdxR-G23, Mkms_1376-mkm-FdxR-G23, MAP4_0440-mao-G23, OCO_40550-mit-G23, OCQ_41640-mir-G23 (3) OCU_40460-mia-G23, MIP_06111-mid-G23, W7S_20245-mmm-G23, OEM_40800-myo-G23, MRGA327_19880-mtg-GU, TBFG_13259-mtf-G24 (18), mt3327-mtc-G24 TBMG_03278-mtb-G24 TBSG_03301-mtk-G24 TBXG_003259-mtz-G24

		MRGA423_20255-mti-G24 CCDC5079_2981-mte-G24 CFBS_3420-mtur-G24 MTCTRI2_3297-mto-G24 CCDC5180_2943-mtl-G24 ERDMAN_3543-mtn-G24 J114_17320-mtue-G24 J112_17365-mtj-G24 MT7199_3272-mtub-G24 TBHG_03166-mtul-G24 HKBT2_3414-mtuu-G24 HKBS1_3417-mtg-G24 MAF_32420-maf-G24 , BN43_60240-mcv-G30, BN45_60260-mcz-G30 (2), Mb3259c-mbo-G24(9), BCG_3353c-mbb-G24, BCG_3260c-mbb-G24, JTY_3255-mbt-G24, BCGMEX_3351c-mbm-G24, K60_041260-mbk-G24,

		K60_040920-mbk-G24, K60_033600-mbk-G24, BCGMEX_3258c-mbm-G25 BN42_41281-mcx-G30, BN44_70011-mcq-GU, OCU_39570-miaG21 (2) OCO_39530-mit-G21, OEM_40050-myo-G21, LG41_18775-mie-G21, OCQ_40760-mir-G21, MAV_4119-mav-G21 (3) LA63_19055-mavr-G21, NF84_18860-mavd-G21 , MAP4_0504-mao-G21, NF84_16680-mavd-G21,(3) MAV_3669-mav-G21, LA63_16845-mavr-G21 MAP4_0923-mao-G21, LH58_16535-mbz-G21, MKAN_24980-mkn-G21, BN42_40756-mcx-G21, K60_028720-mbk-G21, MRGA423_17210-mti-GU, TBFG_12789-mtf-G25 (11)

		MT2846-mtc-G25, TBMG_01198-mtb-G25, TBXG_001187-mtz-G25, CCDC5079_2546-mte-G25, CCDC5180_251-mtl-G25, ERDMAN_3042-mtn-G25, M943_14340-mtx-G25, TBHG_02708-mtul-G25, LH58_14740-mbz-G25, 14740 BN44_60238-mcq-G25 J112_14865-mtj-G07 (14), MRGA327_17010-mtg-G26, CFBS_2933-mtur-G26, MTCTRI2_2829-mto-G26, MCAN_28041-mce-G26, MT7199_2809-mtub-G26, HKBT2_2924-mtuu-G26, HKBS1_2928-mtg-G26, Mb2798c-mbo-G26, BCG_2793c-mbb-G26, JTY_2787-mbt-G26, BCGMEX_2786c-mbm-G26, MAF_27810-maf-G26 27810

		J114_14805-mtue-G26, BN45_51163-mcz-G25, BN43_40463-mcv-G31, MSMEI_1945-msg-G03, ,Mflv_2623-mgi-G03
Group 2	FAD_binding_6 PF00970, NAD_binding_1 PF00175	LI99_21840-msn-G01, (4) MSMEG_4411-msm-G01, LJ00_21835-msb-G01, MSMEI_4304-msg-G01 , OEM_31170-myo-G01, OCQ_32640-mir-G01, LA62_08080-may-G17, (3) NF82_08040-mabo-G17, LA61_07975-maz-G17 LH56_15135-mak-G17, NF90_15630-mys-G17, MMASJCM_1611-mabl-G17,
Group 3	Fer2 PF00111, FAD_binding_6 PF00970 NAD_binding_1 PF00175	MT1987-mtc-G07
Group 4	FAD_binding_6 PF00970, Fer2 PF00111	MAB_0088c-mab-G10, Mflv_3426-mgi-G10, LJ00_18275-msb-G10 (2)

		MSMEI_3589-msg-G10
Group 5	FA_desaturase PF00487,FAD_binding_6 PF00970, NAD_binding_1 PF00175, Fer2 PF00111	FdxB (Rv3554)-Mtu-G04, CCDC5180_3247-mtl-G02, (2) CCDC5079_3295-mte- G04, J113_24860-mtuc-G04, mt3658-mtc-G04, CFBS_3770-mtur-G04 (4) J112_19130-mtj-G04, HKBT2_3764-mtuu-G04, HKBS1_3767-mtg-G04 , TBFG_13587-mtf-G04 (11), TBSG_03620-mtk-G04, TBXG_003569-mtz-G04, MRGA327_21950-mtg-G04, MRGA423_22465-mti-G04 MTCTRI2_3618-mto-G04 MT7199_3616-mtub-G04 J114_19010-mtue-G04 TBHG_03494-mtul-G04 Mb3584-mbo-G04 BCG_3618-mbb-G04 , I917_24940-mtuh-G04

Group 6	NAD_binding_1 PF00175, Fer2 PF00111	D174_13855-mne-G01, MSMEI_4054-msg-G01, LJ00_20590-msb-G01
Group 7	FAD,NAD	NEW-LH54_15880 NEW2-MKAN_15935 NEW-D174_08080 NEW2-Mflv_4699 NEW2-Mmcs_1358 NEW2-Mjls_1392 NEW2-W7S_13715-mmm_G29 NEW2-OEM_26770-myo_G29 NEW2-Mflv_5247 NEW2-Mmcs_2269-mmc_G15 NEW2-Mkms_2316-mkm_G15 NEW2-Mjls_2308 NEW2-Mmcs_0319-mmc_G8

		NEW2-Mkms_0329-mkm_G8 NEW2-MKAN_12135 NEW2-Mmcs_4710-mmc_G9 NEW2-Mkms_4796-mkm_G9 NEW2-Mjls_5095-mjl_G9 NEW2-W7S_18975 NEW2-Mmcs_3712-mmc_G7 NEW2-Mkms_3785-mkm_G7 NEW2-Mjls_3725 NEW2-LJ00_01480 NEW2-G155_01230 NEW2-MKAN_01670 NEW2-MULP_05296(FdxB) NEW2-MKAN_11975 NEW2-G155_16695 NEW2-Mmcs_2875-mmc_G11 NEW2-Mkms_2919-mkm_G11

		NEW2-Mjls_2905-mjl_G11 NEW2-LA62_00445-may_G2 NEW2-NF82_00440-mabo_G2 NEW2-LA61_00450-maz_G2 NEW2-LH56_21915-mak_G2 NEW2-LA62_20430-may_G1 NEW2-LA61_20330-may_G1 NEW2-LH56_04080-mak_G3 NEW2-NF92_04140-mys_G2 NEW2-D174_02960 NEW2-D174_09705 NEW2-Mmcs_1520-mmc_G14 NEW2-Mkms_1543-mkm_G14 MSMEI_4267-msg-G01 Mmcs_2259-mmc-G01 NEW2-Mmcs_2259-mmc_G10

		NEW2-Mkms_2306-mkm_G10 NEW2-Mjls_2298-mjl_G10 NEW2-G155_07985 NEW2-LJ00_09925-msb_G30 NEW2-LI98_09925-msh_G30

Table 4.5. Glutathione reductase type ferredoxin reductase

AdR like	Pyr_redox_2 PF07992	G155_29565-myv-G08, MMASJCM_4256-mabl-G08 (3), NF90_03385-mys-G08 MASS_4170-mabb-GR,LA61_21100-maz (2) LA62_21205-may-G08
	Fer4 PF00037, Pyr_redox_2 PF07992	G155_03130-myv-G01, MASS_0913-mabb-G01, MAB_0930-mab-G01,

		LA61_04605-maz-G01, Mmcs_4462-mkm-G01, Mjls_4845-mjl-G01, JDM601_0812-mjd-G01, Mflv_1720-mgi-G01, Mvan_5031-mva-G01, LI99_28095-msn-G01(5), MSMEG_5681-msm-G01, MSMEI_5531-msg-G01, LJ00_28090-msb-G01, LI98_28100-msh-G01, ML2134-mle-G01, MLBr_02134-mlb (2), MAV_5072-mav-G01, MAV_1015-mav (2), LA63_04500-mavr-G01, NF84_04400-mavd (2), MAP4_3035-mao-G01, OCO_08830-mit-G01, MIP_01480-mid-G01, OCU_08900-mia-G01, OEM_08950-myo-G01, LG41_04370-mie-G01, W7S_04360-mmm-G01,

		OCQ_08980-mir-G01, MMAR_4646-mmi-G01, MUL_0264-mul-G01, MULP_04861-mli-G01, BN45_20176-mcz-G01, BN43_20341-mcv-G01, MT0909-mtc-G01 (27), TBFG_10903-mtf-G01, TBFG_13123-mtf-G01, TBMG_03104-mtb-G01, TBSG_03124-mtk-G01, UDA_0886-mtd-G01, TBXG_003083-mtz-G01, MRGA327_05550-mtg-G01, CFBS_0929-mtur-G01, MTCTRI2_0909-mto-G01, J112_04765-mtj-G01, MT7199_0905-mtub-G01, J114_04715-mtue-G01, M943_04625-mtx-G01 TBHG_00874-mtul-G01 HKBS1_0929-mtg-G01 Mb0910-mbo-G01

		BCG_0938-mbb-G01 JTY_0908-mbt-G01 BCGMEX_0909-mbm-G01 K60_009450-mbk-G01 LH58_04815-mbz-G01 MAF_08950-maf-G01 FprB-Rv0886-Mtu-G01 MCAN_08871-mce-G01 BN44_10967-mcq-G01 HKBT2_0930-mtuu-G09, ERDMAN_3899-mtn-G01,(4) CCDC5079_0817-mte-G01, CCDC5180_0810-mtl-G01, ERDMAN_0979-mtn-G01, D174_07670-mne-G02, MIP_00230-mid-G02, W7S_08345-mmm-G02, MMASJCM_1033-mabl-G01, OCQ_16640-mir-G01
GR type	Pyr_redox_2 PF07992	MAB_3482-mab-G03,(4) LA62_17705-may-G03, NF82_17440-mabo-G03,

		LA61_17605-maz-G03,MASS_3512-mabb-G03,(2) LH56_06695-mak-G03 LJ00_17885-msb-G03,G155_01205-myv-G03,(2) G155_10200-myv-G03, MSMEI_2039-msg-G03,(4) LJ00_10390-msb-G03, LI99_10390-msn-G03, LI98_10390-msh-G03 , Mjls_1578-mjl-G03, Mkms_1632-mkm-G03, Mvan_1910-mva-G03, Mflv_4452-mgi-G03, D174_09620-mne-G03, MULP_03686-mli-G03, MKAN_22480-mkn-G03, OCO_38590-mit-G03 (5) OCQ_39750-mir-G03 OCU_38560-mia-G03 LG41_18315-mie-G03 MIP_05836-mid-G03 OEM_391000-myo-G03 ,

		MAV_4007-mav-G03(3) LA63_18495-mavr-G03 NF84_18305-mavd-G03, OCU_40460-mia-G23 MAP4_0613-mao-G03, ML0666-mle-G03, (2) MLBr_00666-mlb-G03, BN42_41139-mcx-G03, BN45_60104-mcz-G03, MRGA423_19380-mti-G03, Mb3133-mbo-G03 (4) BCG_3131-mbb-G03, BCGMEX_3128-mbm-G03, K60_032230-mbk-G03, MAF_31130-maf-G03, MT7199_3139-mtub-G03, TBMG_00860-mtb-G03 (13), FprA-Rv3106-Mtu-G03, TBSG_00866-mtk-G03, MRGA327_19110-mtg-G03, CFBS_3276-mtur-G03, CCDC5180_2826-mtl-G03, MTCTRI2_3169-mto-G03, UDA_3106-mtd-G03,

		ERDMAN_3402-mtn-G03, J112_16650-mtj-G03, HKBT2_3268-mtuu-G03, HKBS1_3274-mtg-G03, TBHG_03037-mtul-G03 , M943_16035-mtx-G03 (4) MCAN_31331-mce-G03, BN44_60625-mcq-G03, BN43_60100-mcv-G03, J114_16620-mtue-G03, MRGA423_19385-mti
ONFR-like	Pyr_redox_2 PF07992, Reductase_C PF14759	JDM601_1956-mjd-G03, MSMEI_3512-msg-G03,(3) LJ00_17885-msb-G03, LI98_17895-msh-G03, BN45_50134-mcz-G27, BN42_30134-mcx-G27, BN43_31010-mcv-G27, MCAN_18841-mce-G27 (2) BN44_40132-mcq-G27, BCG_1905c-mbb-27,(4) JTY_1889-mbt-G27, BCGMEX_1886c-mbm-G27, K60_019560-mbk-G27 ,

		TBFG_11897-FdxR-FdrA-G19 (23), MT1918-mtc-G19, MT3189-mtc-G19, TBMG_02125-mtb-G19, MRGA327_11545-mtg-G19, TBXG_002107-mtz-G19, TBSG_02136-mtk-G19, HKBT2_1966-mtuu-G19, CCDC5180_1704-mtl-G19, CFBS_1961-mtur-G19, MTCTRI2_1901-mto-G19, MT7199_1895-mtub-G19, J112_09960-mtj-G19, ERDMAN_2061-mtn-G19, J114_09960-mtue-G19, J113_12960-mtuc-G19, M943_09710-mtx-G19, HKBS1_1962-mtg-G19, Mb1900c-mbo-G19, LH58_10020-mbz-G19, MAF_18910-maf-G19, TBFG_11897-mtf-G19, TBHG_01824-mtul-GR , MRGA423_11670-mti-G19,

		LA63_12860-mavr-G02(2) NF84_12705-mavd-G02, LG41_12640-mie-G02, JDM601_0700-mjd-G01, MAP4_4272-mao-G29, MAV_4485-mav-G29, CCDC5180_0631-mtl-GU, BN42_20441-mcx-G28, HKBS1_0723-mtg-G28, MT0716-mtc-G22 (3) ERDMAN_0759-mtn-G22, MT7199_0706-mtub-G22, I917_04905-mtuh-G28, CCDC5079_0640-mte-G28, J113_04870-mtuc-G28, FdrA (Rv0688)-Mtu-G22 (22) TBMG_00701-mtb-G22 TBSG_00705-mtk-G22 TBFG_10702-mtf-G22 TBXG_000694-mtz-G22 MRGA327_04305-mtg-G22 MRGA423_04295-mti-G22

		CFBS_0723-mtur-G22 MTCTRI2_0704-mto-G22 J112_03680-mtj-G22 J114_03670-mtue-G22 HKBT2_0724-mtuu-G22 BCG_0737-mbb-G22 Mb0707-mbo-G22 JTY_0707-mbt-G22 BCGMEX_0708-mbm-G22 K60_007330-mbk-G22 MCAN_06891-mce-G22 MAF_06970-maf-G22 BN44_10756-mcq-G22 BN43_20118-mcv-G22 BN45_10786-mcz-G22 , MKAN_19550-mkn-G27, MMAR_1017-mmi-G27, MULP_01143-mli-G27, MUL_0769-mul-G20, Mvan_0400-mva-G12,

		OCQ_28970-mir-G03, LA62_22195-may-G12,(3) NF82_21885-mabo-G12, LA61_22090-maz-G12 Mvan_0467-mva-G12, Mjls_4216-mjl-G12, G155_23245-myv-G01, MMAR_3153-mmi-G02, Mflv_4591-mgi
	PyrRedox2	NEW-LG40_09280-mks NEW-LH54_09390-mki NEW-MKAN_09430-mkn NEW-D174_23110 NEW-G155_05925 NEW-Mjls_4084 NEW-G155_10535 NEW-D174_03225 NEW-D174_16365 NEW-D174_13835 NEW-Mycch_1556 NEW-MULP_01646

		NEW-MKAN_03850 NEW2-Mmcs_4866Â NEW2-Mkms_4955-mkm_G18 NEW2-Mjls_5234-mjl_G18 NEW-LG40_01300-mks NEW-LH54_01310-mki NEW-MKAN_01290-mkn NEW-MMAR_2931 NEW-MKAN_01240 NEW-MAB_3838c NEW-JDM601_4002

Table 4.6. Ferredoxin Reductases divergent

Group 1	Fer4_15	JDM601_3492-MDJ-G01, G155_20605-myv-G01
Group 2	Fer4	REM2_Fer4_LA63_16020-mavr-G10
Group 3	Fer2	REM2_Fer2_OCO_28550-mit-G01, REM9_J113_06210-mtuc-GR, REM6_Fer2_MSMEG_6836_msn-G16(4) MSMEI_6654-msg-G16 LJ00_33780-msb-G16 LI99_33785-msn-G16
Group 4	Fer_11	MSMEI_1805-msg-G01 LJ00_09210-msb-G01
Group 5	Fer4_8,CCG	LI99_03425-msn-G13, MASS_4335_mabb-G08, BN42_20067-mcx-G13, MT0352-FumaratRed-G13, I917_02395_mtuh-G13, MAV_4817-mav-G13, OCO_47210-mit-G13, OCU_46960-mia-G13,

		OCQ_48240-mir-G13, MIP_07142-mid-G13
Group 6	Fer4_13	MULP_02900-mli-G03, MMAR_2932-mmi-G03

4.4. Conclusion

Redox partners have shown that they can transfer electrons for P450s to function. Number of ferredoxins and ferredoxin reductase have been classified and identified based on their prosthetic groups. A total number of 622 ferredoxins and 374 ferredoxins reductases were obtained and most of them had similar prosthetic groups. All species were categorised accordingly.

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CHAPTER 5

CONCLUSION AND FUTURE WORK

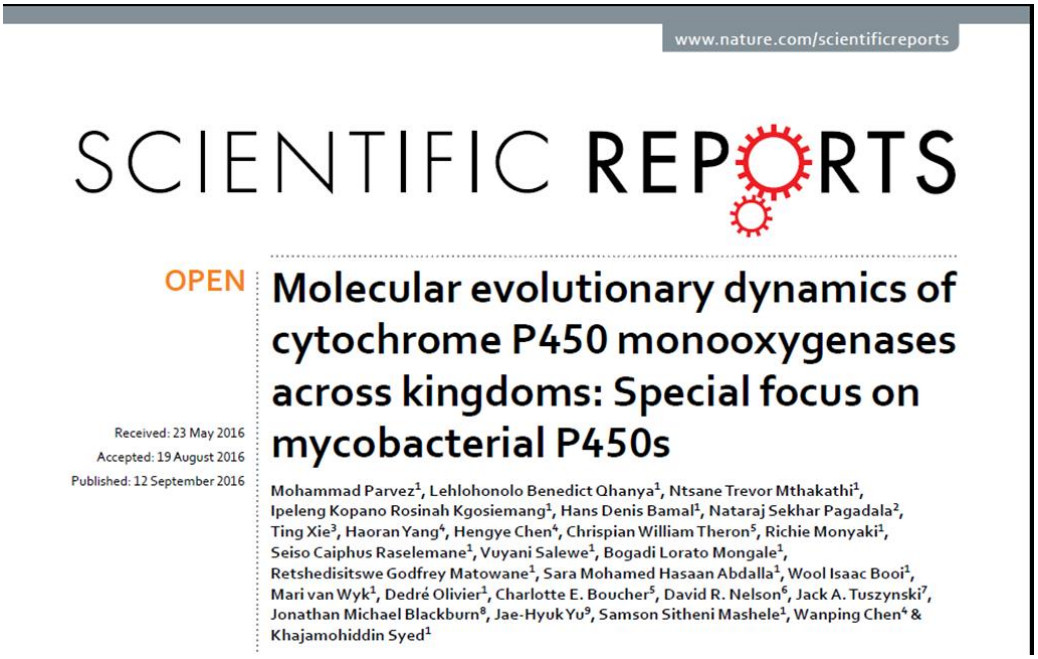
P450 redox partners are very important as they are responsible for transferring electrons to P450s. Most of the P450s, except self-sufficient P450s, need redox partners to perform their reactions. If one can target redox partners it will result inhibition of P450 function and possibly led to the death of an organism. Due to this reason it is possible that P450 redox proteins can serve as novel drug targets against pathogenic organisms.

This study serve as the basis for further exploring P450 redox proteins as drug targets against species belong to the genus *Mycobacterium*. In this study, genome data mining was performed in 81 mycobacterial species and identified possible redox proteins and then these proteins were annotated into ferredoxins and ferredoxin reductases. Furthermore, based on the phylogenetic analysis ferredoxins and ferredoxin reductases were grouped into different groups.

Future work involves genome mapping of these P450 redox proteins to authenticate their capability to transfer electrons to P450s that includes structural analysis (homology modeling based) and identifying the commonly conserved ferredoxins and ferredoxin reductases across the mycobacterial species. The P450 redox proteins that conserved across species and uniquely conserved in different mycobacterial groups will be explored as novel drug targets.

RESEARCH OUTPUTS

Research articles



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SCIENTIFIC REPORTS

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Molecular evolutionary dynamics of cytochrome P450 monooxygenases across kingdoms: Special focus on mycobacterial P450s

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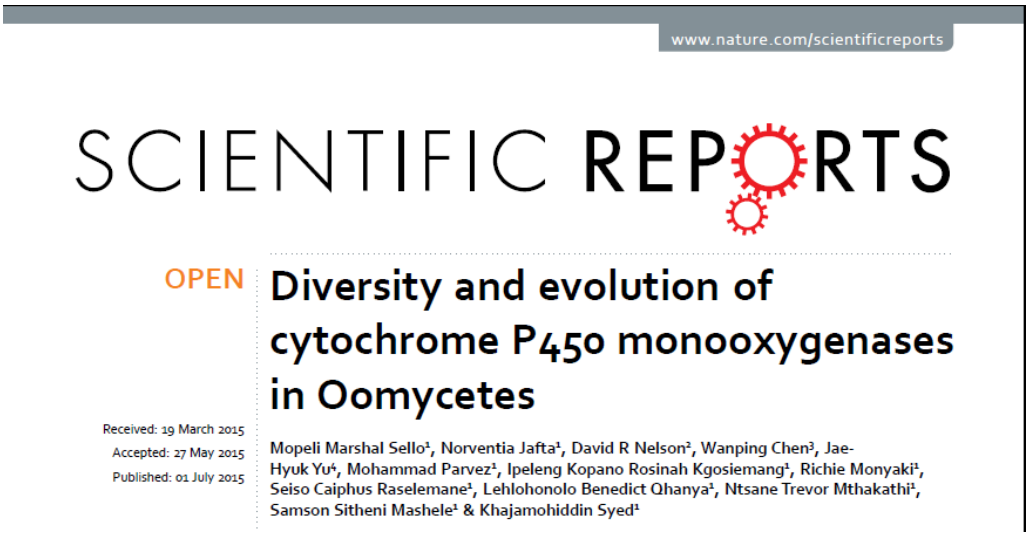

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Diversity and evolution of cytochrome P450 monooxygenases in Oomycetes

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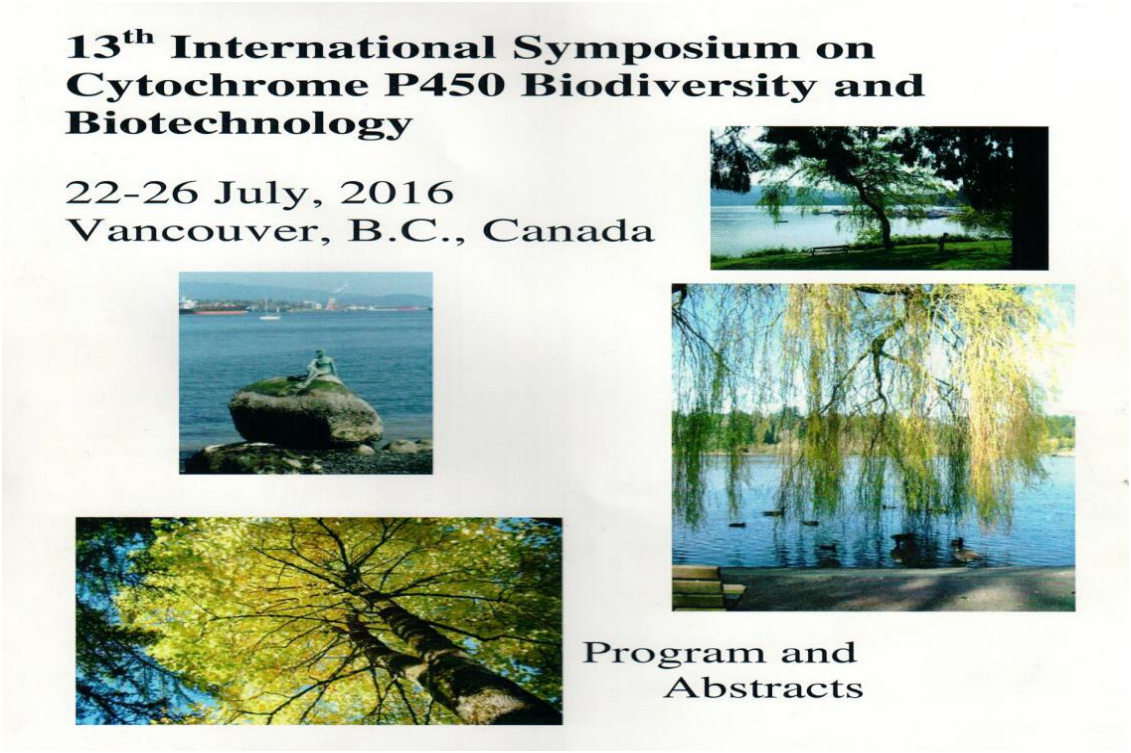
Conference Attendance



\DMP 22

Comparative genomics of cytochrome P450 monooxygenase redox proteins in mycobacteria

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Redox proteins play a key role in organism's physiology per se transferring electrons to different proteins. Redox proteins are indispensable for cytochrome P450 monooxygenases (P450s) reactions. It is known fact that P450s play key role *Mycobacterium tuberculosis*, deadliest human pathogen, physiology and few P450s are found to be critical for its survival. It is logical that if one can inhibit P450 redox enzymes that eventually result not only in loss of all P450s functions but also inhibition of *M. tuberculosis* growth. Hence, P450 redox enzymes can be a novel drug targets. However, to date, comparative study of redox protein in mycobacteria is not reported. Therefore, the aim of this study was to perform comparative genomics of redox partners in mycobacteria. Sixty mycobacterial species genomes available for public use were data-mined for redox proteins. Two methods were used to identify redox proteins. First, proteins were collected using the term "redox protein". Second *M. tuberculosis* redox protein (total 9) were individually blasted against sixty species and hit proteins were collected. A total of 2019 redox proteins were identified in sixty mycobacterial species. Redox proteins number ranged from 8-57 in mycobacteria. Preliminary analysis suggested presence of ferredoxin, oxidoreductase and NADPH:adrenodoxin oxidoreductase etc. *M. abscessus subsp. bolletii* CCUG 48898 contained lower number of redox proteins (8) and *M. smegmatis MC2 155* contained highest number of redox proteins (57). Work is in progress to annotate and perform phylogenetic analysis of identified redox proteins.

P 85-S2

Comparative genomics of cytochrome P450 monooxygenase redox proteins in mycobacteria

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Redox proteins play a key role in organism's physiology per se transferring electrons to different proteins. Redox proteins are indispensible for cytochrome P450 monooxygenases (P450s) reactions. It is known fact that P450s play key role *Mycobacterium tuberculosis*, deadliest human pathogen, physiology and few P450s are found to be critical for its survival. It is logical that if one can inhibit P450 redox enzymes that eventually result not only in loss of all P450s functions but also inhibition of *M. tuberculosis* growth. Hence, P450 redox enzymes can be a novel drug targets. Therefore, the aim of this study was to perform comparative genomics of redox partners in mycobacteria. Sixty mycobacterial species genomes available for public use were data-mined for redox proteins. A total of 2019 redox proteins were identified in sixty mycobacterial species. Redox proteins number ranged from 8-57 in mycobacteria. Preliminary analysis suggested presence of ferredoxin, oxidoreductase and NADPH:adrenodoxin oxidoreductase etc. *M. abscessus* subsp. *bolletii* CCUG 48898 contained lower number of redox proteins (8) and *M. smegmatis* MC2 155 contained highest number of redox proteins (57). Work is in progress to annotate and perform phylogenetic analysis of identified redox proteins.

Media coverage

pressreader

CUT's groundbreaking discovery

New discovery may help fight aquatic animal infection

The New Age (Free State) 17 Jun 2015 News

leading: Research team leader Dr Khajamohiddin Syed and faculty of environmental science acting dean professor Sam Mashele.

pioneers: The CUT science students who helped discover the drug that may help fight aquatic animal infection.

Acting dean of the faculty Prof Sam Mashele said some of the deadliest pathogens in the world were found in the fish farming industry.

He said the discovery was made by researchers from the unit for drug discovery in the institution.

"For many years researchers across the world have been trying to understand these micro- organisms in order to control the disease and develop novel drugs against these pathogens, and CUT researchers are leading the way in finding solutions that will bring an end to this socio-economic challenge facing aquatic farming," Mashele said.

He said microorganisms were widely known in the scientific world and they continued to wreak havoc on the aqua farming sector worldwide.

"They are considered the deadliest of pathogens, causing diminished production of aquatic food," Mashele said.

The team of researchers who discovered the drug were led by Dr Khajamohiddin Syed.

"We collaborated with highly acclaimed international scientists such as professors David Nelson from the University of Tennessee in the US, ae-Hyuk Yu from the University of Wisconsin-Madison and Dr Wanping Chen from Huazhong Agricultural University in China," Mashele said.

"The university researchers are investigating solutions that would sustain the aquatic resources while helping to increase high production levels of aqua farming for commercial purposes, food security and poverty alleviation."

He said their work highlighted the important role aqua farming plays in promoting healthy living and in fighting poverty and hunger.

Syed said aqua farming was a big industry across the world and it involved the farming of fish, shrimps, prawns, squid and octopus and is considered by the UN as an important sector that can provide a livelihood for more than 60 million people in Africa and Asia.

"Consumption of these animals remains a vital source of protein and essential nutrients, especially for developing countries, where they constitute almost half of the total value of their traded communities," Syed said.

"The results of this study have been accepted for publication in the Nature Publication Group journal Scientific Reports, a prestigious multidisciplinary scientific international journal with an impact factor of 5.1."

dag 16 Junie 2015 **Volksblad**

Navorsers by SUT maak deurbraak

Laydene Davids

'n SPAN navorsers aan die Sentrale Universiteit vir Tegnologie (SUT) het 'n wegspringpunt vir 'n middel ontdek wat groot potensiaal toon om siektes, wat deur parasiete veroorsaak word, in seebiere te beëindig.

Navorsers van oor die wêreld sien het jare lank probeer om die waarnatige mikro-organismes te verstaan ten einde die siekte, wat onder meer in visse, garnale, skulvisse en seekatte voorkom, te beheer en 'n middel daarteen te ontwikkel.

Maar meer as 50 jaar lank was dit severgeefs – totdat die navorsers aan die SUT en wêreldekende wetenskaplikes koppe bymekaargesit het.

Dan Maritz, woordvoerder, sê dié span jong navorsers onder leiding van prof Samson Sithembi Mashele en dr. Khajamohiddin Syed loop nou voor om oplossings te vind wat die maatskaplik-ekonomiese uitdagings wat die siektes vir veral die visserybedryf bied, te beëindig.

Syed sê miljoene seediere vrek aarlike weens siektes wat deur parasiete veroorsaak word en dit het 'n regstreekse invloed op die visserybedryf.

Volgens hom is dit alombekend in die wetenskaplike wêreld dat die parasiete (*composite*) chaos in die visserybedryf wêreldwyd saai en die lewensduur van die diere aansienlik verkort.

Die navorsers het die *P400* monocyovase-proteïen in 15 patogeniese genome bestudeer en bevind dit kan as wegspringpunt gebruik word vir 'n middel om die swamagtige mikro-organismes te beveg.

Die navorsers ondersoek dit nou om oplossings te vind om seebulpbronne te beskerm.

Maritz sê hul (die navorsers se) werk beklemtoon die belangrikheid van die visserybedryf in die bevordering van gesonde lewe en die stryd teen armoede en honger.

Die uitkoms van die navorsing is reeds vir plasing in die *Nature Publication Group Journal* aanvaar.

Die wêreldbekende wetenskaplikes wat ook deel van die navorsingspan is, sluit in prof. David R. Nelson van die Universiteit van Tennessee, prof. dae Hyuk Yu van die Universiteit van Wisconsin-Madison, en dr. Wanping Chen Huazhong var die Landbou-universiteit in China.

Die span navorsers aan die Sentrale Universiteit vir Tegnologie (SUT) wat die wegspringpunt vir 'n middel ontdek het om siektes wat deur parasiete veroorsaak word, in seediere te bestry. Hier is van links, voor: dr. Khajamohiddin Syed; middel: Lerato Mongale, dr. Ntsoaki Molebo, Pontsh Jawaharpersaud en Mohammad Parvez agter: prof. Sithembi Mashele, Mopeli Sello, Seiso Baselemane, Lehlohonolo Qwanya, Mthakathi Ntsane, Thapelo Makhele, Euginiah Rampana en Richie Monyaki.

Foto: MLUNGISI LOUW